Industria y Comercio
SUPERINTENDENCIA

Espacio reservado para el adhesivo de radicación

DIRECCIÓN DE NUEVAS CREACIONES
Procedimiento acelerado de exámenes de patente (PPH)

1	**NÚMERO DE SOLICITUD ANTE LA SIC**		
2	**GLOBAL - PPH** **X** PAÍS Estados Unidos	**3**	**PCT – PPH** ☐ PAÍS
4	**PROSUR** ☐ PAÍS	**5**	**Alianza del Pacifico (AdP)** ☐ PAÍS
6	**OFICINA DE PRIMERA PRESENTACIÓN (OPP)** ☐	**7**	**OFICINA DE EXAMEN ANTERIOR (OEA)** ☐
8	**NÚMERO DE SOLICITUD O PUBLICACIÓN DE LA SOLICITUD (OPP)** X **NÚMERO DE SOLICITUD EN OFICINA DE EXAMEN ANTERIOR (OEA):** ☐ **NÚMERO DE SOLICITUD PCT:** ☐		1. US 16/296,194
9	☐ **REPRESENTANTE LEGAL X APODERADO**		

APELLIDOS	NOMBRES	IDENTIFICACIÓN
CASTELLANOS ABONDANO	MARGARITA	C.C .39.779.654 T.P .70.819

DIRECCIÓN	Calle 117 No. 5a-35	No. TELÉFONO	7560770
CIUDAD	Bogotá D.C	CORREO ELECTRÓNICO	patentessic@castellanosyco.co
PAÍS	COLOMBIA	No. RADICACIÓN O PROTOCOLO DE PODER GENERAL	

10 CONDICIONES PARA ACCEDER A ESTE PROCESO:

10.1. DATOS DE PRIORIDAD **X** SI ☐ NO

(33) PAÍS DE ORIGEN	CÓDIGO PAÍS	(31) NÚMERO	(32) FECHA (AAAA/MM/DD)
1. ESTADOS UNIDOS DE AMÉRICA	USA	62/639,988	07 mar. 2018
2. ESTADOS UNIDOS DE AMÉRICA	USA	62/690,933	27 jun. 2018

10.2. DATOS SOLICITUD INTERNACIONAL PCT **X** SI ☐ NO

Solicitud Internacional No.	PCT/US2019/021243	**Fecha**	07 mar. 2019
Publicación Internacional No.	WO/2019/173653	**Fecha**	12 sept. 2019

*El solicitante presenta una copia de la(s) reivindicación(es) patentable(s) u otorgable(s) de la solicitud de la Oficina de Primera Presentación que profirió el examen de patentabilidad, junto con una traducción al castellano. **X** SI ☐ NO

*El solicitante presenta los resultados de búsqueda de la Oficina de Examen Anterior, junto con una traducción al castellano **X** SI ☐ NO

REQUISITOS PARA EL RECONOCIMIENTO DE LOS RESULTADOS DE EXÁMENES DE PATENTABILIDAD EFECTUADOS A SOLICITUDES EXTRANJERAS

Para que la Superintendencia de Industria y Comercio pueda reconocer los resultados de exámenes de patentabilidad producidos por otras Oficinas de Propiedad Industrial se debe cumplir con las siguientes condiciones:

(a) Al momento de solicitar el examen de patentabilidad, si el solicitante pide que se reconozcan exámenes de patentabilidad de otras oficinas extranjeras, deberá aportar junto con el pago de la tasa correspondiente, los siguientes anexos:

(i) Copia de las resoluciones, fallos o decisiones que han sido relevantes para la determinación de la patentabilidad de la(s) solicitud(es) en la Oficina que haya proferido el examen de patentabilidad que contienen reivindicaciones patentables u otorgables que son la base de la petición, y si es del caso, su traducción al castellano. **X** SI ☐ NO

(ii) Copia de todas las reivindicaciones determinadas como patentables u otorgables en la Oficina que profirió el examen de patentabilidad y, si es del caso, su traducción al castellano. **X** SI ☐ NO

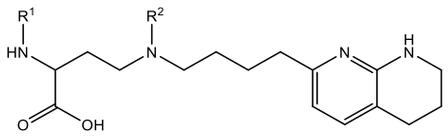
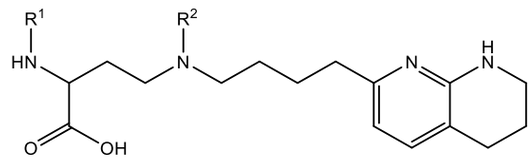
(iii) Copia de los antecedentes, información o documentos citados por el examinador de la Oficina de Primera Presentación del examen de patentabilidad, en las resoluciones, fallos o decisiones correspondientes, incluyendo la literatura no patente. Los documentos de patente deberán presentarse siempre y cuando no estén disponibles para la Superintendencia de Industria y Comercio mediante el simple acceso a bases de datos gratuitas. **X** SI ☐ NO

(iv) Una tabla de correspondencias de las reivindicaciones que han sido determinadas como patentables u otorgables en la solicitud de la Oficina que haya proferido el examen de patentabilidad. . **X** SI ☐ NO

11 FIRMA DEL SOLICITANTE, DEL APODERADO O DEL REPRESENTANTE LEGAL

Junto a cada firma, indicar el nombre del firmante y su calidad (si tal calidad no es obvia al leer el petitorio)



10 (iv)	TABLA DE CORRESPONDENCIA DE REIVINDICACIONES	
Reivindicaciones en la solicitud en Colombia	Reivindicaciones otorgables en la solicitud internacional	Explicación sobre la suficiente correspondencia ó Comentarios que explican la correspondencia
1. Un compuesto de fórmula (II):  (II); o una sal del mismo, en donde: R^1 es C_6-C_{14} arilo o heteroarilo de 5 a 10 miembros en donde el C_6-C_{14} arilo y el heteroarilo de 5 a 10 miembros están opcionalmente sustituidos con R^{1a}; R^2 es hidrógeno; deuterio; C_1-C_6 alquilo opcionalmente sustituido con R^{2a}; -OH; -O-C_1-C_6 alquilo opcionalmente sustituido con R^{2a}; C_3-C_6 cicloalquilo opcionalmente sustituido con R^{2b}; -O-C_3-C_6 cicloalquilo opcionalmente sustituido con R^{2b}; heterociclilo de 3 a 12 miembros opcionalmente sustituido con R^{2c}; o -$S(O)_2R^{2d}$; con la condición de que cualquier átomo de carbono unido directamente	1. Un compuesto de fórmula (II):  (II); o una sal del mismo, en donde: R^1 es C_6-C_{14} arilo o heteroarilo de 5 a 10 miembros en donde el C_6-C_{14} arilo y el heteroarilo de 5 a 10 miembros están opcionalmente sustituidos con R^{1a}; R^2 es hidrógeno; deuterio; C_1-C_6 alquilo opcionalmente sustituido con R^{2a}; -OH; -O-C_1-C_6 alquilo opcionalmente sustituido con R^{2a}; C_3-C_6 cicloalquilo opcionalmente sustituido con R^{2b}; -O-C_3-C_6 cicloalquilo opcionalmente sustituido con R^{2b}; heterociclilo de 3 a 12 miembros opcionalmente sustituido con R^{2c}; o -$S(O)_2R^{2d}$; con la condición de que cualquier átomo de carbono unido directamente	*Las reivindicaciones fueron modificadas voluntariamente para la solicitud en Colombia, a fin de que la materia corresponda con la otorgada en Estados Unidos.* *Por esta razón se hace referencia a las reivindicaciones modificadas.* *En este caso tienen el mismo contenido y todas la reivindicaciones son idénticas.*

a un átomo de nitrógeno esté opcionalmente sustituido con una porción R^{2a} distinta de halógeno; cada R^{1a} es independientemente C_1-C_6 alquilo, C_2-C_6 alquenilo, C_2-C_6 alquinilo, C_3-C_8 cicloalquilo, C_4-C_8 cicloalquenilo, heterociclilo de 3 a 12 miembros, heteroarilo de 5 a 10 miembros, C_6-C_{14} arilo, deuterio, halógeno, -CN, -OR^3, -SR^3, -NR^4R^5, -NO_2, -C=NH(OR^3), -C(O)R^3, -OC(O)R^3, -C(O)OR^3, -C(O)NR^4R^5, -NR^3C(O)R^4, -NR^3C(O)OR^4, -NR^3C(O)NR^4R^5, -S(O)R^3, -$S(O)_2R^3$, -NR^3S(O)R^4, -$NR^3S(O)_2R^4$, -S(O)NR^4R^5, -$S(O)_2NR^4R^5$, o -P(O)(OR^4)(OR^5), en donde cada R^{1a} está, donde sea posible, opcionalmente sustituido de manera independiente con deuterio, halógeno, oxo, -OR^6, -NR^6R^7, -C(O)R^6, -CN, -S(O)R^6, -$S(O)_2R^6$, -P(O)(OR^6)(OR^7), C_3-C_8 cicloalquilo, heterociclilo de 3 a 12 miembros, heteroarilo de 5 a 10 miembros, C_6-C_{14} arilo o C_1-C_6	a un átomo de nitrógeno esté opcionalmente sustituido con una porción R^{2a} distinta de halógeno; cada R^{1a} es independientemente C_1-C_6 alquilo, C_2-C_6 alquenilo, C_2-C_6 alquinilo, C_3-C_8 cicloalquilo, C_4-C_8 cicloalquenilo, heterociclilo de 3 a 12 miembros, heteroarilo de 5 a 10 miembros, C_6-C_{14} arilo, deuterio, halógeno, -CN, -OR^3, -SR^3, -NR^4R^5, -NO_2, -C=NH(OR^3), -C(O)R^3, -OC(O)R^3, -C(O)OR^3, -C(O)NR^4R^5, -NR^3C(O)R^4, -NR^3C(O)OR^4, -NR^3C(O)NR^4R^5, -S(O)R^3, -$S(O)_2R^3$, -NR^3S(O)R^4, -$NR^3S(O)_2R^4$, -S(O)NR^4R^5, -$S(O)_2NR^4R^5$, o -P(O)(OR^4)(OR^5), en donde cada R^{1a} está, donde sea posible, opcionalmente sustituido de manera independiente con deuterio, halógeno, oxo, -OR^6, -NR^6R^7, -C(O)R^6, -CN, -S(O)R^6, -$S(O)_2R^6$, -P(O)(OR^6)(OR^7), C_3-C_8 cicloalquilo, heterociclilo de 3 a 12 miembros, heteroarilo de 5 a 10 miembros, C_6-C_{14} arilo o C_1-C_6	

alquilo opcionalmente sustituido con deuterio, oxo, -OH o halógeno; cada R^{2a}, R^{2b}, R^{2c}, R^{2e} y R^{2f} es independientemente oxo o R^{1a}; R^{2d} es C_1-C_6 alquilo opcionalmente sustituido con R^{2e} o C_3-C_5 cicloalquilo opcionalmente sustituido con R^{2f}; cada R^3 es independientemente hidrógeno, deuterio, C_1-C_6 alquilo, C_2-C_6 alquenilo, C_2-C_6 alquinilo, C_3-C_6 cicloalquilo, C_6-C_{14} arilo, heteroarilo de 5 a 10 miembros o heterociclilo de 3 a 12 miembros, en donde el C_1-C_6 alquilo, C_2-C_6 alquenilo, C_2-C_6 alquinilo, C_3-C_6 cicloalquilo, C_6-C_{14} arilo, heteroarilo de 5 a 10 miembros y heterociclilo de 3 a 12 miembros de R^3 están opcionalmente sustituidos de manera independiente con halógeno, deuterio, oxo, -CN, $-OR^8$, $-NR^8R^9$, $-P(O)(OR^8)(OR^9)$ o C_1-C_6 alquilo opcionalmente sustituido con deuterio, halógeno, -OH u oxo;	alquilo opcionalmente sustituido con deuterio, oxo, -OH o halógeno; cada R^{2a}, R^{2b}, R^{2c}, R^{2e} y R^{2f} es independientemente oxo o R^{1a}; R^{2d} es C_1-C_6 alquilo opcionalmente sustituido con R^{2e} o C_3-C_5 cicloalquilo opcionalmente sustituido con R^{2f}; cada R^3 es independientemente hidrógeno, deuterio, C_1-C_6 alquilo, C_2-C_6 alquenilo, C_2-C_6 alquinilo, C_3-C_6 cicloalquilo, C_6-C_{14} arilo, heteroarilo de 5 a 10 miembros o heterociclilo de 3 a 12 miembros, en donde el C_1-C_6 alquilo, C_2-C_6 alquenilo, C_2-C_6 alquinilo, C_3-C_6 cicloalquilo, C_6-C_{14} arilo, heteroarilo de 5 a 10 miembros y heterociclilo de 3 a 12 miembros de R^3 están opcionalmente sustituidos de manera independiente con halógeno, deuterio, oxo, -CN, $-OR^8$, $-NR^8R^9$, $-P(O)(OR^8)(OR^9)$ o C_1-C_6 alquilo opcionalmente sustituido con deuterio, halógeno, -OH u oxo;	

R^4 y R^5 son cada uno independientemente hidrógeno, deuterio, C_1-C_6 alquilo, C_2-C_6 alquenilo, C_2-C_6 alquinilo, C_3-C_6 cicloalquilo, C_6-C_{14} arilo, heteroarilo de 5 a 6 miembros o heterociclilo de 3 a 6 miembros, en donde el C_1-C_6 alquilo, C_2-C_6 alquenilo, C_2-C_6 alquinilo, C_3-C_6 cicloalquilo, C_6-C_{14} arilo, heteroarilo de 5 a 6 miembros y heterociclilo de 3 a 6 miembros de R^4 y R^5 están opcionalmente sustituidos de manera independiente con deuterio, halógeno, oxo, -CN, -OR^8, -NR^8R^9 o C_1-C_6 alquilo opcionalmente sustituido con deuterio, halógeno, oxo o -OH; o R^4 y R^5 se toman juntos con el átomo al que se unieron para formar un heterociclilo de 3 a 6 miembros opcionalmente sustituido con deuterio, halógeno, oxo, -OR^8, -NR^8R^9 o C_1-C_6 alquilo opcionalmente sustituido con deuterio, halógeno, oxo u -OH;	R^4 y R^5 son cada uno independientemente hidrógeno, deuterio, C_1-C_6 alquilo, C_2-C_6 alquenilo, C_2-C_6 alquinilo, C_3-C_6 cicloalquilo, C_6-C_{14} arilo, heteroarilo de 5 a 6 miembros o heterociclilo de 3 a 6 miembros, en donde el C_1-C_6 alquilo, C_2-C_6 alquenilo, C_2-C_6 alquinilo, C_3-C_6 cicloalquilo, C_6-C_{14} arilo, heteroarilo de 5 a 6 miembros y heterociclilo de 3 a 6 miembros de R^4 y R^5 están opcionalmente sustituidos de manera independiente con deuterio, halógeno, oxo, -CN, -OR^8, -NR^8R^9 o C_1-C_6 alquilo opcionalmente sustituido con deuterio, halógeno, oxo o -OH; o R^4 y R^5 se toman juntos con el átomo al que se unieron para formar un heterociclilo de 3 a 6 miembros opcionalmente sustituido con deuterio, halógeno, oxo, -OR^8, -NR^8R^9 o C_1-C_6 alquilo opcionalmente sustituido con deuterio, halógeno, oxo u -OH;	

R^6 y R^7 son cada uno independientemente hidrógeno, deuterio, C_1-C_6 alquilo opcionalmente sustituido con deuterio, halógeno u oxo, C_2-C_6 alquenilo opcionalmente sustituido con deuterio, halógeno u oxo o C_2-C_6 alquinilo opcionalmente sustituido con deuterio, halógeno u oxo; o R^6 y R^7 se toman juntos con el átomo al que se unieron para formar un heterociclilo de 3 a 6 miembros opcionalmente sustituido con deuterio, halógeno, oxo o C_1-C_6 alquilo opcionalmente sustituido con deuterio, halógeno u oxo; R^8 y R^9 son cada uno independientemente hidrógeno, deuterio, C_1-C_6 alquilo opcionalmente sustituido con deuterio, halógeno u oxo, C_2-C_6 alquenilo opcionalmente sustituido con deuterio, halógeno u oxo o C_2-C_6 alquinilo opcionalmente sustituido con deuterio, halógeno u oxo; o R^8 y R^9 se toman juntos con el átomo al que se unieron para formar un heterociclilo de 3 a 6	R^6 y R^7 son cada uno independientemente hidrógeno, deuterio, C_1-C_6 alquilo opcionalmente sustituido con deuterio, halógeno u oxo, C_2-C_6 alquenilo opcionalmente sustituido con deuterio, halógeno u oxo o C_2-C_6 alquinilo opcionalmente sustituido con deuterio, halógeno u oxo; o R^6 y R^7 se toman juntos con el átomo al que se unieron para formar un heterociclilo de 3 a 6 miembros opcionalmente sustituido con deuterio, halógeno, oxo o C_1-C_6 alquilo opcionalmente sustituido con deuterio, halógeno u oxo; R^8 y R^9 son cada uno independientemente hidrógeno, deuterio, C_1-C_6 alquilo opcionalmente sustituido con deuterio, halógeno u oxo, C_2-C_6 alquenilo opcionalmente sustituido con deuterio, halógeno u oxo o C_2-C_6 alquinilo opcionalmente sustituido con deuterio, halógeno u oxo; o R^8 y R^9 se toman juntos con el átomo al que se unieron para formar un heterociclilo de 3 a 6	

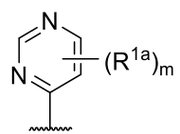
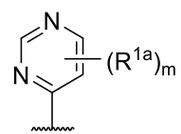
miembros opcionalmente sustituido con deuterio, halógeno, oxo o C_1-C_6 alquilo opcionalmente sustituido con deuterio, oxo o halógeno.	miembros opcionalmente sustituido con deuterio, halógeno, oxo o C_1-C_6 alquilo opcionalmente sustituido con deuterio, oxo o halógeno.	
2. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es heteroarilo de 5 a 10 miembros opcionalmente sustituido con R^{1a}.	2. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es heteroarilo de 5 a 10 miembros opcionalmente sustituido con R^{1a}.	*Tienen el mismo contenido*
3. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es: pirimidinilo, quinazolinilo, pirazolopirimidinilo, pirazinilo, quinolinilo, piridopirimidinilo, tienopirimidinilo, piridinilo, pirrolopirimidinilo, quinoxalinilo, indazolilo, benzotiazolilo, naftalenilo, purininilo o isoquinolinilo; y en donde R^1 es opcionalmente sustituido con deuterio, hidroxi, C_1-C_6 alquilo, C_1-C_6 haloalquilo, C_1-C_6 perhaloalquilo, C_1-C_6 alcoxilo, C_3-C_8 cicloalquilo,	3. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es: pirimidinilo, quinazolinilo, pirazolopirimidinilo, pirazinilo, quinolinilo, piridopirimidinilo, tienopirimidinilo, piridinilo, pirrolopirimidinilo, quinoxalinilo, indazolilo, benzotiazolilo, naftalenilo, purininilo o isoquinolinilo; y en donde R^1 es opcionalmente sustituido con deuterio, hidroxi, C_1-C_6 alquilo, C_1-C_6 haloalquilo, C_1-C_6 perhaloalquilo, C_1-C_6 alcoxilo, C_3-C_8 cicloalquilo,	*Tienen el mismo contenido*

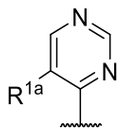
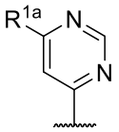
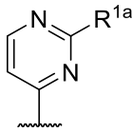
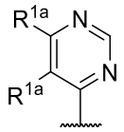
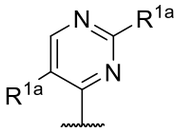
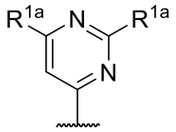
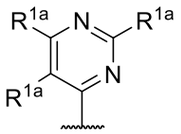
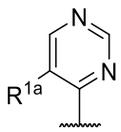
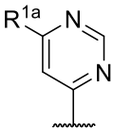
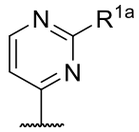
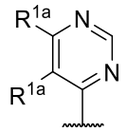
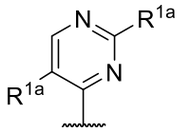
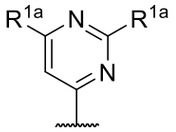
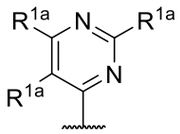
C_3-C_8 halocicloalquilo, C_3-C_8 cicloalcoxilo, heteroarilo de 5 a 10 miembros, C_6-C_{14} arilo, ciano, amino, alquilamino o dialquilamino.	C_3-C_8 halocicloalquilo, C_3-C_8 cicloalcoxilo, heteroarilo de 5 a 10 miembros, C_6-C_{14} arilo, ciano, amino, alquilamino o dialquilamino.	
4. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es: pirimidin-2-ilo, pirimidin-4-ilo, quinazolin-4-ilo, 1H-pirazolo[3,4-d]pirimidin-4-ilo, 1H-pirazolo[4,3-d]pirimidin-7-ilo, pirazin-2-ilo, quinolin-4-ilo, pirido[2,3-d]pirimidin-4-ilo, pirido[3,2-d]pirimidin-4-ilo, pirido[3,4-d]pirimidin-4-ilo, tieno[2,3-d]pirimidin-4-ilo, tieno[3,2-d]pirimidin-4-ilo, tienopirimidin-4-ilo, piridin-2-ilo, piridin-3-ilo, 7H-pirrolo[2,3-d]pirimidin-4-ilo, quinoxalin-2-ilo, 1H-indazol-3-ilo, benzo[d]tiazol-2-ilo, naftalen-1-ilo, 9H-purin-6-ilo o isoquinolin-1-ilo; y en donde R^1 es opcionalmente sustituido con uno o más de deuterio, metilo, ciclopropilo, fluoro, cloro, bromo, difluorometilo, trifluorometilo, metoxi,	4. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es: pirimidin-2-ilo, pirimidin-4-ilo, quinazolin-4-ilo, 1H-pirazolo[3,4-d]pirimidin-4-ilo, 1H-pirazolo[4,3-d]pirimidin-7-ilo, pirazin-2-ilo, quinolin-4-ilo, pirido[2,3-d]pirimidin-4-ilo, pirido[3,2-d]pirimidin-4-ilo, pirido[3,4-d]pirimidin-4-ilo, tieno[2,3-d]pirimidin-4-ilo, tieno[3,2-d]pirimidin-4-ilo, tienopirimidin-4-ilo, piridin-2-ilo, piridin-3-ilo, 7H-pirrolo[2,3-d]pirimidin-4-ilo, quinoxalin-2-ilo, 1H-indazol-3-ilo, benzo[d]tiazol-2-ilo, naftalen-1-ilo, 9H-purin-6-ilo o isoquinolin-1-ilo; y en donde R^1 es opcionalmente sustituido con uno o más de deuterio, metilo, ciclopropilo, fluoro, cloro, bromo, difluorometilo, trifluorometilo, metoxi,	*Tienen el mismo contenido*

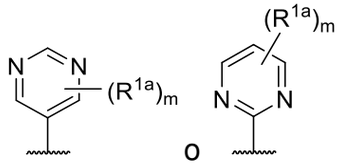
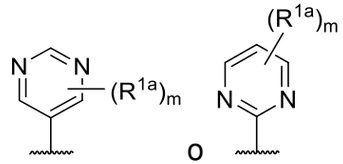
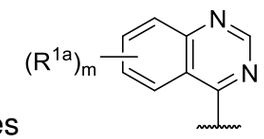
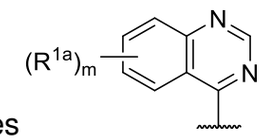
ciano, dimetilamino, fenilo, piridin-3-ilo, o piridin-4-ilo.	ciano, dimetilamino, fenilo, piridin-3-ilo, o piridin-4-ilo.	
5. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es pirimidin-4-ilo opcionalmente sustituido con R^{1a}, en donde cada R^{1a} es independiente heteroarilo de 5 a 10 miembros, o C_1-C_6 alquilo opcionalmente sustituido con halógeno.	5. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es pirimidin-4-ilo opcionalmente sustituido con R^{1a}, en donde cada R^{1a} es independiente heteroarilo de 5 a 10 miembros, o C_1-C_6 alquilo opcionalmente sustituido con halógeno.	*Tienen el mismo contenido*
6. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es quinazolin-4-ilo opcionalmente sustituido con R^{1a}, en donde cada R^{1a} es independiente halógeno, C_1-C_6 alquilo opcionalmente sustituido con halógeno, o C_1-C_6 alcoxi.	6. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es quinazolin-4-ilo opcionalmente sustituido con R^{1a}, en donde cada R^{1a} es independiente halógeno, C_1-C_6 alquilo opcionalmente sustituido con halógeno, o C_1-C_6 alcoxi.	*Tienen el mismo contenido*

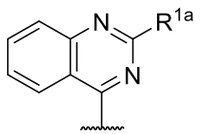
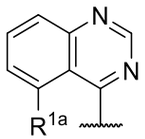
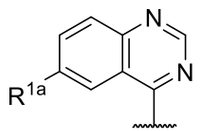
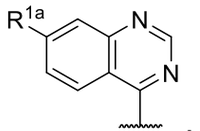
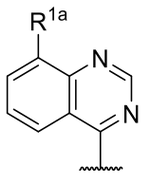
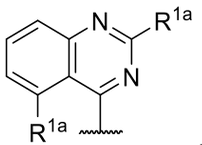
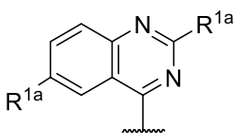
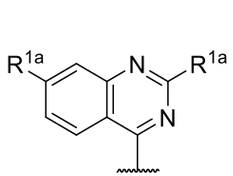
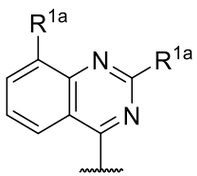
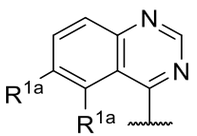
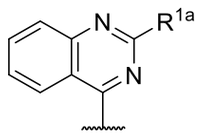
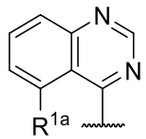
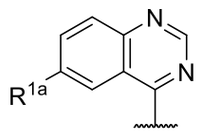
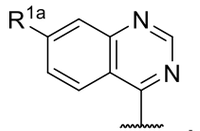
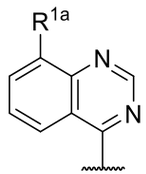
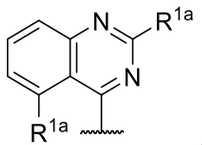
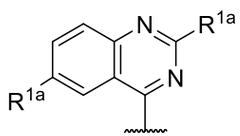
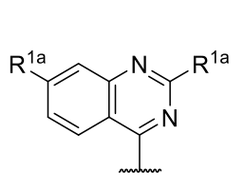
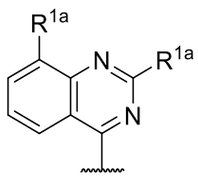
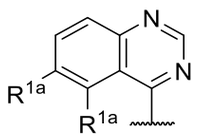
7. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es: hidrógeno, deuterio, hidroxi, C_1-C_6 alquilo, o -O-C_1-C_6 alquilo, y en donde el C_1-C_6 alquilo y -O-C_1-C_6 alquilo de R^2 son opcionalmente sustituidos con deuterio, halógeno, C_1-C_6 alquilo, C_1-C_6 haloalquilo, C_1-C_6 hidroxialquilo, C_1-C_6 alcoxilo, C_3-C_8 cicloalquilo, C_3-C_8 halocicloalquilo, C_3-C_8 cicloalcoxilo, C_6-C_{14} arilo, C_6-C_{14} ariloxi, heteroarilo de 5 a 10 miembros, heteroariloxi de 5 a 10 miembros, heterociclilo de 3 a 12 miembros opcionalmente sustituido con oxo, -C(O)NR^4R^5, -NR^3C(O)R^4 o -$S(O)_2R^3$.	7. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es: hidrógeno, deuterio, hidroxi, C_1-C_6 alquilo, o -O-C_1-C_6 alquilo, y en donde el C_1-C_6 alquilo y -O-C_1-C_6 alquilo de R^2 son opcionalmente sustituidos con deuterio, halógeno, C_1-C_6 alquilo, C_1-C_6 haloalquilo, C_1-C_6 hidroxialquilo, C_1-C_6 alcoxilo, C_3-C_8 cicloalquilo, C_3-C_8 halocicloalquilo, C_3-C_8 cicloalcoxilo, C_6-C_{14} arilo, C_6-C_{14} ariloxi, heteroarilo de 5 a 10 miembros, heteroariloxi de 5 a 10 miembros, heterociclilo de 3 a 12 miembros opcionalmente sustituido con oxo, -C(O)NR^4R^5, -NR^3C(O)R^4 o -$S(O)_2R^3$.	*Tienen el mismo contenido*

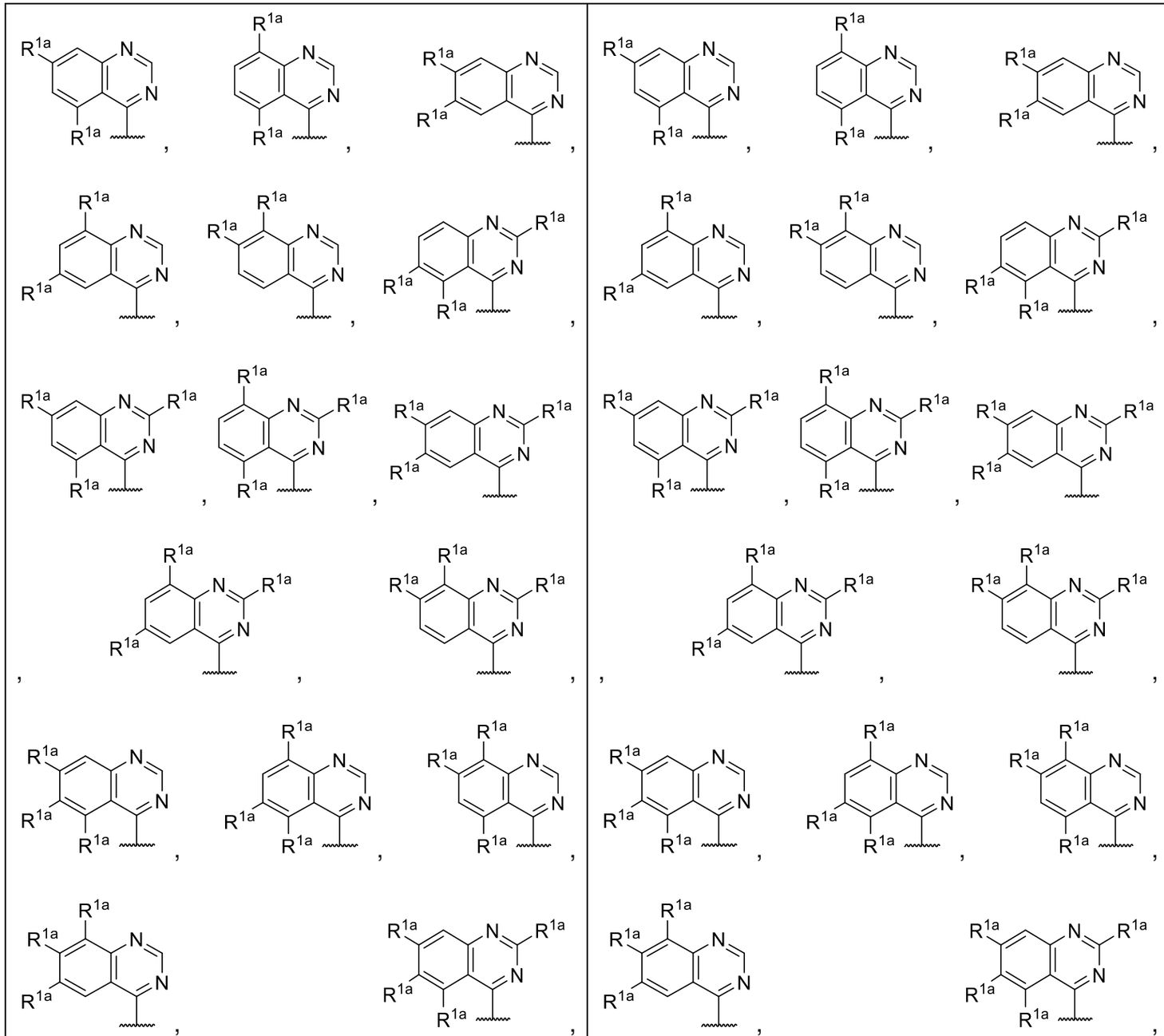
8. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es: metilo, metoxi, etilo, etoxi, propilo, ciclopropilo o ciclobutilo; y en donde R^2 es opcionalmente sustituido con uno o más de hidroxi, metoxi, etoxi, acetamida, fluoro, fluoroalquilo, fenoxi, dimetilamida, metilsulfonilo, ciclopropoxilo, piridin-2-iloxi, piridin-3-iloxi, N-morfolinilo, N-pirrolidin-2-onilo, dimetilpirazol-1-ilo, (1,4-dioxiran-2-ilo) metilo, morfolin-2-ilo, oxetan-3-ilo, fenilo, tetrahidrofuran-2-ilo, o tiazol-2-ilo; cada uno de los cuales es sustituido con 0, 1, 2 o 3 de deuterio, hidroxi, metilo, fluoro, ciano u oxo.	8. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es: metilo, metoxi, etilo, etoxi, propilo, ciclopropilo o ciclobutilo; y en donde R^2 es opcionalmente sustituido con uno o más de hidroxi, metoxi, etoxi, acetamida, fluoro, fluoroalquilo, fenoxi, dimetilamida, metilsulfonilo, ciclopropoxilo, piridin-2-iloxi, piridin-3-iloxi, N-morfolinilo, N-pirrolidin-2-onilo, dimetilpirazol-1-ilo, (1,4-dioxiran-2-ilo) metilo, morfolin-2-ilo, oxetan-3-ilo, fenilo, tetrahidrofuran-2-ilo, o tiazol-2-ilo; cada uno de los cuales es sustituido con 0, 1, 2 o 3 de deuterio, hidroxi, metilo, fluoro, ciano u oxo.	*Tienen el mismo contenido*
9. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es C_1-C_6 alquilo opcionalmente sustituido con:	9. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es C_1-C_6 alquilo opcionalmente sustituido con:	*Tienen el mismo contenido*

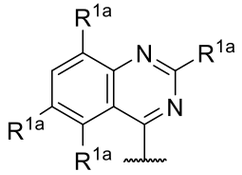
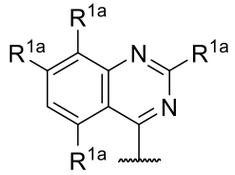
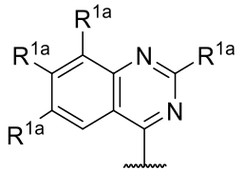
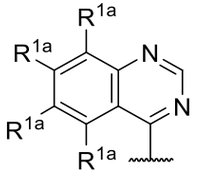
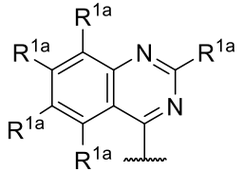
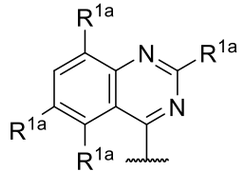
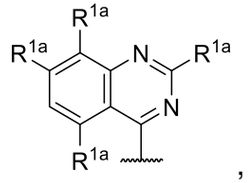
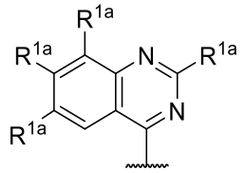
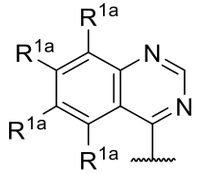
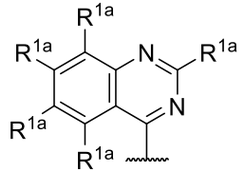
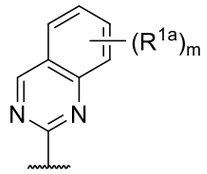
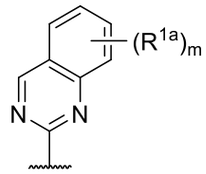
R^{2a}, en donde cada R^{2a} es independientemente: halógeno; C_3-C_8 cicloalquilo opcionalmente sustituido con halógeno; heteroarilo de 5 a 10 miembros opcionalmente sustituido con C_1-C_6 alquilo; $-NR^4R^5$; $-NR^3C(O)R^4$; $-S(O)_2R^3$; oxo, o $-OR^3$, en donde cada R^3 es independientemente: hidrógeno; C_1-C_6 alquilo opcionalmente sustituido con halógeno; C_3-C_6 cicloalquilo opcionalmente sustituido con halógeno; C_6-C_{14} arilo opcionalmente sustituido con halógeno; heteroarilo de 5 a 6 miembros opcionalmente sustituido con halógeno o C_1-C_6 alquilo.	R^{2a}, en donde cada R^{2a} es independientemente: halógeno; C_3-C_8 cicloalquilo opcionalmente sustituido con halógeno; heteroarilo de 5 a 10 miembros opcionalmente sustituido con C_1-C_6 alquilo; $-NR^4R^5$; $-NR^3C(O)R^4$; $-S(O)_2R^3$; oxo, o $-OR^3$, en donde cada R^3 es independientemente: hidrógeno; C_1-C_6 alquilo opcionalmente sustituido con halógeno; C_3-C_6 cicloalquilo opcionalmente sustituido con halógeno; C_6-C_{14} arilo opcionalmente sustituido con halógeno; heteroarilo de 5 a 6 miembros opcionalmente sustituido con halógeno o C_1-C_6 alquilo.	
10. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  , en donde m es 0, 1, 2, o 3 y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo,	10. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  , en donde m es 0, 1, 2, o 3 y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo,	*Tienen el mismo contenido*

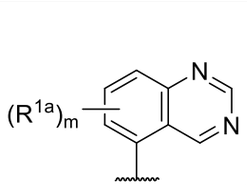
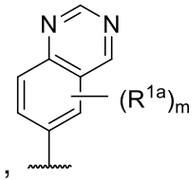
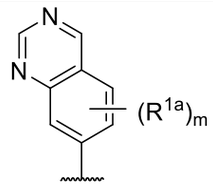
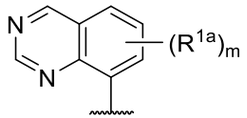
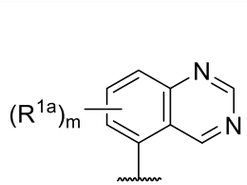
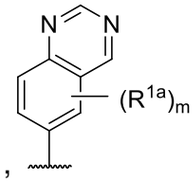
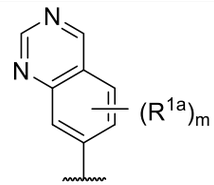
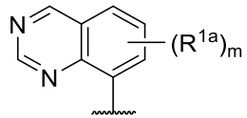
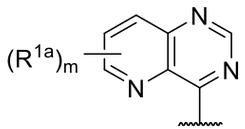
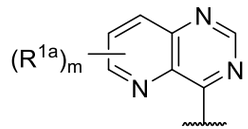
haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.	haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.	
11. El compuesto de la reivindicación 10, o una sal del mismo, en donde R^1 es  ,  ,  ,  ,  ,  , o  , en donde cada R^{1a} es independientemente deuterio, alquilo, haloalquilo, o heteroarilo.	11. El compuesto de la reivindicación 10, o una sal del mismo, en donde R^1 es  ,  ,  ,  ,  ,  , o  , en donde cada R^{1a} es independientemente deuterio, alquilo, haloalquilo, o heteroarilo.	*Tienen el mismo contenido*

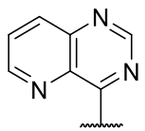
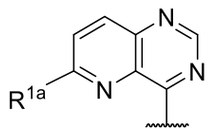
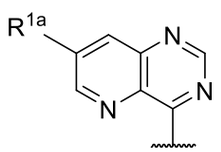
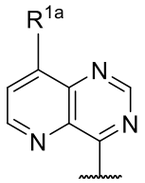
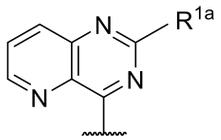
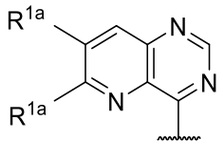
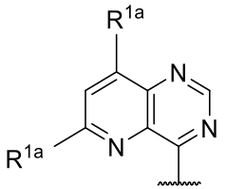
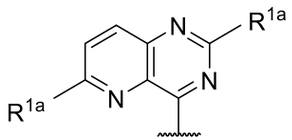
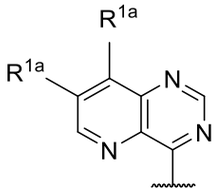
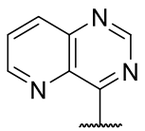
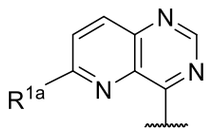
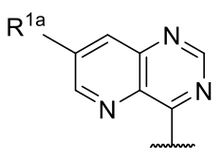
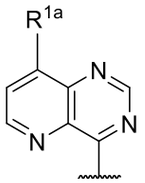
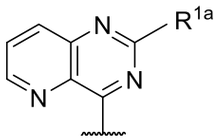
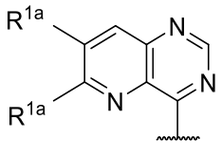
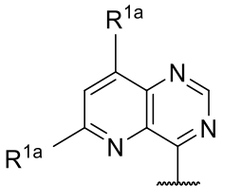
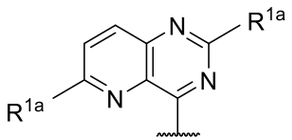
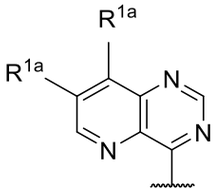
12. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  , en donde m es 0, 1, 2, o 3 y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.	12. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  , en donde m es 0, 1, 2, o 3 y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.	*Tienen el mismo contenido*
13. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  , en donde m es 0, 1, 2, 3, 4, o 5 y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi,	13. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  , en donde m es 0, 1, 2, 3, 4, o 5 y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi,	*Tienen el mismo contenido*

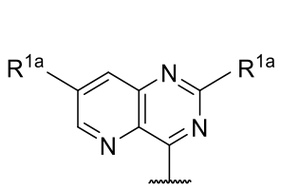
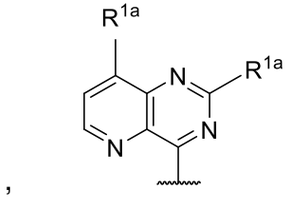
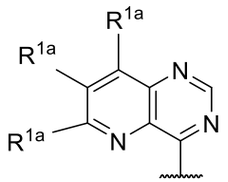
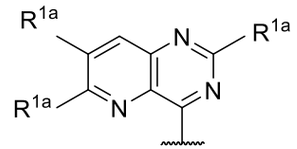
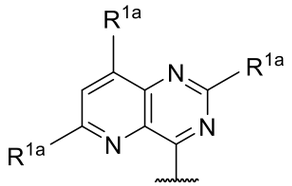
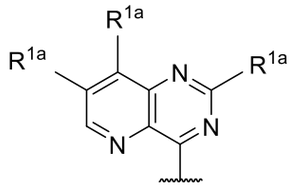
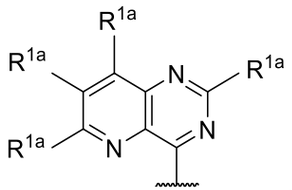
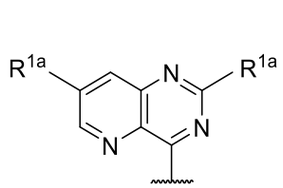
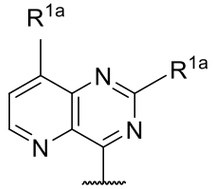
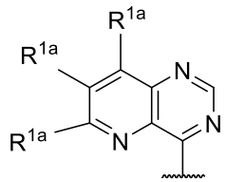
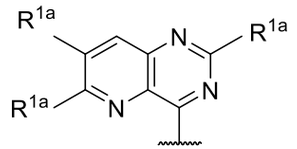
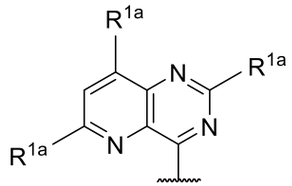
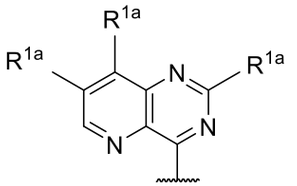
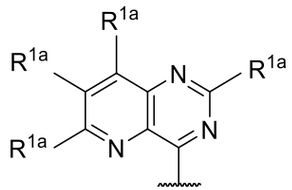
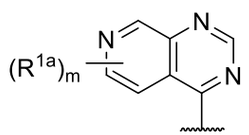
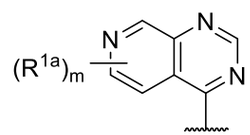
hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.	hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.	
14. El compuesto de la reivindicación 13, o una sal del mismo, en donde R^1 es  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,	14. El compuesto de la reivindicación 13, o una sal del mismo, en donde R^1 es  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,	*Tienen el mismo contenido*

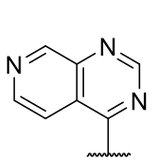
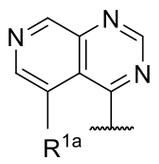
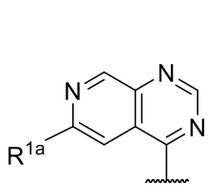
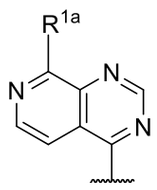
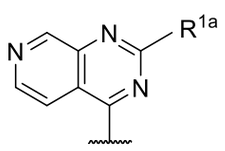
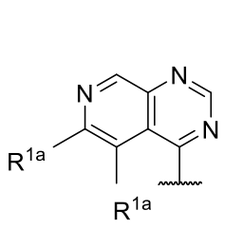
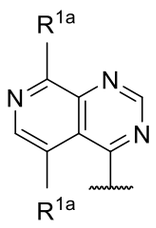
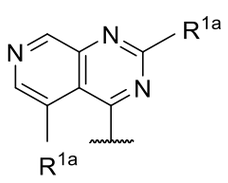
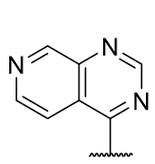
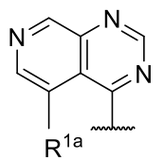
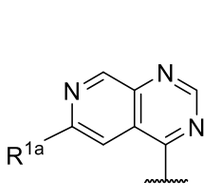
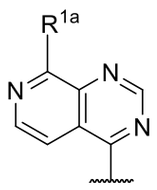
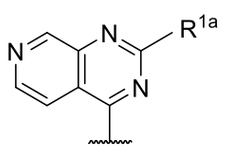
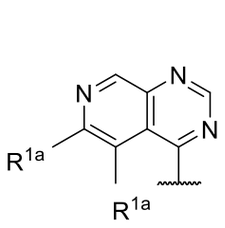
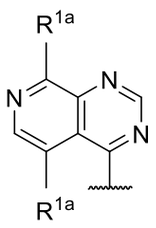
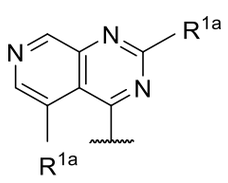


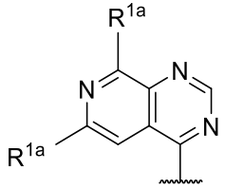
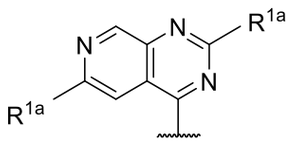
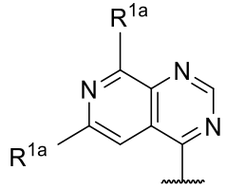
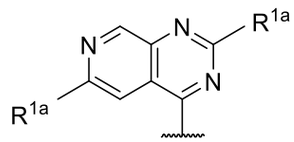
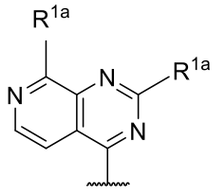
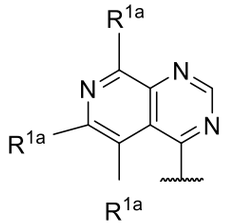
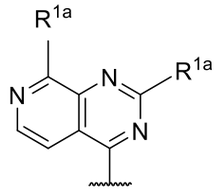
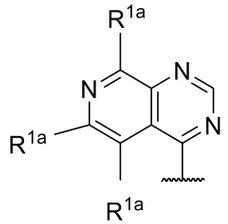
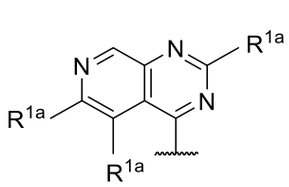
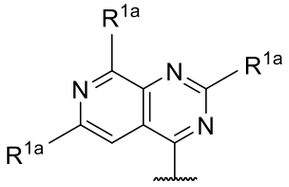
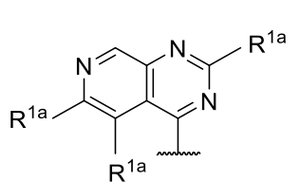
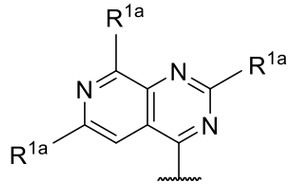
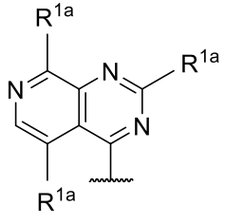
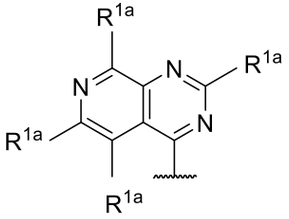
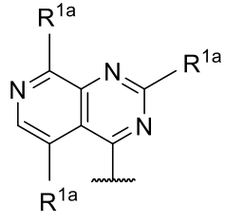
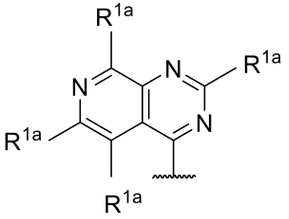
 ,  ,  ,  , o  , en donde cada R^{1a} es independientemente deuterio, halógeno, alquilo, haloalquilo, o alcoxi.	 ,  ,  ,  , o  , en donde cada R^{1a} es independientemente deuterio, halógeno, alquilo, haloalquilo, o alcoxi.	
15. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  ,	15. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  ,	*Tienen el mismo contenido*

 ,  ,  , o  en donde m es 0, 1, 2, 3, 4, o 5 y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.	 ,  ,  , o  en donde m es 0, 1, 2, 3, 4, o 5 y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.	
16. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  en donde m es 0, 1, 2, 3, o 4, y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o	16. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  en donde m es 0, 1, 2, 3, o 4, y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o	*Tienen el mismo contenido*

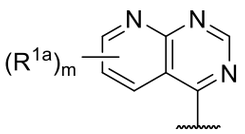
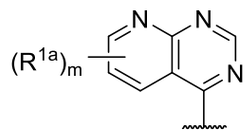
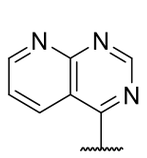
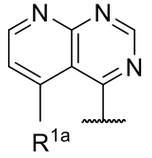
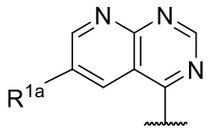
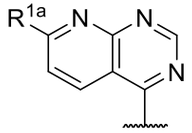
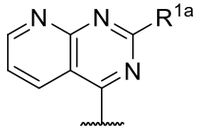
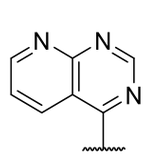
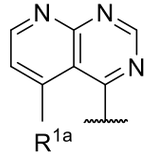
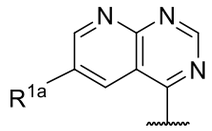
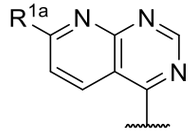
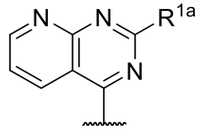
heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.	heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.	
17. El compuesto de la reivindicación 16, o una sal del mismo, en donde R^1 se selecciona del grupo que consiste de  ,  ,  ,  ,  ,  ,  ,  ,  ,	17. El compuesto de la reivindicación 16, o una sal del mismo, en donde R^1 se selecciona del grupo que consiste de  ,  ,  ,  ,  ,  ,  ,  ,  ,	*Tienen el mismo contenido*

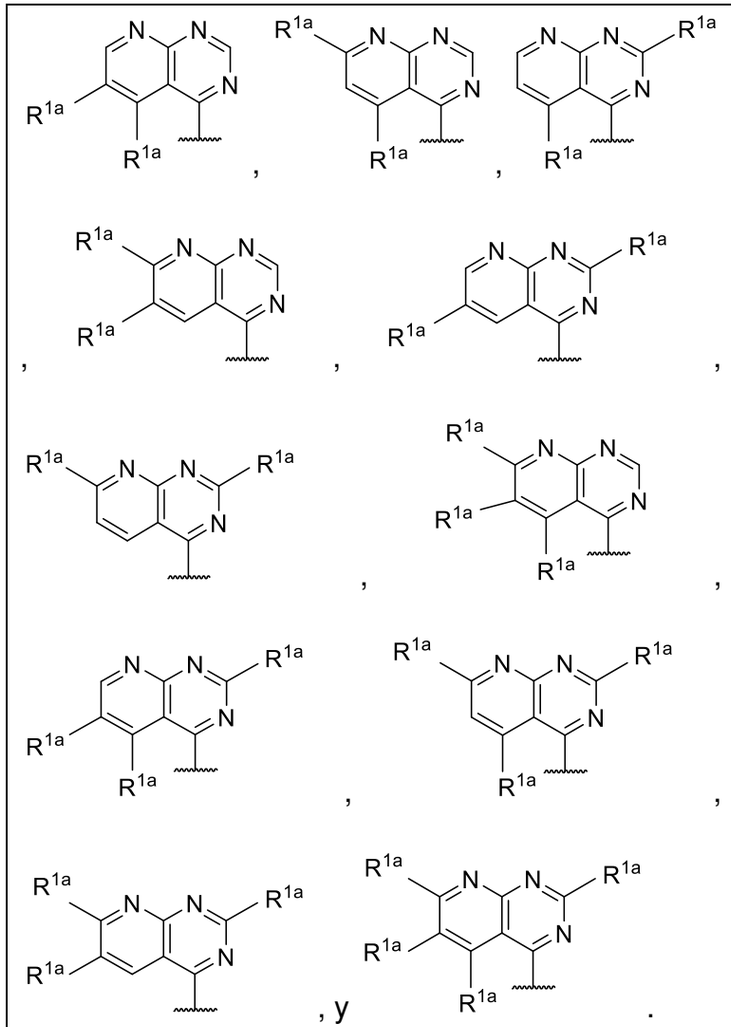
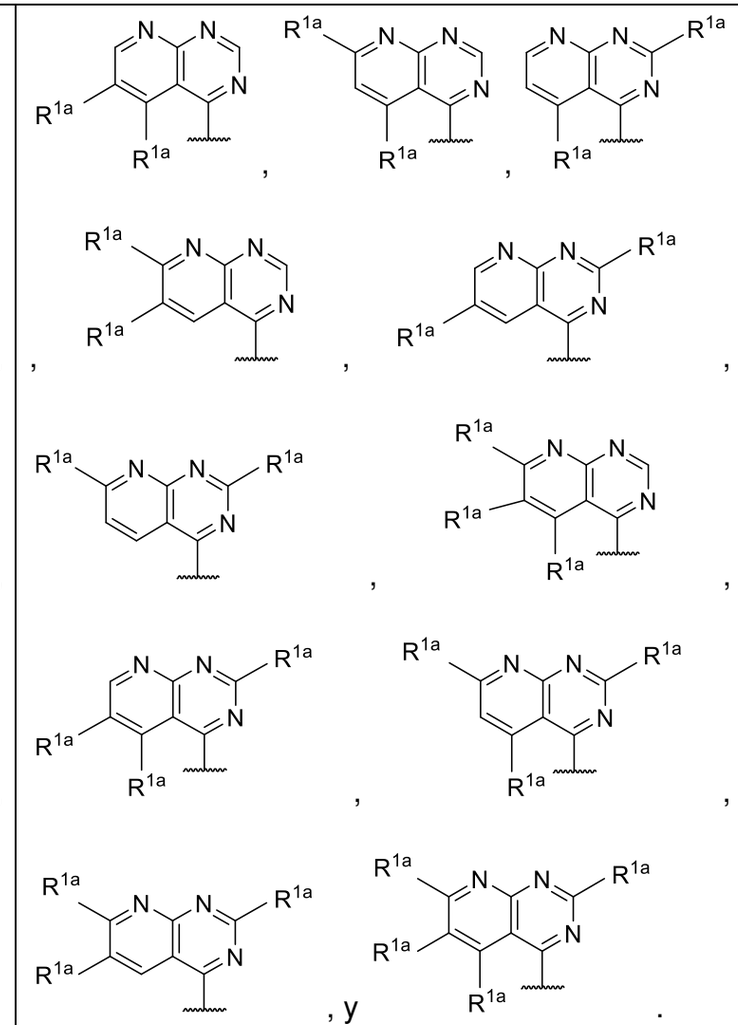
 ,  ,  ,  ,  ,  , y  .	 ,  ,  ,  ,  ,  , y  .	
18. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  en donde m es 0, 1, 2, 3, o 4, y cada R^{1a} es, donde sea	18. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  en donde m es 0, 1, 2, 3, o 4, y cada R^{1a} es, donde sea	*Tienen el mismo contenido*

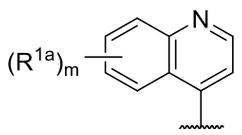
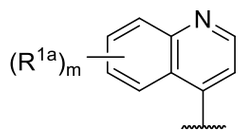
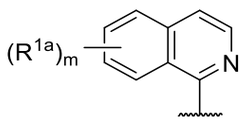
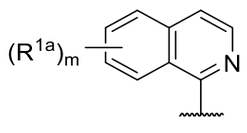
aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.	aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.	
19. El compuesto de la reivindicación 18, o una sal del mismo, en donde R^1 se selecciona del grupo que consiste de  ,  ,  ,  ,  ,  ,  ,  ,	19. El compuesto de la reivindicación 18, o una sal del mismo, en donde R^1 se selecciona del grupo que consiste de  ,  ,  ,  ,  ,  ,  ,  ,	*Tienen el mismo contenido*

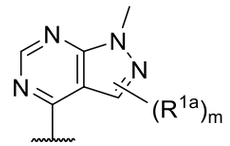
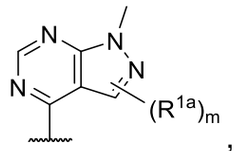

















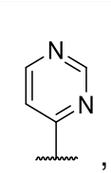
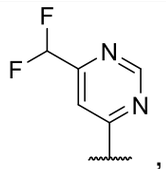
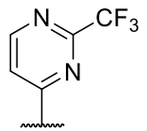
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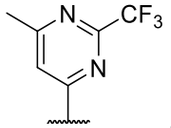
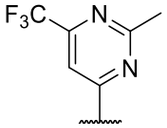
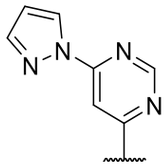
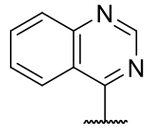
20. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  en donde m es 0, 1, 2, 3, o 4, y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.	20. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  en donde m es 0, 1, 2, 3, o 4, y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.	*Tienen el mismo contenido*
21. El compuesto de la reivindicación 20, o una sal del mismo, en donde R^1 se selecciona del grupo que consiste de  ,  ,  ,  ,  ,	21. El compuesto de la reivindicación 20, o una sal del mismo, en donde R^1 se selecciona del grupo que consiste de  ,  ,  ,  ,  ,	*Tienen el mismo contenido*

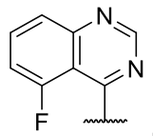
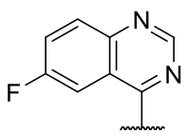
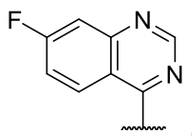



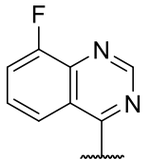
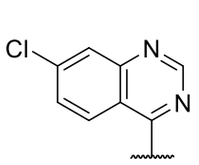
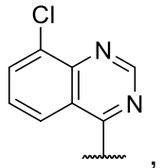
22. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  en donde m es 0, 1, 2, 3, 4, 5, o 6 y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.	22. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  en donde m es 0, 1, 2, 3, 4, 5, o 6 y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.	*Tienen el mismo contenido*
23. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  en donde m es 0, 1, 2, 3, 4, 5, o 6 y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi,	23. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  en donde m es 0, 1, 2, 3, 4, 5, o 6 y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi,	*Tienen el mismo contenido*

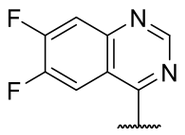
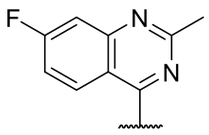
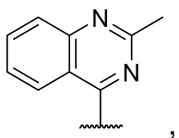
hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.	hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.	
24. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  , en donde m es 0, 1, o 2 y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.	24. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  , en donde m es 0, 1, o 2 y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.	*Tienen el mismo contenido*
25. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 se selecciona del grupo que	25. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 se selecciona del grupo que	*Tienen el mismo contenido*

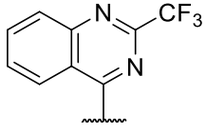
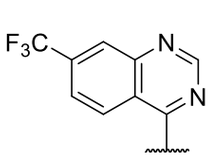
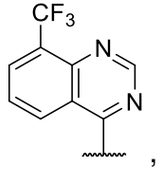
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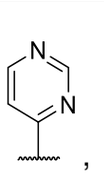
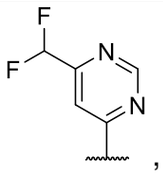
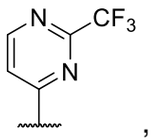
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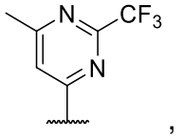
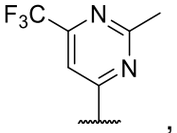
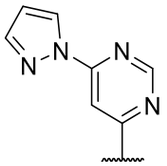
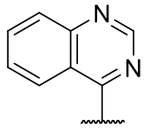
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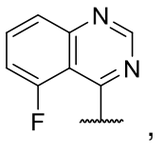
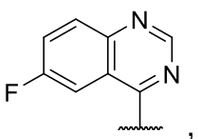
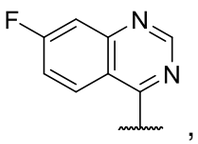
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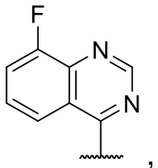
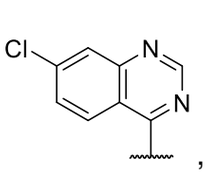
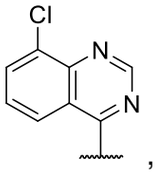
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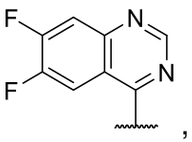
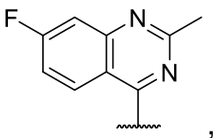
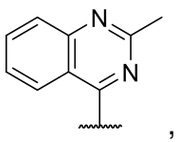
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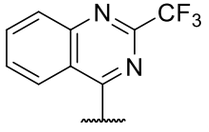
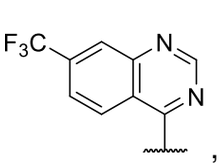
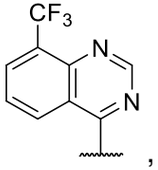
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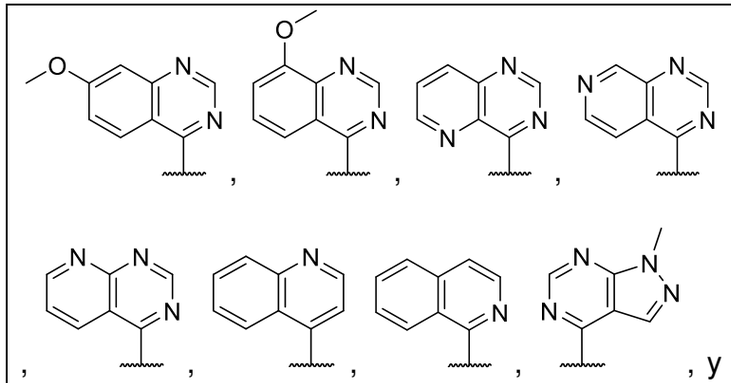
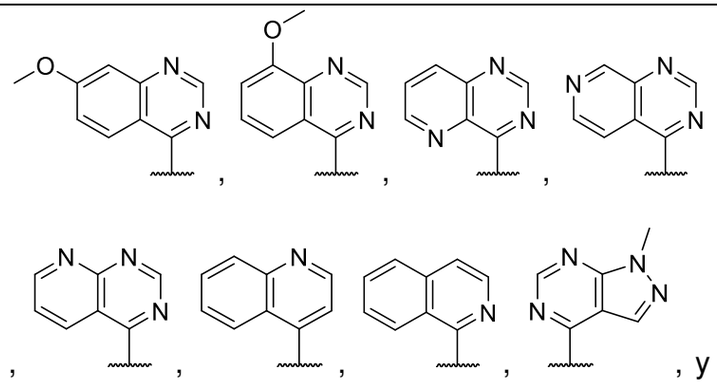
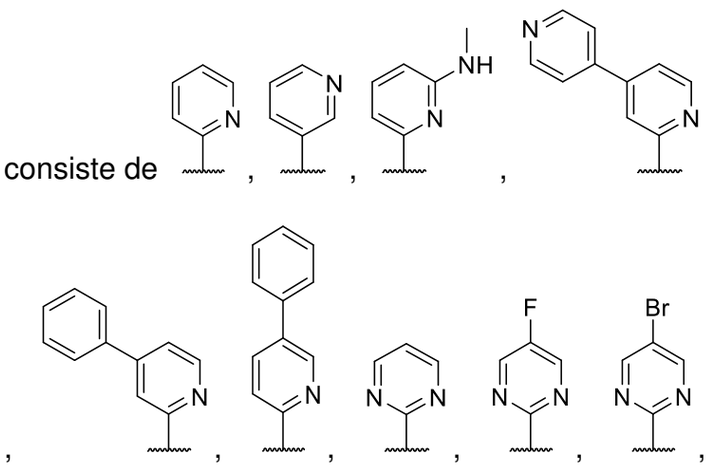
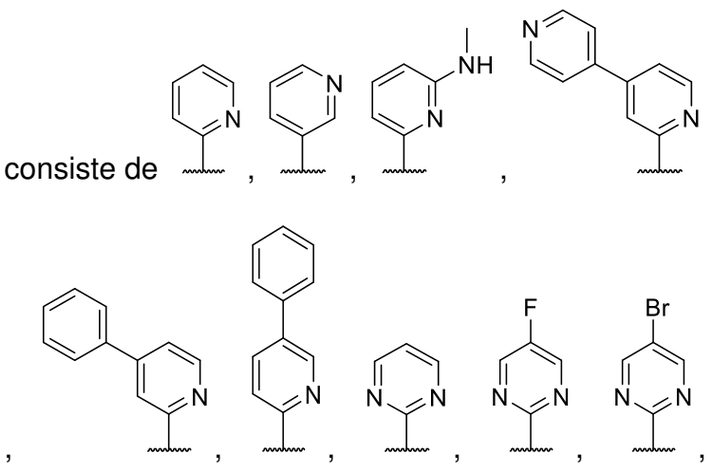
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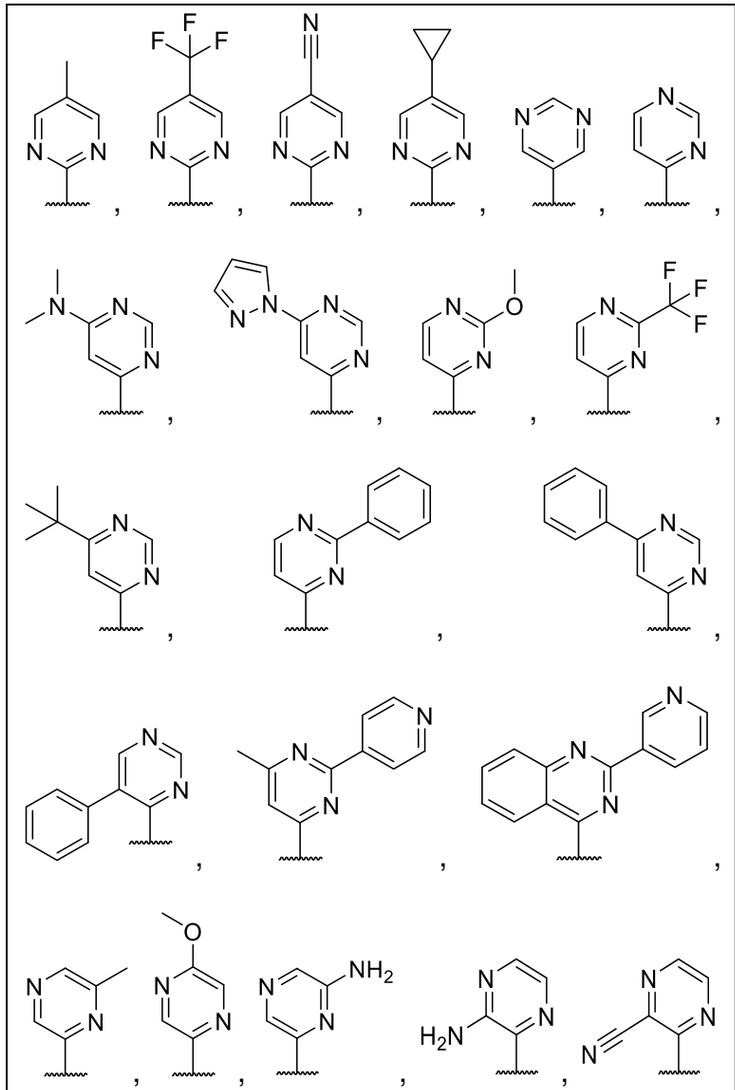
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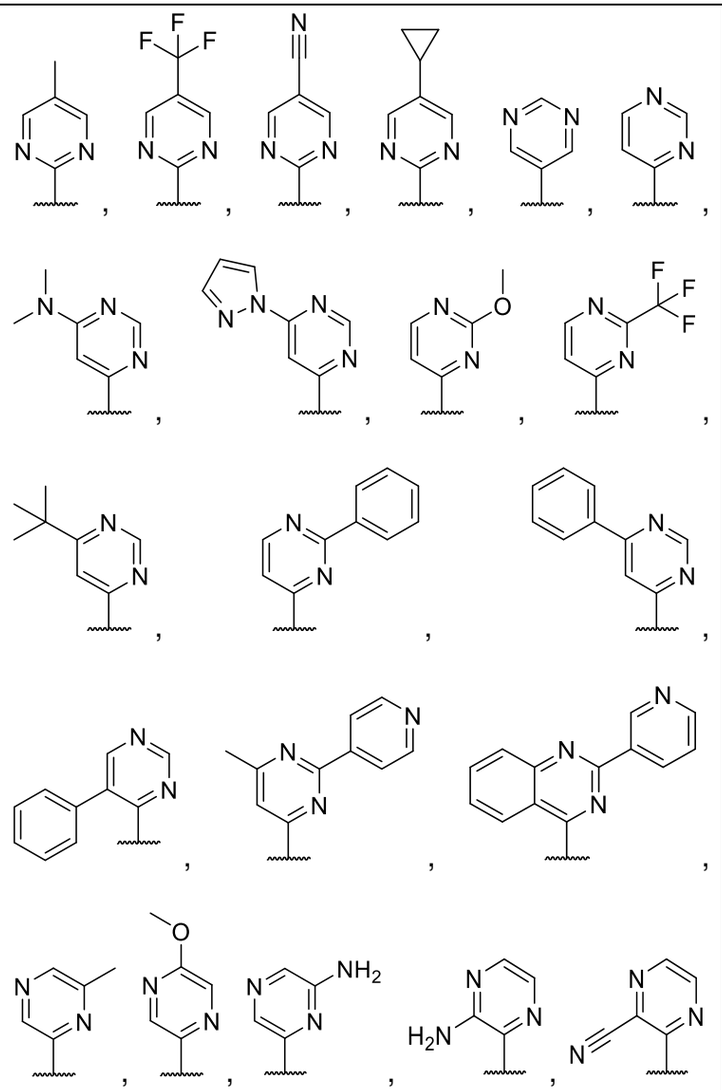
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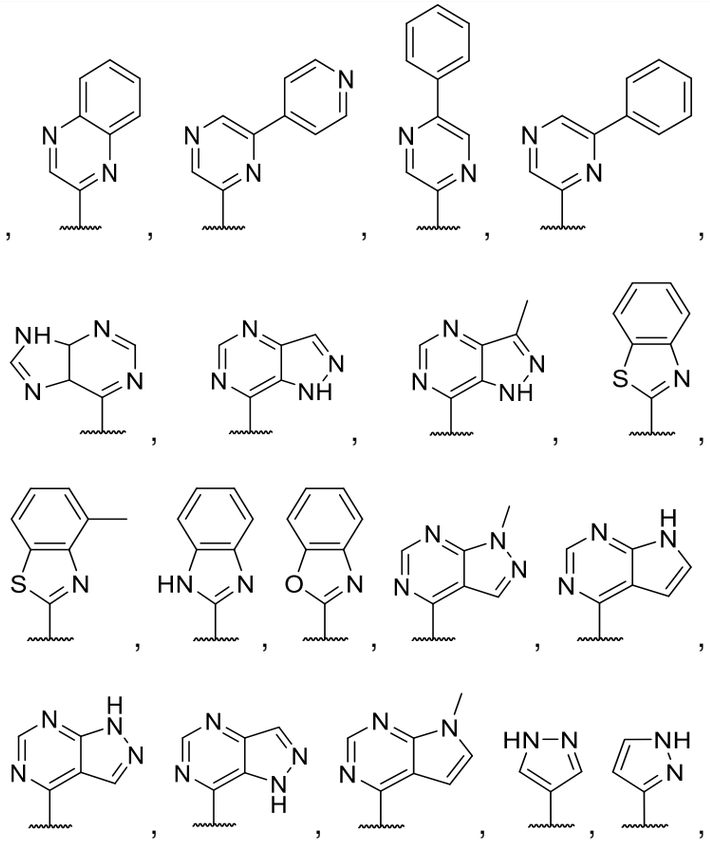
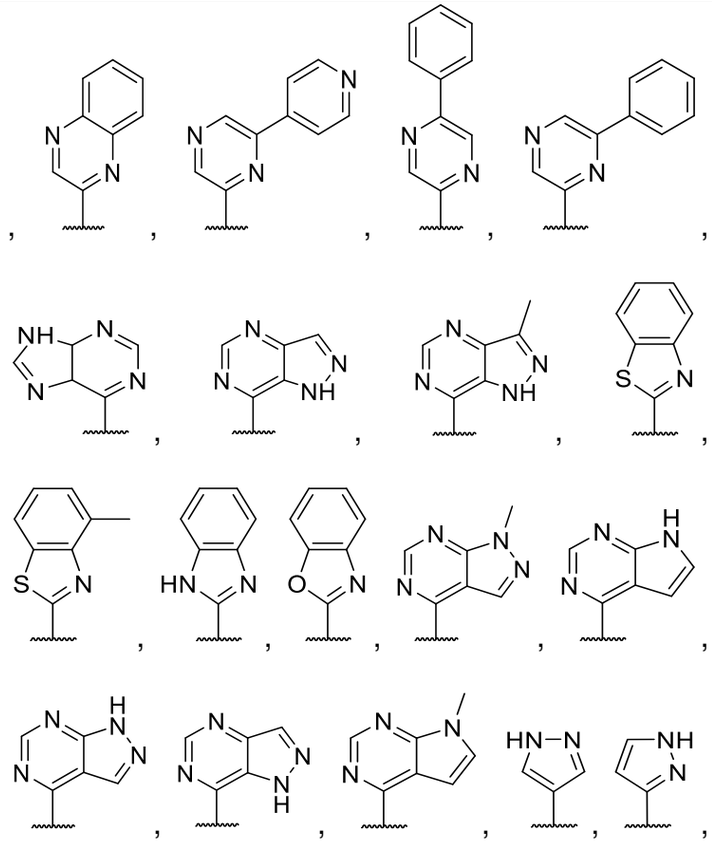
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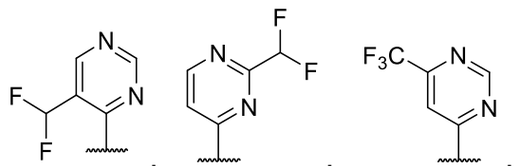
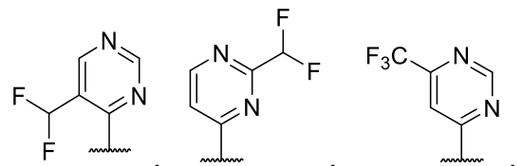
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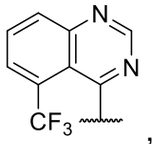
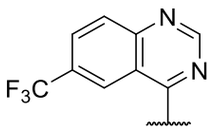
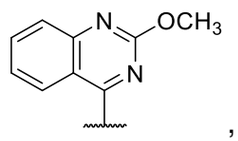
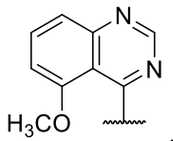
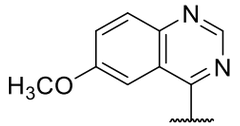
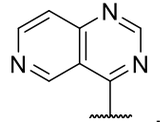
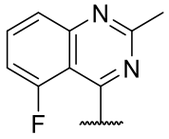
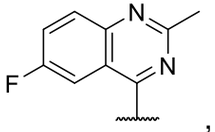
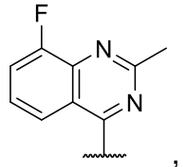
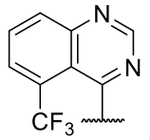
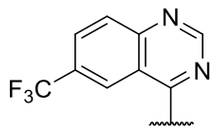
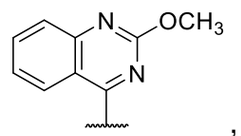
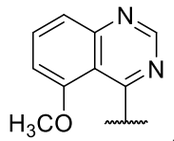
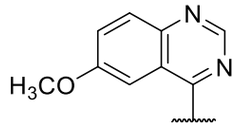
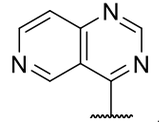
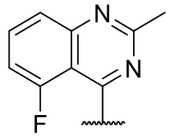
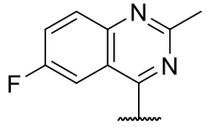
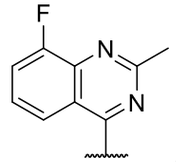
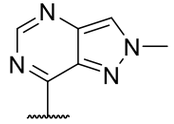
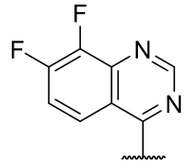
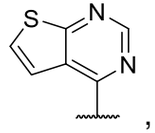
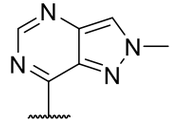
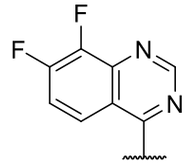
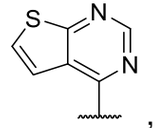
 cualquiera de los grupos anteriores en donde cualquier uno o más átomos de hidrógeno son reemplazados con átomos de deuterio.	 cualquiera de los grupos anteriores en donde cualquier uno o más átomos de hidrógeno son reemplazados con átomos de deuterio.	
26. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 se selecciona del grupo que consiste de 	26. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 se selecciona del grupo que consiste de 	*Tienen el mismo contenido*

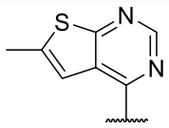
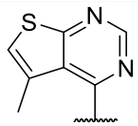
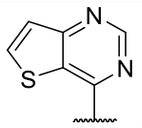
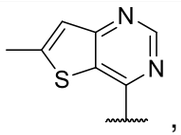
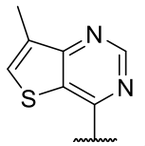
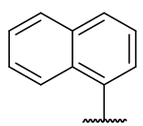
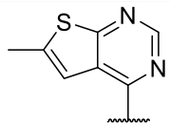
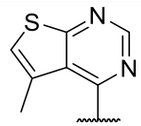
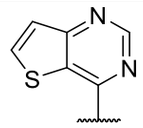
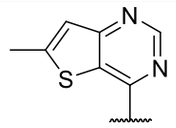
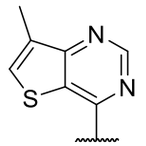
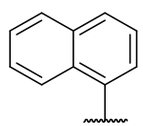
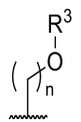
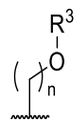


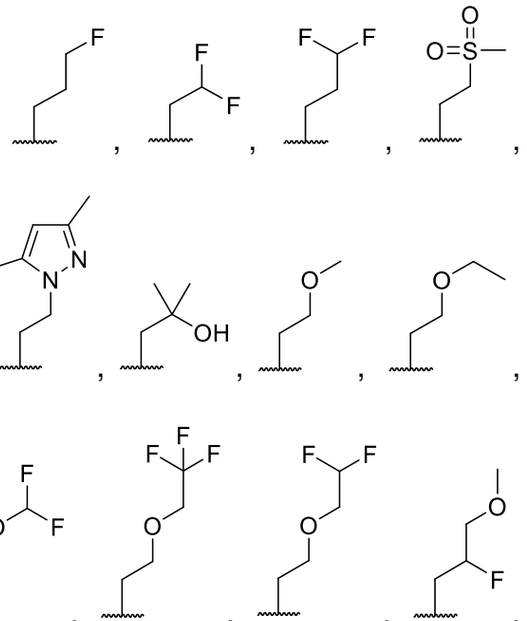
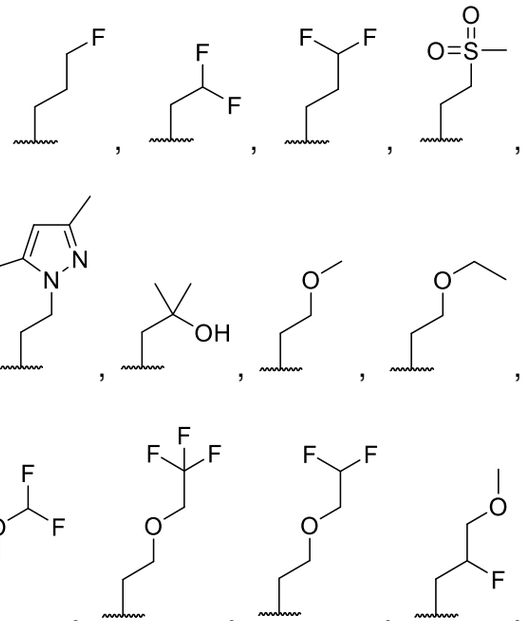


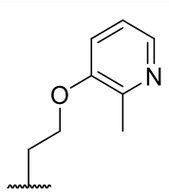
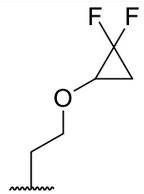
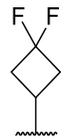
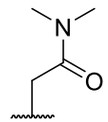
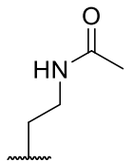
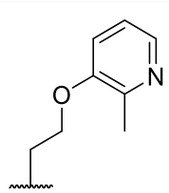
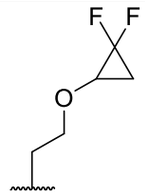
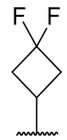
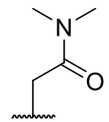
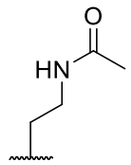
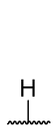
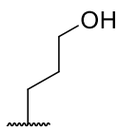
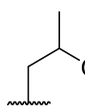
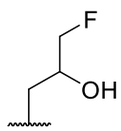
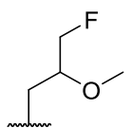
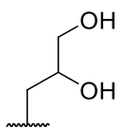
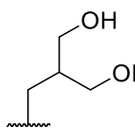
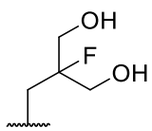
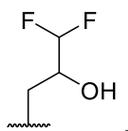
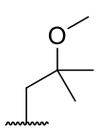
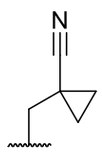
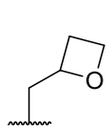
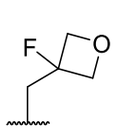
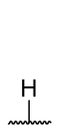
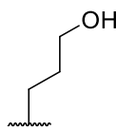
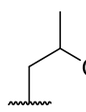
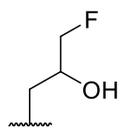
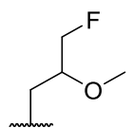
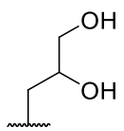
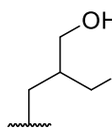
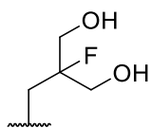
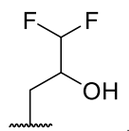
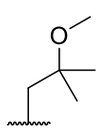
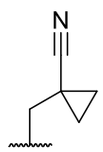
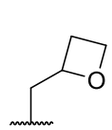
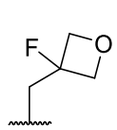
 y cualquiera de los grupos anteriores en donde cualquier uno o más átomos de hidrógeno son reemplazados con átomos de deuterio.	 y cualquiera de los grupos anteriores en donde cualquier uno o más átomos de hidrógeno son reemplazados con átomos de deuterio.	

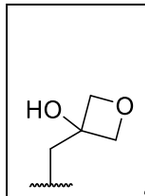
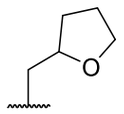
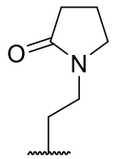
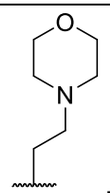
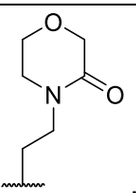
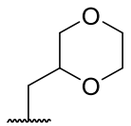
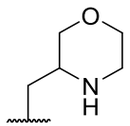
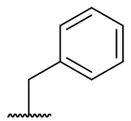
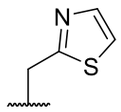
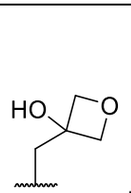
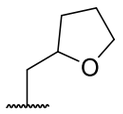
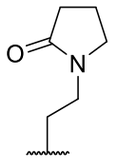
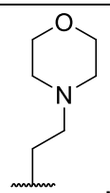
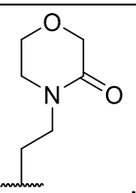
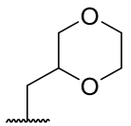
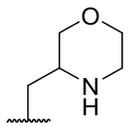
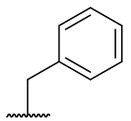
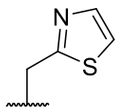
27. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 se selecciona del grupo que consiste de 	27. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 se selecciona del grupo que consiste de 	*Tienen el mismo contenido*

 ,  ,  ,  ,  ,  ,  ,  ,  , y cualquiera de los grupos anteriores en donde cualquier uno o más átomos de hidrógeno son reemplazados con átomos de deuterio.	 ,  ,  ,  ,  ,  ,  ,  ,  , y cualquiera de los grupos anteriores en donde cualquier uno o más átomos de hidrógeno son reemplazados con átomos de deuterio.	
28. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 se selecciona del grupo que consiste de  ,  ,  ,	28. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 se selecciona del grupo que consiste de  ,  ,  ,	*Tienen el mismo contenido*

 ,  ,  ,  ,  ,  , y cualquiera de los grupos anteriores en donde cualquier uno o más átomos de hidrógeno son reemplazados con átomos de deuterio.	 ,  ,  ,  ,  ,  , y cualquiera de los grupos anteriores en donde cualquier uno o más átomos de hidrógeno son reemplazados con átomos de deuterio.	
29. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es  , en donde n es 1, 2, 3, 4, 5, o 6, y R^3 es: C_1-C_2 alquilo opcionalmente sustituido con fluoro; fenilo opcionalmente sustituido con fluoro; piridinilo opcionalmente sustituido con fluoro o metilo; o ciclopropilo opcionalmente sustituido con fluoro.	29. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es  , en donde n es 1, 2, 3, 4, 5, o 6, y R^3 es: C_1-C_2 alquilo opcionalmente sustituido con fluoro; fenilo opcionalmente sustituido con fluoro; piridinilo opcionalmente sustituido con fluoro o metilo; o ciclopropilo opcionalmente sustituido con fluoro.	*Tienen el mismo contenido*

30. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 se selecciona del grupo que consiste de 	30. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 se selecciona del grupo que consiste de 	*Tienen el mismo contenido*

 ,  ,  ,  ,  ,  , y cualquiera de los grupos anteriores en donde cualquier uno o más átomos de hidrógeno son reemplazados con átomos de deuterio.	 ,  ,  ,  ,  ,  , y cualquiera de los grupos anteriores en donde cualquier uno o más átomos de hidrógeno son reemplazados con átomos de deuterio.	
31. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 se selecciona del grupo que consiste de  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,	31. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 se selecciona del grupo que consiste de  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,	*Tienen el mismo contenido*

 ,  ,  ,  ,  ,  ,  ,  ,  ,  , y cualquiera de los grupos anteriores en donde cualquier uno o más átomos de hidrógeno son reemplazados con átomos de deuterio.	 ,  ,  ,  ,  ,  ,  ,  ,  ,  , y cualquiera de los grupos anteriores en donde cualquier uno o más átomos de hidrógeno son reemplazados con átomos de deuterio.	
32. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es: a) C_3-C_5 alquilo sustituido con flúor y -OCH_3, b) C_1-C_6 alquilo opcionalmente sustituido con -OR^3, y cada R^3 es independientemente: fenilo opcionalmente sustituido con flúor; o piridinilo opcionalmente sustituido con flúor o metilo, o c) C_1-C_6 alquilo sustituido con R^{2a} en donde cada R^{2a} es independientemente: halógeno; deuterio;	32. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es: a) C_3-C_5 alquilo sustituido con flúor y -OCH_3, b) C_1-C_6 alquilo opcionalmente sustituido con -OR^3, y cada R^3 es independientemente: fenilo opcionalmente sustituido con flúor; o piridinilo opcionalmente sustituido con flúor o metilo, o c) C_1-C_6 alquilo sustituido con R^{2a} en donde cada R^{2a} es independientemente: halógeno; deuterio;	*Tienen el mismo contenido*

heterociclilo de 3 a 12 miembros opcionalmente sustituido con oxo; C_6-C_{14} arilo opcionalmente sustituido con halógeno o -OR^6; heteroarilo de 5 a 10 miembros opcionalmente sustituido con C_1-C_6 alquilo; C_3-C_8 cicloalquilo opcionalmente sustituido con -CN, halógeno, o -OR^6; o -$S(O)_2R^3$.	heterociclilo de 3 a 12 miembros opcionalmente sustituido con oxo; C_6-C_{14} arilo opcionalmente sustituido con halógeno o -OR^6; heteroarilo de 5 a 10 miembros opcionalmente sustituido con C_1-C_6 alquilo; C_3-C_8 cicloalquilo opcionalmente sustituido con -CN, halógeno, o -OR^6; o -$S(O)_2R^3$.	
33. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es piridilo, indazolilo, 1*H*-pirrolopiridilo, quinolinilo, fenilo, o indanilo, cada uno de los cuales es opcionalmente sustituido con R^{1a}.	33. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es piridilo, indazolilo, 1*H*-pirrolopiridilo, quinolinilo, fenilo, o indanilo, cada uno de los cuales es opcionalmente sustituido con R^{1a}.	*Tienen el mismo contenido*
34. Un compuesto de la reivindicación 1, o una sal del mismo, seleccionado de 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(difluorometil)pirimidin-4-il) amino) ácido butanoico;	34. Un compuesto de la reivindicación 1, o una sal del mismo, seleccionado de 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(difluorometil)pirimidin-4-il) amino) ácido butanoico;	*Tienen el mismo contenido*

4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-hidroxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 2-((7-fluoroquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-hidroxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 2-((7-fluoroquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metilquinazolin-4-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[2,3-d]pirimidin-4-ilamino) ácido butanoico; 2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-(trifluorometil)quinazolin-4-il) amino) ácido butanoico;	4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metilquinazolin-4-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[2,3-d]pirimidin-4-ilamino) ácido butanoico; 2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-(trifluorometil)quinazolin-4-il) amino) ácido butanoico;	

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)quinazolin-4-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((8-(trifluorometil)quinazolin-4-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,2-d]pirimidin-4-ilamino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,4-d]pirimidin-4-ilamino) ácido butanoico; 2-((5-fluoroquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)quinazolin-4-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((8-(trifluorometil)quinazolin-4-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,2-d]pirimidin-4-ilamino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,4-d]pirimidin-4-ilamino) ácido butanoico; 2-((5-fluoroquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((6-fluoroquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((8-fluoroquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6,7-difluoroquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((6-(difluorometil)pirimidin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;	2-((6-fluoroquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((8-fluoroquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6,7-difluoroquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((6-(difluorometil)pirimidin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;	

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;	4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;	

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-(((3,3-difluorociclobutil)metil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-fluoro-2-metilquinazolin-4-il) amino) ácido butanoico; 2-(isoquinolin-1-ilamino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(difluorometoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinolin-4-ilamino) ácido butanoico;	4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-(((3,3-difluorociclobutil)metil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-fluoro-2-metilquinazolin-4-il) amino) ácido butanoico; 2-(isoquinolin-1-ilamino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(difluorometoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinolin-4-ilamino) ácido butanoico;	

2-((7-cloroquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((8-cloroquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-(quinazolin-4-ilamino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metoxiquinazolin-4-il) amino) ácido butanoico; (2S)-4-((2-(2,2-difluorociclopropoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-fluoro-2-metilquinazolin-4-il) amino) ácido butanoico;	2-((7-cloroquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((8-cloroquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-(quinazolin-4-ilamino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metoxiquinazolin-4-il) amino) ácido butanoico; (2S)-4-((2-(2,2-difluorociclopropoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-fluoro-2-metilquinazolin-4-il) amino) ácido butanoico;	

4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((8-metoxiquinazolin-4-il) amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metilquinazolin-4-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 2-((8-cloroquinazolin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((8-metoxiquinazolin-4-il) amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metilquinazolin-4-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 2-((8-cloroquinazolin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 2-(pirido[3,2-d]pirimidin-4-ilamino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,2-d]pirimidin-4-ilamino) ácido butanoico;	4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 2-(pirido[3,2-d]pirimidin-4-ilamino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,2-d]pirimidin-4-ilamino) ácido butanoico;	

4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,2-d]pirimidin-4-ilamino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,2-d]pirimidin-4-ilamino) ácido butanoico;	4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,2-d]pirimidin-4-ilamino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,2-d]pirimidin-4-ilamino) ácido butanoico;	

2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; o 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metilquinazolin-4-il) amino) ácido butanoico.	2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; o 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metilquinazolin-4-il) amino) ácido butanoico.	

35. Un compuesto de la reivindicación 1, o una sal del mismo, seleccionado de 2-((3-cianopirazin-2-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	35. Un compuesto de la reivindicación 1, o una sal del mismo, seleccionado de 2-((3-cianopirazin-2-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	*Tienen el mismo contenido*

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-hidroxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-hidroxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((5-fluoropirimidin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	2-((5-fluoropirimidin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((5-cianopirimidin-2-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;	2-((5-cianopirimidin-2-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;	

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;	2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;	

2-((5-bromopirimidin-2-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	2-((5-bromopirimidin-2-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;	4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;	

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;	2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;	

4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;	4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;	

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fluoropirimidin-2-il) amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico; 4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il)amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fluoropirimidin-2-il) amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico; 4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il)amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; (2S)-4-((oxetan-2-ilmetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((3-hidroxi-2-(hidroximetil)propil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; (2S)-4-((oxetan-2-ilmetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((3-hidroxi-2-(hidroximetil)propil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil) pirimidin-2-il) amino) ácido butanoico;	4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil) pirimidin-2-il) amino) ácido butanoico;	

2-((5-cianopirimidin-2-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	2-((5-cianopirimidin-2-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((5-bromopirimidin-2-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; o 4-(((3-fluorooxetan-3-il) metil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico.	2-((5-bromopirimidin-2-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; o 4-(((3-fluorooxetan-3-il) metil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico.	
36. Un compuesto, o una sal del mismo, seleccionado de 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;	36. Un compuesto, o una sal del mismo, seleccionado de 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;	*Tienen el mismo contenido*

2-((5-cianopirimidin-2-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((7H-pirrolo[2,3-d]pirimidin-4-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	2-((5-cianopirimidin-2-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((7H-pirrolo[2,3-d]pirimidin-4-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-ciclopropilpirimidin-2-il) amino) ácido butanoico; 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-2-ilamino) ácido butanoico; 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-ciclopropilpirimidin-2-il) amino) ácido butanoico; 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-2-ilamino) ácido butanoico; 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico; 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;	4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico; 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;	

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico;	2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico;	

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fluoropirimidin-2-il) amino) ácido butanoico; 4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fluoropirimidin-2-il) amino) ácido butanoico; 4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((5-bromopirimidin-2-il) amino)-4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;	2-((5-bromopirimidin-2-il) amino)-4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;	

4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-metilpirimidin-2-il)amino)ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico;	4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-metilpirimidin-2-il)amino)ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico;	

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metilpirazin-2-il) amino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 2-((5-fluoropirimidin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metilpirazin-2-il) amino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 2-((5-fluoropirimidin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il)amino) ácido butanoico; 2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((6-(dimetilamino)pirimidin-4-il)amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il)amino) ácido butanoico; 2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((6-(dimetilamino)pirimidin-4-il)amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metoxipirazin-2-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico;	4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metoxipirazin-2-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico;	

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) amino)-2-((6-fenilpirazin-2-il)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazol-5-il) amino) ácido butanoico; 2-(benzo[d]oxazol-2-ilamino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) amino)-2-((6-fenilpirazin-2-il)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazol-5-il) amino) ácido butanoico; 2-(benzo[d]oxazol-2-ilamino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-benzo[d]imidazol-2-il) amino) ácido butanoico; 2-(benzo[d]tiazol-2-ilamino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 2-((9H-purin-6-il)amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico;	4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-benzo[d]imidazol-2-il) amino) ácido butanoico; 2-(benzo[d]tiazol-2-ilamino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 2-((9H-purin-6-il)amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico;	

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indazol-3-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indol-3-il) amino) ácido butanoico; 2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indazol-3-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indol-3-il) amino) ácido butanoico; 2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((5-bromopirimidin-2-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;	2-((5-bromopirimidin-2-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;	

4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;	4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;	

4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;	4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;	

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil) amino)-2-((2-(trifluorometil)pirimidin-4-il) amino)ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;	2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil) amino)-2-((2-(trifluorometil)pirimidin-4-il) amino)ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;	

2-((3-cianopirazin-2-il) amino)-4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidi n-4-il) amino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidi n-4-il) amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;	2-((3-cianopirazin-2-il) amino)-4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidi n-4-il) amino) ácido butanoico; 4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidi n-4-il) amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;	

2-((5-cianopirimidin-2-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	2-((5-cianopirimidin-2-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((3-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico;	4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((3-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico;	

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((5-cianopirimidin-2-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;	2-((5-cianopirimidin-2-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;	

2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;	2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;	

2-((5-cianopirimidin-2-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;	2-((5-cianopirimidin-2-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;	

2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;	2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;	

2-((5-cianopirimidin-2-il) amino)-4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;	2-((5-cianopirimidin-2-il) amino)-4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;	

2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;	2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;	

4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il)amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-cianopirimidin-2-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;	4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il)amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-cianopirimidin-2-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;	

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-bromopirimidin-2-il) amino) ácido butanoico; 2-((7H-pirrolo[2,3-d]pirimidin-4-il) amino)-4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-bromopirimidin-2-il) amino) ácido butanoico; 2-((7H-pirrolo[2,3-d]pirimidin-4-il) amino)-4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(dimetilamino)pirimidin-4-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-ciclopropilpirimidin-2-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(tert-butil)pirimidin-4-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;	4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(dimetilamino)pirimidin-4-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-ciclopropilpirimidin-2-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(tert-butil)pirimidin-4-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;	

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((3-cianopirazin-2-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metilpirazin-2-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;	4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((3-cianopirazin-2-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metilpirazin-2-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;	

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico; 2-([4,4'-bipiridin]-2-ilamino)-4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico;	4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico; 2-([4,4'-bipiridin]-2-ilamino)-4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico;	

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((5-bromopirimidin-2-il) amino)-4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fluoropirimidin-2-il) amino) ácido butanoico;	2-((5-bromopirimidin-2-il) amino)-4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fluoropirimidin-2-il) amino) ácido butanoico;	

4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico;	4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico;	

4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico; 4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico; 4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((5-bromopirimidin-2-il) amino)-4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	2-((5-bromopirimidin-2-il) amino)-4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico;	4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico;	

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metilpirazin-2-il) amino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 2-((5-fluoropirimidin-2-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino) ácido butanoico; 2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metilpirazin-2-il) amino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 2-((5-fluoropirimidin-2-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino) ácido butanoico; 2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((6-(dimetilamino)pirimidin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metoxipirazin-2-il) amino) ácido butanoico;	2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((6-(dimetilamino)pirimidin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metoxipirazin-2-il) amino) ácido butanoico;	

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico;	4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico;	

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazol-5-il) amino) ácido butanoico; 2-(benzo[d]oxazol-2-ilamino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-benzo[d]imidazol-2-il) amino) ácido butanoico; 2-(benzo[d]tiazol-2-ilamino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazol-5-il) amino) ácido butanoico; 2-(benzo[d]oxazol-2-ilamino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-benzo[d]imidazol-2-il) amino) ácido butanoico; 2-(benzo[d]tiazol-2-ilamino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 2-((9H-purin-6-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indazol-3-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indol-3-il) amino) ácido butanoico;	4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 2-((9H-purin-6-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indazol-3-il) amino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indol-3-il) amino) ácido butanoico;	

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il) amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico; 2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;	4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il) amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico; 2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;	

4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((2-metoxipirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-metilpirazin-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((2-metoxipirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-metilpirazin-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((3-cianopirazin-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 2-((5-fluoropirimidin-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	2-((3-cianopirazin-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 2-((5-fluoropirimidin-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((6-(dimetilamino)pirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico; 2-((5-metoxipirazin-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;	4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((6-(dimetilamino)pirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico; 2-((5-metoxipirazin-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;	

4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico;	4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico;	

4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico; 2-((9H-purin-6-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-(benzo[d]tiazol-2-ilamino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico; 2-((9H-purin-6-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-(benzo[d]tiazol-2-ilamino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((1-metil-1H-benzo[d]imidazol-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-(benzo[d]oxazol-2-ilamino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1-metil-1H-pirazol-5-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1-metil-1H-indazol-3-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1-metil-1H-indol-3-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il) amino) ácido butanoico;	2-((1-metil-1H-benzo[d]imidazol-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-(benzo[d]oxazol-2-ilamino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1-metil-1H-pirazol-5-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1-metil-1H-indazol-3-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1-metil-1H-indol-3-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il) amino) ácido butanoico;	

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((5-bromopirimidin-2-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(dimetilamino)pirimidin-4-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;	2-((5-bromopirimidin-2-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(dimetilamino)pirimidin-4-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;	

2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fluoropirimidin-2-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fluoropirimidin-2-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metilpirazin-2-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico;	4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metilpirazin-2-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico;	

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metoxipirazin-2-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico;	4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metoxipirazin-2-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico;	

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico; 2-((9H-purin-6-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 2-(benzo[d]tiazol-2-ilamino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-benzo[d]imidazol-2-il) amino) ácido butanoico; 2-(benzo[d]oxazol-2-ilamino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico; 2-((9H-purin-6-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 2-(benzo[d]tiazol-2-ilamino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-benzo[d]imidazol-2-il) amino) ácido butanoico; 2-(benzo[d]oxazol-2-ilamino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazol-5-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indazol-3-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indol-3-il) amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il) amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico; 2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazol-5-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indazol-3-il) amino) ácido butanoico; 4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indol-3-il) amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il) amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico; 2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((5-cianopirimidin-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	2-((5-cianopirimidin-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((2-metoxipirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-metilpirazin-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 2-((5-fluoropirimidin-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	2-((2-metoxipirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-metilpirazin-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 2-((5-fluoropirimidin-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((6-(dimetilamino)pirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico;	2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((6-(dimetilamino)pirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico;	

2-((5-metoxipirazin-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;	2-((5-metoxipirazin-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;	

4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico; 2-((1-metil-1H-pirazol-5-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-(benzo[d]oxazol-2-ilamino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1-metil-1H-benzo[d]imidazol-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico; 2-((1-metil-1H-pirazol-5-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-(benzo[d]oxazol-2-ilamino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1-metil-1H-benzo[d]imidazol-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-(benzo[d]tiazol-2-ilamino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((9H-purin-6-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico; 2-((1-metil-1H-indazol-3-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	2-(benzo[d]tiazol-2-ilamino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((9H-purin-6-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico; 4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico; 2-((1-metil-1H-indazol-3-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((1-metil-1H-indol-3-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-metilpirimidin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico; 2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;	2-((1-metil-1H-indol-3-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-metilpirimidin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico; 2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;	

2-(piridin-2-ilamino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((2-metoxipirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-metilpirazin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	2-(piridin-2-ilamino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((2-metoxipirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-metilpirazin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((3-cianopirazin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 2-((5-fluoropirimidin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	2-((3-cianopirazin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 2-((5-fluoropirimidin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((6-(dimetilamino)pirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico; 2-((5-metoxipirazin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-fenilpirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 2-((6-(dimetilamino)pirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico; 2-((5-metoxipirazin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-fenilpirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((2-fenilpirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-fenilpirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico; 2-((5-fenilpirazin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	2-((2-fenilpirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-fenilpirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico; 2-((5-fenilpirazin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((6-fenilpirazin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1-metil-1H-pirazol-5-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-(benzo[d]oxazol-2-ilamino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1-metil-1H-benzo[d]imidazol-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-(benzo[d]tiazol-2-ilamino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	2-((6-fenilpirazin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1-metil-1H-pirazol-5-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-(benzo[d]oxazol-2-ilamino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1-metil-1H-benzo[d]imidazol-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-(benzo[d]tiazol-2-ilamino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((9H-purin-6-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-fenilpiridin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((4-fenilpiridin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1-metil-1H-indol-3-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1-metil-1H-indazol-3-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il) amino) ácido butanoico;	2-((9H-purin-6-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-fenilpiridin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((4-fenilpiridin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1-metil-1H-indol-3-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1-metil-1H-indazol-3-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il) amino) ácido butanoico;	

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

2-((5-bromopirimidin-2-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metilpirazin-2-il) amino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;	2-((5-bromopirimidin-2-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metilpirazin-2-il) amino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;	

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fluoropirimidin-2-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino) ácido butanoico; 2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(dimetilamino)pirimidin-4-il) amino) ácido butanoico;	4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fluoropirimidin-2-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino) ácido butanoico; 2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(dimetilamino)pirimidin-4-il) amino) ácido butanoico;	

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metoxipirazin-2-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;	2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metoxipirazin-2-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;	

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazol-5-il) amino) ácido butanoico;	4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazol-5-il) amino) ácido butanoico;	

2-(benzo[d]oxazol-2-ilamino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-benzo[d]imidazol-2-il) amino) ácido butanoico; 2-(benzo[d]tiazol-2-ilamino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 2-((9H-purin-6-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico;	2-(benzo[d]oxazol-2-ilamino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-benzo[d]imidazol-2-il) amino) ácido butanoico; 2-(benzo[d]tiazol-2-ilamino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 2-((9H-purin-6-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico;	

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indazol-3-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indol-3-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;	4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indazol-3-il) amino) ácido butanoico; 4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indol-3-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;	

2-((5-cianopirimidin-2-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-	2-((5-cianopirimidin-2-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-	

tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metilpirazin-2-il) amino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fluoropirimidin-2-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-	tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metilpirazin-2-il) amino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fluoropirimidin-2-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-	

7H-pirrolo[2,3-d]pirimidin-4-il) amino) ácido butanoico; 2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(dimetilamino)pirimidin-4-il) amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	7H-pirrolo[2,3-d]pirimidin-4-il) amino) ácido butanoico; 2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(dimetilamino)pirimidin-4-il) amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metoxipirazin-2-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico;	4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metoxipirazin-2-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico;	

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazol-5-il) amino) ácido butanoico; 2-(benzo[d]oxazol-2-ilamino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazol-5-il) amino) ácido butanoico; 2-(benzo[d]oxazol-2-ilamino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-benzo[d]imidazol-2-il) amino) ácido butanoico; 2-(benzo[d]tiazol-2-ilamino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 2-((9H-purin-6-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico;	4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-benzo[d]imidazol-2-il) amino) ácido butanoico; 2-(benzo[d]tiazol-2-ilamino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 2-((9H-purin-6-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico; 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico;	

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indazol-3-il) amino) ácido butanoico; o 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indol-3-il) amino) ácido butanoico.	4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indazol-3-il) amino) ácido butanoico; o 4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indol-3-il) amino) ácido butanoico.	
37. Un compuesto, o una sal del mismo, seleccionado de 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-metoxietil) (5-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) pentil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico;	37. Un compuesto, o una sal del mismo, seleccionado de 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-metoxietil) (5-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) pentil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico;	*Tienen el mismo contenido*

(2S)-2-(quinazolin-4-ilamino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) ((tetrahidrofuran-2-il) metil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 2-((6-(dimetilamino)pirimidin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino) ácido butanoico;	(2S)-2-(quinazolin-4-ilamino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) ((tetrahidrofuran-2-il) metil)amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 2-((6-(dimetilamino)pirimidin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino) ácido butanoico;	

2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il)amino)ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 4-((2-fluoro-3-hidroxi-2-(hidroximetil)propil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((3-hidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;	2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico; 4-((2-(dimetilamino)-2-oxoetil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il)amino)ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico; 4-((2-fluoro-3-hidroxi-2-(hidroximetil)propil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((3-hidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;	

4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-(2-oxopirrolidin-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(benzo[d]tiazol-2-ilamino) ácido butanoico;	4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico; 4-((2-(2-oxopirrolidin-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(benzo[d]tiazol-2-ilamino) ácido butanoico;	

2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico; 2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico; 2-((6-(dimetilamino)pirimidin-4-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico;	4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico; 2-((6-(dimetilamino)pirimidin-4-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico;	

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico; 4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;	4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico; 4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico; 2-((5-cianopirimidin-2-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 2-((5-bromopirimidin-2-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;	

2-((5-ciclopropilpirimidin-2-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 2-((2-(piridin-3-il) quinazolin-4-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 2-((6-fenilpirimidin-4-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 2-((5-fenilpirimidin-4-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 2-(pirimidin-4-ilamino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico;	2-((5-ciclopropilpirimidin-2-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 2-((2-(piridin-3-il) quinazolin-4-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 2-((6-fenilpirimidin-4-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 2-((5-fenilpirimidin-4-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 2-(pirimidin-4-ilamino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico;	

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il) amino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-([4,4'-bipiridin]-2-ilamino)-4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico; (S)-4-((2-(2,2-difluoroetoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-fenilpiridin-2-il)amino)ácido butanoico;	2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il) amino) ácido butanoico; 2-((3-cianopirazin-2-il) amino)-4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-([4,4'-bipiridin]-2-ilamino)-4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico; (S)-4-((2-(2,2-difluoroetoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-fenilpiridin-2-il)amino)ácido butanoico;	

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((6-metilpirazin-2-il)amino)ácido butanoico; 4-((2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinoxalin-2-ilamino)ácido butanoico; 4-((2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((6-metil-2-(piridin-4-il)pirimidin-4-il)amino)ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indazol-3-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(benzo[d]tiazol-2-ilamino) ácido butanoico;	4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((6-metilpirazin-2-il)amino)ácido butanoico; 4-((2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinoxalin-2-ilamino)ácido butanoico; 4-((2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((6-metil-2-(piridin-4-il)pirimidin-4-il)amino)ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indazol-3-il) amino) ácido butanoico; 4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(benzo[d]tiazol-2-ilamino) ácido butanoico;	

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico; 4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(naftalen-1-ilamino)ácido butanoico; 4-((2-morfolinoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; (2S)-4-((2,3-dihidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(naftalen-1-ilamino) ácido butanoico; (2S)-4-((3-fluoro-2-hidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;	4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico; 4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(naftalen-1-ilamino)ácido butanoico; 4-((2-morfolinoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; (2S)-4-((2,3-dihidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(naftalen-1-ilamino) ácido butanoico; (2S)-4-((3-fluoro-2-hidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;	

2-(quinazolin-4-ilamino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (tiazol-2-ilmetil)amino) ácido butanoico; 4-((2-(3-oxomorfolino)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-(benzil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-hidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; (2S)-4-(((1,4-dioxan-2-il) metil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((3-fluoro-2-hidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;	2-(quinazolin-4-ilamino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (tiazol-2-ilmetil)amino) ácido butanoico; 4-((2-(3-oxomorfolino)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-(benzil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-hidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; (2S)-4-(((1,4-dioxan-2-il) metil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((3-fluoro-2-hidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;	

4-((2-hidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; (2S)-4-((morfolin-3-ilmetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; (2S)-4-((3,3-difluoro-2-hidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2,3-dihidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-hidroxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[2,3-d]pirimidin-4-ilamino) ácido butanoico; 4-((2-hidroxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,2-d]pirimidin-4-ilamino) ácido butanoico;	4-((2-hidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; (2S)-4-((morfolin-3-ilmetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; (2S)-4-((3,3-difluoro-2-hidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2,3-dihidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-hidroxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[2,3-d]pirimidin-4-ilamino) ácido butanoico; 4-((2-hidroxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,2-d]pirimidin-4-ilamino) ácido butanoico;	

2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-hidroxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-hidroxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,2-d]pirimidin-4-ilamino) ácido butanoico; 4-(metoxi(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-metoxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-metoxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-hidroxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-hidroxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,2-d]pirimidin-4-ilamino) ácido butanoico; 4-(metoxi(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-metoxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-metoxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-(((3-hidroxioxetan-3-il) metil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-metoxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[2,3-d]pirimidin-4-ilamino) ácido butanoico; 4-((2-metoxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,2-d]pirimidin-4-ilamino) ácido butanoico; 4-((2-metoxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metilquinazolin-4-il) amino) ácido butanoico; 4-(((1-cianociclopropil)metil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;	4-(((3-hidroxioxetan-3-il) metil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((2-metoxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[2,3-d]pirimidin-4-ilamino) ácido butanoico; 4-((2-metoxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,2-d]pirimidin-4-ilamino) ácido butanoico; 4-((2-metoxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metilquinazolin-4-il) amino) ácido butanoico; 4-(((1-cianociclopropil)metil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico; 4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;	

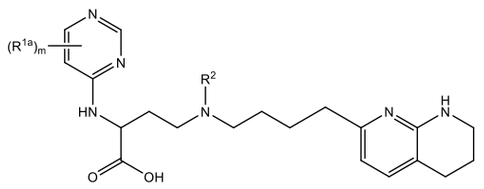
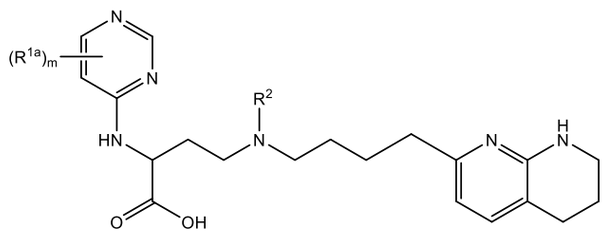
4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metilquinazolin-4-il) amino) ácido butanoico; 4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-fluoro-2-metilquinazolin-4-il) amino) ácido butanoico; 2-(quinazolin-4-ilamino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((8-fluoroquinazolin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((7-fluoroquinazolin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((8-metilquinazolin-4-il) amino) ácido butanoico;	4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metilquinazolin-4-il) amino) ácido butanoico; 4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-fluoro-2-metilquinazolin-4-il) amino) ácido butanoico; 2-(quinazolin-4-ilamino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((8-fluoroquinazolin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((7-fluoroquinazolin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((8-metilquinazolin-4-il) amino) ácido butanoico;	

4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metilquinazolin-4-il) amino) ácido butanoico; 4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-fluoroquinazolin-4-il) amino) ácido butanoico; 4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((8-metilquinazolin-4-il) amino) ácido butanoico; 4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((8-fluoroquinazolin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metilquinazolin-4-il) amino) ácido butanoico; 2-((6-fluoroquinazolin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metilquinazolin-4-il) amino) ácido butanoico; 4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-fluoroquinazolin-4-il) amino) ácido butanoico; 4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((8-metilquinazolin-4-il) amino) ácido butanoico; 4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((8-fluoroquinazolin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metilquinazolin-4-il) amino) ácido butanoico; 2-((6-fluoroquinazolin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;	

4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fluoroquinazolin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(tieno[2,3-d]pirimidin-4-ilamino) ácido butanoico; 4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(tieno[2,3-d]pirimidin-4-ilamino) ácido butanoico; 4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metiltieno[2,3-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metiltieno[2,3-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(tieno[3,2-d]pirimidin-4-ilamino) ácido butanoico;	4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fluoroquinazolin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(tieno[2,3-d]pirimidin-4-ilamino) ácido butanoico; 4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(tieno[2,3-d]pirimidin-4-ilamino) ácido butanoico; 4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metiltieno[2,3-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metiltieno[2,3-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(tieno[3,2-d]pirimidin-4-ilamino) ácido butanoico;	

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metiltieno[3,2-d]pirimidin-4-il) amino) ácido butanoico; 4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(tieno[3,2-d]pirimidin-4-ilamino) ácido butanoico; 4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metiltieno[3,2-d]pirimidin-4-il) amino) ácido butanoico; 4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metiltieno[2,3-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metiltieno[2,3-d]pirimidin-4-il) amino) ácido butanoico;	4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metiltieno[3,2-d]pirimidin-4-il) amino) ácido butanoico; 4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(tieno[3,2-d]pirimidin-4-ilamino) ácido butanoico; 4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metiltieno[3,2-d]pirimidin-4-il) amino) ácido butanoico; 4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metiltieno[2,3-d]pirimidin-4-il) amino) ácido butanoico; 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metiltieno[2,3-d]pirimidin-4-il) amino) ácido butanoico;	

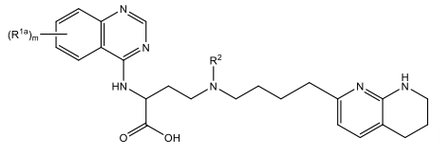
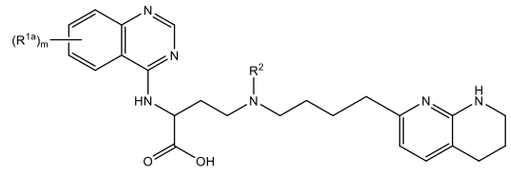
2-((7,8-difluoroquinazolin-4-il) amino)-4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((7,8-difluoroquinazolin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metiltieno[3,2-d]pirimidin-4-il) amino) ácido butanoico; o 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metiltieno[3,2-d]pirimidin-4-il) amino) ácido butanoico.	2-((7,8-difluoroquinazolin-4-il) amino)-4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 2-((7,8-difluoroquinazolin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; 4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metiltieno[3,2-d]pirimidin-4-il) amino) ácido butanoico; o 4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metiltieno[3,2-d]pirimidin-4-il) amino) ácido butanoico.	
38. Una composición farmacéutica que comprende un compuesto de la reivindicación 1, o una sal del mismo, y un portador o excipiente farmacéuticamente aceptable.	38. Una composición farmacéutica que comprende un compuesto de la reivindicación 1, o una sal del mismo, y un portador o excipiente farmacéuticamente aceptable.	*Tienen el mismo contenido*

39. Un kit que comprende un compuesto de la reivindicación 1, o una sal farmacéuticamente aceptable del mismo.	39. Un kit que comprende un compuesto de la reivindicación 1, o una sal farmacéuticamente aceptable del mismo.	*Tienen el mismo contenido*
40. El kit de la reivindicación 39, que además comprende instrucciones para el tratamiento de una enfermedad fibrótica.	40. El kit de la reivindicación 39, que además comprende instrucciones para el tratamiento de una enfermedad fibrótica.	*Tienen el mismo contenido*
41. El compuesto de la reivindicación 1, o una sal farmacéuticamente aceptable del mismo, en donde el compuesto es de la fórmula (II-A):  (II-A), en donde m es 0, 1, 2, o 3.	41. El compuesto de la reivindicación 1, o una sal farmacéuticamente aceptable del mismo, en donde el compuesto es de la fórmula (II-A):  (II-A), en donde m es 0, 1, 2, o 3.	*Tienen el mismo contenido*

42. El compuesto de la reivindicación 1, en donde el compuesto se selecciona de: (S)-2-((5-fluoropirimidin-2-il)amino)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-2-((5-cianopirimidin-2-il)amino)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-(trifluorometil)pirimidin-2-il)amino)ácido butanoico; (S)-2-((5-bromopirimidin-2-il)amino)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((2-(trifluorometil)pirimidin-4-il)amino)ácido butanoico;	42. El compuesto de la reivindicación 1, en donde el compuesto se selecciona de: (S)-2-((5-fluoropirimidin-2-il)amino)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-2-((5-cianopirimidin-2-il)amino)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-(trifluorometil)pirimidin-2-il)amino)ácido butanoico; (S)-2-((5-bromopirimidin-2-il)amino)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((2-(trifluorometil)pirimidin-4-il)amino)ácido butanoico;	*Tienen el mismo contenido*

(S)-2-((6-(1H-pirazol-1-il)pirimidin-4-il)amino)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-fenilpirimidin-4-il)amino)ácido butanoico; (S)-2-((5-ciclopropilpirimidin-2-il)amino)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(pirimidin-4-ilamino)ácido butanoico; (S)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((6-fenilpirimidin-4-il)amino)ácido butanoico; (S)-2-((5-ciclopropilpirimidin-2-il)amino)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;	(S)-2-((6-(1H-pirazol-1-il)pirimidin-4-il)amino)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-fenilpirimidin-4-il)amino)ácido butanoico; (S)-2-((5-ciclopropilpirimidin-2-il)amino)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(pirimidin-4-ilamino)ácido butanoico; (S)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((6-fenilpirimidin-4-il)amino)ácido butanoico; (S)-2-((5-ciclopropilpirimidin-2-il)amino)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;	

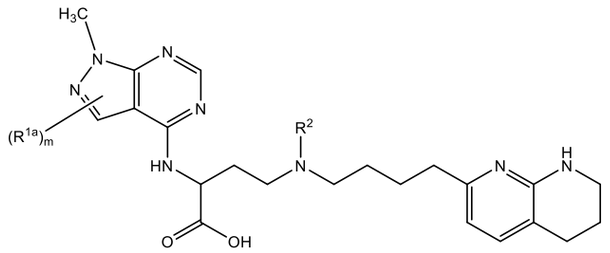
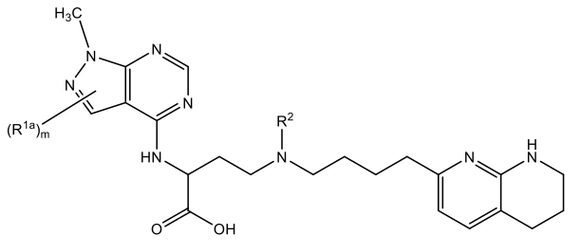
(S)-4-((2-fenoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-fenilpirimidin-4-il)amino)ácido butanoico; (S)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-fenilpirimidin-4-il)amino)ácido butanoico; (S)-2-((3-cianopirazin-2-il)amino)-4-((2-etoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-2-((6-(1H-pirazol-1-il)pirimidin-4-il)amino)-4-((3-fluoropropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; y (S)-2-((3-cianopirazin-2-il)amino)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico, o una sal farmacéuticamente aceptable de éstos.	(S)-4-((2-fenoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-fenilpirimidin-4-il)amino)ácido butanoico; (S)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-fenilpirimidin-4-il)amino)ácido butanoico; (S)-2-((3-cianopirazin-2-il)amino)-4-((2-etoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-2-((6-(1H-pirazol-1-il)pirimidin-4-il)amino)-4-((3-fluoropropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; y (S)-2-((3-cianopirazin-2-il)amino)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico, o una sal farmacéuticamente aceptable de éstos.	

43. El compuesto de la reivindicación 1, o una sal farmacéuticamente aceptable del mismo, en donde el compuesto es de la fórmula (II-B):  (II-B), en donde m es 0, 1, 2, 3, 4, o 5.	43. El compuesto de la reivindicación 1, o una sal farmacéuticamente aceptable del mismo, en donde el compuesto es de la fórmula (II-B):  (II-B), en donde m es 0, 1, 2, 3, 4, o 5.	*Tienen el mismo contenido*
44. El compuesto de la reivindicación 1, en donde el compuesto se selecciona de (S)-2-((7-fluoroquinazolin-4-il)amino)-4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-2-((7-fluoro-2-metilquinazolin-4-il)amino)-4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((8-(trifluorometil)quinazolin-4-il)amino)ácido butanoico;	44. El compuesto de la reivindicación 1, en donde el compuesto se selecciona de (S)-2-((7-fluoroquinazolin-4-il)amino)-4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-2-((7-fluoro-2-metilquinazolin-4-il)amino)-4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((8-(trifluorometil)quinazolin-4-il)amino)ácido butanoico;	*Tienen el mismo contenido*

(S)-2-((6-fluoroquinazolin-4-il)amino)-4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-2-((6,7-difluoroquinazolin-4-il)amino)-4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-2-((7-fluoro-2-metilquinazolin-4-il)amino)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (2S)-4-((2-(2,2-difluorociclopropoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((7-fluoro-2-metilquinazolin-4-il)amino)ácido butanoico; (S)-4-(((S)-3-fluoro-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((2-metilquinazolin-4-il)amino)ácido butanoico; (S)-2-((8-fluoroquinazolin-4-il)amino)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;	(S)-2-((6-fluoroquinazolin-4-il)amino)-4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-2-((6,7-difluoroquinazolin-4-il)amino)-4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-2-((7-fluoro-2-metilquinazolin-4-il)amino)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (2S)-4-((2-(2,2-difluorociclopropoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((7-fluoro-2-metilquinazolin-4-il)amino)ácido butanoico; (S)-4-(((S)-3-fluoro-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((2-metilquinazolin-4-il)amino)ácido butanoico; (S)-2-((8-fluoroquinazolin-4-il)amino)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;	

(S)-2-((7-fluoroquinazolin-4-il)amino)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((8-metilquinazolin-4-il)amino)ácido butanoico; (S)-2-((7,8-difluoroquinazolin-4-il)amino)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico; (S)-4-((2-fenoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico; (S)-4-((2-(3,5-difluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico;	(S)-2-((7-fluoroquinazolin-4-il)amino)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((8-metilquinazolin-4-il)amino)ácido butanoico; (S)-2-((7,8-difluoroquinazolin-4-il)amino)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico; (S)-4-((2-fenoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico; (S)-4-((2-(3,5-difluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico;	

(S)-4-((2-(piridin-2-iloxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico; (S)-4-((2-(2,2-difluoroetoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico; (S)-4-((2-((6-metilpiridin-3-il)oxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico; (S)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico; (S)-4-((2-hidroxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico; (S)-4-(((R)-2-hidroxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico; y	(S)-4-((2-(piridin-2-iloxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico; (S)-4-((2-(2,2-difluoroetoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico; (S)-4-((2-((6-metilpiridin-3-il)oxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico; (S)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico; (S)-4-((2-hidroxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico; (S)-4-(((R)-2-hidroxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico; y	

(S)-4-(((S)-2,3-dihidroxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	(S)-4-(((S)-2,3-dihidroxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	
45. El compuesto de la reivindicación 1, o una sal farmacéuticamente aceptable del mismo, en donde el compuesto es de la fórmula (II-H):  (II-H), donde m es 0, 1, o 2.	45. El compuesto de la reivindicación 1, o una sal farmacéuticamente aceptable del mismo, en donde el compuesto es de la fórmula (II-H):  (II-H), donde m es 0, 1, o 2.	*Tienen el mismo contenido*
46. El compuesto de la reivindicación 1, en donde el compuesto se selecciona de (S)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il)amino)ácido butanoico;	46. El compuesto de la reivindicación 1, en donde el compuesto se selecciona de (S)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il)amino)ácido butanoico;	*Tienen el mismo contenido*

(S)-2-((1H-pirazolo[3,4-d]pirimidin-4-il)amino)-4-((2-fenoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-2-((1H-pirazolo[3,4-d]pirimidin-4-il)amino)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il)amino)ácido butanoico; (S)-4-((2-etoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il)amino)ácido butanoico; (S)-4-((2-(2,2-difluoroetoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il)amino)ácido butanoico; (S)-2-((1H-pirazolo[3,4-d]pirimidin-4-il)amino)-4-((2-(2,2-difluoroetoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;	(S)-2-((1H-pirazolo[3,4-d]pirimidin-4-il)amino)-4-((2-fenoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-2-((1H-pirazolo[3,4-d]pirimidin-4-il)amino)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il)amino)ácido butanoico; (S)-4-((2-etoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il)amino)ácido butanoico; (S)-4-((2-(2,2-difluoroetoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il)amino)ácido butanoico; (S)-2-((1H-pirazolo[3,4-d]pirimidin-4-il)amino)-4-((2-(2,2-difluoroetoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;	

(S)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il)amino)-4-((2-fenoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il)amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)(2-(2,2,2-trifluoroetoxi)etil)amino)ácido butanoico; (S)-2-((1H-pirazolo[3,4-d]pirimidin-4-il)amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)(2-(2,2,2-trifluoroetoxi)etil)amino)ácido butanoico; (S)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(tieno[2,3-d]pirimidin-4-ilamino)ácido butanoico; (S)-4-(((S)-3-fluoro-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(tieno[2,3-d]pirimidin-4-ilamino)ácido butanoico; (S)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(tieno[3,2-d]pirimidin-4-ilamino)ácido butanoico;	(S)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il)amino)-4-((2-fenoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; (S)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il)amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)(2-(2,2,2-trifluoroetoxi)etil)amino)ácido butanoico; (S)-2-((1H-pirazolo[3,4-d]pirimidin-4-il)amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)(2-(2,2,2-trifluoroetoxi)etil)amino)ácido butanoico; (S)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(tieno[2,3-d]pirimidin-4-ilamino)ácido butanoico; (S)-4-(((S)-3-fluoro-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(tieno[2,3-d]pirimidin-4-ilamino)ácido butanoico; (S)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(tieno[3,2-d]pirimidin-4-ilamino)ácido butanoico;	

(S)-4-(((S)-3-fluoro-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(tieno[3,2-d]pirimidin-4-ilamino)ácido butanoico; (S)-4-(((S)-3-fluoro-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((6-metiltieno[3,2-d]pirimidin-4-il)amino)ácido butanoico; y (S)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-metiltieno[2,3-d]pirimidin-4-il)amino)ácido butanoico, o una sal farmacéuticamente aceptable de éstos.	(S)-4-(((S)-3-fluoro-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(tieno[3,2-d]pirimidin-4-ilamino)ácido butanoico; (S)-4-(((S)-3-fluoro-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((6-metiltieno[3,2-d]pirimidin-4-il)amino)ácido butanoico; y (S)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-metiltieno[2,3-d]pirimidin-4-il)amino)ácido butanoico, o una sal farmacéuticamente aceptable de éstos.	
47. El compuesto de la reivindicación 1, en donde el compuesto es (S)-2-((7-fluoro-2-metilquinazolin-4-il)amino)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	47. El compuesto de la reivindicación 1, en donde el compuesto es (S)-2-((7-fluoro-2-metilquinazolin-4-il)amino)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	*Tienen el mismo contenido*

48. El compuesto de la reivindicación 1, en donde el compuesto es (S)-4-((2-hidroxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	48. El compuesto de la reivindicación 1, en donde el compuesto es (S)-4-((2-hidroxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	*Tienen el mismo contenido*
49. El compuesto de la reivindicación 1, en donde el compuesto es (S)-4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	49. El compuesto de la reivindicación 1, en donde el compuesto es (S)-4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	*Tienen el mismo contenido*
50. El compuesto de la reivindicación 1, en donde el compuesto es (S)-4-((2-(3,5-difluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	50. El compuesto de la reivindicación 1, en donde el compuesto es (S)-4-((2-(3,5-difluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	*Tienen el mismo contenido*

51. El compuesto de la reivindicación 1, en donde el compuesto es (S)-4-((2-fenoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-fenilpirimidin-4-il)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	51. El compuesto de la reivindicación 1, en donde el compuesto es (S)-4-((2-fenoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-fenilpirimidin-4-il)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	*Tienen el mismo contenido*
52. El compuesto de la reivindicación 1, en donde el compuesto es (S)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-fenilpirimidin-4-il)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	52. El compuesto de la reivindicación 1, en donde el compuesto es (S)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-fenilpirimidin-4-il)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	*Tienen el mismo contenido*
53. El compuesto de la reivindicación 1, en donde el compuesto es (S)-2-((6-(1H-pirazol-1-il)pirimidin-4-il)amino)-4-((3-fluoropropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	53. El compuesto de la reivindicación 1, en donde el compuesto es (S)-2-((6-(1H-pirazol-1-il)pirimidin-4-il)amino)-4-((3-fluoropropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	*Tienen el mismo contenido*

54. El compuesto de la reivindicación 1, en donde el compuesto es (S)-4-(((S)-3-fluoro-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(tieno[2,3-d]pirimidin-4-ilamino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	54. El compuesto de la reivindicación 1, en donde el compuesto es (S)-4-(((S)-3-fluoro-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(tieno[2,3-d]pirimidin-4-ilamino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	*Tienen el mismo contenido*
55. El compuesto de la reivindicación 1, en donde el compuesto es (S)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il)amino)-4-((2-fenoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	55. El compuesto de la reivindicación 1, en donde el compuesto es (S)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il)amino)-4-((2-fenoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	*Tienen el mismo contenido*
56. El compuesto de la reivindicación 1, en donde el compuesto es (S)-2-((1H-pirazolo[3,4-d]pirimidin-4-il)amino)-4-((2-fenoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	56. El compuesto de la reivindicación 1, en donde el compuesto es (S)-2-((1H-pirazolo[3,4-d]pirimidin-4-il)amino)-4-((2-fenoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	*Tienen el mismo contenido*

57. El compuesto de la reivindicación 1, en donde el compuesto es (S)-2-((1H-pirazolo[3,4-d]pirimidin-4-il)amino)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	57. El compuesto de la reivindicación 1, en donde el compuesto es (S)-2-((1H-pirazolo[3,4-d]pirimidin-4-il)amino)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	*Tienen el mismo contenido*
58. El compuesto de la reivindicación 1, en donde el compuesto es (S)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	58. El compuesto de la reivindicación 1, en donde el compuesto es (S)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.	*Tienen el mismo contenido*
59. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es pirimidin-4-ilo opcionalmente sustituido con R^{1a}, en donde cada R^{1a} es independientemente pirazolilo, metilo, difluorometilo, o trifluorometilo.	59. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es pirimidin-4-ilo opcionalmente sustituido con R^{1a}, en donde cada R^{1a} es independientemente pirazolilo, metilo, difluorometilo, o trifluorometilo.	*Tienen el mismo contenido*

60. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es pirimidin-4-ilo sustituido con metilo y trifluorometilo.	60. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es pirimidin-4-ilo sustituido con metilo y trifluorometilo.	*Tienen el mismo contenido*
61. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es quinazolin-4-ilo opcionalmente sustituido con R^{1a}, en donde cada R^{1a} es independientemente fluoro, cloro, metilo, trifluorometilo o metoxi.	61. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es quinazolin-4-ilo opcionalmente sustituido con R^{1a}, en donde cada R^{1a} es independientemente fluoro, cloro, metilo, trifluorometilo o metoxi.	*Tienen el mismo contenido*
62. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es C_1-C_6 alquilo opcionalmente sustituido con: R^{2a}, en donde cada R^{2a} es independientemente: fluoro, ciclobutilo sustituido con fluoro, pirazolilo sustituido con metilo, o -$S(O)_2CH_3$; o -OR^3, en donde cada R^3 es independientemente: metilo, etilo, difluorometilo, -	62. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es C_1-C_6 alquilo opcionalmente sustituido con: R^{2a}, en donde cada R^{2a} es independientemente: fluoro, ciclobutilo sustituido con fluoro, pirazolilo sustituido con metilo, o -$S(O)_2CH_3$; o -OR^3, en donde cada R^3 es independientemente: metilo, etilo, difluorometilo, -	*Tienen el mismo contenido*

CH_2CHF_2, $-CH_2CF_3$, ciclopropilo sustituido con fluoro, fenilo opcionalmente sustituido con fluoro, o piridinilo opcionalmente sustituido con fluoro o metilo.	CH_2CHF_2, $-CH_2CF_3$, ciclopropilo sustituido con fluoro, fenilo opcionalmente sustituido con fluoro, o piridinilo opcionalmente sustituido con fluoro o metilo.	
63. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es $–CH_2CH_2OCH_3$.	63. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es $–CH_2CH_2OCH_3$.	*Tienen el mismo contenido*
64. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es C_1-C_6 alquilo sustituido con halógeno y $-OR^3$, donde cada R^3 es independientemente C_1-C_6 alquilo.	64. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es C_1-C_6 alquilo sustituido con halógeno y $-OR^3$, donde cada R^3 es independientemente C_1-C_6 alquilo.	*Tienen el mismo contenido*
65. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es C_3-C_6 cicloalquilo opcionalmente sustituido con R^{2b}.	65. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es C_3-C_6 cicloalquilo opcionalmente sustituido con R^{2b}.	*Tienen el mismo contenido*

66. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es C_1-C_6 alquilo opcionalmente sustituido con ciclopropilo.	66. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es C_1-C_6 alquilo opcionalmente sustituido con ciclopropilo.	*Tienen el mismo contenido*
67. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es C_1-C_6 alquilo sustituido con R^{2a} en donde cada R^{2a} es independientemente: heterociclilo de 4 a 5 miembros opcionalmente sustituido con oxo; fenilo opcionalmente sustituido con halógeno o -OR^6; o pirazolilo opcionalmente sustituido con metilo.	67. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es C_1-C_6 alquilo sustituido con R^{2a} en donde cada R^{2a} es independientemente: heterociclilo de 4 a 5 miembros opcionalmente sustituido con oxo; fenilo opcionalmente sustituido con halógeno o -OR^6; o pirazolilo opcionalmente sustituido con metilo.	*Tienen el mismo contenido*
68. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es: pirimidin-2-ilo, pirimidin-4-ilo, quinazolin-4-ilo, 1H-pirazolo[3,4-d]pirimidin-4-ilo, 1H-pirazolo[4,3-d]pirimidin-7-ilo, pirazin-2-ilo, quinolin-4-ilo, pirido[2,3-d]pirimidin-4-ilo, pirido[3,2-d]pirimidin-4-ilo, pirido[3,4-d]pirimidin-4-ilo, tieno[2,3-d]pirimidin-	68. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es: pirimidin-2-ilo, pirimidin-4-ilo, quinazolin-4-ilo, 1H-pirazolo[3,4-d]pirimidin-4-ilo, 1H-pirazolo[4,3-d]pirimidin-7-ilo, pirazin-2-ilo, quinolin-4-ilo, pirido[2,3-d]pirimidin-4-ilo, pirido[3,2-d]pirimidin-4-ilo, pirido[3,4-d]pirimidin-4-ilo, tieno[2,3-d]pirimidin-	*Tienen el mismo contenido*

4-ilo, tieno[3,2-d]pirimidin-4-ilo, tienopirimidin-4-ilo, piridin-2-ilo, piridin-3-ilo, 7H-pirrolo[2,3-d]pirimidin-4-ilo, quinoxalin-2-ilo, 1H-indazol-3-ilo, benzo[d]tiazol-2-ilo, naftalen-1-ilo, 9H-purin-6-ilo, o isoquinolin-1-ilo; y en donde R^1 es opcionalmente sustituido con metilo y fluoro.	4-ilo, tieno[3,2-d]pirimidin-4-ilo, tienopirimidin-4-ilo, piridin-2-ilo, piridin-3-ilo, 7H-pirrolo[2,3-d]pirimidin-4-ilo, quinoxalin-2-ilo, 1H-indazol-3-ilo, benzo[d]tiazol-2-ilo, naftalen-1-ilo, 9H-purin-6-ilo, o isoquinolin-1-ilo; y en donde R^1 es opcionalmente sustituido con metilo y fluoro.	
69. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es: pirimidin-2-ilo, pirimidin-4-ilo, quinazolin-4-ilo, 1H-pirazolo[3,4-d]pirimidin-4-ilo, 1H-pirazolo[4,3-d]pirimidin-7-ilo, pirazin-2-ilo, quinolin-4-ilo, pirido[2,3-d]pirimidin-4-ilo, pirido[3,2-d]pirimidin-4-ilo, pirido[3,4-d]pirimidin-4-ilo, tieno[2,3-d]pirimidin-4-ilo, tieno[3,2-d]pirimidin-4-ilo, tienopirimidin-4-ilo, piridin-2-ilo, piridin-3-ilo, 7H-pirrolo[2,3-d]pirimidin-4-ilo, quinoxalin-2-ilo, 1H-indazol-3-ilo, benzo[d]tiazol-	69. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es: pirimidin-2-ilo, pirimidin-4-ilo, quinazolin-4-ilo, 1H-pirazolo[3,4-d]pirimidin-4-ilo, 1H-pirazolo[4,3-d]pirimidin-7-ilo, pirazin-2-ilo, quinolin-4-ilo, pirido[2,3-d]pirimidin-4-ilo, pirido[3,2-d]pirimidin-4-ilo, pirido[3,4-d]pirimidin-4-ilo, tieno[2,3-d]pirimidin-4-ilo, tieno[3,2-d]pirimidin-4-ilo, tienopirimidin-4-ilo, piridin-2-ilo, piridin-3-ilo, 7H-pirrolo[2,3-d]pirimidin-4-ilo, quinoxalin-2-ilo, 1H-indazol-3-ilo, benzo[d]tiazol-	*Tienen el mismo contenido*

2-ilo, naftalen-1-ilo, 9H-purin-6-ilo, o isoquinolin-1-ilo; y en donde R^1 es opcionalmente sustituido con metilo y trifluorometilo.	2-ilo, naftalen-1-ilo, 9H-purin-6-ilo, o isoquinolin-1-ilo; y en donde R^1 es opcionalmente sustituido con metilo y trifluorometilo.	

UNITED STATES PATENT AND TRADEMARK OFFICE

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NOTICE OF ALLOWANCE AND FEE(S) DUE

25226 7590 06/05/2020
MORRISON & FOERSTER LLP
755 PAGE MILL RD
PALO ALTO, CA 94304-1018

EXAMINER
CHANDRAKUMAR, NIZAL S

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 06/05/2020

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/296,194	03/07/2019	Jacob CHA	76809-20006.00	2171

TITLE OF INVENTION: AMINO ACID COMPOUNDS AND METHODS OF USE

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$500	$0.00	$0.00	$500	09/08/2020

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Maintenance fees are due in utility patents issuing on applications filed on or after Dec. 12, 1980. It is patentee's responsibility to ensure timely payment of maintenance fees when due. More information is available at www.uspto.gov/PatentMaintenanceFees.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via EFS-Web.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

25226 7590 06/05/2020
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Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via EFS-Web or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/296,194	03/07/2019	Jacob CHA	76809-20006.00	2171

TITLE OF INVENTION: AMINO ACID COMPOUNDS AND METHODS OF USE

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$500	$0.00	$0.00	$500	09/08/2020

EXAMINER	ART UNIT	CLASS-SUBCLASS
CHANDRAKUMAR, NIZAL S	1625	546-122000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-09 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. Fees submitted: ❑ Issue Fee ❑ Publication Fee (if required) ❑ Advance Order - # of Copies _____

4b. Method of Payment: *(Please first reapply any previously paid fee shown above)*

❑ Electronic Payment via EFS-Web ❑ Enclosed check ❑ Non-electronic payment by credit card (Attach form PTO-2038)

❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. _____

5. **Change in Entity Status** (from status indicated above)

❑ Applicant certifying micro entity status. See 37 CFR 1.29

❑ Applicant asserting small entity status. See 37 CFR 1.27

❑ Applicant changing to regular undiscounted fee status.

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/296,194	03/07/2019	Jacob CHA	76809-20006.00	2171

25226 7590 06/05/2020

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EXAMINER	
CHANDRAKUMAR, NIZAL S	
ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 06/05/2020

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 16/296,194	Applicant(s) CHA et al.	
	Examiner NIZAL S CHANDRAKUMAR	Art Unit 1625	AIA (FITF) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☑ This communication is responsive to 5/26/2020.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

3. ☑ The allowed claim(s) is/are 4-8,12,15-17,27-49,62,68-72,76-77 and 88-116 . As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see **http://www.uspto.gov/patents/init_events/pph/index.jsp** or send an inquiry to **PPHfeedback@uspto.gov.**

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some *c) ☐ None of the:

   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____ .

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____ .

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☑ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____.
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material _____.
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date. _____.
5. ☑ Examiner's Amendment/Comment
6. ☐ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/NIZAL S CHANDRAKUMAR/
Primary Examiner, Art Unit 1625

Notice of Pre-AIA or AIA Status

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Applicants response filed 5/26/2020 is acknowledged.

Claims 4-8, 12, 15-17, 27-49, 62, 68-72, 76-77, and 88-116 are pending.

Amendments to claims overcome the previously presented rejections.

Claims 4-8, 12, 15-17, 27-49, 62, 68-72, 76-77, and 88-116 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NIZAL S CHANDRAKUMAR whose telephone number is (571)272-6202. The examiner can normally be reached on M-F 8-5 EST.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Kosar can be reached on (571) 272-0913. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see https://ppair-my.uspto.gov/pair/PrivatePair. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/NIZAL S CHANDRAKUMAR/
Primary Examiner, Art Unit 1625

OFICINA DE PATENTES Y MARCAS DE ESTADOS UNIDOS

DEPARTAMENTO DE COMERCIO DE ESTADOS UNIDOS

Oficina de Patentes y Marcas de Estados Unidos

Dirección: COMISIONADO PARA PATENTES

P.O. Box 1450

Alexandria, Virginia 22313-1450

www.uspto.gov

NOTIFICACION DE ACEPTACION Y TASAS PENDIENTES

MORRISON & FOERSTER LLP

755 PAGE MILL RD

PALO ALTO, CA 94304-1018

EXAMINADOR

CHANDRAKUMAR, NIZAL S

UNIDAD DE ARTE 1625 NÚMERO PAPEL

FECHA DE ENVIO: 06/05/2020

SOLICITUD NO.	FECHA PRESENTACION	PRIMER INVENTOR	REFERENCIA ABOGADO	NO. CONFIRMACION
16/296,194	03/07/2019	Jacob CHA	76809-20006.00	2171

TITULO DE LA INVENCIÓN: COMPUESTOS DE AMINOACIDO Y METODOS DE USO

TIPO SOLICITUD	ESTADO DE ENTIDAD	TASA DE EMISION PENDIENTE	TASA DE PUBLICACION PENDIENTE	TASA DE MISION PREV PAGADA	TASAS TOTALES PENDIENTES	FECHA
No provisional	PEQUEÑA	$500	$0.00	$0.00	$500	09/08/2020

LA SOLICITUD IDENTIFICADA ANTERIORMENTE HA SIDO EXAMINADA Y ES ACEPTADA PARA EMISION COMO PATENTE. EL TRAMITE SOBRE LOS MERITOS ESTÁ CERRADO. ESTA NOTIFICACION DE ACEPTACION NO ES UNA CONCESION DE DERECHOS DE PATENTE. ESTA SOLICITUD ESTA SUJETA A REMOCION DE EMISION POR INICIATIVA DE LA OFICINA O POR PETICION DEL SOLICITANTE. VER 37 CFR 1.313 Y MPEP 1308.

LA TASA DE EMISION Y LA TASA DE PUBLICACION (SI SE REQUIERE) DEBEN SER PAGADAS DENTRO DE TRES MESES DESDE LA FECHA DE ENVIO DE ESTA NOTIFICACION O ESTA SOLICITUD SERÁ CONSIDERADA COMO ABANDONADA. ESTE PERIODO ESTATUTARIO NO

PUEDE SER PRORROGADO. VER 356 U.S.C. 151. LA TASA DE EMISION PENDIENTE INDICADA ANTERIORMENTE NO REFLEJA UN CREDITO POR ALGUNA TASA DE EMISION PAGADA PREVIAMENTE EN ESTA SOLICITUD. SI SE HA PAGADO PREVIAMENTE UNA TASA DE EMISION EN ESTA SOLICITUD (COMO SE MUESTRA ANTERIORMENTE), EL REGRESO DE LA PARTE B DE ESTE FORMULARIO SERÁ CONSIDERADO COMO UNA SOLICITUD PARA REAPLICAR LA TASA DE EMISION PREVIAMENTE PAGADA HACIA LA TASA DE EMISION QUE SE DEBE AHORA.

COMO RESPONDER A ESTA NOTIFICACION:

I. Revisar el ESTADO DE ENTIDAD mostrado anteriormente. Si el ESTADO DE ENTIDAD se muestra como PEQUEÑA o MICRO, verificar si el derecho a ese estado de entidad aún aplica.

Si el ESTADO DE ENTIDAD es el mismo como se muestra anteriormente, pagar las TASAS TOTALES PENDIENTES mostradas anteriormente.

Si el ESTADO DE ENTIDAD se cambia del indicado anteriormente, en la PARTE B – TRANSMISION DE TASAS, completar la sección 5 titulada “Cambio en Estado de Entidad (del estado indicado anteriormente)”.

Para propósitos de esta notificación, las tasas de entidad pequeña son ½ de la cantidad de tasas sin descontar, y las tasas de entidad micro son ½ de la cantidad de tasa de entidad pequeña.

II. PARTE B – TRANSMISION DE TASAS, o su equivalente, debe ser completada y devuelta a la Oficina de Patentes y Marcas de Estados Unidos (USPTO) con su TASA DE EMISION y TASA DE PUBLICACION (si se requiere). Si está cargando las tasas a su cuenta de depósito, se debe completar la sección “4b” de la Parte B – Transmisión de Tasas y se debe presentar una copia adicional del formulario. Si se presenta un equivalente de la Parte B, se debe hacer claramente una solicitud de reaplicar una tasa de emisión previamente pagada, y pueden ocurrir retrasos en el procesamiento debido a la dificultad de reconocer el papel como un equivalente de la Parte B.

III. Todas las comunicaciones relacionadas con esta solicitud deben dar el número de solicitud. Por favor dirigir todas las comunicaciones antes de emisión a Mail Stop TASA DE EMISION a menos que se indique lo contrario.

RECORDATORIO IMPORTANTE: Las tasas de mantenimiento son pagables en patentes de utilidad que se emitan para solicitudes presentadas en o después del 12 de diciembre de 1980.

Es responsabilidad del poseedor de la patente asegurar el pago oportuno de las tasas de mantenimiento. Más información está disponible en www.uspto.gov/PatentMaintenanceFees.

PARTE B – TRANSMISION DE TASAS

Complete y envíe este formulario, junto con las tasas aplicables, por correo o fax, o por EFS-Web.

Por correo, enviar a: Mail Stop ISSUE FEE
Comisionado para Patentes
P.O. Box 1450
Alexandria, Virginia 22313-1450

INSTRUCCIONES: Este formulario debe ser usado para transmitir la TASA DE EMISION y la TASA DE PUBLICACION (si se requiere). Los bloques 1 a 5 deben ser completados donde sea adecuado. Toda la correspondencia posterior incluyendo la Patente, órdenes de avance y notificación de tasas de mantenimiento será enviada por correo a la dirección de correspondencia actual como se indica a menos que se corrija a continuación o se dirija de otra forma en el Bloque 1, al (a) especificar una nueva dirección de correspondencia; y/o (b) indicar una "DIRECCION DE PAGO" separada para notificaciones de tasas de mantenimiento

DIRECCION ACTUAL DE CORRESPONDENCIA (Nota: Use el Bloque 1 para cualquier cambio de dirección)

MORRISON & FOERSTER LLP
755 PAGE MILL RD
PALO ALTO, CA 94304-1018

Nota: Un certificado de correo puede ser únicamente usado para correos locales de la Transmisión de Tasas. Este certificado no puede ser usado para cualquier otro papel acompañante. Cada papel adicional, tal como una cesión o dibujo formal, debe tener su propio certificado de correo o transmisión.

Certificado de Correo o Transmisión

Por el presente certifico que esta Transmisión de tasas está siendo depositado con el Servicio Postal de Estados Unidos con franqueo suficiente para correo de primera clase en un sobre dirigido a la dirección Mail Stop ISSUE FEE anterior, o se transmite por facsímil a la USPTO (571-273-2885, en la fecha indicada a continuación.

(Nombre del Depositante)
(Firma)

(Fecha)

SOLICITUD NO.	FECHA PRESENTACION	PRIMER INVENTOR	REFERENCIA ABOGADO	NO. CONFIRMACION
16/296,194	03/07/2019	Jacob CHA	76809-20006.00	2171

TITULO DE LA INVENCION: COMPUESTOS DE AMINOACIDO Y METODOS DE USO

TIPO DE SOL.	ESTADO DE ENTIDAD	TASA DE EMISION	TASA DE PUBLICACION	TASA PAGADA PREVIAMENTE	TOTAL DE TASAS	FECHA DE VENCIMIENTO
no provisional	PEQUEÑA	$500	$0.00	$0.00	$500	09/08/2020

EXAMINADOR	UNIDAD DE ARTE	CLASE-SUBCLASE
CHANDRAKUMAR, NIZAL S	1625	546-122000

1. Cambio de dirección de correspondencia o indicación de “Dirección de Tasa” (37 CFR 1.363).

☐ Cambio de dirección de correspondencia (o formulario de Cambio de Dirección de Correspondencia PTO/SB/122) adjunto

☐ Indicación de “Dirección de Pago” (o formulario de Indicación de “Dirección de Pago” PTO/SB/47; Rev 03-02 o más reciente) adjunto. **Es requerido el uso de un Número de Cliente**.

2. Para imprimir en la página frontal de la patente, lista

(1) Los nombres de hasta 3 abogados de patente registrados o agentes O, alternativamente

(2) El nombre de una única firma (que tiene como un miembro un abogado o agente registrado) y los nombres de hasta 2 abogados de patente o agentes registrados. Si no se indica nombre, ningún nombre será impreso

3. NOMBRE DE CESIONARIO Y DATOS DE RESIDENCIA A SER IMPRESOS EN LA PATENTE (impreso o escrito)

POR FAVOR NOTE: A menos que el cesionario esté identificado a continuación, ningún dato de cesionario aparecerá en la patente. Si un cesionario está identificado a continuación, el documento ha sido presentado para registro como se define en 37 CFR 3.11. Completar este formulario NO es un reemplazo para presentar una cesión.

(A) NOMBRE DE CESIONARIO (B) RESIDENCIA (CIUDAD y ESTADO O PAIS)

Por favor revise la categoría o categorías adecuadas del cesionario (no serán impresas en la patente):

[ ] Individual [ ] Corporación u otra entidad privada [ ] Gubernamental

4a. Se presentan las siguientes tasas:

☐ Tasa de emisión

☐ Tasa de publicación (No se permite descuento por entidad pequeña)

☐ Orden de Avance - # de copias _____

4b. Pago de tasas: (**Por favor reaplicar cualquier tasa de emisión previamente pagada mostrada anteriormente**)

☐ Se adjunta un cheque

☐ Pago por tarjeta de crédito (Se adjunta formulario PTO-2038)

☐ Se autoriza al director a cargar las tasas requeridas, cualquier deficiencia, o acreditar cualquier sobrepago, a la Cuenta de Depósito Número _____

5. **Cambio de Estado de Entidad** (del estado indicado anteriormente)

☐ El Solicitante certifica estado de micro entidad. Ver 37 CFR 1.29

☐ El Solicitante certifica estado de entidad pequeña. Ver 37 CFR 1.27

☐ El Solicitante cambia a estado de tasa regular sin descuento

NOTA: Ausencia de una certificación válida de Estado de Entidad Micro (ver formularios PTO/SB/15A y 15B), el pago de tasa de emisión en la cantidad de entidad micro no será aceptado al riesgo de abandono de la solicitud.

NOTA: Si la solicitud fue previamente bajo el estado de micro entidad, chequeo de este cuadro será tomado como una certificación de pérdida de derecho a estado de entidad micro.

NOTA: Chequear este recuadro se tomará como una notificación de pérdida de derecho a estado de entidad pequeña o micro, como se aplicable

NOTA: Este formulario debe ser firmado de acuerdo con 37 CFR 1.31 y 1.33. Ver 37 CFR 1.4 para requerimientos de firma y certificaciones.

Firma Autorizada _____ Fecha _____

Nombre escrito o impreso _____ Registro No. _____

OFICINA DE PATENTES Y MARCAS DE ESTADOS UNIDOS

DEPARTAMENTO DE COMERCIO DE ESTADOS UNIDOS

Oficina de Patentes y Marcas de Estados Unidos

Dirección: COMISIONADO PARA PATENTES

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SOLICITUD NO.	FECHA PRESENTACION	PRIMER INVENTOR	REFERENCIA ABOGADO	NO. CONFIRMACION
16/296,194	03/07/2019	Jacob CHA	76809-20006.00	2171

MORRISON & FOERSTER LLP

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PALO ALTO, CA 94304-1018

EXAMINADOR

CHANDRAKUMAR, NIZAL S

UNIDAD DE ARTE 1625 NÚMERO PAPEL

FECHA DE ENVIO: 06/05/2020

Determinación de Ajuste de Término de Patente bajo 35 U.S.C. 154 (b)

(Solicitudes presentadas en o después de 29 de mayo de 2000)

La Oficina ha descontinuado el suministro de un cálculo de Ajuste de Término de Patente (PTA) con la Notificación de Aceptación.

La Sección 1(h)(2) de la Ley de Correcciones Técnicas AIA modificó 35 U.S.C. 154(b)(3)(B)(i) para eliminar el requerimiento que la Oficina suministra una determinación de ajuste de término de patente con la notificación de aceptación. Ver Revisiones al Ajuste de Término de Patente, 78 Fed. Reg. 19416, 19417 (Abr. 1, 2013). Por lo tanto, la Oficina ya no suministra más una determinación de ajuste de término de patente inicial con la notificación de aceptación. La Oficina continuará suministrando una determinación de ajuste de término de patente con la Carta de Notificación de Emisión que es enviada al solicitante aproximadamente tres semanas antes de la fecha de emisión de la patente, e incluirá el ajuste de término de patente sobre la patente. Cualquier solicitud para reconsideración de la determinación de ajuste de término de patente (o reintegro del ajuste del término de patente) deberá seguir el proceso indicado en 37 CFR 1.705.

Cualquier pregunta relacionada con la determinación de Extensión o Ajuste del Término de Patente deberá ser dirigida a la Oficina de Administración Legal de Patente en (571)-272-7702. Preguntas relacionadas con pagos de tasas de emisión y publicación deberán ser dirigidas al Centro de Servicio al Cliente de la Oficina de Publicación de Patente en 1-(888)-786-0101 o (571)-272-4200.

Declaración de Autorización de OMB y Carga de PRA para PTOL-85 Parte B

La Ley de Reducción de Trámites (PARA) de 1995 requiere a las agencias Federales a obtener aprobación de la Oficina de Gestión y Presupuesto antes de solicitar la mayoría de tipos de información del público. Cuando la OMB aprueba que una agencia solicite recolectar información del público, la OMB (i) suministra un Número de Control de OMB válido y fecha de vencimiento para que la agencia muestre en el instrumento que será usado para recolectar la información y (ii) requiere que la agencia informe al público acerca del significado legal del Número de Control de OMB de acuerdo con 5 CFR 1320.5(b).

La información recolectada por PTOL-85 Parte B es requerida por 37 CFR 1.311. La información es requerida para obtener o mantener un beneficio por el público el cual es presentar (y procesarla por parte de la USPTO) una solicitud. La confidencialidad se rige por 35 U.S.C. 122 y 37 CFR 1.14. Esta recolección se estima que tome 30 minutos en completarse, incluyendo la recopilación, preparación y presentación del formato de solicitud completo a la USPTO. El tiempo variará dependiendo de cada caso individual. Cualquier comentario sobre la cantidad de tiempo que se requiere para completar este formato y/o sugerencias para reducir esta carga, deben enviarse al Director de Información de la Oficina de Marcas y Patentes de EE.UU., Departamento de Comercio de EE.UU., P.O. Box 1450, Alexandria, Virginia 22313-1450. NO ENVIE TASAS O FORMATOS COMPLETOS A ESTA DIRECCION, ENVIE A: Comisionado de Patentes, P.O. Box 1450, Alexandria, Virginia 22313-1450. Bajo la ley de Reducción de Trámites de 1995, ninguna persona es requerida a responder a una recolección de información a menos que muestre un número de control OMB válido.

Declaración de Ley de Privacidad

La Ley de Privacidad de 1974 (P.L. 93-579) requiere que se suministre cierta información en relación con su presentación del formato adjunto relacionado con una solicitud de patente o patente. En consecuencia, de conformidad con los requerimientos de la Ley, por favor tenga en cuenta que: (1) la autoridad general para la recolección de esta información es 35 U.S.C. 2(b)(2): (2) la entrega de la información solicitada es voluntaria; y (3) el

propósito principal para el cual se utiliza la información por parte de la Oficina de Marcas y Patentes de EE.UU. es para procesar y/o examinar su comunicación relacionada a una solicitud de patente o patente. Si usted no presenta la información solicitada, la Oficina de Marcas y Patentes de EE.UU. no podrá procesar y/o examinar su comunicación, lo cual puede resultar en la terminación de los procedimientos o el abandono de la solicitud o el vencimiento de la patente.

La información suministrada por usted en este formato estará sujeta a los siguientes usos de rutina:

1. La información en este formato será tratada confidencialmente en la medida permitida bajo la Ley de Libertad de Información (5 U.S.C. 552) y la Ley de Privacidad (5 U.S.C 552a). Los Registros de este sistema de registros pueden ser divulgados al Departamento de Justicia para determinar si se requiere divulgar estos registros por la Ley de Libertad de Información.
2. Un registro de este sistema de registros puede ser divulgado, como uso de rutina, en el curso de presentación de evidencia a un tribunal, magistrado, o tribunal administrativo, incluyendo divulgaciones al abogado opositor en el curso de negociaciones de conciliación.
3. Un registro en este sistema de registros puede ser divulgado, como uso de rutina, a un Miembro del Congreso que presente una solicitud relacionada con un individuo, a quien pertenezca el registro, cuando el individuo haya solicitado ayuda del Miembro con respecto a la materia objeto del registro.
4. Un registro en este sistema de registros puede ser divulgado, como uso de rutina, a un contratista de la Agencia que necesite la información con el fin de realizar un contrato. Los receptores de la información estarán obligados a cumplir con los requerimientos de la Ley de Privacidad de 1974, como fue modificada, de acuerdo con a 5 U.S.C. 552a(m).
5. Un registro relacionado con una Solicitud Internacional presentada bajo el Tratado en Cooperación de Patentes en este sistema de registros puede ser divulgado, como uso de rutina, a la Oficina Internacional de la Organización Mundial de Propiedad Intelectual, conforme al Tratado en Cooperación de Patentes.

6. Un registro en este sistema de registros puede ser divulgado, como uso de rutina, a otra agencia federal para propósitos de revisión de Seguridad Nacional (35 U.S.C. 181) y para revisión conforme a la Ley de Energía Atómica (42 U.S.C. 218(c)).
7. Un registro de este sistema de registros puede ser divulgado, como uso de rutina, al Administrador, Servicios Generales, o su designado, durante una inspección de registros realizada por la GSA corno parte de la responsabilidad de esa agencia para recomendar mejoras en las prácticas y programas de manejo de registros, bajo la autoridad de 44 U.S.C. 2904 y 2906. Dicha divulgación deberá hacerse de acuerdo con las regulaciones de la GSA que rigen la inspección de registros para este propósito, y cualquier otra directiva relevante (es decir, GSA o Comercio). Dicha divulgación no será usada para tomar determinaciones sobre individuos.
8. Un registro de este sistema de registros será divulgado, como uso de rutina, al público después de la publicación de la solicitud de conformidad con 35 U.S.C. 122(b) o la emisión de una patente de conformidad con 35 U.S.C. 151. Además, un registro puede ser divulgado, sujeto a las limitaciones de 37 CFR 1.14, como uso de rutina, al público si el registro fue presentado en una solicitud la cual fue abandonada o en la cual se terminaros los procedimientos y dicha solicitud es referenciada por una solicitud publicada, una solicitud abierta para inspección pública o una patente emitida.
9. Un registro de este sistema de registros puede ser divulgado, como uso de rutina, a una agencia de cumplimiento de ley Federal, Estatal, o local, si la USPTO es consciente de una violación o potencial violación de ley o regulación.

Notificación de Concesión	**Solicitud No.** 16/296,194	**Solicitante(s)** CHA y otros	
	Examinador NIZAL S. CHANDRAKUMAR	**Unidad de Arte** 1625	**Estado AIA (FITF)** Sí

-- La FECHA DE ENVIO de esta comunicación aparece en la hoja de cubierta con la dirección de correspondencia--

Todas las reivindicaciones son concedidas, TRÁMITE SOBRE EL FONDO ESTÁ (O PERMANECE) CERRADO en esta solicitud. Si no se incluye acá (o enviada previamente), una Notificación de Concesión (PTOL-85) u otra comunicación adecuada será enviada en su debido momento. **ESTA NOTIFICACION DE CONCESION NO ES UNA CONCESION DE DERECHOS DE PATENTE**. Esta solicitud está sujeta a retiro de emisión a la iniciativa de la Oficina o a petición del solicitante. Ver 37 CFR 1.313 y MPEP 1308.

1. ☒ Esta comunicación responde a 5/26/2020.

☐Una declaración bajo **37 CFR 1.130(b)** se presentó el_____.

2. ☐ Se hizo una elección por el solicitante en respuesta a un requerimiento de restricción definido durante la entrevista el ____; el requerimiento de restricción y la elección se han incorporado en esta acción.

3. ☒ Las reivindicaciones concedidas son 4-8,12,15-17,27-49,62,68-72,-76-77 y 88-116. Como resultado de las reivindicaciones aceptadas, usted puede ser elegible del beneficio del programa de **Autopista de Trámite de Patente** en una oficina de propiedad intelectual participante para la correspondiente solicitud. Para más información, por favor ver http://www.uspto.gov/patents/init_events/pph/index.jsp o enviar una pregunta a PPHfeedback@uspto.gov.

4. ☐ Se reconoce una reivindicación de prioridad extranjera bajo 35 USC sección 119(a)-(d) o (f).

Copias certificadas:

a) ☐ Todas b) ☐ Algunas c) ☐ Ninguna de las:

1. ☐ Copias certificadas de los documentos de prioridad se han recibido.

2. ☐ Copias certificadas de los documentos de prioridad se han recibido en la Solicitud No. ____.

3. ☐ Copias de las copias certificadas de los documentos de prioridad se han recibido en esta solicitud de fase nacional de la Oficina Internacional (Regla PCT 17.2 (a)).

* Copias certificadas no recibidas: _____.

El Solicitante tiene TRES MESES A PARTIR DE LA “FECHA DE ENVIO” de esta comunicación para presentar una respuesta que cumpla con los requerimientos indicados anteriormente. Falla en cumplir a tiempo resultará en el ABANDONO de esta solicitud.

ESTE PERIODO DE TRES MESES NO ES EXTENSIBLE

5. ☐ Se deben presentar FIGURAS CORREGIDAS (como “hojas de reemplazo”).

☐ Incluyendo cambios requeridos por la Enmienda/Comentario del Examinador adjunto o en la Acción Oficial de Papel No./Fecha de Envío ____.

Los indicios de identificación tal como el número de solicitud (ver 37 CFR 1.84(c)) se deben escribir en las figuras en el frente (no atrás) de cada hoja. Las hojas de reemplazo deben estar etiquetadas como tal en el encabezado de acuerdo con 37 CFR 1.121(d).

6. ☐ Se debe presentar DEPOSITO DE y/o INFORMACIÓN acerca del depósito de MATERIAL BIOLOGICO. Note el comentario del Examinador adjunto con relación al REQUERIMIENTO PARA EL DEPOSITO DE MATERIAL BIOLOGICO.

Adjunto(s)

1. ☐ Notificación de Referencias Citadas (PTO-892)
2. ☒ Declaraciones de Divulgación de Información (PTO/SB/08), Papel No./Fecha Envío ____
3. ☐ Comentario del Examinador con Relación a Requerimiento para Depósito de Material Biológico
4. ☐ Resumen de Entrevista (PTO-413), Papel No./Fecha Envío ____.
5. ☐ Enmienda/Comentario del Examinador
6. ☐ Declaración del Examinador de Razones para Concesión.
7. ☐ Otro ____.

/NIZAL S CHANDRAKUMAR/ Examinador Principal, Unidad de Arte 1625	

Notificación de Estado Pre-AIA o AIA

La presente solicitud, presentada en o después del 16 de marzo de 2013, está siendo examinada bajo las disposiciones de primer inventor en presentar del AIA.

Se reconoce la respuesta de los Solicitantes presentada el 5/26/2020.

Las reivindicaciones 4-8, 12, 15-17, 27-49, 62, 68-72, 76-77, y 88-116 están pendientes.

Las modificaciones a las reivindicaciones superan las objeciones presentadas anteriormente.

Las reivindicaciones 4-8, 12, 15-17, 27-49, 62, 68-72, 76-77, y 88-116 son aceptadas.

Cualquier inquietud relacionada con esta comunicación o comunicaciones anteriores del examinador debe ser dirigida a NIZAL S CHANDRAKUMAR cuyo número telefónico es (571)272-6202. El examinador normalmente está disponible de L-V 8-5 EST.

También hay disponibles entrevistas con el examinador vía teléfono, en persona, y video conferencia usando una herramienta de colaboración basada en web suministrada por la USPTO. Para agendar una entrevista, se invita al solicitante a utilizar la Solicitud Automática de Entrevistas de la USPTO (AIR) en http://www.uspto.gov/interviewpractice.

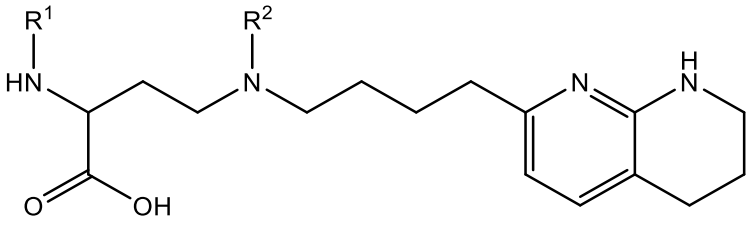
Si los intentos por comunicarse con el examinador por teléfono no son exitosos, el supervisor del examinador, Andrew Kosar puede ser contactado en (571) 272-0913. El número de teléfono de fax para la organización donde esta solicitud o procedimiento es asignado es 571-273-8300.

Información relacionada con el estado de una solicitud puede ser obtenida del sistema de Recuperación de Información de Solicitud de Patente (PAIR). La información de estado para solicitudes publicadas puede ser obtenido del PAIR Privado o el PAIR Público. La información del estado para solicitudes no publicadas está disponible únicamente mediante el PAIR Privado. Para más información acerca del sistema PAIR, vea https://ppair-my.uspto.gov/pair/PrivatePair. Si tiene inquietudes sobre el acceso al sistema PAIR Privado, contacte el Centro de Negocios Electrónicos (EBC) en 866-217-9197 (totalmente gratis). Si desea ayuda de un Representante de Servicio al Cliente de la USPTO o acceso al sistema automático de información, llame al 800-786-9199 (EN EE.UU. O CANADA) o 571-272-1000.

/NIZAL S CHANDRAKUMAR/

Examinador Principal, Unidad del Arte 1625

Claim 1. A compound of formula (II):



(II);

or a salt thereof, wherein:

R^1 is C_6-C_{14} aryl or 5- to 10-membered heteroaryl wherein the C_6-C_{14} aryl and 5- to 10-membered heteroaryl are optionally substituted by R^{1a};

R^2 is hydrogen; deuterium; C_1-C_6 alkyl optionally substituted by R^{2a}; -OH; -O-C_1-C_6 alkyl optionally substituted by R^{2a}; C_3-C_6 cycloalkyl optionally substituted by R^{2b}; -O-C_3-C_6 cycloalkyl optionally substituted by R^{2b}; 3- to 12-membered heterocyclyl optionally substituted by R^{2c}; or -$S(O)_2R^{2d}$; with the proviso that any carbon atom bonded directly to a nitrogen atom is optionally substituted with an R^{2a} moiety other than halogen;

each R^{1a} is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_8 cycloalkyl, C_4-C_8 cycloalkenyl, 3- to 12-membered heterocyclyl, 5- to 10-membered heteroaryl, C_6-C_{14} aryl, deuterium, halogen, -CN, -OR^3, -SR^3, -NR^4R^5, -NO_2, -C=NH(OR^3), -$C(O)R^3$, -$OC(O)R^3$, -$C(O)OR^3$, -$C(O)NR^4R^5$, -$NR^3C(O)R^4$, -$NR^3C(O)OR^4$, -$NR^3C(O)NR^4R^5$, -$S(O)R^3$, -$S(O)_2R^3$, -$NR^3S(O)R^4$, -$NR^3S(O)_2R^4$, -$S(O)NR^4R^5$, -$S(O)_2NR^4R^5$, or -$P(O)(OR^4)(OR^5)$, wherein each R^{1a} is, where possible, independently optionally substituted by deuterium, halogen, oxo, -OR^6, -NR^6R^7, -$C(O)R^6$, -CN, -$S(O)R^6$, -$S(O)_2R^6$, -$P(O)(OR^6)(OR^7)$, C_3-C_8 cycloalkyl, 3- to 12-membered heterocyclyl, 5- to 10-membered heteroaryl, C_6-C_{14} aryl, or C_1-C_6 alkyl optionally substituted by deuterium, oxo, -OH or halogen;

each R^{2a}, R^{2b}, R^{2c}, R^{2e}, and R^{2f} is independently oxo or R^{1a};

R^{2d} is C_1-C_6 alkyl optionally substituted by R^{2e} or C_3-C_5 cycloalkyl optionally substituted by R^{2f};

each R^3 is independently hydrogen, deuterium, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_6-C_{14} aryl, 5- to 10-membered heteroaryl or 3- to 12-membered heterocyclyl, wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_6-C_{14} aryl, 5- to 10-membered heteroaryl and 3- to 12-membered heterocyclyl of R^3 are independently optionally substituted by halogen, deuterium, oxo, -CN, $-OR^8$, $-NR^8R^9$, $-P(O)(OR^8)(OR^9)$, or C_1-C_6 alkyl optionally substituted by deuterium, halogen, -OH or oxo;

R^4 and R^5 are each independently hydrogen, deuterium, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_6-C_{14} aryl, 5- to 6-membered heteroaryl or 3- to 6-membered heterocyclyl, wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_6-C_{14} aryl, 5- to 6-membered heteroaryl and 3- to 6-membered heterocyclyl of R^4 and R^5 are independently optionally substituted by deuterium, halogen, oxo, -CN, $-OR^8$, $-NR^8R^9$ or C_1-C_6 alkyl optionally substituted by deuterium, halogen, -OH or oxo;

or R^4 and R^5 are taken together with the atom to which they attached to form a 3- to 6-membered heterocyclyl optionally substituted by deuterium, halogen, oxo, $-OR^8$, $-NR^8R^9$ or C_1-C_6 alkyl optionally substituted by deuterium, halogen, oxo or -OH;

R^6 and R^7 are each independently hydrogen, deuterium, C_1-C_6 alkyl optionally substituted by deuterium, halogen, or oxo, C_2-C_6 alkenyl optionally substituted by deuterium, halogen, or oxo, or C_2-C_6 alkynyl optionally substituted by deuterium, halogen, or oxo;

or R^6 and R^7 are taken together with the atom to which they attached to form a 3- to 6-membered heterocyclyl optionally substituted by deuterium, halogen, oxo or C_1-C_6 alkyl optionally substituted by deuterium, halogen, or oxo; and

R^8 and R^9 are each independently hydrogen, deuterium, C_1-C_6 alkyl optionally substituted by deuterium, halogen, or oxo, C_2-C_6 alkenyl optionally substituted by deuterium, halogen or oxo, or C_2-C_6 alkynyl optionally substituted by deuterium, halogen, or oxo;

or R^8 and R^9 are taken together with the atom to which they attached to form a 3-6 membered heterocyclyl optionally substituted by deuterium, halogen, oxo or C_1-C_6 alkyl optionally substituted by deuterium, oxo, or halogen.

Claim 2. The compound of claim 1, or a salt thereof, wherein R^1 is 5- to 10-membered heteroaryl optionally substituted by R^{1a}.

Claim 3. The compound of claim 1, or a salt thereof, wherein R^1 is:

pyrimidinyl, quinazolinyl, pyrazolopyrimidinyl, pyrazinyl, quinolinyl, pyridopyrimidinyl, thienopyrimidinyl, pyridinyl, pyrrolopyrimidinyl, quinoxalinyl, indazolyl, benzothiazolyl, naphthalenyl, purinyl, or isoquinolinyl; and

wherein R^1 is optionally substituted by deuterium, hydroxy, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 perhaloalkyl, C_1-C_6 alkoxyl, C_3-C_8 cycloalkyl, C_3-C_8 halocycloalkyl, C_3-C_8 cycloalkoxyl, 5- to 10-membered heteroaryl, C_6-C_{14} aryl, cyano, amino, alkylamino, or dialkylamino.

Claim 4. The compound of claim 1, or a salt thereof, wherein R^1 is:

pyrimidin-2-yl, pyrimidin-4-yl, quinazolin-4-yl, 1H-pyrazolo[3,4-d]pyrimidin-4-yl, 1H-pyrazolo[4,3-d]pyrimidin-7-yl, pyrazin-2-yl, quinolin-4-yl, pyrido[2,3-d]pyrimidin-4-yl, pyrido[3,2-d]pyrimidin-4-yl, pyrido[3,4-d]pyrimidin-4-yl, thieno[2,3-d]pyrimidin-4-yl, thieno[3,2-d]pyrimidin-4-yl, thienopyrimidin-4-yl, pyridin-2-yl, pyridin-3-yl, 7H-pyrrolo[2,3-d]pyrimidin-4-yl, quinoxalin-2-yl, 1H-indazol-3-yl, benzo[d]thiazol-2-yl, naphthalen-1-yl, 9H-purin-6-yl, or isoquinolin-1-yl; and

wherein R^1 is optionally substituted by one or more deuterium, methyl, cyclopropyl, fluoro, chloro, bromo, difluoromethyl, trifluoromethyl, methoxy, cyano, dimethylamino, phenyl, pyridin-3-yl, or pyridin-4-yl.

Claim 5. The compound of claim 1, or a salt thereof, wherein R^1 is pyrimidin-4-yl optionally substituted by R^{1a}, wherein each R^{1a} is independently 5- to 10-membered heteroaryl, or C_1-C_6 alkyl optionally substituted by halogen.

Claim 6. The compound of claim 1, or a salt thereof, wherein R^1 is quinazolin-4-yl optionally substituted by R^{1a}, wherein each R^{1a} is independently halogen, C_1-C_6 alkyl optionally substituted by halogen, or C_1-C_6 alkoxy.

Claim 7. The compound of claim 1, or a salt thereof, wherein R^2 is:

hydrogen,

deuterium,

hydroxy,

C_1-C_6 alkyl, or

-O-C_1-C_6 alkyl, and

wherein the C_1-C_6 alkyl and -O-C_1-C_6 alkyl of R^2 are optionally substituted with deuterium, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 alkoxyl, C_3-C_8 cycloalkyl, C_3-C_8 halocycloalkyl, C_3-C_6 cycloalkoxyl, C_6-C_{14} aryl, C_6-C_{14} aryloxy, 5- to 10-membered heteroaryl, 5- to 10-membered heteroaryloxy, 3- to 12-membered heterocyclyl optionally substituted with oxo, -C(O)NR^4R^5, -NR^3C(O)R^4, or -$S(O)_2R^3$.

Claim 8. The compound of claim 1, or a salt thereof, wherein R^2 is:

methyl, methoxy, ethyl, ethoxy, propyl, cyclopropyl, or cyclobutyl; and

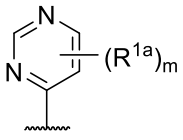
wherein R^2 is optionally substituted with one or more of hydroxy, methoxy, ethoxy, acetamide, fluoro, fluoroalkyl, phenoxy, dimethylamide, methylsulfonyl, cyclopropoxyl, pyridin-2-yloxy, pyridin-3-yloxy, N-morpholinyl, N-pyrrolidin-2-onyl, dimethylpyrazol-1-yl, (1,4-dioxan-2-yl) methyl, morpholin-2-yl, oxetan-3-yl, phenyl, tetrahydrofuran-2-yl, or thiazol-2-yl;

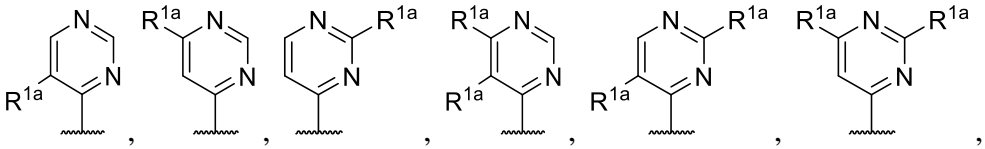
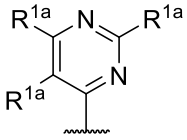
each of which is substituted with 0, 1, 2, or 3 of deuterium, hydroxy, methyl, fluoro, cyano, or oxo.

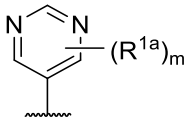
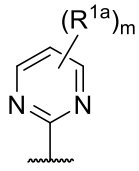
Claim 9. The compound of claim 1, or a salt thereof, wherein R^2 is C_1-C_6 alkyl optionally substituted by:

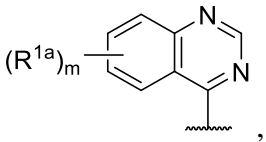
R^{2a}, wherein each R^{2a} is independently: halogen; C_3-C_8 cycloalkyl optionally substituted by halogen; 5- to 10-membered heteroaryl optionally substituted by C_1-C_6 alkyl; -NR^4R^5; -NR^3C(O)R^4; -$S(O)_2R^3$; oxo, or

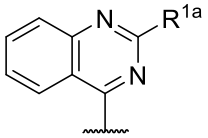
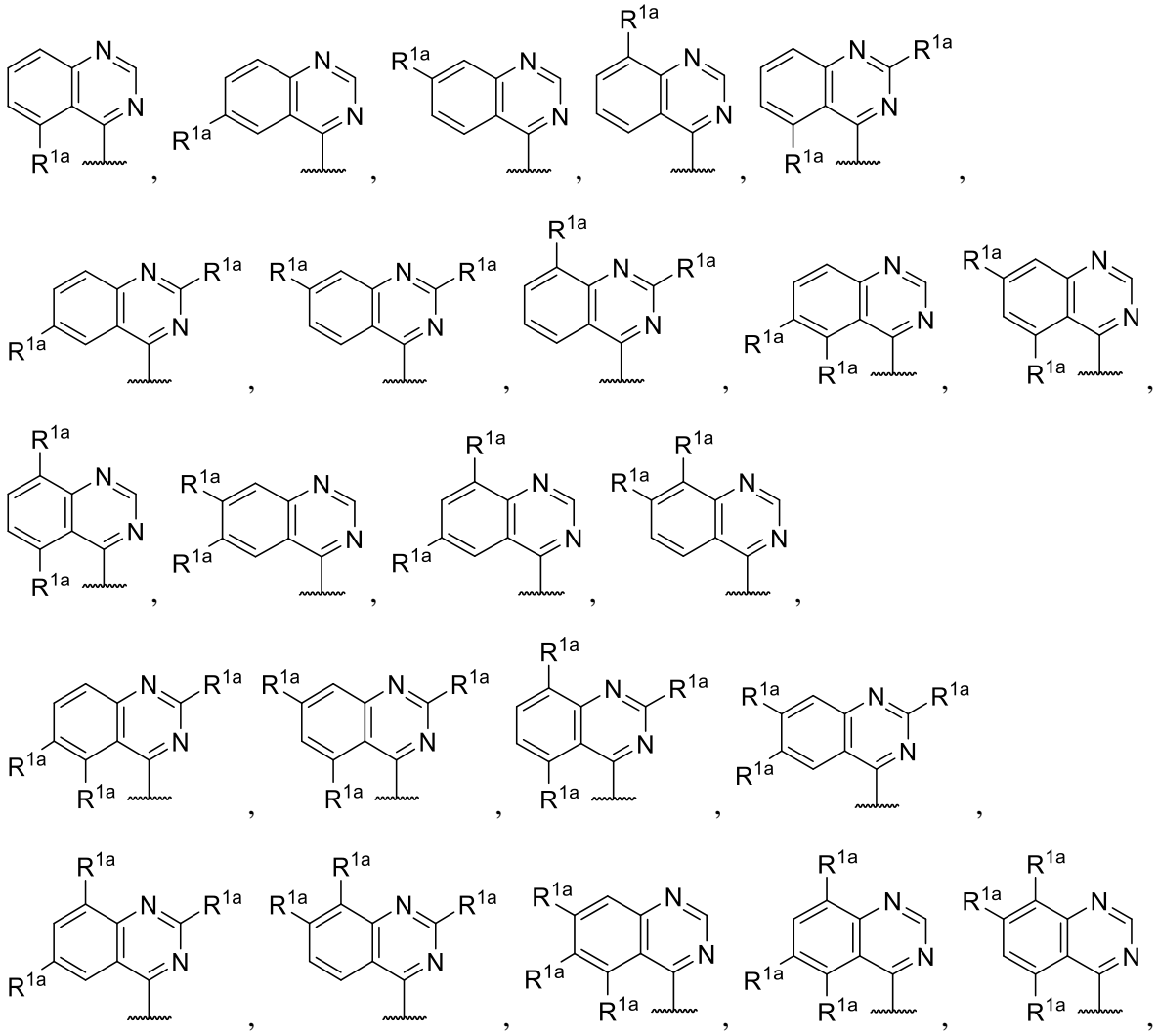
-OR^3, wherein each R^3 is independently: hydrogen; C_1-C_6 alkyl optionally substituted by halogen; C_3-C_6 cycloalkyl optionally substituted by halogen; C_6-C_{14} aryl optionally substituted by halogen; 5- to 6-membered heteroaryl optionally substituted by halogen or C_1-C_6 alkyl

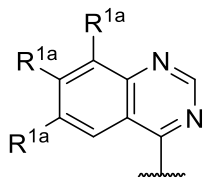
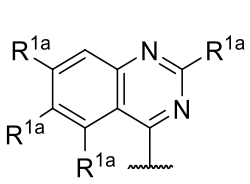
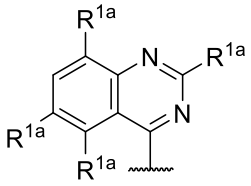
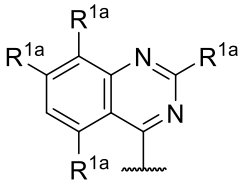
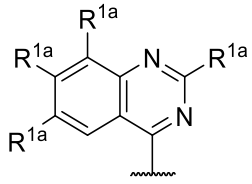
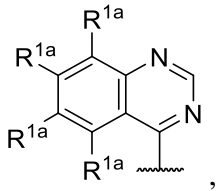
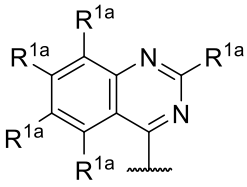
Claim 10. The compound of claim 1, or a salt thereof, wherein R^1 is  , wherein m is 0, 1, 2, or 3 and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium.

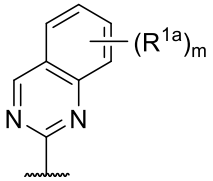
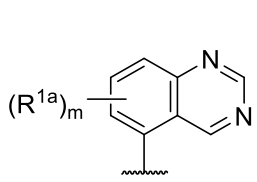
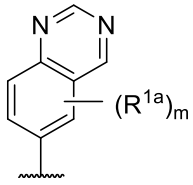
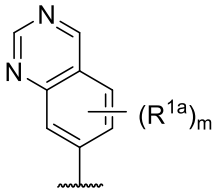
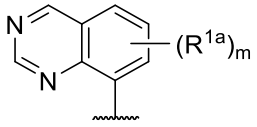
Claim 11. The compound of claim 10, or a salt thereof, wherein R^1 is  , or  , wherein each R^{1a} is independently deuterium, alkyl, haloalkyl, or heteroaryl.

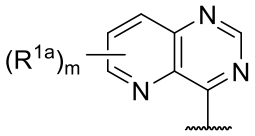
Claim 12. The compound of claim 1, or a salt thereof, wherein R^1 is  or  , wherein m is 0, 1, 2, or 3 and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium.

Claim 13. The compound of claim 1, or a salt thereof, wherein R^1 is  , wherein m is 0, 1, 2, 3, 4, or 5 and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium.

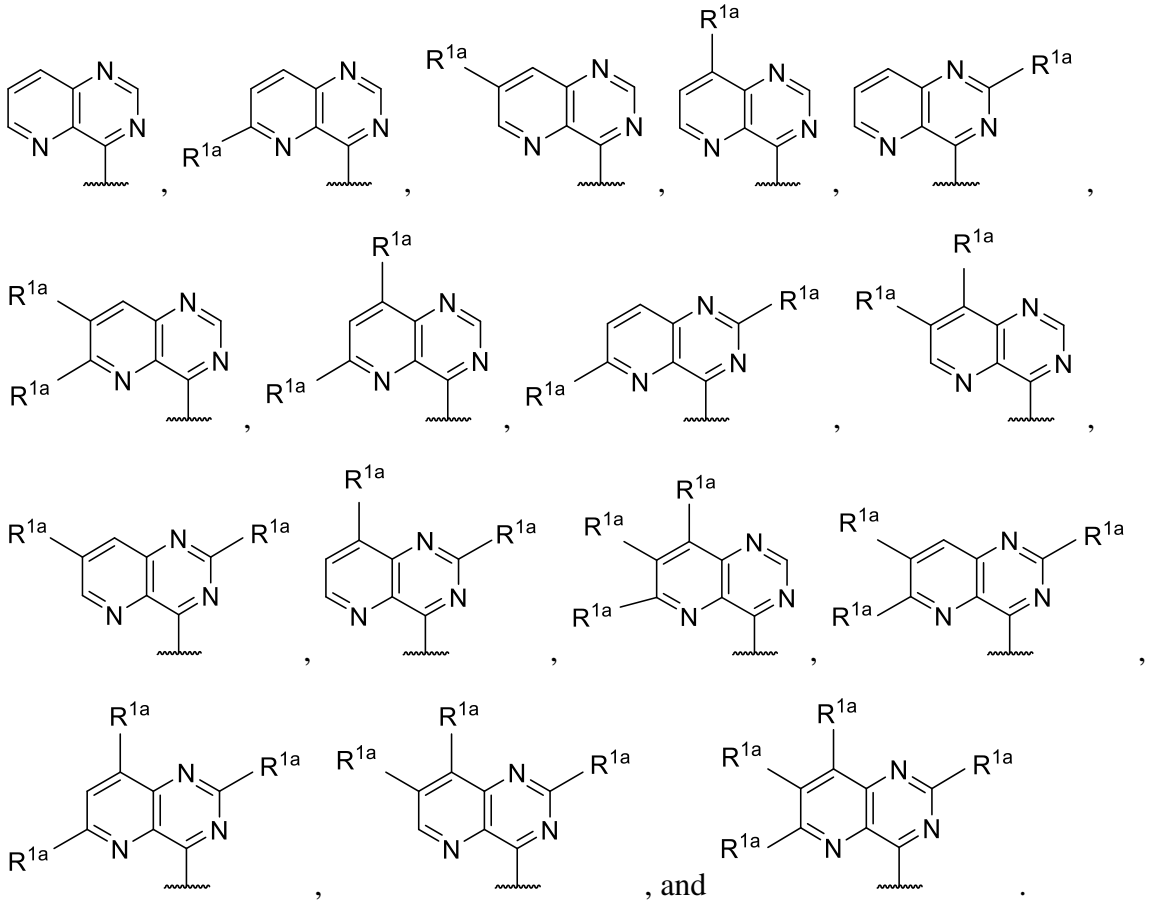
Claim 14. The compound of claim 13, or a salt thereof, wherein R^1 is  , 

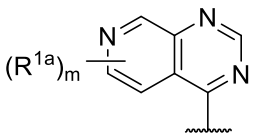







, wherein each R^{1a} is independently deuterium, halogen, alkyl, haloalkyl, or alkoxy.

Claim 15. The compound of claim 1, or a salt thereof, wherein R^1 is 




wherein m is 0, 1, 2, 3, 4, or 5 and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium.

Claim 16. The compound of claim 1, or a salt thereof, wherein R^1 is 
, wherein m is 0, 1, 2, 3, or 4, and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium.

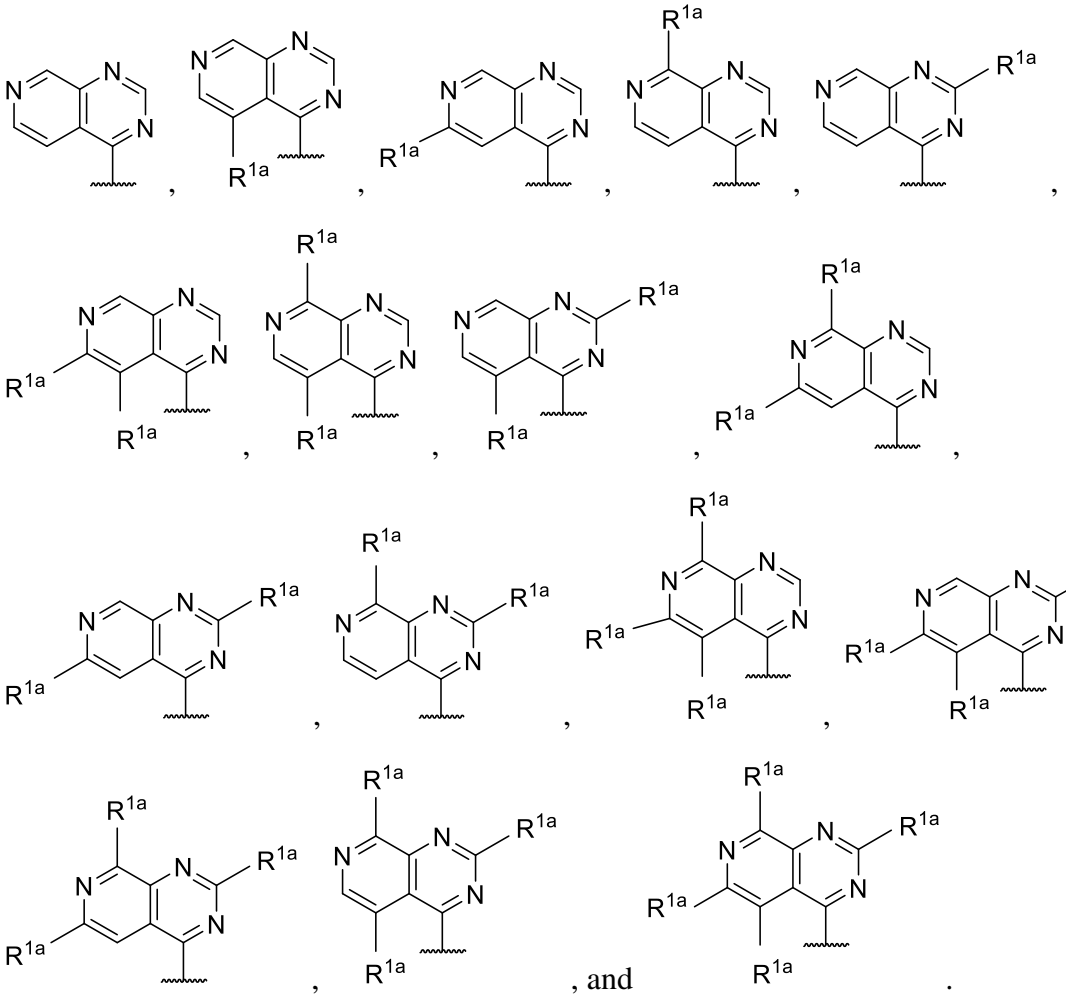
Claim 17. The compound of claim 16, or a salt thereof, wherein R^1 is selected from the group consisting of

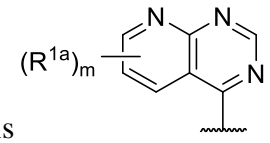




Claim 18. The compound of claim 1, or a salt thereof, wherein R^1 is , wherein m is 0, 1, 2, 3, or 4, and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium.

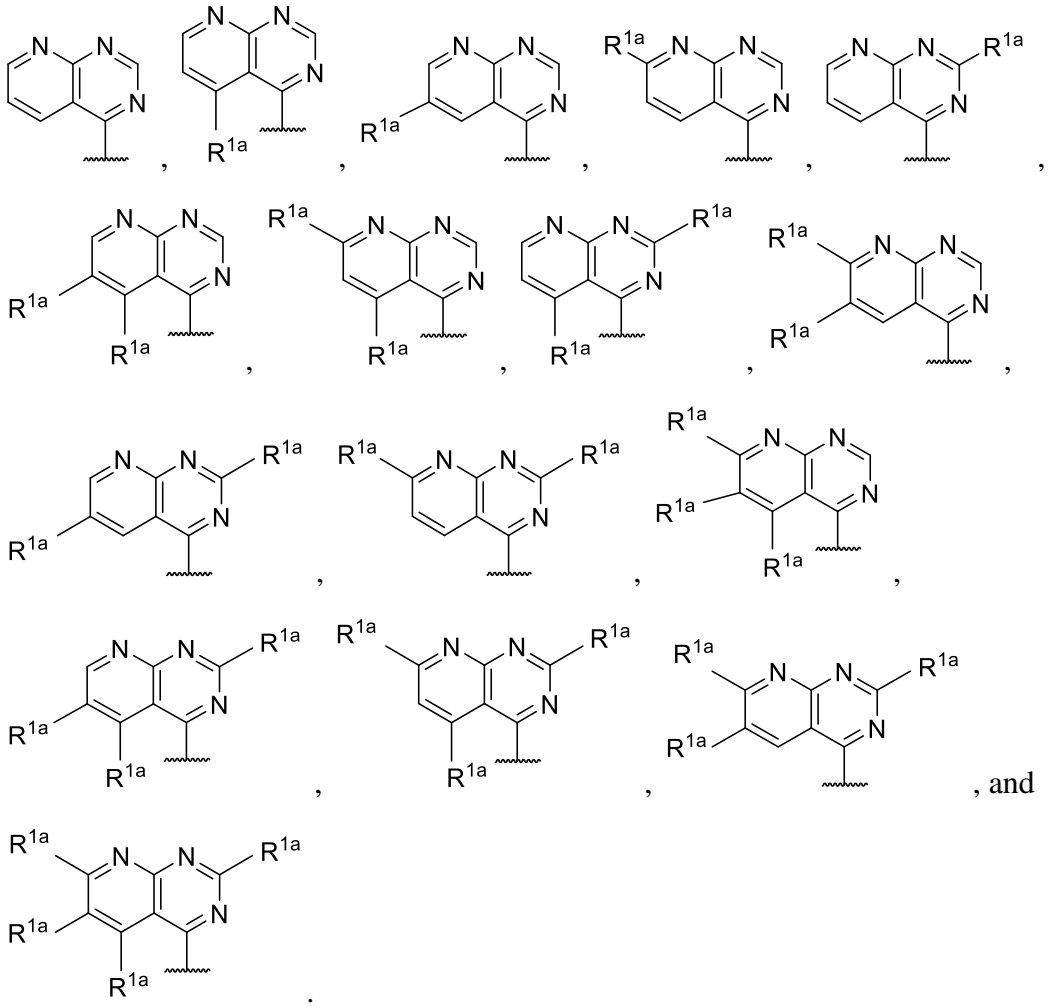
Claim 19. The compound of claim 18, or a salt thereof, wherein R^1 is selected from the group consisting of





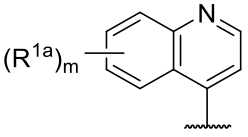
Claim 21. The compound of claim 1, or a salt thereof, wherein R^1 is , wherein m is 0, 1, 2, 3, or 4, and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium.

Claim 21. The compound of claim 21, or a salt thereof, wherein R^1 is selected from the group consisting of

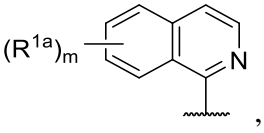


, and

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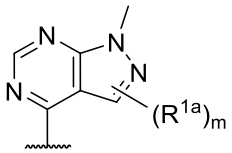


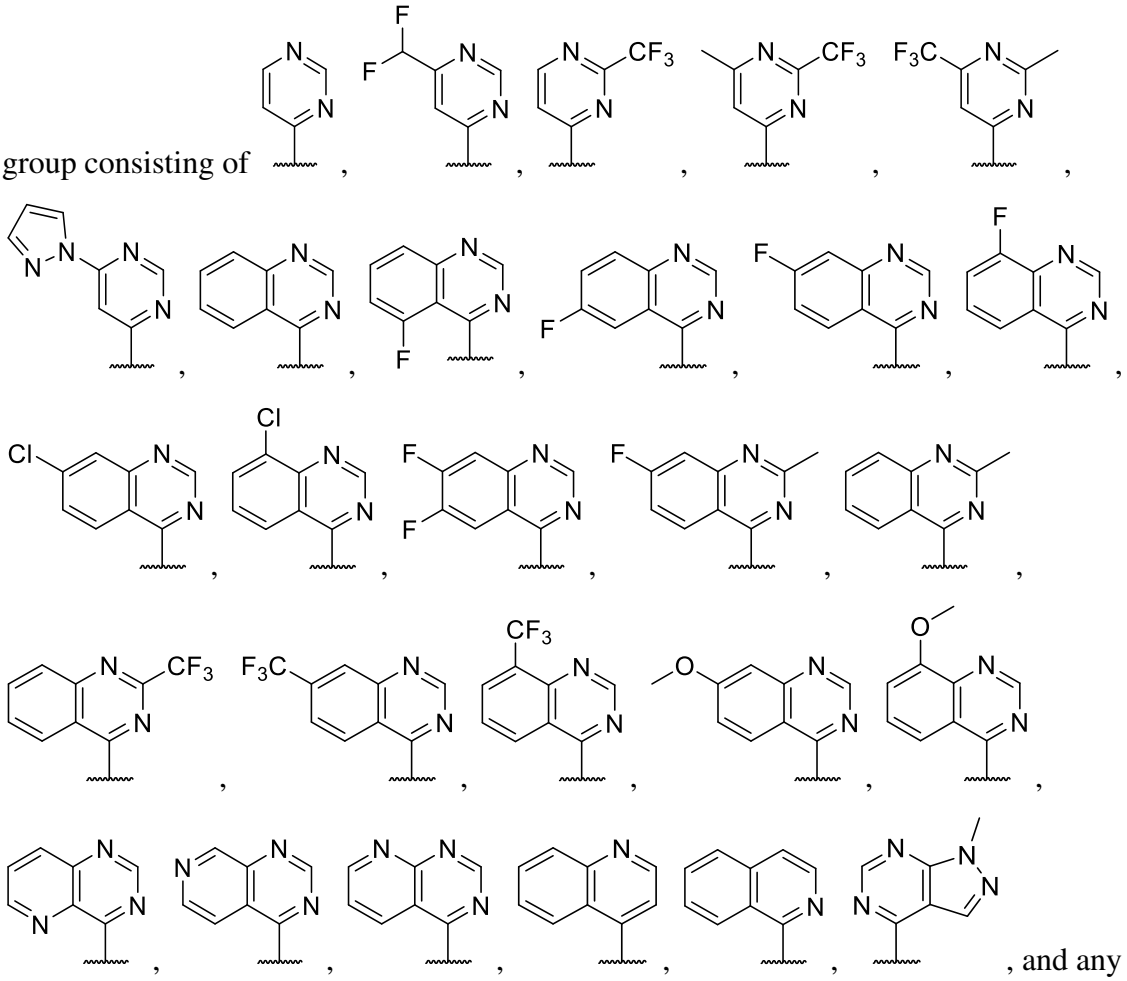
Claim 22. The compound of claim 1, or a salt thereof, wherein R^1 is , wherein m is 0, 1, 2, 3, 4, 5, or 6 and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium.

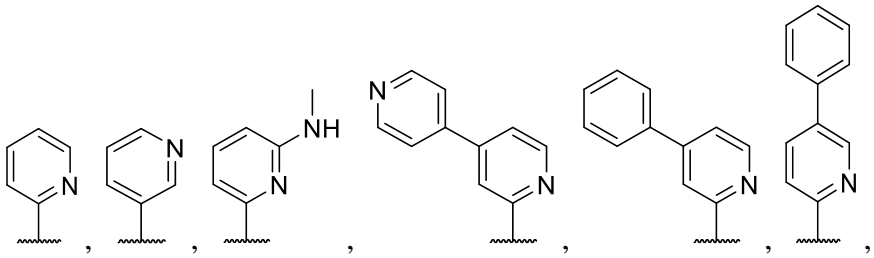
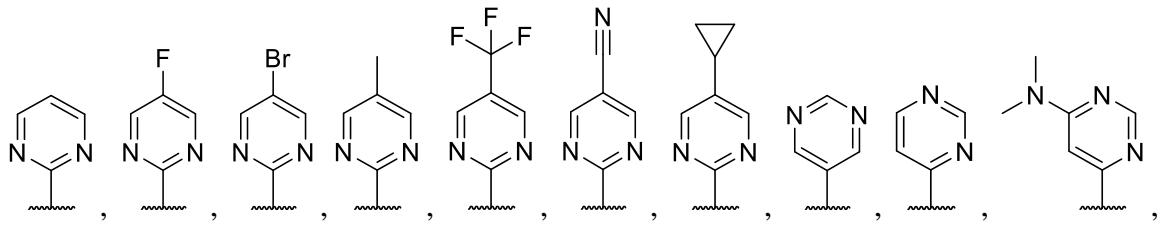
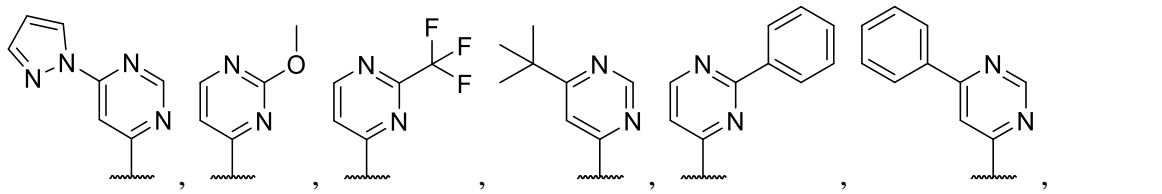
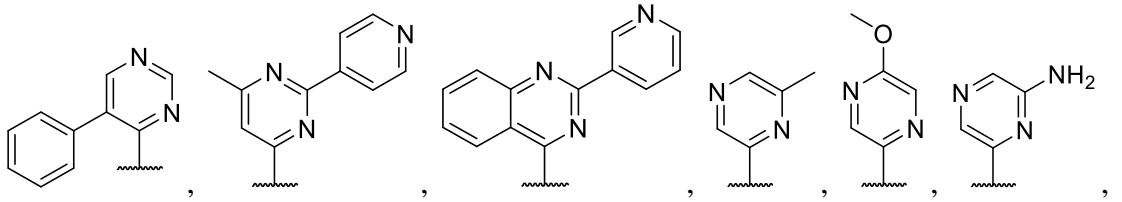
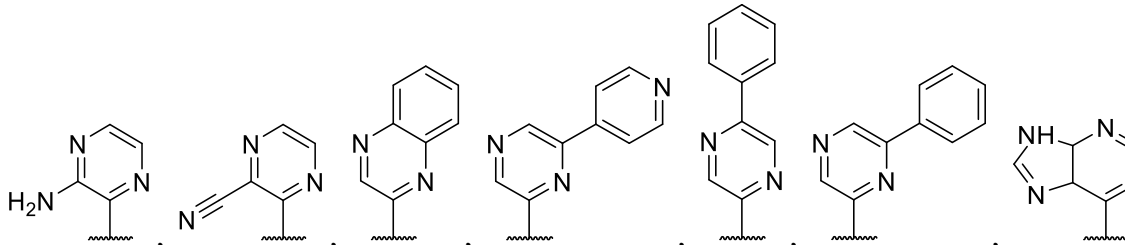
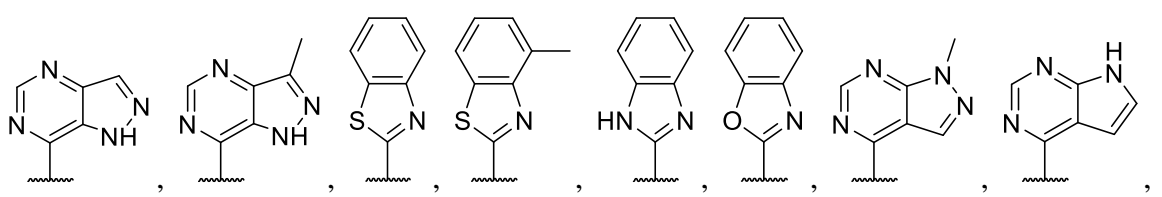
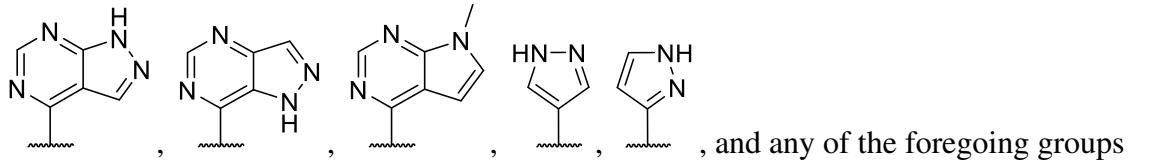


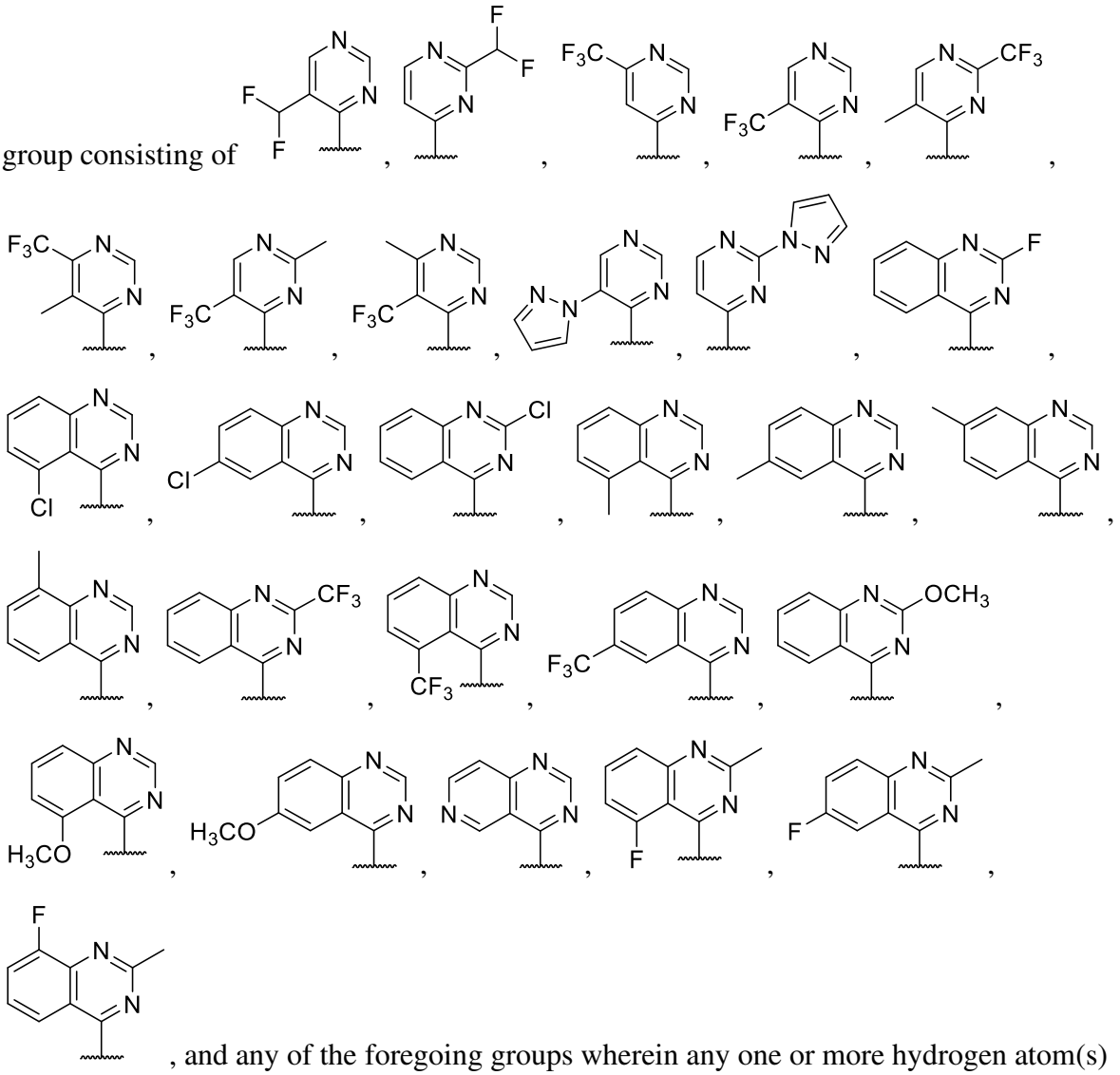
Claim 23. The compound of claim 1, or a salt thereof, wherein R^1 is , wherein m is 0, 1, 2, 3, 4, 5, or 6 and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl,

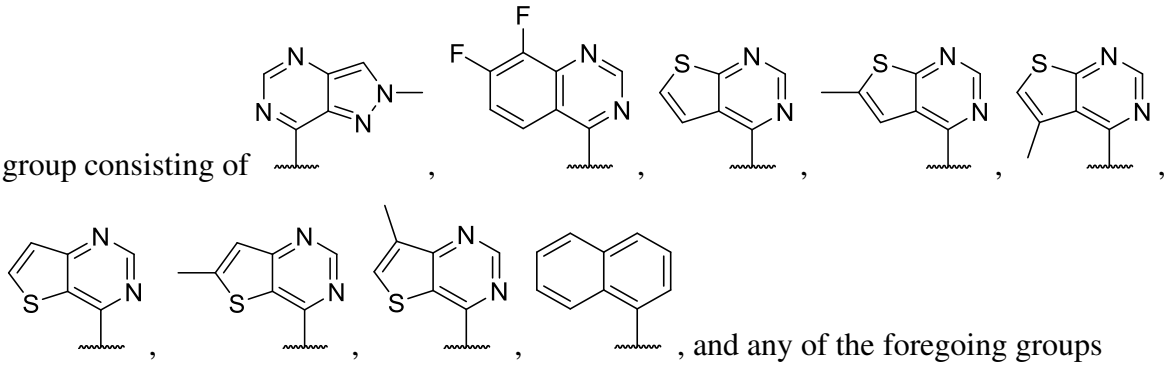
alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium.

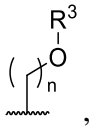
Claim 24. The compound of claim 1, or a salt thereof, wherein R^1 is  , wherein m is 0, 1, or 2 and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium.

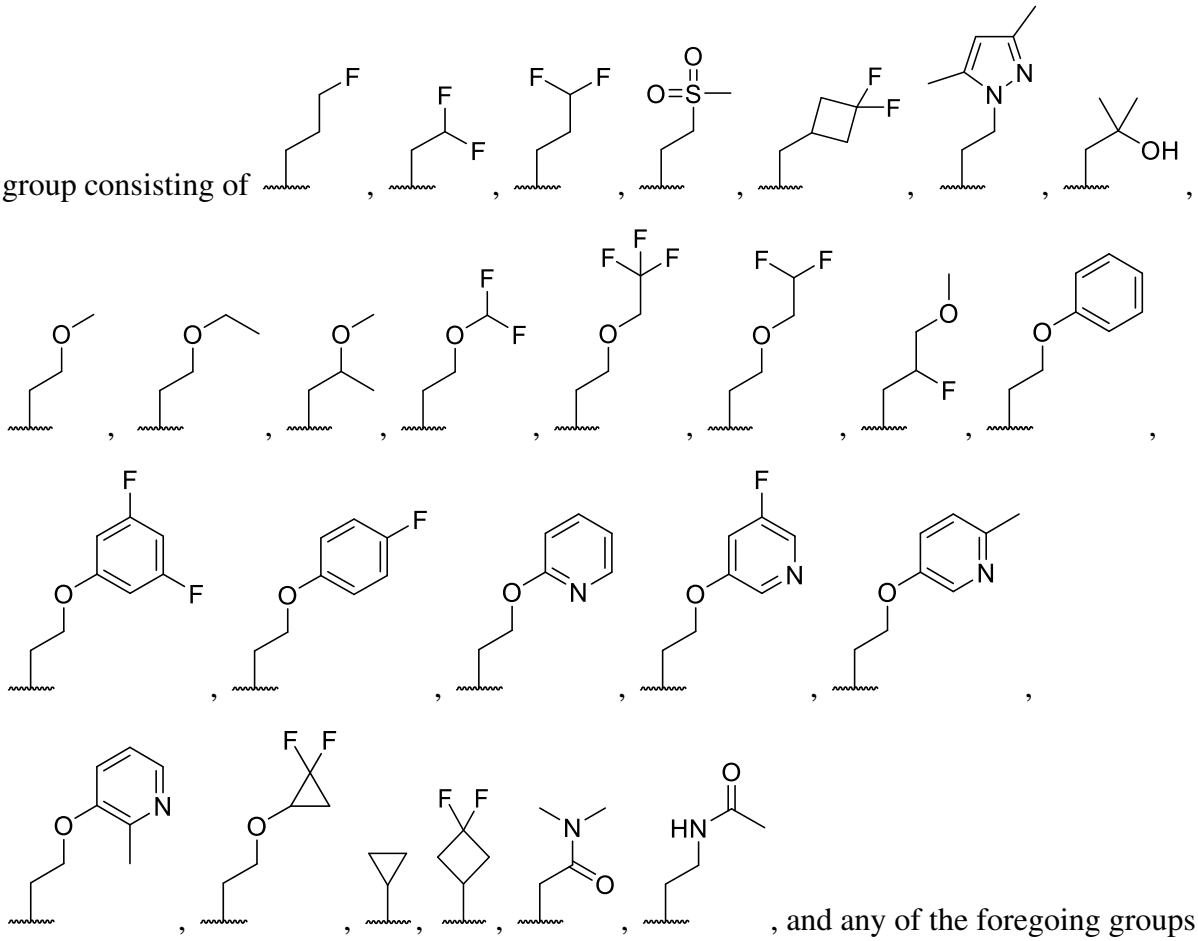
Claim 25. The compound of claim 1, or a salt thereof, wherein R^1 is selected from the group consisting of  , and any of the foregoing groups wherein any one or more hydrogen atom(s) are replaced with deuterium atom(s).

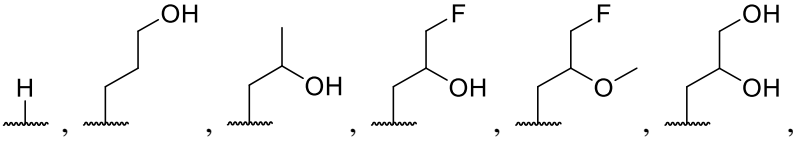
Claim 26. The compound of claim 1, or a salt thereof, wherein R^1 is selected from the group consisting of  ,  ,  ,  ,  ,  ,  , and any of the foregoing groups wherein any one or more hydrogen atom(s) are replaced with deuterium atom(s).

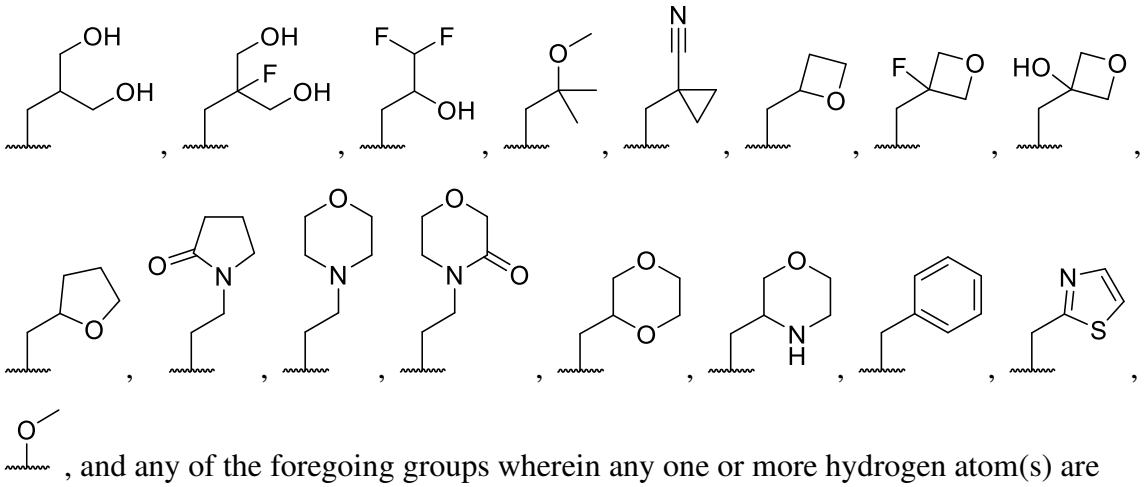
Claim 27. The compound of claim 1, or a salt thereof, wherein R^1 is selected from the group consisting of  , and any of the foregoing groups wherein any one or more hydrogen atom(s) are replaced with deuterium atom(s).

Claim 28. The compound of claim 1, or a salt thereof, wherein R^1 is selected from the group consisting of  , and any of the foregoing groups wherein any one or more hydrogen atom(s) are replaced with deuterium atom(s).

Claim 29. The compound of claim 1, or a salt thereof, wherein R^2 is  , wherein n is 1, 2, 3, 4, 5, or 6, and R^3 is: C_1-C_2 alkyl optionally substituted by fluoro; phenyl optionally substituted by fluoro; pyridinyl optionally substituted by fluoro or methyl; or cyclopropyl optionally substituted by fluoro.

Claim 30. The compound of claim 1, or a salt thereof, wherein R^2 is selected from the group consisting of  , and any of the foregoing groups wherein any one or more hydrogen atom(s) are replaced with deuterium atom(s).

Claim 31. The compound of claim 1, or a salt thereof, wherein R^2 is selected from the group consisting of  ,



, and any of the foregoing groups wherein any one or more hydrogen atom(s) are replaced with deuterium atom(s).

Claim 32. The compound of claim 1, or a salt thereof, wherein R^2 is:

a) C_3-C_5 alkyl substituted by both fluorine and -OCH_3,

b) C_1-C_6 alkyl optionally substituted by -OR^3, and each R^3 is independently: phenyl optionally substituted by fluorine; or pyridinyl optionally substituted by fluorine or methyl, or

c) C_1-C_6 alkyl substituted by R^{2a} wherein each R^{2a} is independently: halogen; deuterium; 3- to 12-membered heterocyclyl optionally substituted by oxo; C_6-C_{14} aryl optionally substituted by halogen or –OR^6; 5- to 10-membered heteroaryl optionally substituted by C_1-C_6 alkyl; C_3-C_8 cycloalkyl optionally substituted by -CN, halogen, or –OR^6; or -$S(O)_2R^3$.

Claim 33. The compound of claim 1, or a salt thereof, wherein R^1 is pyridyl, indazolyl, 1*H*-pyrrolopyridyl, quinolinyl, phenyl, or indanyl, each of which is optionally substituted by R^{1a}.

Claim 34. A compound of claim 1, or a salt thereof, selected from

4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-(difluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

4-((2-hydroxy-2-methylpropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

2-((7-fluoroquinazolin-4-yl) amino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((3,3-difluorocyclobutyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-methylquinazolin-4-yl) amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrido[2,3-d]pyrimidin-4-ylamino) butanoic acid;

2-((7-fluoro-2-methylquinazolin-4-yl) amino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((7-(trifluoromethyl)quinazolin-4-yl) amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(trifluoromethyl)quinazolin-4-yl) amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((8-(trifluoromethyl)quinazolin-4-yl) amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrido[3,2-d]pyrimidin-4-ylamino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrido[3,4-d]pyrimidin-4-ylamino) butanoic acid;

2-((5-fluoroquinazolin-4-yl) amino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-fluoroquinazolin-4-yl) amino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((8-fluoroquinazolin-4-yl) amino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6,7-difluoroquinazolin-4-yl) amino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-methyl-6-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

2-((6-(difluoromethyl)pyrimidin-4-yl) amino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-methyl-2-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

4-((2-(methylsulfonyl)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((3,3-difluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((3-fluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

2-((7-fluoro-2-methylquinazolin-4-yl) amino)-4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-(((3,3-difluorocyclobutyl)methyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((7-fluoro-2-methylquinazolin-4-yl) amino) butanoic acid;

2-(isoquinolin-1-ylamino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(difluoromethoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinolin-4-ylamino) butanoic acid;

2-((7-chloroquinazolin-4-yl) amino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((8-chloroquinazolin-4-yl) amino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-(quinazolin-4-ylamino)-4-((4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl) (2-(2,2,2-trifluoroethoxy)ethyl)amino) butanoic acid;

2-((7-fluoro-2-methylquinazolin-4-yl) amino)-4-((2-(4-fluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((3-fluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((7-methoxyquinazolin-4-yl) amino) butanoic acid;

(2S)-4-((2-(2,2-difluorocyclopropoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((7-fluoro-2-methylquinazolin-4-yl) amino) butanoic acid;

4-((3-fluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((8-methoxyquinazolin-4-yl) amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-methylquinazolin-4-yl) amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

2-((8-chloroquinazolin-4-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((2-(2,2-difluoroethoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

2-(pyrido[3,2-d]pyrimidin-4-ylamino)-4-((4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl) (2-(2,2,2-trifluoroethoxy)ethyl)amino) butanoic acid;

4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

2-((7-fluoro-2-methylquinazolin-4-yl) amino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrido[3,2-d]pyrimidin-4-ylamino) butanoic acid;

4-((2-ethoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

2-((7-fluoro-2-methylquinazolin-4-yl) amino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrido[3,2-d]pyrimidin-4-ylamino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrido[3,2-d]pyrimidin-4-ylamino) butanoic acid;

2-((7-fluoro-2-methylquinazolin-4-yl) amino)-4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((2-(dimethylamino)-2-oxoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

2-((7-fluoro-2-methylquinazolin-4-yl) amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid; or

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-methylquinazolin-4-yl) amino) butanoic acid.

Claim 35. A compound of claim 1, or a salt thereof, selected from

2-((3-cyanopyrazin-2-yl) amino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

4-((2-hydroxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

2-((3-cyanopyrazin-2-yl) amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-fluoropyrimidin-2-yl) amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1H-pyrazolo[4,3-d]pyrimidin-7-yl) amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrimidin-4-yl) amino) butanoic acid;

2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-(methylsulfonyl)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(methylsulfonyl)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((2-(methylsulfonyl)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(methylsulfonyl)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

4-((2-(methylsulfonyl)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrimidin-4-yl) amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl) amino)-4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-fluoropyrimidin-2-yl) amino) butanoic acid;

4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-methyl-2-(pyridin-4-yl) pyrimidin-4-yl) amino) butanoic acid;

4-((2-(4-fluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl)amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-(methylsulfonyl)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((2-(methylsulfonyl)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrimidin-4-yl) amino) butanoic acid;

(2S)-4-((oxetan-2-ylmethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((3-hydroxy-2-(hydroxymethyl)propyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((3,3-difluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((3,3-difluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

4-((3,3-difluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

4-((3,3-difluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl) amino)-4-((3,3-difluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((3-fluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

4-((3-fluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl) pyrimidin-2-yl) amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((2-(4-fluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(4-fluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

4-((2-(dimethylamino)-2-oxoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

4-((2-(dimethylamino)-2-oxoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrimidin-4-yl) amino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-(4-fluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((2-(4-fluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(dimethylamino)-2-oxoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl) amino)-4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid; or

4-(((3-fluorooxetan-3-yl) methyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid.

Claim 36. A compound, or a salt thereof, selected from

4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((7H-pyrrolo[2,3-d]pyrimidin-4-yl) amino)-4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-cyclopropylpyrimidin-2-yl) amino) butanoic acid;

4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-2-ylamino) butanoic acid;

4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrimidin-4-yl) amino) butanoic acid;

4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrimidin-4-yl) amino) butanoic acid;

2-((1H-pyrazolo[4,3-d]pyrimidin-7-yl) amino)-4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-methoxypyrimidin-4-yl) amino) butanoic acid;

4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yl) amino) butanoic acid;

4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl) amino)-4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yl) amino) butanoic acid;

4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-methyl-2-(pyridin-4-yl) pyrimidin-4-yl) amino) butanoic acid;

4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-phenylpyrimidin-4-yl) amino) butanoic acid;

2-((3-cyanopyrazin-2-yl) amino)-4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-fluoropyrimidin-2-yl) amino) butanoic acid;

4-((3,3-difluorocyclobutyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((3,3-difluorocyclobutyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridi n-2-yl) butyl)amino) butanoic acid;

4-((3,3-difluorocyclobutyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((3,3-difluorocyclobutyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((3,3-difluorocyclobutyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((3,3-difluorocyclobutyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((3,3-difluorocyclobutyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl) amino)-4-((3,3-difluorocyclobutyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((3,3-difluorocyclobutyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

4-((3,3-difluorocyclobutyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((3,3-difluorocyclobutyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((3,3-difluorocyclobutyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-phenylpyrimidin-4-yl) amino) butanoic acid;

2-((3-cyanopyrazin-2-yl) amino)-4-((3,3-difluorocyclobutyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((3,3-difluorocyclobutyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((5-methylpyrimidin-2-yl)amino)butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyridin-3-ylamino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyridin-2-ylamino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1H-pyrazolo[4,3-d]pyrimidin-7-yl) amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-methoxypyrimidin-4-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-methylpyrazin-2-yl) amino) butanoic acid;

2-((3-cyanopyrazin-2-yl) amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

2-((5-fluoropyrimidin-2-yl) amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((7-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl)amino) butanoic acid;

2-((6-(tert-butyl)pyrimidin-4-yl) amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl) amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

2-((6-(dimethylamino)pyrimidin-4-yl)amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinoxalin-2-ylamino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-methoxypyrazin-2-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-methyl-2-(pyridin-4-yl) pyrimidin-4-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-(pyridin-4-yl) pyrazin-2-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrazin-2-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl) amino)-2-((6-phenylpyrazin-2-yl)amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazol-5-yl) amino) butanoic acid;

2-(benzo[d]oxazol-2-ylamino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-benzo[d]imidazol-2-yl) amino) butanoic acid;

2-(benzo[d]thiazol-2-ylamino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yl) amino) butanoic acid;

2-((9H-purin-6-yl)amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyridin-2-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((4-phenylpyridin-2-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-indazol-3-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-indol-3-yl) amino) butanoic acid;

2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-(methylsulfonyl)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((2-(methylsulfonyl)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(methylsulfonyl)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-(methylsulfonyl)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((2-(methylsulfonyl)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((2-(methylsulfonyl)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(methylsulfonyl)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl) amino)-4-((2-(methylsulfonyl)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((3-cyanopyrazin-2-yl) amino)-4-((2-(methylsulfonyl)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(methylsulfonyl)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

4-((3,3-difluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((3,3-difluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((3,3-difluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((3,3-difluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((3,3-difluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((3,3-difluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((3,3-difluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl) amino)-4-((3,3-difluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((3,3-difluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

2-((3-cyanopyrazin-2-yl) amino)-4-((3,3-difluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((3,3-difluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yl) amino) butanoic acid;

4-((3,3-difluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

4-((3,3-difluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((3,3-difluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((3,3-difluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((3-fluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((3-fluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((3-fluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((3-fluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((3-fluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((3-fluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((3-fluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl) amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl) amino)butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl) amino)-4-((3-fluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((3-fluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

2-((3-cyanopyrazin-2-yl) amino)-4-((3-fluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((3-fluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yl) amino) butanoic acid;

4-((3-fluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

4-((3-fluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrimidi n-4-yl) amino) butanoic acid;

4-((3-fluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrimidi n-4-yl) amino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyridin-2-ylamino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl) amino)-4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

2-((3-cyanopyrazin-2-yl) amino)-4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((3-methyl-1H-pyrazolo[4,3-d]pyrimidin-7-yl) amino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyridin-2-yl) amino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((4-phenylpyridin-2-yl) amino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrazin-2-yl) amino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrimidin-4-yl) amino) butanoic acid;

2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl) amino)-4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

4-((2-(4-fluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((2-(4-fluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(4-fluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-(4-fluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((2-(4-fluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((2-(4-fluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(4-fluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl) amino)-4-((2-(4-fluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(4-fluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-(4-fluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-(4-fluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

4-((2-(4-fluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yl) amino) butanoic acid;

4-((2-ethoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((2-ethoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-ethoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-ethoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((2-ethoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((2-ethoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-ethoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl) amino)-4-((2-ethoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-ethoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

2-((3-cyanopyrazin-2-yl) amino)-4-((2-ethoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-ethoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-ethoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yl) amino) butanoic acid;

4-((2-ethoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

4-((2-ethoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-methylpyrimidin-2-yl)amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyridin-3-ylamino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-cyanopyrimidin-2-yl) amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-bromopyrimidin-2-yl) amino) butanoic acid;

2-((7H-pyrrolo[2,3-d]pyrimidin-4-yl) amino)-4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1H-pyrazolo[4,3-d]pyrimidin-7-yl) amino)-4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-methoxypyrimidin-4-yl) amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-(dimethylamino)pyrimidin-4-yl) amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-cyclopropylpyrimidin-2-yl) amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-(tert-butyl)pyrimidin-4-yl) amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((7-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl) amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((3-cyanopyrazin-2-yl) amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-methylpyrazin-2-yl) amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinoxalin-2-ylamino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-methyl-2-(pyridin-4-yl) pyrimidin-4-yl) amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yl) amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((4-phenylpyridin-2-yl) amino) butanoic acid;

2-([4,4'-bipyridin]-2-ylamino)-4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrazin-2-yl) amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrazin-2-yl) amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-(pyridin-4-yl) pyrazin-2-yl) amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

4-((2-(dimethylamino)-2-oxoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((2-(dimethylamino)-2-oxoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(dimethylamino)-2-oxoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-(dimethylamino)-2-oxoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((2-(dimethylamino)-2-oxoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1H-pyrazolo[4,3-d]pyrimidin-7-yl) amino)-4-((2-(dimethylamino)-2-oxoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((2-(dimethylamino)-2-oxoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(dimethylamino)-2-oxoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl) amino)-4-((2-(dimethylamino)-2-oxoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(dimethylamino)-2-oxoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-fluoropyrimidin-2-yl) amino) butanoic acid;

4-((2-(dimethylamino)-2-oxoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

2-((3-cyanopyrazin-2-yl) amino)-4-((2-(dimethylamino)-2-oxoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(dimethylamino)-2-oxoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-(dimethylamino)-2-oxoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-(dimethylamino)-2-oxoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-(dimethylamino)-2-oxoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-methyl-2-(pyridin-4-yl) pyrimidin-4-yl) amino) butanoic acid;

4-((2-(dimethylamino)-2-oxoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

4-((2-(dimethylamino)-2-oxoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((4-phenylpyridin-2-yl) amino) butanoic acid;

4-((2-(2,2-difluoroethoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((2-(2,2-difluoroethoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(2,2-difluoroethoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-(2,2-difluoroethoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((2-(2,2-difluoroethoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(2,2-difluoroethoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-methylpyrimidin-2-yl) amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyridin-3-ylamino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyridin-2-ylamino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1H-pyrazolo[4,3-d]pyrimidin-7-yl) amino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-methoxypyrimidin-4-yl) amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-methylpyrazin-2-yl) amino) butanoic acid;

2-((3-cyanopyrazin-2-yl) amino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

2-((5-fluoropyrimidin-2-yl) amino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((7-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl) amino) butanoic acid;

2-((6-(tert-butyl)pyrimidin-4-yl) amino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl) amino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

2-((6-(dimethylamino)pyrimidin-4-yl) amino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinoxalin-2-ylamino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-methoxypyrazin-2-yl) amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-methyl-2-(pyridin-4-yl) pyrimidin-4-yl) amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-(pyridin-4-yl) pyrazin-2-yl) amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrazin-2-yl) amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrazin-2-yl) amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazol-5-yl) amino) butanoic acid;

2-(benzo[d]oxazol-2-ylamino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-benzo[d]imidazol-2-yl) amino) butanoic acid;

2-(benzo[d]thiazol-2-ylamino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[4,3-d]pyrimidin-7-yl) amino) butanoic acid;

2-((9H-purin-6-yl) amino)-4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyridin-2-yl) amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((4-phenylpyridin-2-yl) amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-indazol-3-yl) amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-indol-3-yl) amino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinoxalin-2-ylamino) butanoic acid;

4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-methylpyrimidin-2-yl) amino) butanoic acid;

4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyridin-3-ylamino) butanoic acid;

2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyridin-2-ylamino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1H-pyrazolo[4,3-d]pyrimidin-7-yl) amino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((2-methoxypyrimidin-4-yl) amino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-methylpyrazin-2-yl) amino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((3-cyanopyrazin-2-yl) amino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

2-((5-fluoropyrimidin-2-yl) amino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((7-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl) amino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(tert-butyl)pyrimidin-4-yl) amino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl) amino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

2-((6-(dimethylamino)pyrimidin-4-yl) amino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinoxalin-2-ylamino) butanoic acid;

2-((5-methoxypyrazin-2-yl) amino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrimidin-4-yl) amino) butanoic acid;

2-((6-methyl-2-(pyridin-4-yl) pyrimidin-4-yl) amino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-(pyridin-4-yl) pyrazin-2-yl) amino) butanoic acid;

4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrazin-2-yl) amino) butanoic acid;

4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrazin-2-yl) amino) butanoic acid;

4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((4-phenylpyridin-2-yl) amino) butanoic acid;

4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((4-phenylpyridin-2-yl) amino) butanoic acid;

2-((9H-purin-6-yl) amino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1-methyl-1H-pyrazolo[4,3-d]pyrimidin-7-yl) amino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-(benzo[d]thiazol-2-ylamino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1-methyl-1H-benzo[d]imidazol-2-yl) amino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-(benzo[d]oxazol-2-ylamino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1-methyl-1H-pyrazol-5-yl) amino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1-methyl-1H-indazol-3-yl) amino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1-methyl-1H-indol-3-yl) amino)-4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-methylpyrimidin-2-yl) amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyridin-3-ylamino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyridin-2-ylamino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1H-pyrazolo[4,3-d]pyrimidin-7-yl) amino)-4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-methoxypyrimidin-4-yl) amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(dimethylamino)pyrimidin-4-yl) amino)-4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl) amino)-4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(tert-butyl)pyrimidin-4-yl) amino)-4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((7-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl) amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-fluoropyrimidin-2-yl) amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

2-((3-cyanopyrazin-2-yl) amino)-4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-methylpyrazin-2-yl) amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrazin-2-yl) amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrazin-2-yl) amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-(pyridin-4-yl) pyrazin-2-yl) amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-methyl-2-(pyridin-4-yl) pyrimidin-4-yl) amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-methoxypyrazin-2-yl) amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinoxalin-2-ylamino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((4-phenylpyridin-2-yl) amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyridin-2-yl) amino) butanoic acid;

2-((9H-purin-6-yl) amino)-4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[4,3-d]pyrimidin-7-yl) amino) butanoic acid;

2-(benzo[d]thiazol-2-ylamino)-4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-benzo[d]imidazol-2-yl) amino) butanoic acid;

2-(benzo[d]oxazol-2-ylamino)-4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazol-5-yl) amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-indazol-3-yl) amino) butanoic acid;

4-((2-((5-fluoropyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-indol-3-yl) amino) butanoic acid;

4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-methylpyrimidin-2-yl) amino) butanoic acid;

4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyridin-3-ylamino) butanoic acid;

2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyridin-2-ylamino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1H-pyrazolo[4,3-d]pyrimidin-7-yl) amino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((2-methoxypyrimidin-4-yl) amino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-methylpyrazin-2-yl) amino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((3-cyanopyrazin-2-yl) amino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

2-((5-fluoropyrimidin-2-yl) amino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((7-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl) amino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(tert-butyl)pyrimidin-4-yl) amino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl) amino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

2-((6-(dimethylamino)pyrimidin-4-yl) amino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinoxalin-2-ylamino) butanoic acid;

2-((5-methoxypyrazin-2-yl) amino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrimidin-4-yl) amino) butanoic acid;

2-((6-methyl-2-(pyridin-4-yl) pyrimidin-4-yl) amino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-(pyridin-4-yl) pyrazin-2-yl) amino) butanoic acid;

4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrazin-2-yl) amino) butanoic acid;

4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrazin-2-yl) amino) butanoic acid;

2-((1-methyl-1H-pyrazol-5-yl) amino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-(benzo[d]oxazol-2-ylamino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1-methyl-1H-benzo[d]imidazol-2-yl) amino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-(benzo[d]thiazol-2-ylamino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1-methyl-1H-pyrazolo[4,3-d]pyrimidin-7-yl) amino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((9H-purin-6-yl) amino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyridin-2-yl) amino) butanoic acid;

4-((2-((2-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyridin-2-yl) amino) butanoic acid;

2-((1-methyl-1H-indazol-3-yl) amino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1-methyl-1H-indol-3-yl) amino)-4-((2-((6-methylpyridin-3-yl) oxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-methylpyrimidin-2-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyridin-3-ylamino) butanoic acid;

2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

2-(pyridin-2-ylamino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1H-pyrazolo[4,3-d]pyrimidin-7-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((2-methoxypyrimidin-4-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-methylpyrazin-2-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((3-cyanopyrazin-2-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

2-((5-fluoropyrimidin-2-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((7-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(tert-butyl)pyrimidin-4-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

2-((6-(dimethylamino)pyrimidin-4-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinoxalin-2-ylamino) butanoic acid;

2-((5-methoxypyrazin-2-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-phenylpyrimidin-4-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((2-phenylpyrimidin-4-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-phenylpyrimidin-4-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-methyl-2-(pyridin-4-yl) pyrimidin-4-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-(pyridin-4-yl) pyrazin-2-yl) amino) butanoic acid;

2-((5-phenylpyrazin-2-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-phenylpyrazin-2-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1-methyl-1H-pyrazol-5-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-(benzo[d]oxazol-2-ylamino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1-methyl-1H-benzo[d]imidazol-2-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-(benzo[d]thiazol-2-ylamino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1-methyl-1H-pyrazolo[4,3-d]pyrimidin-7-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((9H-purin-6-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-phenylpyridin-2-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((4-phenylpyridin-2-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1-methyl-1H-indol-3-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1-methyl-1H-indazol-3-yl) amino)-4-((2-(pyridin-2-yloxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-methylpyrimidin-2-yl) amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyridin-3-ylamino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyridin-2-ylamino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1H-pyrazolo[4,3-d]pyrimidin-7-yl) amino)-4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-methoxypyrimidin-4-yl) amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-methylpyrazin-2-yl) amino) butanoic acid;

2-((3-cyanopyrazin-2-yl) amino)-4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-fluoropyrimidin-2-yl) amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((7-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl) amino) butanoic acid;

2-((6-(tert-butyl)pyrimidin-4-yl) amino)-4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl) amino)-4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-(dimethylamino)pyrimidin-4-yl) amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinoxalin-2-ylamino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-methoxypyrazin-2-yl) amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-methyl-2-(pyridin-4-yl) pyrimidin-4-yl) amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-(pyridin-4-yl) pyrazin-2-yl) amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrazin-2-yl) amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrazin-2-yl) amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazol-5-yl) amino) butanoic acid;

2-(benzo[d]oxazol-2-ylamino)-4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-benzo[d]imidazol-2-yl) amino) butanoic acid;

2-(benzo[d]thiazol-2-ylamino)-4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[4,3-d]pyrimidin-7-yl) amino) butanoic acid;

2-((9H-purin-6-yl) amino)-4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyridin-2-yl) amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((4-phenylpyridin-2-yl) amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-indazol-3-yl) amino) butanoic acid;

4-((2-(3,5-difluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-indol-3-yl) amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-methylpyrimidin-2-yl) amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyridin-3-ylamino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyridin-2-ylamino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((1H-pyrazolo[4,3-d]pyrimidin-7-yl) amino)-4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-methoxypyrimidin-4-yl) amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-methylpyrazin-2-yl) amino) butanoic acid;

2-((3-cyanopyrazin-2-yl) amino)-4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-fluoropyrimidin-2-yl) amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((7-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl) amino) butanoic acid;

2-((6-(tert-butyl)pyrimidin-4-yl) amino)-4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl) amino)-4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-(dimethylamino)pyrimidin-4-yl) amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinoxalin-2-ylamino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-methoxypyrazin-2-yl) amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-methyl-2-(pyridin-4-yl) pyrimidin-4-yl) amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-(pyridin-4-yl) pyrazin-2-yl) amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrazin-2-yl) amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrazin-2-yl) amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazol-5-yl) amino) butanoic acid;

2-(benzo[d]oxazol-2-ylamino)-4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-benzo[d]imidazol-2-yl) amino) butanoic acid;

2-(benzo[d]thiazol-2-ylamino)-4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-pyrazolo[4,3-d]pyrimidin-7-yl) amino) butanoic acid;

2-((9H-purin-6-yl) amino)-4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyridin-2-yl) amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((4-phenylpyridin-2-yl) amino) butanoic acid;

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-indazol-3-yl) amino) butanoic acid; or

4-((2-(3,5-dimethyl-1H-pyrazol-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-indol-3-yl) amino) butanoic acid.

Claim 37. A compound, or a salt thereof, selected from

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((2-methoxyethyl) (5-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) pentyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinoxalin-2-ylamino) butanoic acid;

(2S)-2-(quinazolin-4-ylamino)-4-((4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl) ((tetrahydrofuran-2-yl) methyl)amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((3-fluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((3,3-difluoropropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

2-((6-(dimethylamino)pyrimidin-4-yl) amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(tert-butyl)pyrimidin-4-yl) amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((7-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl) amino) butanoic acid;

2-((2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yl) amino)-4-((2-phenoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2,2-difluoroethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyridin-2-ylamino) butanoic acid;

4-((2-(dimethylamino)-2-oxoethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yl)amino)butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yl) amino) butanoic acid;

4-((2-fluoro-3-hydroxy-2-(hydroxymethyl)propyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((3-hydroxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((2-(4-fluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrazin-2-yl) amino) butanoic acid;

4-((2-(2-oxopyrrolidin-1-yl) ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

2-((3-cyanopyrazin-2-yl) amino)-4-(cyclopropyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((3-cyanopyrazin-2-yl) amino)-4-((2-(4-fluorophenoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(benzo[d]thiazol-2-ylamino) butanoic acid;

2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl) (2-(2,2,2-trifluoroethoxy)ethyl)amino) butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl) amino)-4-((2-(2,2-difluoroethoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(2,2-difluoroethoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-(2,2-difluoroethoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-(2,2-difluoroethoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-(pyridin-3-yl) quinazolin-4-yl) amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((2-(2,2-difluoroethoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(2,2-difluoroethoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrimidin-4-ylamino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-methoxypyrimidin-4-yl) amino) butanoic acid;

2-((6-(dimethylamino)pyrimidin-4-yl) amino)-4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((6-(tert-butyl)pyrimidin-4-yl) amino)-4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-phenylpyrimidin-4-yl) amino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-phenylpyrazin-2-yl) amino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-phenylpyrazin-2-yl) amino) butanoic acid;

4-((4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl) (2-(2,2,2-trifluoroethoxy)ethyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl) amino) butanoic acid;

2-((5-cyanopyrimidin-2-yl) amino)-4-((4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl) (2-(2,2,2-trifluoroethoxy)ethyl)amino) butanoic acid;

2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl) amino)-4-((4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl) (2-(2,2,2-trifluoroethoxy)ethyl)amino) butanoic acid;

2-((5-bromopyrimidin-2-yl) amino)-4-((4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl) (2-(2,2,2-trifluoroethoxy)ethyl)amino) butanoic acid;

4-((4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl) (2-(2,2,2-trifluoroethoxy)ethyl)amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl) amino) butanoic acid;

2-((5-cyclopropylpyrimidin-2-yl) amino)-4-((4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl) (2-(2,2,2-trifluoroethoxy)ethyl)amino) butanoic acid;

2-((3-cyanopyrazin-2-yl) amino)-4-((4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl) (2-(2,2,2-trifluoroethoxy)ethyl)amino) butanoic acid;

2-((2-(pyridin-3-yl) quinazolin-4-yl) amino)-4-((4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl) (2-(2,2,2-trifluoroethoxy)ethyl)amino) butanoic acid;

2-((6-phenylpyrimidin-4-yl) amino)-4-((4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl) (2-(2,2,2-trifluoroethoxy)ethyl)amino) butanoic acid;

2-((5-phenylpyrimidin-4-yl) amino)-4-((4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl) (2-(2,2,2-trifluoroethoxy)ethyl)amino) butanoic acid;

2-(pyrimidin-4-ylamino)-4-((4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl) (2-(2,2,2-trifluoroethoxy)ethyl)amino) butanoic acid;

2-((6-(1H-pyrazol-1-yl) pyrimidin-4-yl) amino)-4-((4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl) (2-(2,2,2-trifluoroethoxy)ethyl)amino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-methylpyrimidin-2-yl) amino) butanoic acid;

2-((3-cyanopyrazin-2-yl) amino)-4-((2-(2,2-difluoroethoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-([4,4'-bipyridin]-2-ylamino)-4-((2-(2,2-difluoroethoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-(2,2-difluoroethoxy)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((4-phenylpyridin-2-yl) amino) butanoic acid;

(S)-4-((2-(2,2-difluoroethoxy)ethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((5-phenylpyridin-2-yl)amino)butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((7-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl) amino) butanoic acid;

4-((2-fluoro-3-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((6-methylpyrazin-2-yl)amino)butanoic acid;

4-((2-fluoro-3-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(quinoxalin-2-ylamino)butanoic acid;

4-((2-fluoro-3-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((6-methyl-2-(pyridin-4-yl)pyrimidin-4-yl)amino)butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((1-methyl-1H-indazol-3-yl) amino) butanoic acid;

4-((2-acetamidoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(benzo[d]thiazol-2-ylamino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyridin-3-ylamino) butanoic acid;

4-((2-methoxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(naphthalen-1-ylamino)butanoic acid;

4-((2-morpholinoethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

(2S)-4-((2,3-dihydroxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((2-methoxyethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(naphthalen-1-ylamino) butanoic acid;

(2S)-4-((3-fluoro-2-hydroxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

2-(quinazolin-4-ylamino)-4-((4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl) (thiazol-2-ylmethyl)amino) butanoic acid;

4-((2-(3-oxomorpholino)ethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-(benzyl(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((2-hydroxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

(2S)-4-(((1,4-dioxan-2-yl) methyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((3-fluoro-2-hydroxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((2-hydroxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

(2S)-4-((morpholin-3-ylmethyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

(2S)-4-((3,3-difluoro-2-hydroxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((2,3-dihydroxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((2-hydroxy-2-methylpropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrido[2,3-d]pyrimidin-4-ylamino) butanoic acid;

4-((2-hydroxy-2-methylpropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrido[3,2-d]pyrimidin-4-ylamino) butanoic acid;

2-((7-fluoro-2-methylquinazolin-4-yl) amino)-4-((2-hydroxy-2-methylpropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-hydroxy-2-methylpropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((2-fluoro-3-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrido[3,2-d]pyrimidin-4-ylamino) butanoic acid;

4-(methoxy(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((2-methoxy-2-methylpropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

2-((7-fluoro-2-methylquinazolin-4-yl) amino)-4-((2-methoxy-2-methylpropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-(((3-hydroxyoxetan-3-yl) methyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((2-methoxy-2-methylpropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrido[2,3-d]pyrimidin-4-ylamino) butanoic acid;

4-((2-methoxy-2-methylpropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(pyrido[3,2-d]pyrimidin-4-ylamino) butanoic acid;

4-((2-methoxy-2-methylpropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-methylquinazolin-4-yl) amino) butanoic acid;

4-(((1-cyanocyclopropyl)methyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((3-fluoro-2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(quinazolin-4-ylamino) butanoic acid;

4-((3-fluoro-2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((2-methylquinazolin-4-yl) amino) butanoic acid;

4-((3-fluoro-2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((7-fluoro-2-methylquinazolin-4-yl) amino) butanoic acid;

2-(quinazolin-4-ylamino)-4-((4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((8-fluoroquinazolin-4-yl) amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((7-fluoroquinazolin-4-yl) amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((8-methylquinazolin-4-yl) amino) butanoic acid;

4-((3-fluoro-2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((7-methylquinazolin-4-yl) amino) butanoic acid;

4-((3-fluoro-2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((7-fluoroquinazolin-4-yl) amino) butanoic acid;

4-((3-fluoro-2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((8-methylquinazolin-4-yl) amino) butanoic acid;

4-((3-fluoro-2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((8-fluoroquinazolin-4-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((7-methylquinazolin-4-yl) amino) butanoic acid;

2-((6-fluoroquinazolin-4-yl) amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((3-fluoro-2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-fluoroquinazolin-4-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(thieno[2,3-d]pyrimidin-4-ylamino) butanoic acid;

4-((3-fluoro-2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(thieno[2,3-d]pyrimidin-4-ylamino) butanoic acid;

4-((3-fluoro-2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-methylthieno[2,3-d]pyrimidin-4-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-methylthieno[2,3-d]pyrimidin-4-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(thieno[3,2-d]pyrimidin-4-ylamino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-methylthieno[3,2-d]pyrimidin-4-yl) amino) butanoic acid;

4-((3-fluoro-2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-(thieno[3,2-d]pyrimidin-4-ylamino) butanoic acid;

4-((3-fluoro-2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((6-methylthieno[3,2-d]pyrimidin-4-yl) amino) butanoic acid;

4-((3-fluoro-2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-methylthieno[2,3-d]pyrimidin-4-yl) amino) butanoic acid;

4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((5-methylthieno[2,3-d]pyrimidin-4-yl) amino) butanoic acid;

2-((7,8-difluoroquinazolin-4-yl) amino)-4-((3-fluoro-2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

2-((7,8-difluoroquinazolin-4-yl) amino)-4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino) butanoic acid;

4-((3-fluoro-2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((7-methylthieno[3,2-d]pyrimidin-4-yl) amino) butanoic acid; or

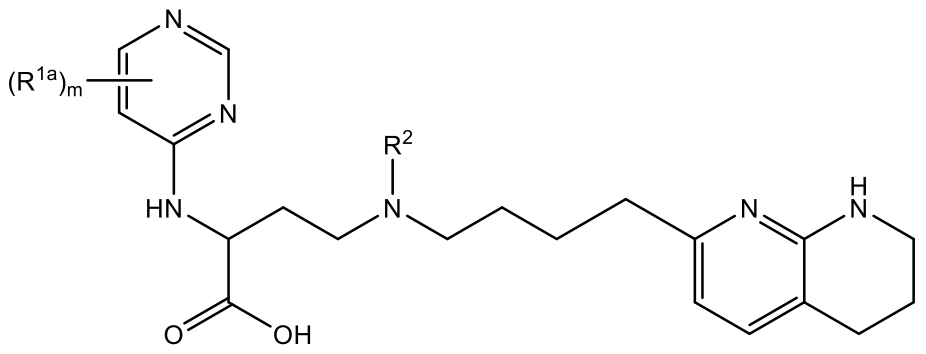
4-((2-methoxypropyl) (4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl) butyl)amino)-2-((7-methylthieno[3,2-d]pyrimidin-4-yl) amino) butanoic acid.

Claim 38. A pharmaceutical composition comprising a compound of claim 1, or a salt thereof, and a pharmaceutically acceptable carrier or excipient.

Claim 39. A kit comprising a compound of claim 1, or a pharmaceutically acceptable salt thereof.

Claim 40. The kit of claim 39, further comprising instructions for the treatment of a fibrotic disease.

Claim 41. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is of the formula (II-A):



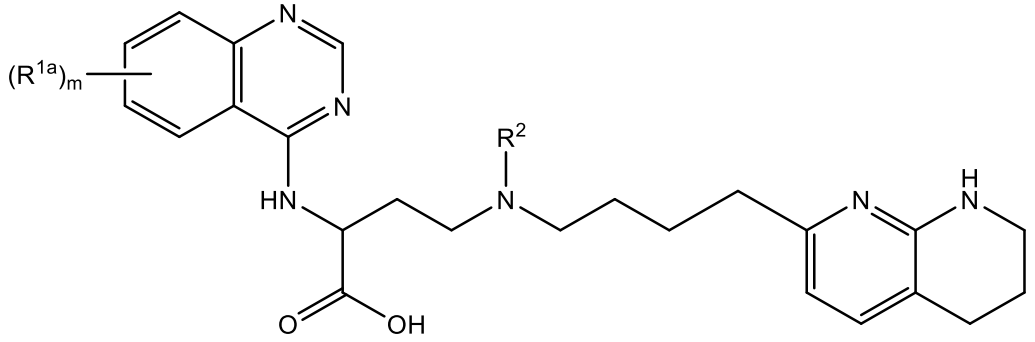
(II-A),

where m is 0, 1, 2, or 3.

Claim 42. **(Allowed)** The compound of claim 1, wherein the compound is selected from:
(S)-2-((5-fluoropyrimidin-2-yl)amino)-4-(((R)-2-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid;
(S)-2-((5-cyanopyrimidin-2-yl)amino)-4-(((S)-2-fluoro-3-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid;
(S)-4-(((S)-2-fluoro-3-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)butanoic acid;
(S)-2-((5-bromopyrimidin-2-yl)amino)-4-(((S)-2-fluoro-3-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid;
(S)-4-(((S)-2-fluoro-3-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((2-(trifluoromethyl)pyrimidin-4-yl)amino)butanoic acid;
(S)-2-((6-(1H-pyrazol-1-yl)pyrimidin-4-yl)amino)-4-(((S)-2-fluoro-3-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid;
(S)-4-(((S)-2-fluoro-3-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((5-phenylpyrimidin-4-yl)amino)butanoic acid;
(S)-2-((5-cyclopropylpyrimidin-2-yl)amino)-4-(((R)-2-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid;
(S)-4-(((S)-2-fluoro-3-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(pyrimidin-4-ylamino)butanoic acid;
(S)-4-(((S)-2-fluoro-3-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((6-phenylpyrimidin-4-yl)amino)butanoic acid;

(S)-2-((5-cyclopropylpyrimidin-2-yl)amino)-4-(((S)-2-fluoro-3-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid;
(S)-4-((2-phenoxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((5-phenylpyrimidin-4-yl)amino)butanoic acid;
(S)-4-((2-(4-fluorophenoxy)ethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((5-phenylpyrimidin-4-yl)amino)butanoic acid;
(S)-2-((3-cyanopyrazin-2-yl)amino)-4-((2-ethoxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid;
(S)-2-((6-(1H-pyrazol-1-yl)pyrimidin-4-yl)amino)-4-((3-fluoropropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid; and
(S)-2-((3-cyanopyrazin-2-yl)amino)-4-((2-(4-fluorophenoxy)ethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid,
or a pharmaceutically acceptable salt thereof.

Claim 43. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is of the formula (II-B):



(II-B),

where m is 0, 1, 2, 3, 4, or 5.

Claim 44. **(Allowed)** The compound of claim 1, wherein the compound is selected from:
(S)-2-((7-fluoroquinazolin-4-yl)amino)-4-((2-methoxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid;
(S)-2-((7-fluoro-2-methylquinazolin-4-yl)amino)-4-((2-methoxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid;
(S)-4-((2-methoxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((8-(trifluoromethyl)quinazolin-4-yl)amino)butanoic acid;

(S)-2-((6-fluoroquinazolin-4-yl)amino)-4-((2-methoxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid;
(S)-2-((6,7-difluoroquinazolin-4-yl)amino)-4-((2-methoxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid;
(S)-2-((7-fluoro-2-methylquinazolin-4-yl)amino)-4-((2-(4-fluorophenoxy)ethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid;
(2S)-4-((2-(2,2-difluorocyclopropoxy)ethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((7-fluoro-2-methylquinazolin-4-yl)amino)butanoic acid;
(S)-4-(((S)-3-fluoro-2-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((2-methylquinazolin-4-yl)amino)butanoic acid;
(S)-2-((8-fluoroquinazolin-4-yl)amino)-4-(((R)-2-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid;
(S)-2-((7-fluoroquinazolin-4-yl)amino)-4-(((R)-2-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid;
(S)-4-(((R)-2-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((8-methylquinazolin-4-yl)amino)butanoic acid;
(S)-2-((7,8-difluoroquinazolin-4-yl)amino)-4-(((R)-2-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid;
(S)-4-((2-methoxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(quinazolin-4-ylamino)butanoic acid;
(S)-4-((2-phenoxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(quinazolin-4-ylamino)butanoic acid;
(S)-4-((2-(3,5-difluorophenoxy)ethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(quinazolin-4-ylamino)butanoic acid;
(S)-4-((2-(pyridin-2-yloxy)ethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(quinazolin-4-ylamino)butanoic acid;
(S)-4-((2-(2,2-difluoroethoxy)ethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(quinazolin-4-ylamino)butanoic acid;
(S)-4-((2-((6-methylpyridin-3-yl)oxy)ethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(quinazolin-4-ylamino)butanoic acid;
(S)-4-(((R)-2-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(quinazolin-4-ylamino)butanoic acid;

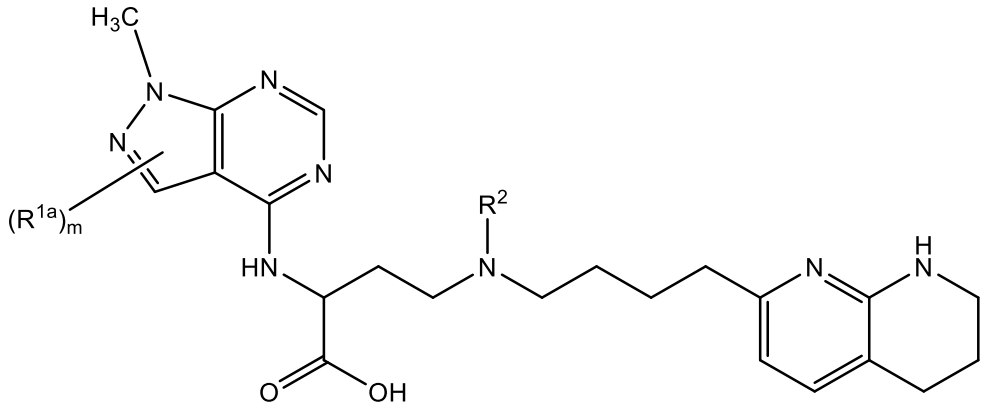
(S)-4-((2-hydroxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(quinazolin-4-ylamino)butanoic acid;

(S)-4-(((R)-2-hydroxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(quinazolin-4-ylamino)butanoic acid; and

(S)-4-(((S)-2,3-dihydroxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(quinazolin-4-ylamino)butanoic acid,

or a pharmaceutically acceptable salt thereof.

Claim 45. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is of the formula (II-H):



(II-H),

where m is 0, 1, or 2.

Claim 46. **(Allowed)** The compound of claim 1, wherein the compound is selected from:

(S)-4-(((R)-2-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)amino)butanoic acid;

(S)-2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl)amino)-4-((2-phenoxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid;

(S)-2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl)amino)-4-((2-(4-fluorophenoxy)ethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid;

(S)-4-((2-(4-fluorophenoxy)ethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yl)amino)butanoic acid;

(S)-4-((2-ethoxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yl)amino)butanoic acid;

(S)-4-((2-(2,2-difluoroethoxy)ethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)amino)butanoic acid;

(S)-2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl)amino)-4-((2-(2,2-difluoroethoxy)ethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid;
(S)-2-((2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yl)amino)-4-((2-phenoxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid;
(S)-2-((1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)amino)-4-((4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)(2-(2,2,2-trifluoroethoxy)ethyl)amino)butanoic acid;
(S)-2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl)amino)-4-((4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)(2-(2,2,2-trifluoroethoxy)ethyl)amino)butanoic acid;
(S)-4-(((R)-2-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(thieno[2,3-d]pyrimidin-4-ylamino)butanoic acid;
(S)-4-(((S)-3-fluoro-2-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(thieno[2,3-d]pyrimidin-4-ylamino)butanoic acid;
(S)-4-(((R)-2-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(thieno[3,2-d]pyrimidin-4-ylamino)butanoic acid;
(S)-4-(((S)-3-fluoro-2-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(thieno[3,2-d]pyrimidin-4-ylamino)butanoic acid;
(S)-4-(((S)-3-fluoro-2-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((6-methylthieno[3,2-d]pyrimidin-4-yl)amino)butanoic acid; and
(S)-4-(((R)-2-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((5-methylthieno[2,3-d]pyrimidin-4-yl)amino)butanoic acid,
or a pharmaceutically acceptable salt thereof.

Claim 47. **(Allowed)** The compound of claim 1, wherein the compound is (S)-2-((7-fluoro-2-methylquinazolin-4-yl)amino)-4-((2-(4-fluorophenoxy)ethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid, or a pharmaceutically acceptable salt thereof.

Claim 48. The compound of claim 1, wherein the compound is (S)-4-((2-hydroxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(quinazolin-4-ylamino)butanoic acid, or a pharmaceutically acceptable salt thereof.

Claim 49. The compound of claim 1, wherein the compound is (S)-4-((2-methoxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(quinazolin-4-ylamino)butanoic acid, or a pharmaceutically acceptable salt thereof.

Claim 50. The compound of claim 1, wherein the compound is (S)-4-((2-(3,5-difluorophenoxy)ethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(quinazolin-4-ylamino)butanoic acid, or a pharmaceutically acceptable salt thereof.

Claim 51. The compound of claim 1, wherein the compound is (S)-4-((2-phenoxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((5-phenylpyrimidin-4-yl)amino)butanoic acid, or a pharmaceutically acceptable salt thereof.

Claim 52. The compound of claim 1, wherein the compound is (S)-4-((2-(4-fluorophenoxy)ethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((5-phenylpyrimidin-4-yl)amino)butanoic acid, or a pharmaceutically acceptable salt thereof.

Claim 53. The compound of claim 1, wherein the compound is (S)-2-((6-(1H-pyrazol-1-yl)pyrimidin-4-yl)amino)-4-((3-fluoropropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid, or a pharmaceutically acceptable salt thereof.

Claim 54. The compound of claim 1, wherein the compound is (S)-4-(((S)-3-fluoro-2-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(thieno[2,3-d]pyrimidin-4-ylamino)butanoic acid, or a pharmaceutically acceptable salt thereof.

Claim 55. The compound of claim 1, wherein the compound is (S)-2-((2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yl)amino)-4-((2-phenoxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid, or a pharmaceutically acceptable salt thereof.

Claim 56. The compound of claim 1, wherein the compound is (S)-2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl)amino)-4-((2-phenoxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid, or a pharmaceutically acceptable salt thereof.

Claim 57. The compound of claim 1, wherein the compound is (S)-2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl)amino)-4-((2-(4-fluorophenoxy)ethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid, or a pharmaceutically acceptable salt thereof.

Claim 58. The compound of claim 1, wherein the compound is (S)-4-((2-(4-fluorophenoxy)ethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yl)amino)butanoic acid, or a pharmaceutically acceptable salt thereof.

Claim 59. The compound of claim 1, or a salt thereof, wherein R^1 is pyrimidin-4-yl optionally substituted by R^{1a}, wherein each R^{1a} is independently pyrazolyl, methyl, difluoromethyl, or trifluoromethyl.

Claim 60. The compound of claim 1, or a salt thereof, wherein R^1 is pyrimidin-4-yl substituted by both methyl and trifluoromethyl.

Claim 61. The compound of claim 1, or a salt thereof, wherein R^1 is quinazolin-4-yl optionally substituted by R^{1a}, wherein each R^{1a} is independently fluoro, chloro, methyl, trifluoromethyl or methoxy.

Claim 62. The compound of claim 1, or a salt thereof, wherein R^2 is C_1-C_6 alkyl optionally substituted by:

R^{2a}, wherein each R^{2a} is independently: fluoro, cyclobutyl substituted by fluoro, pyrazolyl substituted by methyl, or $-S(O)_2CH_3$; or

$-OR^3$, wherein each R^3 is independently: methyl, ethyl, difluoromethyl, $-CH_2CHF_2$, $-CH_2CF_3$, cyclopropyl substituted by fluoro, phenyl optionally substituted by fluoro, or pyridinyl optionally substituted by fluoro or methyl.

Claim 63. The compound of claim 1, or a salt thereof, wherein R^2 is $–CH_2CH_2OCH_3$.

Claim 64. The compound of claim 1, or a salt thereof, wherein R^2 is C_1-C_6 alkyl substituted by both halogen and $-OR^3$, wherein each R^3 is independently C_1-C_6 alkyl.

Claim 65. The compound of claim 1, or a salt thereof, wherein R^2 is C_3-C_6 cycloalkyl optionally substituted by R^{2b}.

Claim 66. The compound of claim 1, or a salt thereof, wherein R^2 is C_1-C_6 alkyl optionally substituted by cyclopropyl.

Claim 67. The compound of claim 1, or a salt thereof, wherein R^2 is C_1-C_6 alkyl substituted by R^{2a} wherein each R^{2a} is independently: 4- to 5-membered heterocyclyl optionally substituted by oxo; phenyl optionally substituted by halogen or $–OR^6$; or pyrazolyl optionally substituted by methyl.

Claim 68. The compound of claim 1, or a salt thereof, wherein R^1 is:

pyrimidin-2-yl, pyrimidin-4-yl, quinazolin-4-yl, 1H-pyrazolo[3,4-d]pyrimidin-4-yl, 1H-pyrazolo[4,3-d]pyrimidin-7-yl, pyrazin-2-yl, quinolin-4-yl, pyrido[2,3-d]pyrimidin-4-yl, pyrido[3,2-d]pyrimidin-4-yl, pyrido[3,4-d]pyrimidin-4-yl, thieno[2,3-d]pyrimidin-4-yl, thieno[3,2-d]pyrimidin-4-yl, thienopyrimidin-4-yl, pyridin-2-yl, pyridin-3-yl, 7H-pyrrolo[2,3-d]pyrimidin-4-yl, quinoxalin-2-yl, 1H-indazol-3-yl, benzo[d]thiazol-2-yl, naphthalen-1-yl, 9H-purin-6-yl, or isoquinolin-1-yl; and

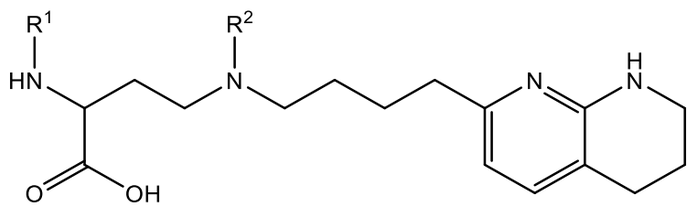
wherein R^1 is optionally substituted by methyl and fluoro.

Claim 69. The compound of claim 1, or a salt thereof, wherein R^1 is:

pyrimidin-2-yl, pyrimidin-4-yl, quinazolin-4-yl, 1H-pyrazolo[3,4-d]pyrimidin-4-yl, 1H-pyrazolo[4,3-d]pyrimidin-7-yl, pyrazin-2-yl, quinolin-4-yl, pyrido[2,3-d]pyrimidin-4-yl, pyrido[3,2-d]pyrimidin-4-yl, pyrido[3,4-d]pyrimidin-4-yl, thieno[2,3-d]pyrimidin-4-yl, thieno[3,2-d]pyrimidin-4-yl, thienopyrimidin-4-yl, pyridin-2-yl, pyridin-3-yl, 7H-pyrrolo[2,3-d]pyrimidin-4-yl, quinoxalin-2-yl, 1H-indazol-3-yl, benzo[d]thiazol-2-yl, naphthalen-1-yl, 9H-purin-6-yl, or isoquinolin-1-yl; and

wherein R^1 is optionally substituted by methyl and trifluoromethyl.

1. Un compuesto de fórmula (II):



(II);

o una sal del mismo, en donde:

R^1 es C_6-C_{14} arilo o heteroarilo de 5 a 10 miembros en donde el C_6-C_{14} arilo y el heteroarilo de 5 a 10 miembros están opcionalmente sustituidos con R^{1a};

R^2 es hidrógeno; deuterio; C_1-C_6 alquilo opcionalmente sustituido con R^{2a}; -OH; -O-C_1-C_6 alquilo opcionalmente sustituido con R^{2a}; C_3-C_6 cicloalquilo opcionalmente sustituido con R^{2b}; -O-C_3-C_6 cicloalquilo opcionalmente sustituido con R^{2b}; heterociclilo de 3 a 12 miembros opcionalmente sustituido con R^{2c}; o -$S(O)_2R^{2d}$; con la condición de que cualquier átomo de carbono unido directamente a un átomo de nitrógeno esté opcionalmente sustituido con una porción R^{2a} distinta de halógeno;

cada R^{1a} es independientemente C_1-C_6 alquilo, C_2-C_6 alquenilo, C_2-C_6 alquinilo, C_3-C_8 cicloalquilo, C_4-C_8 cicloalquenilo, heterociclilo de 3 a 12 miembros, heteroarilo de 5 a 10 miembros, C_6-C_{14} arilo, deuterio, halógeno, -CN, -OR^3, -SR^3, -NR^4R^5, -NO_2, -C=NH(OR^3), -$C(O)R^3$, -$OC(O)R^3$, -$C(O)OR^3$, -$C(O)NR^4R^5$, -$NR^3C(O)R^4$, -$NR^3C(O)OR^4$, -$NR^3C(O)NR^4R^5$, -$S(O)R^3$, -$S(O)_2R^3$, -$NR^3S(O)R^4$, -$NR^3S(O)_2R^4$, -$S(O)NR^4R^5$, -$S(O)_2NR^4R^5$, o -$P(O)(OR^4)(OR^5)$, en donde cada R^{1a} está, donde sea posible, opcionalmente sustituido de manera independiente con deuterio, halógeno, oxo, -OR^6, -NR^6R^7, -$C(O)R^6$, -CN, -$S(O)R^6$, -$S(O)_2R^6$, -$P(O)(OR^6)(OR^7)$, C_3-C_8 cicloalquilo, heterociclilo de 3 a 12 miembros, heteroarilo de 5 a 10 miembros, C_6-C_{14} arilo o C_1-C_6 alquilo opcionalmente sustituido con deuterio, oxo, -OH o halógeno;

cada R^{2a}, R^{2b}, R^{2c}, R^{2e} y R^{2f} es independientemente oxo o R^{1a};

R^{2d} es C_1-C_6 alquilo opcionalmente sustituido con R^{2e} o C_3-C_5 cicloalquilo opcionalmente sustituido con R^{2f};

cada R^3 es independientemente hidrógeno, deuterio, C_1-C_6 alquilo, C_2-C_6 alquenilo, C_2-C_6 alquinilo, C_3-C_6 cicloalquilo, C_6-C_{14} arilo, heteroarilo de 5 a 10 miembros o heterociclilo de 3 a 12 miembros, en donde el C_1-C_6 alquilo, C_2-C_6 alquenilo, C_2-C_6 alquinilo, C_3-C_6 cicloalquilo, C_6-C_{14} arilo, heteroarilo de 5 a 10 miembros y heterociclilo de 3 a 12 miembros de R^3 están opcionalmente sustituidos de manera independiente con halógeno, deuterio, oxo, -CN, -OR^8, -NR^8R^9, -$P(O)(OR^8)(OR^9)$ o C_1-C_6 alquilo opcionalmente sustituido con deuterio, halógeno, -OH u oxo;

R^4 y R^5 son cada uno independientemente hidrógeno, deuterio, C_1-C_6 alquilo, C_2-C_6 alquenilo, C_2-C_6 alquinilo, C_3-C_6 cicloalquilo, C_6-C_{14} arilo, heteroarilo de 5 a 6 miembros o heterociclilo de 3 a 6 miembros, en donde el C_1-C_6 alquilo, C_2-C_6 alquenilo, C_2-C_6 alquinilo, C_3-C_6 cicloalquilo, C_6-C_{14} arilo, heteroarilo de 5 a 6 miembros y heterociclilo de 3 a 6 miembros de R^4 y R^5 están opcionalmente sustituidos de manera independiente con deuterio, halógeno, oxo, -CN, -OR^8, -NR^8R^9 o C_1-C_6 alquilo opcionalmente sustituido con deuterio, halógeno, oxo o -OH;

o R^4 y R^5 se toman juntos con el átomo al que se unieron para formar un heterociclilo de 3 a 6 miembros opcionalmente sustituido con deuterio, halógeno, oxo, -OR^8, -NR^8R^9 o C_1-C_6 alquilo opcionalmente sustituido con deuterio, halógeno, oxo u -OH;

R^6 y R^7 son cada uno independientemente hidrógeno, deuterio, C_1-C_6 alquilo opcionalmente sustituido con deuterio, halógeno u oxo, C_2-C_6 alquenilo opcionalmente sustituido con deuterio, halógeno u oxo o C_2-C_6 alquinilo opcionalmente sustituido con deuterio, halógeno u oxo;

o R^6 y R^7 se toman juntos con el átomo al que se unieron para formar un heterociclilo de 3 a 6 miembros opcionalmente sustituido con deuterio, halógeno, oxo o C_1-C_6 alquilo opcionalmente sustituido con deuterio, halógeno u oxo;

R^8 y R^9 son cada uno independientemente hidrógeno, deuterio, C_1-C_6 alquilo opcionalmente sustituido con deuterio, halógeno u oxo, C_2-C_6 alquenilo opcionalmente sustituido con deuterio, halógeno u oxo o C_2-C_6 alquinilo opcionalmente sustituido con deuterio, halógeno u oxo;

o R^8 y R^9 se toman juntos con el átomo al que se unieron para formar un heterociclilo de 3 a 6 miembros opcionalmente sustituido con deuterio, halógeno, oxo o C_1-C_6 alquilo opcionalmente sustituido con deuterio, oxo o halógeno.

2. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es heteroarilo de 5 a 10 miembros opcionalmente sustituido con R^{1a}.

3. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es:

pirimidinilo, quinazolinilo, pirazolopirimidinilo, pirazinilo, quinolinilo, piridopirimidinilo, tienopirimidinilo, piridinilo, pirrolopirimidinilo, quinoxalinilo, indazolilo, benzotiazolilo, naftalenilo, purininilo o isoquinolinilo; y

en donde R^1 es opcionalmente sustituido con deuterio, hidroxi, C_1-C_6 alquilo, C_1-C_6 haloalquilo, C_1-C_6 perhaloalquilo, C_1-C_6 alcoxilo, C_3-C_8 cicloalquilo, C_3-C_8 halocicloalquilo, C_3-C_8 cicloalcoxilo, heteroarilo de 5 a 10 miembros, C_6-C_{14} arilo, ciano, amino, alquilamino o dialquilamino.

4. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es:

pirimidin-2-ilo, pirimidin-4-ilo, quinazolin-4-ilo, 1H-pirazolo[3,4-d]pirimidin-4-ilo, 1H-pirazolo[4,3-d]pirimidin-7-ilo, pirazin-2-ilo, quinolin-4-ilo, pirido[2,3-d]pirimidin-4-ilo, pirido[3,2-d]pirimidin-4-ilo, pirido[3,4-d]pirimidin-4-ilo, tieno[2,3-d]pirimidin-4-ilo, tieno[3,2-d]pirimidin-4-ilo, tienopirimidin-4-ilo, piridin-2-ilo, piridin-3-ilo, 7H-pirrolo[2,3-d]pirimidin-4-ilo, quinoxalin-2-ilo, 1H-indazol-3-ilo, benzo[d]tiazol-2-ilo, naftalen-1-ilo, 9H-purin-6-ilo o isoquinolin-1-ilo; y

en donde R^1 es opcionalmente sustituido con uno o más de deuterio, metilo, ciclopropilo, fluoro, cloro, bromo, difluorometilo, trifluorometilo, metoxi, ciano, dimetilamino, fenilo, piridin-3-ilo, o piridin-4-ilo.

5. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es pirimidin-4-ilo opcionalmente sustituido con R^{1a}, en donde cada R^{1a} es independiente heteroarilo de 5 a 10 miembros, o C_1-C_6 alquilo opcionalmente sustituido con halógeno.

6. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es quinazolin-4-ilo opcionalmente sustituido con R^{1a}, en donde cada R^{1a} es independiente halógeno, C_1-C_6 alquilo opcionalmente sustituido con halógeno, o C_1-C_6 alcoxi.

7. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es:

hidrógeno,

deuterio,

hidroxi,

C_1-C_6 alquilo, o

-O-C_1-C_6 alquilo, y

en donde el C_1-C_6 alquilo y -O-C_1-C_6 alquilo de R^2 son opcionalmente sustituidos con deuterio, halógeno, C_1-C_6 alquilo, C_1-C_6 haloalquilo, C_1-C_6 hidroxialquilo, C_1-C_6 alcoxilo, C_3-C_8 cicloalquilo, C_3-C_8 halocicloalquilo, C_3-C_8 cicloalcoxilo, C_6-C_{14} arilo, C_6-C_{14} ariloxi, heteroarilo de 5 a 10 miembros, heteroariloxi de 5 a 10 miembros, heterociclilo de 3 a 12 miembros opcionalmente sustituido con oxo, -$C(O)NR^4R^5$, -$NR^3C(O)R^4$ o -$S(O)_2R^3$.

8. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es:

metilo, metoxi, etilo, etoxi, propilo, ciclopropilo o ciclobutilo; y

en donde R^2 es opcionalmente sustituido con uno o más de hidroxi, metoxi, etoxi, acetamida, fluoro, fluoroalquilo, fenoxi, dimetilamida, metilsulfonilo, ciclopropoxilo, piridin-2-iloxi, piridin-3-iloxi, N-morfolinilo, N-pirrolidin-2-onilo, dimetilpirazol-1-ilo, (1,4-dioxiran-2-ilo) metilo, morfolin-2-ilo, oxetan-3-ilo, fenilo, tetrahidrofuran-2-ilo, o tiazol-2-ilo;

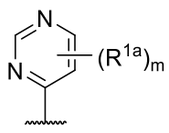
cada uno de los cuales es sustituido con 0, 1, 2 o 3 de deuterio, hidroxi, metilo, fluoro, ciano u oxo.

9. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es C_1-C_6 alquilo opcionalmente sustituido con:

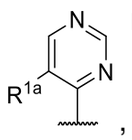
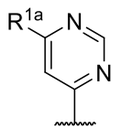
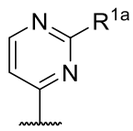
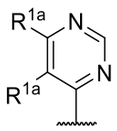
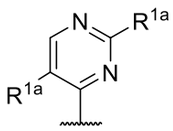
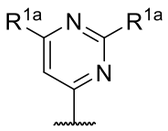
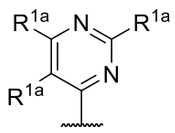
R^{2a}, en donde cada R^{2a} es independientemente: halógeno; C_3-C_8 cicloalquilo opcionalmente sustituido con halógeno; heteroarilo de 5 a 10 miembros opcionalmente sustituido con C_1-C_6 alquilo; $-NR^4R^5$; $-NR^3C(O)R^4$; $-S(O)_2R^3$; oxo, o

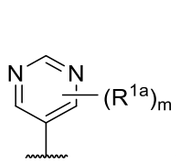
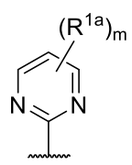
$-OR^3$, en donde cada R^3 es independientemente: hidrógeno; C_1-C_6 alquilo opcionalmente sustituido con halógeno; C_3-C_6 cicloalquilo opcionalmente sustituido con halógeno; C_6-C_{14} arilo opcionalmente sustituido con halógeno; heteroarilo de 5 a 6 miembros opcionalmente sustituido con halógeno o C_1-C_6 alquilo.

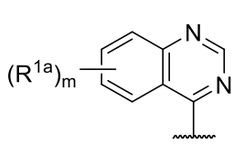
10. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es

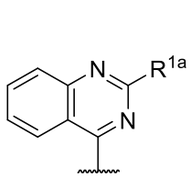
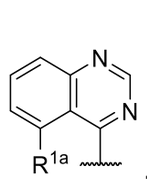
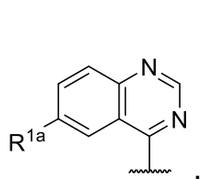
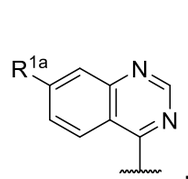
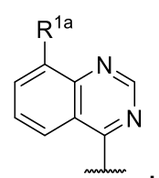


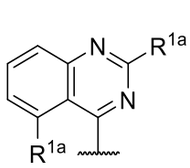
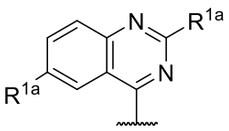
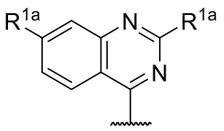
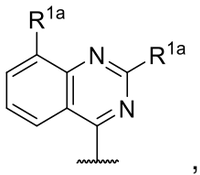
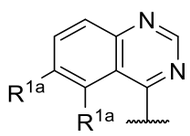
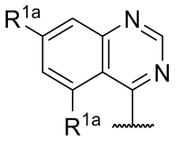
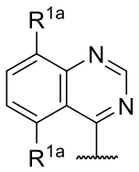
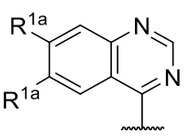
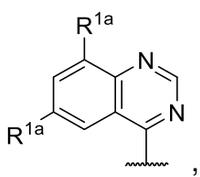
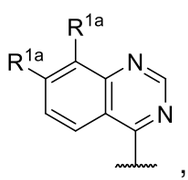
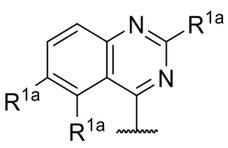
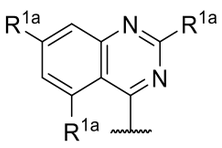
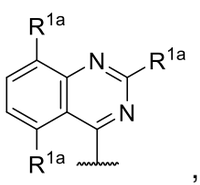
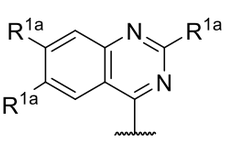
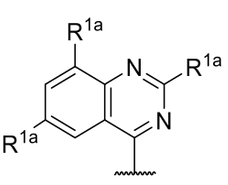
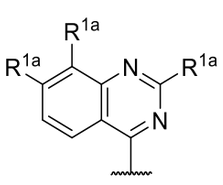
, en donde m es 0, 1, 2, o 3 y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.

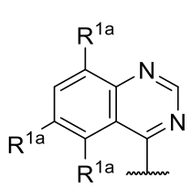
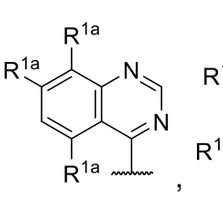
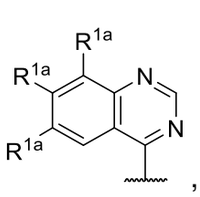
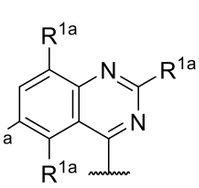
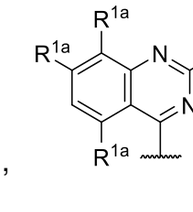
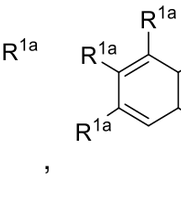
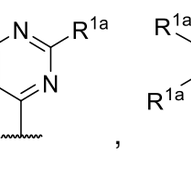
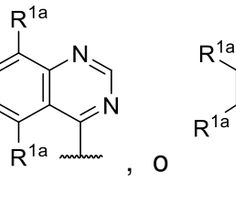
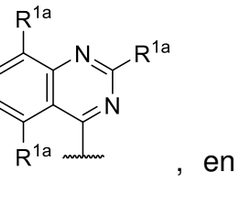
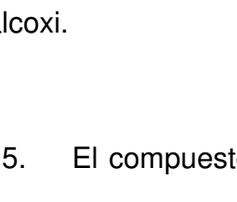
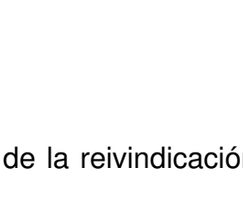
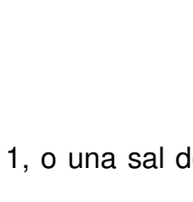
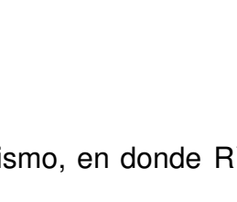
11. El compuesto de la reivindicación 10, o una sal del mismo, en donde R^1 es  ,  ,  ,  ,  ,  , o  , en donde cada R^{1a} es independientemente deuterio, alquilo, haloalquilo, o heteroarilo.

12. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  o  , en donde m es 0, 1, 2, o 3 y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.

13. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  , en donde m es 0, 1, 2, 3, 4, o 5 y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.

14. El compuesto de la reivindicación 13, o una sal del mismo, en donde R^1 es  ,  ,  ,  ,  ,


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, o

, en donde cada R^{1a} es independientemente deuterio, halógeno, alquilo, haloalquilo, o alcoxi.

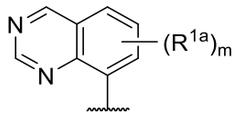
15. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es

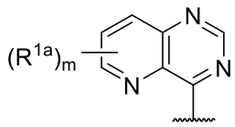
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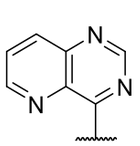
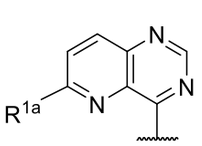
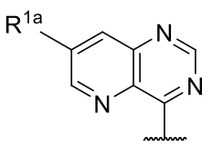
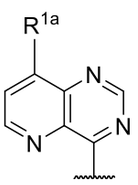
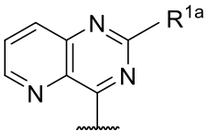
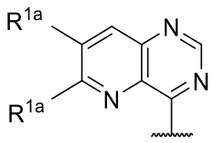
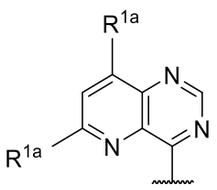
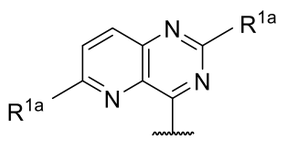
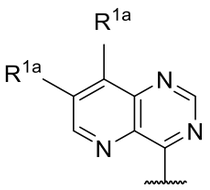
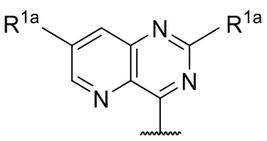
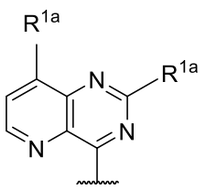
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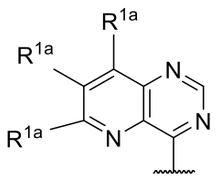
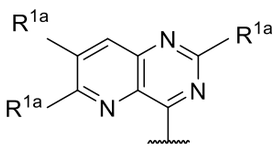
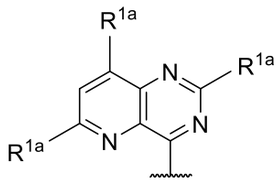
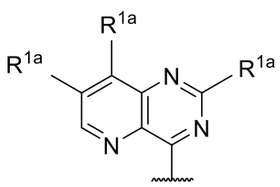
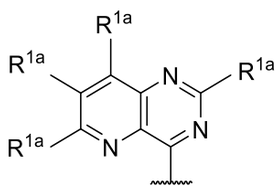
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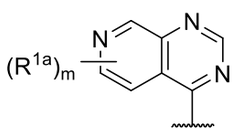
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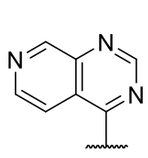
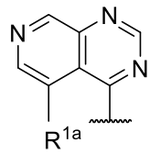
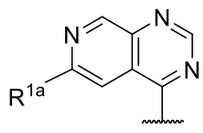
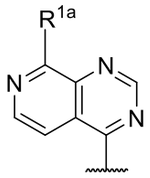
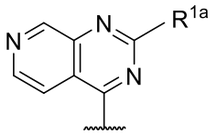
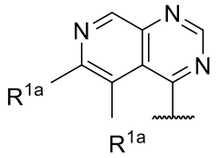
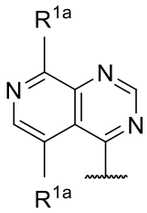
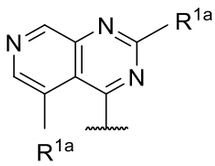
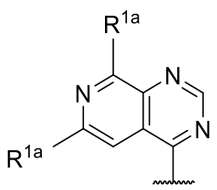
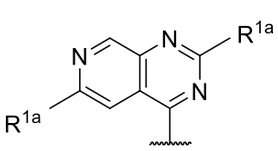
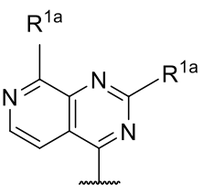
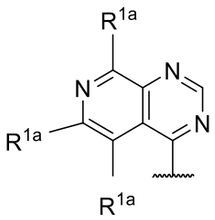
 en donde m es 0, 1, 2, 3, 4, o 5 y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.

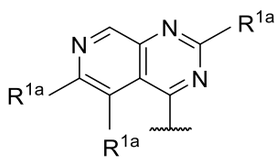
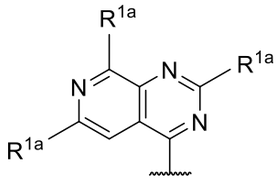
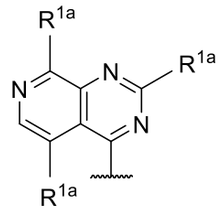
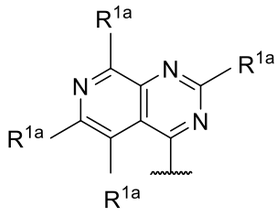
16. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  en donde m es 0, 1, 2, 3, o 4, y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.

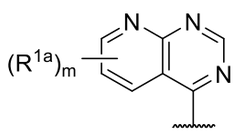
17. El compuesto de la reivindicación 16, o una sal del mismo, en donde R^1 se selecciona del grupo que consiste de  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,

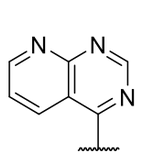
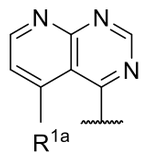
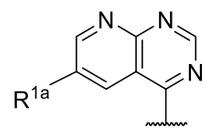
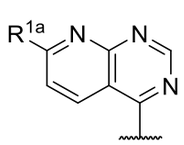
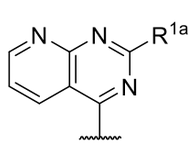
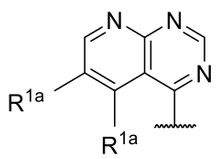
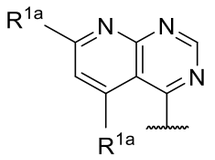
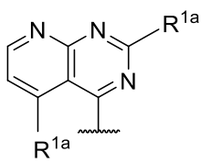
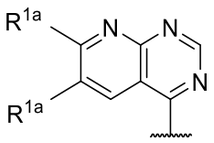
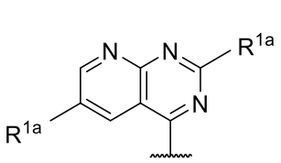
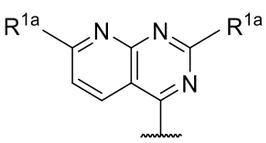

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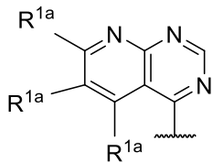
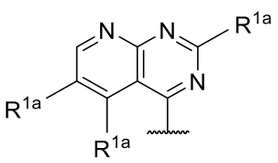
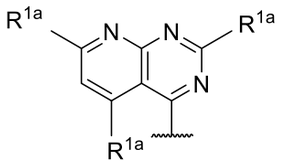
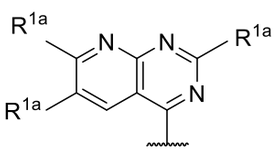
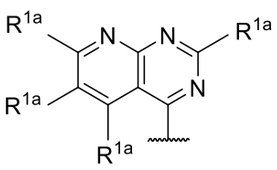
18. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es  en donde m es 0, 1, 2, 3, o 4, y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.

19. El compuesto de la reivindicación 18, o una sal del mismo, en donde R^1 se selecciona del grupo que consiste de

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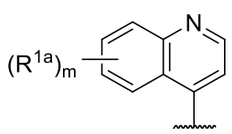

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20. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es

en donde m es 0, 1, 2, 3, o 4, y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.

21. El compuesto de la reivindicación 20, o una sal del mismo, en donde R^1 se selecciona del grupo que consiste de

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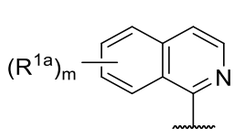






22. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es



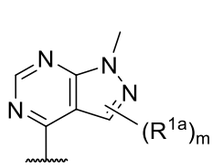
en donde m es 0, 1, 2, 3, 4, 5, o 6 y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.

23. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es



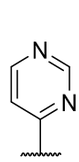
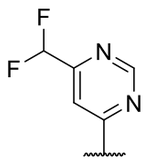
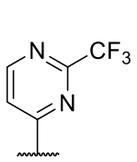
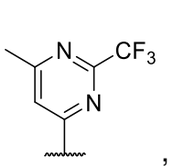
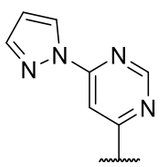
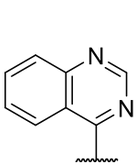
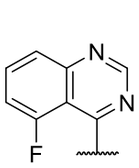
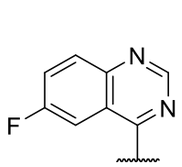
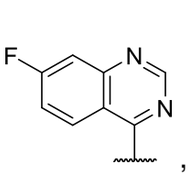
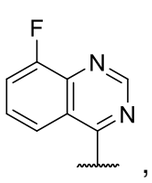
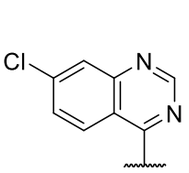
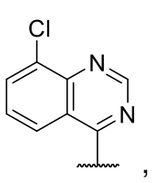
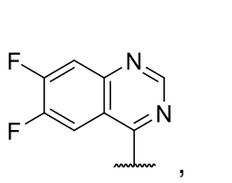
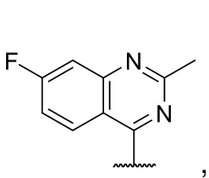
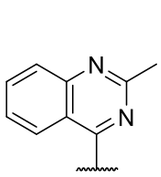
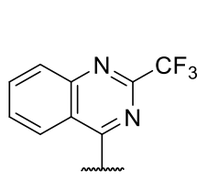
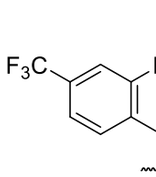
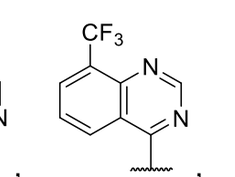
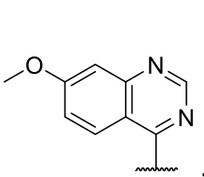
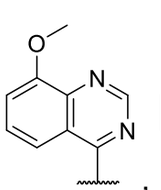
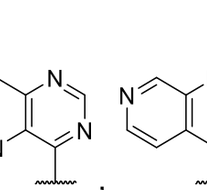
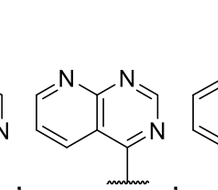
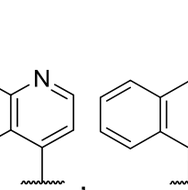
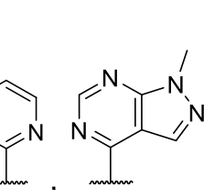
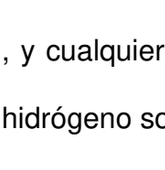
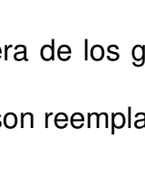
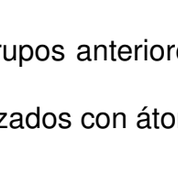
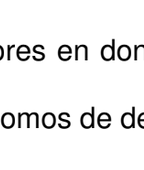
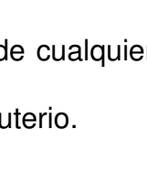
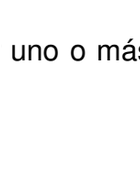
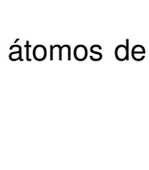
en donde m es 0, 1, 2, 3, 4, 5, o 6 y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.

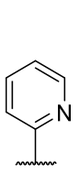
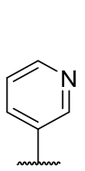
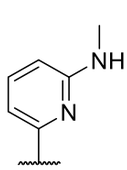
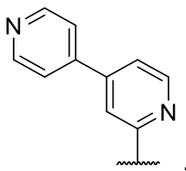
24. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es

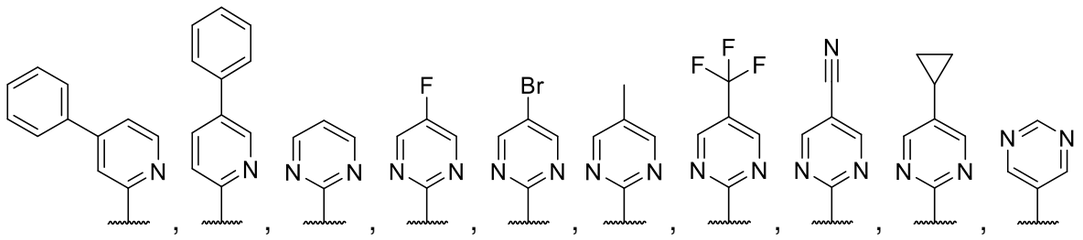
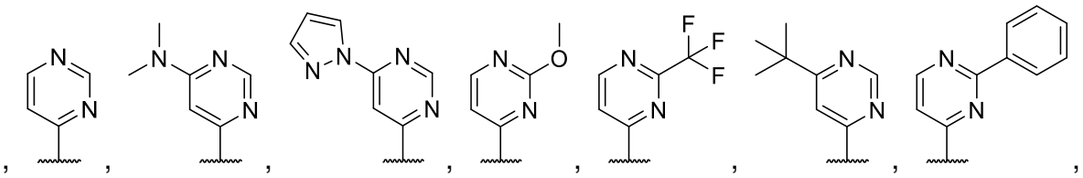
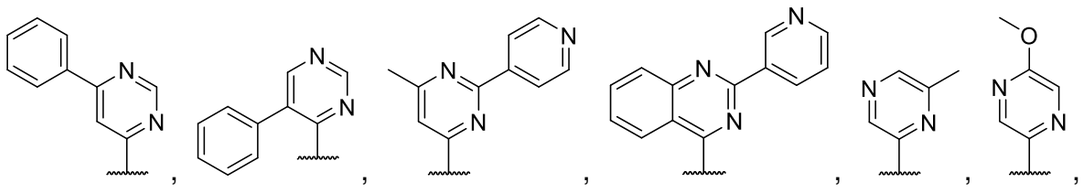
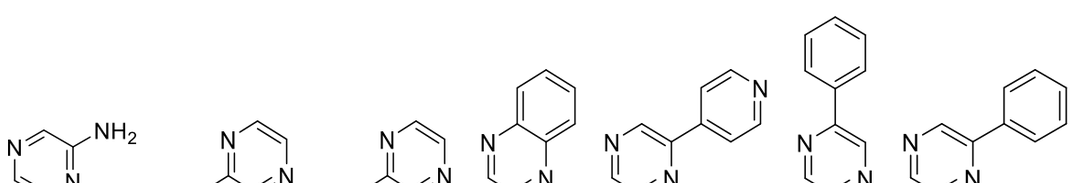
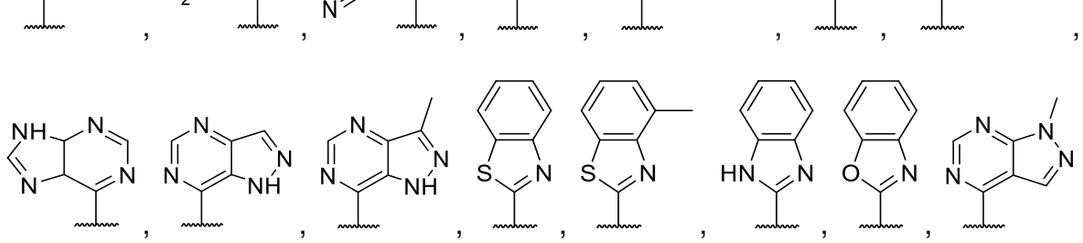


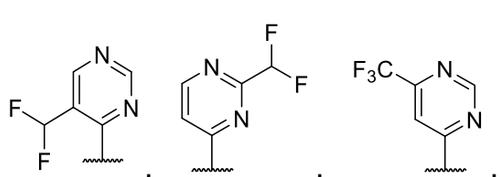
, en donde m es 0, 1, o 2 y cada R^{1a} es, donde sea aplicable, independientemente deuterio, halógeno, alquilo, haloalquilo, alcoxi, hidroxi, -CN, o

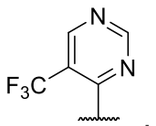
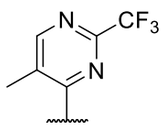
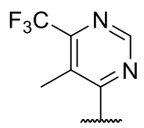
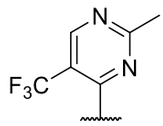
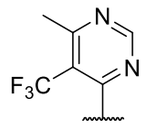
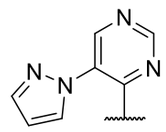
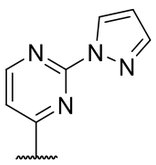
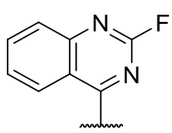
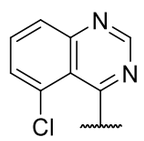
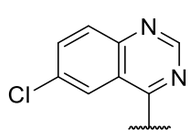
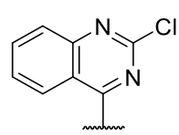
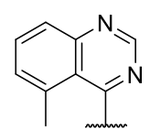
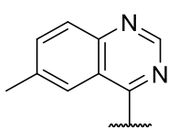
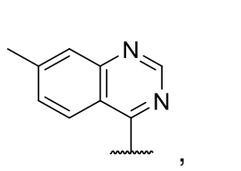
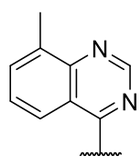
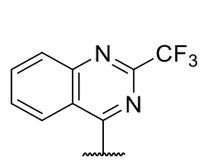
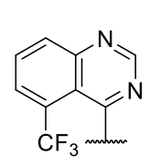
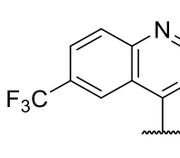
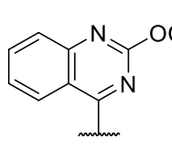
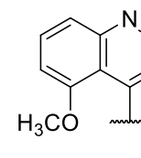
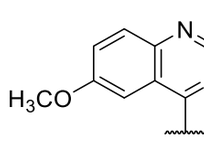
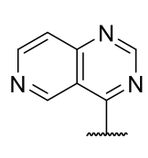
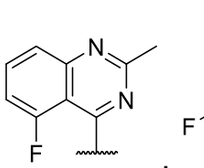
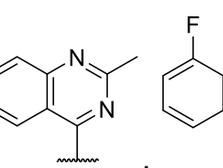
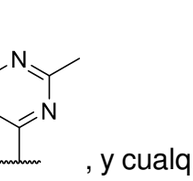
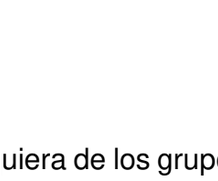
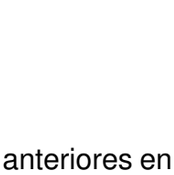
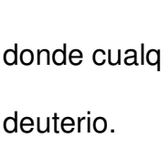
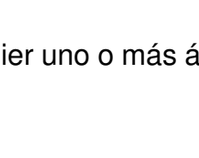
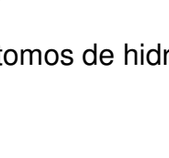
heteroarilo, en donde el alquilo, haloalquilo, alcoxi, hidroxi, y heteroarilo de R^{1a} son independientemente opcionalmente sustituidos con deuterio.

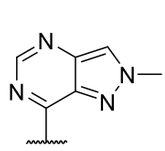
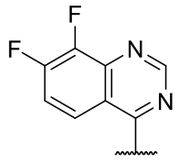
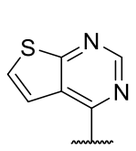
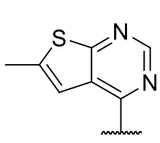
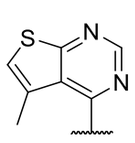
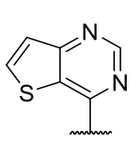
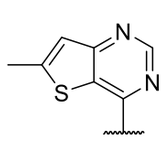
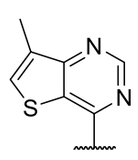
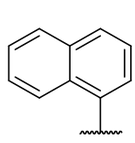
25. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 se selecciona del grupo que consiste de  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , y cualquiera de los grupos anteriores en donde cualquier uno o más átomos de hidrógeno son reemplazados con átomos de deuterio.

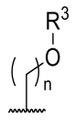
26. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 se selecciona del grupo que consiste de  ,  ,  ,  ,

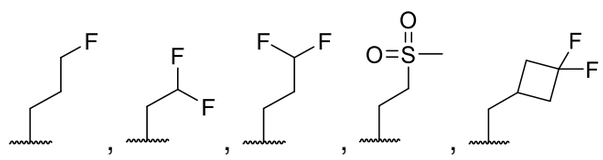
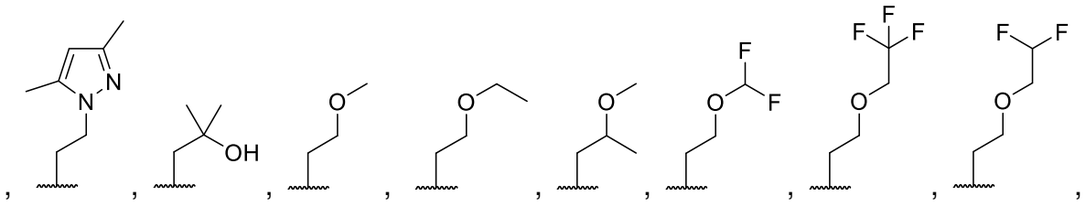
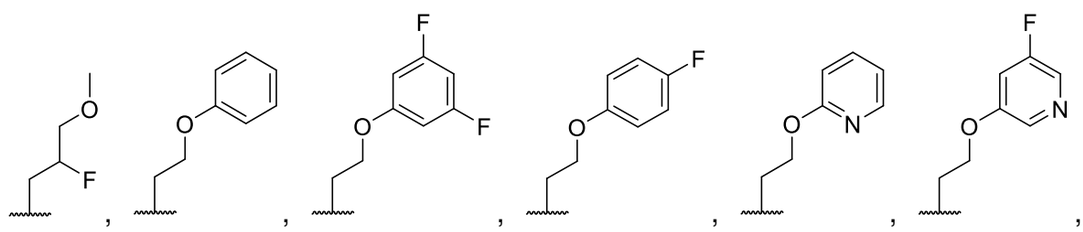





, y cualquiera de los grupos anteriores en donde cualquier uno o más átomos de hidrógeno son reemplazados con átomos de deuterio.

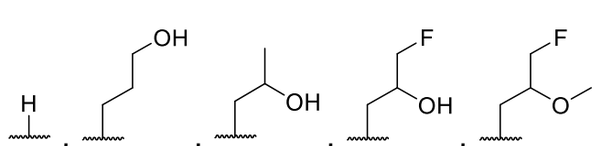
27. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 se selecciona del grupo que consiste de  ,

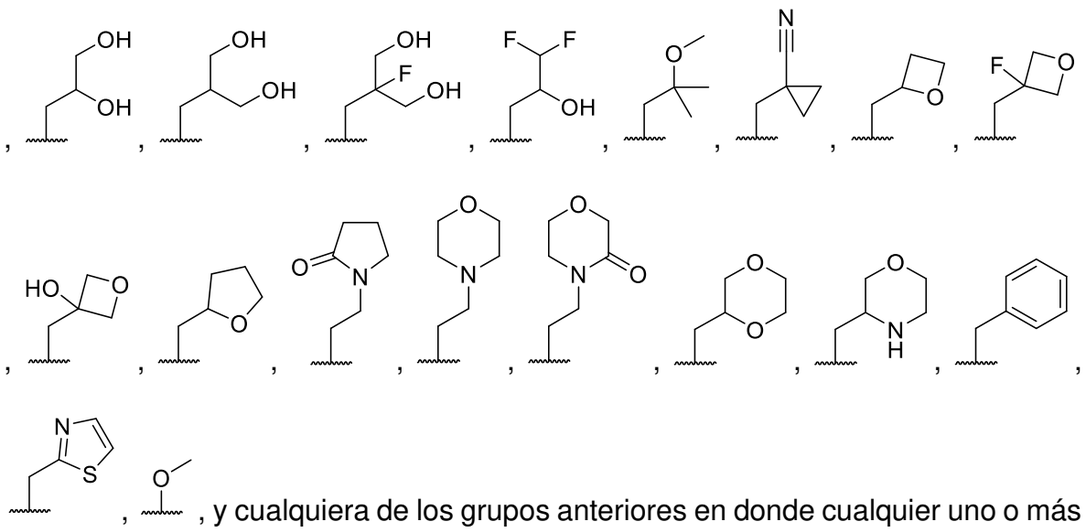
 ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , y cualquiera de los grupos anteriores en donde cualquier uno o más átomos de hidrógeno son reemplazados con átomos de deuterio.

28. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 se selecciona del grupo que consiste de  ,  ,  ,  ,  ,  ,  ,  ,  , y cualquiera de los grupos anteriores en donde cualquier uno o más átomos de hidrógeno son reemplazados con átomos de deuterio.

29. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es  , en donde n es 1, 2, 3, 4, 5, o 6, y R^3 es: C_1-C_2 alquilo opcionalmente sustituido con fluoro; fenilo opcionalmente sustituido con fluoro; piridinilo opcionalmente sustituido con fluoro o metilo; o ciclopropilo opcionalmente sustituido con fluoro.

30. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 se selecciona del grupo que consiste de  ,  ,  , y cualquiera de los grupos anteriores en donde cualquier uno o más átomos de hidrógeno son reemplazados con átomos de deuterio.

31. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 se selecciona del grupo que consiste de 



, y cualquiera de los grupos anteriores en donde cualquier uno o más átomos de hidrógeno son reemplazados con átomos de deuterio.

32. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es:

a) C_3-C_5 alquilo sustituido con flúor y -OCH_3,

b) C_1-C_6 alquilo opcionalmente sustituido con -OR^3, y cada R^3 es independientemente: fenilo opcionalmente sustituido con flúor; o piridinilo opcionalmente sustituido con flúor o metilo, o

c) C_1-C_6 alquilo sustituido con R^{2a} en donde cada R^{2a} es independientemente: halógeno; deuterio; heterociclilo de 3 a 12 miembros opcionalmente sustituido con oxo; C_6-C_{14} arilo opcionalmente sustituido con halógeno o -OR^6; heteroarilo de 5 a 10 miembros opcionalmente sustituido con C_1-C_6 alquilo; C_3-C_8 cicloalquilo opcionalmente sustituido con -CN, halógeno, o -OR^6; o -$S(O)_2R^3$.

33. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es piridilo, indazolilo, 1*H*-pirrolopiridilo, quinolinilo, fenilo, o indanilo, cada uno de los cuales es opcionalmente sustituido con R^{1a}.

34. Un compuesto de la reivindicación 1, o una sal del mismo, seleccionado de

4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(difluorometil)pirimidin-4-il) amino) ácido butanoico;

4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

4-((2-hidroxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

2-((7-fluoroquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metilquinazolin-4-il) amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[2,3-d]pirimidin-4-ilamino) ácido butanoico;

2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-(trifluorometil)quinazolin-4-il) amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)quinazolin-4-il) amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((8-(trifluorometil)quinazolin-4-il) amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,2-d]pirimidin-4-ilamino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,4-d]pirimidin-4-ilamino) ácido butanoico;

2-((5-fluoroquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-fluoroquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((8-fluoroquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6,7-difluoroquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

2-((6-(difluorometil)pirimidin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-(((3,3-difluorociclobutil)metil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-fluoro-2-metilquinazolin-4-il) amino) ácido butanoico;

2-(isoquinolin-1-ilamino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(difluorometoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinolin-4-ilamino) ácido butanoico;

2-((7-cloroquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((8-cloroquinazolin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-(quinazolin-4-ilamino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico;

2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metoxiquinazolin-4-il) amino) ácido butanoico;

(2S)-4-((2-(2,2-difluorociclopropoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-fluoro-2-metilquinazolin-4-il) amino) ácido butanoico;

4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((8-metoxiquinazolin-4-il) amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metilquinazolin-4-il) amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

2-((8-cloroquinazolin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

2-(pirido[3,2-d]pirimidin-4-ilamino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico;

4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,2-d]pirimidin-4-ilamino) ácido butanoico;

4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,2-d]pirimidin-4-ilamino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,2-d]pirimidin-4-ilamino) ácido butanoico;

2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; o

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metilquinazolin-4-il) amino) ácido butanoico.

35. Un compuesto de la reivindicación 1, o una sal del mismo, seleccionado de

2-((3-cianopirazin-2-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

4-((2-hidroxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

2-((3-cianopirazin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-fluoropirimidin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;

2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fluoropirimidin-2-il) amino) ácido butanoico;

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico;

4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

2-((5-ciclopropilpirimidin-2-il)amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;

(2S)-4-((oxetan-2-ilmetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((3-hidroxi-2-(hidroximetil)propil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

2-((5-ciclopropilpirimidin-2-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil) pirimidin-2-il) amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

2-((5-ciclopropilpirimidin-2-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico; o

4-(((3-fluorooxetan-3-il) metil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico.

36. Un compuesto, o una sal del mismo, seleccionado de

4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((7H-pirrolo[2,3-d]pirimidin-4-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-ciclopropilpirimidin-2-il) amino) ácido butanoico;

4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-2-ilamino) ácido butanoico;

4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;

4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;

2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico;

4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico;

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

2-((5-ciclopropilpirimidin-2-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico;

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico;

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico;

2-((3-cianopirazin-2-il) amino)-4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fluoropirimidin-2-il) amino) ácido butanoico;

4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridi n-2-il) butil)amino) ácido butanoico;

4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

2-((5-ciclopropilpirimidin-2-il) amino)-4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;

4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;

4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico;

2-((3-cianopirazin-2-il) amino)-4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((3,3-difluorociclobutil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-metilpirimidin-2-il)amino)ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metilpirazin-2-il) amino) ácido butanoico;

2-((3-cianopirazin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

2-((5-fluoropirimidin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il)amino) ácido butanoico;

2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

2-((6-(dimetilamino)pirimidin-4-il)amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metoxipirazin-2-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) amino)-2-((6-fenilpirazin-2-il)amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazol-5-il) amino) ácido butanoico;

2-(benzo[d]oxazol-2-ilamino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-benzo[d]imidazol-2-il) amino) ácido butanoico;

2-(benzo[d]tiazol-2-ilamino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico;

2-((9H-purin-6-il)amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indazol-3-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indol-3-il) amino) ácido butanoico;

2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((3-cianopirazin-2-il) amino)-4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(metilsulfonil)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

2-((5-ciclopropilpirimidin-2-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

2-((3-cianopirazin-2-il) amino)-4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico;

4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;

4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;

4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico;

4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil) amino)-2-((2-(trifluorometil)pirimidin-4-il) amino)ácido butanoico;

2-((5-ciclopropilpirimidin-2-il) amino)-4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

2-((3-cianopirazin-2-il) amino)-4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico;

4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidi n-4-il) amino) ácido butanoico;

4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidi n-4-il) amino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

2-((3-cianopirazin-2-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((3-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;

2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico;

4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

2-((3-cianopirazin-2-il) amino)-4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico;

4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

4-((2-etoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il)amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-cianopirimidin-2-il) amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-bromopirimidin-2-il) amino) ácido butanoico;

2-((7H-pirrolo[2,3-d]pirimidin-4-il) amino)-4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(dimetilamino)pirimidin-4-il) amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-ciclopropilpirimidin-2-il) amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(tert-butil)pirimidin-4-il) amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((3-cianopirazin-2-il) amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metilpirazin-2-il) amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico;

2-([4,4'-bipiridin]-2-ilamino)-4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fluoropirimidin-2-il) amino) ácido butanoico;

4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

2-((3-cianopirazin-2-il) amino)-4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico;

4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

4-((2-(dimetilamino)-2-oxoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico;

4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il) amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metilpirazin-2-il) amino) ácido butanoico;

2-((3-cianopirazin-2-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

2-((5-fluoropirimidin-2-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino) ácido butanoico;

2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

2-((6-(dimetilamino)pirimidin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metoxipirazin-2-il) amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazol-5-il) amino) ácido butanoico;

2-(benzo[d]oxazol-2-ilamino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-benzo[d]imidazol-2-il) amino) ácido butanoico;

2-(benzo[d]tiazol-2-ilamino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico;

2-((9H-purin-6-il) amino)-4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indazol-3-il) amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indol-3-il) amino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico;

4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il) amino) ácido butanoico;

4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico;

2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((2-metoxipirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-metilpirazin-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((3-cianopirazin-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

2-((5-fluoropirimidin-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

2-((6-(dimetilamino)pirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico;

2-((5-metoxipirazin-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;

2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico;

4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico;

4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico;

4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico;

4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico;

2-((9H-purin-6-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-(benzo[d]tiazol-2-ilamino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1-metil-1H-benzo[d]imidazol-2-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-(benzo[d]oxazol-2-ilamino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1-metil-1H-pirazol-5-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1-metil-1H-indazol-3-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1-metil-1H-indol-3-il) amino)-4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il) amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(dimetilamino)pirimidin-4-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fluoropirimidin-2-il) amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

2-((3-cianopirazin-2-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metilpirazin-2-il) amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metoxipirazin-2-il) amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico;

2-((9H-purin-6-il) amino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico;

2-(benzo[d]tiazol-2-ilamino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-benzo[d]imidazol-2-il) amino) ácido butanoico;

2-(benzo[d]oxazol-2-ilamino)-4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazol-5-il) amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indazol-3-il) amino) ácido butanoico;

4-((2-((5-fluoropiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indol-3-il) amino) ácido butanoico;

4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il) amino) ácido butanoico;

4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico;

2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((2-metoxipirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-metilpirazin-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((3-cianopirazin-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

2-((5-fluoropirimidin-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

2-((6-(dimetilamino)pirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico;

2-((5-metoxipirazin-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;

2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico;

4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico;

4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico;

2-((1-metil-1H-pirazol-5-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-(benzo[d]oxazol-2-ilamino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1-metil-1H-benzo[d]imidazol-2-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-(benzo[d]tiazol-2-ilamino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((9H-purin-6-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico;

4-((2-((2-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico;

2-((1-metil-1H-indazol-3-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1-metil-1H-indol-3-il) amino)-4-((2-((6-metilpiridin-3-il) oxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-metilpirimidin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico;

2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

2-(piridin-2-ilamino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((2-metoxipirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-metilpirazin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((3-cianopirazin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

2-((5-fluoropirimidin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

2-((6-(dimetilamino)pirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico;

2-((5-metoxipirazin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-fenilpirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((2-fenilpirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-fenilpirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico;

2-((5-fenilpirazin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-fenilpirazin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1-metil-1H-pirazol-5-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-(benzo[d]oxazol-2-ilamino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1-metil-1H-benzo[d]imidazol-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-(benzo[d]tiazol-2-ilamino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((9H-purin-6-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-fenilpiridin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((4-fenilpiridin-2-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1-metil-1H-indol-3-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1-metil-1H-indazol-3-il) amino)-4-((2-(piridin-2-iloxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il) amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metilpirazin-2-il) amino) ácido butanoico;

2-((3-cianopirazin-2-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fluoropirimidin-2-il) amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino) ácido butanoico;

2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(dimetilamino)pirimidin-4-il) amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metoxipirazin-2-il) amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazol-5-il) amino) ácido butanoico;

2-(benzo[d]oxazol-2-ilamino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-benzo[d]imidazol-2-il) amino) ácido butanoico;

2-(benzo[d]tiazol-2-ilamino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico;

2-((9H-purin-6-il) amino)-4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indazol-3-il) amino) ácido butanoico;

4-((2-(3,5-difluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indol-3-il) amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il) amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((1H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metilpirazin-2-il) amino) ácido butanoico;

2-((3-cianopirazin-2-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fluoropirimidin-2-il) amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino) ácido butanoico;

2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(dimetilamino)pirimidin-4-il) amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metoxipirazin-2-il) amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metil-2-(piridin-4-il) pirimidin-4-il) amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-(piridin-4-il) pirazin-2-il) amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazol-5-il) amino) ácido butanoico;

2-(benzo[d]oxazol-2-ilamino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-benzo[d]imidazol-2-il) amino) ácido butanoico;

2-(benzo[d]tiazol-2-ilamino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico;

2-((9H-purin-6-il) amino)-4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpiridin-2-il) amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico;

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indazol-3-il) amino) ácido butanoico; o

4-((2-(3,5-dimetil-1H-pirazol-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indol-3-il) amino) ácido butanoico.

37. Un compuesto, o una sal del mismo, seleccionado de

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((2-metoxietil) (5-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) pentil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinoxalin-2-ilamino) ácido butanoico;

(2S)-2-(quinazolin-4-ilamino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) ((tetrahidrofuran-2-il) metil)amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((3-fluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((3,3-difluoropropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

2-((6-(dimetilamino)pirimidin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino) ácido butanoico;

2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino)-4-((2-fenoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2,2-difluoroetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-2-ilamino) ácido butanoico;

4-((2-(dimetilamino)-2-oxoetil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il)amino)ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il) amino) ácido butanoico;

4-((2-fluoro-3-hidroxi-2-(hidroximetil)propil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((3-hidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico;

4-((2-(2-oxopirrolidin-1-il) etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

2-((3-cianopirazin-2-il) amino)-4-(ciclopropil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((3-cianopirazin-2-il) amino)-4-((2-(4-fluorofenoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(benzo[d]tiazol-2-ilamino) ácido butanoico;

2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico;

2-((5-ciclopropilpirimidin-2-il) amino)-4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-(piridin-3-il) quinazolin-4-il) amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirimidin-4-ilamino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metoxipirimidin-4-il) amino) ácido butanoico;

2-((6-(dimetilamino)pirimidin-4-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((6-(tert-butil)pirimidin-4-il) amino)-4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-fenilpirimidin-4-il) amino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-fenilpirazin-2-il) amino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fenilpirazin-2-il) amino) ácido butanoico;

4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino)-2-((5-(trifluorometil)pirimidin-2-il) amino) ácido butanoico;

2-((5-cianopirimidin-2-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico;

2-((1H-pirazolo[3,4-d]pirimidin-4-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico;

2-((5-bromopirimidin-2-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico;

4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino)-2-((2-(trifluorometil)pirimidin-4-il) amino) ácido butanoico;

2-((5-ciclopropilpirimidin-2-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico;

2-((3-cianopirazin-2-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico;

2-((2-(piridin-3-il) quinazolin-4-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico;

2-((6-fenilpirimidin-4-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico;

2-((5-fenilpirimidin-4-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico;

2-(pirimidin-4-ilamino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico;

2-((6-(1H-pirazol-1-il) pirimidin-4-il) amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (2-(2,2,2-trifluoroetoxi)etil)amino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metilpirimidin-2-il) amino) ácido butanoico;

2-((3-cianopirazin-2-il) amino)-4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-([4,4'-bipiridin]-2-ilamino)-4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-(2,2-difluoroetoxi)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((4-fenilpiridin-2-il) amino) ácido butanoico;

(S)-4-((2-(2,2-difluoroetoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-fenilpiridin-2-il)amino)ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metil-7H-pirrolo[2,3-d]pirimidin-4-il) amino) ácido butanoico;

4-((2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((6-metilpirazin-2-il)amino)ácido butanoico;

4-((2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinoxalin-2-ilamino)ácido butanoico;

4-((2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((6-metil-2-(piridin-4-il)pirimidin-4-il)amino)ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((1-metil-1H-indazol-3-il) amino) ácido butanoico;

4-((2-acetamidoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(benzo[d]tiazol-2-ilamino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(piridin-3-ilamino) ácido butanoico;

4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(naftalen-1-ilamino)ácido butanoico;

4-((2-morfolinoetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

(2S)-4-((2,3-dihidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((2-metoxietil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(naftalen-1-ilamino) ácido butanoico;

(2S)-4-((3-fluoro-2-hidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

2-(quinazolin-4-ilamino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil) (tiazol-2-ilmetil)amino) ácido butanoico;

4-((2-(3-oxomorfolino)etil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-(benzil(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((2-hidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

(2S)-4-(((1,4-dioxan-2-il) metil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((3-fluoro-2-hidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((2-hidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

(2S)-4-((morfolin-3-ilmetil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

(2S)-4-((3,3-difluoro-2-hidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((2,3-dihidroxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((2-hidroxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[2,3-d]pirimidin-4-ilamino) ácido butanoico;

4-((2-hidroxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,2-d]pirimidin-4-ilamino) ácido butanoico;

2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-hidroxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-hidroxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((2-fluoro-3-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,2-d]pirimidin-4-ilamino) ácido butanoico;

4-(metoxi(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((2-metoxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

2-((7-fluoro-2-metilquinazolin-4-il) amino)-4-((2-metoxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-(((3-hidroxioxetan-3-il) metil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((2-metoxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[2,3-d]pirimidin-4-ilamino) ácido butanoico;

4-((2-metoxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(pirido[3,2-d]pirimidin-4-ilamino) ácido butanoico;

4-((2-metoxi-2-metilpropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metilquinazolin-4-il) amino) ácido butanoico;

4-(((1-cianociclopropil)metil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(quinazolin-4-ilamino) ácido butanoico;

4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((2-metilquinazolin-4-il) amino) ácido butanoico;

4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-fluoro-2-metilquinazolin-4-il) amino) ácido butanoico;

2-(quinazolin-4-ilamino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((8-fluoroquinazolin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((7-fluoroquinazolin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((8-metilquinazolin-4-il) amino) ácido butanoico;

4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metilquinazolin-4-il) amino) ácido butanoico;

4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-fluoroquinazolin-4-il) amino) ácido butanoico;

4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((8-metilquinazolin-4-il) amino) ácido butanoico;

4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((8-fluoroquinazolin-4-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metilquinazolin-4-il) amino) ácido butanoico;

2-((6-fluoroquinazolin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-fluoroquinazolin-4-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(tieno[2,3-d]pirimidin-4-ilamino) ácido butanoico;

4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(tieno[2,3-d]pirimidin-4-ilamino) ácido butanoico;

4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metiltieno[2,3-d]pirimidin-4-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metiltieno[2,3-d]pirimidin-4-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(tieno[3,2-d]pirimidin-4-ilamino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metiltieno[3,2-d]pirimidin-4-il) amino) ácido butanoico;

4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-(tieno[3,2-d]pirimidin-4-ilamino) ácido butanoico;

4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((6-metiltieno[3,2-d]pirimidin-4-il) amino) ácido butanoico;

4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metiltieno[2,3-d]pirimidin-4-il) amino) ácido butanoico;

4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((5-metiltieno[2,3-d]pirimidin-4-il) amino) ácido butanoico;

2-((7,8-difluoroquinazolin-4-il) amino)-4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

2-((7,8-difluoroquinazolin-4-il) amino)-4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino) ácido butanoico;

4-((3-fluoro-2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metiltieno[3,2-d]pirimidin-4-il) amino) ácido butanoico; o

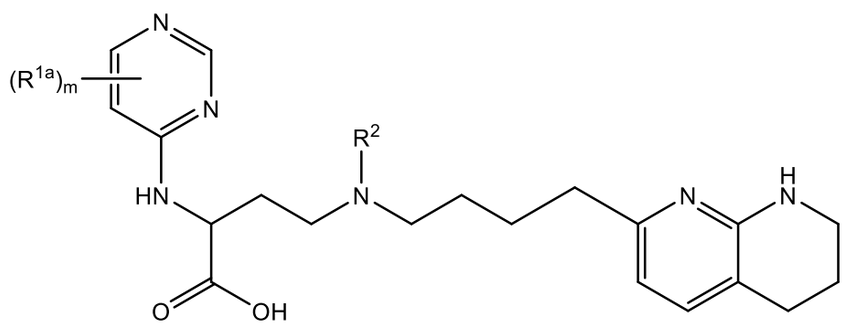
4-((2-metoxipropil) (4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il) butil)amino)-2-((7-metiltieno[3,2-d]pirimidin-4-il) amino) ácido butanoico.

38. Una composición farmacéutica que comprende un compuesto de la reivindicación 1, o una sal del mismo, y un portador o excipiente farmacéuticamente aceptable.

39. Un kit que comprende un compuesto de la reivindicación 1, o una sal farmacéuticamente aceptable del mismo.

40. El kit de la reivindicación 39, que además comprende instrucciones para el tratamiento de una enfermedad fibrótica.

41. El compuesto de la reivindicación 1, o una sal farmacéuticamente aceptable del mismo, en donde el compuesto es de la fórmula (II-A):



(II-A),

en donde m es 0, 1, 2, o 3.

42. El compuesto de la reivindicación 1, en donde el compuesto se selecciona de:

(S)-2-((5-fluoropirimidin-2-il)amino)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;

(S)-2-((5-cianopirimidin-2-il)amino)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;

(S)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-(trifluorometil)pirimidin-2-il)amino)ácido butanoico;

(S)-2-((5-bromopirimidin-2-il)amino)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;

(S)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((2-(trifluorometil)pirimidin-4-il)amino)ácido butanoico;

(S)-2-((6-(1H-pirazol-1-il)pirimidin-4-il)amino)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;

(S)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-fenilpirimidin-4-il)amino)ácido butanoico;

(S)-2-((5-ciclopropilpirimidin-2-il)amino)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;

(S)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(pirimidin-4-ilamino)ácido butanoico;

(S)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((6-fenilpirimidin-4-il)amino)ácido butanoico;

(S)-2-((5-ciclopropilpirimidin-2-il)amino)-4-(((S)-2-fluoro-3-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;

(S)-4-((2-fenoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-fenilpirimidin-4-il)amino)ácido butanoico;

(S)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-fenilpirimidin-4-il)amino)ácido butanoico;

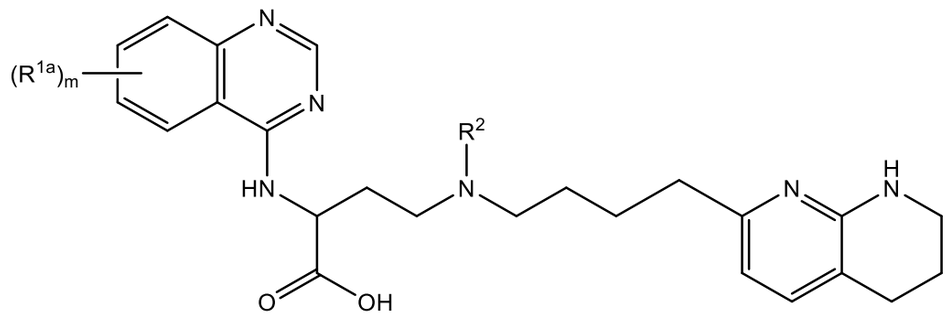
(S)-2-((3-cianopirazin-2-il)amino)-4-((2-etoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;

(S)-2-((6-(1H-pirazol-1-il)pirimidin-4-il)amino)-4-((3-fluoropropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico; y

(S)-2-((3-cianopirazin-2-il)amino)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico,

o una sal farmacéuticamente aceptable de éstos.

43. El compuesto de la reivindicación 1, o una sal farmacéuticamente aceptable del mismo, en donde el compuesto es de la fórmula (II-B):



(II-B),

en donde m es 0, 1, 2, 3, 4, o 5.

44. El compuesto de la reivindicación 1, en donde el compuesto se selecciona de (S)-2-((7-fluoroquinazolin-4-il)amino)-4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;

(S)-2-((7-fluoro-2-metilquinazolin-4-il)amino)-4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;

(S)-4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((8-(trifluorometil)quinazolin-4-il)amino)ácido butanoico;

(S)-2-((6-fluoroquinazolin-4-il)amino)-4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;

(S)-2-((6,7-difluoroquinazolin-4-il)amino)-4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;

(S)-2-((7-fluoro-2-metilquinazolin-4-il)amino)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;

(2S)-4-((2-(2,2-difluorociclopropoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((7-fluoro-2-metilquinazolin-4-il)amino)ácido butanoico;

(S)-4-(((S)-3-fluoro-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((2-metilquinazolin-4-il)amino)ácido butanoico;

(S)-2-((8-fluoroquinazolin-4-il)amino)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;

(S)-2-((7-fluoroquinazolin-4-il)amino)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;

(S)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((8-metilquinazolin-4-il)amino)ácido butanoico;

(S)-2-((7,8-difluoroquinazolin-4-il)amino)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;

(S)-4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico;

(S)-4-((2-fenoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico;

(S)-4-((2-(3,5-difluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico;

(S)-4-((2-(piridin-2-iloxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico;

(S)-4-((2-(2,2-difluoroetoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico;

(S)-4-((2-((6-metilpiridin-3-il)oxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico;

(S)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico;

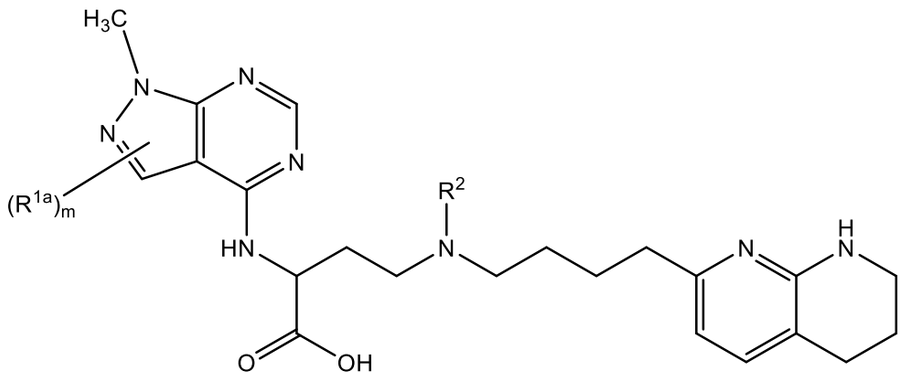
(S)-4-((2-hidroxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico;

(S)-4-(((R)-2-hidroxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico; y

(S)-4-(((S)-2,3-dihidroxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico,

o una sal farmacéuticamente aceptable del mismo.

45. El compuesto de la reivindicación 1, o una sal farmacéuticamente aceptable del mismo, en donde el compuesto es de la fórmula (II-H):



(II-H), donde m es 0, 1, o 2.

46. El compuesto de la reivindicación 1, en donde el compuesto se selecciona de (S)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il)amino)ácido butanoico;

(S)-2-((1H-pirazolo[3,4-d]pirimidin-4-il)amino)-4-((2-fenoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;

(S)-2-((1H-pirazolo[3,4-d]pirimidin-4-il)amino)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;

(S)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il)amino)ácido butanoico;

(S)-4-((2-etoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il)amino)ácido butanoico;

(S)-4-((2-(2,2-difluoroetoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il)amino)ácido butanoico;

(S)-2-((1H-pirazolo[3,4-d]pirimidin-4-il)amino)-4-((2-(2,2-difluoroetoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;

(S)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il)amino)-4-((2-fenoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico;

(S)-2-((1-metil-1H-pirazolo[3,4-d]pirimidin-4-il)amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)(2-(2,2,2-trifluoroetoxi)etil)amino)ácido butanoico;

(S)-2-((1H-pirazolo[3,4-d]pirimidin-4-il)amino)-4-((4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)(2-(2,2,2-trifluoroetoxi)etil)amino)ácido butanoico;
(S)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(tieno[2,3-d]pirimidin-4-ilamino)ácido butanoico;
(S)-4-(((S)-3-fluoro-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(tieno[2,3-d]pirimidin-4-ilamino)ácido butanoico;
(S)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(tieno[3,2-d]pirimidin-4-ilamino)ácido butanoico;
(S)-4-(((S)-3-fluoro-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(tieno[3,2-d]pirimidin-4-ilamino)ácido butanoico;
(S)-4-(((S)-3-fluoro-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((6-metiltieno[3,2-d]pirimidin-4-il)amino)ácido butanoico; y
(S)-4-(((R)-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-metiltieno[2,3-d]pirimidin-4-il)amino)ácido butanoico,
o una sal farmacéuticamente aceptable de éstos.

47. El compuesto de la reivindicación 1, en donde el compuesto es (S)-2-((7-fluoro-2-metilquinazolin-4-il)amino)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.

48. El compuesto de la reivindicación 1, en donde el compuesto es (S)-4-((2-hidroxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.

49. El compuesto de la reivindicación 1, en donde el compuesto es (S)-4-((2-metoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.

50. El compuesto de la reivindicación 1, en donde el compuesto es (S)-4-((2-(3,5-difluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(quinazolin-4-ilamino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.

51. El compuesto de la reivindicación 1, en donde el compuesto es (S)-4-((2-fenoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-fenilpirimidin-4-il)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.

52. El compuesto de la reivindicación 1, en donde el compuesto es (S)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((5-fenilpirimidin-4-il)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.

53. El compuesto de la reivindicación 1, en donde el compuesto es (S)-2-((6-(1H-pirazol-1-il)pirimidin-4-il)amino)-4-((3-fluoropropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.

54. El compuesto de la reivindicación 1, en donde el compuesto es (S)-4-(((S)-3-fluoro-2-metoxipropil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-(tieno[2,3-d]pirimidin-4-ilamino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.

55. El compuesto de la reivindicación 1, en donde el compuesto es (S)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il)amino)-4-((2-fenoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.

56. El compuesto de la reivindicación 1, en donde el compuesto es (S)-2-((1H-pirazolo[3,4-d]pirimidin-4-il)amino)-4-((2-fenoxietil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.

57. El compuesto de la reivindicación 1, en donde el compuesto es (S)-2-((1H-pirazolo[3,4-d]pirimidin-4-il)amino)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.

58. El compuesto de la reivindicación 1, en donde el compuesto es (S)-4-((2-(4-fluorofenoxi)etil)(4-(5,6,7,8-tetrahidro-1,8-naftiridin-2-il)butil)amino)-2-((2-metil-2H-pirazolo[4,3-d]pirimidin-7-il)amino)ácido butanoico, o una sal farmacéuticamente aceptable del mismo.

59. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es pirimidin-4-ilo opcionalmente sustituido con R^{1a}, en donde cada R^{1a} es independientemente pirazolilo, metilo, difluorometilo, o trifluorometilo.

60. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es pirimidin-4-ilo sustituido con metilo y trifluorometilo.

61. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es quinazolin-4-ilo opcionalmente sustituido con R^{1a}, en donde cada R^{1a} es independientemente fluoro, cloro, metilo, trifluorometilo o metoxi.

62. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es C_1-C_6 alquilo opcionalmente sustituido con:

R^{2a}, en donde cada R^{2a} es independientemente: fluoro, ciclobutilo sustituido con fluoro, pirazolilo sustituido con metilo, o $-S(O)_2CH_3$; o

$-OR^3$, en donde cada R^3 es independientemente: metilo, etilo, difluorometilo, $-CH_2CHF_2$, $-CH_2CF_3$, ciclopropilo sustituido con fluoro, fenilo opcionalmente sustituido con fluoro, o piridinilo opcionalmente sustituido con fluoro o metilo.

63. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es $–CH_2CH_2OCH_3$.

64. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es C_1-C_6 alquilo sustituido con halógeno y $-OR^3$, donde cada R^3 es independientemente C_1-C_6 alquilo.

65. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es C_3-C_6 cicloalquilo opcionalmente sustituido con R^{2b}.

66. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es C_1-C_6 alquilo opcionalmente sustituido con ciclopropilo.

67. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^2 es C_1-C_6 alquilo sustituido con R^{2a} en donde cada R^{2a} es independientemente: heterociclilo de 4 a 5 miembros opcionalmente sustituido con oxo; fenilo opcionalmente sustituido con halógeno o $-OR^6$; o pirazolilo opcionalmente sustituido con metilo.

68. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es:

pirimidin-2-ilo, pirimidin-4-ilo, quinazolin-4-ilo, 1H-pirazolo[3,4-d]pirimidin-4-ilo, 1H-pirazolo[4,3-d]pirimidin-7-ilo, pirazin-2-ilo, quinolin-4-ilo, pirido[2,3-d]pirimidin-4-ilo, pirido[3,2-d]pirimidin-4-ilo, pirido[3,4-d]pirimidin-4-ilo, tieno[2,3-d]pirimidin-4-ilo, tieno[3,2-d]pirimidin-4-ilo, tienopirimidin-4-ilo, piridin-2-ilo, piridin-3-ilo, 7H-pirrolo[2,3-d]pirimidin-4-ilo, quinoxalin-2-ilo, 1H-indazol-3-ilo, benzo[d]tiazol-2-ilo, naftalen-1-ilo, 9H-purin-6-ilo, o isoquinolin-1-ilo; y

en donde R^1 es opcionalmente sustituido con metilo y fluoro.

69. El compuesto de la reivindicación 1, o una sal del mismo, en donde R^1 es:

pirimidin-2-ilo, pirimidin-4-ilo, quinazolin-4-ilo, 1H-pirazolo[3,4-d]pirimidin-4-ilo, 1H-pirazolo[4,3-d]pirimidin-7-ilo, pirazin-2-ilo, quinolin-4-ilo, pirido[2,3-d]pirimidin-4-ilo, pirido[3,2-d]pirimidin-4-ilo, pirido[3,4-d]pirimidin-4-ilo, tieno[2,3-d]pirimidin-4-ilo, tieno[3,2-d]pirimidin-4-ilo, tienopirimidin-4-ilo, piridin-2-ilo, piridin-3-ilo, 7H-pirrolo[2,3-d]pirimidin-4-ilo, quinoxalin-2-ilo, 1H-indazol-3-ilo, benzo[d]tiazol-2-ilo, naftalen-1-ilo, 9H-purin-6-ilo, o isoquinolin-1-ilo; y

en donde R^1 es opcionalmente sustituido con metilo y trifluorometilo.

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Classification and Natural History of the Idiopathic Interstitial Pneumonias

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In the American Thoracic Society/European Respiratory Society consensus classification, idiopathic interstitial pneumonias are classified into seven clinicopathologic entities. The classification is largely based on histopathology, but depends on the close interaction of clinician, radiologist, and pathologist. An accurate diagnosis can be very difficult, especially when deciding between idiopathic pulmonary fibrosis and fibrotic nonspecific interstitial pneumonia; better diagnostic markers are needed. The prognosis of idiopathic pulmonary fibrosis is very poor, with median survival of 2–4 yr after the diagnosis, yet the course of individual patients is highly variable. Predicting prognosis in the individual patient is challenging but various clinical and radiologic variables have been identified. According to several recent clinical trials, the natural history of this disease may involve periods of relative stability punctuated by acute exacerbations of disease that result in substantial morbidity or death. Nonspecific interstitial pneumonia is characterized by a distinct histopathologic appearance and a better prognosis than idiopathic pulmonary fibrosis. However, there is still confusion and controversy over the relationship between idiopathic pulmonary fibrosis and fibrotic nonspecific interstitial pneumonia.

Keywords: acute exacerbation; idiopathic pulmonary fibrosis, classification, natural history, prognosis; nonspecific interstitial pneumonia

The idiopathic interstitial pneumonias (IIPs) are a group of diffuse parenchymal lung diseases of unknown etiology with varying degrees of inflammation and fibrosis. In 1969, Liebow and Carrington published a landmark histopathologic classification schema for the IIPs consisting of five patterns: usual interstitial pneumonia (UIP), bronchiolitis obliterans interstitial pneumonia and diffuse alveolar damage, desquamative interstitial pneumonia, lymphocytic interstitial pneumonia (LIP), and giant cell interstitial pneumonia (1). Katzenstein and Myers emphasized the need for consistent histopathologic criteria for the classification of the IIPs and incorporated several key distinguishing features: the temporal heterogeneity of inflammation and fibrosis, the extent of inflammation, the extent of fibroblastic proliferation, the extent of accumulation of intraalveolar macrophages, and the presence of honeycombing or hyaline membranes (2).

The histopathologic classification of the IIPs has evolved over time, most recently codified in the American Thoracic Society/European Respiratory Society (ATS/ERS) 2002 consensus classification statement (3) (Table 1). This classification separates the IIPs into seven clinicopathologic entities (in order of relative frequency): idiopathic pulmonary fibrosis (IPF; frequency, $\sim$ 47 to 64%), nonspecific interstitial pneumonia (NSIP; frequency, $\sim$ 14 to 36%), respiratory bronchiolitis–associated interstitial lung disease, respiratory bronchiolitis–associated interstitial lung disease/desquamative interstitial pneumonia (frequency, $\sim$ 10 to 17%), cryptogenic organizing pneumonia (frequency, $\sim$ 4 to 12%), acute interstitial pneumonia (frequency $<$ 2%), and LIP (frequency $<$ 2%). Although the histopathologic patterns provide the basis for the ATS/ERS classification, it is no longer the "gold standard" for the classification of the IIPs (3). The ATS/ERS consensus statement emphasizes the importance of dynamic interactions among clinicians, radiologists, and pathologists to arrive at a final clinico-radiologic-pathologic diagnosis. This new multidisciplinary gold standard for the diagnosis of the IIPs is a combined clinico-radiographic-pathologic analysis arrived at by a dynamic, integrated process among clinicians, radiologists, and pathologists (when a surgical lung biopsy is available) that improves diagnostic confidence and interobserver agreement and should be routinely employed in the diagnosis of the IIPs (3, 4).

The discussion of all seven forms of IIP is beyond the scope of this short review; several reviews on these entities have been recently published (5–8). Table 2 summarizes some of the key features of the IIPs. The pathologic, physiologic, and radiologic aspects of these diseases and the approach to treatment are discussed in more detail by other authors in this series. This review will focus on IPF and NSIP.

IPF

IPF is the most common interstitial lung disease of unknown etiology. According to the current ATS/ERS definition, IPF is a distinctive type of chronic fibrosing interstitial pneumonia of unknown cause limited to the lungs and associated with a surgical lung biopsy showing a histopathologic pattern of UIP (*see* Visscher and Myers, pages 322–329).

WHO IS AT RISK OF IPF?

IPF occurs worldwide and the majority of the patients reported are white (10–14). IPF mainly affects people over 50 yr of age; approximately two-thirds are over the age of 60 yr at the time of presentation. The incidence is estimated at 10.7 cases per 100,000 per year for males and 7.4 cases per 100,000 per year for females (15, 16). The prevalence of IPF is estimated at 20/100,000 for males and 13/100,000 for females (15, 16). The majority of patients with IPF are current or former smokers, and cigarette smoking has been identified in some studies as a risk factor for developing IPF (12).

WHAT CAUSES IPF?

The pathogenesis of IPF remains unknown. During the past decade, there has been a shift away from the pathogenesis theory of generalized inflammation progressing to widespread parenchymal

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TABLE 1. HISTOPATHOLOGIC CLASSIFICATION SCHEMES OF IDIOPATHIC INTERSTITIAL PNEUMONIAS

Liebow and Carrington (1969) (1)	Katzenstein and Myers (1998) (2)	ATS/ERS (2002) (3)	
		Histologic Pattern	Clinico-Radiographic-Pathologic Diagnosis
UIP	UIP	UIP	Idiopathic pulmonary fibrosis
DIP	DIP	DIP	Desquamative interstitial pneumonia
	RB-ILD	RB	Respiratory bronchiolitis interstitial lung disease
LIP		LIP	Lymphoid interstitial pneumonia
GIP			
BIP		OP	Cryptogenic organizing pneumonia
	AIP	DAD	Acute interstitial pneumonia
	NSIP	NSIP	Nonspecific interstitial pneumonia

Definition of abbreviations: AIP = acute interstitial pneumonia; BIP = bronchiolitis obliterans interstitial pneumonia and diffuse alveolar damage; DAD = diffuse alveolar damage; DIP = desquamative interstitial pneumonia; GIP = giant cell interstitial pneumonia; LIP = lymphocytic interstitial pneumonia; NSIP = nonspecific interstitial pneumonia; OP = organizing pneumonia; RB = respiratory bronchiolitis; RB-ILD = respiratory bronchiolitis–interstitial lung disease; UIP = usual interstitial pneumonia.

fibrosis toward a paradigm of disordered fibroproliferation and alveolar epithelial cell function (17). A complete discussion of the current understanding of the pathogenesis of IPF is found elsewhere in this monograph.

HOW IS IPF DIAGNOSED?

Clinical Features

Most patients present with gradual onset (> 6 mo) of dyspnea and/or a nonproductive cough. Constitutional symptoms are rare. Bibasilar fine inspiratory crackles (so-called Velcro crackles) are the most frequent physical examination finding and digital clubbing is seen in 25 to 50% of patients. Features of right heart failure and peripheral edema develop late in the clinical course.

Pulmonary function tests often reveal restrictive impairment (decreased static lung volumes), reduced diffusing capacity for carbon monoxide, and arterial hypoxemia exaggerated or elicited by exercise (*see* Martinez and Flaherty, pages 315–321).

Bronchoalveolar lavage (BAL) fluid cellular analysis shows increased neutrophils and eosinophils; lymphocytosis is not a usual feature.

The chest roentgenogram typically reveals diffuse reticular opacities (*see* Misumi and Lynch, pages 307–314). The chest radiograph lacks diagnostic specificity. In addition, the chest radiograph correlates poorly with the histopathologic pattern, the anatomic distribution of disease, and the severity of disease, with the exception of honeycombing, which is quite specific for IPF. High-resolution computed tomography (HRCT) is significantly more sensitive and specific for the diagnosis of IPF and

TABLE 2. CLINICAL, RADIOLOGIC, AND HISTOLOGIC FEATURES, TREATMENT, AND PROGNOSIS OF THE IDIOPATHIC INTERSTITIAL PNEUMONIAS

	Idiopathic Pulmonary Fibrosis	NSIP	DIP, RB-ILD	Cryptogenic Organizing Pneumonia	Acute Interstital Pneumonia	Lymphocytic Interstitial Pneumonia
Duration of illness	Chronic (> 12 mo)	Subacute to chronic (mo to yr)	Subacute (wk to mo);	Subacute (< 3 mo)	Abrupt (1 to 2 wk)	Chronic (> 12 mo)
HRCT	• Peripheral, subpleural, basal predominance • Reticular opacities • Architectural distortion • Traction bronchiectasis/ bronchiolectasis • Honeycombing	• Peripheral, subpleural, basal, symmetric • Ground-glass attenuation • Consolidation (uncommon) • Lower lobe volume loss • Subpleural sparing may be seen	• DIP: diffuse ground-glass opacity in the middle and lower lung zones • RB-ILD: bronchial wall thickening; centrilobular nodules; patchy ground-glass opacity	• Subpleural or peribronchial • Patchy consolidation • Nodules	• Diffuse, bilateral • Ground-glass opacities often with lobular sparing	• Diffuse • Centrilobular nodules, • Ground-glass attenuation, • Septal and bronchovascular thickening, • Thin-walled cysts
Treatment	Poor response to corticosteroid or cytotoxic agents	Corticosteroid responsiveness	Smoking cessation, effectiveness of corticosteroid unknown	Corticosteroid responsiveness	Effectiveness of corticosteroid unknown	Corticosteroid responsiveness
Prognosis	5-yr mortality, 80% (median survival 2–3 yr)	Cellular NSIP: 5-yr mortality < 10% (median survival > 10 yr) Fibrotic NSIP: 5-yr mortality 10% (median survival 6–8 yr)	RB-ILD: no deaths reported DIP: 5-yr mortality < 5%	5-yr mortality < 5% (deaths rare)	60% mortality in < 6 mo	Limited data, not well defined

Definition of abbreviations: NSIP = nonspecific interstitial pneumonia; RB-ILD = respiratory bronchiolitis–interstitial lung disease.
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has replaced conventional chest radiography as the preferred imaging method (Table 2) (19). The presence of extensive ground-glass opacities, nodules, upper lobe or mid-zone predominance of findings, and significant hilar or mediastinal lymphadenopathy should question the radiographic diagnosis of IPF. HRCT can make a confident, highly specific diagnosis of IPF in half to two-thirds of patients with IIP (20, 21).

Surgical Lung Biopsy

The definitive diagnosis of IPF requires a histopathologic pattern of UIP found on surgical lung biopsy (3, 22). The specific features of UIP are described by Visscher and Myers (9). In addition to UIP pattern, the diagnosis of IPF requires the following: (*1*) exclusion of other known causes of interstitial lung disease, (*2*) characteristic abnormalities on HRCT scan, and (*3*) a restrictive ventilatory defect and/or impaired gas exchange (22). In the absence of a surgical lung biopsy, a presumptive diagnosis of IPF can be made based on clinical, radiologic, and physiologic criteria (Table 3). In the immunocompetent adult, the presence of all major diagnostic criteria and at least three of the four minor criteria increases the likelihood of a correct clinical diagnosis of IPF (20).

Increasingly, HRCT has been shown to provide a high degree of specificity in the diagnosis of IPF. Several studies have demonstrated that, when present, these clinical criteria are highly specific ($> 90\%$) for the presence of UIP on surgical lung biopsy (20, 21). Their sensitivity, however, is only around 50%. Therefore, in a subset of patients with IPF, the diagnosis can be confirmed with a high degree of confidence even in the absence of surgical lung biopsy (3, 22).

In rare cases of IPF, the HRCT pattern may be more informative than the surgical lung biopsy pattern. Biopsies that show a fibrosing NSIP pattern in patients with clinical and radiographic features consistent with IPF (especially honeycomb lung) tend to behave like, and should therefore be regarded as, IPF. This further emphasizes the importance of a combined clinico-radiographic-histopathologic diagnostic approach to IPF.

WHAT IS THE NATURAL HISTORY AND PROGNOSIS OF IPF?

The natural history of IPF is not well defined. While the course of IPF is typically described as one of relentless decline in respiratory function, the course of individual patients is highly variable and some patients remain stable for extended periods of time without treatment (Figure 1).

TABLE 3. AMERICAN THORACIC SOCIETY/EUROPEAN RESPIRATORY SOCIETY CRITERIA FOR DIAGNOSIS OF IDIOPATHIC PULMONARY FIBROSIS IN ABSENCE OF SURGICAL LUNG BIOPSY*

Major Criteria (Must Have All Four)

1. Exclusion of other known causes of ILD, such as certain drug toxicities, environmental exposures, and connective tissue diseases
2. Abnormal pulmonary function studies that include evidence of restriction (reduced VC, often with an increased FEV_1/FVC ratio) and impaired gas exchange (increased $P[A\text{-}a]_{O_2}$, decreased Pa_{O_2} with rest or exercise or decreased D_{LCO})
3. Bibasilar reticular abnormalities with minimal ground-glass opacities on HRCT scans
4. Transbronchial lung biopsy or BAL showing no features to support an alternative diagnosis

Minor Criteria (Must Have Three of Four)

1. Age > 50 yr
2. Insidious onset of otherwise unexplained dyspnea on exertion
3. Duration of illness > 3 mo
4. Bibasilar, inspiratory crackles

Definition of abbreviations: BAL = bronchoalveolar lavage; D_{LCO} = diffusing capacity of the lung for carbon monoxide; HRCT = high-resolution computed tomography; ILD = interstitial lung disease; $P(A\text{-}a)_{O_2}$ = alveolar-arterial pressure difference for O_2.

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* See text for details.

Estimates of survival in IPF are dependent on the time point from which they are calculated: time of first radiographic abnormality, time of onset of symptoms, or time of diagnosis. Basilar reticular opacities are often visible on chest imaging studies several years before the development of symptoms. Among asymptomatic patients with IPF (diagnosed by radiographic abnormalities found on routine chest X-ray screening and lung biopsy showing UIP), symptoms developed about 1,000 d after the recognition of the radiologic abnormality (23). Many studies have reported that the median duration of symptoms before the diagnosis of IPF is 1 to 2 yr (23–31). Thus, the diagnosis of IPF may be delayed 5 or more yr from the time of onset. Compared with survival from the time of diagnosis, median survival from the development of symptoms is approximately 48 mo shorter, illustrating the impact the time point chosen can have on survival estimates (Figure 2). The median survival in most studies performed after the development of new IIP classification is between 2 and 4 yr (average, 3 yr) after the diagnosis is made, and the 5-yr survival is between 20 and 40% (24–31). Survival of the prevalent cases is longer than that of incident cases, likely because prevalence studies exclude those who died quickly of aggressive disease (i.e., survival bias) (32).

New insight into the natural history of IPF comes from several recent well-designed clinical trials (33–35). Although these trials confirmed the high mortality associated with this disease, the mean change in lung function was surprisingly small. In a randomized, placebo-controlled trial of IFN-γ1b, subjects who survived to Week 72 had a decrease in mean FVC % predicted from 64.5 to 61.0%, and a decrease in mean D_{LCO}% predicted from 37.8 to 37.0% (33). Similarly, a randomized, placebo-controlled trial of acetylcysteine demonstrated a mean reduction of VC during 12 mo of 190 ml (7.5% of baseline) and mean decline in D_{LCO} of 0.70 mmol/min/kPa. (13.3% of baseline) in the placebo group (34). Finally, in a randomized, placebo-controlled trial of pirfenidone, a decline in VC of only 130 ml was observed in the placebo group at 9 mo (35).

The discordance between the rate of decline in pulmonary function and mortality suggests that the clinical course of IPF may be less a gradual decline and more a steplike process, with periods of relative stability punctuated by periods of acute decompensation that may be associated with high mortality (Figure 1). These acute decompensations have received increasing attention over the last several years and have been termed acute exacerbations of IPF.

Acute Exacerbation of IPF

Acute deterioration in IPF—that is, an abrupt and unexpected worsening of the underlying lung disease—may occur secondary to infections, pulmonary embolism, pneumothorax, or heart failure (36). Often, however, there is no identifiable cause for the acute decline, and these episodes are called "acute exacerbations" or "accelerated phase" of IPF (37–40).

Acute exacerbations of IPF are increasingly recognized as common and highly morbid clinical events (35, 37–44) (Table 4). Martinez and colleagues retrospectively analyzed the course of 168 patients with IPF (45). Over a median period of 76 wk, 21% of these patients died, and 47% of these deaths followed an acute deterioration in the patient's clinical status. Azuma and colleagues prospectively reported 35 patients with untreated IPF and found a 14% incidence (five cases) of acute exacerbation (35). The impact of acute exacerbation on mortality was unclear as the number of cases was small and only one of the patients died. Rice and colleagues in a review of autopsy findings conclude

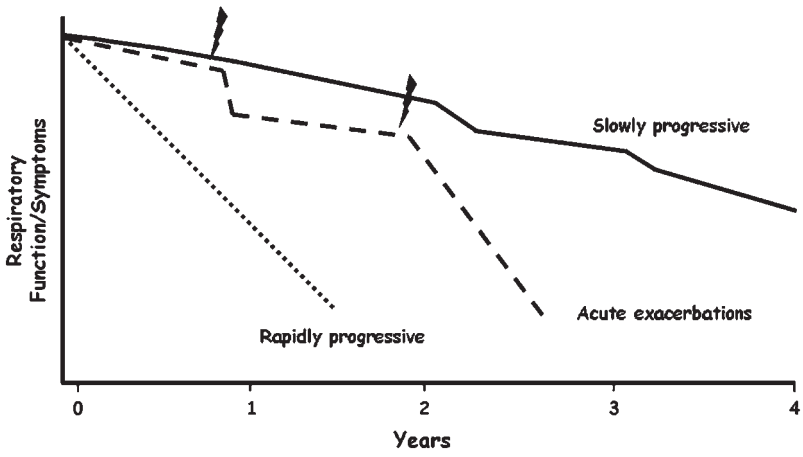


Figure 1. Schematic drawing of the potential clinical course of patients with idiopathic pulmonary fibrosis (IPF). The majority of patients with IPF show a relatively slow decline in functional status after diagnosis. Others appear to have episodes of acute clinical deterioration (acute exacerbations) that precede and possibly initiate the terminal phase of their illness. A minority of patients appear to have a short duration of illness with a more rapidly progressive clinical course. *Jagged mark* = acute exacerbations.

that acute exacerbations associated with a histopathologic pattern of diffuse alveolar damage may be a common terminal event (46). Recent studies have suggested mortality rates from 20 to 86% (35, 41–43).

Acute exacerbation of IPF has not been well defined clinically. Most diagnostic criteria are modeled after those of Kondoh and include acute subjective worsening, new radiographic abnormalities, and evidence of impaired gas exchange (38). Because of the importance of acute exacerbations of IPF to our understanding of the natural history the disease, a consensus definition should be developed and the etiology, risk factors, pathogenesis, treatment, prognosis, and predictors need to be studied. We propose that the definition of acute exacerbation of IPF require subjective and objective evidence of deterioration and exclusion of common alternative etiologies, such as infection, pulmonary embolism, heart failure, and pneumothorax (Table 5).

Predictors of Prognosis of IPF

Predicting survival based on baseline clinical variables has proven challenging. A number of parameters at the time of diagnosis have been proposed as predictors of worse survival in IPF: increasing age, male sex, degree of dyspnea, smoking history, severity of lung function and radiographic abnormality, neutrophilia or eosinophilia on BAL, honeycombing on HRCT, and the extent of fibroblastic foci on surgical lung biopsy specimens (24, 47, 48). Among the demographic and physiologic variables, patient age at the time of diagnosis and reduced lung function appear to be relatively consistent prognostic markers, but even these are inconsistent.

A study by Flaherty and colleagues suggests that the HRCT pattern adds important prognostic information. Among patients with IPF, a HRCT consistent with definite IPF was associated with worse survival than a HRCT that was indeterminate (median survival, 2.08 [95% confidence interval (CI), 1.30–3.98] vs. 5.76 [95% CI, 4.03 to not available], respectively) (49).

Recently, oxygen desaturation during 6 min of walking has been demonstrated to predict survival in IPF (50). End of exercise Sp_{O_2}, change in Sp_{O_2} with exercise, walk distance, and walk velocity were also correlated with survival in a 5-yr follow-up study in patients with IPF (51). Considering its simplicity and practicality, the prognostic value of this test should be investigated further.

Composite indices containing multiple parameters may be more accurate than single parameters. King and colleagues generated a clinico-radiologic-physiologic score from a large cohort of patients with biopsy-proven IPF using clinical, radiographic,

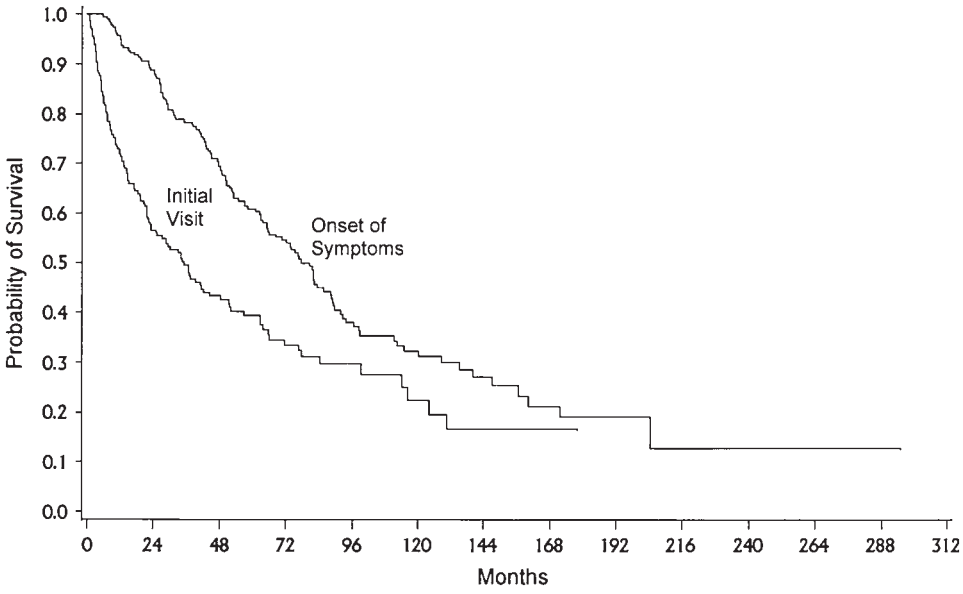


Figure 2. Kaplan-Meier plot of survival probability from the time of the onset of symptoms (median survival was 80.8 mo; 95% confidence interval, 65.5–89.3) compared with the time from initial visit (median survival was 35.2 mo; 95% confidence interval, 23.2–48.5; n = 238). Reprinted by permission from Reference 13.

TABLE 4. ACUTE EXACERBATIONS IN IDIOPATHIC PULMONARY FIBROSIS

Publication	Study Population	Study Design	Frequency of Acute Exacerbations	Mortality Rate after Acute Exacerbations
Kim, 2006 (41)	147	Retrospective cohort	9.6% (2-yr incidence)	78% (overall, 82% died within 3 mo)
Parambil, 2005 (42)	7	Case series	Not available	86%
Azuma, 2005 (35)	107	Prospective RCT	7% (6-mo incidence)	20%
Kubo, 2005 (43)	56	Prospective RCT	57% (3-yr incidence)	30%
Kondoh, 2005 (44)	27	Prospective cohort	22% (mean follow-up 49.5 mo)	100%
Ambrosini, 2003 (39)	5	Case series	Not available	80%
Akira, 1997 (40)	17	Case series	Not available	53%
Kondoh, 1993 (38)	3	Case series	Not available	0%
Kondo, 1989 (37)	155	Survey	57.6% (no time period defined)	95.5%
Kondo, 1989 (37)	22	Retrospective cohort	18% (no time period defined)	100%

and physiologic (including exercise test) features to predict survival (13). Wells and colleagues derived a composite physiologic index (CPI) from simple spirometry and $D_{L_{CO}}$ and demonstrated that CPI was linked to mortality more closely than the individual pulmonary function test values (52). The CPI score is easier to generate than the clinico-radiologic-physiologic score because no radiographic scoring or exercise data are required. However, the validity of these composite indices requires more study.

Finally, several studies have shown that serial changes in dyspnea and lung function are predictive of survival (27–29, 53). Change in FVC during the initial 6 mo seems to be better than change in $D_{L_{CO}}$ as a predictor of mortality in patients with moderately severe disease (27–29).

WHAT IS THE TREATMENT FOR IPF?

The treatment of IPF is discussed by elsewhere in this issue by Walter and coworkers (pages 330–338).

NSIP

For many years, it was recognized that lung biopsy samples from some patients with IIP do not fit into any well-defined histologic pattern. In 1994, Katzenstein and Fiorelli assigned the term "nonspecific interstitial pneumonia" to this histopathologic group (55). Importantly, the NSIP pattern is found on surgical lung biopsies from nonidiopathic forms of interstitial lung disease, such as connective tissue disease, hypersensitivity pneumonitis, poorly resolved diffuse alveolar damage, LIP, and a variety of exposures. It has been suggested that NSIP may represent an injury pattern common to many settings, rather than a specific disease, and that idiopathic NSIP (i.e., the clinical condition) may represent subclinical forms of these alternative diagnoses.

The concept of NSIP as a separate disease entity is attractive, however, because it can explain some of the historical heterogeneity in the clinical behavior of IPF. Many patients previously labeled as having IPF had cellular biopsies (prominent lymphoplasmacytic inflammation), BAL lymphocytosis, a dramatic response to steroids, and better long-term prognosis. On re-review, many of these steroid-responsive, cellular, lymphocyte-predominant cases represented NSIP (i.e., their surgical lung biopsy showed NSIP pattern, not UIP pattern). Based on this observation, the ATS/ERS classification schema for the IIPs included idiopathic NSIP as a provisional clinical diagnosis and recommended further study and characterization of this condition.

Nicholson has proposed that fibrotic NSIP pattern may be a relatively "inactive" UIP pattern (56). However, in a study comparing lung biopsy and subsequent explant tissue in patients with IIP, Katzenstein and colleagues found no explants showing UIP pattern to be preceded by biopsy findings of the NSIP pattern, which was interpreted as evidence against the evolution from NSIP to IPF (57). Furthermore, surgical lung biopsy specimens of early stages from patients with IPF who were detected by CT scan showed the same temporal heterogeneity (i.e., UIP pattern) as seen in advanced cases of IPF; NSIP pattern was not observed (26). Based on these data, current evidence suggest that, in general, idiopathic fibrosing NSIP pattern represents a distinct clinical condition, and not an early (or inactive) stage of IPF (58). The finding of both UIP and NSIP pattern in multiple biopsies from the same patients (59, 60) raises the possibility that NSIP pattern may, on occasion, be a nonspecific manifestation of IPF. However, more data are required to clarify this issue.

TABLE 5. PROPOSED DIAGNOSTIC CRITERIA FOR ACUTE EXACERBATIONS IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS

1. Subjective worsening of dyspnea or cough within the last 30 d
2. New ground-glass opacities or consolidation on chest imaging studies (chest radiograph or HRCT)
3. One of the following:
   a. Decline of $\geq$ 10% in absolute FVC
   b. Decline of $\geq$ 10 mm Hg in Pa_{O_2}
   c. Decline of $\geq$ 5% in Sp_{O_2}
4. Negative respiratory culture for respiratory pathogens (positive culture defined as moderate or heavy growth of sputum or endotracheal aspirate or quantitative culture by mini-BAL $\geq 10^3$ cfu/ml, protected brush specimen $\geq 10^3$ cfu/ml or BAL $\geq 10^4$ cfu/ml)
5. No evidence of pulmonary embolism, congestive heart failure, pneumothorax as cause of acute worsening

Definition of abbreviations: BAL = bronchoalveolar lavage; HRCT = high-resolution computed tomography.

WHO IS AT RISK OF NSIP?

NSIP occurs worldwide and the majority of the patients reported are white. The incidence and prevalence are unknown. The mean age of patients with NSIP is a decade younger than the patients with IPF (median age of onset is 40 and 50 yr respectively) (3, 23, 25, 29, 53). NSIP appears to be more common in women, although this needs further clarification. There is not an association with cigarette smoking.

WHAT CAUSES NSIP?

The pathogenesis of NSIP is unknown. Many investigators suspect it to be an autoimmune disease because of the common appearance of this pattern in patients with connective tissue disease, especially systemic sclerosis and polymyositis-dermatomyositis. As mentioned previously, it is also possible that idiopathic NSIP may represent subclinical forms of other

nonidiopathic interstitial lung diseases (e.g., hypersensitivity pneumonitis). Clearly, this issue needs additional study.

WHAT ARE THE CLINICAL FEATURES OF NSIP?

The clinical presentation of NSIP generally consists of the subacute onset of dyspnea or nonproductive cough. Constitutional symptoms are rare, although a low-grade fever is sometimes reported. The median duration of symptoms before diagnosis varies from 6 to 18 mo. Clubbing is found in about 10% of patients. In contrast to IPF, serologic abnormalities (antinuclear antibodies and rheumatoid factor) may be positive in low titer. More than half of the patients have an increased percentage of lymphocytes in the BAL fluid. Pulmonary function tests often reveal restrictive impairment, reduced diffusing capacity for carbon monoxide, and arterial hypoxemia exaggerated or elicited by exercise (18). The radiologic and histopathologic findings will be discussed by other authors in this issue (9, 19).

HOW IS NSIP DIAGNOSED?

As with all IIPs, the diagnosis of NSIP depends on a combination of clinical, radiologic, and histopathologic findings. NSIP is characterized pathologically by varying degrees of inflammation and fibrosis and by temporal homogeneity (i.e., uniformity of fibrosis), which is distinct from UIP pattern. Nonetheless, fibrotic NSIP pattern can be difficult to distinguish from UIP pattern, and significant interobserver variability exists even among expert histopathologists (30, 61). Therefore, even though the current ATS/ERS classification is based on histopathologic pattern, additional diagnostic methods, such as microarray analysis, are needed to better distinguish the two diseases. (62).

WHAT IS THE TREATMENT FOR NSIP?

Patients with NSIP have a better outcome than patients with IPF, with many showing improvement after treatment with corticosteroids. Importantly, there are no controlled data on which to judge the effectiveness of therapy. Retrospective reviews of patients with NSIP show around a third will improve pulmonary function with therapy and the majority of the rest will stabilize (30, 63). Patients with NSIP may require the addition of immunosuppressive agents as the initial response to corticosteroids alone may not be adequate. Patients with moderate to severe impairment are at particular risk for progressive or poorly responsive disease (53). It has been suggested that patients with fibrosing NSIP be treated with the combination of corticosteroid and immunosuppressant therapy to prevent the development of an irreversible fibrosis (44). Further studies are needed to compare the effect of corticosteroid therapy with corticosteroid and immunosuppressant combination therapy for idiopathic fibrosing NSIP (44).

WHAT IS THE NATURAL HISTORY AND PROGNOSIS OF NSIP?

The clinical course of idiopathic NSIP has not been well studied. The prognosis of cellular NSIP is excellent with few reported deaths (29, 53). The course of fibrotic NSIP is worse, with reported median survival ranging from 6 to 13.5 yr (25, 29, 49, 53, 60). Travis and colleagues reported the 10-yr survival of fibrotic NSIP to be 35% (31). Nicholson and colleagues reported a 5-yr survival of only 43% (30). Nagai and colleagues reported deterioration of lung function despite treatment in 5 of 17 patients, and 2 of them died (48). Kondoh and colleagues showed that 25% worsened or died after a mean follow-up of 92 mo (44). Further studies with long-term follow-up in larger number of patients are required to clarify the course and prognostic marker in this disease.

CONCLUSIONS

Following the development of the ATS/ERS consensus classification, we have been able to classify the IIPs more clearly. HRCT has become central to the diagnosis of the IIPs, and a multidisciplinary approach to the diagnosis of these conditions is paramount. IPF has the worst prognosis among the chronic IIPs. However, the clinical course of IPF may not be as indolent and steadily progressive as classically described. Periods of relative stability may instead be punctuated with acute exacerbations of disease that cause new lung injury, acute decline, and, frequently, death. Predicting prognosis in the individual patient with IPF is challenging but various clinical and radiologic variables have been identified. NSIP has been proposed as a separate entity among the IIPs. There is little evidence to support the idea that NSIP progresses to IPF; rather, NSIP may be a unique form of IIP, although further clarification of the relationship of NSIP to collagen vascular disease, hypersensitivity pneumonitis, and other nonidiopathic forms of interstitial lung disease is needed. NSIP appears more responsive to corticosteroid and immunomodulatory therapy, and has better survival than IPF.

Conflict of Interest Statement: D.S.K. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. H.R.C. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. T.E.K. has served on advisory boards for Actelion (compensation: 2003 = $11,725; 2004 = $9,940; 2005 = $15,000), for InterMune (2003 = $21,000; 2004 = $15,000; 2005 = $20,000), and for GlaxoSmithKline (2004 = $12,625; 2005 = $10,000), and has served as a consultant for Nektar, Alexza, AstraZeneca, Biogen, Centocor, Fibrogen, Genzyme, Human Genome Sciences, Merck, and CoTherix, and none of these exceeded $10,000 per company per year in any of the preceding 3 yr.

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Idiopathic Nonspecific Interstitial Pneumonia
Lung Manifestation of Undifferentiated Connective Tissue Disease?

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***Rationale*: The American Thoracic Society/European Respiratory Society International Consensus Classification panel identified the clinical entity idiopathic nonspecific interstitial pneumonia (NSIP) as a provisional diagnosis and recommended further study.**

***Objectives*: We hypothesized that idiopathic NSIP is an autoimmune disease and the lung manifestation of undifferentiated connective tissue disease (UCTD), a recently described, distinct entity.**

***Methods*: We studied 28 consecutive patients with idiopathic interstitial pneumonia (IIP) enrolled in the University of California, San Francisco Interstitial Lung Disease Center who met prespecified criteria for UCTD, as follows: at least one clinical manifestation of connective tissue disease, serologic evidence of systemic inflammation in the absence of clinical infection, and absence of sufficient American College of Rheumatology criteria for another connective tissue disease. Medical record reviews, evaluation of radiographs, and scoring of lung biopsies were performed. The control group consisted of all other patients (n = 47) with IIP who did not meet the UCTD criteria.**

***Measurements and Main Results*: The patients with UCTD were more likely to be women, younger, and nonsmokers than the IIP control subjects. Compared with the control group, patients with UCTD-ILD were significantly more likely to have ground-glass opacity on high-resolution computed tomography (HRCT) and NSIP pattern on biopsy, and less likely to have honeycombing on HRCT or usual interstitial pneumonia on biopsy. At our center, the majority of patients classified as idiopathic NSIP (88%) met the criteria for UCTD.**

***Conclusions*: Most patients diagnosed with idiopathic NSIP meet the case definition of UCTD. Furthermore, these results show that the clinical entity idiopathic NSIP is different from idiopathic pulmonary fibrosis and appears to be an autoimmune disease.**

Keywords: idiopathic interstitial pneumonia; systemic rheumatic disease; undifferentiated connective tissue; collagen vascular; autoimmune disease

AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

The clinical entity idiopathic nonspecific interstitial pneumonia is a provisional diagnosis and needs further study. Undifferentiated connective tissue disease is a recognized disease entity, but the pulmonary manifestations are not described. Their relationship is unknown.

What This Study Adds to the Field

Patients previously classified as having idiopathic nonspecific interstitial pneumonia have clinical, serologic, radiographic, and pathologic characteristics that are highly suggestive of autoimmune disease and meet criteria for undifferentiated connective tissue disease.

Before the last decade, a subset of the patients diagnosed as having idiopathic pulmonary fibrosis (IPF) had cellular biopsies (prominent lymphoplasmacytic inflammation), bronchoalveolar lavage lymphocytosis, a clinical response to steroids, and a better long-term prognosis (1–4). On review of the lung histopathology, most of these cases were reclassified as nonspecific interstitial pneumonia (NSIP) (i.e., their surgical lung biopsy showed a pattern, termed NSIP, distinct from usual interstitial pneumonia [UIP], the pattern characteristic of IPF) (5, 6). Consequently, the 2002 American Thoracic Society/European Respiratory Society (ATS/ERS) International Consensus Panel for Classification of Interstitial Lung Disease included idiopathic NSIP as a provisional clinical diagnosis and recommended further study and characterization of this condition (7).

The histopathologic pattern of NSIP has been found in a wide variety of clinical and radiologic contexts (8–10). Recently, NSIP has been identified as the most common histopathologic pattern found in patients with connective tissue disease (CTD) who meet established American College of Rheumatology (ACR) criteria (11–13).

Rheumatologic studies have estimated that up to 25% of patients with features of a systemic autoimmune disease do not fulfill ACR classification criteria for CTD (14–18). These patients are considered to have diffuse or undifferentiated CTD (UCTD). The majority of such cases (65–94%) after years of follow-up do not develop into a "differentiated" CTD (e.g., rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, mixed CTD) (14–19). Consequently, it has been proposed that UCTD represents a distinct clinical entity with the following criteria: signs and symptoms suggestive of a CTD, positive serologic results, and disease duration of at least 1 year (19–21). The most common clinical manifestations of UCTD include the following: Raynaud's phenomenon, arthritis/arthralgias, pleuritis/pericarditis, sicca symptoms, cutaneous involvement (photosensitivity, rash), esophageal involvement, fever, and myositis (14). The specific pulmonary manifestations of UCTD have not been studied.

We hypothesized that the clinical entity "idiopathic NSIP" is an autoimmune disease and, furthermore, is the lung manifestation of UCTD. Applying prespecified diagnostic criteria for UCTD to a cohort of patients with idiopathic interstitial pneumonia (IIP), we studied these patients' clinical manifestations, radiographic findings, and lung histopathologic patterns. Next, we compared the patients with UCTD with all other patients with IIP enrolled at the University of California, San Francisco (UCSF), over the same period. Last, we determined what proportion of patients with IIP and a lung biopsy showing NSIP pattern met the case definition for UCTD. Some of the results

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of this study were presented in abstract form at the ATS International Conference in May 2007 (22).

METHODS

Study Subjects and Diagnostic Criteria

We reviewed the medical records of patients consecutively enrolled in the UCSF Interstitial Lung Disease longitudinal database with a diagnosis of IIP from January 1, 2004, to November 1, 2006. Enrollment included completion of a written survey and permission to review all medical records. The UCSF Committee on Human Research approved the study, and subjects provided informed consent.

Patients were considered to have UCTD if review of their medical record identified signs or symptoms and laboratory findings that met the prespecified criteria for UCTD as defined in Table 1. Patients with a defined CTD according to current ACR criteria, or a known cause of interstitial lung disease (ILD) (e.g., hypersensitivity pneumonitis, drug-induced lung disease) were excluded. Using this approach, 28 patients were identified who met the criteria for UCTD. For the control group, we reviewed the medical records of all the other patients with IIP (n = 47) from our original query and who did not meet the case definition for UCTD.

Clinical and Radiographic Characteristics

Patients entered into the database had the following clinical characteristics documented at the time of the first visit: age, ethnicity, sex, date of first symptom onset (cough, dyspnea, or wheeze), symptoms or signs of CTD (Table 1), smoking status, physical exam findings, pulmonary function tests, and serologic tests (the battery of individual tests were determined by individual clinician judgment). Serologic studies were performed in a variety of laboratories, including referring clinics/hospitals and at the study hospital, using standard techniques (23, 24). All laboratory tests were ordered as part of clinical evaluation and not performed for the purposes of this study.

High-resolution computed tomography (HRCT) scans of the chest were performed on all patients at the time of initial evaluation. For this study, the films were reviewed in a blinded fashion by chest radiologists experienced in the interpretation of diffuse lung disease. The specific findings on HRCT were documented for the index scan (first documenting presence of ILD).

TABLE 1. DIAGNOSTIC CRITERIA FOR PATIENTS WITH UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE*

Diagnostic Criteria	Presence of
Symptoms associated with connective tissue disease	At least one of the following symptoms: 1. Raynaud's phenomenon 2. Arthralgias/multiple joint swelling 3. Photosensitivity 4. Unintentional weight loss 5. Morning stiffness 6. Dry mouth or dry eyes (sicca features) 7. Dysphagia 8. Recurrent unexplained fever 9. Gastroesophageal reflux 10. Skin changes (rash) 11. Oral ulceration 12. Nonandrogenic alopecia 13. Proximal muscle weakness
Evidence of systemic inflammation in the absence of infection	Positive findings for at least one of the following: 1. Antinuclear antigen 2. Rheumatoid factor 3. Anti–SCL 70 antibody 4. SS-A or SS-B 5. Jo-1 antibody, 6. Sedimentation rate (> two times normal), C-reactive protein

* Criteria are derived from References 18, 20, and 21.

Pathologic Analysis

All lung biopsy specimens were reviewed by a lung pathologist at UCSF with experience and advanced training in the evaluation of diffuse lung disease, and were classified using the histopathologic patterns described in the ATS/ERS International Consensus Classification of the IIPs (7). Specific features on histopathology were prospectively documented and a major histopathologic pattern was assigned as part of clinical care and without knowledge of this particular study.

Determination of Overlap between UCTD and IIP with Biopsy Pattern of NSIP

After the above analyses were performed, the entire UCSF ILD longitudinal database was reviewed to identify all patients classified as IIP with a surgical biopsy documenting an NSIP pattern. This list was then cross-referenced with all patients fulfilling criteria for UCTD. The proportion of patients with UCTD among those with IIP and a biopsy showing NSIP was determined.

Statistical Analysis

Continuous data are expressed as means or medians with observed range. Categorical data are expressed as percentages. Comparisons between groups were made using the *t* test, χ^2 test, or Fisher exact test as appropriate. All p values corresponded to two-sided tests and statistical significance was defined as a p value of less than 0.05. All analyses were performed with STATA statistical software (version 9.2; Stata Corp., College Station, TX).

RESULTS

Study Population

Two hundred and eighty patients were enrolled in the UCSF database during the study period (78 with IIP, 53 with defined CTDs, 44 with sarcoidosis, 40 with hypersensitivity pneumonitis, 28 with drug-induced ILD, 6 with asbestosis, 31 with miscellaneous other diagnoses or diagnostic uncertainty but not believed to be idiopathic). Among the established CTD-associated ILDs (cases that were excluded from this study), 33 had scleroderma, 8 had rheumatoid arthritis, 7 had dermatomyositis/polymyositis, 3 had primary Sjögren's disease, 1 had systemic lupus erythematosus, and 1 had mixed connective tissue disease.

Seventy-five subjects with IIP had adequate data and 28 of these met criteria for UCTD (37%). This represents approximately 10% (period prevalence) of all patents enrolled in the UCSF ILD clinic during the study period. Forty-seven control patients with IIP who did not meet criteria for UCTD constituted the control cohort (Figure 1A). Of these, 41 were diagnosed as IPF, 2 as having idiopathic NSIP, 1 with desquamative interstitial pneumonia, and 3 did not have a biopsy and a final clinical diagnosis was inconclusive (the differential diagnosis was fibrotic NSIP vs. IPF).

Demographic and Clinical Characteristics

Demographic and clinical characteristics of the 28 patients with UCTD and the 47 control patients with IIP studied are shown in Table 2. Sixty-eight percent of the patients with UCTD were women compared with 23% of the IIP control subjects ($p < 0.0001$). The mean age of disease onset (defined by first attributable lung symptom) was 50 years for the patients with UCTD and 65 years for the control subjects with IIP ($p < 0.0001$). Forty-three percent of patients with UCTD and 75% of the control IIP patients were ever-smokers ($p = 0.006$). The most common ethnicity in both groups of patients was white.

As expected based on the case criteria, systemic but not respiratory symptoms could differentiate between the patients with UCTD and the other IIP control subjects. All patients presented with dyspnea. Dry cough was somewhat less common in the UCTD group (82 vs. 98%, $p = 0.015$). In the UCTD group,

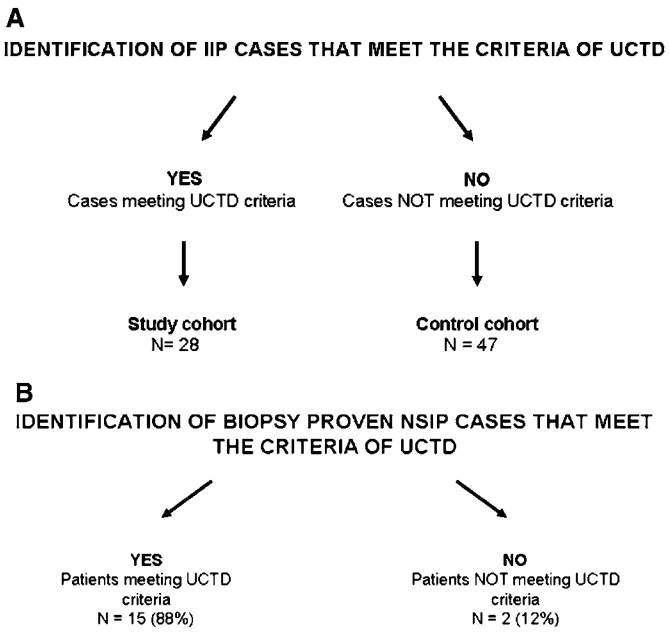


Figure 1. (*A*) Flow diagram for determining undifferentiated connective tissue disease (UCTD) cases and control subjects. All cases enrolled from January 1, 2004, to November 1, 2006, with diagnosis of idiopathic interstitial pneumonia (IIP; n = 75) were reviewed to identify those that met the criteria for UCTD (*see* Table 1). (*B*) Flow diagram showing the proportion of patients with nonspecific interstitial pneumonia (NSIP) on biopsy that met the criteria for UCTD. All cases enrolled from January 1, 2004, to November 1, 2006, with a diagnosis of IIP and with a lung biopsy showing an NSIP pattern were examined (n = 17).

the most common systemic symptoms were arthralgias/joint swelling (64%) and Raynaud's phenomenon (61%). Other common findings included the following: esophageal symptoms such as gastroesophageal reflux (65%) and dysphagia (36%), dry mouth or eyes (29%), recurrent unexplained fever (25%), rash (25%), and morning stiffness (18%). Twenty-four (86%) of the patients with UCTD had at least two symptoms, whereas 19 (67%) had at least three systemic symptoms. Twelve (43%) of the patients had both arthralgias and Raynaud's phenomenon. In the control group, these symptoms were much less common. Clubbing was seen in 7% of those with UCTD and in 26% of control subjects ($p = 0.048$), whereas inspiratory crackles were common in both groups (89 and 96%, respectively).

Laboratory and Physiologic Findings

Laboratory data are displayed in Table 3. A positive antinuclear antibody was the most common serologic abnormality in patients with UCTD (64%), with a median titer of 1:320. In addition, these patients frequently had a sedimentation rate more than two times the upper limit of normal (67%). A positive antinuclear antibody was decidedly uncommon in the control group (6%), and when present, was of low titer (1:40 and 1:80).

The pulmonary function abnormalities were similar between the two groups and demonstrated restrictive defects with diffusion impairments.

Chest Imaging Findings

Results of the comparison between the two groups for characteristic features on HRCT are shown in Table 4. The finding of ground-glass opacity extending beyond areas of adjacent reticulation was highly associated with the UCTD patient group (odds ratio [OR], 49; $p < 0.0001$). In addition, the finding of consolidation was also associated with having UCTD (OR, 10; $p = 0.025$). In contrast, the finding of honeycombing (OR for UCTD, 0.06; $p < 0.0001$) and traction bronchiectasis (OR for UCTD, 0.23; $p = 0.006$) was much more characteristic of the other IIPs than with UCTD. Mosaic perfusion was more common in the UCTD group but the difference was not statistically significant ($p = 0.36$). Reticulation was a common feature in both groups.

Histopathologic Findings

Table 5 shows the histopathologic patterns for all study patients who underwent surgical lung biopsy (n = 40; 18 [64%] met criteria for UCTD, and 22 [47%] had other IIPs) and provides a comparison between the UCTD and control groups. Overall, UIP was the most common pattern (50%) followed by NSIP (43%). There was one case each of organizing pneumonia, desquamative interstitial pneumonia, and nonclassifiable fibrosis.

Among the 28 cases who met the UCTD criteria, 18 underwent surgical lung biopsy, the NSIP pattern was present in 15 patients (OR, 50; $p < 0.0001$); in the remaining three cases, there was one case each of organizing pneumonia, UIP, and nonclassifiable fibrosis. Among the 22 cases with IIP who underwent surgical lung biopsy and who did not meet the UCTD case definition, two patients had an NSIP pattern found on lung biopsy. Therefore, among all patients enrolled in the UCSF database with IIP and an NSIP pattern on surgical lung biopsy during this study period (n = 17), 15 (88%) met our case definition for UCTD (Figure 1B). It is noteworthy that the two patients who did not meet the UCTD case definition met the systemic symptom criteria and had ground-glass opacity on HRCT but did not meet serologic criteria; however, complete serologic panels were not performed. The UIP pattern was strongly associated with the other IIP group (OR for control subjects, 111; OR for UCTD, 0.009; $p < 0.0001$).

DISCUSSION

Even in the absence of a defined CTD, 10 to 20% of patients with IIP have systemic symptoms (fever, arthralgias, Raynaud's phenomenon) and serologic abnormalities (elevated erythrocyte sedimentation rate, antinuclear antibodies, or rheumatoid factor) suggestive of an autoimmune process (25–27). Following the 2002 ATS/ERS international consensus classification of the IIPs, it has been noted that most patients with these findings are classified among the patients with idiopathic NSIP (3, 28). In addition, it is now recognized that the vast majority of ILD associated with defined CTD is characterized by the histopathologic pattern of NSIP (11–13) and a predominance of ground-glass opacities on HRCT (13, 29, 30), especially in systemic sclerosis, Sjögren's syndrome, and dermatomyositis/polymyositis. A recent ATS working group described idiopathic NSIP as a distinct clinical entity that occurs mostly in middle-aged women who are never-smokers and who often have positive serologic tests for collagen vascular disease (31). Fujita and coworkers recently reported in a case series that the clinical and pathologic features of patients with idiopathic NSIP and those with CTD-associated NSIP were qualitatively similar (32). Given the above, we hypothesized that the clinical entity "idiopathic NSIP" is an autoimmune disease and the lung manifestation of UCTD, an increasingly recognized and distinct CTD. Our results provide strong evidence to support this hypothesis. In addition, the high prevalence ($\sim 10\%$) of these patients in a tertiary referral center population demonstrates the importance of this disorder.

Several characteristics of the current study enhance the validity of the results: the systematic prospective assessment for symptoms of CTD, detailed information on clinical and

TABLE 2. DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF PATIENTS WITH UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE COMPARED WITH PATIENTS WITH IDIOPATHIC INTERSTITIAL PNEUMONIA

Characteristics	Patients with UCTD* (*n = 28*)	Patients with other IIP† (*n = 47*)	p Value‡
Age at first lung symptom, yr, mean (range)	50 (31–68)	65 (41–86)	< 0.0001
Age at first enrollment, yr, mean (range)	54 (33–69)	69 (46–90)	< 0.0001
Sex, n (%)			
Men	9 (32)	36 (77)	< 0.0001
Women	19 (68)	11 (23)	
Smoking status, n (%)			
Ever	12 (43)	35 (75)	0.006
Never	16 (57)	12 (25)	
Former	12 (43)	32 (68)	
Current	0	3 (11)	
Ethnic background, n (%)			
White	19 (68)	39 (83)	0.077
Black	1 (4)	4 (9)	
Hispanic	4 (14)	4 (9)	
Asian	3 (11)	0 (0)	
Other	1 (4)	0 (0)	
Symptoms and signs at presentation, n (%)			
Lung related			
Dyspnea	28 (100)	47 (100)	
Cough	23 (82)	46 (98)	0.015
Wheeze	2 (7)	1 (2)	0.284
Systemic			
Arthralgias/joint swelling	18 (64)	6 (13)	< 0.001
GERD	18 (65)	16 (34)	0.011
Raynaud's phenomenon	17 (61)	0 (0)	< 0.001
Dysphagia	10 (36)	2 (4)	< 0.001
Sicca symptoms	8 (29)	6 (13)	0.089
Recurrent fever	7 (25)	2 (4)	0.007
Skin changes (rash)	7 (25)	1 (2)	0.002
Morning stiffness	5 (18)	0 (0)	0.003
Unintentional weight loss	3 (11)	5 (11)	0.992
Proximal muscle weakness	3 (11)	0 (0)	0.022
Oral ulcerations	1 (4)	0 (0)	0.192
Photosensitivity	0	0	
Alopecia (nonandrogenic)	0	0	
Bibasilar inspiratory crackles	25 (89)	45 (96)	0.278
Clubbing	2 (7)	12 (26)	0.048

Definitions of abbreviations: GERD = gastroesophageal reflux disease; IIP = idiopathic interstitial pneumonia; UCTD = undifferentiated connective tissue disease.

* Includes patients with UCTD (*see* Table 1 for definitions).

† IIP control subjects (clinical diagnoses include 24 subjects with idiopathic pulmonary fibrosis, 3 with idiopathic nonspecific interstitial pneumonia, and 1 with desquamative interstitial pneumonia).

‡ χ^2 or Fisher exact test, where appropriate.

radiographic characteristics, and documentation of specific histopathologic findings. This study is the first to apply specific criteria for the diagnosis of UCTD to characterize patients with associated ILD. We show that patients with UCTD and ILD bear striking similarities to the more established CTDs in terms of clinical characteristics (female, younger, nonsmoker predilection, high titer-positive antinuclear antibodies (ANA), absence of clubbing), radiographic features (presence of significant ground-glass opacity and absence of honeycombing), and histopathologic patterns (NSIP predominant). We believe this study provides important insight into the underlying pathogenesis of these patients—that of autoimmunity.

Autoimmune disease predominantly affecting a single-organ system is well described (33, 34). The establishment of these diseases as autoimmune in nature has largely been based on clinical and laboratory evidence of autoimmunity, and histologic findings of a lymphocytic infiltrate in the affected organ (33, 34). In autoimmune pancreatitis, internationally recognized criteria are based on a combination of the findings of abdominal imaging, laboratory testing (positive autoantibodies), and histology (lymphoplasmacytic infiltrate) (35). Other investigators have suggested the inclusion of a clinical response to steroids in the criteria (36). In autoimmune hepatitis, the diagnosis is based on characteristic clinical features (e.g., female predilection, systemic symptoms such as arthralgias), circulating autoantibodies (e.g., ANA titer greater than 1:80), abnormal levels of serum globulins, and a compatible histologic picture (chronic hepatitis with a plasma cell infiltrate) (34). Although the causes of autoimmune hepatitis and pancreatitis are unknown, aberrant autoreactivity is believed to have a role in its pathogenesis. Based on similar clinical, laboratory, and histopathologic criteria, we believe our findings suggest that idiopathic NSIP represents a form of autoimmune pneumonitis.

In the 2002 ATS/ERS international consensus statement on the classification of IIP, it was stated that, "the concept of an idiopathic form of NSIP presents a problem for the clinician because there is no recognized and distinctive clinical description for patients presenting with this histologic pattern on lung biopsy" (7). Our study suggests that the application of diagnostic criteria for UCTD may be able to distinguish these patients based on a thorough systematic review of symptoms or signs of CTD and serologic studies before obtaining surgical lung biopsy.

TABLE 3. LABORATORY AND PULMONARY FUNCTION DATA OF PATIENTS WITH UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE COMPARED WITH PATIENTS WITH IDIOPATHIC INTERSTITIAL PNEUMONIA

	UCTD*		Other IIP Patients†	
Characteristic	No. of Patients Examined	Median or Number (%)	No. of Patients Examined	Median or Number (%)
Laboratory				
Anti–nuclear antibody, positive	28	18 (64)	33	2 (6)
Anti–nuclear antibody titer, median (range)	18	320 (40–1,280)	2	60 (40–80)
Rheumatoid factor, positive	26	5 (19)	29	2 (7)
Anti–SSA‡ antibody, positive	17	2 (12)	6	0 (0)
Anti–SSB§ antibody, positive	17	0	6	0 (0)
Anti–SCL‖ 70 antibody, positive	19	1 (5)	9	0 (0)
CCP¶ positive	3	0	2	0 (0)
Anti-RNP, positive	9	0	3	0 (0)
Sedimentation rate ($> 2\times$ normal)	12	8 (67)	4	0 (0)
Anti–Jo1** antibody, positive	9	2 (22)	1	0 (0)
Other serology,†† positive	15	9 (60)	9	0 (0)
Pulmonary function tests at presentation				
FVC, % predicted (range)	28	62.5 (38–104)	46	69 (36–119)
D_{LCO}, % predicted (range)	27	47 (16–64)	44	47 (14–73)
TLC, % predicted (range)	24	66 (47–87)	39	64 (45–101)

Definition of abbreviations: anti-RNP = antiribonucleoprotein; IIP = idiopathic interstitial pneumonia; UCTD = undifferentiated connective tissue disease.

* Includes patients with UCTD (*see* Table 1 for definition).

† IIP control subjects (clinical diagnoses include 41 with idiopathic pulmonary fibrosis, 2 with idiopathic nonspecific interstitial pneumonia, 1 with desquamative interstitial pneumonia, and 3 with inconclusive nonspecific interstitial pneumonia vs. idiopathic pulmonary fibrosis).

‡ Also known as anti–Ro antibody.

§ Also known as anti–La antibody.

‖ Also known as anti–topoisomerase I antibody.

¶ Also known as anti–cyclic citrullinated peptide antibody.

** Also known as anti–histidyl-tRNA synthetase.

†† Other labs included C-reactive protein, creatine kinase, aldolase.

It has been known for some time that the pulmonary manifestations of CTD occasionally precede the more typical systemic manifestations by months or years (especially in rheumatoid arthritis, systemic lupus erythematosus, and polymyositis/dermatomyositis) (37). Consequently, we expect that some of the patients included in our UCTD cohort will go on to develop sufficient criteria to be classified as another disease entity. However, if patients with ILD behave similarly to those with UCTD in general, this is likely to be a minority of patients (e.g., 25%) (14–19). Furthermore, among those patients with UCTD that does evolve into another disorder, the majority do so within the first year of follow-up (19). It should be noted that our UCTD patients with ILD had mean disease duration (first pulmonary symptom onset until presentation) of approximately 3.5 years at the time of enrollment.

We have demonstrated that the most common clinical manifestations in patients with UCTD and ILD are diffuse arthralgias, Raynaud's phenomenon, and esophageal symptoms, whereas oral ulcerations, renal and neurologic disease (data not shown), alopecia, clubbing, and muscle weakness are uncommon. This relative frequency of findings are similar to what has been observed in other non-ILD UCTD cohorts (19). These findings, if replicated, may inform subsequent development of more specific classification criteria for this form of CTD.

TABLE 4. HIGH-RESOLUTION COMPUTED TOMOGRAPHY FINDINGS IN PATIENTS WITH UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE COMPARED WITH PATIENTS WITH IDIOPATHIC INTERSTITIAL PNEUMONIA

Characteristic	UCTD* n 28 (%)	Other IIP† n = 47 (%)	OR (*95% CI*)	p Value‡
Ground-glass opacity§	21 (75)	4 (9)	49 (10–261)	< 0.0001
Consolidation	5 (21)	1 (2)	10 (1.0–483)	0.025
Reticulation	24 (86)	45 (96)	0.20 (0.02–1.40)	0.100
Traction bronchiectasis	18 (64)	37 (79)	0.23 (0.07–0.73)	0.006
Honeycombing	3 (11)	37 (79)	0.06 (0.01–0.22)	< 0.0001
Mosaic perfusion	4 (14)	2 (4)	2.7 (0.29–34)	0.356

Definition of abbreviations: CI = confidence interval; IIP = idiopathic interstitial pneumonia; OR = odds ratio; UCTD = undifferentiated connective tissue disease.

* Includes patients with UCTD (*see* Table 1 for definition).

† IIP control subjects (clinical diagnoses include 41 with idiopathic pulmonary fibrosis, 2 with idiopathic nonspecific interstitial pneumonia, 1 with desquamative interstitial pneumonia, and 3 with inconclusive nonspecific interstitial pneumonia vs. idiopathic pulmonary fibrosis).

‡ χ^2 or Fisher exact test, where appropriate.

§ Defined as a significant amount of ground-glass opacification beyond that associated with reticulation.

TABLE 5. HISTOPATHOLOGIC FINDINGS IN PATIENTS WITH UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE COMPARED WITH PATIENTS WITH IDIOPATHIC INTERSTITIAL PNEUMONIA

Histopathologic Pattern	All Patients n = 40 (%)	UCTD* n = 18 (%)	Other IIP† n = 22 (%)	OR (95% CI)	p Value‡
Nonspecific interstitial pneumonia pattern	17 (42.5)	15 (83)	2 (9)	50 (6–566)	< 0.0001
Usual interstitial pneumonia	20 (50)	1 (6)	19 (86)	0.009 (0.0002–0.114)	< 0.0001
Organizing pneumonia	1 (2.5)	1 (6)	0 (0)	NS	0.450
Desquamative interstitial pneumonia	1 (2.5)	0 (0)	1 (5)	NS	1
Nonclassifiable fibrosis	1 (2.5)	1 (6)	0 (0)	NS	1

Definition of abbreviations: CI = confidence interval; IIP = idiopathic interstitial pneumonia; NS = not significant; OR = odds ratio; UCTD = undifferentiated connective tissue disease.

* Includes patients with UCTD (*see* Table 1 for definition).

† IIP control subjects (clinical diagnoses include 41 with idiopathic pulmonary fibrosis, 2 with idiopathic nonspecific interstitial pneumonia, 1 with desquamative interstitial pneumonia, and 3 with inconclusive nonspecific interstitial pneumonia vs. idiopathic pulmonary fibrosis).

‡ χ^2 or Fisher exact test, where appropriate.

There are a number of limitations of this study. First, in keeping with the most recently published literature on the topic (19, 20), we chose to only require one connective tissue symptom for the diagnosis of UCTD. This approach may sacrifice some specificity and potentially lead to misclassification. If present, the direction of misclassification would be expected to bias our results toward the null hypothesis, because patients without true UCTD would have been misclassified as cases instead of control subjects. Importantly, the overwhelming majority of patients with UCTD-ILD had more than one symptom (86%) and most had at least three symptoms (67%). Second, although the study demonstrated several highly statistically significant associations, the sample size limited our power to examine some of the less dramatic but potentially insightful associations (e.g., mosaic perfusion on HRCT or germinal centers on histopathology). Third, the retrospective design limited our ability to acquire a complete serologic panel on all patients. Consequently, in our case definition, we had to include a requirement for at least one of several potential autoantibodies/inflammatory markers. In addition, we included sedimentation rate and C-reactive protein (in absence of infection) in our criteria to be as inclusive as possible because of the absence of prior description of UCTD in the setting of ILD. Although these tests are relatively nonspecific, they are frequently used to monitor disease activity of rheumatic diseases (38). We would note again, however, that if misclassification occurred, it would have been expected to bias our results toward the null hypothesis. In future prospective studies, it will be important to perform comprehensive laboratory and serologic panels on all patients to more precisely elucidate these patterns.

In summary, we have demonstrated that most patients previously classified as having idiopathic NSIP have clinical, serologic, radiographic, and pathologic characteristics that are suggestive of autoimmune disease and meet criteria for UCTD. Future studies should confirm these findings in other cohorts of patients with ILD, define the natural history of UCTD-ILD, and identify appropriate targets for well-designed controlled studies of therapeutic interventions.

Conflict of Interest Statement: B.W.K. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. H.R.C. has served on an advisory board for InterMune. L.K. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. D.I.D. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. P.J.W. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. B.E. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. K.D.J. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. T.E.K. has served on advisory boards for Actelion, InterMune, GlaxoSmithKline, and served as a consultant for Nektar, Alexza, AstraZeneca, Biogen, Centocor, Fibrogen, Genzyme, Human Genome Sciences, Merck, and CoTherix.

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Biochemistry

Luminescent oxygen channeling immunoassay: Measurement of particle binding kinetics by chemiluminescence

(homogeneous immunoassay/singlet oxygen/latex beads/antenna)

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ABSTRACT **A method for monitoring formation of latex particle pairs by chemiluminescence is described. Molecular oxygen is excited by a photosensitizer and an antenna dye that are dissolved in one of the particles. $^1\Delta_g O_2$ diffuses to the second particle and initiates a high quantum yield chemiluminescent reaction of an olefin that is dissolved in it. The efficiency of $^1\Delta_g O_2$ transfer between particles is ≈3.5%. The technique permits real-time measurement of particle binding kinetics. Second-order rate constants increase with the number of receptor binding sites on the particles and approach diffusion control. By using antibody-coated particles, a homogenous immunoassay capable of detecting ≈4 amol of thyroid-stimulating hormone in 12 min was demonstrated. Single molecules of analyte produce particle heterodimers that are detected even when no larger aggregates are formed.**

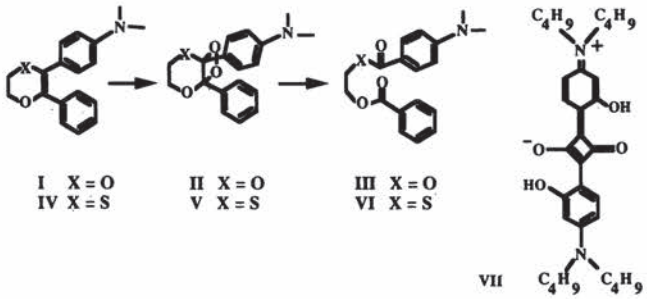
Measurement of ligand–receptor binding events by standard methods such as radioimmunoassay and ELISA requires a physical separation of bound and free labeled ligand or receptor. "Homogeneous" methods avoid this troublesome step because the signal from the label is modulated by the molecular binding event (1). Among the more sensitive of these methods is enzyme channeling immunoassay (2) in which a binding event brings two enzymes together at a surface. One enzyme produces a product that is a chromogenic substrate for the second enzyme. Because of slow diffusion at the surface, the first product has a higher local concentration than in the bulk solution and selectively reacts with the proximate second enzyme.

An alternative homogeneous method utilizes immunochemical aggregation of ligand- or receptor-labeled particles (latex agglutination) (3). Detection of agglutination by conventional light scattering requires formation of large aggregates and has limited sensitivity. Low-angle light scattering measurements provide higher sensitivity but require rigorously exclusion of adventitious particles (4, 5).

In the present study, nonenzymatic channeling of $^1\Delta_g O_2$ is used to provide exquisitely sensitive real-time monitoring of particle–particle interactions. The method, called luminescent oxygen channeling immunoassay (LOCI), exploits the short diffusion distance of $^1\Delta_g O_2$ to initiate a chemiluminescent reaction near the site that it was formed. Unlike methods that use light scattering, LOCI is relatively insensitive to interference by particles or other substances present in biological samples.

MATERIALS AND METHODS

Chemicals. Dioxene **I**, thioxene **IV**, and the squarate dye **VII** were prepared by modifications of literature methods (6–8). Aminodextran having one amine per seven glucose units was



prepared by adding concentrated ammonia to 500-kDa dextran (Pharmacia) that had been activated by reaction with epichlorohydrin and $Zn(BF_4)_2$. The product was purified by precipitation with methanol. Fluorescein-biotin (Fl-biotin) was prepared by 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDAC) coupling of Fl-5′-COOH to 1,12-diamino-4,9-dioxadodecane followed by reaction with biotinyl-6-aminohexanoic acid *N*-hydroxysuccinimide ester (biotin-LC-NHS, Pierce). Bis-(6-hydroxyhexyl) disulfide and 6-aminohexanol 5′-phosphate esters of dA_{40} and dT_{40} were from Midland Certified Reagent (Midland, TX). $(dT)_{40}$-digoxin was prepared by periodate oxidation of the vicinal glycol of digoxin, reductive amination with β-alanyl β-alanine, and EDAC coupling with the 6-aminohexanol oligonucleotide ester. Fl-5′-$CONH(CH_2)_6NHCOCH_2OCH_2CONH(CH_2)_6NH_2$ (Fl-X_{22}) was prepared from diglycolic acid and excess 1,6-diaminohexane followed by coupling to Fl-5′-COOH. Antibodies and digoxigenin-3-one *O*-carboxymethyloxime (CMO-Dig) were from Syva. CMO-Dig was combined with EDAC and Fl-X_{22} to give Fl-X_{22}-CMO-Dig. Chloroaluminum phthalocyanine tetrasulfonic acid [$PC(SO_3H)_4AlCl$] and chloroaluminum tetra-*n*-decylphthalocyanine [$PC(dec)_4AlCl$] were purchased from Ultra Diagnostics (Seattle). All other compounds were from Pierce, Aldrich, or Sigma except as indicated.

Buffers. The standard buffer was 50 mM sodium phosphate/0.15 M NaCl, pH 7.0. The assay buffer was 0.1 M Tris·HCl/0.3 M NaCl/bovine serum albumin (1 mg/ml), pH 8.2.

Antibody Conjugates. Anti-thyroid-stimulating hormone (TSH) antibodies, anti-$TSH_{\beta 1}$ and anti-$TSH_{\beta 2}$, were to nonoverlapping epitopes. Anti-$TSH_{\beta 1}$ was derivatized with sulfosuccinimidyl 4-(maleimidomethyl)cyclohexane-1-car-

Abbreviations: TTA, 3-(2-thienoyl)-1,1,1-trifluoroacetone; Phen, 1,10-phenanthroline; TOPO, trioctylphosphine oxide; Chl, chlorophyll a; CMO-Dig, digoxigenin-3-one *O*-carboxymethyloxime; Fl, fluorescein; $PC(SO_3H)_4AlCl$, chloroaluminum phthalocyanine tetrasulfonic acid; $PC(dec)_4AlCl$, chloroaluminum tetra-*n*-decylphthalocyanine; EDAC, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide; SAv, streptavidin; TSH, thyroid-stimulating hormone; LOCI, luminescent oxygen channeling immunoassay; RLU, relative light unit(s).

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boxylate (sulfo-SMCC). The bis-(6-hydroxyhexyl) disulfide 5′-phosphate ester of dT_{40} was reduced with tris-(2-carboxyethyl)phosphine (Molecular Probes) at pH 5.3 and condensed with the antibody at pH 6.0 at 4°C under argon. The conjugate was purified over protein A-Sepharose followed by DEAE-Sephadex. A dT_{40}/protein molar ratio of 1:1 was determined from the absorption at 260 and 280 nm.

Biotinylated anti-$TSH_{\beta 2}$ and anti-digoxin were prepared from biotin-LC-NHS followed by dialysis. The number of biotins was determined by titration of the protein amines with 2,4,6-trinitrobenzenesulfonic acid.

Streptavidin (SAv) and anti-Fl antibodies were thiolated with *N*-succinimidyl *S*-acetylthioacetate and subsequent treatment with 0.1 mM hydroxylamine for 1 h under argon.

Dyeing of Latex Particles. Polystyrene latex particles (175 nm) having about 8.3 carboxyl groups per nm^2 of surface (Bangs Laboratories, Carmel, IN) were stirred with 3.3 mM compound **I** or **IV** with or without 15.5 mM $Eu(TTA)_3$ [where TTA is 3-(2-thienoyl)-1,1,1-trifluoroacetone] and 15.5 mM 1,10-phenanthroline (Phen) or 20 mM trioctylphosphine oxide (TOPO) in 8:1:1 (vol/vol) ethylene glycol/benzyl alcohol/water for 8–10 min at 110°C. The particles were diluted with equal volumes of ethanol, centrifuged, washed with water, and sonicated. Chemiluminescer particles contained 10 mM **I** ($\copyright_I$) or >10 mM **I** or **IV** together with ≈100 mM $Eu(TTA)_3$ ($\copyright_{I/Eu(TTA)_3/TOPO}$ or $\copyright_{IV/Eu(TTA)_3/Phen}$, respectively). A similar procedure was used to incorporate chlorophyll a (Chl) and **VII** into latex particles to give sensitizer particles, $\bullet_{Chl}$ and $\bullet_{Chl/VII}$. The absorption spectra of the dyes in polystyrene particles were nearly the same as in toluene.

Surface Modification of Latex Particles. Maleimide-substituted dextran was prepared from amino-dextran and sulfo-SMCC followed by dialysis. Typically ≈35% of the amino groups reacted. Dyed 175-nm latex particles were coupled to the amino-dextran with EDAC followed by centrifugation, washing, and sonication. After incubation with excess thiolated SAv, antibody, or dA_{40} for 16 h at 20°C, the reactive groups were capped with mercaptoacetic acid followed by excess iodoacetic acid. Binding capacities were measured using [^{3}H]biotin, Fl, or Fl-labeled dT_{40}.

Binding of bioTin, FI-X_{22}-, or dT_{40}-labeled antibodies or ligands to coated particles was carried out by incubation at 4°C in assay buffer with periodic sonication. Binding was assumed to be quantitative. Dynamic light scattering measurements showed that any bead aggregation was reversed by a final sonication in the presence of the free label.

Chemiluminescent Measurements. Standard irradiation conditions for dioxene **I** particles included irradiation at 37°C for 1 min with a 150-W Dolan–Jenner tungsten/halogen lamp equipped with a 0.71-cm-diameter glass fiber optic bundle and a 610-nm cutoff filter. Chemiluminescent emission was then monitored for 20 s with a Turner (Palo Alto, CA) TC20e luminometer equipped with a 550-nm cutoff filter. A light output of 1 relative light unit (RLU) was near the minimum reproducible signal. Thioxene **IV** particles were irradiated for 1 s at 37°C, and after 50 ms, the emission was monitored for 1 s by using a photomultiplier tube equipped with a 620-nm band pass filter and automated shutter.

Chemiluminescence quantum yields were determined relative to that of **II** (ϕ_{CL} = 0.021 at 20°C vs. a ^{14}C standard) (6). The amount of dioxetane **II** produced during irradiation of **I** in 0.1 μM $PC(dec)_4AlCl$ in toluene was determined from the fluorescence of its decomposition product **III**. A similar yield was assumed for the conversion of **IV** to **V** corrected for the higher rate of reaction of **IV** with $^1\Delta_gO_2$ (see below). The quantum yields were measured in the presence and absence of added $Eu(TTA)_3Phen$.

Quantum yields of chemiluminescer-dyed particles were determined by irradiation of particle suspensions in 0.2 μM $PC(SO_3H)_4AlCl$ and standard buffer at 25°C. The diester **III** was determined after centrifugation of the particles and dissolution in dioxane. It was assumed that the rates of reaction of $^1\Delta_gO_2$ with **I** and **IV** in particles were the same because of the rate-leveling effect of very fast reactions by polystyrene (9). The total light output was determined by extrapolation to zero irradiation time to account for light emitted during irradiation. Light intensities were also measured after a steady state of the dioxetanes was reached.

Quantum Yield of $^1\Delta_gO_2$ Formation. Sensitizer-dyed particles in standard buffer were irradiated and the rates of $^1\Delta_gO_2$ formation were monitored by the disappearance of 9,10-bis-(carboxyethyl)anthracene. Quantum yields were calculated by comparing with the rate of $^1\Delta_gO_2$ formation during irradiation of 2 nM $PC(SO_3H)_4AlCl$ (ϕ = 0.4) (10).

Kinetic Measurements. Rates of binding of receptor-labeled particles to ligand-labeled particles were determined in assay buffer at 37°C without stirring. Reactions involving $\copyright_{I/Eu(TTA)_3/TOPO}$ were stopped by addition of 0.25 mM biotin prior to measuring the signal. Reactions involving $\copyright_{IV/Eu(TTA)_3/Phen}$ were measured in real time.

RESULTS

Chemiluminescent Particles. Dioxene **I** reacts rapidly with $^1\Delta_gO_2$ ($k = 7.5 \times 10^7\ M^{-1}\cdot s^{-1}$) (11). The resulting dioxetane **II** is reported to undergo nearly quantitative first-order decay to the diester **III** in toluene at 25°C with chemiluminesence emission at 360 and 400 nm (ϕ_{CL} = 0.021) (6). The quantum yield has now been found to increase to 0.15 in the presence of 0.5 mM $Eu(TTA)_3Phen$. Only europium emission (predominantly at 613 nm) was observed, and the decay rate of **II** was doubled (Table 1). Thioxene **IV** reacted even more rapidly with $^1\Delta_gO_2$ ($k = 1.9 \times 10^8\ s^{-1}$) but with only weak emission at 370 nm. Added $Eu(TTA)_3Phen$ had less effect on the decay rate but produced strong concentration-dependent emission at 613 nm (ϕ_{CL} = 0.20 at 5 mM chelate and ϕ_{CL} = 0.37 on extrapolation to infinite chelate concentration).

Irradiation of suspensions of $\copyright_{I/Eu(TTA)_3/TOPO}$ or $\copyright_{IV/Eu(TTA)_3/Phen}$ particles in aqueous solutions of $PC(SO_3H)_4AlCl$ at 37°C produced delayed emission at 613 nm that decayed with multiphasic kinetics (Table 1). The quantum yields were high (0.31 and 0.46, respectively) and independent of the irradiation intensity. In contrast, $\copyright_I$ particles emitted at 360 nm with ϕ_{CL} = 0.011.

The fraction of $^1\Delta_gO_2$ entering the particles that reacts with the dioxene **I** was determined by irradiating suspensions of $\copyright_I$ in 1 μM $PC(SO_3H)_4AlCl$. The total amount of diester **III** formed (III_T) was found to increase with the dioxene concentration in the particles according to the following equation:

$$\frac{1}{III_T} = \frac{1}{(^1\Delta_gO_2)_T} + \frac{k_d + k_{out}}{k_r(^1\Delta_gO_2)_T} \cdot \frac{1}{[I]},$$

which is derived from the following approximate kinetic model:

Table 1. Chemiluminescent quantum yields and decay rates of dioxetanes produced on irradiation of **I** and **IV**

	Toluene (25°C)		Particles (37°C)	
	ϕ_{CL}	$\tau_{1/2}$, s	ϕ_{CL}	$\tau_{1/2}$, s
I	0.021	2370	0.011	50
I $Eu(TTA)_3Phen$	0.15 (0.5)	1280	0.31 (100)*	50
IV	Very low	2.2		
IV $Eu(TTA)_3Phen$	0.37†	1.8	0.46 (100)	0.6

$\tau_{1/2}$ is the time for 50% decrease in signal during multiphasic decay. Numbers in parentheses indicate the concentration of Eu in mM.
*$Eu(TTA)_3TOPO$ used instead of $Eu(TTA)_3Phen$.
†Extrapolated to infinite [Eu].

$$(^1\Delta_gO_2)_{aq} + (I)_{ps} \underset{k_{out}}{\overset{k_{in}}{\rightleftarrows}} (^1\Delta_gO_2 + I)_{ps}$$

$$(^1\Delta_gO_2 + I)_{ps} \xrightarrow{k_d} (^3O_2 + I)_{ps}$$

$$(^1\Delta_gO_2 + I)_{ps} \xrightarrow{k_r} (III)_{ps},$$

where ps refers to polystyrene, and the integrated total $^1\Delta_gO_2$ that enters the particles, $(^1\Delta_gO_2)_T$, is assumed to be independent of the concentration of I in the particles. Based on the extrapolated yield at infinite [I], 10 mM I trapped 65% of the $^1\Delta_gO_2$ entering the particles.

Sensitizer Particles. The efficiency of $^1\Delta_gO_2$ formation was measured by irradiating suspensions of sensitizer particles in standard buffer containing the $^1\Delta_gO_2$ trap, 9,10-bis-(carboxyethyl)anthracene. Chl (ε_{670} = 82,000) was a relatively efficient oxygen sensitizer, but significantly greater $^1\Delta_gO_2$ yield could be achieved by also including the very strongly absorbing 1,3-bis(*N*,*N*-dibutyl-4-amino-3-hydroxyphenyl)squaraine **VII** (ε_{648} = 330,000). This highly fluorescent compound, which by itself is a poor sensitizer, presumably serves as an antenna to collect light and transfer energy from its excited singlet state to Chl (Fig. 1).

The absolute rate of $^1\Delta_gO_2$ formation from an optimally dyed dextran-coated $\bullet_{Chl/VII}$ particle under standard irradiation conditions was about 11,000 $^1\Delta_gO_2$ molecules per s (ϕ = 0.018). This rate increased by about 20% upon saturating the buffer with pure oxygen instead of air.

Particle Coating. Nonspecific binding interactions of particles were greatly reduced by coating with dextran. The apparent particle diameters usually increased from 175 nm to 200–240 nm during the coating process. Generic receptors were bound to the dextran to permit quantitative functionalization of the particles with antibodies or haptens that were appropriately labeled with biotin, dT_{40}, or Fl-X_{22}. Typically, the number of receptors per particle was 300–500 anti-Fl IgGs, 2000–4000 SAvs, or 400–700 oligonucleotides.

LOCI Signal. Chemiluminescent emission at 613 nm was observed after irradiation (>610 nm) of a suspension of $\bullet_{Chl/VII}$(anti-Fl)$_{450}$·(Fl-X_{22}-biotin)$_{450}$ and $©_{I/Eu(TTA)_3/TOPO}$·(SAv)$_{4000}$. The signal increased linearly with increasing concentration of the chemiluminescent particles (43 μRLU for each chemiluminescer particle added) and peaked at equal concentration of the two particles (32 μRLU). At chemiluminescer particle excess, it approached a slightly lower plateau near 29 μRLU for each sensitizer particle (Fig. 2).

Initially, a rosette of sensitizer particles would be expected to form about each added chemiluminescer particle. The signal arising from a single particle pair interaction should then be the observed signal per chemiluminescer particle divided by the number of sensitizer particles in the rosette. When the chemiluminescer particles are in excess they should completely surround each sensitizer particle. The signal from a single particle pair interaction should then be the observed signal per sensitizer particle divided by the number of chemiluminescer particles in the rosette. A minimum of six spherical particles bound to a central particle is required to block additional binding and a maximum of 12 particles can bind if perfectly ordered. Random binding was calculated by computer modeling to yield an average rosette of 8.3 particles surrounding the central particle. A particle pair, therefore, gives rise to 3.6–7.2 μRLU (sensitizer particle excess) or 2.4–4.8 μRLU (chemiluminescer particle excess). This difference in response may result from competition between the chemiluminescer particles for a limited supply of $^1\Delta_gO_2$ when in chemiluminescer particle excess.

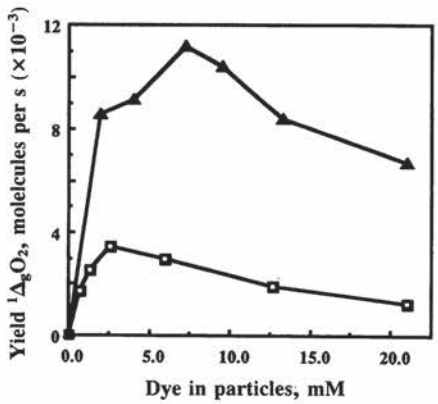


FIG. 1. Yields of $^1\Delta_gO_2$ per particle during irradiation of 200 μg of latex particles containing various amounts of Chl (squares) or 3.5 mM Chl and various amounts of **VII** (triangles) suspended in 100 μM anthracene-9,10-dipropionic acid in standard buffer.

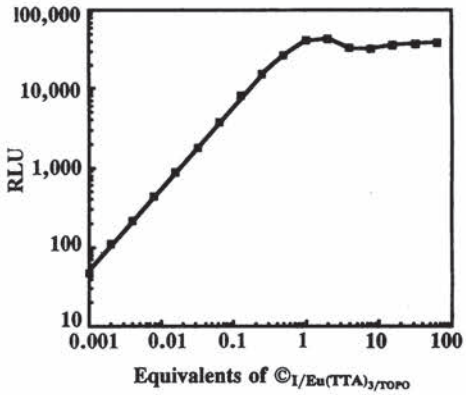


FIG. 2. Suspensions of 22 pM $\bullet_{Chl/VII}$(anti-Fl)$_{450}$·(Fl-X_{22}-biotin)$_{450}$ in 0.5 ml of assay buffer were incubated for 2 h with various amounts of $©_{I/Eu(TTA)_3/TOPO}$(SAv)$_{4000}$. The suspensions were then diluted 1:5 and irradiated at >610 nm for 1 min, and the signal was measured over 20 s.

Direct evidence that the LOCI signal could be generated from individual particle pairs was obtained by transmission electron microscopy. For this purpose $\bullet_{Chl/VII}$(anti-Fl)$_{450}$ particles were incubated with $©_{I/Eu(TTA)_3/TOPO}$(SAv)$_{4000}$ particles in the presence of anti-digoxin-(biotin)$_5$ and Fl-X_{22}-CMO-Dig. Based on the LOCI signal 1.3–2.6 × 10^8 particle pairs should have formed. This was near to the electron microscopically determined number of 3.3 × 10^8 particle pairs with almost no larger aggregates.

Few compounds could be found that interfere with singlet oxygen channeling. These were compounds that quench or react very rapidly with $^1\Delta_gO_2$. Thus 1 mM sodium azide or 5 mM ascorbate resulted in a 50% reduction in the signal from particle pairs. Since azide, which quenches $^1\Delta_gO_2$ in water with high efficiency (k_q = 5 × 10^8 $M^{-1}\cdot s^{-1}$) (12) displayed typical Stern–Volmer quenching of the LOCI signal, channeling must be due primarily or exclusively to $^1\Delta_gO_2$.

To estimate the local concentration and efficiency of capture of $^1\Delta_gO_2$ within a particle pair, the LOCI chemiluminescence was compared to the chemiluminescence and the yield of diester **III** when $©_{I/Eu(TTA)_3/TOPO}$ particles were exposed to a known $^1\Delta_gO_2$ concentration. A concentration of 7.8 pM $^1\Delta_gO_2$ during irradiation of 1 μM $PC(SO_3H)_4AlCl$ was calculated from the ratio of the measured $^1\Delta_gO_2$ formation rate to its decay rate in water of 5 × 10^5 s^{-1} (13). When uncoated $©_I$ particles were present in this solution, an average of 780 molecules per min of the diester **III** was formed in each particle. Since the presence of coordinatively saturated $Eu(TTA)_3$ would not be expected to interfere, the same rate was assumed for $©_{I/Eu(TTA)_3/TOPO}$ particles. [This assumption was used because of difficulties in measuring **III** in the presence of $Eu(TTA)_3$.] Under these conditions,

$©_{I/Eu(TTA)_3/TOPO}$ particles produced a signal of 0.28 μRLU per particle, which was reduced to 0.17 μRLU after coating with dextran. By using the above LOCI signal of 3.6–7.2 μRLU per particle pair, the local $^1\Delta_gO_2$ concentration experienced by a chemiluminescer particle in a particle pair is calculated to be 0.17–0.33 nM and 10,000–20,000 molecules per min of the diester **III** are formed.

Binding Kinetics. LOCI could be used to monitor the rate of particle dimer formation. Various concentrations of $©_{I/Eu(TTA)_3/TOPO}(SAv)_{2800}$ were mixed with a suspension of 4.89 pM $●_{Chl/VII}(anti\text{-}Fl)_{450}$·$(Fl\text{-}X_{22}\text{-}digoxin)_{46}$·[anti-digoxin-$(biotin)_5]_{25}$ particles at 37°C. With equimolar concentrations, typical second-order kinetics ($k = 2.3 \times 10^9$ $M^{-1}\cdot s^{-1}$) were observed up to 78% of the signal extrapolated to infinite time. The same rate constant was obtained from initial rates. The infinity point (2.8 μRLU per particle pair) was close to that obtained independently from the titration data (3.6–7.2 μRLU per particle pair).

The effect of receptor surface density on particle–particle binding rates was studied with 2.8 pM $©_{IV/Eu(TTA)_3/Phen}$-$(SAv)_{3400}$·[$(biotin)_5$-anti-digoxin]$_n$ and 2.8 pM $●_{Chl/VII}(dA_{40})_{540}$·$(dT_{40}\text{-}digoxin)_{300}$. Rates were measured as a function of the number of anti-digoxin IgGs (n) that were bound to the chemiluminescer particle. The relative rate constants initially increased nearly linearly with n but increased less rapidly at higher surface densities (Fig. 3).

Assay Response. Highly sensitive detection of digoxin, a typical small molecule analyte, was possible by incubating a suspension of $©_{IV/Eu(TTA)_3/Phen}(SAv)_{3400}$·$(biotin\text{-}anti\text{-}digoxin)_{12}$ and serum, adding $●_{Chl/VII}(dA_{40})_{540}$·$(dT_{40}\text{-}digoxin)_{300}$, and measuring the signal. The total assay time was only 63 s (Fig. 4). Increasing the concentration of either particle resulted in proportional increases in the signal. Since the incubation periods were substantially shorter than required for complete particle binding (≈3 min), the signal increases primarily reflect incomplete particle binding.

Human TSH was selected as a model multiepitopic analyte because of its exceptionally low concentration in hyperthyroid patient serum. $©_{IV/Eu(TTA)_3/Phen}(dA_{40})_{540}$·$(dT_{40}\text{-}anti\text{-}TSH_{\beta 1})_{250}$ particles (9.3 pM) and anti-$TSH_{\beta 2}$-$(biotin)_{15}$ (6.7 nM) were incubated in a 1:3 dilution of serum in assay buffer for 8 min. The solution was then diluted 1:6 with 17 pM $●_{Chl/VII}(SAv)_{2000}$ particles and incubated an additional 4 min. The assay response was linear over four orders of magnitude

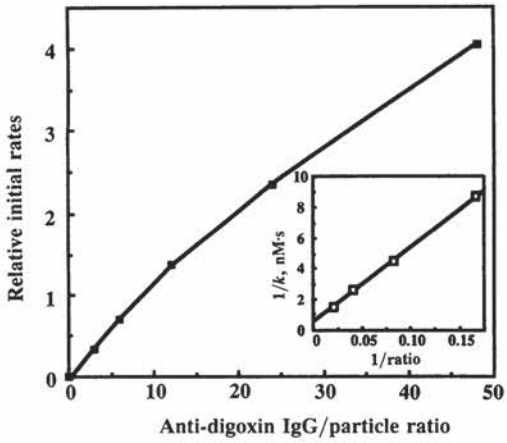


FIG. 3. Effect of anti-digoxin/particle ratios on the kinetics of binding to digoxin-coupled particles. $●_{Chl/VII}(dA_{40})_{540}$·$(dT_{40}\text{-}digoxin)_{300}$ (2.8 pM) was incubated at 37°C in assay buffer with $©_{IV/Eu(TTA)_3/Phen}(SAv)_{3400}$·[$(biotin)_5$-anti-digoxin]$_n$ (2.8 pM) having different amounts of anti-digoxin IgG. The initial rates, followed over 95 s, were normalized (*Inset*) using the independently measured second-order rate constant of 3.8×10^8 $M^{-1}\cdot s^{-1}$ for $n = 24$. Ratio refers to anti-digoxin IgG/particle ratio.

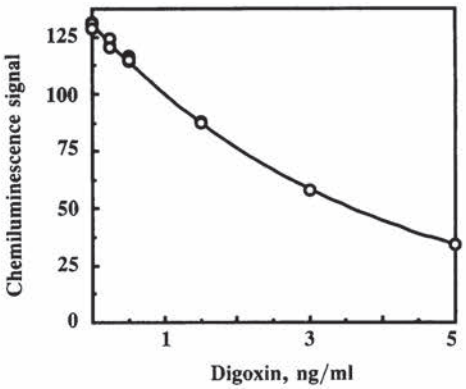


FIG. 4. Serum (50 μl) was incubated with 16 pM $©_{IV/Eu(TTA)_3/Phen}(SAv)_{3400}$·[$(biotin)_5$-anti-digoxin]$_{12}$ (350 μl) in assay buffer at 37°C for 33 s. The suspension was then diluted with 600 μl of 30 pM $●_{Chl/VII}(dA_{40})_{540}$·$(dT_{40}\text{-}digoxin)_{300}$, incubated for 20 s, irradiated, and measured. Duplicate points are shown.

and the signal from 4.2 amol of TSH (2.5×10^6 molecules) was fully resolved (≈6 σ above background). This limit was imposed by a background signal attributable to nonspecific binding between the sensitizer and chemiluminescer particles that increased linearly with time. At zero TSH concentration, there were also smaller time-independent contributions to background due to the instrument, the autochemiluminescence of the chemiluminescer, and $^1O_2$ migration to unbound chemiluminescer particles. The intensity of the latter was about equal to the specific signal at the detection limit.

DISCUSSION

Latex agglutination methods for rapid immunochemical detection generally employ relatively insensitive light-scattering measurements (3). Although it is possible to detect immunochemical formation of particle pairs by low-angle light scattering or by using flow systems such as the optical-pulse particle analyzer (14), these methods require rigorously particle-free solvents and impractically low particle concentrations (4, 5). The present study takes advantage of the short diffusion distance of $^1\Delta_gO_2$ produced in one particle to cause preferential reaction within a particle pair. The ensuing chemiluminescent reaction in an adjacent particle permits ready monitoring of particle pair formation without interference from particles in the sample. The long wavelength emission of chemiluminescent reagents, **I** and **IV**, in the presence of a europium chelate minimizes interference by biological substances, most of which absorb at shorter wavelength. Some precedence for the method can be found in the known selective cytotoxic effect of $^1\Delta_gO_2$ formed upon irradiation of sensitizers that are immunochemically targeted to cells. Direct antibody–dye conjugates have been used for *in vivo* photodynamic therapy (15) and dye-labeled liposomes bound to antibodies exhibit selective *in vitro* killing of T lymphocytes (16).

The LOCI method permits real-time monitoring of particle binding. The second-order rate constant at 37°C for the reaction of biotinylated particles (125 per particle) with particles heavily labeled with avidin (2800 per particle) was 2.3×10^9 $M^{-1}\cdot s^{-1}$. This approached the calculated bimolecular diffusion-controlled rate constant in buffer (9.0×10^9 $M^{-1}\cdot s^{-1}$) (17) and was similar to the rate constant for dimerization of oppositely charged latex particles (18). In contrast, digoxin-labeled particles (300 per particle) bind to particles labeled with anti-digoxin antibodies at a lower rate that is dependent on the antibody surface density. This behavior is consistent with formation of particle–particle encounter complexes that dissociate at a rate competitive with particle binding within the complex. The rate constant is given by

$$k = k_+ k_{on} D_s A_s / (k_{on} D_s A_s + k_-),$$

where k_+ and k_- are, respectively, the rate constants for formation and dissociation of the encounter complex; D_s and A_s are the fractional surface densities of the digoxin and the antibody; and k_{on} is the first order rate constant for binding within the encounter complex. Extrapolation to infinite A_s (Fig. 3 *Inset*) gave $k_+ = 2 \times 10^9\ M^{-1} \cdot s^{-1}$, which approximated the rate constant for avidin particle–biotin particle binding. Since the rate was unaffected by variations in the surface concentration of the digoxin, it is probably close to the maximum achievable. Previously estimated antibody-mediated particle dimerization rate constants were 100-fold lower despite very high antibody surface density (19), possibly because the antibody orientation was not controlled.

Based on Fick's First Law, a chemiluminescer particle in a particle pair experiences a $^1\Delta_g O_2$ concentration at a distance r from the center of an irradiated sensitizer particle of:

$$c(r) = \frac{S}{4\pi r D(1 + a/d)} \exp[-(r - a)/d],$$

where S is the rate of formation of $^1\Delta_g O_2$ by the particle (taken here as 11,000 s^{-1}), a is the radius of the polystyrene portion of the sensitizer particle (87.5 nm), d is the $^1\Delta_g O_2$ diffusion length $(D/k_d)^{1/2}$ (≈80 nm), k_d is the $^1\Delta_g O_2$ decay constant in water, and D is the diffusion coefficient in water. At 37°C the relative $^1\Delta_g O_2$ concentration is negligible beyond ≈250 nm from the surface (Fig. 5). For particles separated by 50 nm of dextran, the mean $^1\Delta_g O_2$ concentration at the surface of the chemiluminescer particle would be 0.2–0.3 nM $^1\Delta_g O_2$. This is consistent with the experimentally derived local $^1\Delta_g O_2$ concentration of 0.17–0.33 nM.

Data relating to the transfer efficiency of $^1\Delta_g O_2$ between adjacent particles are summarized in Table 2. Since it was found that **III** was produced at a rate of 10,000–20,000 molecules per min in a particle pair and 11,000 $^1\Delta_g O_2$ per s are formed during the 1-min standard irradiation conditions, the $^1\Delta_g O_2$ capture efficiency is 1.5–3.0%. The $^1\Delta_g O_2$ transfer efficiency between two bound particles is higher (2.3–4.6%) because only 65% of the $^1\Delta_g O_2$ entering the chemiluminescent particles reacts with **I**. Based on the chemiluminescence quantum yield of the dioxetane **II** in particles (31%), 4600 ± 1500 photons were emitted per binding event of which ≈10% were emitted during the 20-s monitoring period.

The TSH assay data are informative as to the limits of sensitivity of LOCI. A linear response to TSH concentrations down to <0.1% of the particle concentration illustrates that a single TSH molecule affects particle pair formation and that particle pairing is sufficient to obtain a signal. However, detection of TSH was limited to ≈4 amol (90 fM in serum) despite sufficient instrumental sensitivity. This limit was primarily due to time-dependent nonspecific binding of the particles. Drift of $^1\Delta_g O_2$ to unbound particles produced a less troublesome time-independent background, which was of a magnitude consistent with the expected steady-state concentration of $^1\Delta_g O_2$ (1 pM).

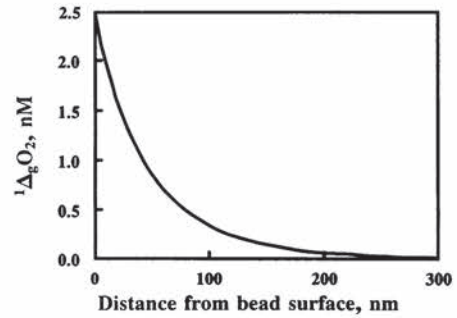


FIG. 5. Concentration of $^1\Delta_g O_2$ calculated as a function of distance from a 175-nm particle producing 11,000 $^1\Delta_g O_2$ per s.

Table 2. Efficiency of $^1\Delta_g O_2$ channeling within pairs of $\bullet_{Chl/VII}$ and $\copyright_{I/Eu(TTA)_3/TOPO}$ particles under standard 1-min irradiation conditions

Parameter	Value
Rate of $^1\Delta_g O_2$ production by $\bullet_{Chl/VII}$, s^{-1}	11,000
Efficiency of $^1\Delta_g O_2$ transfer between particles	0.035 ± 0.012
Fraction of $^1\Delta_g O_2$ entering a particle that reacts with **I**	0.65
Chemiluminescence quantum yield of **II**	0.31
Photons emitted per particle pair	4600 ± 1500

It is noteworthy that 10^2–10^3 fewer photons are emitted per analyte molecule in LOCI than in homogenous fluorescence immunoassay methods (20). Nevertheless LOCI is $>10^3$ more sensitive due to the inherently lower background emission of chemiluminescence. The method is, therefore, applicable to a broad range of analytes such as nucleic acids, antibodies, and antigens. Because no separation step is necessary, there may also be an opportunity to make direct measurements of components of fragile biological structures such as organelles and cell surfaces. Additionally, the ability to follow binding kinetics offers the opportunity to gain greater understanding of the detailed processes associated with particle–particle interactions.

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MINI-REVIEW

Role of the Development Scientist in Compound Lead Selection and Optimization

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ABSTRACT: The R&D process for bringing drugs from discovery laboratories to the marketplace is undergoing rapid change, as enabled by new technologies and as demanded by the global pharmaceutical business environment. One consequence of the accelerated R&D paradigm is a blurring of the traditional discovery-development interface, which in turn impacts the traditional roles of discovery and development scientists. R&D organizations must find ways to screen out rapidly compounds that have relatively poor probability of successful registration. Quality of development candidates can be favorably influenced by early consideration of "developability" criteria along with receptor-based potency and specificity. Computational approaches and/or high-throughput experimental determinations will be used increasingly to profile compound characteristics which influence "developability." If such criteria are considered at the time of lead selection and optimization, the compound attrition rate during later development should be decreased from the historical norm. This article discusses the emerging role of development scientists during small-molecule lead selection and optimization. The changing role of development scientists also has implications for graduate curricula in the pharmaceutical sciences. © 2000 Wiley-Liss, Inc. and the American Pharmaceutical Association J Pharm Sci 89: 145–154, 2000

INTRODUCTION

The research-based pharmaceutical industry has faced growing challenges in recent years as a result of increased economic and regulatory pressures. Rising health care costs, increasing price pressure from managed care organizations, international price controls, rapid appearance of generic products (or competition within a therapeutic class) in the market, and more stringent regulatory policies have compelled the research-based pharmaceutical companies to refine and accelerate their drug discovery–development processes.[1–3] While the advent of genomics, combinatorial chemistry, and other drug discovery innovations and technologies have resulted in an unprecedented abundance of new targets and potential drug candidates, additional productivity pressures require R & D organizations to rapidly screen out compounds that do not have a high probability of successful registration and commercialization.[4] R&D spending by US pharmaceutical companies in 1999 is expected to be ~$21.1 billion (an ~11% increase over 1998) compared to a total R&D expenditure of $6.5 billion ten years ago.[5] Thus, while the research-based

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pharmaceutical industry has added powerful new technologies to enhance discovery output, the rate of entry of new chemical entities into the market may still be slower than desired for long-term growth and commercial success, especially if development resources are constrained and the odds of successful nonclinical and clinical development are not improved over the historical norm. Simply increasing the quantity of compounds in development, i.e., playing the numbers game, may not in itself yield better results. Rather, the quality of drug candidates must also be improved by setting judicious selection criteria at an early stage.[6]

Given the historical success rate of ~40% for discovery compounds going from preclinical testing into humans, and only 10% of those making it into the market,[7] a major challenge for the research-based pharmaceutical companies is, simply put, to decrease the attrition rate during development. The historical average 90% attrition rate is no longer compatible with long-term success.

This review article will focus on the role of the development scientist, in the small-molecules area, during compound lead selection and optimization to improve the efficiency of the discovery process (viz., quality of compounds selected to enter development) and thereby increase the probability of success. The development scientist can contribute to an environment where lead selection is no longer based predominantly on iterative SAR methods but is also influenced by "developability" information generated using computational methods and systematic experimental approaches. Although organizations differ, for purposes of this article the development disciplines involved during candidate selection shall include Pharmaceutics, ADME, Toxicology, Analytical R & D, and Process Chemistry. These disciplines will assess the developability of the potential drug candidate based on its safety profile, synthetic route, and biopharmaceutical properties.[7]

TRADITIONAL DISCOVERY–DEVELOPMENT INTERFACE

Traditionally (through the late 1980s), the medicinal chemist in drug discovery has focused on ligand selectivity and specificity (K_i).[8,9] Although the medicinal chemists were aware of the importance of physicochemical properties such as MW, log *P*, solubility, and ADME properties (bioavailability, clearance), these were often not weighted highly relative to K_i during compound selection. *In vitro* screening methods for target specificity often resulted in compounds that were excellent ligands but not necessarily good development candidates, since lead compounds which are high-affinity ligands usually tend toward high molecular weights and increased lipophilicity, which may result in poor absorption.[10] Additionally, *in vitro* screening methods for affinity often use nonaqueous solvents, and thus poorly water soluble compounds may emerge as optimal leads. In this way, traditional optimization designs may actually be counterproductive since they may systematically select against favorable delivery properties.[9]

After a drug candidate was selected in this way, development scientists were given the task of efficiently synthesizing the molecule, formulating it, and testing it for biopharmaceutical properties. Even though the development scientists had a good understanding of the factors that affect success further along the pipeline, there was often little interaction between the discovery scientists and development scientists during compound lead selection. As a result of this paradigm and the differences in the mindsets of discovery and development scientists, [11] the latter were often faced with difficult challenges to "fix" a compound's development liabilities, and high attrition (or slow development) often resulted. The traditional development paradigm thus also tended to increase development time and cost. As pointed out in a recent article, "an efficacious but non-absorbed agent is no better than a well absorbed but inefficacious one."[9]

Toxicity of the drug candidate, lack of efficacy, and poor biopharmaceutical properties (termed "inappropriate pharmacokinetics" in one study[12]) are some of the primary reasons for failure and/or slowdown (Table I). The poor biopharmaceutical properties are often attributable to poor chemical stability in the gut, poor solubility (and hence dissolution rate), poor permeability (and hence absorption), and poor metabolic and/or elimination profile. For example, during the development of MK-678, a cyclic hexapeptide, it was initially mistakenly believed that susceptibility to enzymatic cleavage was the only obstacle to oral bioavailability.[8] Although MK-678 was stable to relevant proteases its oral bioavailability was <5%, demonstrating that stability to proteases was a necessary but not sufficient condition for adequate bioavailability. Later studies suggested that the secondary amide bonds within MK-678 allowed

Table I. Reasons for Failure and/or Slow Down of Compounds in Development

Reasons for Failure[a]	Reasons for Slow Down[b]
Poor biopharmaceutical properties, 39%	Synthetic complexity
Lack of efficacy, 29%	Ambiguous toxicity finding
Toxicity, 21%	Poor biopharmaceutical properties
Market reasons, 6%	Low potency
	Inherently time-intensive target indication

[a] Source for reasons for failure: ref. 12.
[b] Not an exhaustive list.

for extensive solvation, thus decreasing absorption and contributing to poor bioavailability.[8] These and other factors such as hydrogen bonding potential or polar surface area and susceptibility to efflux pumps must also be taken into consideration during lead identification and optimization. In another instance, special formulation efforts such as using a liquid-filled soft gelatin capsule were used at Pfizer to bring CP-212454, a poorly aqueous-soluble CCK-B receptor antagonist, as a candidate into development. [13] However, it was later established that oxidative degradation of the compound in the formulation would preclude it from being developed. As a result, the focus was shifted toward identifying a more soluble analogue to yield higher exposure in humans from a conventional oral dosage form.[13]

EMERGING MULTIVARIATE OPTIMIZATION

To overcome some of the pitfalls associated with the traditional lead identification and optimization process, many pharmaceutical companies have taken steps in the early- to mid-1990s to integrate the functions of discovery and development scientists.[14,15] Development scientists should ideally become involved in the drug discovery program in the early lead identification stages and then continue to provide input during *in vitro* and *in vivo* optimization. For example, at Wyeth-Ayerst, discovery teams together with an early development team champion the identification of a candidate for drug development.[16] Interestingly, the development team is present in nascent form during discovery stages and assesses the "readiness" of the molecule for development. This is because within Wyeth-Ayerst it was found that the root of a significant portion of early development problems and their solutions lies in the discovery phase, and therefore the importance of thinking about development during the discovery phase was recognized. [16] Several pharmaceutical companies have recently incorporated high-throughput screens to profile compounds for properties such as solubility, metabolic stability, permeability, P450 inhibition, etc. and have used the data base to help select improved candidates for development.[17] Dupont has developed a fluorescence assay-based automated high-throughput screen to eliminate highly electrophilic compounds (propensity to conjugate with glutathione) which may have undesirable safety or ADME properties.[18] Such preclinical assessment tools could identify likely early failures in development without spending resources on clinical trials.

As a consequence of combinatorial chemistry approaches, the number of compounds available for evaluation has increased dramatically.[19,20] While in the past a chemist could make a few hundred compounds a year, it is now possible to synthesize ~10^4 compounds per chemist–year.[5] Within a given project (pharmacologic target), these compounds often span a variety of chemotypes and each chemotype offers thousands of compounds. With the arrival of combinatorial chemistry in pharmaceutical lead optimization, there are now two routes for proceeding in the discovery of new drugs. One route is the application of automated synthesis to prepare large numbers of new compounds and then screen every one of them for various properties. The other route is to use a rational drug design approach wherein the compounds, albeit in large numbers, are synthesized based on molecular modeling techniques and iterative structure-based ligand design.[21,22] Although both routes have their pros and cons, it is suggested that "building in" the appropriate properties into the molecules at the time of chemotype selection and lead optimization is critical even as new technologies are embraced in the race for new drugs.

In the early stages of a directed discovery effort, where thousands of compounds are being screened, it is prudent to obtain estimates (through computational approaches where possible) of important biopharmaceutical properties such as solubility, permeability, potential for metabolism, etc., to provide guidance to the medicinal chemist in making strategic decisions about arriving at preferred chemotypes.[10,23,24] At the *in vitro* screening stage, it may be useful to estimate

relevant developability criteria through medium- or high-throughput screens, so that the chemist can steer away from "problematic" chemotypes while trying to enhance the selectivity and specificity of the candidates. As the discovery program advances to the *in vivo* screening stage, the candidate field should be narrowed substantially. More detailed and precise experimental work can then be initiated on a case-by-case basis so that the discovery–development team can arrive at a handful of potential candidates for ultimate selection for development. The team must ensure that the decision factors are appropriately weighted such that essential properties are not weeded out while the desirable properties are maximized. For example, for intravenous delivery of a promising anticancer compound reasonable aqueous solubility is desirable but may not be essential since, in consideration of the potentially great medical benefit, the development team could consider alternative nonaqueous or partially aqueous solubilization systems. Larger infusion volumes (of a more dilute solution) may also be considered for clinical administration, although this may be less practical in preclinical models. Such "extreme" formulation approaches, however, may be unacceptable when developing a compound for use in a less dire or partially satisfied medical need, and thus low aqueous solubility may be a reason to reject a compound. What we describe here is thus a holistic approach to optimization of development candidates based on evaluation of multiple variables at various tiers. Similar rational, systematic approaches are fast emerging within the industry as a workable means to decrease the compound attrition rate during drug development.

One of the challenges in the new development process is to decide the value of the information obtained on a series of compounds as a function of time (i.e., the temporal sequence within the discovery pipeline). At the earliest stages of a discovery program, very little or no bulk drug substance is available for evaluation. At this stage, compound profiling information may be generated *"in silico"* (i.e., derived from molecular structure by computational algorithms). The quality and utility of such *in silico* data must be evaluated carefully by the project team as many algorithms inherently lack precision. Once the compound is available, albeit in very small amounts, automated systems may be developed to generate profiling information in a high-throughput mode. After a high-throughput screen, compounds of interest can be further supplied to allow more precise measurements of key parameters, where the value of the data warrants the additional effort. For example, although fundamental preclinical PK–PD relationships may be helpful in compound evaluation, attempts to develop extensive PK–PD correlation in preclinical models may not often be justified. This is because the relevance of these data to the clinical situation is often tenuous, even though reliable PK–PD data may be obtained in multiple animal models.[25] In cases where the pharmacology of a novel target requires preclinical validation, this may be achieved by a constant i.v. infusion whereby the plasma levels can be controlled with reasonable precision.

As described above, if the shift from traditional methods to a more holistic approach is implemented, the closer integration of discovery and development activities affords the opportunity to design drug candidates which not only have good pharmacological properties but also have good biopharmaceutical properties. Such a multivariate optimization, however, necessarily requires compromise and judgment calls as to which criteria are critical and how much weight should be given to each. For example, factors such as potency, solubility, pK_a, lipophilicity, metabolic stability, absorption, excretion, protein binding, and toxicity affect the performance of a drug intended for oral administration. These factors are intimately linked and any chemical structural modifications to modulate one property selectively may adversely affect one or more of the other key properties. The concept of multivariate optimization, therefore, will not guarantee success of the candidate in the clinic, but it should increase the chances of success during development. Additionally, while the optimization strategy will not yield the "perfect" candidate, several strategic considerations also impinge on development candidate selection. These considerations include unmet medical need and patient demographics, global business/marketing potential, nature of the competition, and innovativeness/medical breakthrough potential. Each of these factors must be weighed in addition to developability in choosing drug candidates and in setting the go/no-go hurdles for the project.

Identifying the right candidate for development may thus be viewed as a balancing act of finding the "leaders" versus eliminating the "laggards." In an ideal situation, the lead selection and optimization process should first eliminate

the poor compounds and from the remaining pool of acceptable compounds, the winner compound(s) should be picked. The criteria should also be set in such a way that the chances of rejecting a good compound are minimized.

Clearly, early identification of compounds with high potential for development requires a multidisciplinary approach. Table II lists the developability properties that may be assessed by the functional areas at various stages of the discovery process. Recognition of overlaps between the functional areas is important and active collaboration is essential for ultimate success.

Even after following a systematic process to arrive at a developable candidate, compounds with liabilities from a developability perspective may still emerge, and the integration of discovery and development may continue through exploratory clinical programs as shown in Scheme 1. This scheme reflects a recent trend in the pharmaceutical industry wherein companies have tested several drug candidates in the clinic before selecting the drug to be fully developed and registered. The rapid testing of a series of potential drug candidates in humans (Phase I/II), in parallel where possible, is employed to validate and feed back information to preclinical models for subsequent discovery iterations. The pyrone-based HIV-1 protease inhibitors (Pharmacia and Upjohn) are a good example of this type of development.[26] The first-generation pyrone (PNU-96988) and the second-generation cyclooctylpyrone (PNU-103017) were tested through Phase I single- and multiple-dose clinical trials to gain insight into the human tolerance, clinical pharmacokinetics, and biopharmaceutical properties of this novel structural class of compounds. On the basis of the information gathered, a superior dihydropyrone analog (PNU-140690) was subsequently designed which showed better potency, lower protein binding, greater permeability, and greater metabolic stability. Such a scheme may be particularly relevant for "first-in-class" compounds where there is a higher risk due to absence of prior clinical information and the therapeutic potential is not proven in humans. While the company advances compound(s) which may not be fully optimized quickly into the clinic to obtain safety and proof-of-concept, discovery efforts are continued to enhance the properties of the drug candidates. The PK–PD data from the first clinical studies provide feedback to guide design and selection of superior candidates. According to this strategy, discovery does not end when a compound is selected for initial clinical evaluation, but continues at least until a candidate enters full clinical efficacy trials aimed at product registration.

PREDICTIVE TECHNIQUES

With the recent influx of large numbers of compounds, the future demands increasing use of computational methods. These include predictive/computational models for physicochemical properties (solubility, pK_a, $\log P$), and more recent emphasis on prediction of pharmacokinetic and toxicology profiles. For example, several recent publications have shown that quantitative relationships using $M \log P$, H bonding, polarity, and a molecular size descriptor may be used to predict permeability across physiological barriers with reasonable success.[27–30] QSAR models have also been developed to predict potential for eye irritation on the basis of aqueous solubility of the irritant and its strength of binding to the mucus membrane.[31]

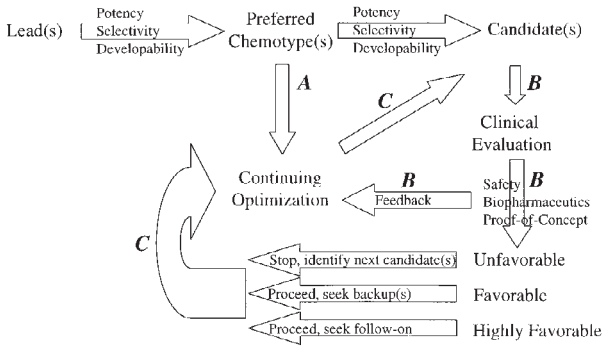
Various commercial interests are currently engaged in development of models to predict molecular attributes including permeability and other ADME properties. Typically, these employ a "training set" of data to regress molecular properties against various structural descriptors, e.g., molecular surface area calculations. The predictive power of such models depends on the size and diversity of the training set and on the extent of extrapolation which may be attempted. At this point, although properties might be predicted for conceptualized structures, the scientist must still do the conceptualizing. As this field advances, machine-learning might be coupled to such models, whereby the model could be queried to suggest structural modifications to shift properties in the desired direction.

In a recent seminar at Bristol-Myers Squibb, Dr. Michael Wise (Pembroke College, Cambridge University) discussed simulation of metabolic pathways by *in silico* biochemistry.[32] Current state-of-the-art computational approaches do not scale well (i.e., it becomes disproportionately harder to simulate larger-pathway systems) and cannot reliably model non-steady-state behavior, especially highly nonlinear systems such as cascades. Dr. Wise described a data flow computational approach which models metabolic processes as a network of reactions occurring at physiologically relevant concentrations. For example, direction of a reaction depends on the rela-

Table II. Assessment of Some Developability Criteria at Various Stages of Drug Discovery (Example Shown Is for Compounds Intended for Oral Delivery, and the List Is Not Comprehensive)

Discovery Stage	Early	In Vitro	In Vivo	Candidate Selection
Activity	Screening for "hits"	Chemical analoging	Optimization	Selection for development
Number of compounds	Thousands	Hundreds	Dozen(s)	1–5
Pharmaceutics	In silico approaches (log *P*, pK_a, solubility)	High-throughput aqueous solubility, potential for chemical instability, prodrug potential	pK_a, pH-solubility profile, chemical stability, log *P*, nonaqueous solubility	Crystallinity, hygroscopicity, salt potential, solid-state stability, pH-stability, other delivery attributes, overall formulation potential
ADME	In silico approaches[a] (predictive ADME)	Caco-2 permeability, protein binding, cytochrome P450 inhibition and metabolic stability	Oral bioavailability, clearance, elimination half-life in animal model(s)	Oral bioavailability in multiple species, dose and formulation dependence
Process chemistry	–	–	Core process chemistry, potential synthetic difficulties	Yield, crystallinity, purity, enantiomeric purity, chemical and physical form, cost-of-goods
Toxicology	In silico approaches[a] (predictive toxicology)	Hepatotoxicity, cell-based assays	Pharmacology-based assays, mutagenicity, teratogenicity	Carcinogenicity, in vivo toxicology
Analytical R&D	–	Chemical structure profiling	Chemical structure profiling	Assay development, impurity issues

[a] Computational models under development.



Scheme 1. Integration of drug discovery and development. Discovery, Non-clinical Development and Clinical Development collaborate to identify compound(s) with high probability of successful registration and commercialization. Pathways ***A*** and ***B*** are conducted in parallel to guide selection of the next generation of candidates (pathway ***C***), should they be needed.

tive concentration of reactants (based on K_{eq}) and relative affinities of the enzyme for the competing reactants (modeled by relative $1/K_m$ values). The flux through a pathway is therefore the sum of the fluxes through the chains of reactions. Dr. Wise commented that this "black box" approach to enzyme reactions is novel and will take about 5 years to be fully implemented. A preliminary version of the system, lacking much of the final functionality but illustrating the ideas, has been published.[33]

In addition to *in silico* methods, several high throughput *in vitro* methods have been developed to estimate ADME properties in both humans and animals.[34] Examples include Caco-2 permeability studies to study transport mechanism, metabolism studies with the common cytochrome P450 isozymes to determine susceptibility and identify metabolites by LC/MS, and ELISA-based assays for studying cytochrome P450 induction potential. LC/MS is rapidly becoming the analytical tool of choice during metabolism studies because in addition to being highly selective and sensitive, the method can accelerate *in vitro* screening procedures significantly. Additional advantages of using such *in vitro* methods are that they require limited amounts of material, are amenable to moderate/high throughput, do not suffer from inter-animal variability, and provide an opportunity for parallel optimization of potency and bioavailability. A recent example illustrated the use of *in vitro* intestinal tissues and Caco-2 cell models and *in vivo* intraduodenal/intraportal models in the design of orally active endothelin receptor antagonists. With these ADME models, a structure–transport relationship was established, enabling the design and identification of an orally active compound.[35]

In vivo ADME screening of compounds increasingly involves so-called cassette dosing where multiple compounds are mixed, dosed simultaneously, and the plasma samples are analyzed for individual compounds.[34] While such a method can provide preclinical data rapidly on multiple compounds, some caution must be exercised due to the possibility of misleading data as a result of drug–drug interactions. For example, an interesting situation arose in Glaxo-Wellcome during cassette dosing of a group of compounds known to have dose-dependent pharmacokinetics in rats. One of these compounds had an apparent oral bioavailability of >300% when the oral dosing cassette data were compared to the corresponding intravenous cassette data. When dosed singly, the oral bioavailability was <10%. Saturation of clearance by first-pass metabolism was hypothesized as the reason for this observation when cassette dosing was employed.[36] Plasma pooling and continuous withdrawal of samples are other techniques used as fast screening tools for discovery candidates.[34] In plasma pooling, the volume of the sample is selected to represent the corresponding sampling interval, and time-averaged concentrations are used to determine AUC.[37] This method can often provide PK data in close agreement with more labor- and time-intensive traditional methods.[38]

Besides predictive ADME capability, the other area of greatest need is the ability to predict the toxicological profile of compounds during lead selection. The current GLP methods rely primarily on animal data and are sequential and resource-intensive. As in the other functional areas, the trend is toward earlier prediction or detection of potential toxicological liabilities by *in silico* and moderate-throughput *in vitro* screens, respectively. The latter are designed to detect potential for mutagenesis, teratogenesis, carcinogenesis, and specific organ toxicities. However, it is still unclear if these *in vitro* models will be usable in a high-throughput mode. Other current efforts are aimed at mechanistic understanding of toxicity at the molecular level by conducting studies with hepatocytes, liver slices and/or microsomes, and isolated proteins with specific experimental endpoints. One example of a predictive toxicology model arose during the discovery of PNU-101033E, a compound for asthma, where occur-

rence of phospholipidosis was correlated to gall bladder toxicity in several lab species.[39] An *in vitro* phospholipidosis assay was subsequently developed and was used in a moderate throughput screen to arrive at potential leads, one of which is now in clinical trials.[34,40]

A FUTURISTIC VIEW

Recently, PriceWaterhouseCoopers (PWC) asserted that the pressure for resources and greater competition for patients will compel the pharmaceutical industry to substantially truncate the clinical trials process and radically change pharmaceutical R & D.[5] They speculate that emerging techniques such as single-cell differential gene expression and target searches will enable the industry to identify targets with the ideal physiological and pathological characteristics. Armed with these leads, companies may someday be able to perform *in silico* clinical trials based on computer models that test for human safety, efficacy, and drug–drug interactions. Although admittedly the regulatory agencies may not accept such evidence for some time, the authors of the PWC report[5] suggest that in the future the industry may be able to go from test tube directly to human efficacy trials.

IMPLICATIONS FOR TRAINING AND SKILL SETS OF DEVELOPMENT SCIENTISTS

Given the complex, multidisciplinary approach to lead candidate selection and optimization, the training and skill sets of development scientists can have a significant impact on their effectiveness at the discovery–development interface. As much as it is important to pick winner development candidates, it is equally important to train winner scientists in the collaborative discovery–development arena. The development scientists should of course be experts in their fields and be able to set the critical developability criteria in their area of expertise. Additionally, they should be familiar with the language and problem-solving approaches of the other areas and be able to communicate effectively with the synthetic organic chemists, biologists, and other discovery-related disciplines. Developing an understanding of the role of informatics, combinatorial chemistry and high-throughput techniques with special regard to automation and miniaturization is critical. The development scientist should also have a fundamental understanding of the overall discovery process including genomics, target selection, screening to identify "hits" and leads, and finally, the candidate selection and optimization process.

All of this requires the development scientist to have multidisciplinary training along with the ability to think critically, to solve scientific problems, and to communicate effectively. A pharmaceutical scientist involved in the drug discovery process should be able to interface with the chemists and provide input on relevant biopharmaceutical properties. He/she has to have a sound background in physical and organic chemistry to predict/determine and alter properties such as solubility, chemical stability, pK_a and to examine the potential to prepare suitable prodrugs. He/she should also be able to interface with the pharmacokineticist to understand the issues associated with bioavailability, distribution, and elimination and to understand the physiological barriers to absorption at the cellular level. The pharmaceutical scientist should of course be able to conduct preformulation studies (physical profiling, chemical form selection, etc.) and prepare suitable prototype formulations for *in vitro*/*in vivo* testing. The breadth of background required to function effectively at the discovery–development interface poses significant challenges to universities in developing their graduate curricula, especially when combined with the more traditional areas of training in pharmaceutical technology and manufacturing operations. One result may be more specialization, either as a strategic choice of the particular college and faculty, or if offered as different curriculum "concentrations." Students or recent graduates might also gain valuable experience through industrial internships and/or focused on-the-job training. Certainly universities must balance breadth of expertise with depth to prepare well-rounded scientists for the pharmaceutical industry.

SUMMARY AND CONCLUSIONS

The R & D process for bringing new drugs from the discovery laboratories to the marketplace is undergoing significant and rapid change. Change is demanded by the realities of the global pharmaceutical marketplace and is enabled by powerful new technologies. One consequence of the new R & D paradigm is a blurring of the traditional discovery–development interface, which in turn impacts the traditional roles of discovery and de-

velopment scientists. The future will likely depend on achieving the proper balance between the quantity of candidates brought into development and their quality as influenced by early consideration of development criteria along with receptor-based potency and specificity. Early use of computational approaches followed by high throughput experimental determinations may become the norm as best practices are adopted to improve the chances of successful preclinical and clinical development. Although traditional clinical trials will continue to be conducted and are unlikely to be replaced by "virtual bodies" or *in silico* clinical trials for some years, in the near term research-based pharmaceutical companies must continue to expand and refine computational approaches to preclinical compound assessment and must manage the resulting data bases efficiently. If developability criteria are considered at the time of lead selection and optimization, the compound attrition rate during clinical development should be decreased from the historical norm. Development scientists play a critical role in ensuring that this occurs and is managed appropriately in development candidate selection. Interestingly, as the research-based pharmaceutical companies are moving towards more rapid and efficient R & D processes, the U.S. FDA has also responded to these increased pressures through several initiatives recognizing that "neither FDA nor industry can change unilaterally."[41] It is hoped that the universities are also attentive to these ongoing changes and are adapting their curricula to meet the future demand for pharmaceutical scientists with appropriately broadened perspectives and skill sets.

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CHAPTER NINETEEN

Analog Design

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1 INTRODUCTION

This chapter is limited to nonprotein therapeutic candidates. The rapidly evolving field of peptide analogs and peptidomimetic agents merits and requires separate and extensive consideration. In any strategy aimed at designing new drug molecules or analogs of known biologically active compounds, there are no absolute rules for procedure or guidelines; the knowledge, imagination, and intuition of the medicinal chemist are the most important factors for success. Analog design is as much an art as it is a science. The concept of analog design presupposes that a lead has been obtained, i.e., a chemical compound has been identified that possesses a desirable pharmacological property. The search for and identification of leads is a challenge and is a separate topic. It is sufficient for the present discussion to note that lead compounds are frequently identified as endogenous participants (hormones, neurotransmitters, second messengers, or enzyme cofactors) in the body's biochemistry and physiology, or a lead may result from routine, random biological screening of natural products or of synthetic organic molecules that were

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created for purposes other than for use as drugs.

Analog design is most fruitful in the study of pharmacologically active molecules that are structurally specific: their biological activity depends on the nature and the details of their chemical structure. Hence, seemingly minor modification of the molecule may result in a profound change in pharmacological response (increase, diminish, completely destroy, or alter the nature of the response). In pursuing analog design and synthesis, it must be recognized that the newly created analogs are different chemical entities from the lead compound. It is not possible to retain all and exactly the same solubility and solvent partition characteristics, chemical reactivity and stability, acid or base strength, and/or *in vivo* metabolism properties of the lead compound. Thus, although the new analog may demonstrate pharmacological similarity to the lead compound, it is not likely to be identical to it, nor will its similarities and differences always be predictable.

The goal of analog design is twofold: (*1*) to modify the chemical structure of the lead compound to retain or reinforce the desirable pharmacologic effect while minimizing unwanted pharmacological (e.g., toxicity, side effects, or undesirable metabolism) and physical and chemical properties (e.g., poor solubility and solvent partitioning characteristics or chemical instability), which may result in a superior therapeutic agent; and (*2*) to use target analogs as pharmacological probes (i.e., tools used for the study of fundamental pharmacological and physiological phenomena) to gain greater insight into the pharmacology of the lead molecule and perhaps to reveal new knowledge of basic biology. Studies of analog structure–activity relationships may increase the chemist's ability to predict optimum chemical structural parameters for a given pharmacological effect.

Analog design is greatly facilitated if the chemist can initially define the pharmacophore of the lead compound: that combination of atoms within the molecule that is responsible for eliciting the desired pharmacologic effect. Analog design may be directed toward maintaining this combination of atoms intact in a newly designed molecule or toward a carefully planned, systematic modification of the pharmacophore. If the chemist is uncertain about the composition of the pharmacophoric portion of the molecule, a prime initial goal of analog design should be to define the pharmacophore. The chemist addresses the following questions: What change(s) can be made in the lead molecule that permit(s) retention or reinforcement of the basic pharmacological action? and What change can be made in the molecule that diminishes, destroys, or qualitatively changes the basic pharmacological action? The ideal program of analog design should involve a *single* structural change in the lead molecule with each new compound designed and synthesized. An analog in which multiple changes in the structure of the lead molecule have been made simultaneously may occasionally produce a molecule with highly desirable pharmacologic effects but relatively little useful information will be gained from such a molecule. It cannot be readily determined which change (or which combination of changes) was responsible for the enhancement of the desired pharmacology. On a practical basis, it is frequently chemically impossible to effect only one discrete change in the lead molecule; one simple molecular structural alteration will influence many structural and chemical parameters. Nonetheless, the chemist should be cognizant of the disadvantages inherent in "shotgun" modification of lead molecules.

In analog design, molecular modifications of the lead compound can involve one or more of the following strategies:

1. Bioisosteric replacement.
2. Design of rigid analogs.

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3. Homologation of alkyl chain(s) or alteration of chain branching, design of aromatic ring position isomers, and alteration of ring size.
4. Alteration of stereochemistry, or design of geometric isomers or stereoisomers.
5. Design of fragments of the lead molecule that contain the pharmacophoric group (bond disconnection).
6. Alteration of interatomic distances within the pharmacophoric group or in other parts of the molecule.

None of these strategies is inherently preferable to the others; all merit the chemist's attention and consideration. Application of combinations of these strategies to the lead molecule may be highly advantageous. Considering the possible permutations and combinations of these changes that are possible within a single lead molecule, it is obvious that the number of analogs that can be designed from a single lead compound is large. Some structural changes that might be proposed are chemically impossible, e.g., the molecule is incapable of existence, or it represents an overwhelmingly formidable synthetic challenge. These negative factors will diminish the population of possible analogs to be considered for synthesis; nevertheless, the chemist will always be confronted with myriad possible target molecules, resulting from a lead molecule. Rational decisions must be made concerning which compounds should be synthesized, and synthetic priorities must be established for target compounds. It is reasonable that, all other factors being equal, the chemist should synthesize the less challenging targets first. Beyond this truism, the chemist's best resources are his or her intuition and imagination. Selection and application of specific molecular modification strategies depends on the chemical structure of the lead compound and, to a certain extent, on the pharmacologic action to be studied.

All of the strategies of analog design as well as subsequent decisions concerning target compounds to be synthesized can be facilitated by computer-assisted molecular modeling techniques, which may give the chemist further insights into structural, stereochemical, and electronic implications of the proposed molecular modification.

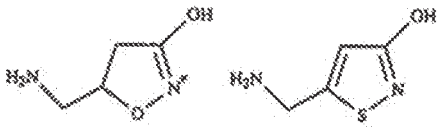
2 BIOISOSTERIC REPLACEMENT

The concept of bioisosterism derives from the observation that certain physical properties of chemically different substances (e.g., carbon monoxide and nitrogen and ketene and diazomethane) are strikingly similar (1). These similarities were rationalized on the basis that carbon monoxide and elemental nitrogen each have 14 orbital electrons, and similarly, diazomethane and ketene each have 22 orbital electrons. Medicinal chemists have expanded and adapted the original concept to the analysis of biological activity. The following definition has been provided: "Bioisosteres are groups or molecules which have chemical and physical properties producing broadly similar biological properties" (2). This definition might be expanded to include the concept that bioisosteres may produce opposite biological effects, and these effects are frequently a reflection of some action on the same physiological process or at the same receptor site. Bioisosteric similarity of molecules is commonly assigned on the basis of the number of valence electrons of an atom or a group of atoms rather than on the number of total orbital electrons, as was originally specified by Langmuir. In a remarkable number of instances, compounds result that have similar (or even diametrically opposite) pharmacologic effects to the parent compound. The significant concept is that the bioisosteres are affecting, in some fashion, the same receptor site or pharmacological mechanism.

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Categories of classic isosteres have been illustrated (2) (Table 19.1).

Dihydromuscimol 1 and thiomuscimol 2 are cyclic analogs of γ-aminobutyric acid (GABA) in which the C=N moiety of the heterocyclic ring is bioisosteric with the C=O of GABA. In addition, the -S- moiety of thiomuscimol is bioisosteric with the ring -O- of dihydromuscimol. Both structures (1) and (2) are highly potent agonists at GABA-A receptors (3). A classic bioisosteric replacement study was reported for a methoxytetrahydropyran-derived inhibitor (4) of 5-lipoxygenase (4) (Table 19.2). None of the isosteric replacements was as potent as the lead compound (4). However, the thio isostere (5) approaches the oxygen compound (4) in potency, and

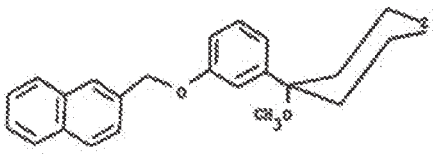


(1) (2)



(3)

Table 19.2 Inhibition of 5-Lipoxygenase



Structure	Z	IC_{50} (μM)
(4)	O	0.07
(5)	S	0.4
(6)	CH_2	2.6
(7)	C=O	3.4
(8)	SO	4.2
(9)	SO_2	10.6
(10)	NCH_3	>40

Table 19.1 Bioisosteric Atoms and Groups

1. *Univalent*

-F —OH -NH_2 -CH_3 -Cl
-SH PH_2
-I -t-C_4H_9
-Br -i-C_3H_7

2. *Bivalent*

-O- -S- -Se- $-CH_2-$ -NH-
COOR COSR $COCH_2R$ CONHR

3. *Trivalent*

-N= -CH=
-P= -As=

4. *Quadrivalent*



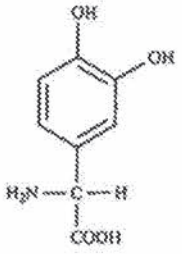
5. *Ring equivalents*

-CH=CH- -S- (e.g., benzene-thiophene)
=CH- =N- (e.g., benzene-pyridine)
-O- -S- $-CH_2-$ -NH-

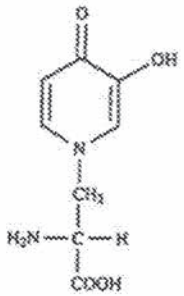
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subsequent studies may reveal other advantages of the sulfur compound as a therapeutic agent candidate.

Because of its bioisosteric similarity to the normal substrate L-dopa (11), L-mimosine (12) inhibits the enzyme tyrosinase (5). These compounds exemplify a situation in which bioisosteres display *opposite* pharmacological effects at the same receptor.



(11)

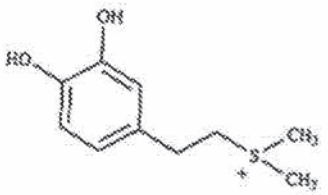


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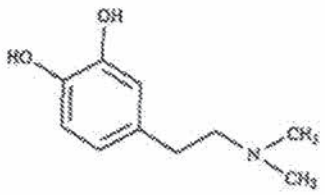
The sulfonium isostere (13) of *N,N*-dimethyldopamine (14) retains the dopaminergic agonist effect displayed by structure (14) (6).

The fact that structure (13) bears a permanent unit positive charge was invoked in support of the hypothesis that β-phenethylamines such as structure (14) interact with the dopamine receptor(s) in their protonated (cationic) form.

Bioisosteric replacement strategy has



(13)



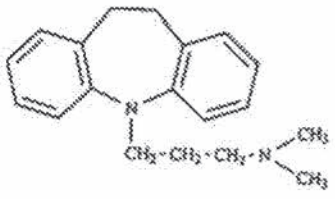
(14)

been fruitful in design of tricyclic antidepressants, using the dibenzazepine derivative imipramine (15) as the lead.

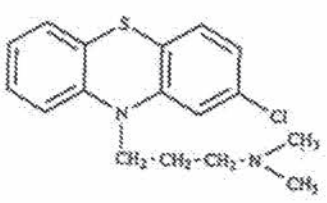
The structural similarity between imipramine (15) and the phenothiazine antipsychotics [typified by chlorpromazine (16)] is apparent. Although these two bioisosteric molecules have different pharmacological uses and likely have different mechanism and sites of action in the central nervous system (7), they share the property of being psychotropic agents. In the antidepressant dibenzocycloheptene derivative amitriptyline (17), the ring nitrogen of imipramine is replaced by an exocyclic olefinic moiety. Demexiptiline (18), doxepin (19), and dothiepin (20) represent other bioisosteric modifications of imipramine that possess antidepressant activity (8).

While the strategy of bioisosteric replacement may be a powerful and highly productive tool in analog design, Thornber (2) has emphasized that fundamental chemical and physical chemical changes will result from this molecular modification, which may in themselves profoundly affect the pharmacological action of the resulting molecules. Possible modifications include change in size of the atom involved in the bioisosteric replacement, change in the shape of the substituted group and possible resulting change in the shape of the entire molecule, differences in bond angles, change in partition coefficient, change in pK_a of the molecule; alteration of chemical reactivity and chemical stability of the

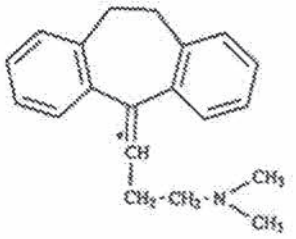
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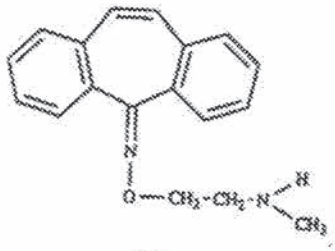
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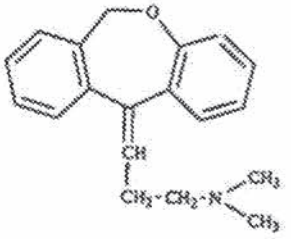
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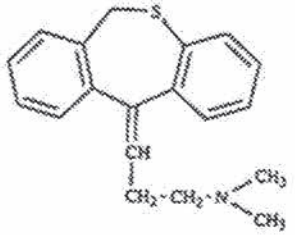
(17)



(18)



(19)



(20)

molecule with accompanying alteration of the nature of *in vivo* metabolism of the molecule, and change in hydrogen bonding capacity. The effect and pharmacological significance of many of these parameters are unpredictable and must be determined experimentally.

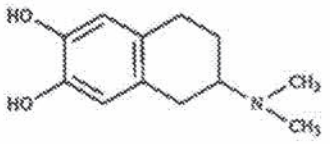
3 RIGID ANALOGS

Imposition of some degree of molecular rigidity into a flexible organic molecule (by incorporation of elements of the flexible molecule into a rigid ring system or by introduction of a carbon–carbon double or triple bond) may result in potent, biologically active agents that show a higher degree of specificity of pharmacological effect. There are two possible advantages to this technique (9): the three-dimensional geometry of the pharmacophore can be determined and the key functional groups are held in one position, or in the case of a semirigid structure, these groups are constrained to a limited range of steric dispositions and interatomic distances. By the rigid analog strategy, it is possible to approximate "frozen" specific conformations of a flexible lead molecule, which may

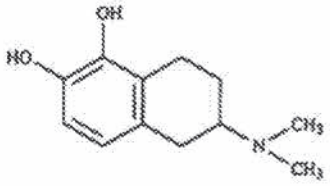
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provide enhanced pharmacological effect and may assist in defining and understanding structure–activity parameters. Computer-based molecular modeling has been shown to be a useful tool in designing rigid analogs.

The semirigid tetralin congeners (21, 22) of *N,N*-dimethyldopamine (14) represent different rotameric conformations of the aromatic ring of dopamine as the aromatic ring relates to the ethylamine side chain when the ring and the side chain are coplanar. Structural constraints of the tetralin ring system impose this restricted geometry on the dopamine moiety. Compounds (21) and (22) display different spectra of effects at different subpopulations of dopamine receptors (10) which likely reflect different conformations assumed by the flexible dopamine molecule at its various *in vivo* sites of action.

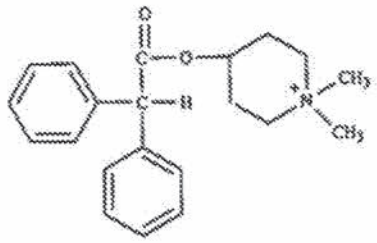


(21)

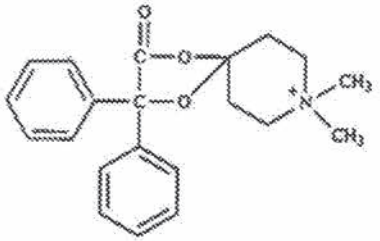


(22)

Restriction of conformational freedom of the acyl moiety in 4-DAMP (23) (an antimuscarinic compound displaying higher affinity at ileal M_3 acetylcholine receptors than at atrial M_2-receptors) was imposed by the structure of the spiro-compound (24) (11).



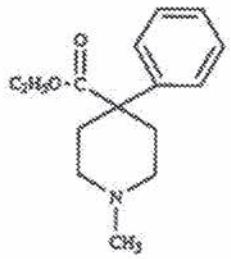
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(24)

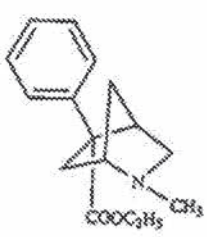
Spiro-DAMP (24) was slightly more potent at M_2 muscarinic receptors than at M_3 receptors. It was proposed that the geometry of the spiro-molecule might reflect the receptor-bound conformation of 4-DAMP (23); this conformation differs from that observed in the crystal structure of 4-DAMP.

Imposition of rigidity into the piperidine ring of meperidine (25) by introduction of a methylene group between carbons 3 and 6 resulted in the epimers (26) and (27), frozen conformations of meperidine (12).

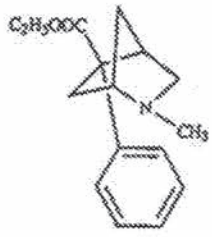


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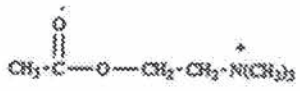
(26)



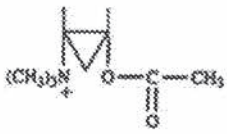
(27)

Isomer (27) was six times as potent as isomer (26), and it was twice as potent as meperidine itself.

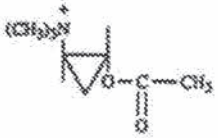
Incorporation of the choline portion of the neurotransmitter acetylcholine (28) into a cyclopropane ring system resulted in cis- and trans-1,2-disubstituted molecules (29), (30) in which the acetylcholine molecule is frozen into folded ("cisoid") and extended ("transoid") conformations.



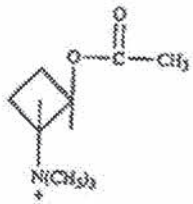
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(29)



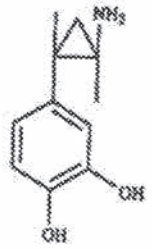
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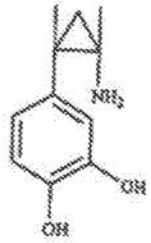
(31)

The (1*S*), (2*S*)-(+)-trans-isomer (30) was somewhat more potent than acetylcholine itself in assays for muscarinic agonism (13) and it was an excellent substrate for acetylcholinesterase. The (±)-cis-isomer (29) was almost inert at muscarinic and nicotinic receptors and was a poor substrate for acetylcholinesterase. These data were taken as evidence that the flexible acetylcholine molecule interacts with muscarinic receptors in an extended geometry of the chain of atoms (14). When this semirigid analog strategy for acetylcholine was applied to a cyclobutane ring system [compound (31)], there was a marked loss of pharmacological effect (15). This result is enigmatic; differences in interatomic distances and bond angles in the pharmacophoric moiety as well as differences in the amount of extraneous molecular bulk seem insufficient to account for the dramatic difference in pharmacological potencies between the three- and the four-membered ring systems.

The cyclopropane ring has been employed to impart a degree of rigidity to the side chain of dopamine [structures (32), (33)] (16).



(32)



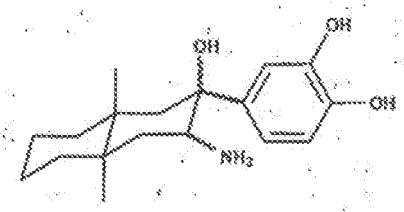
(33)

Neither isomer displayed effects at dopamine receptors, but both were α-adrenoceptor agonists, with the (±)-trans-isomer (32) approximately five times more potent than (±)-cis-isomer (33). It has been suggested (17) that these findings are significant in solving the problem of the

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preferred conformation of β-phenethylamines at the α-adrenoceptor.

The β-phenylethanolamine moiety was incorporated into the *trans*-decalin ring system (34) and the racemic modifications of all four possible isomers were prepared as significant frozen conformations of the flexible norepinephrine molecule (18). All four compounds displayed approximately equal (extremely low) potency. The achievement of conformational integrity by incorporation of a flexible pharmacophore into a bulky, complex molecule may be at the expense of biological activity.

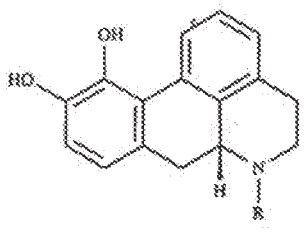


(34)

4 HOMOLOGATION OF ALKYL CHAIN OR ALTERATION OF CHAIN BRANCHING, CHANGES IN RING SIZE, AND RING POSITION ISOMERS

Change in the size or branching of an alkyl chain on a bioactive molecule may have a profound (and sometimes unpredictable) effect on physical and pharmacological properties. An increase in the number of carbons in a chain may significantly increase the lipophilic character of the molecule and change the partition coefficient, which may be reflected in the biology of the compound: alteration of absorption, transport, and excretion properties. Alteration of the size and/or shape of an alkyl substituent can affect the conformational preference of a flexible molecule and may alter the spatial relationships of the components of the pharmacophore, which may be reflected in the ability of the molecule to achieve complimentarity with its receptor or with the catalytic surface of a metabolizing enzyme. The alkyl group itself may represent a binding site with the receptor (via hydrophobic interactions), and alteration of the chain may alter its binding capacity. Conversely, extension of an alkyl chain or branching of it may introduce sufficient extraneous bulk into the molecule to interfere with its optimal interaction with the receptor or with metabolizing enzymes. Position isomers of substituents (even alkyl groups) on aromatic rings may possess different pharmacological properties. In addition to their ability to alter electron distribution in an aromatic ring system, position isomers may differ in their complimentarity to *in vivo* receptors, and a substituent position on a ring may influence the spatial occupancy of the ring system with respect to the remainder of a conformationally variable molecule. What sometimes has been trivialized and denigrated as "methyl group roulette" may indeed be an important parameter in the design of analogs.

Homologation of the *N*-alkyl chain in norapomorphine 35 from methyl (36) to ethyl (37) to *n*-propyl (38) produced increases in emetic action in dogs and in



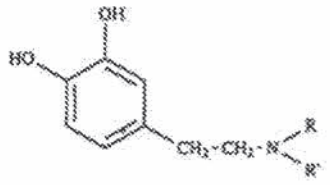
(35) R = H (38) R = *n*-C_3H_7

(36) R = CH_3 (39) R = *n*-C_4H_9

(37) R = C_2H_5

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stereotypy responses in rodents (19, 20). The homolog, *n*-butyl (39) demonstrated a tremendous loss in potency and activity compared with the lower homologs (20). Studies of *N,N*- dialkylated dopamines (40)–(43) revealed that combinations of alkyl groups may impart a high degree of dopamine agonist effects (21).



(40) R = R' = CH_3

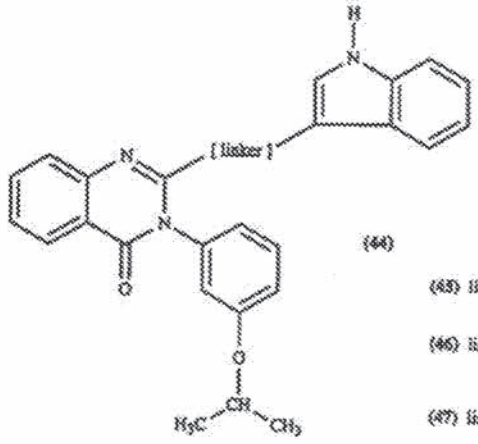
(41) R = R' = *n*-C_3H_7

(42) R = *n*-C_3H_7; R' = *n*-C_4H_9

(43) R = R' = *n*-C_4H_9

Thus, *N,N*-dimethyldopamine (40) is extremely potent in certain assays for dopaminergic agonism, and *N,N*-di-*n*-propyldopamine (41) (22) and *N*-*n*-propyl-*N*-*n*-butyldopamine (42) (23) are potent dopaminergic agonists, whereas *N,N*-di-*n*-butyldopamine (43) is inert (22). It seems likely that the enhanced dopaminergic agonist effects conferred by *N*-ethyl and *n*-propyl groups on aporphine and β-phenethylamine-derived molecules are not related merely to enhanced lipophilic character or to partitioning phenomena, but rather to the likelihood that the 2- and 3-carbon chains have a positive affinity for subsites on certain dopamine receptors. These receptor subsites do not accommodate longer chains (e.g., *n*-butyl).

The alkyl linker between the two heterocyclic ring systems in compound (44) was modified in studies of the ability of analogs to bind to the cholecystokinin-B receptor (24). When this linking group was ethylene (45), extremely potent receptor binding resulted. Introduction of carbon–carbon unsaturation into the linker (46) resulted in a 16-fold decrease in binding ability; this suggests a deleterious effect of conformational restriction and limitation of molecular flexibility on biological activity. Branching of the linker chain with a methyl



(44)

(45) linker =

(46) linker =

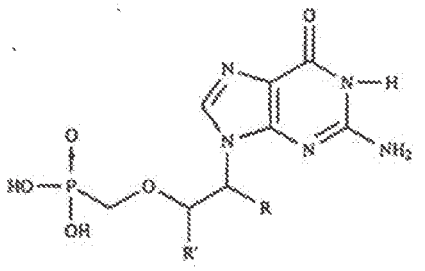
(47) linker =

(48) linker =

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group adjacent to the quinazolinone ring (47) produced a 350-fold decrease in binding potency. However, chain branching with a methyl group in the alternate position on the dimethylene chain produced a compound (48) whose potency was of the same order of magnitude as the extremely potent lead compound (45). The exponential difference in receptor binding ability exhibited by the two isomeric-branched chain-linker compound (47) and (48) was ascribed to unfavorable steric interactions between the receptor and the linker methyl group of structure 47 (24). Isomers such as structures (47) and (48) may generate useful computer-generated molecular modeling data with respect to the preferred conformation of the ligand for optimum receptor interaction and the definition of receptor topography.

A study (25) of (phosphonomethoxy) ethylguanidines (49)–(52) as antiviral agents revealed that branching of the ethylene chain by introduction of a methyl at position 1′ (51) diminished antiviral activity 25-fold and diminished toxicity 16-fold compared to the unmethylated system (49).



(49) R = R′ = H

(50) R = H ; R′ = CH_3

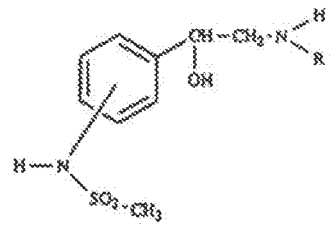
(51) R=CH_3 ; R′ = H

(52) R = H ; R′ = *gem* - di - CH_3

In contrast, (*R*)-(50), the 2′-methyl congener, exhibited only a 5-fold decrease in antiviral potency as compared to compound (49), but it also exhibited a 30-fold lessening of toxicity to provide a substantial increase in therapeutic index over compound (49). The 2′, 2′-*gem*-dimethyl congener (52) was somewhat less potent than the (*R*)-2′-monomethyl compound (50) and was markedly more toxic. The (*S*)-2′-methyl analog (50) exhibited a decidedly lower therapeutic ratio than its (*R*)-enantiomer, demonstrating pharmacological difference between stereoisomers.

Closely related to the alteration of chain length and/or branching is alteration of ring size. A methoxytetrahydrofuran derivative (53) (Table 19.3) showed activity as an inhibitor of 5-lipoxygenase (4). The size of the oxygen-containing ring as well as the position of the oxygen member with respect to the methoxy and aryl substituents was varied, as shown in Table 19.3. The (seven-membered) oxepane ring derivative (58) and the (six-membered) tetrahydropyran ring derivative (57) showed enhanced potency over the tetrahydrofuran lead compound (53).

In a series of arylsulfonamidophenethanolamines (59) (26), derivatives bearing the sulfonamido group meta to the ethanolamine side chain displayed properties of a β-adrenoceptor partial agonist, whereas those bearing the sulfonamido group in the para position were β-antagonists (26).

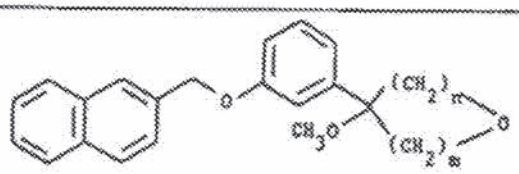


(59)

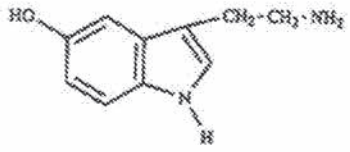
The phenolic group of serotonin (60) was incorporated into a pyran ring (61) (27), which represents an alkyl substituent at position 4 of the indole ring system.

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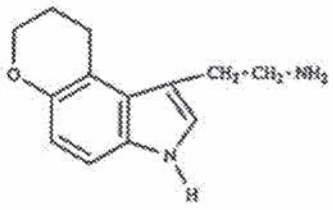
Table 19.3 Inhibition of Lipoxygenase



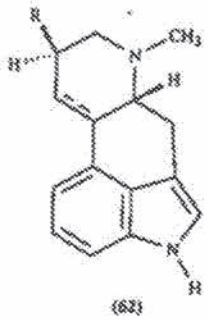
Structure	n	m	IC_{50} (μM)
(53)	1	2	0.7
(54)	1	1	2.5
(55)	1	3	1.7
(56)	1	4	2.5
(57)	2	2	0.07
(58)	2	3	0.2



(60)



(61)



(62)

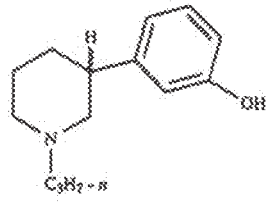
This analog lost serotonin-like affinity for 5-HT_1 receptors, but it is potent and selective for 5-HT_2 receptors. The low affinity for 5-HT_1 receptors was rationalized, in part, on the basis of steric interference between the dihydropyran ring and the aminoethyl side chain which inhibits the tryptamine system from assuming the folded "ergot alkaloid-like" conformation, as illustrated in structure (62), which probably approximates the conformation of serotonin at 5-HT_1 receptors.

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5 ALTERATION OF STEREOCHEMISTRY AND DESIGN OF STEREOISOMERS AND GEOMETRIC ISOMERS

The earlier, almost universally accepted, opinion that, in the case of chiral molecules one enantiomer would be expected to demonstrate pharmacological activity and the other enantiomer should be expected to be pharmacologically inert is not valid. It must be anticipated that all stereoisomers of an organic molecule will exhibit frequently widely different and unpredictable pharmacological effects.

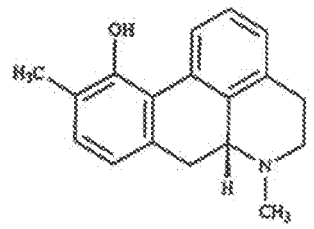
(±)-3-(3-Hydroxyphenyl)-*N*-*n*-propylpiperidine ("3-PPP") (63) was described (28) as having highly selective action at dopaminergic autoreceptors.



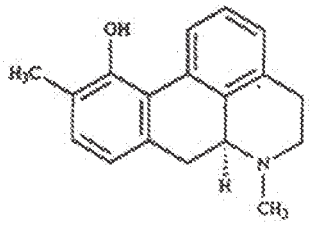
(63)

This racemate was resolved (29). At high doses the (*R*)-enantiomer selectively stimulated presynaptic dopaminergic receptor sites, while at lower doses, it selectively stimulated postsynaptic receptor sites. In contrast, the (*S*)-enantiomer stimulated presynaptic dopamine receptors and at the same dose level, it blocked postsynaptic dopamine receptors. Thus this enantiomer exhibits a bifunctional mode of dopaminergic attenuation, that of presynaptic agonism and postsynaptic antagonism. The pharmacological effects of the racemic modification are the sum total of the complex activities of the two enantiomers, and the observed pharmacology of racemic 3-PPP is not an accurate reflection of the pharmacological potential of the individual enantiomers. Pharmacological testing of only a racemic modification is inadequate and may be misleading.

(*R*)-(−)-11-Hydroxy-10-methylaporphine (64) is a highly selective serotonergic 5-HT_{1A} agonist (30).



(64)



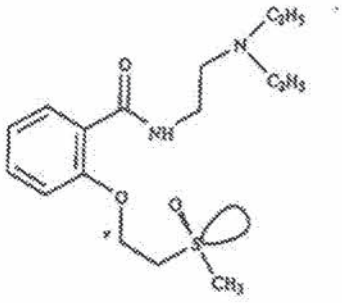
(65)

Remarkably, the (*S*)-enantiomer (65) is a potent antagonist at this same subpopulation of serotonin receptors (31). The phenomenon of enantiomers which possess opposite effects (agonist–antagonist) at the same receptor, once considered to be extremely rare, has recently been noted more often, probably due to the increasing recognition by chemists and pharmacologists that each member of an enantiomeric pair may possess its own unique and unpredictable pharmacology.

In addition to stereochemistry about a carbon center, other potentially chiral atoms offer possibilities for pharmacological significance. A gastroprokinetic com-

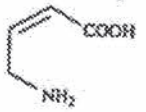
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pound (66) with serotonergic activity bears a chiral sulfoxide moiety (32). The enantiomers are equipotent, but the (*S*)-isomer demonstrates a greater intrinsic activity than the (*R*).



(66)

cis- and *trans*-4-Aminocrotonic acids (67), (68) were prepared (33) as congeners of γ-Aminobutyric acid (GABA) (3).



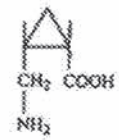
(67)



(68)



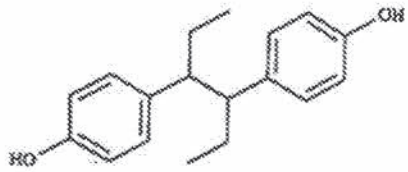
(69)



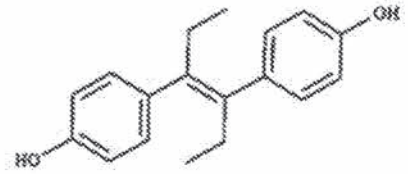
(70)

The folded *cis*-isomer (67) was inert in assays for GABA agonism, whereas the extended *trans*-isomer (68) was active. These data demonstrate biological differences of geometric isomers, which in turn involve yet another structural parameter: imposition of a degree of structural rigidity upon the molecule. A parallel strategy to the *cis*/*trans* GABA congeners (67) and (68) addressed *cis*- and *trans*-1,2-disubstituted cyclopropane derivatives (69) and (70) whose relative effects at GABA receptors paralleled those of the olefinic derivatives (34).

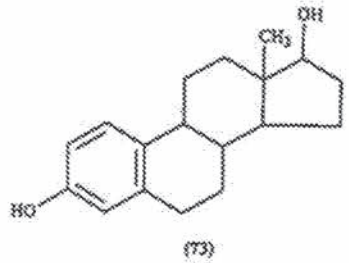
Hexestrol (71), the saturated congener of diethylstilbestrol (72), is the *meso*-form of the molecule. It has the greatest estrogenic potency of the three possible stereoisomers (35). In diethylstilbestrol (72), the E-isomer (trans), has 10 times the estrogenic potency of the Z-isomer (cis); this effect has been rationalized because the E-geometric isomer is an open chain analog of the natural estrogen estradiol (73) (36). In dienestrol (74), the geometric isomerism possible with olefinic moieties has been invoked to achieve a similar kind of open chain analogy to the steroid ring system as in diethylstilbestrol, and a high level of estrogenic activity results.



(71)

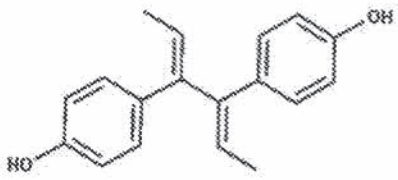


(72)



(73)

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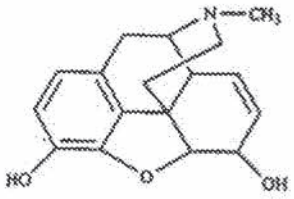


(74)

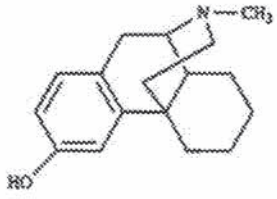
6 FRAGMENTS OF THE LEAD MOLECULE

Design of fragments of a lead molecule is based on the premise that lead molecules, especially polycyclic natural products, may be more structurally complex than is necessary for optimal pharmacologic effect. Buried within the structure of such a lead compound is a pharmacophoric moiety that, if it can be clearly defined, may be "dissected out" to result in a biologically active, simpler molecule that may itself be used as a lead in further analog design. A bond disconnection strategy may be employed, in which bonds in the chemical structure are broken or removed to destroy one or more of the rings. The result may be a valuable drug that is more accessible (through chemical synthesis) than the original lead molecule. A disadvantage to this strategy of drug design is that greater flexibility may be introduced into a rigid molecule, and the conformational integrity of the pharmacophore that may have existed in the original lead molecule is compromised or lost, sometimes at the expense of activity/potency. There may be a similar destruction of chiral centers, which may be undesirable.

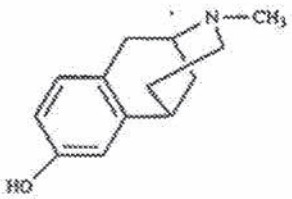
Morphine (75) can be cited as a lead molecule to illustrate fragment analog design.



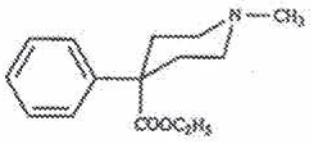
(75)



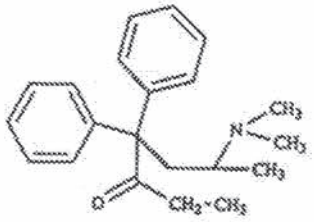
(76)



(77)



(78)

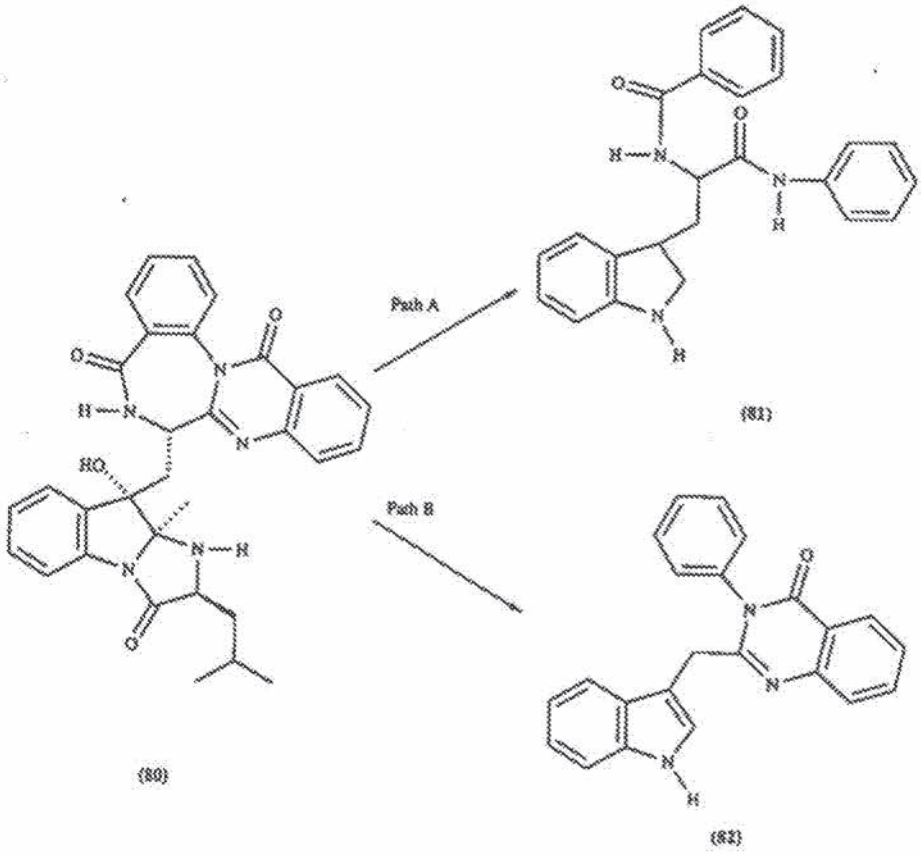


(79)

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The analgestic pharmacophore of morphine has been defined (37) as the basic nitrogen, an aromatic ring (the "A" ring) three carbon atoms removed from the nitrogen, and a quaternary carbon adjacent to the aromatic ring, which provides a region of molecular bulk (37). A bond disconnection strategy involved disruption of the hydrofuran ring to give rise to morphinan ring derivatives, e.g., levorphanol (76), whose pharmacological effects closely parallel those of morphine (38). Further simplification of the morphine ring system led to benzomorphan derivatives, typified by metazocine (77), in which morphine like narcotic analgesic activity is retained. Finally, 4-phenylpiperidine derivatives typified by meperidine (78) and the noncyclic system methadone (79) present the putative analgesic pharmacophore with a seemingly minimal number of extraneous atoms. These simple compounds retain narcotic analgesic activity. It must be noted, however, that the discovery of analgesic activity in 4-phenylpiperidine derivatives was not a result of a systematic structure-activity study of the morphine molecule, but was serendipitous (39).

Asperlicin (80), a potent cholecystokinin-A antagonist, was subjected to two different bond disconnection strategies, as indicated (40).

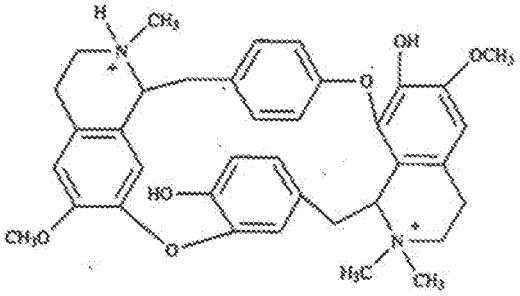


(80) (81) (82)

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Path A leads to tryptophan derivatives (81), some of which are potent cholecystokinin antagonists (41). Some quinazolinone derivatives (82) of disconnection pathway B showed extremely high potency and excellent selectivity as cholecystokinin-B receptor subtype ligands (24). A combination of X-ray crystallography and computer-based molecular modeling was utilized in the decision making process in the bond disconnection (24) and in the design of specific target molecules.

The myoneural blocking pharmacophore in *d*-tubocurarine (83) includes the two cationic heads (a quaternary ammonium group and a protonated tertiary amine); the cationic heads are separated by ten atoms (nine carbons and one oxygen).



(83)

$$(CH_3)_3\overset{+}{N}-(CH_2)_{10}-\overset{+}{N}(CH_3)_3$$

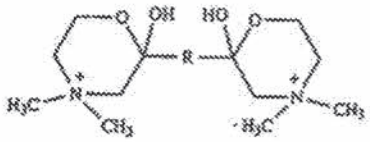
(84)

Based on these parameters, a simple molecule, (decamethonium) (84), in which two trimethylammonium heads are separated by 10 methylene groups to approximate the internitrogen distance in *d*-tubocurarine, was designed independently by two groups of investigators (42, 43). This synthetic fragment/analog of *d*-tubocurarine exhibits a high degree of potency and activity in production of flaccid paralysis of skeletal muscles, superficially like that of the lead compound. However, *d*-tubocurarine's myoneural blockade is of the nondepolarizing type whereas decamethonium produces a depolarizing type of skeletal muscle blockade. This fundamental difference in mechanism of action is due in part to the flexibility of the decamethonium molecule compared with *d*-tubocurarine. The difference in mechanism of action of the two myoneural blocking agents results in a considerable difference in the spectrum and severity of side effects and in the technique of employment in clinical practice. In all types of analog design, changes in chemical structure may result in changes in mechanism of action, even though the chemical nature of the pharmacophoric group may not be altered.

7 VARIATION IN INTERATOMIC DISTANCES

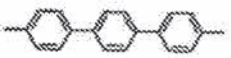
Alteration of distances between portions of the pharmacophore of a molecule (or even between other portions) may produce profound qualitative and/or quantitative changes in pharmacological actions. In a series of congeners of hemicholinium (85), the central biphenyl portion of the molecule was changed to terphenyl (86) and to *p*-phenylene (87). Both changes resulted in profound loss of myoneural blocking activity (44). This result was ascribed to alteration of the interquaternary nitrogen distance of 14.4 Å in hemicholinium (85) (which was assumed to be the optimum for myoneural blockade) to 18.4 Å in the terphenyl analog and to 10.2 Å in the *p*-phenylene analog. The central biphenyl "spacer" in hemicholinium (85) was changed to a 2,7-disubstituted phenanthrene (88), *trans*,*trans*-4,4-bicyclohexyl (89), and 2,2'-dimethylbiphenyl (90). In all three of these systems the 14.4-Å interquaternary distance in hemicholinium (85) was maintained; all of these congeners were quali-

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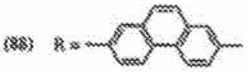
(85) R =



(86) R =



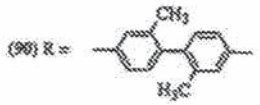
(87) R =



(88) R =



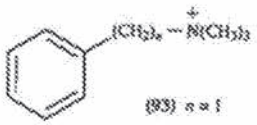
(89) R =



(90) R =

(91) R = $-(CH_2)_6-$

(92) R = $-(CH_2)_7-$



(93) $n = 1$

(94) $n = 2$

(95) $n = 3$

tatively and quantitatively similar to hemicholinium in inhibition of neuromuscular transmission. Conformational analysis of the polyalkylene congeners (91 and 92) demonstrated that when the flexible polyalkylene chain is maximally extended and in a staggered conformation, the interquaternary distance in the hexamethylene congener (91) is approximately 14 Å, and in the heptamethylene congener (92) it is approximately 15 Å. Both compounds exhibited hemicholinium-like inhibition of neuromuscular transmission, although they were less potent than hemicholinium (45). This diminution of potency might be ascribed to the compromising of another structural parameter in the hemicholinium molecule: the rigidity of the central biphenyl spacer unit that maintains the internitrogen distance.

In a series of phenylalkylenetrimethylammonium derivatives (93)–(95), nicotinic agonism is maximal when $n = 3$ [compound (95)].

It was concluded (46) that a moiety (benzene ring) with high electron density three or four single bond lengths (approx. 6 Å) from the cationic center is a requirement for nicotinic agonism in the series (46).

In α,ω-bis-trimethylammonium polymethylene compounds (96–99), maximal activity for blockade of autonomic ganglia resides in those derivatives where $n = 5$ or 6 (96 and 97) (47, 48)

$(CH_3)_3\overset{+}{N}-(CH_2)_n-\overset{+}{N}(CH_3)_3$

(96) $n = 5$ (98) $n = 16$

(97) $n = 6$ (99) $n = 18$

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Ganglionic effects drop drastically when $n = 4$ or 7. These observations have been rationalized on the basis of attainment of optimal interquaternary distance in the penta- and hexamethylene congeners for optimal interaction with ganglionic receptor subsites. Remarkably, as the number of methylene groups in compound (96) is further greatly expanded, a high level of ganglionic blocking potency returns. The hexadecyl and octadecyl congeners (98) and (99) are approximately four times as potent at autonomic ganglia as the penta- and hexamethylene compounds. As was mentioned previously, polymethylene bis-quaternary systems, in which the cationic heads are separated by 10 methylene groups, have potent effects at myoneural junctions and little action at autonomic ganglia. Thus extension of a *bis*-quaternary polyalkylene molecule from 5 or 6 methylenes to 10 produces a pharmacological change from ganglionic blockade to myoneural blockade, and further extension to 16 or 18 methylenes results in loss of myoneural effects and a return of ganglionic blocking action.

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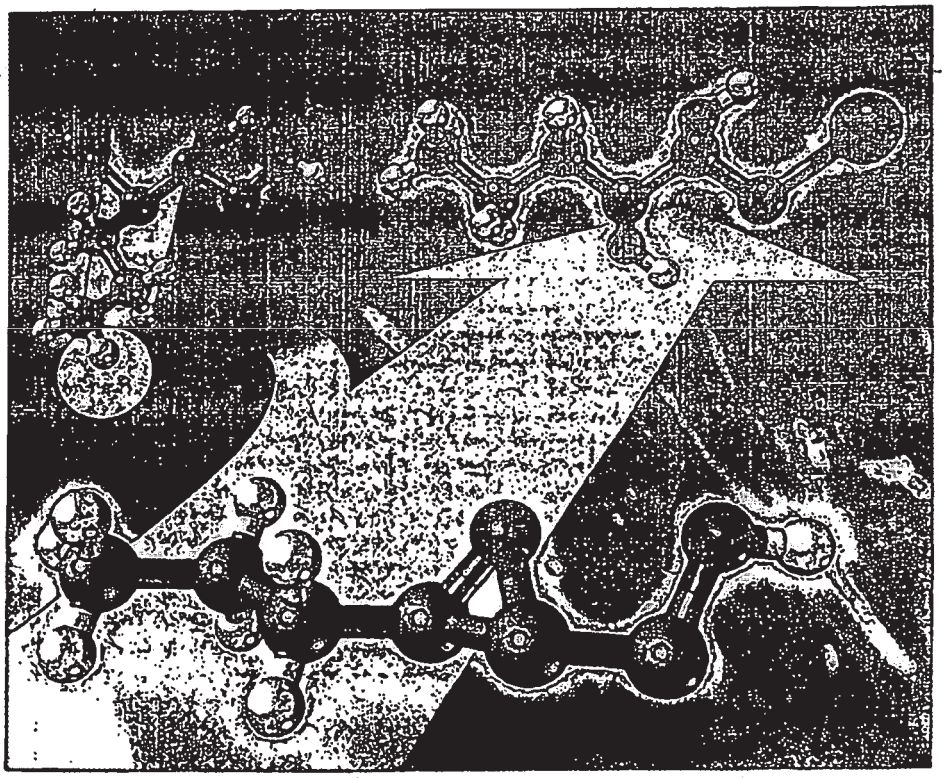
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F. Zaragoza Dörwald

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Side Reactions in Organic Synthesis

A Guide to Successful Synthesis Design



Florencio Zaragoza Dörwald

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Preface

Most non-chemists would probably be horrified if they were to learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why.

Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such work.

This book attempts to highlight the competing processes and limitations of some of the most common and important reactions used in organic synthesis. Awareness of these limitations and problem areas is important for the design of syntheses, and might also aid elucidation of the structure of unexpected products. Two chapters of this book cover the structure–reactivity relationship of organic compounds, and should also aid the design of better syntheses.

Chemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious). Nevertheless, I have ventured to describe some reactions as difficult or impossible. A talented chemist might, however, succeed in performing such reactions anyway, for what I congratulate him in advance. The aim of this book is not to stop the reader from doing bold experiments, but to help him recognize his experiment as bold, to draw his attention to potential problems, and to inspire, challenge, and motivate.

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1
Organic Synthesis: General Remarks

1.1
Introduction

Organic reactions almost never yield exclusively the desired product. Students learn this when they perform their first synthesis in the laboratory, for example the synthesis of anisole from phenol. Although the starting materials, the intermediates, and the product are all colorless, the reaction mixture will turn uncannily dark. This darkening shows that in reality much more is going on in addition to the expected process, and that obviously quite complex chemistry must be occurring, giving rise to extended conjugated polyenes from simple starting materials. Fortunately these dyes are usually formed in minute amounts only and the student will hopefully also learn not to be scared by color effects, and that even from pitch-black reaction mixtures colorless crystals may be isolated in high yield.

Because most reactions yield by-products and because isolation and purification of the desired product are usually the most difficult parts of a preparation, the work-up of each reaction and the separation of the product from by-products and reagents must be carefully considered while planning a synthesis. If product isolation seems to be an issue, the work-up of closely related examples from the literature (ideally two or three from different authors) should be studied. Many small, hydrophilic organic compounds which should be easy to prepare are still unknown, not because nobody has attempted to make them, but because isolation and purification of such compounds can be very difficult. Therefore the solubility of the target compound in water and in organic solvents, and its boiling or melting point, should be looked up or estimated, because these will aid choice of the right work-up procedure.

The chemical stability of the target compound must also be taken into account while planning its isolation. Before starting a synthesis one should also have a clear idea about which analytical tools will be most appropriate for following the progress of the reaction and ascertaining the identity and purity of the final product. Last, but not least, the toxicity and mutagenicity of all reagents, catalysts, solvents, products, and potential by-products should be looked up or estimated, and appropriate precautionary measures should be taken.

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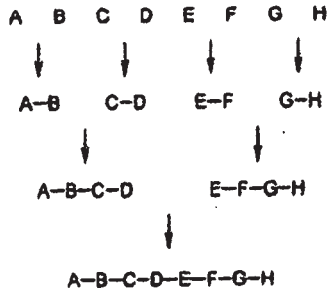
1.2
Synthesis Design

The synthesis of a structurally complex compound requires careful retrosynthetic analysis to identify the shortest synthetic strategies which are most likely to give rapid access to the target compound, ideally in high yield and purity. It is critical to keep the synthesis as short as possible, because, as discussed throughout this book, each reaction can cause unexpected problems, especially when working with structurally complex intermediates. Also for synthesis of "simple-looking" structures several different approaches should be considered, because even structurally simple compounds often turn out not to be so easy to make as initially thought.

1.2.1
Convergent vs Linear Syntheses

If a target compound can be assembled from a given number of smaller fragments, the highest overall yields will usually be obtained if a convergent rather than linear strategy is chosen (Scheme 1.1). In a convergent assembly strategy the total number of reactions and purifications for all atoms or fragments of the target are kept to a

convergent strategy:



7 reactions, total yield with respect to monomer A: 51%
(for 80% yield per coupling step)

linear strategy:

A → A–B → A–B–C → A–B–C–D → A–B–C–D–E →
A–B–C–D–E–F → A–B–C–D–E–F–G → A–B–C–D–E–F–G–H

7 reactions, total yield with respect to monomer A: 21%
(for 80% yield per coupling step)

Scheme 1.1. Convergent and linear assembly strategies.

minimum. If a linear strategy is chosen the first fragment (A in Scheme 1.1) will be subjected to a large number of reactions and purifications, and the total yield with regard to this first fragment will be rather low. Syntheses should be organized in such a way that expensive and/or structurally complex fragments are subjected to the fewest possible number of transformations.

1.2.2 Retrosynthetic Analysis

1.2.2.1 Introduction

When planning a synthesis, the most suitable starting materials should be chosen. These should be structurally and/or stereochemically as closely related to the target as possible, to keep the synthesis brief. The first steps of a good synthesis may even be low-yielding (if the products are easy to purify), because at these early stages little work and reagents have been invested and the intermediates are still cheap. Poor yields at later stages of a multistep synthesis, however, strongly reduce its usefulness, because most steps of the synthesis will have to be run on a large scale, using large amounts of solvents and reagents, to obtain a small amount only of the final product, which will, accordingly, be rather expensive.

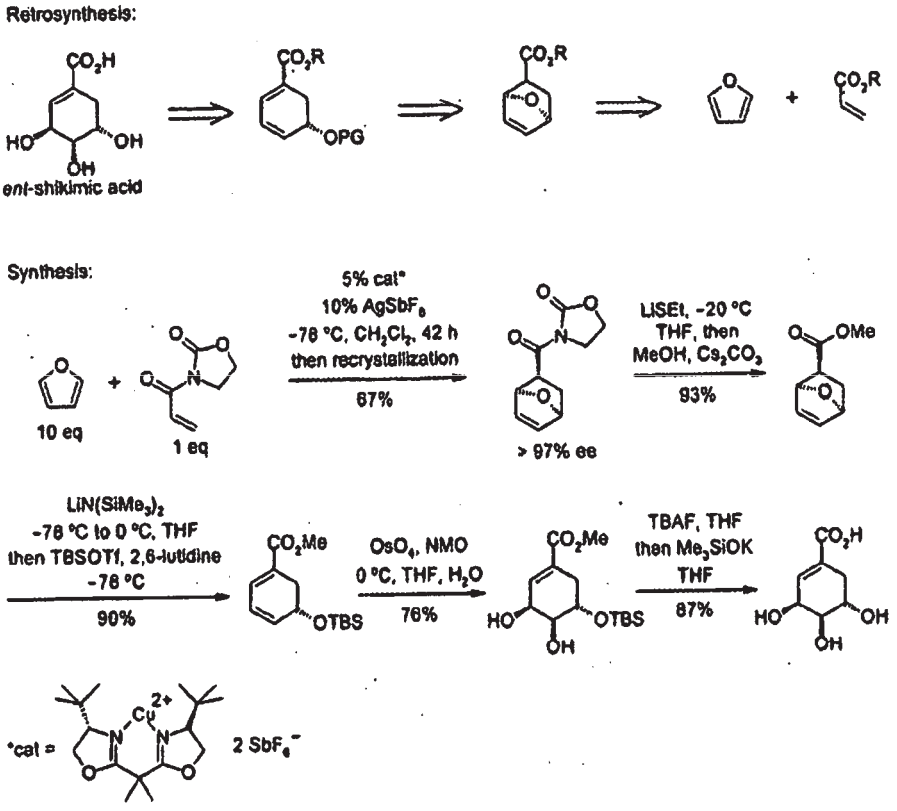
In a retrosynthesis the easiest bonds to make are often cleaved first (i.e. these bonds will be made at the end of the synthesis), yielding several fragments which can be joined together at late stages of the synthesis, using straightforward and high-yielding chemistry. Such reactions would usually be condensations, for example acetal, amide, or ester formation, or the formation of carbon–heteroatom bonds, but might also be high-yielding C–C bond-forming reactions if the required reaction conditions are compatible with all the structural elements of the final product.

If the target contains synthetically readily accessible substructures (e.g. cyclic elements accessible by well established cycloaddition or cyclization reactions), these might be chosen as starting point of a disconnection [1]. If such substructures are not present, their generation by introduction of removable functional groups (e.g. by converting single bonds into double bonds or by formal oxidation of methylene groups to carbonyl groups, Scheme 1.5) should be attempted. If this approach fails to reveal readily accessible substructures, the functional groups present in the target structure which might assist the stepwise construction of the carbon framework must be identified, and the bonds on the shortest bond paths between these groups should be considered as potential sites of disconnection (Scheme 1.3). Retro-aldol or Mannich reactions, optionally combined with the "Umpolung" of functional groups, have been the most common and successful tools for disconnection of intricate carbon frameworks, but any other, high-yielding C–C bond-forming reaction can also be considered. As illustrated by the examples discussed below, a good retrosynthesis requires much synthetic experience, a broad knowledge of chemical reactivity, and the ability to rapidly recognize synthetically accessible substructures.

1.2.2.2 Shikimic Acid

In Scheme 1.2 one possible retrosynthetic analysis of the unnatural enantiomer of shikimic acid, a major biosynthetic precursor of aromatic α-amino acids, is sketched. Because *cis* dihydroxylations can be performed with high diastereoselectivity and yield, this step might be placed at the end of a synthesis, what leads to a cyclohexadienoic acid derivative as an intermediate. Chemoselective dihydroxylation of this compound should be possible, because the double bond to be oxidized is less strongly deactivated than the double bond directly bound to the (electron-withdrawing) carboxyl group.

Despite being forbidden by the Baldwin rules (5-*endo*-trig ring opening; see Section 9.2), cyclohexadienoic acid derivatives such as that required for this synthesis can be prepared by base-induced ring scission of 7-oxanorbornene derivatives, presumably because of the high strain-energy of norbornenes. The required 7-oxanorbornene, in turn, should be readily accessible from furan and an acrylate via the

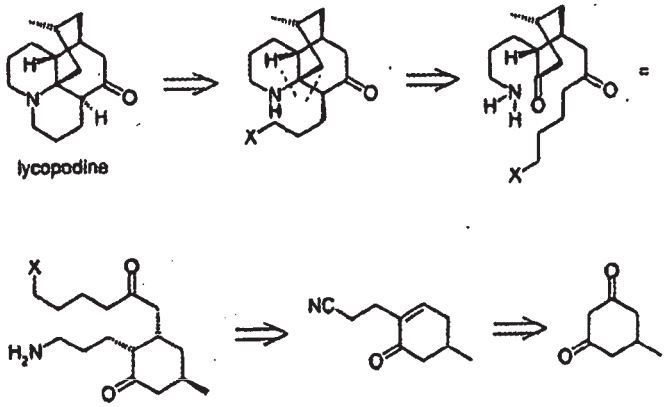


Scheme 1.2. Retrosynthetic analysis and synthesis of *ent*-shikimic acid [2].

Diels–Alder reaction. With the aid of an enantiomerically pure Lewis acid this Diels–Alder reaction yields a highly enantiomerically enriched 7-oxanorbornene, so that the remaining steps of this elegant synthesis only need to proceed diastereoselectively and without racemization.

1.2.2.3 Lycopodine

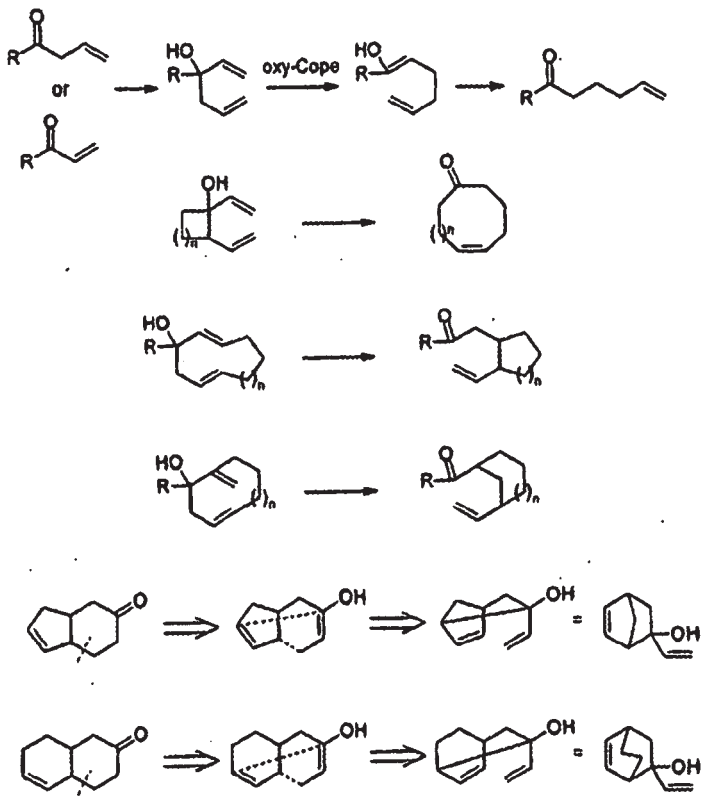
A further target which contains a readily accessible and easily recognizable substructure is the alkaloid lycopodine. Being a β-amino ketone, a possible retrosynthesis could be based on an intramolecular Mannich reaction, as outlined in Scheme 1.3. In this case two of the targets four rings would be generated in one step by a Mannich condensation; this significantly reduces the total number of steps required. A robust, intramolecular *N*-alkylation was chosen as last step. Realization of this synthetic plan led to a synthesis of racemic lycopodine in only eight steps with a total yield of 13 % [3]. Fortunately the Mannich reaction yielded an intermediate with the correct relative configuration.



Scheme 1.3. Retrosynthesis of lycopodine based on an intramolecular Mannich reaction [3].

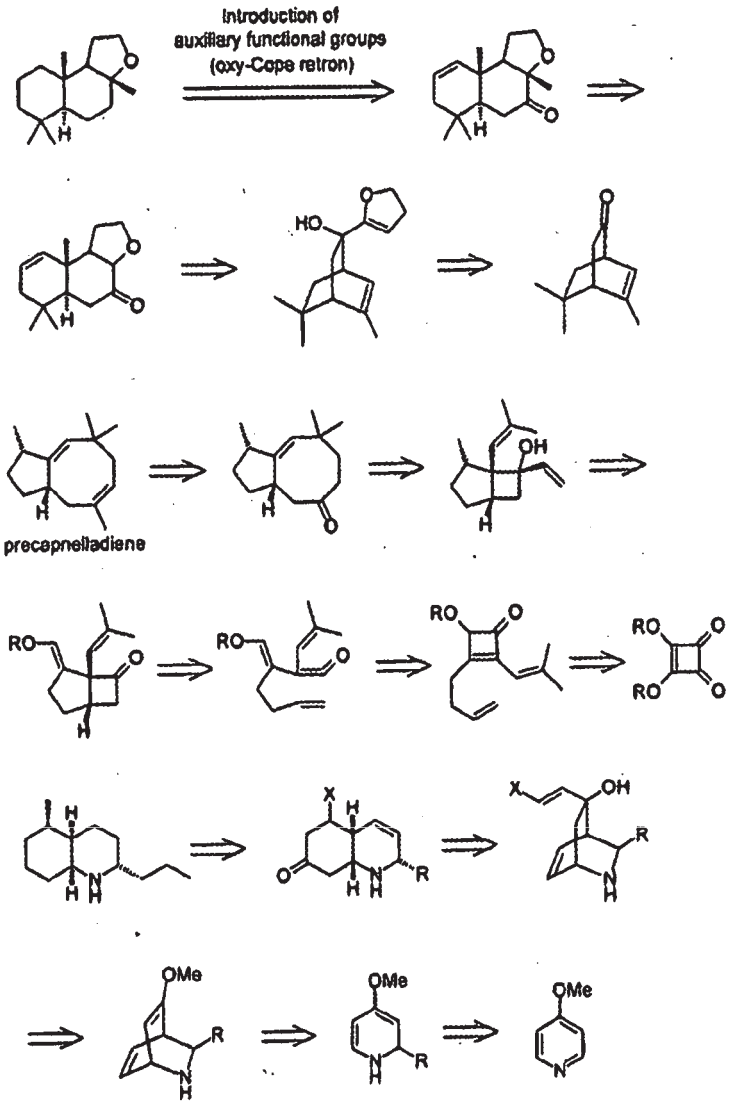
1.2.2.4 The Oxy-Cope Rearrangement

Less obvious than the retrosyntheses discussed above are those based on intramolecular rearrangements, because these often involve a major change of connectivity between atoms. For instance, exploitation of oxy-Cope rearrangements as synthetic tools requires some practice and the ability to recognize the substructures accessible via this reaction from readily available starting materials. Oxy-Cope rearrangements yield 4-penten-1-yl ketones by formal allylation of a vinyl ketone at the β position or γ-vinylation of an allyl ketone (Scheme 1.4). This rearrangement can be used to prepare decalins [4] or perhydroindenes [5, 6] from bicyclo[2.2.2]octenones or norbornenones, respectively, which can be prepared by using the Diels–Alder reaction. Moreover, oxy-Cope rearrangements may be used for ring expansions or contractions.



Scheme 1.4. The oxy-Cope rearrangement.

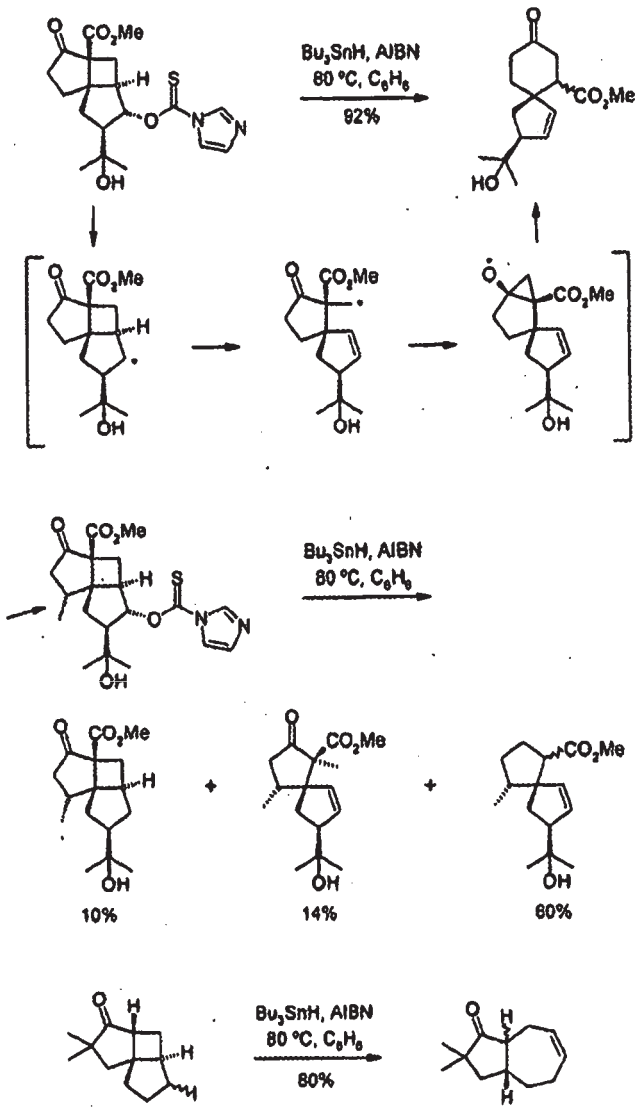
Numerous natural products have been prepared using the oxy-Cope rearrangement as the key step [5], in particular, and with high virtuosity, by the group of L.A. Paquette [4, 6, 7]. Three examples of retrosynthetic analyses of natural products or analogs thereof based on the oxy-Cope rearrangement are shown in Scheme 1.5. Because all the products are devoid of a keto group, the required 4-penten-1-yl ketone substructure (i.e. the oxy-Cope retron [1]) must be introduced during the retrosynthesis in such a way that accessible starting materials result.



Scheme 1.5. Retrosynthesis of an ambergris-type ether, of precapnelladiene, and of an alkaloid based on the oxy-Cope rearrangement [8–10].

1.2.2.5 Conclusion

As will be shown throughout this book, the outcome of organic reactions is highly dependent on all structural features of a given starting material, and unexpected products may readily be formed. Therefore, while planning a multistep synthesis, it is important to keep the total number of steps as low as possible.



Scheme 1.6. Rearrangement of polycyclic cyclobutylmethyl radicals [11, 12].

Even the most experienced chemist will not be able to foresee all potential pitfalls of a synthesis, specially so if multifunctional, structurally complex intermediates must be prepared. The close proximity or conformational fixation of functional groups in a large molecule can alter their reactivity to such an extent that even simple chemical transformations can no longer be performed [11]. Small structural variations of polyfunctional substrates might, therefore, bring about an unforeseeable change in reactivity.

Examples of closely related starting materials which upon treatment with the same reagents yield completely different products are sketched in Scheme 1.6. The additional methyl group present in the second starting material slows addition to the carbonyl group of the radical formed by ring scission of the cyclobutane ring, and thus prevents ring expansion to the cyclohexanone. Removal of the methoxycarbonyl group leads to cleavage of a different bond of the cyclobutane ring and thereby again to a different type of product [12].

The understanding and prediction of such effects and the development of milder and more selective synthetic transformations, applicable to the synthesis of highly complex structures or to the selective chemical modification of proteins, DNA, or even living cells will continue to be the challenge for current and future generations of chemists.

1.3
Hard and Soft Acids and Bases

One of the most useful tools for predicting the outcome of chemical reactions is the principle of hard and soft acids and bases (HSAB), formulated by Pearson in 1963 [13–15]. This principle states that hard acids will react preferentially with hard bases, and soft acids with soft bases, "hard" and "soft" referring to sparsely or highly polarizable reactants. A selection of hard and soft Lewis acids and bases is given in Table 1.1.

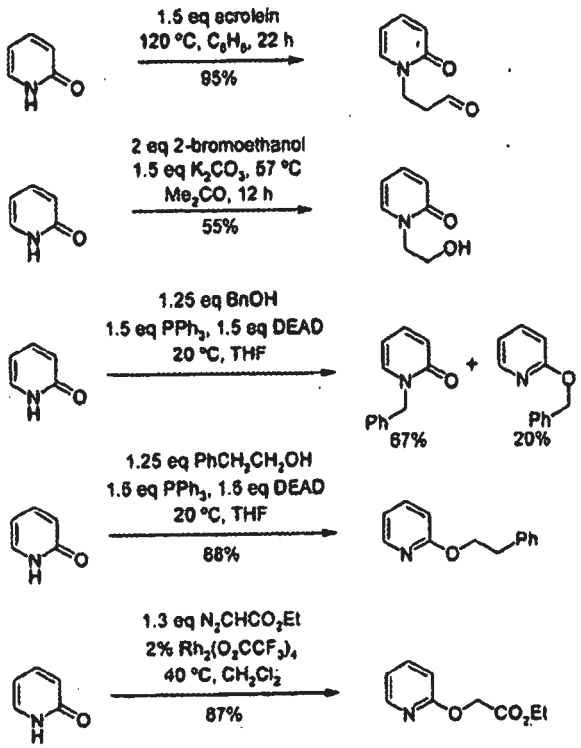
Several chemical observations can be readily explained with the aid of the HSAB principle. For instance, the fact that the early transition metals in high oxidation states, for example titanium(IV), do not usually form complexes with alkenes, carbon monoxide, or phosphines, but form stable oxides instead can be attributed to their hardness. The late transition metals, on the other hand, being highly polarizable, because of their almost completely filled *d* orbitals, readily form complexes with soft bases such as alkenes, carbanions, and phosphines, and these complexes are often unreactive towards water or oxygen. For the same reason, in alkali or early transition metal enolates the metal is usually bound to oxygen, whereas enolates of late transition metals usually contain M–C bonds [17, 18]. While alkali metal alkyls or Grignard reagents react with enones presumably by initial coordination of the metal to oxygen followed by transfer of the alkyl group to the carbonyl carbon atom [16, 19], organocuprates or organopalladium compounds preferentially coordinate and transfer their organic residue to soft C–C double bonds.

Table 1.1. Hard and soft Lewis acids and bases [13, 15, 16] (Z = electron-withdrawing group, M = metal). The acidic or basic centers in molecules are in italics.

Hard acids (non-metals)	Borderline acids (non-metals)	Soft acids (non-metals)
H^+, $B(OR)_3$, BF_3, BCl_3, RCO^+, CO_2, NC^+, R_3Si^+, Si^{4+}, RPO_2^+, $ROPO_2^+$, As^{3+}, RSO_2^+, $ROSO_2^+$, SO_3, Se^{3+}, Cl^{7+}, I^{7+}, I^{5+}	BR_3, R^+ (softer $CH_3^+ > RCH_2^+ > R_2CH^+ > R_3C^+ >$ vinyl$^+ \approx C_6H_5^+ \approx$ RC≡C$^+$ harder), RCHO, R_2CO, $R_2C{=}NR$, NO^+, SO_2	BH_3, Ar–Z, C=C–Z, quinones, carbenes, HO^+, RO^+, RS^+, RSe^+, RTe^+, Br_2, Br^+, I_2, I^+
Hard acids (metals)	**Borderline acids (metals)**	**Soft acids (metals)**
Li^+, Na^+, K^+, $BeMe_2$, Be^{2+}, $RMgX$, Mg^{2+}, Ca^{2+}, Sr^{2+}, $AlCl_3$, $AlMe_3$, AlH_3, $Al(OR)_3$, Al^{3+}, $GaMe_3$, Ga^{3+}, $InMe_3$, In^{3+}, SnR_3^+, $SnMe_2^{2+}$, Sn^{2+}, Sc^{3+}, La^{3+}, $Ti(OR)_4$, Ti^{4+}, Zr^{4+}, VO_2^+, Cr^{3+}, Fe^{3+}, Co^{3+}, Ir^{3+}, Th^{4+}, UO_2^{2+}, Pu^{4+}, Yb^{3+}	GaH_3, $Sn(OR)_4$, $SnCl_4$, Pb^{2+}, Sb^{3+}, Bi^{3+}, $Sc(OTf)_3$, $ScCl_3$, Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, RZn^+, Zn^{2+}, $Yb(OTf)_3$, $YbCl_3$	Cs^+, $TlMe_3$, Tl^+, Tl^{3+}, $Pd(PAr_3)_2$, $Pd(PAr_3)_2^{2+}$, Pd^{2+}, Pt^{2+}, Cu^+, Ag^+, Au^+, CdR^+, Cd^{2+}, HgR^+, Hg^+, Hg^{2+}, M^0
Hard bases	**Borderline bases**	**Soft bases**
NH_3, RNH_2, R_2N^-, N_2H_4, H_2O, OH^-, ROH, RO^-, R_2O, RCO_2^-, CO_3^{2-}, NO_3^-, PO_4^{3-}, SO_4^{2-}, ClO_4^-, F^-, Cl^-	AlH_4^-, N_2, N_3^-, $PhNH_2$, R_3N, C_5H_5N, $R_2C{=}NR$, NO_2^-, SO_3^{2-}, Br^-	H^-, BH_4^-, R^- (softer RC≡C$^-$ > vinyl$^-$ > R_3C^- harder), C_6H_6, $R_2C{=}CR_2$, RC≡CR, CN^-, RNC, CO, PR_3, $P(OR)_3$, AsR_3, RS^-, SCN^-, RSH, R_2S, $S_2O_3^{2-}$, RSe^-, I^-

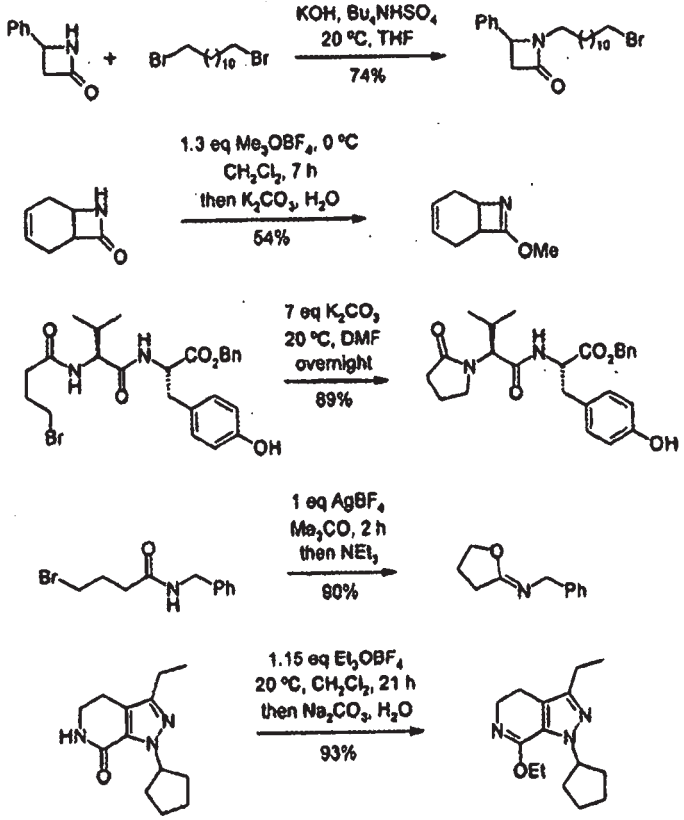
HSAB is particularly useful for assessing the reactivity of ambident nucleophiles or electrophiles, and numerous examples of chemoselective reactions given throughout this book can be explained with the HSAB principle. Hard electrophiles, for example alkyl triflates, alkyl sulfates, trialkyloxonium salts, electron-poor carbenes, or the intermediate alkoxyphosphonium salts formed from alcohols during the Mitsunobu reaction, tend to alkylate ambident nucleophiles at the hardest atom. Amides, enolates, or phenolates, for example, will often be alkylated at oxygen by hard electrophiles whereas softer electrophiles, such as alkyl iodides or electron-poor alkenes, will preferentially attack amides at nitrogen and enolates at carbon.

2-Pyridone is *O*-alkylated more readily than normal amides, because the resulting products are aromatic. With soft electrophiles, however, clean *N*-alkylations can be performed (Scheme 1.7). The Mitsunobu reaction, on the other hand, leads either to mixtures of *N*- and *O*-alkylated products or to *O*-alkylation exclusively, probably because of the hard, carbocation-like character of the intermediate alkoxyphosphonium cations. Electrophilic rhodium carbene complexes also preferentially alkylate the oxygen atom of 2-pyridone or other lactams [20] (Scheme 1.7).



Scheme 1.7. Regioselective alkylation of 2-pyridone [20–22].

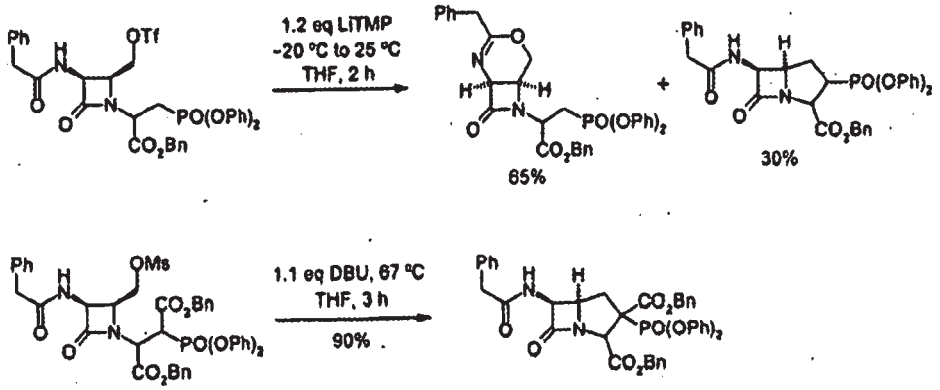
Lactams and some non-cyclic, secondary amides (RCONHR) can be alkylated with high regioselectivity either at nitrogen (Section 6.6) or at oxygen. *N*-Alkylations are generally conducted under basic reaction conditions whereas *O*-alkylations are often performed with trialkyloxonium salts, dialkyl sulfates, or alkyl halides/silver salts without addition of bases. Protonated imino ethers are formed; these are usually not isolated but are converted into the free imino ethers with aqueous base during the work-up. Scheme 1.8 shows examples of the selective alkylation of lactams and of the formation of 2-pyrrolidinones or 2-iminotetrahydrofurans by cyclization of 4-bromobutyramides.



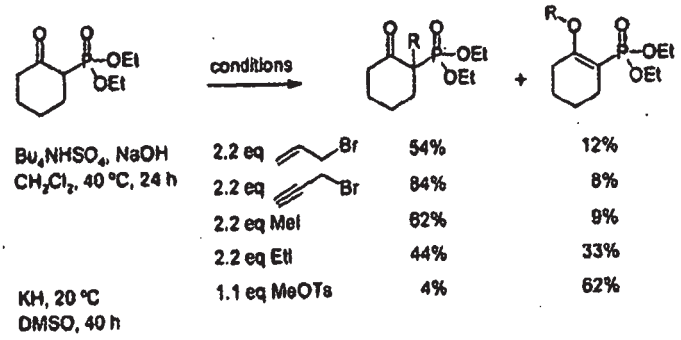
Scheme 1.8. Regioselective alkylation of amides [23–27].

The triflate sketched in Scheme 1.9 mainly alkylates the amide at oxygen, instead of alkylating the softer, lithiated phosphonate. Selective *C*-alkylation can be achieved in this instance by choosing a less reactive mesylate as electrophile and by enhancing the acidity of the phosphonate.

The regioselectivity of the alkylation of enolates can also be controlled by the hardness of the alkylating agent [29]. As illustrated by the examples in Scheme 1.10, allyl, propargyl, or alkyl bromides or iodides mainly yield *C*-alkylated products, whereas the harder sulfonates preferentially alkylate at oxygen.



Scheme 1.9. Intramolecular alkylation of amides and phosphonates [28].

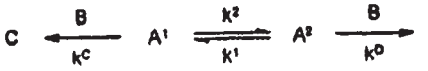


Scheme 1.10. Regioselective alkylation of enolates [30, 31].

1.4 The Curtin–Hammett Principle

In the 1940s the idea was prevalent among chemists that the conformation of a reactant could be determined from the structure of a reaction product, i.e. the major conformer would yield the major product. This assumption was shown to be incorrect by Curtin and Hammett in the 1950s [32].

For a reaction in which a starting material A is an equilibrium mixture of two conformers (or diastereomers, tautomers, rotamers, etc.) A^1 and A^2 (Eq. 1.1), two extreme situations can be considered – one in which equilibration of A^1 and A^2 is slow if compared with their reaction with B ($k^1, k^2 \ll k^C, k^D$), and one in which equilibration of A^1 and A^2 is much faster than their reaction with B ($k^1, k^2 \gg k^C, k^D$).



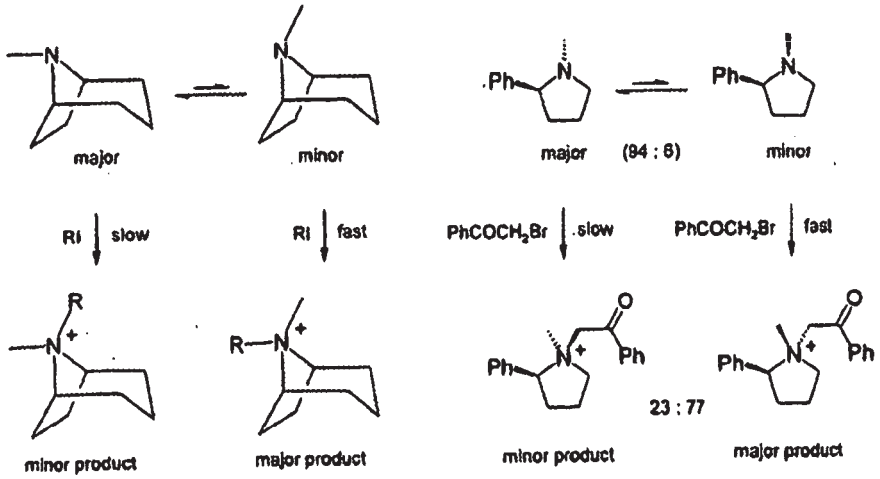
(Eq. 1.1)

If equilibration of A^1 and A^2 is slow, the product ratio [C]/[D] will be equal to the ratio of conformers of the starting material A ($[A^1]/[A^2]$) and independent of the ratio k^C/k^D. If equilibration is rapid, however, the amount of C and D formed will depend both on the ratio of starting materials ($[A^1]/[A^2]$) and on the ratio of the two reaction rate constants k^C and k^D: $[D]/[C] = [A^2]/[A^1] \times k^D/k^C$ [32].

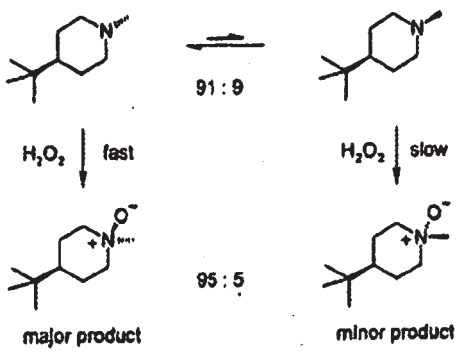
The main implication of these derivations is that if equilibration is rapid, the product ratio cannot always be intuitively predicted if the reaction rates k^C and k^D are unknown. Because energy-rich conformers, present in low concentrations only, are often more reactive than more stable conformers, it is not unusual for the main product of a reaction to result from a minor conformer which cannot even be observed.

Two examples of such situations are sketched in Scheme 1.11. Quaternization of tropane occurs mainly from the less hindered "pyrrolidine side" (equatorial attack at the piperidine ring), even though the main conformer of tropane has an equatorial methyl group. Similarly, 1-methyl-2-phenylpyrrolidine yields mainly an *anti* alkylated product via alkylation of the minor *cis* conformer when treated with phenacyl bromide [33]. In both instances the less stable conformer is more reactive to such an extent that the major product of the reaction results from this minor conformer. A further notable example of a reaction in which the main product results from a minor but more reactive intermediate is the enantioselective hydrogenation of α-acetamidocinnamates with a chiral rhodium-based catalyst [34].

This does, however, not need to be so. Oxidation of 1-methyl-4-*tert*-butylpiperidine, for example, yields mainly the amine *N*-oxide derived from the most stable conformer (Scheme 1.12). In this example the more energy-rich (less stable) conformer reacts more slowly than the major conformer.



Scheme 1.11. Diastereoselective quaternization of tertiary amines [32, 33, 35].



Scheme 1.12. Diastereoselective oxidation of 4-*tert*-butyl-1-methylpiperidine [32, 36, 37].

To conclude, the Curtin–Hammett principle states that the relative amounts of products formed from two interconverting conformers depend on the reactivity of these two conformers if the interconversion of these conformers is rapid, and cannot always be intuitively predicted.

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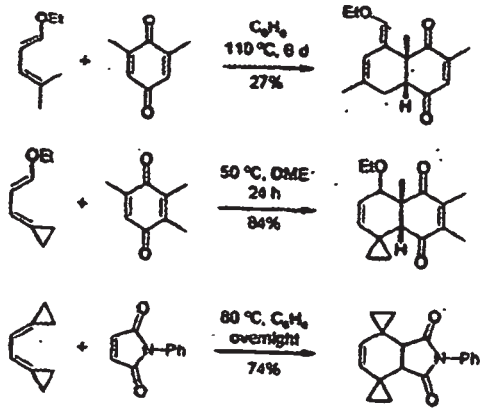
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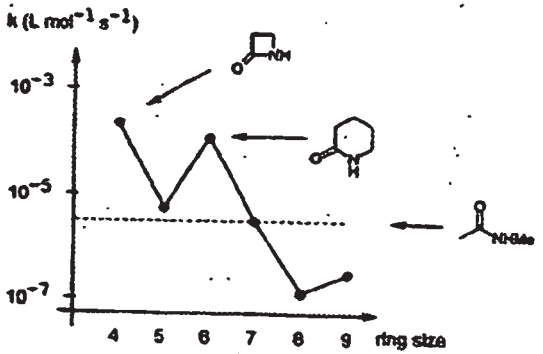
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Scheme 3.7. Diels–Alder reactions with cyclopropylidenes [22–24].

ring scission. Eight- and nine-membered lactams are more resistant to nucleophilic hydrolysis than non-cyclic amides; this might be because of an increase in transannular repulsive van der Waals interactions during the addition of hydroxide to these amides.

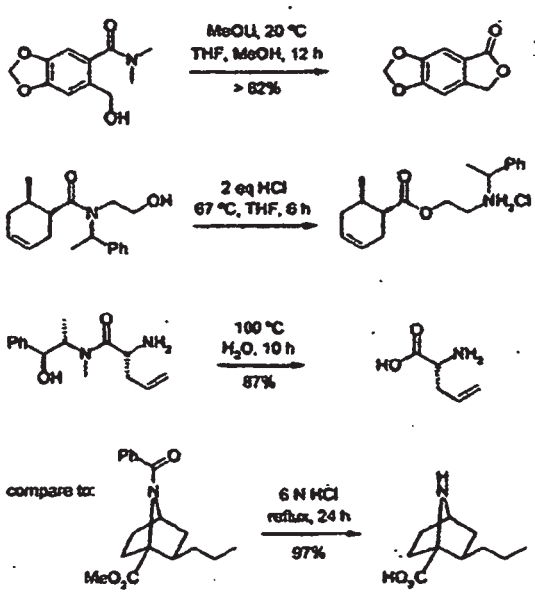


Scheme 3.8. Rates of lactam hydrolysis with aqueous base [25]. For comparison, the rate of hydrolysis of *N*-methylacetamide is shown.

3.3 Incompatible Functional Groups

It goes without saying that a compound will decompose or oligomerize if it contains functional groups which can react with each other. Because intramolecular reactions often proceed at much higher rates than their intermolecular variants, functional group incompatibilities may arise unexpectedly, involving groups which would not react intermolecularly. For instance, many phthalic acid, maleic acid, or 2-(hydroxymethyl)benzoic acid derivatives are notoriously sensitive because of the close proximity of the two functional groups (Scheme 3.9). Similarly, amides of 2-aminoethanols rearrange readily to esters under acidic reaction conditions [26] and undergo hydrolysis under mildly basic conditions, mainly because the hydroxyl group is close to the amide bond (Scheme 3.9). Normal amides usually require treatment with highly concentrated mineral acids at high temperatures to undergo hydrolysis (last example, Scheme 3.9).

Mannich bases (2-aminoethyl ketones) are another class of inherently unstable compounds which often undergo facile thermal elimination of the amine to yield a vinyl ketone [30]. Chemically related to Mannich bases are 2- or 4-(aminomethyl)-



Scheme 3.9. Hydrolysis of amides with and without intramolecular assistance [26–29].

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8
Palladium-catalyzed C–C Bond Formation

8.1
Introduction

The development in recent decades of numerous different Pd-catalyzed C–C bond-forming reactions has had a huge impact on synthetic organic chemistry [1–10]. Several classes of compounds, for example unsymmetrical biaryls or substituted polyenes, which were difficult if not impossible to synthesize in the 1950s, can now be readily prepared under mild conditions with high regio- and stereoselectivity via Pd-catalyzed cross-coupling reactions. The compatibility of Pd-catalysis with many functional groups and protic solvents, together with its broad scope, has secured a central role for this chemistry in organic synthesis.

The most important Pd-catalyzed C–C bond-forming reactions proceed according to the mechanisms outlined in Schemes 8.3 and 8.6. In these reactions a Pd(0) complex, which can be generated in situ by reduction of Pd(II), undergoes oxidative addition to an organic halide or sulfonate to yield an organopalladium(II) complex. This reaction is rapid with aryl or vinyl halides but proceeds more slowly with alkyl halides [9]. The reactivity decreases in the order $RI > ROTf \approx RBr \gg RCl \gg RF$ [11], and electron-poor aryl or vinyl halides react with Pd(0) complexes faster than electron-rich halides. The resulting organopalladium(II) complex can react with alkenes or a variety of organometallic compounds, forming the C–C bond and regenerating the catalytically active Pd(0) complex.

8.2
Chemical Properties of Organopalladium Compounds

The synthetically most important Pd-catalyzed C–C bond-forming reactions proceed via intermediate square planar organopalladium(II) complexes of the type $PdRL_3$, in which the ligands L are usually halide or phosphine ligands. Organopalladium(II) complexes are rather stable organometallic compounds which can be readily prepared and isolated [12–14]. Complexes such as $PdArL_2X$ with L representing phosphines or amines and X being a halogen do not usually react with water, and Pd-mediated C–C bond-forming reactions can be conducted in the presence of water

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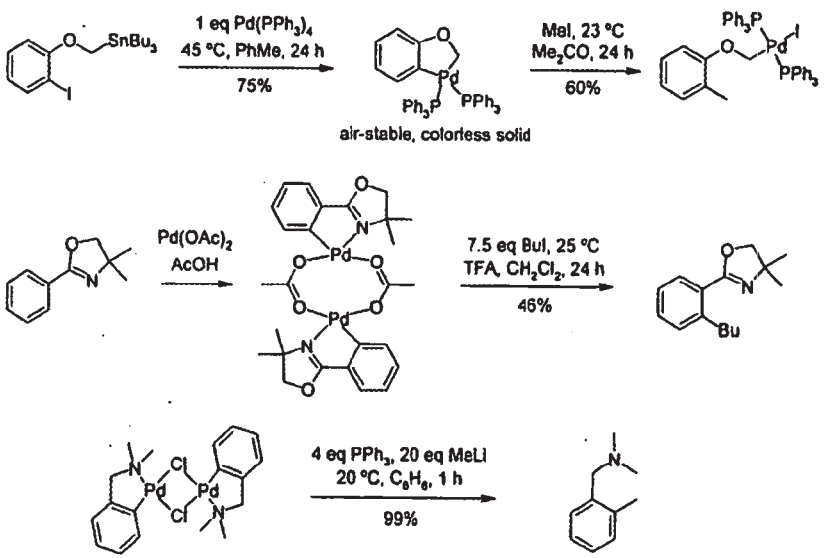
or in water alone [15–20]. Water may even be beneficial for some types of Pd-catalyzed reaction [21]. Organopalladium complexes such as $PdArL_2X$ react with water only if L or X are very weak ligands (e.g. acetone [22]). These weak ligands can be displaced by water, and in the resulting complexes hydrolysis of the Pd–C bond can occur to yield a hydrocarbon.

The products of the thermolysis of $PdAr(Hal)(PAr_3)_2$ depend on the substitution pattern of the aryl groups, on the halide, on the solvent, and on the temperature chosen. Heating of $PdAr(Hal)(PAr_3)_2$, in the absence of other reagents, to temperatures above 50 °C leads to the reversible migration of aryl groups from palladium to phosphorus via intermediate formation of tetraarylphosphonium salts [11, 23, 24] (see Section 8.6). This migration proceeds more readily with electron-rich Pd-bound aryl groups [25]. Strong heating yields phosphonium salts, phosphines, biaryls Ar–Ar, reduced arenes ArH (the Ar group originating from both Pd-bound and phosphorus-bound aryl groups), and metallic palladium [11, 26], probably via homolytic Pd–C bond fission [27]. Heating in the presence of phosphines can lead to the reductive elimination of aryl halides [28].

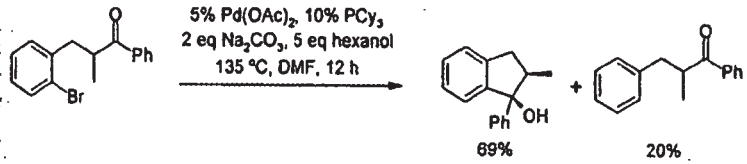
Complexes such as $PdArL_2X$ are usually stable in air, but treatment with strong oxidants leads to cleavage of the Pd–C bond to yield phenols [29, 30]. Carbon monoxide cleanly converts organopalladium(II) complexes into acyl complexes (L_3PdCOR) [31, 32].

The metal-bound carbon atom in organopalladium(II) complexes can formally react either as an electrophile or as a nucleophile. Treatment of arylpalladium(II) complexes with alkyl halides, for example, yields products of homo- or cross-coupling, possibly via intermediate formation of hexacoordinated Pd(IV) complexes [31, 33] (Scheme 8.1). Treatment of the same type of complex with alkyl Grignard reagents or other carbon nucleophiles, on the other hand, also yields the corresponding alkyl arenes via nucleophilic displacement of a ligand followed by reductive elimination (Scheme 8.1).

Organopalladium complexes do usually not transfer a formal carbanion to aldehydes or ketones, but intramolecular Barbier-type reactions of this kind have been observed (Scheme 8.2).



Scheme 8.1. Reaction of arylpalladium(II) complexes with electrophilic and nucleophilic alkylating reagents [34–36].



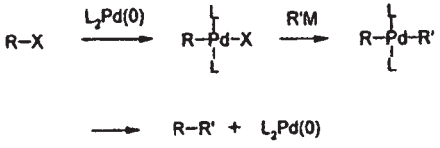
Scheme 8.2. Palladium-mediated Barbier-type cyclization of a bromoaryl ketone [37].

8.3
Mechanisms of Pd-catalyzed C–C Bond Formation

8.3.1
Cross-coupling

For Pd-catalyzed cross-coupling reactions the organopalladium complex is generated from an organic electrophile RX and a Pd(0) complex in the presence of a carbon nucleophile. Not only organic halides but also sulfonium salts [38], iodonium salts [39], diazonium salts [40], or thiol esters (to yield acylpalladium complexes) [41] can be used as electrophiles. With allylic electrophiles (allyl halides, esters, or carbonates, or strained allylic ethers and related compounds) Pd-η^3-π-allyl complexes are formed; these react as soft, electrophilic allylating reagents.

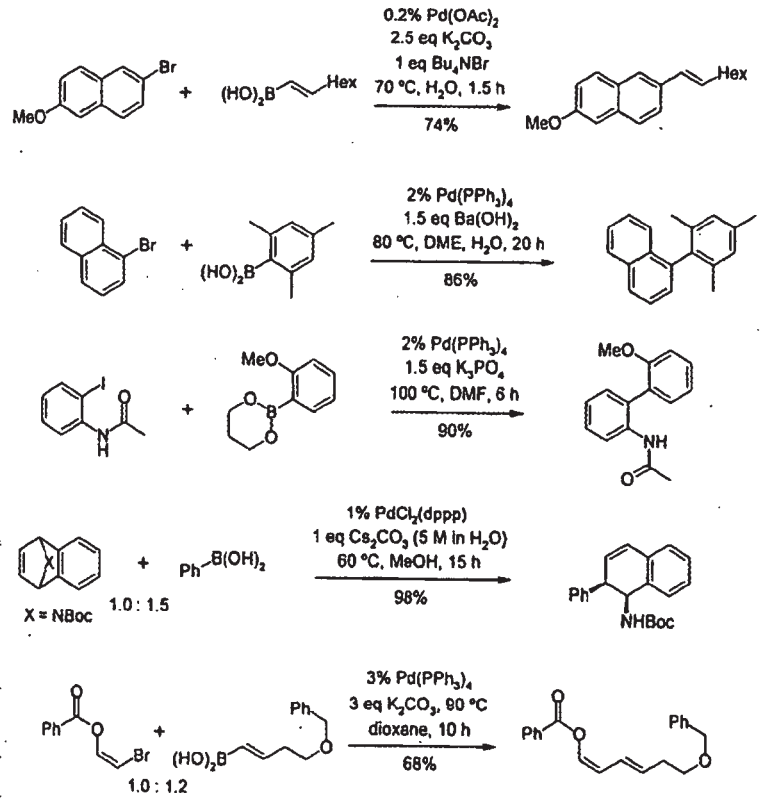
Organopalladium complexes formed by oxidative insertion of Pd(0) into C–X bonds can undergo ligand exchange with other organometallic reagents R'M or with compounds with nucleophilic carbon (enolates, phenols, electron-rich heteroarenes) to yield diorganylpalladium(II) complexes (Scheme 8.3). These may undergo reductive elimination to yield the cross-coupled product R–R' and the catalytically active Pd(0) complex (Scheme 8.3) [42].



Scheme 8.3. Simplified mechanism of Pd-catalyzed cross-coupling reactions. R, R' = aryl, vinyl, alkynyl, allyl, benzyl, alkyl, acyl; M = MgX, ZnX, $B(OR)_2$, BR_2, SnR_3.

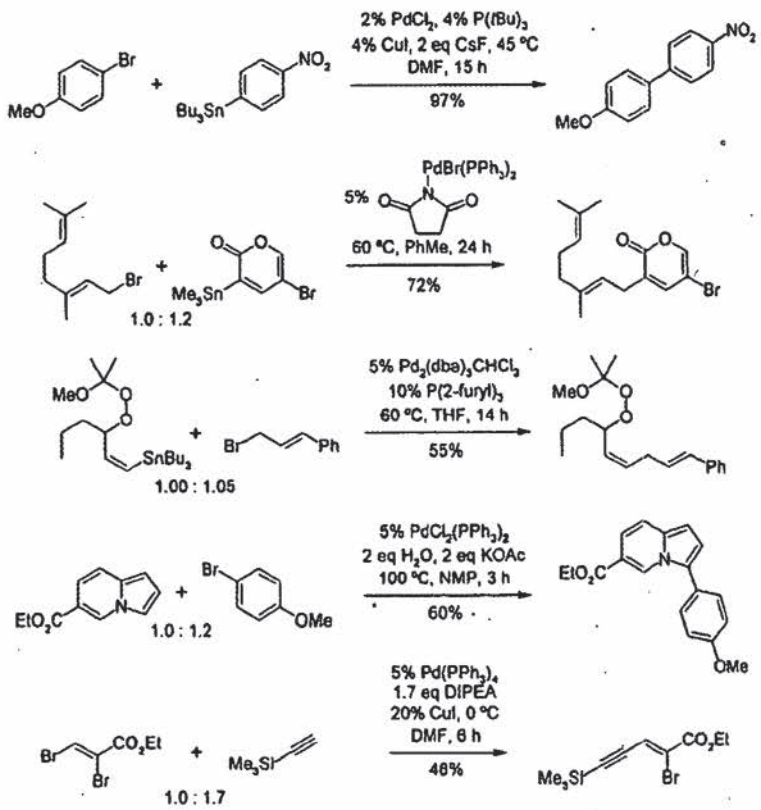
The synthetically most exploited cross-coupling variants are those in which the organometallic components are organoboron (Suzuki reaction), organotin (Stille reaction), organozinc (Negishi reaction), or alkynylcopper derivatives (Sonogashira reaction). The advantages of these reagents, if compared with the more polar organolithium or Grignard reagents (which also undergo Pd-mediated cross-coupling reactions) are their low reactivity toward most functional groups, their stability, and the consequent simplicity of their handling. Other nucleophilic reagents which can displace the leaving group X from complexes $PdRL_2X$ include cyanide [43], enolates [3, 44–51], phenols [52–54], indoles [55], indolizines (Scheme 8.5) [56], pyrroles, furans, thiophenes, imidazoles, thiazoles, and related compounds [57–62]. With most of these reagents a new Pd–C bond is presumably formed on displacement of the ligand X.

Aryl-bound functional groups which are tolerated in Pd-mediated arylations include *ortho*-alkynyl [63], *ortho*-vinyl [64], *ortho*-nitro [65], and *ortho*-formyl groups [66]. Some examples of Pd-mediated cross-coupling reactions are depicted in Schemes 8.4 and 8.5, to illustrate the required conditions and scope of these reactions.



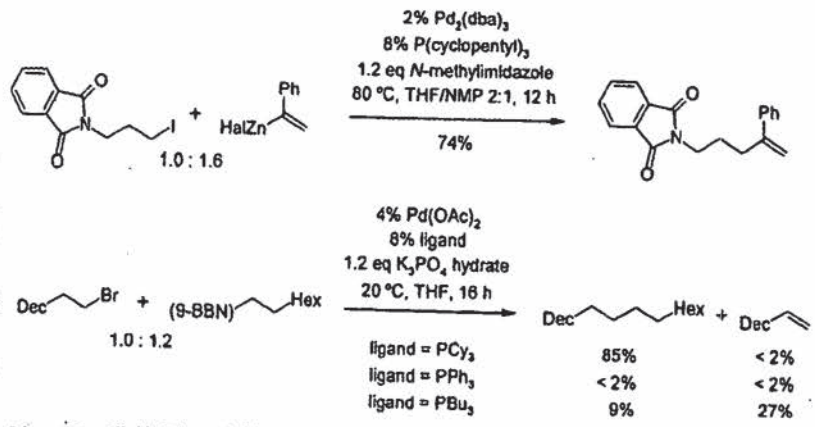
Scheme 8.4. Palladium-catalyzed cross-coupling reactions of boron derivatives [18, 66–68].

Organometallic reagents of low nucleophilicity, for example nitroaryl stannanes [69], undergo transmetalation only slowly; this can lead to low yields of cross-coupling products [69]. Catalytic amounts of CsF and CuI, together with a palladium source and a phosphine can bring about cross-coupling of such unreactive stannanes (first reaction, Scheme 8.5) [69].



Scheme 8.5. Palladium-catalyzed cross-coupling reactions of stannanes and other carbon nucleophiles with aryl, allyl, and vinyl bromides [56, 69–72].

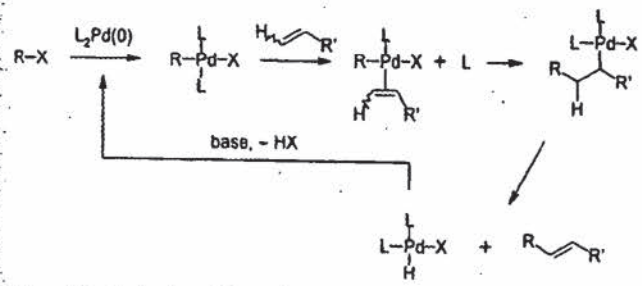
Alkylpalladium complexes generated by oxidative addition of Pd(0) to alkyl halides with a β hydrogen can undergo β-elimination to yield an alkene and a Pd-hydrido complex (as in the Heck reaction; Scheme 8.7). Nevertheless, this process is relatively slow compared with transmetalations and reductive eliminations, and simple alkyl halides or tosylates with β hydrogen can be cross-coupled with carbon nucleophiles under optimized conditions if the nucleophile is sufficiently reactive [9, 73–75] (Scheme 8.6).



Scheme 8.6. Alkyl halides with β hydrogen in palladium-mediated cross-couplings [76, 77].

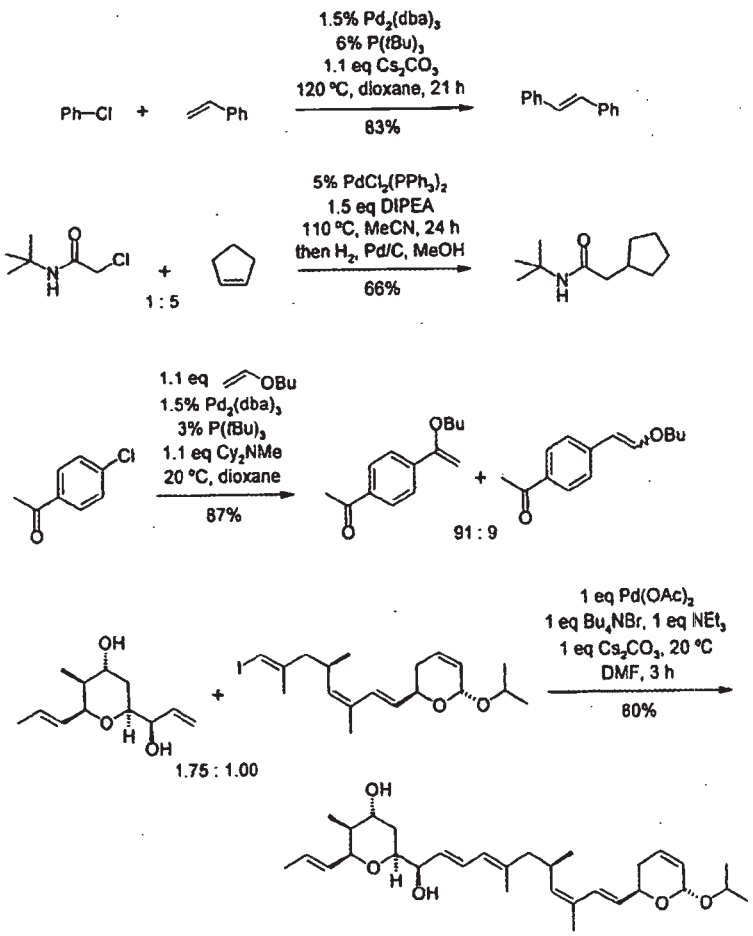
8.3.2 The Heck Reaction

If the initial organopalladium complex is formed in the presence of an alkene, transfer of the organyl group to the alkene can occur (Heck reaction, Scheme 8.7) [5, 78]. Electron-deficient and electron-rich alkenes and even some arenes [79] can be used. In the last step of this process a Pd-hydrido complex is formed by β-hydride elimination, leading to the formation of the C–C double bond. In the presence of bases the hydrido complex eliminates HX, regenerating the catalytically active Pd(0) complex (Scheme 8.7).



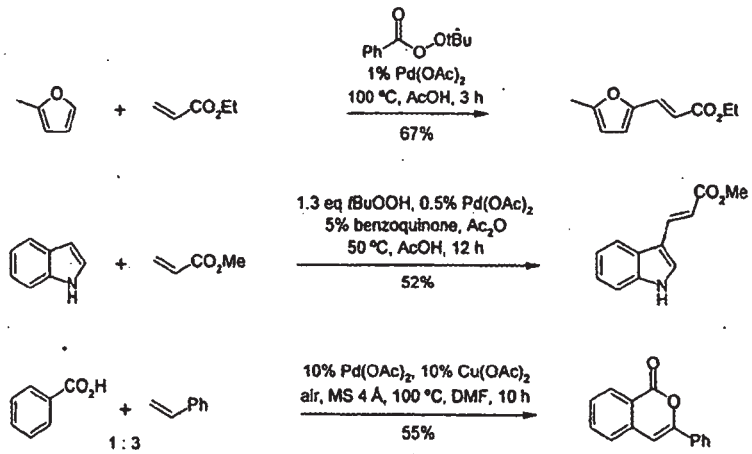
Scheme 8.7. Mechanism of the Heck reaction.

Representative examples of Heck reactions are depicted in Scheme 8.8. Terminal alkenes react faster than internal alkenes, and the formation of mixtures of products resulting from further arylation or vinylation of the initial product is therefore only observed when a large excess of halide and long reaction times are employed. Electron-poor alkenes usually react more rapidly than electron-rich alkenes, and the new C–C bond is usually formed at the most electron-deficient carbon atom.



Scheme 8.8. Examples of Heck reactions [80–84].

Direct palladation of C–H bonds can be achieved by treatment of, for example, electron-rich arenes with Pd(II) salts (see also Section 8.11). After cross-coupling via reductive elimination the resulting Pd(0) must be reoxidized to Pd(II) if Pd-catalysis is the aim [85]. Reoxidation of Pd(0) with Cu or Ag salts (as in the Wacker process) is not always well suited for C–C bond-forming reactions [86], but other oxidants, for example peroxides, have been used with success (Scheme 8.9). The required presence of oxidants in the reaction mixture limits the scope of these reactions to oxidation-resistant starting materials.



Scheme 8.9. Formation of C–C bonds via intermediate palladation of C–H bonds [86–88].

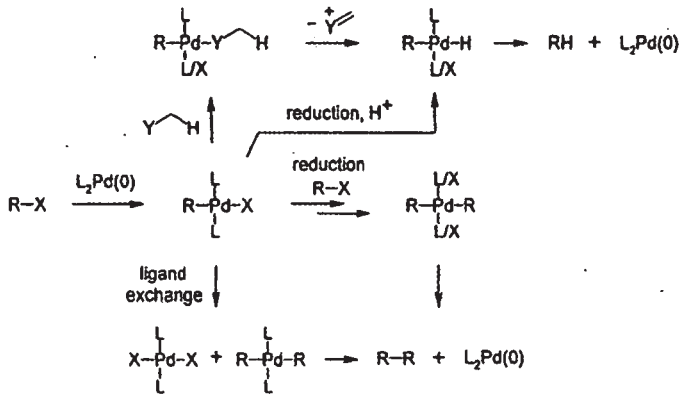
The large number of highly diverse examples of high-yielding Pd-catalyzed organic reactions might give the non-specialist the impression that almost any conceivable transformation might work in the presence of a suitable Pd catalyst. This is, of course, not true, and even the most robust Pd-catalyzed processes have their limitations. Some of these will be discussed in the following sections. The most important unwanted processes which can compete with Pd(0)-catalyzed C–C bond formation include homocoupling or reduction of the halide and homocoupling, C-protonation, or oxidation of the organometallic reagent.

8.4 Homocoupling and Reduction of the Organyl Halide

As mentioned in Section 8.2, organopalladium(II) complexes can react with organyl halides to yield products of cross-coupling. The formation of large amounts of symmetric biaryls as a result of homocoupling of the aryl halide is often observed during

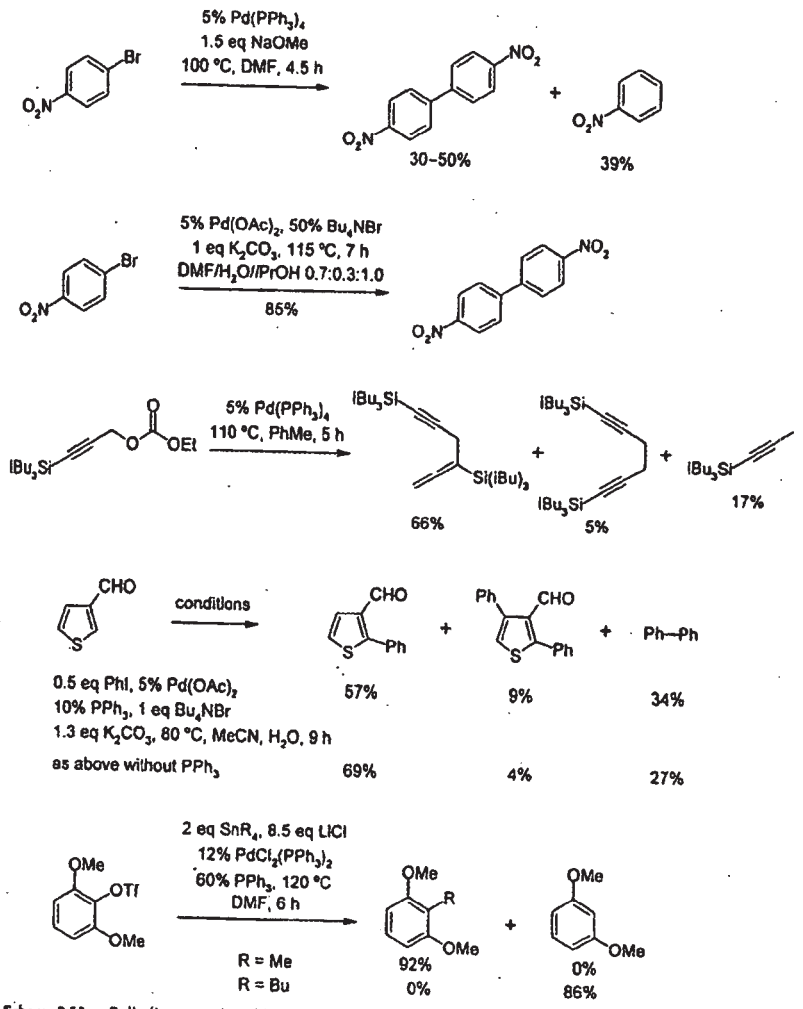
the coupling of aryl halides with weak nucleophiles or unreactive alkenes. This reaction may proceed via transient formation of Pd(IV) complexes. Another possible mechanism of this homocoupling is reduction of the intermediate organopalladium(II) complex to a Pd(0) complex which then undergoes a second oxidative addition to the halide to yield a diorganylpalladium(II) complex (Scheme 8.10) [89]. Alternatively, the initially formed Pd(II) complex can undergo ligand exchange with itself to yield diorganylpalladium(II) complexes and complexes without organyl groups [90]. This process will compete most efficiently with Stille and Suzuki cross-couplings if the stannane or boronic acid is electron-deficient, sterically hindered, or otherwise unreactive and undergoes transmetalation only slowly. Benzylic halides and 2-halopyridines are particularly prone to undergo homocoupling (and reduction) [62, 91, 92].

Reduction of the halide to a hydrocarbon is another common side reaction of Pd-mediated cross-couplings. This hydrodehalogenation can proceed via reductive elimination from a hydrido complex $PdRL_2H$, which can be formed from the initial product of oxidative addition ($PdRL_2X$) by ligand exchange with an alkoxide, an amine, or an organometallic reagent containing β hydrogen, followed by β-hydride elimination (and formation of a carbonyl compound [93, 94], an imine [1], or an alkene [36], respectively). Hydrodehalogenation is, therefore, often observed in palladium-catalyzed reactions of aryl halides with alcoholates [95] or amines [96], but can be largely suppressed by use of sterically demanding phosphines, which accelerate reductive elimination of the arylamine from aryl(amido)palladium(II) complexes at the expense of β-hydride elimination [1, 97]. Alternative routes to hydrido complexes include the reduction of Pd(II) complexes to Pd(0) complexes, followed by protonation [98] (Scheme 8.10). It has been observed that arenes are formed during the reduction of a Pd(II) catalyst precursor to Pd(0) in the presence of aryl halides [97], but the precise mechanism of this process remains unknown.



Scheme 8.10. Possible mechanisms of the Pd-catalyzed reduction and homocoupling of organic halides. X = halide, triflate; Y = R_2C^-, NHR, O^-.

Reducing agents which have been used to promote the Pd-mediated homocoupling of organyl halides include hydroquinone [99], zinc powder [15, 100, 101], magnesium [101], tetra(dimethylamino)ethene [102], tertiary aliphatic amines [103–105], and aliphatic alcohols [104, 106]. However, as mentioned above, homocoupling can also proceed in the absence of reducing agents [107]. As illustrated by the examples illustrated in Scheme 8.11, the reaction conditions for homocouplings do not differ

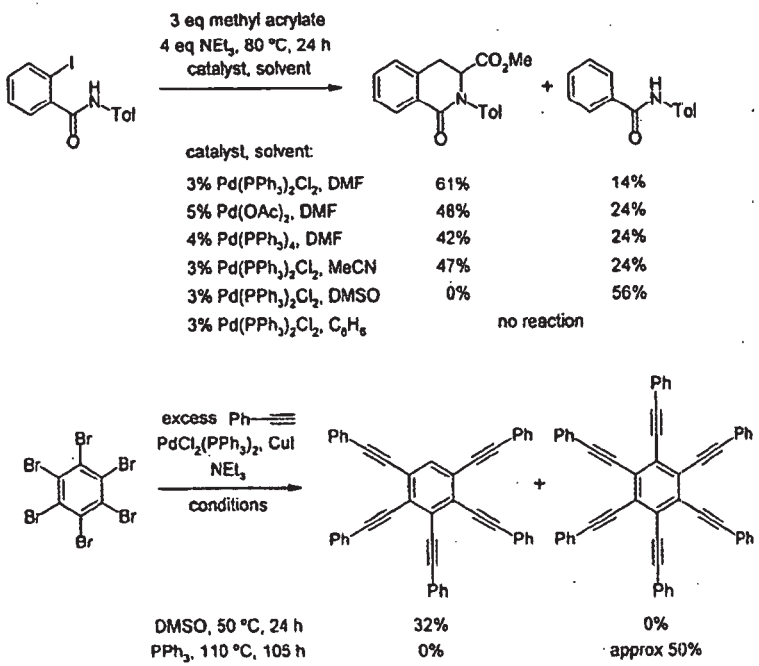


Scheme 8.11. Palladium-catalyzed homocoupling and reduction of organyl halides, carbonates, and triflates [57, 94, 104, 108, 109].

much from those used for Heck reactions or some cross-couplings, and homocoupling can therefore compete with these.

Reduction of the starting halide to a hydrocarbon should, at least in theory, be suppressible by strong ligands (e.g. chelating diphosphines), which will not be readily displaced by alcoholates or amines. Reduction should proceed swiftly if only weak, readily displaceable ligands are present in the reaction mixture [80], together with efficient reducing agents such as amines or alcoholates with α hydrogen.

The amount and type of base chosen can also have an impact on the extent of homocoupling and reduction of aryl halides in the presence of Pd(0). KO*t*Bu has been reported to increase the rate of homocoupling [46], whereas NaH can bring about quick reduction of some aryl halides [46, 47]. Higher reaction temperatures can lead to larger amounts of biaryls and to less hydrodehalogenation [15]. In the absence of strong reducing reagents or bases clean homocoupling of aryl halides without any reduction can occasionally be achieved [89] (Scheme 8.11). As illustrated by the examples depicted in Scheme 8.12, the amount of reduced product can also depend on the solvent. Reduction and homocoupling of the halide can, of course, also be suppressed by adding to the reaction mixture an efficient transmetalating reagent, a reactive alkene, or another reagent which can react quickly with the initially formed product of oxidative addition before it is converted to a hydrido com-



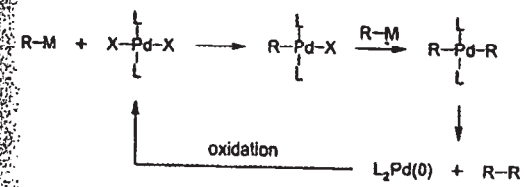
Scheme 8.12. Palladium-catalyzed reduction of organyl halides [112, 113].

plex. Thus, Heck or Sonogashira reactions are usually performed in the presence of amines, and even preformed complexes of palladium with aliphatic amines can be used as catalysts for Suzuki couplings, with no reduction of the halide being observed [110]. Similarly, carbon monoxide reacts much more rapidly with organopalladium complexes than do hydrogen or other reducing agents [111], and aryl or vinyl halides can be cleanly converted into aldehydes by treatment with mixtures of carbon monoxide and hydrogen without competing hydrodehalogenation [32].

8.5
Homocoupling and Oxidation of the Carbon Nucleophile

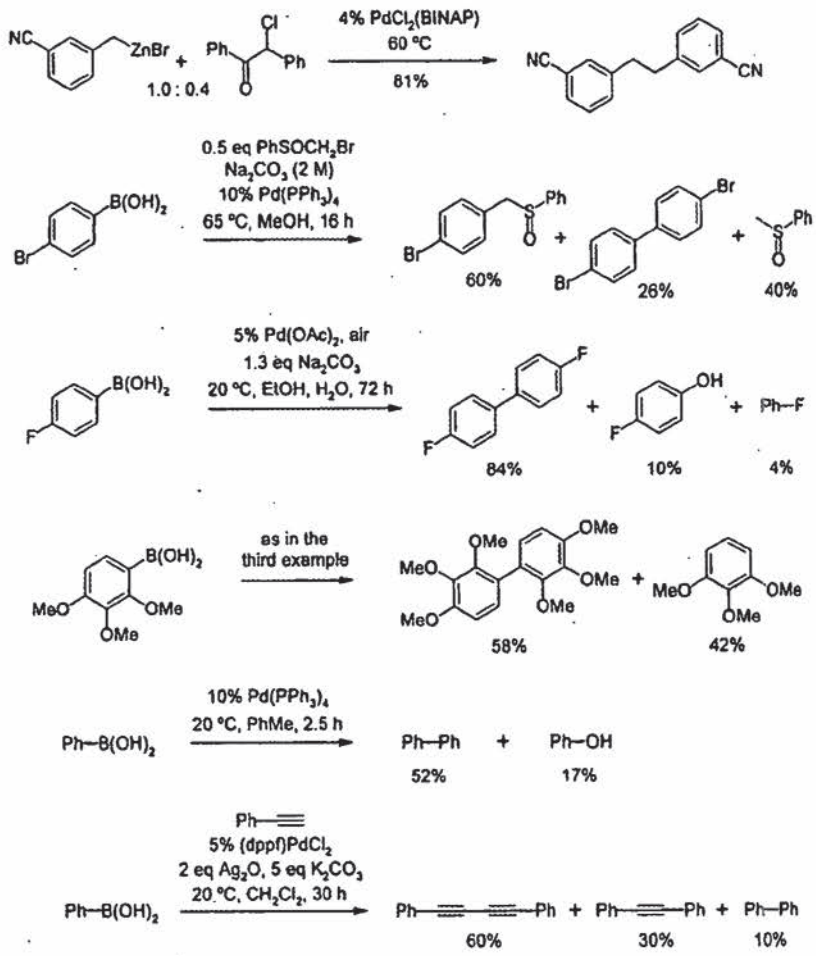
Most transition metal-catalyzed cross-coupling reactions also yield small quantities of the product of homocoupling of the nucleophilic reactant [16, 114, 115]. In particular terminal alkynes [116, 117] or metalated terminal alkynes [118] readily dimerize to the corresponding 1,3-butadiynes (Scheme 8.14).

Homocoupling of the carbon nucleophiles might proceed by the mechanism shown in Scheme 8.13. Stannanes or boronic acids, for instance, can sequentially displace either halides or organyl groups from Pd(II) complexes to yield new diorganylpalladium(II) complexes [67, 101, 116], which can undergo reductive elimination to yield a hydrocarbon and Pd(0). In the presence of an oxidant, a Pd(II) complex can be regenerated and homocoupling of the stannane or boronic acid will proceed with catalytic amounts of Pd [119, 120]. For arylboronic acids the type of base chosen can affect the extent of homocoupling: with NaOH and NEt_3 significantly more symmetric biaryl is sometimes formed than with CsF, K_3PO_4, or Na_2CO_3 as bases [16]. The reason for this behavior is not well understood.



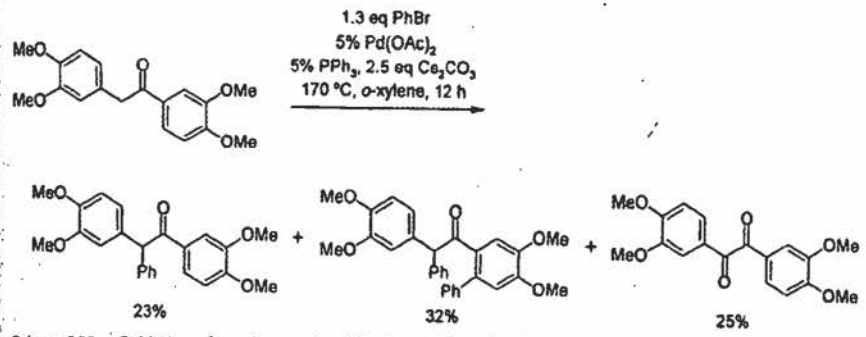
Scheme 8.13. Possible mechanism of the homocoupling of the organometallic component of Pd-mediated cross-couplings [119, 121].

Numerous examples of unwanted or deliberate Pd-mediated homocoupling of organometallic reagents have been reported (Scheme 8.14) [38, 122, 123]. Suitable oxidants include α-halo ketones [116, 124, 125] (which can, therefore, not be used as electrophilic component in cross-coupling reactions), oxygen [120, 124, 126], 1,2-diiodoethene [127], 2,3-dibromopropionic acid esters [119], and $CuCl_2$ [128].



Scheme 8.14. Palladium-mediated homocoupling of carbon nucleophiles [117, 120, 121, 125, 129].

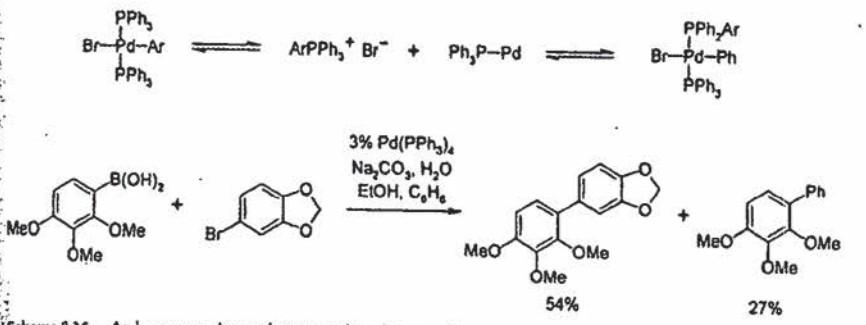
Occasionally hydroxylation of the carbon nucleophile is observed during Pd-catalyzed C–C bond formation (Scheme 8.15; third reaction in Scheme 8.14 [121]). These reactions may in some instances proceed by a mechanism analogous to the Wacker reaction [130], or to the hydroxylation of organometallic compounds or boranes by peroxides or air (Section 3.5).



Scheme 8.15. Oxidation of a carbon nucleophile during Pd-catalyzed cross-coupling [48].

8.6
Transfer of Aryl Groups from the Phosphine Ligand

During arylations of carbon nucleophiles with aryl halides in the presence of palladium triarylphosphine complexes products containing the aryl group of the phosphine can result (Scheme 8.16). These reactions proceed via reversible arylation of the Pd-bound phosphine, which occurs at temperatures above 50 °C, particularly readily in the presence of iodide [11] (see Section 8.2). Electron-deficient aryl groups usually migrate less readily than electron-rich groups [23, 25].



Scheme 8.16. Aryl group exchange between phosphines and palladium [11, 131].

This unwanted side reaction can be suppressed by keeping the amount of catalyst as small as possible, by using sterically demanding trialkyl phosphine ligands, by conducting the reaction in solvents of low polarity, such as CH_2Cl_2 (instead of THF or DMF), or by using phosphine-free catalysts [23, 38, 62, 132–134].

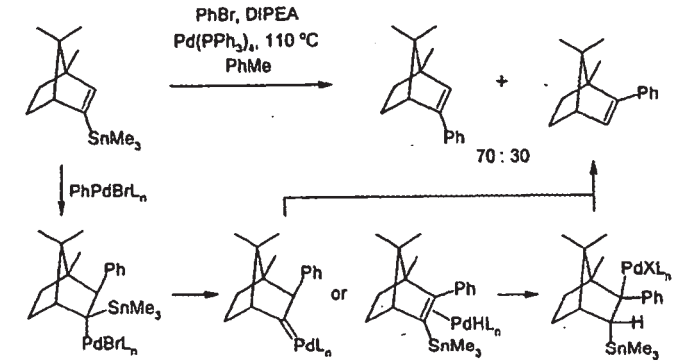
8.7
ipso- vs *cine*-Substitution at Vinylboron and Vinyltin Derivatives

Cross-coupling reactions with vinylboronic acids can yield either the normal product (*ipso*-substitution of boron) or a regioisomer formed via a Heck-type reaction (*cine*-substitution; Scheme 8.17) [135]. Formation of the normal product (1-phenylhexene in Scheme 8.17) requires a base capable of binding to the boronic acid, thereby increasing the nucleophilicity of the boron-bound carbon atom (typically ROM, MOH, M_2CO_3, M_3PO_4, where M = alkali metal [136]). Products of *cine*-substitution result when tertiary amines are used as bases, i.e. under Heck-type reaction conditions.

Similarly, vinylstannanes can also yield products of *cine*-substitution (Scheme 8.17), specially if tin and an electron-withdrawing or aryl group are bound to the same carbon atom [40, 137–141]. It has been suggested that formation of these products proceeds via intermediate formation of a palladium carbene complex [138, 140] or via reversible β-hydride elimination [141], and can be avoided by addition of Cu(I) salts [142], which increase the rate of Stille coupling, or by protecting vinylic C–H groups by transient silylation [143].



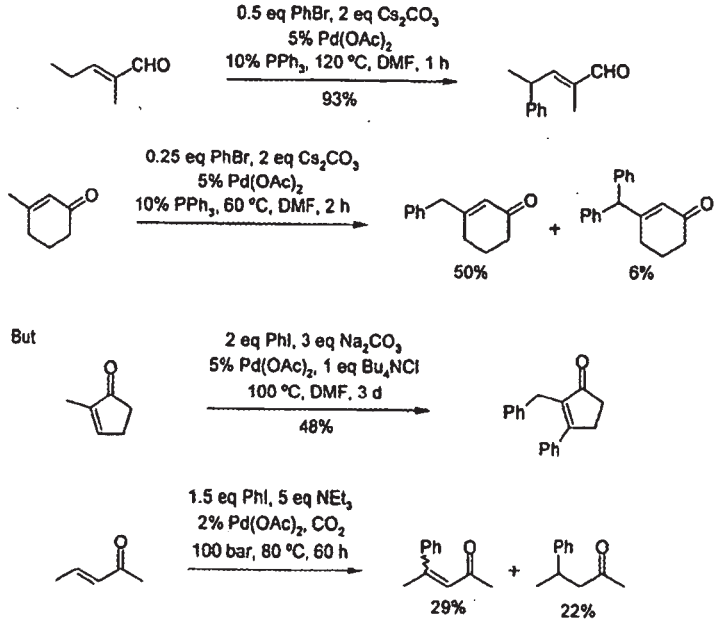
3% $Pd(PPh_3)_4$, 80 °C, C_6H_6, no base, 6 h	0%
3% $Pd(PPh_3)_4$, 80 °C, C_6H_6, 2 eq NaOH, 2 h	99% (100 : 0)
3% $Pd(PPh_3)_4$, 80 °C, DMF, 5 eq NEt_3, 20 h	54% (10 : 90)
3% Pd black, 80 °C, DMF, 5 eq NEt_3, 20 h	94% (4 : 96)
3% Pd black, 80 °C, DMF, 2 eq NaOH, 6 h	86% (56 : 44)



Scheme 8.17. Regioselectivity of cross-coupling reactions with vinylboronic acids and vinylstannanes [9, 144].

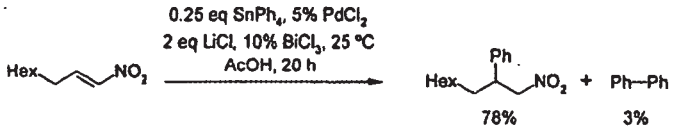
8.8
Allylic Arylation and Hydrogenation as Side Reactions of the Heck Reaction

Alkenes substituted with electron-withdrawing groups and with an allylic, acidified C–H group can react with organopalladium complexes under basic conditions either as carbon nucleophiles (cross-coupling) or as alkenes (Heck reaction). Highly substituted alkenes will undergo Heck reaction only slowly, so that their reaction as carbon nucleophiles might become the main reaction pathway (first two reactions, Scheme 8.18). Few examples of such reactions have been reported, however, and, as illustrated by the last two examples in Scheme 8.18, not all enones or enals react this way.



Scheme 8.18. Heck reaction vs allylic arylation [145–147].

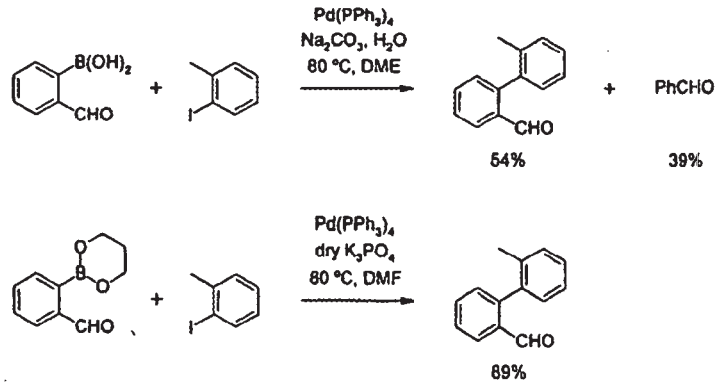
Aliphatic amines can be readily oxidized by Pd(II) to imines or iminium salts and hydrido complexes. The latter can transfer hydrogen to alkenes, leading to the formation of alkanes as byproducts of the Heck reaction (last example, Scheme 8.18). Such reactions can be avoided by using alkali carbonates as base instead of aliphatic amines [148]. Treatment of stannanes or organoboron derivatives with electron-deficient alkenes under acidic reaction conditions can also lead to formal products of Michael addition instead of the products of a Heck-type reaction [149, 150] (Scheme 8.19).



Scheme 8.19. Arylation of electron-poor alkenes under acidic reaction conditions [150].

8.9
Protodemetalation of the Carbon Nucleophile

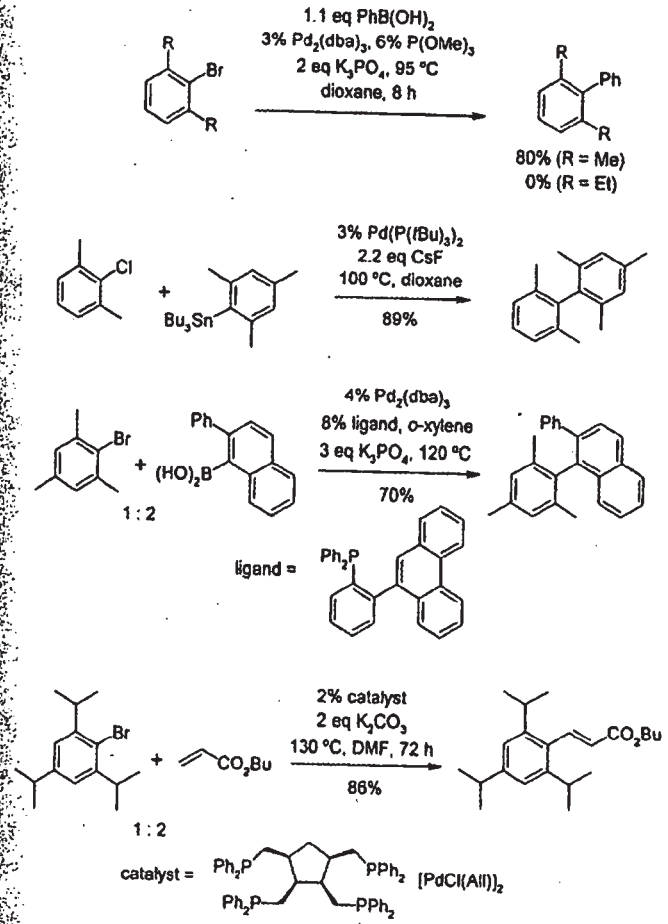
Boranes and, to a lesser extent, boronic acids can undergo slow hydrolysis (protodeboration) in the presence of protic solvents. This unwanted reaction can become predominant if a cross-coupling reaction only proceeds slowly (e.g. with electron-rich, sterically demanding, or unreactive halides; Scheme 8.20; see also Scheme 8.14) or if the boron derivative is particularly sensitive, for example 2-formylphenylboronic acid. In such instances the reaction should be performed under anhydrous conditions in an aprotic solvent with a boronic acid ester [151] or a stannane.



Scheme 8.20. Protodeboration of boronic acids in the presence of water [66].

8.10
Sterically Hindered Substrates

Cross-couplings of 2,6-disubstituted aryl halides, stannanes, or boronic acids proceed less readily than with sterically less demanding starting materials and might require a careful optimization of the reaction conditions (Scheme 8.21) [109]. Reduction or hydrolysis to the corresponding arenes will usually compete effectively with these slow cross-couplings, which should therefore be conducted under anhydrous conditions and in the absence of reducing agents. It has been found that sterically demanding phosphines are particularly well suited to Suzuki or Stille couplings of sterically demanding starting materials. Thus, neither the coupling of mesitylboronic acid and iodomesitylene with $Pd(PPh_3)_4$ [66, 151] nor the coupling of mesitylmagnesium bromide and 2-chloro-*m*-xylene or bromomesitylene with 1,3-(2-mesityl)imidazol-2-ylidene Pd complexes [115] yield the desired 2,6,2′,6′-tetrasubstituted biaryls. Compounds of this type can, however, be prepared by using sterically demanding phosphines as ligands (Scheme 8.21). Heck reactions with sterically demanding aryl halides can, similarly, also be performed successfully with the aid of sterically demanding phosphines (last example, Scheme 8.21).

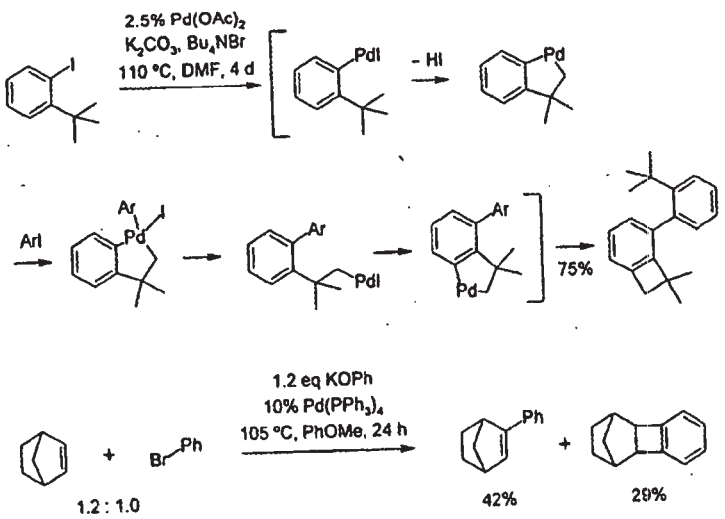


Scheme 8.21. Palladium-mediated C–C bond formation with sterically demanding substrates [152–155].

8.11 Cyclometalation

In transition metal complexes of suitable geometry the metal may undergo intramolecular oxidative insertion into C–H bonds. Intermediates of Pd-catalyzed C–C bond formation can also undergo such cyclometalations to yield "palladacycles". This can give rise to unexpected products or, if the palladacycles are too stable, the catalyst will be consumed and no further reaction will occur. At high temperatures reductive elimination from such complexes can occur to yield cyclic products.

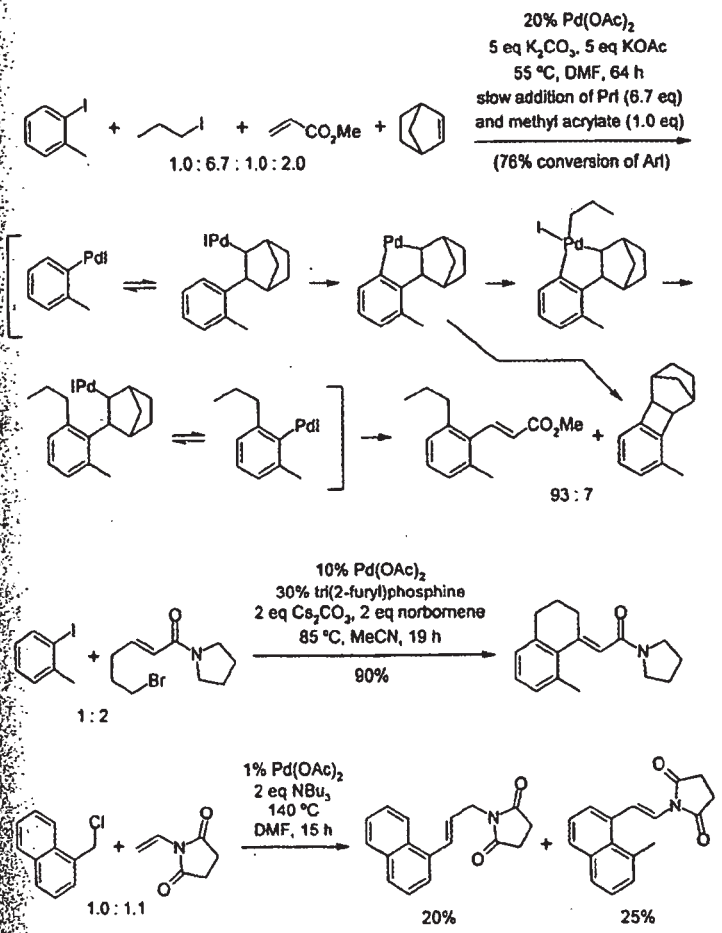
In the first example sketched in Scheme 8.22 a palladacycle is formed by intramolecular insertion of Pd into a methyl C–H group after intermolecular oxidative addition to the C–I group. The resulting intermediate does not undergo reductive elimination to yield a benzocyclobutene, probably because it is less strained than the final intermediate of this process. First after cross-coupling with a second aryl iodide followed by a second cyclometalation the resulting palladacycle undergoes reductive elimination to yield a benzocyclobutene. Similarly, Heck reactions with norbornene can also give rise to cyclobutanes (second reaction, Scheme 8.22).



Scheme 8.22. Cyclopalladation during Pd-mediated homocoupling of aryl iodides [156] and Heck reaction with norbornene [157]. Ar = 2-(tBu)C_6H_4.

Other intermediates which can undergo similar cyclometalations include (2-methoxyphenyl)palladium [158, 159] and (1-naphthylmethyl)palladium complexes (Scheme 8.23) [160]. Cyclometalation is usually promoted by high temperatures, and if these are necessary the yield of cross-coupling reactions with substrates prone to undergo cyclopalladation (for example 2-bromoanisole) can drop dramatically [43].

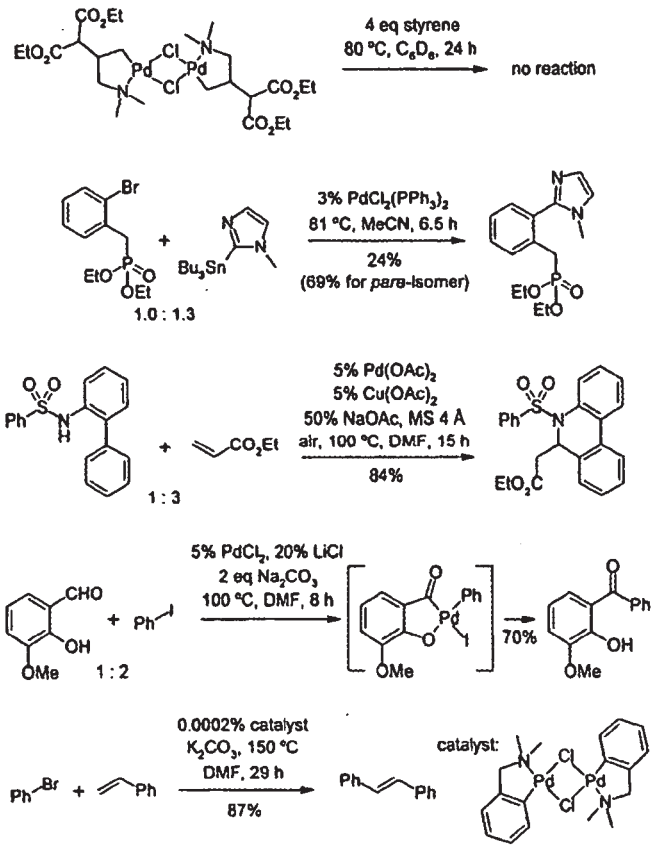
Another example of transient formation of a palladacycle is the Pd-mediated *ortho*-alkylation and *ipso*-vinylation of aryl iodides depicted in Scheme 8.23. In this multicomponent reaction the ability of norbornene to undergo reversible arylation and palladacycle formation is exploited. This reaction also illustrates that aryl halides undergo oxidative addition to Pd faster than do alkyl halides, and that aryl–alkyl bond-formation by reductive elimination also proceeds faster than alkyl–alkyl bond-formation. The large excess of alkyl iodide used in these reactions prevents the formation of biaryls. Benzocyclobutenes can also be formed in this reaction, in particular when the alkyl group on the aryl iodide is sterically demanding or when a secondary alkyl iodide is used [161].



Scheme 8.23. Palladium-mediated C–C bond formation via cyclopalladation [160–162].

8.12 Chelate Formation

Organic compounds can react with Pd salts to form stable chelates via oxidative C–H insertion and simultaneous bond formation with a further coordination site in the molecule, for example an aliphatic amine, a hydrazone, a carboxylate, a phenolate, a phosphine, or a thioether [13, 14, 51, 163]. Such cyclic complexes can be significantly more stable than related, non-cyclic organopalladium complexes, and might no longer undergo cross-coupling or Heck reactions under the usual conditions [164]. For instance, although Heck reactions can usually be performed with internal alkenes [165], only terminal alkenes or allene react intermolecularly with isolated 2-(aminomethyl)arylpalladium complexes [166, 167]. 3-(Dialkylamino)propylpalladium complexes are even less reactive (Scheme 8.24) [168], and five-membered Pd-chelates with sulfur or phosphorus ligands are unreactive towards alkenes [166, 169]. Accordingly, aryl halides with strongly chelating *ortho*-substituents will undergo transition metal-catalyzed C–C bond formation only sluggishly or not at all (Scheme 8.24). Some palladacycles or Pd-chelates are even sufficiently stable to be useful catalysts for cross-coupling or Heck reactions, and can be recovered unchanged because they do not undergo cross-coupling during these reactions (Scheme 8.24) [78, 170–172]. 2-(Hydroxymethyl)aryl halides or 2-(acylamino)aryl halides have, however, been used with success in Pd-mediated cross-coupling reactions [66, 173]. Similarly, in the third example in Scheme 8.24 the intermediate sulfonylamino chelate is sufficiently labile to undergo Heck reaction with ethyl acrylate.



Scheme 8.24. Reactions involving Pd-chelates [51, 88, 174–176].

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9 Cyclizations

9.1 Introduction

Cyclic compounds are mainly prepared from non-cyclic starting materials either by cycloaddition reactions or by cyclization. Whereas in cycloadditions the ring size of the product is determined by the reaction mechanism of a given cycloaddition, cyclizations enable the use of most bond-forming reactions and, in principle, enable access to any ring size. Certain rings, however, are more difficult to prepare than others, and because oligomerization competes with all cyclizations, slow cyclizations will have a detrimental effect on the yield of cyclic products. In this section some of the critical structural considerations for successful cyclizations will be presented and examples of difficult cyclizations will be discussed.

9.2 Baldwin's Cyclization Rules

In the 1970s J.E. Baldwin proposed a set of qualitative generalizations for the probability of formation of cyclic compounds, based on the favored trajectories for the approach of one reactant to another [1–5]. Cyclizations were organized according to the ring size formed, whether the breaking bond is located in (endo) or outside (exo) the newly formed ring, and the hybridization of the (mostly uncharged) carbon atom with the highest *s* character involved in bond formation (tet, trig, or dig for sp^3-, sp^2-, or *sp*-hybridized carbon, respectively). Baldwin's rules state that 3 to 6-endo-tet, 3 to 5-endo-trig, and 3 and 4-exo-dig processes are unfavorable, whereas all remaining cyclizations are allowed (Scheme 9.1).

These rules do not apply strictly, but provide useful guidelines for synthesis design. The rules are generally not applicable to electrocyclic reactions or to substrates containing non-second-period elements (e.g. P or S), because their longer bond lengths imply different geometric constraints.

An example of a forbidden 6-endo-tet process would be the intramolecular alkylation of a carbanion via a six-membered transition state (Scheme 9.2). Because such an alkylation would proceed via the SN2 mechanism and would require a linear

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