

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO	
RAD: 15-269914- -1	FECHA: 2015-12-17 14:58:12
DEP: 2020 DIRECCION DE NUEVAS CREACIONES	EVE: 378 FASE NACIONAL INCLUIDO CAPITULO I
TRA: 11 PCT-PATENTE DE INVENCION CAPITULOS I Y II	FOLIOS: 10
ACT: 519 TRASLADOINFORME	

DIRECCIÓN DE NUEVAS CREACIONES

2020
Bogotá, D.C.,

Abogado(a)/Señor(a)
LUZ CLEMENCIA DE PÁEZ

Asunto: Radicación: 15-269914- -1
Trámite: 11
Evento: 378
Actuación: 519
Oficio: 15281
Folios: 10

Patente de Invención	X			Patente de Modelo de Utilidad	
Vía Nacional					
Vía PCT (Fase Nacional)	X	Capítulo I	X	Capítulo II	
No. Solicitud Internacional	PCT/US2012/052882				
Fecha de Presentación Internacional	29/08/2012				

Como resultado del examen de fondo realizado, con fundamento en el Artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina, se comunica:

1. Documentos estudiados

Descripción:	Radicado N° 15-269914-00000-0000	11/Noviembre/2015
Reivindicaciones:	Radicado N° 15-269914-00000-0000	11/Noviembre/2015
Oposición:	Radicado N° 14-065677-00001-0000	Lafrancol S.A.S 10/Julio/2014
Respuesta de la solicitante:	Radicado N° 14-065677-00006-0000	19/Enero/2015
Prioridad:	US 61/528,609	29/Agosto/2011

2. Análisis de la Prioridad

Se acepta la reivindicación de prioridad porque ésta solicitud fue presentada dentro del plazo establecido (Art. 9 D 486) y su contenido técnico corresponde con el de la prioridad reivindicada.

3. Presentación de solicitudes Fraccionarias (Art 36 D 486)

Se acepta para examen la solicitud fraccionaria presentada e identificada como 15-269914-00000-0000, porque no implica ampliación de la materia contenida en la solicitud inicial.

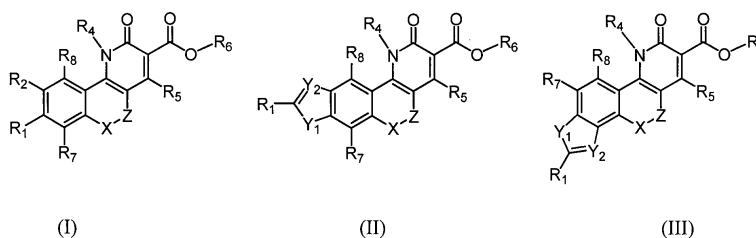
4. Objeto de la invención

De acuerdo con lo establecido en el numeral 1.2.2.2 del capítulo primero del Título X de la Circular Única para efectos del examen de patentabilidad, se tendrá en cuenta la tasa pagada por la solicitante al momento de comenzar el examen para las reivindicaciones adicionales; esto es que cuando la solicitud contenga más de diez (10) reivindicaciones y no se haya pagado la tasa complementaria, sólo se estudiarán las cubiertas por la tasa pagada. En el presente caso se estudiarán las reivindicaciones 1 a 9 del capítulo reivindicatorio (Radicado N°. 15-269914-00000-0000).

Título de la solicitud: "COMPUESTOS ANTIBACTERIANOS Y MÉTODOS PARA SU USO"

El problema planteado en esta solicitud consiste en la necesidad de proporcionar nuevos agentes antibacterianos debido al aumento de la resistencia bacteriana a los antibióticos convencionales.

Para resolver este problema técnico la solicitud en estudio proporciona compuestos, formas y composiciones farmacéuticas de los mismos para tratar o mejorar una infección bacteriana resistente a múltiples fármacos. La solicitud se refiere a un compuesto de formula (I), formula (II) o formula (III).



El objeto de la presente solicitud se relaciona con la Clasificación Internacional de Patentes (CIP): A61K 31/473.

5. De la solicitud de patente

Título

El título de la solicitud es general y ambiguo, puesto que menciona de manera genérica compuestos con actividad como antibacterianos lo cual incluye una gran variedad de compuestos que no están comprendidos dentro del objeto de la solicitud. Se sugiere incluir las características estructurales comunes a los compuestos reclamados, con el fin de hacer el título un poco más concreto y pertinente.

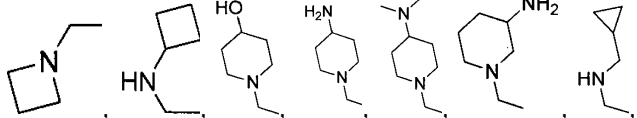
Reivindicaciones (Art 30 D 486, Art 22 PCT)

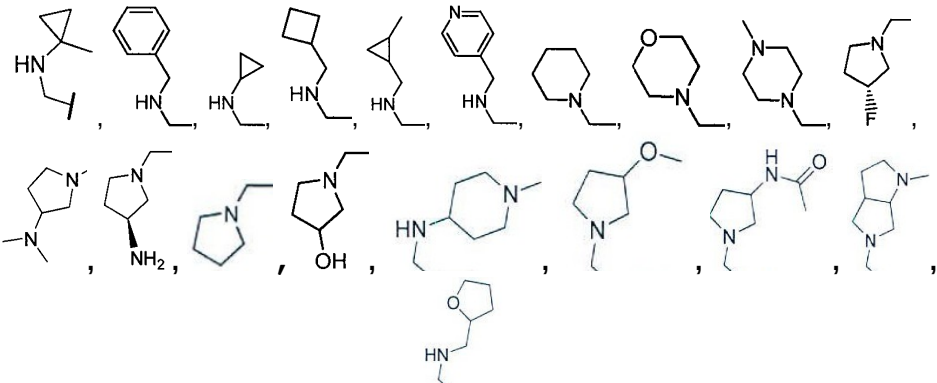
1. La reivindicación 1 no es clara porque:

- La fórmula estructural presentada en la reivindicación 1 no corresponde con la encontrada en el capítulo descriptivo (Pág. 8), puesto que el sustituyente en la posición 3 del anillo de piridona es $-C(=O)-CH_3$ en la fórmulas II de la reivindicación, mientras que es un grupo $-C(=O)-CR^6$ en la formula II del capítulo descriptivo. Dado que la reivindicación indica la presencia del

sustituyente R⁶, esta Oficina considera que esta inconsistencia resulta de un error material, y realizará el estudio teniendo en cuenta las características estructurales de la fórmula encontrada en el capítulo descriptivo. Se sugiere a la solicitante realizar la corrección correspondiente en la estructura presentada.

- La reivindicación 4 no es concisa porque no define los grupos alquilo que hacen parte de los sustituyentes mencionados en esta reivindicación. Se sugiere incluir la definición de dichos grupos.
- La reivindicación 7 no es clara porque la forma en que están nombrados los compuestos no cumplen con las normas IUPAC. Se le recuerda a la solicitante que para nombrar ácidos carboxílicos es necesario empezar el nombre con la palabra “ácido” continuar con la nomenclatura del compuesto y finalizar con la palabra “carboxílico”, por lo que se sugiere que se hagan las correcciones necesarias a los nombres de los compuestos que se reclaman.
- La reivindicación 8 no se encuentra soportada en la descripción, puesto que en ella no se demuestra desarrollo de hidratos, solvatos, clatratos, isotopologos, polimorfos o tautómeros de los compuestos allí reclamados, por lo que se sugiere a la solicitante eliminar dichos términos de la reivindicación.
- La reivindicación 9 no es clara ya que al tratarse de una composición farmacéutica sus características técnicas esenciales son sus ingredientes y la proporción o concentración de los mismos. De esta forma, se sugiere evitar el uso de las expresiones “cantidad eficaz” y “excipiente farmacéuticamente aceptable”, puesto que hacen referencia a la función o actividad de los ingredientes de la composición, la cual no es una característica técnica esencial que permita diferenciar las composiciones reclamadas del estado de la técnica. De esta forma se sugiere caracterizar los ingredientes por su nombre IUPAC, Denominación común internacional o estructura, y su proporción o concentración usando rangos concretos.
- La reivindicación 1 no es concisa porque las definiciones de R, R₃, R₄, R₅, R₆, R₇, R₈, X Y₁, Y₂ y Z son muy genéricas y dan lugar a una gran variedad de compuestos no sustentados por la descripción. Se sugiere restringir la solicitud a una razonable generalización del tipo de compuestos que ha sido sintetizado ó probado, es decir, que se encuentran debidamente sustentados.

Sustituciones	Soporte de los ejemplos presentados
X	-CH ₂ -, -CH ₂ CH ₂ -, -C(CH ₃)-CH ₂ -, -CH=CH-, -C(CH ₃)=CH-, -CH(OH)CH(OH)-, -O-, -O-CH ₂ -, -N(CH ₃)-CH ₂ -, -NH-CH ₂ -, -NH-CH ₂ CH ₂ -, enlace.
Z	-CH ₂ -, -CH(CH ₃)-,
Y ₁	-N(CH ₃)-
Y ₂	-CH-
R ₁	-H, -CH ₂ NH ₂ , -CH ₂ NHCH ₃ , -CH ₂ NHCH ₂ CH ₃ , -CH ₂ NHCH(CH ₃) ₂ , -CH ₂ NHC(CH ₃) ₃ , -CH ₂ N(CH ₂ CH ₃) ₂ , -CH ₂ NHCH ₂ CH ₂) ₂ CH ₃ , -CH ₂ NHCH ₂ C≡CH, -CH ₂ N(CH ₃) ₂ , -CH ₂ NH(CH ₂) ₃ CH ₃ , -CH ₂ NH(CH ₂) ₄ CH ₃ , -CH ₂ NH(CH ₂) ₅ CH ₃ , -, -CH ₂ NH(CH ₂) ₆ CH ₃ , -CH ₂ NH(CH ₂) ₇ CH ₃ , -CH ₂ NH(CH ₂) ₈ CH ₃ , -CH ₂ N(CH ₃)(CH ₂) ₂ N(CH ₃) ₂ , CH ₂ NH(CH ₂) ₂ CH ₃ -(CH ₂) ₂ NHCH ₂ CH ₃ , -N(CH ₃) ₂ , -NH(CH ₂) ₂ N(CH ₃) ₂ , -CH ₂ NH(CH ₂) ₂ NHCH ₃ , -CH ₂ NH(CH ₂) ₂ NH ₂ , -CH ₂ NHC(CH ₃)CH ₂ CH ₃ , -CH ₂ NHCH ₂ CH ₂ OH, -CH ₂ NH(CH ₂) ₂ OCH ₃ , -CH ₂ N(CH ₃)(CH ₂) ₂ OH, -CH ₂ NHCH(CH ₃)CH ₂ OCH ₃ , -CH ₂ NHCH(CH ₃)CH ₂ OH, -CH ₂ NHCH ₂ CH=CH ₂ , -CH ₂ NHCH ₂ C(CH ₃) ₃ , -CH ₂ NHCH ₂ CH(CH ₃) ₂ , -CH ₂ NHCH(CH ₃)CH ₂ N(CH ₃) ₂ ,  -CH ₂ NHCH(CH ₃)CH ₂ CH ₃ ,

Sustituciones	Soporte de los ejemplos presentados
	
R ₂ /R ₇ /R ₈	-H, -F
R ₄	-H, -CH ₃ , -CH ₂ CH ₃
R ₅	-OH
R ₆	-H

Se sugiere a la solicitante hacer las aclaraciones necesarias.

Descripción (Art 28 D 486)

La descripción no soporta adecuadamente el alcance dado por el capítulo reivindicatorio, dado que los ejemplos de compuestos mostrados resultan ser insuficientes para la gran variedad de compuestos reclamados.

Compuestos en los que R⁶ es diferente a hidrógeno, Z es diferente a -CH₂- o -CH(CH₃)-, Y₁ es diferente de -N(CH₃)-, Y₂ es diferente a -CH-, R₅ es diferentes de -OH, y donde R₂, R₇, R₈, son diferentes de H, no se encuentran ejemplificados. De esta forma no existe evidencia de su actividad farmacológica, por lo que se desconoce si comparten o no la actividad de los compuestos que sí fueron evaluados. Es imposible atribuir la actividad de los compuestos ensayados a la gran variedad de compuestos que se encuentran al alcance de la reivindicación 1, por lo que se considera que no existe una divulgación suficiente de la materia allí reclamada.

Dado que las características mencionadas anteriormente son comunes en los ejemplos presentados por la solicitante, es evidente que estos sustituyentes son esenciales para la actividad biológica de los compuestos reclamados, por lo que se sugiere a la solicitante que lo plantee de esa forma.

Se sugiere a la solicitante hacer las aclaraciones necesarias.

6. Análisis de las Oposiciones

Argumentaciones de Lafrancol S.A.S

La opositora manifiesta que las composiciones y combinaciones farmacéuticas que comprenden una cantidad eficaz de un agente antibiótico o antibacteriano tales como Cefixima, Linezolid, entre muchos otros, útiles en el tratamiento o mejora de infecciones bacterianas causadas por patógenos Gram-negativos y Gram-positivos de tipo salvaje, son prácticas y eventos totalmente conocidos en la industria farmacéutica, por lo que manifiesta que carecen de los requisitos de novedad y nivel inventivo. Igualmente, indica que la solicitud pretende obtener patente de composiciones farmacéuticas que involucran agentes tales como Cefixime y Linezolid, entre muchos otros, señalando que no puede

la solicitante acceder a beneficios patentarios sobre composiciones y combinaciones farmacéuticas que comprenden moléculas que se encuentran descubiertas y plenamente identificadas en el sector químico-farmacéutico, manifestando que en documentos como “The Merck Index” se evidencia que el principio activo Cefixime se encuentra bajo el conocimiento público desde un tiempo considerable, y que el mismo ostenta beneficios patentarios bajo los documentos EP 30630 y US 4409214 (Años 1981 y 1983) respectivamente y que por su parte la molécula Linezolid ostenta beneficios patentarios bajo los documentos WO 9507271 y US 5688792 (Años 1995 y 1997) respectivamente.

Asimismo la opositora señala que la solicitud pretende proteger objetos que no son considerados invenciones, tales como métodos de tratamiento y las combinaciones de productos conocidos.

Por último la opositora manifiesta que la solicitud carece de los requisitos de Novedad y Nivel inventivo, fundamentales para otorgársele el privilegio de patente de invención, si se tiene cuenta la materia revelada en documentos como:

- US 2008/0312292 A1 (Yasui et al).
- US 2010/0069380 A1 (Choi et al).
- US 2010/0261706 A1 (Jagtap et al).
- US 4,474,786 A (Smith et al).
- US 2007/0249583 A1 (Stein et al).

Respuestas de la Solicitante

La solicitante llama la atención sobre la poca argumentación de la sociedad opositora y la ausencia de un estudio al objeto de la solicitud en el escrito de oposición, resaltando que se limita a reproducir una copia de los documentos citados en el informe de búsqueda internacional sin tener siquiera en cuenta la clasificación dada a los mismos, concluyendo que la oposición carece de argumentos sobre la falta de novedad o nivel inventivo de la solicitud.

Frente a la afirmación de la opositora sobre el incumplimiento de los requisitos de novedad, nivel inventivo y aplicación industrial, la solicitante se refiere al hallazgo por parte de la autoridad internacional, la cual encontró que las reivindicaciones 2, 4 y 7-10 cumplen con dichos requisitos.

Finalmente, con respecto a los argumentos referidos a que la solicitud reclama métodos de tratamiento y a combinaciones que comprenden Cefixime y Linezolid, la solicitante reitera que dichas reivindicaciones han sido eliminadas.

Respuesta del Examinador Técnico

En segundo lugar, con respecto al argumento de la opositora según el cual la actual solicitud reclama métodos de tratamiento y combinaciones, esta Oficina encuentra que dicha afirmación no es pertinente, en vista de que la materia reclamada en el capítulo reivindicatorio radicado bajo el No. 15-269914-00000-00000, el cual no contiene materia que pueda ser considerada como no patentable.

Por otra parte, frente al documento “*The Merck Index*” citado en el escrito de oposición de la Lafrancol S.A.S esta Oficina aclara que no hace referencia a compuestos con las características estructurales de las formulas (I), (II) y (II) reclamados en la actual solicitud, es decir no divulga las características técnicas esenciales de la materia reclamada, por lo que no se considera relevante para el análisis de patentabilidad de la solicitud.

Con respecto a los documentos citados en el escrito de oposición esta oficina considera que:

- El documento US 2008/0312292 A1 (Yasui et al), proporciona compuestos con acción antipruritica, los cuales son agonistas de los receptores de cannabinoides. Los cuales no se encuentran relacionados estructural ni funcionalmente con los compuestos objeto de la solicitud, por lo que esta Oficina considera que este documento no afecta los requisitos de patentabilidad de la solicitud en estudio.
- Por su parte el documento US 2010/0069380 A1 (Choi et al), se refiere a compuestos que modulan la actividad de la peptidil tRNA hidrolasa bacteriana, así como composiciones que los comprenden y métodos para prevenir o inhibir la proliferación bacteriana o alguno de sus síntomas. Esta Oficina encuentra que los compuestos divulgados en este documento comparten algunas de las características esenciales con los ahora reclamados, por lo que se considera pertinente para evaluar los requisitos de patentabilidad de la presente solicitud.
- A su vez, el documento US 2010/0261706 A1 (Jagtap et al), proporciona compuestos tetraciclicos análogos o derivados de 1H-indeno[1,2-b]piridin-2(5H)-ona, útiles para el tratamiento de una variedad de enfermedades y trastornos. Estos compuestos difieren de los reclamados en el anillo A que se encuentra fusionado a la piridona, el cual no se encuentra en los compuestos reclamados; puesto que este documento menciona que dichos compuestos son útiles para el tratamiento de una serie de trastornos, mas no se refiere particularmente a la acción de los mismos como agentes antibacteriales, esta Oficina considera que no afecta los requisitos de patentabilidad de la solicitud en estudio.
- De la misma forma, en cuanto al documento US 4,474,786 A (Smith et al), que se refiere a compuestos derivados de lactamas tricíclicas útiles para incrementar la contractilidad cardiaca, esta Oficina considera que dada la diferencia en número de anillos y disposición espacial de los mismos con los compuestos reclamados por la solicitud, y teniendo en cuenta que pertenecen a otro campo técnico, este documento no se considera relevante para el análisis de patentabilidad de la solicitud en cuestión.
- Por último, el documento US 2007/0249583 A1 (Stein et al) proporciona compuestos inhibidores de la HMG CoA reductasa, y por lo tanto útiles como inhibidores de la síntesis de colesterol, sin embargo los compuestos allí divulgados difieren de los reclamados por la ausencia de un grupo ceto en el anillo de piridina, es decir en que no se presenta el anillo de piridona de los compuestos reclamados, y dado que pertenecen a otro campo técnico, este documento no se considera relevante para el análisis de patentabilidad de la solicitud en cuestión.

En conclusión, la materia divulgada en el documento US 2010/0069380, afecta los requisitos de patentabilidad de la presente solicitud, por lo que la oposición se considera fundada.

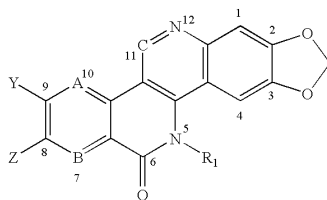
7. Determinación del Estado de la Técnica

El estado de la técnica se determinó con base en la fecha de presentación de la solicitud de prioridad: 29 de agosto de 2011 y se encontraron los siguientes documentos que anticipan el objeto de esta solicitud:

Ítem	Documento	Título	Fecha de Publicación
D1	US 20050009825	"Cytotoxic agents"	13/Enero/2005
D2	Ramesh, D et al. <i>Indian Journal of Chemistry- Section B</i> Vol.47B(05)	"Synthesis of novel naphtho[2,1-b]furo[3,2-b]pyridine derivatives as potential antimicrobial agents"	Mayo de 2008

El documento D1¹ divulga compuestos inhibidores de la topoisomerasa I y/o II, que muestran actividad citotóxica, los cuales corresponden a la fórmula I (Pág. 1, Párr. [0004])

¹<https://www.google.com.co/patents/US20050009825>



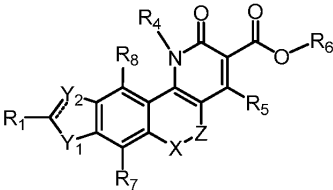
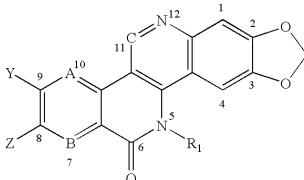
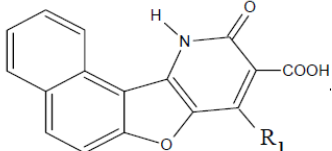
El documento D2² divulga la síntesis y caracterización de compuestos derivados de nafto[2,1-b]furo[3,2-b]piridina útiles como agentes antimicrobianos (Resumen).

8. Examen de Patentabilidad (Art 14 D486)

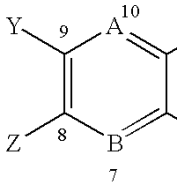
Nivel inventivo (Art 18 D486)

La reivindicación 1 consiste en: “Un compuesto de fórmula (II) (...)” (Radicado N°. 15-269914-00000-00000).

Comparación de las características técnicas esenciales, con las del estado de la técnica:

Características esenciales	D1	D2
Compuestos de fórmula II  o una forma del mismo, en el cual	 (Pág. 50, Reivindicación 1)	 8a-c (Pág. 755, esquema 1, compuestos 5a-c, 6a-c, y 8a-c)
X es un enlace, N(R₁₄), S, O, -CH(R₉)-, -CH(R₉)-CH(R₁₀)-, -CH(R₉)-CH(R₁₀)-CH(R₁₁)-, -C(R₉)=C(R₁₀)-, -C(R₉)=C(R₁₀)-CH(R₁₁)-, -CH(R₉)-C(R₁₀)=C(RU)-, -O-CH(R₁₀)-, -CH(R₉)-O-, -N(R₁₄)-CH(R₁₀)-, -CH(R₉)-N(R₁₄)-, -S-CH(R₁₀)-, -CH(R₉)-S-, -O-CH(R₁₀)-CH(Rn)-, -CH(R₉)-O-CH(R₁₁)-, -CH(R₉)-CH(R₁₀)-O-, -N(R₁₄)-CH(R₁₀)-CH(R₁₁)-, -CH(R₉)-N(R₁₄)-CH(R₁₁)-, -CH(R₉)-CH(R₁₀)-N(R₁₄)-, -S-CH(R₁₀)-CH(R₁₁)-, -CH(R₉)-S-CH(R₁₁)-, -CH(R₉)-CH(R₁₀)-S-, -O-C(O)-CH(R₁₁)-, -C(O)-O-CH(R₁₁)-, -CH(R₉)-O-C(O)-, -CH(R₉)-C(O)-O-, -N(R₁₄)-C(O)-CH(R₁₁)-, -C(O)-N(R₁₄)-CH(R₁₁)-, -CH(R₉)-N(R₁₄)-C(O)-, -CH(R₉)-C(O)-N(R₁₄)-, -S-C(O)-CH(Ru)-, -C(O)-S-CH(R₁₁)-, -CH(R₉)-S-C(O)- o -CH(R₉)-C(O)-S-;	N	enlace
Y₁ es -N(R₁₂)- o -O-	-O-	
Y₂ es -C(R₁₃)-, -N(R₁₂)- o -O- En el que la línea discontinua representa un doble enlace que esta presente cuando Y₂ es -C(R₁₃)- y ausente cuando Y₂ es -N(R₁₂)- o -O	-O-	
Z es N(R₁₄), S, O, C(O) -CH(R₃)-	-C(=O)-	-O-

Características esenciales	D1	D2
R₁ es C₃₋₁₄cicloalquilo seleccionado de entre ciclopropilo, ciclobutilo, ciclopentilo, ciclohexilo o cicloheptilo; fenilo; heteroarilo seleccionado de pirrolilo, tiazolilo, triazolilo-1H 1,2,3-, 1H-tetrazolilo, 2H-tetrazolilo, imidazolilo o piridinilo; heterociclilo seleccionado en cada caso, cuando está presente, entre azetidino, pirrolidino, tetrahydrofurano, piperidino, piperazino, morfolino, 1, 4- diazepano, 1,3-dioxolano, 2,5- dihidro-1H-pirrolilo, dihidro-1H- imidazolilo, 1,4,5,6- tetrahydropirimidin, 1,2, 3,6- tetrahydropiridinilo; tetrahydro-2H- pirano, indolino, 2,3- dihydrobenzo[d]oxazolilo, benzo- 2H-3,4-dihidro[b][1,4] oxazino, 3,4-dihidroisoquinolino- (1 H)-il, 1,2,3,4-tetrahydroisoquinolino, 1,2,3,4-tetrahydroquinoxalino, hexahidropirrol[3,4-b][1,4] oxazin-(2H)-il, (4aR,7aS)- hexahidropirrol[3, 4-b][1, 4] oxazin-(4aH)ilo, 3,4-dihidro-2H- pirido[3,2-b][1,4]oxazino, (cis)- octahidrociclopenta[c]pirrolilo, hexahidropirrol[3,4-b] pirrol (1H) il, (3aR, 6aR) hexahidropirrol [3,4-b] pirrol (1H) il, (3aR, 6aS) - hexahidropirrol[3,4 -c]pirrol (1H)- il, 5H-pirrol[3,4-b]piridin (1H)-il, 5,7-dihidro-6H-pirrol[3, 4- b]piridinilo, tetrahydro- 1H- pirrol[3, 4-b]piridin(2H,7H,7aH) -il, hexahidro-1H-pirrol[3,4- b]piridin(2H)-il, (4aR,7aR) hexahidro1H-pirrol[3, 4-b] piridin(2H)-il, octahidro-6H- pirrol[3, 4-b]piridinilo, 2,3, 4,9- tetrahydro-1H-carbazolilo, 1,2,3,4- tetrahydropirazino[1,2-a] indol-8- ilo, 2,3-dihidro-1H-pirrol [1,2- a]indolilo, (3aR,6aR)- hexahidrociclopenta[c]pirrol(1H)il, (3aR,4R,6aS)- hexahidrociclopenta[c]pirrol(1H)il, (3aR, 4S, 6aS)- hexahidrociclopenta[c]pirrol(1H) il, (3aR,5r,6aS)- hexahidrociclopenta[c]pirrol(1H)- il,1,3-dihidro-2H-isoindolilo, octahidro-2H-isoindolilo, (3aS)-1, 3,3a, 4,5,6-hexahidro-2H -isoindolil, (3aR,4R,7aS) -1H- isoindol- (3H, 3aH, 4H, 5H, 6H, 7H, 7aH) -il, (3aR, 7aS) octahidro- 2H-isoindolilo, (3aR, 4R, 7aS) octahidro-2H-isoindolilo, (3aR, 4S, 7aS) octahidro-2H-isoindolilo, 2,5- diazabicyclo [2.2. 1] heptanilo, 2- azabicyclo [2.2.1] hept-5-enil, 3- azabicyclo [3.1.0] hexanilo, (LR,	-H	-H

Características esenciales	D1	D2
5S, 6S) -3- azabicyclo [3.1.0] hexanilo, (cis, cis) -3-azabicyclo [3.1.0] hexanilo, 3,6- diazabicyclo [3.1.0] hexanilo, (LS, 5R, 6R) -3- azabicyclo [3.2.0] heptanilo, (LS, 5R, 6S) - 3- azabicyclo [3.2.0] heptanilo, 5-azaespiro [2.4] heptanilo, 2,6-diazaespiro [3.3] heptanilo, 2,5- diazaespiro [3.4] octanilo, 2,6-diazaespiro [3.4] octanilo, 2, 7-diazaespiro [3.5] nonanilo, 2,7- diazaespiro [4.4] nonanilo, 2-azaespiro [4,5] decanilo o 2,8-diazaespiro [4.5] decanilo.		
R ₂ es hidrógeno, halógeno, hidroxilo, C ₁₋₆ alquilo, amino, C ₁₋₆ alquilo-amino o (C ₁₋₆ alquilo) ₂ - amino		Se fusionan con un cuarto anillo de benceno
R ₇ y R ₈ son hidrógeno, halógeno, hidroxilo, C ₁₋₈ alquilo, amino, C ₁₋₈ alquil-amino, (C ₁₋₈ alquilo) ₂ -amino		
R ₄ es hidrógeno, hidroxilo, C ₁₋₈ alquilo, arilo C ₁₋₈ alquilo, donde el arilo es opcionalmente sustituido con un sustituyente adicional seleccionado entre C ₁₋₈ alquilo, halo- C ₁₋₈ alquilo, C ₁₋₈ alcoxi o alcoxi- C ₁₋₈ alquilo;	R ⁶ es H, C ₁₋₈ alquilo, C ₂₋₈ alquenilo, cicloalquilo, arilo, heteroarilo, aril- C ₁₋₈ alquilo, heteroaril- C ₁₋₈ alquilo sustituidos o no sustituido,	-H
R ₅ es hidrógeno, halógeno, hidroxilo, C ₁₋₈ alquilo, carboxilo, amino, C ₁₋₈ alquil-amino, (C ₁₋₈ alquilo) ₂ -amino o C ₁₋₈ alquil-SO ₂ - amino.		-CH ₃ en a
		-C ₆ H ₅ en b
		-OH en c
R ₆ es hidrógeno o C ₁₋₈ alquilo		No se menciona

El documento D1 se considera el estado de la técnica cercano a la solicitud definida en la reivindicación 1 porque da a conocer compuestos de fórmula (I) que actúan como inhibidores de la topoisomerasa I y/o II, útiles como agentes antibacterianos (Pág. 23, Párr. [0374]).

La diferencia entre la solicitud, definida en la reivindicación 1 y los compuestos divulgados en D1 consiste en que los compuestos reclamados son tetracíclicos, mientras que los compuestos divulgados por el documento D1 son tricíclicos.

No hay evidencia de un efecto técnico asociado a la modificación de la estructura central de los compuestos reclamados, toda vez que el documento D1 no muestra una evaluación del efecto como agentes antibacterianos de los compuestos allí reclamados, de esta forma no es posible realizar una comparación entre estos compuestos y los reclamados por la solicitud.

Por lo tanto, el problema técnico objetivo que pretende resolver esta invención se puede considerar como la necesidad de proporcionar compuestos alternativos a los divulgados en D1 que posean actividad antibacteriana.

Sin embargo, compuestos derivados de piridona que comprenden un núcleo central tricíclico se encuentran divulgados en el documento D2 que se refiere a la producción y caracterización de compuestos derivados de nafto[2,1-b]furo[3,2-b]piridina, donde el

grupo pridin-2-ona comprende un sustituyente de ácido carboxílico en posición 3 de dicho anillo, que son útiles como agentes antimicrobianos (Resumen).

En consecuencia, la persona del oficio normalmente versada en la materia, modificaría el anillo central de los compuestos divulgados por el documento D1, incluyendo un sustituyente de ácido carboxílico en posición 3 del anillo de grupo pridin-2-ona de acuerdo a lo divulgado en D2, para llegar así al objeto de la reivindicación 1 de la solicitud. Por lo cual se considera obvia.

En consecuencia, la reivindicación 1 de acuerdo con lo divulgado en los documentos D1 y D2, carece de Nivel Inventivo.

Puesto que las reivindicaciones dependientes 2 - 12 no mencionan características inventivas adicionales tampoco se pueden considerar inventivas.

Conclusión:

Las reivindicaciones 1-12 cumplen el requisito de novedad (Art. 16), pero no cumplen con el requisito de nivel inventivo (Art. 18).

9. Conclusión

Los requisitos de Patentabilidad de la presente solicitud están afectados así:

Ítem	Documento	Reivindicaciones afectadas	Requisito que afecta
D1	US 20050009825	1-12	Nivel Inventivo
D2	Ramesh, D et al. <i>Indian Journal of Chemistry</i> -Section B Vol.47B(05)	1-12	Nivel Inventivo

En cumplimiento del artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina, se le indica que debe dar respuesta dentro del término de sesenta (60) días contados a partir del día siguiente de la fecha de notificación de la presente comunicación. En caso de no dar respuesta al presente requerimiento, o si a pesar de la respuesta subsistieran los impedimentos para la concesión, se denegará la patente.

Se invita al solicitante se sirva indicar, si así lo considera, su renuncia al término faltante de sesenta (60) días para dar respuesta a este requerimiento y presentarla por escrito.

Finalmente, se le recuerda al solicitante que si como respuesta a este requerimiento llegara a modificar el capítulo reivindicatorio y éste contenga más de diez (10) reivindicaciones, no pagará la tasa de modificación voluntaria pero sí la correspondiente al pago por reivindicación adicional.

Notifíquese el presente oficio conforme a lo dispuesto en el numeral 5.2, literal e), del capítulo quinto del título primero de la Circular Única No. 10 de 2001.



JOSÉ LUIS SALAZAR LÓPEZ
Director de Nuevas Creaciones (c)

El anterior requerimiento fue notificado por fijación en lista, de fecha 2015-12-22

Elaboró: Ruth Andrea Rodriguez
Revisó: Dayron Alexander Ramirez Reyes

INFORME DE BÚSQUEDA DE PATENTES PARA EL RADICADO 15-269914-00000-0000						
CRITERIOS PARA LA BÚSQUEDA						
Palabras clave utilizadas		antibacterial				
CLASIFICACIONES INTERNACIONALES UTILIZADAS PARA LA BÚSQUEDA		A61K31/473 C07D495/04				
BASES DE DATOS CONSULTADAS.						
Google patents		Espacenet		Science direct		Patbase
INFORMES DE EXÁMENES REALIZADOS EN OTRAS OFICINAS						
Oficina	Fecha del examen o de reporte de búsqueda de documentos	Anterioridades encontradas para el examen o reportados en el examen de búsqueda(relacionarlos todos)	Reiv. afectadas	RELEVANCIA (requisito que afecta)	FUERON TENIDOS EN CUENTA PARA EL EXAMEN EN LA OFICINA COLOMBIANA	
					SI	NO
EUROPE	07/03/13	US2008312292				X
		US2010069380				X
		US2010261706				X
		US4474786				X
		US2007249583				X
DOCUMENTOS ADICIONALES ENCONTRADOS POR EL EXAMINADOR DE ACUERDO A LOS CRITERIOS DE BÚSQUEDA.						
US 20050009825						
Ramesh, D et al. Synthesis of novel naphtho[2,1-b]furo[3,2-b]pyridine derivatives as potential antimicrobial agents. <i>Indian Journal of Chemistry-Section B</i> Vol.47B(05)						
BÚSQUEDA DE SECUENCIAS						
Número de depósito / patente y N° de secuencia % de identidad						
SEQ ID NO (de la solicitud)	NCBI	The Lens	EMBL-EBI	DDJB	Genome Quest	
N/A						

Ruth Rodriguez

Search history

- Search 1: TAC=(mGluR5 AND pyridine) (Results 119)
- Search 2: TAC=(mGluR5 AND pyridine) and CPC=(C07D213/74) (Results 5)
- Search 3: TAC=(mGluR5 AND pyridine) and CPC=(C07D237/22) (Results 0)
- Search 4: TAC=(mGluR5) and CPC=(C07D213/74) (Results 13)
- Search 5: TAC=(mGluR5) and CPC=(C07D237/22) (Results 1)
- Search 6: TAC=(mGluR5) and CPC=(C07D239/42) (Results 7)
- Search 7: [SP]: 1. a compound of formula i [ftimg=31947663] wherein y is n or ch with the proviso that y can only be ch, if at least one of u, v or w are n u is n or c-r4 v and w are independently n or ch with the proviso that only one of u, v or w can be simultaneously nitrogen r4 is hydrogen, methyl or halogen r1 is phenyl or heteroaryl, which are optionally substituted by halogen, lower alkyl or lower alkoxy r is hydrogen or lower alkyl r2 is hydrogen, lower alkyl, lower alkoxy, cf3 or s-lower alkyl r3/r3' are, independently from each other, hydrogen, lower alkyl or lower alkoxy or r3 and r3' form together a c3-5-cycloalkyl-, tetrahydrofuran- or an oxetane-ring or a pharmaceutically acceptable acid addition salt, a racemic mixture, or its corresponding enantiomer and/or optical isomer and/or stereoisomer thereof. 2. the compound of claim 1 having the formula [ftimg=31947664] wherein y is n u is -ch- or n v and w are independently n or ch with the proviso that only one of u, v or w can be simultaneously nitrogen r1 is phenyl, which is optionally substituted by halogen r is hydrogen or lower alkyl r2 is lower alkyl, lower alkoxy, cf3 or s-lower alkyl r3/r3' are independently from each other hydrogen or lower alkyl or a pharmaceutically acceptable acid addition salt, a racemic mixture, or its corresponding enantiomer and/or optical isomer and/or stereoisomer thereof. 3. a compound of claim 2, selected from the group consisting of 2,2-dimethyl-n-(5-phenylethynyl-pyridin-2-yl)-propionamide, n-(5-phenylethynyl-pyridin-2-yl)-butyramide, pentanoic acid (5-phenylethynyl-pyridin-2-yl)-amide, 3-methyl-n-(5-phenylethynyl-pyridin-2-yl)-butyramide, (rs)-2-methyl-pentanoic acid (5-phenylethynyl-pyridin-2-yl)-amide, 2-methylsulfanyl-n-(5-phenylethynyl-pyridin-2-yl)-acetamide, 2,2-dimethyl-n-(5-phenylethynyl-pyrimidin-2-yl)-propionamide, 2,2,n-trimethyl-n-(5-phenylethynyl-pyrimidin-2-yl)-propionamide, 2,2-dimethyl-n-(6-phenylethynyl-pyridazin-3-yl)-propionamide, 2-methoxy-n-(5-phenylethynyl-pyridin-2-yl)-acetamide, n-[5-(3-fluoro-phenylethynyl)-pyridin-2-yl]-2,2-dimethyl-propionamide, 2-methoxy-2-methyl-n-(5-phenylethynyl-pyridin-2-yl)-propionamide, n-[5-(3-fluoro-phenylethynyl)-pyridin-2-yl]-2-methoxy-2-methyl-propionamide, n-[5-(2,5-difluoro-phenylethynyl)-pyridin-2-yl]-2-methoxy-2-methyl-propionamide, n-[5-(3-chloro-phenylethynyl)-pyridin-2-yl]-3,3,3-trifluoro-2,2-dimethyl-propionamide and n-[6-(3-chloro-phenylethynyl)-pyridazin-3-yl]-2,2-dimethyl-propionamide. 4. the compound of claim 1 having the formula [ftimg=31947665] wherein r1 is phenyl or heteroaryl, which are optionally substituted by halogen, lower alkyl or lower alkoxy r is hydrogen or lower alkyl r2 is hydrogen, lower alkyl, lower alkoxy, cf3 or s-lower alkyl r3/r3' are, independently from each other, hydrogen, lower alkyl or lower alkoxy or r3 and r3' form together a c3-5-cycloalkyl-, tetrahydrofuran- or an oxetane-ring or a pharmaceutically acceptable acid addition salt, a racemic mixture, or its corresponding enantiomer and/or optical isomer and/or stereoisomer thereof. 5. a compound of claim 4 selected from the group consisting of 2,2-dimethyl-n-(5-phenylethynyl-pyridin-2-yl)-propionamide, n-(5-phenylethynyl-pyridin-2-yl)-butyramide, pentanoic acid (5-phenylethynyl-pyridin-2-yl)-amide, 3-methyl-n-(5-phenylethynyl-pyridin-2-yl)-butyramide, (rs)-2-methyl-pentanoic acid (5-phenylethynyl-pyridin-2-yl)-amide, 2-methylsulfanyl-n-(5-phenylethynyl-pyridin-2-yl)-acetamide, 2-methoxy-n-(5-phenylethynyl-pyridin-2-yl)-acetamide, n-[5-(3-fluoro-phenylethynyl)-pyridin-2-yl]-2,2-dimethyl-propionamide, 2-methoxy-2-methyl-n-(5-phenylethynyl-pyridin-2-yl)-propionamide, n-[5-(3-fluoro-phenylethynyl)-pyridin-2-yl]-2-methoxy-2-methyl-propionamide, n-[5-(2,5-difluoro-phenylethynyl)-pyridin-2-yl]-2-methoxy-2-methyl-propionamide, n-[5-(3-chloro-phenylethynyl)-pyridin-2-yl]-3,3,3-trifluoro-2,2-dimethyl-propionamide and n-[5-(3-chloro-phenylethynyl)-pyridazin-3-yl]-2,2-dimethyl-propionamide. 6. the compound of claim 1 having the formula [ftimg=31947666] wherein r1 is phenyl or heteroaryl, which are optionally substituted by halogen, lower alkyl or lower alkoxy r is hydrogen or lower alkyl r2 is hydrogen, lower alkyl, lower alkoxy, cf3 or s-lower alkyl r3/r3' are, independently from each other, hydrogen, lower alkyl or lower alkoxy or r3 and r3' form together a c3-5-cycloalkyl-, tetrahydrofuran- or an oxetane-ring or a pharmaceutically acceptable acid addition salt, a racemic mixture, or its corresponding enantiomer and/or optical isomer and/or stereoisomer thereof. 7. a compound of claim 6 selected from 2,2-dimethyl-n-(5-phenylethynyl-pyrimidin-2-yl)-propionamide or 2,2,n-trimethyl-n-(5-phenylethynyl-pyrimidin-2-yl)-propionamide. 8. the compound of claim 1 having the formula [ftimg=31947667] wherein r1 is phenyl or heteroaryl, which are optionally substituted by halogen, lower alkyl or lower alkoxy r is hydrogen or lower alkyl r2 is hydrogen, lower alkyl, lower alkoxy, cf3 or s-lower alkyl r3/r3' are independently from each other hydrogen, lower alkyl or lower alkoxy or r3 and r3' form together a c3-5-cycloalkyl-, tetrahydrofuran- or an oxetane-ring or a pharmaceutically acceptable acid addition salt, a racemic mixture, or its corresponding enantiomer and/or optical isomer and/or stereoisomer thereof. 9. a compound of claim 8, selected from 2,2-dimethyl-n-(6-phenylethynyl-pyridazin-3-yl)-propionamide or n-[6-(3-chloro-phenylethynyl)-pyridazin-3-yl]-2,2-dimethyl-propionamide. 10. the compound of claim 1 having the formula [ftimg=31947668] wherein r1 is phenyl or heteroaryl, which are optionally substituted by halogen, lower alkyl or lower alkoxy r is hydrogen or lower alkyl r2 is hydrogen, lower alkyl, lower alkoxy, cf3 or s-lower alkyl r3/r3' are independently from each other hydrogen, lower alkyl or lower alkoxy or r3 and r3' form together a c3-5-cycloalkyl-, tetrahydrofuran- or an oxetane-ring or a pharmaceutically acceptable acid addition salt, a racemic mixture, or its corresponding enantiomer and/or optical isomer and/or stereoisomer thereof. 11. the compound of claim 1 having the formula [ftimg=31947669] wherein r1 is phenyl or heteroaryl, which are optionally substituted by halogen, lower alkyl or lower alkoxy r is hydrogen or lower alkyl r2 is hydrogen, lower alkyl, lower alkoxy, cf3 or s-lower alkyl r3/r3' are independently from each other hydrogen, lower alkyl or lower alkoxy or r3 and r3' form together a c3-5-cycloalkyl-, tetrahydrofuran- or an oxetane-ring or a pharmaceutically acceptable acid addition salt, a racemic mixture, or its corresponding enantiomer and/or optical isomer and/or stereoisomer thereof. 12. a process for preparation of a compound of claim 1 comprising a) reacting a compound of formula [ftimg=31947670] with a suitable compound of formula [ftimg=31947671] to a compound of formula [ftimg=31947672] wherein the substituents are defined in claim 1, or if desired, converting the compounds obtained into pharmaceutically acceptable acid addition salts, or b) reacting a compound of formula [ftimg=31947673] with a suitable compound of formula [ftimg=31947674] to a compound of formula [ftimg=31947675] wherein the substituents are defined in claim 1, or if desired, converting the compounds obtained into pharmaceutically acceptable acid addition salts, or c) reacting a compound of formula [ftimg=31947676] with a suitable compound of formula [ftimg=31947677] to a compound of formula [ftimg=31947678] wherein the substituents are defined in claim 1, or d) reacting a compound of formula [ftimg=31947679] with a suitable compound of formula r-hal to a compound of formula [ftimg=31947680] wherein r is alkyl and hal is halogen and wherein the other substituents are defined in claim 1, or if desired, converting the compounds obtained into pharmaceutically acceptable acid addition salts. 13. a pharmaceutical composition comprising a compound of claim 1 together with at least one therapeutically inert carrier. (Results 99)
- Search 8: (7) AND PD=(2005 OR 2007 OR 2003 OR 2006 OR 2004 OR 2008 OR 2011 OR 2002 OR 2009 OR 2000 OR 2001 OR 2010) (Results 83)
- Search 9: (8) AND IPC=(C07) (Results 83)
- Search 10: fn=(42647780 or 42647780 or 32886770 or 32849686 or 32886770 or 33397783 or 32090793 or 42647780 or 44320998) (Results 6)
- Search 11: TAC=(c-kit OR PDGFR) and CPC=(C07D498/04) (Results 8)
- Search 12: TAC=(c-kit OR PDGFR) and CPC=(C07D471/04 or C07D491/044 or C07D491/048 or C07D491/107 or C07D498/04) (Results 134)
- Search 13: (12) AND PD=(2007 OR 2006 OR 2005 OR 2008 OR 2009 OR 2011 OR 2010 OR 2012 OR 2003 OR 2004 OR 2002) (Results 112)
- Search 14: PN=(wo2013033167) (Results 1)
- Search 15: fn=(53180003 or 53179963 or 34298802 or 52846395 or 53180003 or 53179963 or 53179963 or 30222475 or 43941857 or 32711703 or 30737034 or 41802181 or 53182986 or 53183176) (Results 11)
- Search 16: PN=(WO2013033167) (Results 1)
- Search 17: fn=(53180003 or 53179963 or 34298802 or 52846395 or 53180003 or 53179963 or 53179963 or 30222475 or 43941857 or 32711703 or 30737034 or 41802181 or 53182986 or 53183176) (Results 11)
- Search 18: [SP]: 1. a method for treating a disease or disorder where modulation of a kinase is implicated, wherein the method comprises administering to a system or subject in need of such treatment an effective amount of a compound of formula (i) or formula (ii), or pharmaceutically acceptable salt thereof, [ftimg=68000466] wherein: m is 1 and r20 is selected from h, halo, c1-c6alkyl, c1-c6haloalkyl, c1-c6haloalkoxy, deuterium, deuterated c1-c6alkyl, -cn, -(cr92)nor4, -c(o)r4, -(cr92)nc -o(o)r4, r10, -(cr92)nr10, -((cr92)no)tr4, -(cr92)no(cr92)nr7, -(cr92)nc(o)r4, -c(o)n(r4)2, -or4, and -(cr92)ncn or m is 4 and r20 is deuterium r1 is selected from c1-c6alkyl and halo each r11 is independently selected from h, halo and c1-c6alkyl i1 is a bond, -nh- or -c(o)nh- i2 is -(cr92)n-, -chr6-, -(cr92)no-, -nh-, -(cr92)nc -o-, -c(o)o(cr92)n-, -(cr92)noc(o)nr4-, -(cr92)nnr4c(o)(cr92)n-, -(cr92)nnr4c(o)-, or -(cr92)nnr4c(o)-o- r2 is r3 or i2r3 r3 is selected from an unsubstituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a piperidinone, a oxazolidin-2-one, pyrrolidinone, a pyrrolidin-2-one and a substituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, wherein the substituted 4-6 membered heterocycloalkyl of r3 is substituted with 1-4 substituents independently selected from c1-c6alkyl halo, -cn, c1-c6haloalkyl, -or4, -c(o)or4, -c(o)r4, -c(o)r7, -c(o)or5, -(cr92)nor4, -o(cr92)nor4, -c(o)o(cr92)nor4, -n(r4)2, -c(o)nr42, -nr4c(o)or4, -nr4c(o)(cr92)nor4, -nr4(cr92)nor4, -nr4s(-o)2r4, -n(c(o)or4)2, r8, -(cr92)nr8,

deuterated c1-c6alkoxy, -s(-o)2r4, -s(-o)2r7, -s(-o)2r8, -s(-o)2n(r4)2, -s(-o)2nhc(-o)or4, -s(-o)2(cr92)nc(-o)or4, s(-o)2(cr92)nor4, a spiro attached dioxolane, a spiro attached dioxolane which is substituted with c1-c6alkyl, a spiro attached dioxane, a spiro attached tetrahydrofuranly, a spiro attached oxetane, a spiro attached cyclobutanone, a spiro attached cyclobutanol, a c1 alkyl bridge, an unsubstituted 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s and a 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s substituted with 1-3 substituents independently selected from c1-c6alkyl, halo, c1-c6haloalkyl, c1-c6haloalkoxy, -or4 and r8 each r4 is independently selected from h and c1-c6alkyl r5 is an unsubstituted c3-c8cycloalkyl, an unsubstituted 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n or o or a c3-c8cycloalkyl substituted with 1-3 substituents independently selected from c1-c6alkyl each r6 is independently selected from -nr4c(o)or4, -or4 and -(cr92)nor4 each r7 is independently selected from c1-c6haloalkyl r8 is selected from an unsubstituted phenyl, unsubstituted 5-6 membered heteroaryl with 1-3 heteroatoms independently selected from n, o and s, an unsubstituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, an unsubstituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, an unsubstituted c3-c8cycloalkyl, a substituted 5-6 membered heteroaryl with 1-3 heteroatoms independently selected from n, o and s, a substituted phenyl, a substituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, a substituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a substituted phenyl, a tetrahydro-1h-oxazolo [3,4-a]pyrazin-3(5h)-one, an oxazolidin-2-one, pyrrolidinone and a pyrrolidin-2-one, wherein the substituted phenyl, the substituted 5-6 membered heteroaryl with 1-2 heteroatoms independently selected from n, o and s, the substituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, substituted c3-c8cycloalkyl and substituted 4-6 membered heterocycloalkyl of r8 are substituted with 1-3 substituents independently selected from c1-c6alkyl, -(cr92)2nor4, -(cr92)2nr5, -(c(r92)2)nc(o)or4, -c(o)or4 and -s(o)2r4 each r9 is independently selected from h and c1-c6alkyl r10 is selected from an unsubstituted phenyl, unsubstituted 5-6 membered heteroaryl with 1-2 heteroatoms independently selected from n, o and s, an unsubstituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, an unsubstituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, an unsubstituted c3-c8cycloalkyl, a substituted 5-6 membered heteroaryl with 1-2 heteroatoms independently selected from n, o and s, a substituted phenyl, a substituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, a substituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a substituted c3-c8cycloalkyl, an oxazolidin-2-one, pyrrolidinone and a pyrrolidin-2-one, wherein the substituted phenyl, the substituted 5-6 membered heteroaryl with 1-2 heteroatoms independently selected from n, o and s, the substituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, substituted c3-c8cycloalkyl and substituted 4-6 membered heterocycloalkyl of r8 are substituted with 1-3 substituents independently selected from c1-c6alkyl [me], -(cr92)2nor4, -(cr92)2nr5, -(c(r92)2)nc(o)or4 and -s(o)2r4 t is 1, 2 or 3, and each n is independently selected from 1, 2, 3 and 4 wherein the kinase is selected from c-kit, pdgfra and pdgfr beta, and wherein the disease is selected from asthma, allergic rhinitis, allergic sinusitis and crohn's disease. 2. the method of claim 1, wherein the compound is a compound of formula (ia), formula (iia), formula (ib) or formula (iib): [ftimg=68000467] wherein: m is 1 and r20 is selected from h, halo, c1-c6alkyl, c1-c6haloalkyl, c1-c6haloalkoxy, deuterium, deuterated c1-c6alkyl, -cn, -(cr92)nr4, -c(o)r4, -(cr92)nc(-o)or4, r10, -(cr92)nr10, -(cr92)no)tr4, -(cr92)no (cr92)nr7, -(cr92)nc(-o)r4, -c(-o)n(r4)2, -or4, and -(cr92)ncn or m is 4 and r20 is deuterium r1 is selected from c1-c6alkyl and halo each r11 is independently selected from h, halo and c1-c6alkyl l2 is -(cr92)n-, -chr6-, -(cr92)no-, -nh-, -(cr92)nc(-o)-, -c(-o)o(cr92)n-, -(cr92)noc(-o)nr4-, -(cr92)nnr4c(-o)(cr92)n-, -(cr92)nnr4c(-o)-, or -(cr92)nnr4c(-o)-o- r2 is r3 or l2r3 r3 is selected from an unsubstituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a piperidinone, an oxazolidin-2-one, pyrrolidinone, a pyrrolidin-2-one and a substituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, wherein the substituted 4-6 membered heterocycloalkyl of r3 is substituted with 1-4 substituents independently selected from c1-c6alkyl halo, -cn, c1-c6haloalkyl, -or4, -c(-o)or4, -c(-o)r4, -c(-o)r7, -c(-o)r5, -(cr92)nor4, -o(cr92)nor4, -c(-o)o(cr92)nor4, -n(r4)2, -c(-o)nr42, -nr4c(-o)or4, -nr4c(-o)(cr92)nor4, -nr4c(cr92)nor4, -nr4s(-o)2r4, -n(c(-o)or4)2, r8, -(cr92)nr8, deuterated c1-c6alkoxy, -s(-o)2r4, -s(-o)2r7, -s(-o)2r8, -s(-o)2n(r4)2, -s(-o)2nhc(-o)or4, -s(-o)2(cr92)nc(-o)or4, s(-o)2(cr92)nor4, a spiro attached dioxolane, a spiro attached dioxolane which is substituted with c1-c6alkyl, a spiro attached dioxane, a spiro attached tetrahydrofuranly, a spiro attached oxetane, a spiro attached cyclobutanone, a spiro attached cyclobutanol, a c1 alkyl bridge, an unsubstituted 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s and a 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s substituted with 1-3 substituents independently selected from c1-c6alkyl, halo, c1-c6haloalkyl, c1-c6haloalkoxy, -or4 and r8 each r4 is independently selected from h and c1-c6alkyl r5 is an unsubstituted c3-c8cycloalkyl, an unsubstituted 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n or o or a c3-c8cycloalkyl substituted with 1-3 substituents independently selected from c1-c6alkyl r6 is independently selected from -nr4c(o)or4, -or4 and -(cr92)nor4 each r7 is independently selected from c1-c6haloalkyl r8 is selected from an unsubstituted phenyl, unsubstituted 5-6 membered heteroaryl with 1-3 heteroatoms independently selected from n, o and s, an unsubstituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, an unsubstituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a substituted phenyl, a substituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, a substituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a substituted c3-c8cycloalkyl, a tetrahydro-1h-oxazolo[3,4-a]pyrazin-3(5h)-one, an oxazolidin-2-one, pyrrolidinone and a pyrrolidin-2-one, wherein the substituted phenyl, the substituted 5-6 membered heteroaryl with 1-2 heteroatoms independently selected from n, o and s, the substituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, substituted c3-c8cycloalkyl and substituted 4-6 membered heterocycloalkyl of r8 are substituted with 1-3 substituents independently selected from c1-c6alkyl, -(cr92)2nor4, -(cr92)2nr5, -(c(r92)2)nc(o)or4, -c(o)or4 and -s(o)2r4 each r9 is independently selected from h and c1-c6alkyl r10 is selected from an unsubstituted phenyl, unsubstituted 5-6 membered heteroaryl with 1-2 heteroatoms independently selected from n, o and s, an unsubstituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, an unsubstituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, an unsubstituted c3-c8cycloalkyl, a substituted 5-6 membered heteroaryl with 1-4 heteroatoms selected from n, a substituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a substituted phenyl, a substituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, a substituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, the substituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, substituted c3-c8cycloalkyl, an oxazolidin-2-one, pyrrolidinone and a pyrrolidin-2-one, wherein the substituted phenyl, the substituted 5-6 membered heteroaryl with 1-2 heteroatoms independently selected from n, o and s, the substituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, substituted c3-c8cycloalkyl and substituted 4-6 membered heterocycloalkyl of r8 are substituted with 1-3 substituents independently selected from c1-c6alkyl, -(cr92)2nor4, -(cr92)2nr5, -(c(r92)2)nc(o)or4, -c(o)or4 and -s(o)2r4 t is 1, 2 or 3, and each n is independently selected from 1, 2, 3 and 4. 3. the method of claim 1, wherein r1 is selected from -ch3 and f. 4. the method of claim 3, wherein r1 is -ch3. 5. the method of claim 1, wherein each r11 is independently selected from h, f and -ch3. 6. the method of claim 5, wherein each r11 is h. 7. the method of claim 1, wherein r3 is selected from an unsubstituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n and o, a piperidinone, an oxazolidin-2-one, pyrrolidinone, a pyrrolidin-2-one and a substituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n and o, wherein the substituted 4-6 membered heterocycloalkyl of r3 is substituted with 1-4 substituents independently selected from c1-c6alkyl, halo, -cn, c1-c6haloalkyl, -or4, -c(-o)or4, -c(-o)r4, -c(-o)r7, -c(-o)r5, -(cr92)nor4, -c(-o)o(cr92)nor4, -c(-o)nr42, -nr4c(-o)or4, -nr4c(-o)(cr92)nor4, -r8, -(cr92)nr8, -s(-o)2r4, -s(-o)2r7, -s(-o)2r8, -s(-o)2n(r4)2, -s(-o)2nhc(-o)or4, -s(-o)2(cr92)nor4, -s(-o)2(cr92)nc(-o)or4 and a c1 alkyl bridge. 8. the method of claim 7, wherein each r4 is independently selected from h, methyl, ethyl, propyl, butyl, i-propyl and t-butyl. 9. the method of claim 7, wherein each r5 is cyclopropyl, cyclopropyl substituted with a methyl or morpholinyl. 10. the method of claim 7, wherein each r7 is independently selected from ch2f, -chf2, -ch2chf2, -ch2cf3 and -cf3. 11. the method of claim 7, wherein each r9 is independently selected from h, methyl and ethyl. 12. the method of claim 7, wherein r8 is selected from an unsubstituted phenyl, unsubstituted 5-6 membered heteroaryl with 1-3 heteroatoms independently selected from n and o, an unsubstituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, an unsubstituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n and o, a substituted 5-6 membered heteroaryl with 1-3 heteroatoms independently selected from n and o, a substituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, a substituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n and o, and a tetrahydro-1h-oxazolo[3,4-a]pyrazin-3(5h)-one, wherein the substituted 5-6 membered heteroaryl with 1-3 heteroatoms independently selected from n and o, the substituted 5 membered heteroaryl with 1-4 heteroatoms selected from n and substituted 4-6 membered heterocycloalkyl of r8 are substituted with 1-3 substituents independently selected from c1-c6alkyl and -c(-o)or4. 13. the method of claim 12, wherein r8 is selected from pyridinyl, pyrazolyl tetrahydrofuranly, tetrahydropranyl, pyrrolidinyl, piperidinyl, pyrimidinyl and oxadiazolyl, each of which is unsubstituted or substituted with 1-2 substituents independently selected from ch3 and c(-o)oc(ch3)3. 14. the method of claim 7, wherein r3 is selected from azetidinyl, azetidin-1-yl, azetidin-2-yl, azetidin-3-yl, pyrrolidinyl, pyrrolidin-1-yl, pyrrolidin-2-yl, pyrrolidin-3-yl, piperidinyl, piperidin-1-yl, piperidin-2-yl, piperidin-3-yl, piperidin-4-yl, tetrahydropranyl, tetrahydropryan-2-yl, tetrahydropryan-3-yl, tetrahydropryan-4-yl, tetrahydrofuran-2-yl, tetrahydrofuran-3-yl, oxetanyl, oxetan-2-yl, oxetan-3-yl, morpholinyl, morpholin-2-yl, morpholin-3-yl and morpholin-4-yl, each of which is unsubstituted or each of which is substituted with 1-4 substituents independently selected from -ch3, -ch2ch3, f, -cf3, -cn, -oh, -c(-o)cf3, -och3, -c(-o)och3, -c(-o)ch3, -c(-o)och2ch2och3, -c(-o)och2ch3, -c(-o)oc(ch3)3, -ch2oh, -ch2och3, -ch2ch2ch2och3, -nhc(-o)oc(ch3)3, -nhc(-o)och3, -c(-o)n(ch3)2, -s(-o)2ch3, -s(-o)2ch2ch3, -s(-o)2ch2ch2ch3, -s(-o)2ch2ch2ch2ch3, -s(-o)2ch(ch3)2, -s(-o)2ch2ch2c(-o)och3, -s(-o)2ch2ch2och3, -s(-o)2ch2f, -s(-o)2nh2, -s(-o)2nhc(-o)oc(ch3)3, a c1alkyl bridge, -c(-o)or5, -s(-o)2r8, -(cr92)nr8 and r8. 15. the method of claim 14, wherein: r3 is azetidinyl substituted with -c(-o)och3. 16. the method of claim 14, wherein m is 1 and r20 is selected from h, halo, c1-c6alkyl, c1-c6haloalkyl, deuterium, deuterated c1-c6alkyl, -cn, -(cr92)nor4, -c(o)r4, -(cr92)nc(-o)or4, r10, -(cr92)nr10, -(cr92)no(cr92)nr7, -(cr92)nc(-o)r4, -or4, and -(cr92)ncn. 17. the method of claim 16, wherein m is 1 r20 is selected from h, -d-, f-, ch3, -cf3, -cn, -ch2ch2ch2cn, -ch2ch2cn, -och3, -ch2ch2c(-o)oc(ch3)3, -c(-o)ch3, -ch2ch2c(-o)ch3, -cd3, -ch2oh, -ch2ch2c(ch3)2oh, -ch2c(ch3)2oh, -c(ch3)2oh, -ch2och3, -ch2och2cf3, -ch2och2chf2, and -ch2och2ch2f. 18. the method of claim 17, wherein m is 1 and r20 is -ch3. 19. the method of claim 17, wherein m is 1 and r20 is h. 20. the method of claim 16, wherein: r10 is selected from morpholinyl, piperidinyl, piperidin-1-yl, piperidin-2-yl, piperidin-3-yl, piperidin-4-yl, piperazinyl, piperazin-1-yl, pyrazolyl, pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, triazolyl, 1h-1,2,3-triazol-1-yl, 4h-1,2,4-triazol-3-yl, 1h-1,2,4-triazol-5-yl, thiazolyl, thiazol-4-yl, thiazol-5-yl, imidazolyl, imidazol-1-yl, imidazol-2-yl, each of which is unsubstituted or each of which is substituted with 1-3 substituents independently selected from c1-c6alkyl, -(cr92)nor4, -(cr92)2nc(o)or4, -(cr92)2nr5 and -s(-o)2r4, or r10 is selected from an oxazolidin-2-one and a pyrrolidin-2-one. 21. the method of claim 20, wherein: r10 is selected from morpholinyl, piperidinyl, piperidin-1-yl, piperidin-2-yl, piperidin-3-yl, piperidin-4-yl, piperazinyl, piperazin-1-yl, pyrazolyl, pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, triazolyl, 1h-1,2,3-triazol-4-yl, 4h-1,2,4-triazol-3-yl, 1h-1,2,4-triazol-5-yl, thiazolyl, thiazol-4-yl, thiazol-5-yl, imidazolyl, imidazol-1-yl, imidazol-2-yl, each of which is unsubstituted or each of which is substituted with 1-3 substituents independently selected from -ch3, -ch2ch2oh, -ch2c(o)oh, -ch2ch2oh, -ch2c(ch3)2oh, -s(o)2ch3 and -ch2ch2-r5. 22. the method of claim 15, wherein m is 4 and r20 is deuterium. 23. the method of claim 1, wherein the compound is selected from: n-{5-[3-(azetidin-1-yl)-1,2,4-oxadiazol-5-yl]-2-methylphenyl}imidazol[1,2-a]pyridine-3-carboxamide n-{5-[3-(3,3-difluoroazetidin-1-yl)-1,2,4-oxadiazol-5-yl]-2-methylphenyl}imidazol[1,2-a]pyridine-3-carboxamide n-(2-methyl-5-{3-[(1s,4s)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl]-1,2,4-oxadiazol-5-yl}phenyl)imidazo[1,2-a]pyridine-3-carboxamide n-{5-[3-(4,4-difluoropiperidin-1-yl)-1,2,4-oxadiazol-5-yl]-2-methylphenyl}imidazo[1,2-a]pyridine-3-carboxamide n-{5-[3-(4-fluoropiperidin-1-yl)-1,2,4-oxadiazol-5-yl]-2-methylphenyl}imidazo[1,2-a]pyridine-3-carboxamide n-{5-[5-(3-hydroxy-3-(trifluoromethyl)azetidin-1-yl)-1,2,4-oxadiazol-3-yl]-2-methylphenyl}-6-methylimidazo[1,2-a]pyridine-3-carboxamide n-{2-methyl-5-{5-(oxolan-3-yl)-1,2,4-oxadiazol-3-yl}phenyl}imidazo[1,2-a]pyridine-3-carboxamide n-{2-methyl-5-[5-(oxan-2-yl)-1,2,4-oxadiazol-3-yl}phenyl}imidazo[1,2-a]pyridine-3-carboxamide methyl 2-[3-{3-{imidazo[1,2-a]pyridine-3-amido}-4-methylphenyl}-1,2,4-oxadiazol-5-yl]piperidine-1-carboxylate n-{5-[5-(5-difluoroaxan-2-yl)-1,2,4-oxadiazol-3-yl]-2-methylphenyl}imidazo[1,2-a]pyridine-3-carboxamide n-{5-[5-[(2s)-5,5-difluoroaxan-2-yl]-1,2,4-oxadiazol-3-yl]-2-methylphenyl}imidazo[1,2-a]pyridine-3-carboxamide n-{5-[5-[(2r)-5,5-difluoroaxan-2-yl]-1,2,4-oxadiazol-3-yl]-2-methylphenyl}imidazo[1,2-a]pyridine-3-amido)-4-methylphenyl]-1,2,4-oxadiazol-3-yl]-2-methylphenyl}imidazo[1,2-a]pyridine-3-carboxamide tert-butyl 3-[3-{3-{imidazo[1,2-a]pyridine-3-amido)-4-methylphenyl]-1,2,4-oxadiazol-3-yl}azetidine-1-carboxylate n-{5-[5-(1-methanesulfonylazetidin-3-yl)-1,2,4-oxadiazol-3-yl]-2-methylphenyl}imidazo[1,2-a]pyridine-3-carboxamide methyl 3-[3-{3-{imidazo[1,2-a]pyridine-3-amido)-4-methylphenyl]-1,2,4-oxadiazol-3-yl}azetidine-1-carboxylate n-(2-methyl-5-{5-[1-(propane-1-sulfonyl)azetidin-3-yl]-1,2,4-oxadiazol-3-yl}phenyl)imidazo[1,2-a]pyridine-3-carboxamide n-{2-methyl-5-[5-(ethanesulfonyl)azetidin-3-yl]-1,2,4-oxadiazol-3-yl}phenyl}imidazo[1,2-a]pyridine-3-carboxamide n-{2-methyl-5-[5-(3-(3-difluoroazetidin-1-yl)methyl]-1,2,4-oxadiazol-3-yl)-2-methylphenyl}imidazo[1,2-a]pyridine-3-carboxamide n-{2-methyl-5-[5-(morpholin-4-ylmethyl)-1,2,4-oxadiazol-3-yl]phenyl}imidazo[1,2-a]pyridine-3-carboxamide n-(2-methyl-5-[5-(1-sulfamoylazetidin-3-yl)-1,2,4-oxadiazol-3-yl]phenyl)imidazo[1,2-a]pyridine-3-carboxamide tert-butyl (2s)-2-[3-{3-{imidazo[1,2-a]pyridine-3-amido)-4-methylphenyl]-1,2,4-oxadiazol-5-yl}azetidine-1-carboxylate n-{5-[5-(2s)-1-methanesulfonylazetidin-2-yl]-1,2,4-oxadiazol-3-yl]-2-methylphenyl}imidazo[1,2-a]pyridine-3-carboxamide methyl n-{3-[3-{3-{imidazo[1,2-a]pyridine-3-amido)-4-methylphenyl]-1,2,4-oxadiazol-5-yl}oxetan-3-yl]carbamate tert-butyl 3-[3-(4-fluoro-3-{imidazo[1,2-a]pyridine-3-amido)phenyl]-1,2,4-oxadiazol-5-yl]azetidine-1-carboxylate n-{5-[5-(1-(ethanesulfonyl)azetidin-3-yl)-1,2,4-oxadiazol-3-yl]-2-fluorophenyl}imidazo[1,2-a]pyridine-3-carboxamide n-{5-[5-{3-(3,3-difluoropyrrolidin-1-yl)methyl}-1,2,4-oxadiazol-3-yl]-2-methylphenyl}imidazo[1,2-a]pyridine-3-carboxamide n-{5-[5-{4,4-difluoropiperidin-1-yl}methyl]-1,2,4-oxadiazol-3-yl]-2-methylphenyl}imidazo[1,2-a]pyridine-3-carboxamide n-{5-[5-{1-(butane-1-sulfonyl)azetidin-3-yl]-1,2,4-oxadiazol-3-yl]-2-methylphenyl}imidazo[1,2-a]pyridine-3-carboxamide methyl 4-[3-{3-{imidazo[1,2-a]pyridine-3-amido)-4-methylphenyl]-1,2,4-oxadiazol-5-yl]piperidine-1-carboxylate n-{5-[5-(1-methanesulfonylpiperidin-4-yl)-1,2,4-oxadiazol-3-yl]-2-methylphenyl}imidazo[1,2-a]pyridine-3-carboxamide n-{5-[5-(4-methanesulfonylmorpholin-2-yl)-1,2,4-oxadiazol-3-yl]-2-methylphenyl}imidazo[1,2-a]pyridine-3-carboxamide n-{5-[5-(2s)-1-methanesulfonylpyrrolidin-2-yl]-1,2,4-oxadiazol-3-yl]-2-methylphenyl}imidazo[1,2-a]pyridine-3-carboxamide n-{5-[5-[(2r)-4-methanesulfonylmorpholin-2-yl]-1,2,4-oxadiazol-3-yl]-2-

21: [SP] 1. a method for treating a disease or disorder where modulation of a kinase is implicated, wherein the method comprises administering to a system or subject in need of such treatment an effective amount of a compound of formula (i) or formula (ii), or pharmaceutically acceptable salt thereof, [ftimg=68000467] wherein: m is 1 and r20 is selected from h, halo, c1-c6alkyl, c1-c6haloalkoxy, deuterium, deuterated c1-c6alkyl, -cn, -(cr92)nr4, -(c-o)r4, -(cr92)nc -(o)r4, r10, -(cr92)nr10, -(cr92)no)r4, -(cr92)no(c)r92nr7, -(cr92)nc-(o)r4, -(c-o)(r4)2, -or4, and -(cr92)ncn or m is 4 and r20 is deuterium r1 is selected from c1-c6alkyl and halo each r11 is independently selected from h, halo and c1-c6alkyl 11 is a bond, -nh-, or -(c-o)nh- 12 is -(cr92)n-, -chr6-, -(cr92)no-, -nh-, -(cr92)nc -(o)-, -(c-o)(c92)nr-, -(cr92)nc(c-o)nr4-, -(cr92)nnr4c-(o)(cr92)nr-, -(cr92)nnr4c-(o)-, r3 or 12r3 r3 is selected from an unsubstituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a piperidinone, an oxazolidin-2-one, pyrrolidinone, a pyrrolidin-2-one and a substituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, wherein the substituted 4-6 membered heterocycloalkyl of r3 is substituted with 1-4 substituents independently selected from c1-c6alkyl halo, -cn, c1-c6haloalkyl, -or4, -(c-o)r4, -(c-o)r4, -(c-o)r7, -(c-o) or5, -(cr92)nr4, -(c92)nr4, -(c-o)(c92)nr4, -(n)r4)2, -(c-o)r4r2, -nr4c-(o)r4, -nr4c-(o)(cr92)nr4, -nr4(c92)nr4, -nr4s-(o)2r4, -n-(c-o)r4r2, r8, -(cr92)nr8, deuterated c1-c6alkoxy, -(s-o)2r4, -(s-o)2r7, -(s-o)2r8, -(s-o)2n(r4)2, -(s-o)2nhc-(o)r4, -(s-o)2(c92)nc-(o)r4, -(s-o)2(c92)nc-(o)r4, a spiro attached dioxolane, a spiro attached dioxolane which is substituted with c1-c6alkyl, a spiro attached dioxane, a spiro attached tetrahydrofuran, a spiro attached oxetane, a spiro attached cyclobutanone, a spiro attached cyclobutanol, a c1 alkyl bridge, an unsubstituted 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s and a 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s substituted with 1-3 substituents independently selected from c1-c6alkyl, halo, c1-c6haloalkyl, c1-c6haloalkoxy, -or4 and r8 each r4 is independently selected from h and c1-c6alkyl r5 is an unsubstituted c3-c8cycloalkyl, an unsubstituted 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n or o or a c3-c8cycloalkyl substituted with 1-3 substituents independently selected from c1-c6alkyl each r6 is independently selected from -nr4c(o)r4, -or4 and -(cr92)nr4 each r7 is independently selected from c1-c6haloalkyl r8 is selected from an unsubstituted phenyl, unsubstituted 5-6 membered heterocycloalkyl with 1-3 heteroatoms independently selected from n, o and s, an unsubstituted 5 membered heterocycloalkyl with 1-4 heteroatoms selected from n, an unsubstituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a substituted phenyl, a substituted 5 membered heterocycloalkyl with 1-4 heteroatoms selected from n, o and s, a substituted phenyl, a substituted 5 membered heterocycloalkyl with 1-4 heteroatoms selected from n, o and s, a substituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a substituted c3-c8cycloalkyl, a tetrahydro-1h-oxazolo [3,4-a]pyrazin-3(5h)-one, an oxazolidin-2-one, pyrrolidinone and a pyrrolidin-2-one, wherein the substituted phenyl, the substituted 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, the substituted 5 membered heterocycloalkyl with 1-4 heteroatoms selected from n, substituted c3-c8cycloalkyl and substituted 4-6 membered heterocycloalkyl of r8 are substituted with 1-3 substituents independently selected from c1-c6alkyl, -(cr92)nr4, -(c92)nr5, -(c92)nc(o)r4, -(c-o)r4 and -(s-o)2r4 each r9 is independently selected from h and c1-c6alkyl r10 is selected from an unsubstituted phenyl, unsubstituted 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, an unsubstituted 5 membered heterocycloalkyl with 1-4 heteroatoms selected from n, an unsubstituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, an unsubstituted c3-c8cycloalkyl, a substituted 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a substituted phenyl, a substituted 5 membered heterocycloalkyl with 1-4 heteroatoms selected from n, a substituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a substituted c3-c8cycloalkyl, an oxazolidin-2-one, pyrrolidinone and a pyrrolidin-2-one, wherein the substituted phenyl, the substituted 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, the substituted 5 membered heterocycloalkyl with 1-4 heteroatoms selected from n, substituted c3-c8cycloalkyl and substituted 4-6 membered heterocycloalkyl of r8 are substituted with 1-3 substituents independently selected from c1-c6alkyl [me], -(cr92)nr4, -(c92)nr5, -(c92)2nc(o)r4 and -(s-o)2r4 t is 1, 2 or 3, and each n is independently selected from 1, 2, 3 and 4 wherein the kinase is selected from c-kit, pdgfra and pdgfr beta, and wherein the disease is selected from asthma, allergic rhinitis, allergic sinusitis and crohn's disease. 2. the method of claim 1, wherein the compound is a compound of formula (ia), formula (iia), formula (ib) or formula (iib): [ftimg=68000467] wherein: m is 1 and r20 is selected from h, halo, c1-c6alkyl, c1-c6haloalkoxy, c1-c6haloalkoxy, deuterium, deuterated c1-c6alkyl, -cn, -(cr92)nr4, -(c-o)r4, -(cr92)nc-(o)r4, r10, -(cr92)nr10, -((cr92)no)r4, -(cr92)no (cr92)nr7, -(cr92)nc-(o)r4, -(c-o)(r4)2, -or4, and -(cr92)ncn or m is 4 and r20 is deuterium r1 is selected from c1-c6alkyl and halo each r11 is independently selected from h, halo and c1-c6alkyl 12 is -(cr92)n-, -chr6-, -(cr92)no-, -nh-, -(cr92)nc-(o)-, -(c-o)(c92)nr-, -(cr92)no(c-o)nr4-, -(cr92)nnr4c-(o)(cr92)nr-, -(cr92)nnr4c-(o)-, or -(cr92)nnr4c-(o)- r2 is r3 or 12r3 r3 is selected from an unsubstituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a piperidinone, an oxazolidin-2-one, pyrrolidinone, a pyrrolidin-2-one and a substituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, wherein the substituted 4-6 membered heterocycloalkyl of r3 is substituted with 1-4 substituents independently selected from c1-c6alkyl halo, -cn, c1-c6haloalkoxy, -or4, -(c-o)r4, -(c-o)r4, -(c-o)r7, -(c-o) or5, -(cr92)nr4, -(c92)nr4, -(c-o)(c92)nr4, -(c-o)(c92)nr4, -(c-o)(c92)nr4, -(n)r4)2, -(c-o)r4r2, r8, -(cr92)nr8, deuterated c1-c6alkoxy, -(s-o)2r4, -(s-o)2r7, -(s-o)2r8, -(s-o)2n(r4)2, -(s-o)2nhc-(o)r4, -(s-o)2(c92)nc-(o)r4, -(s-o)2(c92)nr4, a spiro attached dioxolane, a spiro attached dioxane, a spiro attached tetrahydrofuran, a spiro attached oxetane, a spiro attached cyclobutanone, a spiro attached cyclobutanol, a c1 alkyl bridge, an unsubstituted 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s and a 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s substituted with 1-3 substituents independently selected from c1-c6alkyl, halo, c1-c6haloalkyl, c1-c6haloalkoxy, -or4 and r8 each r4 is independently selected from h and c1-c6alkyl r5 is an unsubstituted c3-c8cycloalkyl, an unsubstituted 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n or o or a c3-c8cycloalkyl substituted with 1-3 substituents independently selected from c1-c6alkyl each r6 is independently selected from -nr4c(o)r4, -or4 and -(cr92)nr4 each r7 is independently selected from c1-c6haloalkyl r8 is selected from an unsubstituted phenyl, unsubstituted 5-6 membered heterocycloalkyl with 1-3 heteroatoms independently selected from n, o and s, an unsubstituted 5 membered heterocycloalkyl with 1-4 heteroatoms selected from n, an unsubstituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a substituted phenyl, a substituted 5 membered heterocycloalkyl with 1-4 heteroatoms selected from n, o and s, a substituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a substituted c3-c8cycloalkyl, a tetrahydro-1h-oxazolo [3,4-a]pyrazin-3(5h)-one, an oxazolidin-2-one, pyrrolidinone and a pyrrolidin-2-one, wherein the substituted phenyl, the substituted 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, the substituted 5 membered heterocycloalkyl with 1-4 heteroatoms selected from n, substituted c3-c8cycloalkyl and substituted 4-6 membered heterocycloalkyl of r8 are substituted with 1-3 substituents independently selected from c1-c6alkyl [me], -(cr92)nr4, -(c92)nr5, -(c92)2nc(o)r4 and -(s-o)2r4 t is 1, 2 or 3, and each n is independently selected from 1, 2, 3 and 4 wherein the kinase is selected from c-kit, pdgfra and pdgfr beta, and wherein the disease is selected from asthma, allergic rhinitis, allergic sinusitis and crohn's disease. 2. the method of claim 1, wherein the compound is a compound of formula (ia), formula (iia), formula (ib) or formula (iib): [ftimg=68000467] wherein: m is 1 and r20 is selected from h, halo, c1-c6alkyl, c1-c6haloalkoxy, c1-c6haloalkoxy, deuterium, deuterated c1-c6alkyl, -cn, -(cr92)nr4, -(c-o)r4, -(cr92)nc-(o)r4, r10, -(cr92)nr10, -((cr92)no)r4, -(cr92)no (cr92)nr7, -(cr92)nc-(o)r4, -(c-o)(r4)2, -or4, and -(cr92)ncn or m is 4 and r20 is deuterium r1 is selected from c1-c6alkyl and halo each r11 is independently selected from h, halo and c1-c6alkyl 12 is -(cr92)n-, -chr6-, -(cr92)no-, -nh-, -(cr92)nc-(o)-, -(c-o)(c92)nr-, -(cr92)no(c-o)nr4-, -(cr92)nnr4c-(o)(cr92)nr-, -(cr92)nnr4c-(o)-, or -(cr92)nnr4c-(o)- r2 is r3 or 12r3 r3 is selected from an unsubstituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a piperidinone, an oxazolidin-2-one, pyrrolidinone, a pyrrolidin-2-one and a substituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, wherein the substituted 4-6 membered heterocycloalkyl of r3 is substituted with 1-4 substituents independently selected from c1-c6alkyl halo, -cn, c1-c6haloalkoxy, -or4, -(c-o)r4, -(c-o)r4, -(c-o)r7, -(c-o) or5, -(cr92)nr4, -(c92)nr4, -(c-o)(c92)nr4, -(c-o)(c92)nr4, -(c-o)(c92)nr4, -(n)r4)2, -(c-o)r4r2, r8, -(cr92)nr8, deuterated c1-c6alkoxy, -(s-o)2r4, -(s-o)2r7, -(s-o)2r8, -(s-o)2n(r4)2, -(s-o)2nhc-(o)r4, -(s-o)2(c92)nc-(o)r4, -(s-o)2(c92)nr4, a spiro attached dioxolane, a spiro attached dioxane, a spiro attached tetrahydrofuran, a spiro attached

Search [SP]: cross-reference to related applications this application is a continuation of prior application ser. no. 14/031,792, filed sep. 19, 2013, which is a continuation

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associated myelopathy.the term "carrier," as used herein, refers to chemical compounds or agents that facilitate the incorporation of a compound described herein into cells or tissues.the terms "co-administration" or "combined administration" or the like as used herein are meant to encompass administration of the selected therapeutic agents to a single patient, and are intended to include treatment regimens in which the agents are not necessarily administered by the same route of administration or at the same time.the term "dermatological disease" or "dermatological disorder," as used herein refers to a skin disorder. such dermatological disorders include, but are not limited to, proliferative or inflammatory disorders of the skin such as, atopic dermatitis, bullous disorders, collagenoses, contact dermatitis eczema, kawasaki disease, rosacea, sjogren-larsson syndrome, actinic keratosis, basal cell carcinoma and urticaria.the term "diluent," as used herein, refers to chemical compounds that are used to dilute a compound described herein prior to delivery. diluents can also be used to stabilize compounds described herein.the terms "effective amount" or "therapeutically effective amount," as used herein, refer to a sufficient amount of a compound described herein being administered which will relieve to some extent one or more of the symptoms of the disease or condition being treated. the result can be reduction and/or alleviation of the signs, symptoms, or causes of a disease, or any other desired alteration of a biological system. for example, an "effective amount" for therapeutic uses is the amount of the composition comprising a compound as disclosed herein required to provide a clinically significant decrease in disease symptoms. an appropriate "effective" amount in any individual case may be determined using techniques, such as a dose escalation study.the terms "enhance" or "enhancing," as used herein, means to increase or prolong either in potency or duration a desired effect. thus, in regard to enhancing the effect of therapeutic agents, the term "enhancing" refers to the ability to increase or prolong, either in potency or duration, the effect of other therapeutic agents on a system. an "enhancing-effective amount," as used herein, refers to an amount adequate to enhance the effect of another therapeutic agent in a desired system.the terms "fibrosis" or "fibrosis disease," as used herein, refers to conditions that follow acute or chronic inflammation and are associated with the abnormal accumulation of cells and/or collagen and include but are not limited to fibrosis of individual organs or tissues such as the heart, kidney, joints, lung, or skin, and includes such disorders as idiopathic pulmonary fibrosis and cryptogenic fibrosing alveolitis.the term "inflammatory disease or disorders," as used herein, refers to those diseases or conditions that are characterized by one or more of the signs of pain (dolor, from the generation of noxious substances and the stimulation of nerves), heat (calor, from vasodilatation), redness (rubor, from vasodilatation and increased blood flow), swelling (tumor, from excessive inflow or restricted outflow of fluid), and loss of function (functio laesa, which may be partial or complete, temporary or permanent). inflammation takes many forms and includes, but is not limited to, inflammation that is one or more of the following: acute, adhesive, atrophic, catarrhal, chronic, cirrhotic, diffuse, disseminated, exudative, fibrinous, fibrosing, focal, granulomatous, hyperplastic, hypertrophic, interstitial, metastatic, necrotic, obliterative, parenchymatous, plastic, productive, proliferous, pseudomembranous, purulent, sclerosing, seroplastic, serous, simple, specific, subacute, suppurative, toxic, traumatic, and/or ulcerative. inflammatory disorders further include, without being limited to those affecting the blood vessels (polyarteritis, temporal arthritis) joints (arthritis: crystalline, osteo-, psoriatic, reactive, rheumatoid, reiter's) gastrointestinal tract (disease) skin (dermatitis) or multiple organs and tissues (systemic lupus erythematosus).as used herein, the term "inhibit", "inhibition" or "inhibiting" refers to the reduction or suppression of a given condition, symptom, or disorder, or disease, or a significant decrease in the baseline activity of a biological activity or process.the term "pharmaceutically acceptable," as used herein, refers to a material, such as a carrier or diluent, which does not abrogate the biological activity or properties of the compounds described herein. such materials are administered to an individual without causing undesirable biological effects or interacting in a deleterious manner with any of the components of the composition in which it is contained.the term "pharmaceutically acceptable" carrier, as used herein, includes any and all solvents, dispersion media, coatings, surfactants, antioxidants, preservatives (e.g., antibacterial agents, antifungal agents), isotonic agents, absorption delaying agents, salts, preservatives, drug stabilizers, binders, excipients, disintegration agents, lubricants, sweetening agents, flavoring agents, dyes, and the like and combinations thereof, as would be known to those skilled in the art (see, for example, remington's pharmaceutical sciences, 18th ed. mack printing company, 1990, pp. 1289-1329). except insofar as any conventional carrier is incompatible with the active ingredient, its use in the therapeutic or pharmaceutical compositions is contemplated.the term "pharmaceutically acceptable salt," as used herein, refers to a formulation of a compound that does not cause significant irritation to an organism to which it is administered and does not abrogate the biological activity and properties of the compounds described herein.the terms "combination" or "pharmaceutical combination," as used herein mean a product that results from the mixing or combining of more than one active ingredient and includes both fixed and non-fixed combinations of the active ingredients. the term "fixed combination" means that the active ingredients, by way of example, a compound of formula (i) or formula (ii) and an additional therapeutic agent, are both administered to a patient simultaneously in the form of a single entity or dosage. the term "non-fixed combination" means that the active ingredients, by way of example, a compound of formula (i) or formula (ii) and an additional therapeutic agent, are both administered to a patient as separate entities either simultaneously, concurrently or sequentially with no specific time limits, wherein such administration provides therapeutically effective levels of the 2 compounds in the body of the patient. the latter also applies to cocktail therapy, e.g. the administration of 3 or more active ingredients.the terms "composition" or "pharmaceutical composition," as used herein, refers to a mixture of at least one compound, such as the compounds of formula (i) or formula (ii) provided herein, with at least one and optionally more than one other pharmaceutically acceptable chemical components, such as carriers, stabilizers, diluents, dispersing agents, suspending agents, thickening agents, and/or excipients.the term "respiratory disease," as used herein, refers to diseases affecting the organs that are involved in breathing, such as the nose, throat, larynx, trachea, bronchi, and lungs. respiratory diseases include, but are not limited to, asthma, adult respiratory distress syndrome and allergic (extrinsic) asthma, non-allergic (intrinsic) asthma, acute severe asthma, chronic asthma, clinical asthma, nocturnal asthma, allergen-induced asthma, aspirin-sensitive asthma, exercise-induced asthma, isocapnic hyperventilation, child-onset asthma, adult-onset asthma, cough-variant asthma, occupational asthma, steroid-resistant asthma, seasonal asthma, seasonal allergic rhinitis, perennial allergic rhinitis, chronic obstructive pulmonary disease, including chronic bronchitis or emphysema, pulmonary hypertension, interstitial lung fibrosis and/or airway inflammation and cystic fibrosis, and hypoxia.the term "subject" or "patient," as used herein, encompasses mammals and non-mammals. examples of mammals include, but are not limited to, humans, chimpanzees, apes, monkeys, cattle, horses, sheep, goats, swine rabbits, dogs, cats, rats, mice, guinea pigs, and the like. examples of non-mammals include, but are not limited to, birds, fish and the like. frequently the subject is a human, and may be a human who has been diagnosed as in need of treatment for a disease or disorder disclosed herein.as used herein, a subject is "in need of" a treatment if such subject would benefit biologically, medically or in quality of life from such treatment.the term "c-kit inhibitor," as used herein, refers to a compound which inhibits c-kit kinase.the term "disease or disorder associated with c-kit activity," as used herein, refers to any disease state associated with a c-kit kinase. such diseases or disorders include, but are not limited to, a mast-cell associated disease, inflammatory diseases, respiratory diseases, fibrosis diseases, a dermatological disease, metabolic diseases and autoimmune diseases, such as, by way of example only, asthma, dermatitis, allergic rhinitis, pulmonary fibrosis, hepatic fibrosis, cardiac fibrosis, scleroderma, irritable bowel syndrome (ibs), inflammatory bowel disease (ibd), urticaria, rheumatoid arthritis, multiple sclerosis, uticaria, pulmonary arterial hypertension (pah), primary pulmonary hypertension (pph), dermatosis, diabetes, type i diabetes and type ii diabetes.the term "pdgfr inhibitor," as used herein, refers to a compound which inhibits pdgfr kinase.the term "disease or disorder associated with pdgfr activity," as used herein, refers to any disease state associated with a pdgfr kinase. such diseases or disorders include, but are not limited to, inflammatory diseases, respiratory diseases, fibrosis diseases, metabolic diseases and autoimmune diseases, such as, by way of example only, asthma, dermatitis, allergic rhinitis, scleroderma, irritable bowel syndrome (ibs), inflammatory bowel disease (ibd), urticaria, rheumatoid arthritis, multiple sclerosis, pulmonary arterial hypertension and diabetes.the term "an optical isomer" or "a stereoisomer," as used herein, refers to any of the various stereo isomeric configurations which may exist for a given compound of the present invention and includes geometric isomers. it is understood that a substituent may be attached at a chiral center of a carbon atom. the term "chiral" refers to molecules which have the property of non-superimposability on their mirror image partner, while the term "achiral" refers to molecules which are superimposable on their mirror image partner. therefore, the invention includes enantiomers, diastereomers or racemates of the compound. "enantiomers" are a pair of stereoisomers that are non-superimposable mirror images of each other. a 1:1 mixture of a pair of enantiomers is a "racemic" mixture. the term is used to designate a racemic mixture where appropriate."diastereoisomers" are stereoisomers that have at least two asymmetric atoms, but which are not mirror-images of each other. the absolute stereochemistry is specified according to the cahn-ingold-prelog r-s system. when a compound is a pure enantiomer the stereochemistry at each chiral carbon may be specified by either r or s. resolved compounds whose absolute configuration is unknown can be designated (+) or (-) depending on the direction (dextro- or levorotatory) which they rotate plane polarized light at the wavelength of the sodium d line. certain compounds described herein contain one or more asymmetric centers or axes and may thus give rise to enantiomers, diastereomers, and other stereoisomeric forms that may be defined, in terms of absolute stereochemistry, as (r)- or (s)-.the term "a therapeutically effective amount" of a compound of the present invention, as used herein, refers to an amount of the compound of the present invention that will elicit the biological or medical response of a subject, for example, reduction or inhibition of an enzyme or a protein activity, or ameliorate symptoms, alleviate conditions, slow or delay disease progression, or prevent a disease, etc. in one non-limiting embodiment, the term "a therapeutically effective amount" refers to the amount of the compound of the present invention that, when administered to a subject, is effective to (1) at least partially alleviating, inhibiting, preventing and/or ameliorating a condition, or a disorder or a disease (i) mediated by c-kit kinase or c-kit and pdgfr kinases, or (ii) associated with c-kit kinase or c-kit and pdgfr kinase activity, or (iii) characterized by activity (normal or abnormal) of c-kit kinase or c-kit and pdgfr kinases or (2) reducing or inhibiting the activity of c-kit kinase or c-kit and pdgfr kinases or (3) reducing or inhibiting the expression of c-kit kinase or c-kit and pdgfr kinases. in another non-limiting embodiment, the term "a therapeutically effective amount" refers to the amount of the compound of the present invention that, when administered to a cell, or a tissue, or a non-cellular biological material, or a medium, is effective to at least partially reducing or inhibiting the activity of c-kit kinase or c-kit and pdgfr kinases or at least partially reducing or inhibiting the expression of c-kit kinase or c-kit and pdgfr kinases.the terms "treat", "treating" or "treatment," as used herein, refers to methods of alleviating, abating or ameliorating a disease or condition symptoms, preventing additional symptoms, ameliorating or preventing the underlying metabolic causes of symptoms, inhibiting the disease or condition, arresting the development of the disease or condition, relieving the disease or condition, causing regression of the disease or condition, relieving a condition caused by the disease or condition, or stopping the symptoms of the disease or condition either prophylactically and/or therapeutically.in addition, as used herein, the term "treat", "treating" or "treatment" of any disease or disorder refers in one embodiment, to ameliorating the disease or disorder (i.e., slowing or arresting or reducing the development of the disease or at least one of the clinical symptoms thereof). in another embodiment "treat", "treating" or "treatment" refers to alleviating or ameliorating at least one physical parameter including those which may not be discernible by the patient. in yet another embodiment, "treat", "treating" or "treatment" refers to modulating the disease or disorder, either physically, (e.g., stabilization of a discernible symptom), physiologically, (e.g., stabilization of a physical parameter), or both. in yet another embodiment, "treat", "treating" or "treatment" refers to preventing or delaying the onset or development or progression of the disease or disorder.the compound names provided herein were obtained using chemdraw ultra 10.0 (cambridgesoft(r)) or jchem version 5.3.1 (chemaxon).unless specified otherwise, the term "compounds of the present invention" or "compounds provided herein" refers to compounds of formula (i) and formula (ii), and subformulae thereof (such as formula (ia), formula (iia), formula (ib), formula (iib), formula (ic), formula (iic), formula (id), formula (iid), formula (ie), formula (iie), formula (if) and formula (iif)), and pharmaceutically acceptable salts, hydrates or solvates, stereoisomers (including diastereoisomers and enantiomers), tautomers and isotopically labeled compounds (including deuterium substitutions) thereof. compounds of the present invention further comprise polymorphs of compounds of formula (i) and formula (ii) (or subformulae thereof) and salts thereof.as used herein, the term "a," "an," "the" and similar terms used in the context of the present invention (especially in the context of the claims) are to be construed to cover both the singular and plural unless otherwise indicated herein or clearly contradicted by the context.all methods described herein can be performed in any suitable order unless otherwise indicated herein or otherwise clearly contradicted by context. the use of any and all examples, or exemplary language (e.g. "such as") provided herein is intended merely to better illuminate the invention and does not pose a limitation on the scope of the invention otherwise claimed.various enumerated embodiments of the invention are described herein. it will be recognized that features specified in each embodiment may be combined with other specified features to provide further embodiments of the present invention.description of the preferred embodimentsprovided herein are compounds, pharmaceutically acceptable salts, solvates, n-oxides and isomers thereof, that are inhibitors of c-kit kinase or c-kit and pdgfr kinases. certain embodiments of compounds provided herein have an ic50 for pdgfr inhibition to ic50 for c-kit inhibition ratio (ic50 pdgfr/ic50 c-kit) in the range of 750 to 1000. certain embodiments of compounds provided herein have an ic50 for pdgfr inhibition to ic50 for c-kit inhibition ratio (ic50 pdgfr/ic50 c-kit) in the range of 500 to 750. certain embodiments of compounds provided herein have an ic50 for pdgfr inhibition to ic50 for c-kit inhibition ratio (ic50 pdgfr/ic50 c-kit) in the range of 250 to 500. certain embodiments of compounds provided herein have an ic50 for pdgfr inhibition to ic50 for c-kit inhibition ratio (ic50 pdgfr/ic50 c-kit) in the range of 100 to 250. certain embodiments of compounds provided herein have an ic50 for pdgfr inhibition to ic50 for c-kit inhibition ratio (ic50 pdgfr/ic50 c-kit) in the range of 75 to 100. certain embodiments of compounds provided herein have an ic50 for pdgfr inhibition to ic50 for c-kit inhibition ratio (ic50 pdgfr/ic50 c-kit) in the range of 50 to 75. certain embodiments of compounds provided herein have an ic50 for pdgfr inhibition to ic50 for c-kit inhibition ratio (ic50 pdgfr/ic50 c-kit) in the range of 25 to 50. certain embodiments of compounds provided herein have an ic50 for pdgfr inhibition to ic50 for c-kit inhibition ratio (ic50 pdgfr/ic50 c-kit) in the range of 10 to 25. certain embodiments of compounds provided herein have an ic50 for pdgfr inhibition to ic50 for c-kit inhibition ratio (ic50 pdgfr/ic50 c-kit) in the range of 7.5 to 10. certain embodiments of compounds provided herein have an ic50 for pdgfr inhibition to ic50 for c-kit inhibition ratio (ic50 pdgfr/ic50 c-kit) in the range of 5 to 7.5. certain embodiments of compounds provided herein have an ic50 for pdgfr inhibition to ic50 for c-kit inhibition ratio (ic50 pdgfr/ic50 c-kit) in the range of 2.5 to 5. certain embodiments of compounds provided herein have an ic50 for pdgfr inhibition to ic50 for c-kit inhibition ratio (ic50 pdgfr/ic50 c-kit) in the range of 1 to 2.5. certain embodiments of compounds provided herein have an ic50 for ic50 for pdgfr inhibition to c-kit inhibition ratio (ic50 pdgfr/ic50 c-kit) in the range of 0.95 to 2.5.also provided herein are pharmaceutical compositions that include such compounds. further provided herein are methods for the treatment of diseases and/or disorders associated with c-kit kinase or c-kit and pdgfr kinases using such compounds and pharmaceutical compositions.the c-kit kinase, or c-kit

and pdgfr kinase, inhibitors of the present invention are compounds having the structure of formula (i) or formula (ii), and pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof: [ftimg=680000442] wherein: m is 1 and r20 is selected from h, halo, c1-c6alkyl, c1-c6haloalkyl, c1-c6haloalkoxy, deuterium, deuterated c1-c6alkyl, -cn, -(cr92)nor4, -(c(o)r4), -(cr92)nc(o)or4, r10, -(cr92)nr10, -((cr92)no)tr4, -(cr92)no(cr92)nr7, -(cr92)nc(o)r4, -(c(o)n(r4)2, -or4, and -(cr92)ncnor m is 4 and r20 is deuteriumr1 is selected from c1-c6alkyl and haloeach r11 is independently selected from h, halo and c1-c6alkylr11 is a bond, -nh- or -c(o)nh-12 is -(cr92)n-, -chr6-, -(cr92)no-, -nh-, -(cr92)nc(o)-, -(c(o)o(cr92)n-, -(cr92)noc(o)nr4-, -(cr92)nnr4c(o)(cr92)n-(cr92)nnr4c(o)-, or -(cr92)nnr4c(o)o-r2 is r3 or l2r3r3 is selected from an unsubstituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a piperidinone, an oxazolidin-2-one, pyrrolidinone, a pyrrolidin-2-one and a substituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, wherein the substituted 4-6 membered heterocycloalkyl of r3 is substituted with 1-4 substituents independently selected from c1-c6alkyl halo, -cn, c1-c6haloalkyl, -or4, -(c(o)or4, -(c(o)r4), -(c(o)r7, -(c(o)or5, -(cr92)nor4, -(o(cr92)nor4, -(c(o)o(cr92)nor4, -n(r4)2, -(c(o)nr42, -nr4c(o)or4, -nr4c(o)(cr92)nor4, -nr4(cr92)nor4, -nr4s(o)2r4, -n(c(o)or4)2, r8, -(cr92)nr8, deuterated c1-c6alkoxy, -(o)2r4, -(o)2r7, -(s(o)2r8, -(s(o)2n(r4)2, -(s(o)2nhc(o)or4, -(s(o)2(cr92)nc(o)or4, s(o)2(cr92)nor4, a spiro attached dioxolane, a spiro attached dioxolane which is substituted with c1-c6alkyl, a spiro attached dioxane, a spiro attached tetrahydrofuran, a spiro attached oxetane, a spiro attached cyclobutanone, a spiro attached cyclobutanol, a c1 alkyl bridge, an unsubstituted 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s and a 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, wherein the substituted 4-6 membered heterocycloalkyl of r3 is substituted with 1-4 substituents independently selected from c1-c6alkyl halo, c1-c6haloalkyl, c1-c6haloalkoxy, -or4 and r8each r4 is independently selected from h and c1-c6alkylr5 is an unsubstituted c3-c8cycloalkyl, an unsubstituted 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n or o or a c3-c8cycloalkyl substituted with 1-3 substituents independently selected from c1-c6alkyleach r6 is independently selected from -nr4c(o)or4, -or4 and -(cr92)nor4each r7 is independently selected from c1-c6haloalkylr8 is selected from an unsubstituted phenyl, unsubstituted 5-6 membered heteroaryl with 1-3 heteroatoms independently selected from n, o and s, an unsubstituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, an unsubstituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a substituted phenyl, a substituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, a substituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a substituted c3-c8cycloalkyl, a substituted 5-6 membered heteroaryl with 1-3 heteroatoms independently selected from n, o and s, a substituted phenyl, a substituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, substituted c3-c8cycloalkyl and substituted 4-6 membered heterocycloalkyl of r8 are substituted with 1-3 substituents independently selected from c1-c6alkyl, -(cr92)nor4, -(cr92)nr5, -(cr92)nc(o)or4, -(c(o)or4 and -(s(o)2r4each r9 is independently selected from h and c1-c6alkylr10 is selected from an unsubstituted phenyl, unsubstituted 5-6 membered heteroaryl with 1-2 heteroatoms independently selected from n, o and s, an unsubstituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, an unsubstituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, an unsubstituted c3-c8cycloalkyl, a substituted 5-6 membered heteroaryl with 1-2 heteroatoms independently selected from n, o and s, a substituted phenyl, a substituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, a substituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a substituted c3-c8cycloalkyl, an oxazolidin-2-one, pyrrolidinone and a pyrrolidin-2-one, wherein the substituted phenyl, the substituted 5-6 membered heteroaryl with 1-2 heteroatoms independently selected from n, o and s, the substituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, substituted c3-c8cycloalkyl and substituted 4-6 membered heterocycloalkyl of r8 are substituted with 1-3 substituents independently selected from c1-c6alkyl [me], -(cr92)nor4, -(cr92)nr5, -(cr92)nc(o)or4 and -(s(o)2r4t is 1, 2 or 3, andeach n is independently selected from 1, 2, 3 and 4.in certain embodiments of compounds of formula (i) or formula (ii), and the pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, the compound of formula (i) or formula (ii) is a compound having a structure of formula (ia), formula (iia), formula (ib) or formula (iib):[ftimg=68000043] wherein: m is 1 and r20 is selected from h, halo, c1-c6alkyl, c1-c6haloalkyl, c1-c6haloalkoxy, deuterium, deuterated c1-c6alkyl, -cn, -(cr92)nor4, -(c(o)r4, -(cr92)nc(o)or4, r10, -((cr92)no)tr4, -(cr92)no(cr92)nr7, -(cr92)nc(o)r4, -(c(o)n(r4)2, -or4, and -(cr92)ncnor m is 4 and r20 is deuteriumr1 is selected from c1-c6alkyl and haloeach r11 is independently selected from h, halo and c1-c6alkylr12 is -(cr92)n-, -chr6-, -(cr92)no-, -nh-, -(cr92)nc(o)-, -(c(o)o(cr92)n-, -(cr92)noc(o)nr4-, -(cr92)nnr4c(o)(cr92)n-, -(cr92)nnr4c(o)-, or -(cr92)nnr4c(o)o-r2 is r3 or l2r3r3 is selected from an unsubstituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a piperidinone, an oxazolidin-2-one, pyrrolidinone, a pyrrolidin-2-one and a substituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, wherein the substituted 4-6 membered heterocycloalkyl of r3 is substituted with 1-4 substituents independently selected from c1-c6alkyl halo, -cn, c1-c6haloalkyl, -or4, -(c(o)or4, -(c(o)r4, -(c(o)r7, -(c(o)or5, -(cr92)nor4, -(o(cr92)nor4, -(c(o)o(cr92)nor4, -n(r4)2, -(c(o)nr42, -nr4c(o)or4, -nr4c(o)(cr92)nor4, -nr4(cr92)nor4, -nr4s(o)2r4, -n(c(o)or4)2, r8, -(cr92)nr8, deuterated c1-c6alkoxy, -(o)2r4, -(o)2r7, -(s(o)2r8, -(s(o)2n(r4)2, -(s(o)2nhc(o)or4, -(s(o)2(cr92)nc(o)or4, s(o)2(cr92)nor4, a spiro attached dioxolane, a spiro attached dioxolane which is substituted with c1-c6alkyl, a spiro attached dioxane, a spiro attached tetrahydrofuran, a spiro attached oxetane, a spiro attached cyclobutanone, a spiro attached cyclobutanol, a c1 alkyl bridge, an unsubstituted 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s and a 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, wherein the substituted 4-6 membered heterocycloalkyl of r3 is substituted with 1-4 substituents independently selected from c1-c6alkyl halo, c1-c6haloalkyl, c1-c6haloalkoxy, -or4 and r8each r4 is independently selected from h and c1-c6alkylr5 is an unsubstituted c3-c8cycloalkyl, an unsubstituted 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n or o or a c3-c8cycloalkyl substituted with 1-3 substituents independently selected from c1-c6alkyleach r6 is independently selected from -nr4c(o)or4, -or4 and -(cr92)nor4each r7 is independently selected from c1-c6haloalkylr8 is selected from an unsubstituted phenyl, unsubstituted 5-6 membered heteroaryl with 1-3 heteroatoms independently selected from n, o and s, an unsubstituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, an unsubstituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a substituted phenyl, a substituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, substituted c3-c8cycloalkyl and substituted 4-6 membered heterocycloalkyl of r8 are substituted with 1-3 substituents independently selected from c1-c6alkyl [me], -(cr92)nor4, -(cr92)nr5, -(cr92)nc(o)or4 and -(s(o)2r4t is 1, 2 or 3, andeach n is independently selected from 1, 2, 3 and 4.in certain embodiments of compounds of formula (i) or formula (ii), and the pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, the compound of formula (i) or formula (ii), is a compound having a structure of formula (ia), formula (iia), formula (ib), formula (iib), formula (ic), formula (iic), formula (id), formula (iid), formula (ie), formula (iie), formula (if) or formula (iif): [ftimg=68000044][ftimg=68000045][ftimg=68000046] wherein: m is 1 and r20 is selected from h, halo, c1-c6alkyl, c1-c6haloalkyl, c1-c6haloalkoxy, deuterium, deuterated c1-c6alkyl, -cn, -(cr92)nor4, -(c(o)r4, -(cr92)nc(o)or4, r10, -(cr92)no)tr4, -(cr92)no(cr92)nr7, -(cr92)nc(o)r4, -(c(o)n(r4)2, -or4, and -(cr92)ncnor m is 4 and r20 is deuteriumr1 is selected from c1-c6alkyl and haloeach r11 is independently selected from h, halo and c1-c6alkylr12 is -(cr92)n-, -chr6-, -(cr92)no-, -nh-, -(cr92)nc(o)-, -(c(o)o(cr92)n-, -(cr92)noc(o)nr4-, -(cr92)nnr4c(o)(cr92)n-, -(cr92)nnr4c(o)-, or -(cr92)nnr4c(o)o-r2 is r3 or l2r3r3 is selected from an unsubstituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a piperidinone, an oxazolidin-2-one, pyrrolidinone, a pyrrolidin-2-one and a substituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, wherein the substituted 4-6 membered heterocycloalkyl of r3 is substituted with 1-4 substituents independently selected from c1-c6alkyl halo, -cn, c1-c6haloalkyl, -or4, -(c(o)or4, -(c(o)r4, -(c(o)r7, -(c(o)or5, -(cr92)nor4, -(o(cr92)nor4, -(c(o)o(cr92)nor4, -n(r4)2, -(c(o)nr42, -nr4c(o)or4, -nr4c(o)(cr92)nor4, -nr4(cr92)nor4, -nr4s(o)2r4, r8, -(cr92)nr8, deuterated c1-c6alkoxy, -(o)2r4, -(o)2r7, -(s(o)2r8, -(s(o)2n(r4)2, -(s(o)2nhc(o)or4, -(s(o)2(cr92)nc(o)or4, s(o)2(cr92)nor4, a spiro attached dioxolane, a spiro attached dioxolane which is substituted with c1-c6alkyl, a spiro attached dioxane, a spiro attached tetrahydrofuran, a spiro attached oxetane, a spiro attached cyclobutanone, a spiro attached cyclobutanol, a c1 alkyl bridge, an unsubstituted 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s and a 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s substituted with 1-3 substituents independently selected from c1-c6alkyl, halo, c1-c6haloalkyl, c1-c6haloalkoxy, -or4 and r8each r4 is independently selected from h and c1-c6alkylr5 is an unsubstituted c3-c8cycloalkyl, an unsubstituted 5-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n or o or a c3-c8cycloalkyl substituted with 1-3 substituents independently selected from c1-c6alkyleach r6 is independently selected from -nr4c(o)or4, -or4 and -(cr92)nor4each r7 is independently selected from c1-c6haloalkylr8 is selected from an unsubstituted phenyl, unsubstituted 5-6 membered heteroaryl with 1-3 heteroatoms independently selected from n, o and s, an unsubstituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, an unsubstituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a substituted phenyl, a substituted 5 membered heteroaryl with 1-4 heteroatoms selected from n, a substituted 4-6 membered heterocycloalkyl with 1-2 heteroatoms independently selected from n, o and s, a substituted c3-c8cycloalkyl, a substituted 5-6 membered heteroaryl with 1-4 heteroatoms selected from n, substituted c3-c8cycloalkyl and substituted 4-6 membered heterocycloalkyl of r8 are substituted with 1-3 substituents independently selected from c1-c6alkyl [me], -(c(r92)nr5, -(c(r92)nc(o)or4 and -(s(o)2r4t is 1, 2 or 3, andeach n is independently selected from 1, 2, 3 and 4.the compounds of formula (i) or formula (ii), pharmaceutically acceptable salts, solvates, n-oxides and isomers thereof, and pharmaceutical compositions provided herein also includes all suitable isotopic variations of such compounds, and pharmaceutically acceptable salts, solvates, n-oxides and isomers thereof, and pharmaceutical compositions. therefore, any formula given herein is also intended to represent unlabeled forms as well as isotopically labeled forms of the compounds. isotopically labeled compounds have structures depicted by the formulas given herein except that one or more atoms are replaced by an atom having a selected atomic mass or mass number. examples of isotopes that can be incorporated into compounds of the invention include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorous, fluorine, and chlorine, such as 2h, 3h, 11c, 13c, 14c, 15n, 18f 31p, 32p, 35s, 36cl, 125i respectively. the invention includes various isotopically labeled compounds as defined herein, for example those into which radioactive isotopes, such as 3h and 14c, or those into which non-radioactive isotopes, such as 2h and 13c are present. such isotopically labelled compounds are useful in metabolic studies (with 14c), reaction kinetic studies (with, for example 2h or 3h), detection or imaging techniques, such as positron emission tomography (pet) or single-photon emission computed tomography (spect) including drug or substrate tissue distribution assays, or in radioactive treatment of patients. in particular, an 18f or labeled compound may be particularly desirable for pet or spect studies. isotopically-labeled compounds of formula (i) can generally be prepared by conventional techniques known to those skilled in the art or by processes analogous to those described in the accompanying examples and preparations using an appropriate isotopically-labeled reagents in place of the non-labeled reagent previously employed.further, substitution with heavier isotopes, particularly deuterium (i.e., 2h or d) may afford certain therapeutic advantages resulting from greater metabolic stability, for example increased in vivo half-life or reduced dosage requirements or an improvement in therapeutic index. it is understood that deuterium in this context is regarded as a substituent of a compound of the formula (i). the concentration of such a heavier isotope, specifically deuterium, may be defined by the isotopic enrichment factor. the term "isotopic enrichment factor" as used herein means the ratio between the isotopic abundance and the natural abundance of a specified isotope. if a substituent in a compound of this invention is denoted deuterium, such compound has an isotopic enrichment factor for each designated deuterium atom of at least 3500 (52.5 percent deuterium incorporation at each designated deuterium atom), at least 4000 (60 percent deuterium incorporation), at least

4500 (67.5 percent deuterium incorporation), at least 5000 (75 percent deuterium incorporation), at least 5500 (82.5 percent deuterium incorporation), at least 6000 (90 percent deuterium incorporation), at least 6333.3 (95 percent deuterium incorporation), at least 6466.7 (97 percent deuterium incorporation), at least 6600 (99 percent deuterium incorporation), or at least 6633.3 (99.5 percent deuterium incorporation).pharmaceutically acceptable solvates in accordance with the invention include those wherein the solvent of crystallization may be isotopically substituted, e.g. d₂o, d₆-acetone, d₆-dms_o.compounds of the invention, i.e. compounds of formula (i) and formula (ii) that contain groups capable of acting as donors and/or acceptors for hydrogen bonds may be capable of forming co-crystals with suitable co-crystal formers. these co-crystals may be prepared from compounds of formula (i) by known co-crystal forming procedures. such procedures include grinding, heating, co-subliming, co-melting, or contacting in solution compounds of formula (i) with the co-crystal former under crystallization conditions and isolating co-crystals thereby formed. suitable co-crystal formers include those described in wo 2004/078163. hence the invention further provides co-crystals comprising a compound of formula (i) and formula (ii).processes for making compounds of formula (i) or formula (ii)general procedures for preparing compounds of formula (i) or formula (ii) are described in the examples, infra. in the reactions described, reactive functional groups, for example hydroxy, amino, imino, thio or carboxy groups, where these are desired in the final product, may be protected to avoid their unwanted participation in the reactions. conventional protecting groups may be used in accordance with standard practice (see e.g., t. w. greene and p. g. m. wuts in "protective groups in organic chemistry," john wiley and sons, 1991).in certain embodiments, the compounds of formula (i) or formula (ii) provided herein are prepared as a pharmaceutically acceptable acid addition salt by reacting the free base form of the compound of formula (i) or formula (ii) with a stoichiometric amount of an appropriate pharmaceutically acceptable organic acid or inorganic acid or a suitable anion exchange reagent. in other embodiments, a pharmaceutically acceptable base addition salt of compounds of formula (i) or formula (ii) is prepared by reacting the free acid form of the compound of formula (i) or formula (ii) with a stoichiometric amount of an appropriate pharmaceutically acceptable organic base or inorganic base or a suitable ion exchange reagent. such reactions are typically carried out in water or in an organic solvent, or in a mixture of the two. generally, use of non-aqueous media like ether, ethyl acetate, ethanol, isopropanol, or acetonitrile is desirable, where practicable.alternatively, the salt forms of the compounds of formula (i) or formula (ii) are prepared using salts of the starting materials or intermediates. in certain embodiments, the compounds of formula (i) or formula (ii) are in the form of other salts including, but not limited to, oxalates and trifluoroacetates. in certain embodiments, hemisalts of acids and bases are formed, for example, hemisulphate and hemicalcium salts.such pharmaceutically acceptable acid addition salts of compounds of formula (i) or formula (ii) include, but are not limited to, a hydrobromide, hydrochloride, sulfate, nitrate, succinate, maleate, formate, acetate, adipate, besylate, bicarbonate/carbonate, propionate, fumarate, citrate, tartrate, lactate, benzoate, salicylate, glutamate, aspartate, p-toluenesulfonate, benzenesulfonate, methanesulfonate, ethanesulfonate, ethanedisulfonate, camphorsulfonate, chlorotheophyllonate, naphthalenesulfonate (e.g. 2-naphthalenesulfonate), hexanoate salt, bisulphate/sulphate, borate, camsylate, cyclamate, edisylate, esylate, gluceptate, gluconate, glucuronate, hexafluorophosphate, hibenzate, hippurate, hydrochloride/chloride, hydrobromide/bromide, hydroiodide/iodide, isethionate, lactobionate, laurysulphate, malate, malonate, mandelate, mesylate, methylsulphate, naphthoate, napsylate, naphthylate, 2-napsylate, nicotinate, octadecanoate, oleate, orotate, oxalate, palmitate, pamoate, phosphate/hydrogen phosphate/dihydrogen phosphate, polygalacturonate, pyroglutamate, saccharate, stearate, sulfosalicylate, tannate, tosylate, trifluoroacetate and xinofoate salts.the organic acid or inorganic acids used to form certain pharmaceutically acceptable acid addition salts of compounds of formula (i) or formula (ii) include, but are not limited to, hydrobromic acid, hydrochloric acid, sulfuric acid, nitric acid, phosphoric acid, succinic acid, maleic acid, malonic acid, mandelic acid, formic acid, acetic acid, propionic acid, glycolic acid, oxalic acid, fumaric acid, citric acid, tartaric acid, lactic acid, benzoic acid, salicylic acid, glutamic acid, aspartic acid, toluenesulfonic acid, sulfosalicylic acid, benzenesulfonic acid, methanesulfonic acid, ethanesulfonic acid, naphthalenesulfonic acid, such as 2-naphthalenesulfonic acid, or hexanoic acid.such pharmaceutically acceptable base addition salt of compounds of formula (i) or formula (ii) include, but are not limited to, ammonium, aluminium, arginine, benzathine, calcium, choline, copper, diethylamine, diolamine, glycine, isopropylamine, cholineate, diethanolamine, piperazine, iron, lysine, magnesium, meglumine, olamine, potassium, silver, sodium, tromethamine and zinc salts.the organic or inorganic bases used to form certain pharmaceutically acceptable base addition salt of compounds of formula (i) or formula (ii) include, but are not limited to, salts derived from ammonium salts and metals from columns i to xii of the periodic table, or salts derived from primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines, basic ion exchange resins, and the like.in certain embodiments, the free acid or free base forms of the compounds of formula (i) or formula (ii) provided herein are prepared from the corresponding base addition salt or acid addition salt from, respectively. for example a compound formula (i) in an acid addition salt form is converted to the corresponding free base by treating with a suitable base (by way of example only, an ammonium hydroxide solution, a sodium hydroxide, and the like). for example, a compound of formula (i) in a base addition salt form is converted to the corresponding free acid by treating with a suitable acid (by way of example only, hydrochloric acid).lists of additional suitable salts can be found, e.g., in "remington's pharmaceutical sciences", 20th ed., mack publishing company, easton, pa., (1985) and in "handbook of pharmaceutical salts: properties, selection, and use" by stahl and wermuth (wiley-vch, weinheim, germany, 2002).in certain embodiments, compounds of formula (i) or formula (ii) in unoxidized form are prepared from n-oxides of compounds formula (i) or formula (ii) by treating with a reducing agent (by way of example only, sulfur, sulfur dioxide, triphenyl phosphine, lithium borohydride, sodium borohydride, phosphorus trichloride, tribromide, or the like) in a suitable inert organic solvent (by way of example only, acetonitrile, ethanol, aqueous dioxane, or the like) at 0 to 80 degrees centigrade in certain embodiments, compounds of formula (i) or formula (ii) are prepared as protected derivatives using methods known to those of ordinary skill in the art. a detailed description of the techniques applicable to the creation of protecting groups and their removal can be found in t. w. greene, "protecting groups in organic chemistry," 3rd edition, john wiley and sons, inc., 1999. in certain embodiments, compounds of formula (i) or formula (ii) are prepared or formed, as solvates (e.g., hydrates). in certain embodiments, hydrates of compounds of formula (i) or formula (ii) are prepared by recrystallization from an aqueous/organic solvent mixture, using organic solvents such as dioxin, tetrahydrofuran or methanol.furthermore, the compounds of the present invention, including their salts, can also be obtained in the form of their hydrates, or include other solvents used for their crystallization. the compounds of the present invention may inherently or by design form solvates with pharmaceutically acceptable solvents (including water) therefore, it is intended that the invention embrace both solvated and unsolvated forms. the term "solvate" refers to a molecular complex of a compound of the present invention (including pharmaceutically acceptable salts thereof) with one or more solvent molecules. such solvent molecules are those commonly used in the pharmaceutical art, which are known to be innocuous to the recipient, e.g., water, ethanol, and the like. the term "hydrate" refers to the complex where the solvent molecule is water. the compounds of the present invention, including salts, hydrates and solvates thereof, may inherently or by design form polymorphs.any asymmetric atom (e.g., carbon or the like) of the compound(s) of the present invention can be present in racemic or enantiomerically enriched, for example the (r)-, (s)- or (r,s)-configuration. in certain embodiments, each asymmetric atom has at least 50 percent enantiomeric excess, at least 60 percent enantiomeric excess, at least 70 percent enantiomeric excess, at least 80 percent enantiomeric excess, at least 90 percent enantiomeric excess, at least 95 percent enantiomeric excess, or at least 99 percent enantiomeric excess in the (r)- or (s)-configuration. substituents at atoms with unsaturated double bonds may, if possible, be present in cis-(z)- or trans-(e)-form.accordingly, as used herein a compound of the present invention can be in the form of one of the possible isomers, rotamers, atropisomers, tautomers or mixtures thereof, for example, as substantially pure geometric (cis or trans) isomers, diastereomers, optical isomers (antipodes), racemates or mixtures thereof.any resulting mixtures of isomers can be separated on the basis of the physicochemical differences of the constituents, into the pure or substantially pure geometric or optical isomers, diastereomers, racemates, for example, by chromatography and/or fractional crystallization.any resulting racemates of final products or intermediates can be resolved into the optical antipodes by known methods, e.g., by separation of the diastereomeric salts thereof, obtained with an optically active acid or base, and liberating the optically active acidic or basic compound. in particular, a basic moiety may thus be employed to resolve the compounds of the present invention into their optical antipodes, e.g., by fractional crystallization of a salt formed with an optically active acid, e.g., tartaric acid, dibenzoyl tartaric acid, diacetyl tartaric acid, di-o,o'-p-toluoyl tartaric acid, mandelic acid, malic acid or camphor-10-sulfonic acid. racemic products can also be resolved by chiral chromatography, e.g., high pressure liquid chromatography (hplc) using a chiral adsorbent.in certain embodiments, compounds of formula (i) or formula (ii) are prepared as their individual stereoisomers. in other embodiments, the compounds of formula (i) or formula (ii) provided herein are prepared as their individual stereoisomers by reacting a racemic mixture of the compound with an optically active resolving agent to form a pair of diastereoisomeric compounds, separating the diastereomers and recovering the optically pure enantiomers. in certain embodiments, resolution of enantiomers is carried out using covalent diastereomeric derivatives of the compounds of formula (i) or formula (ii), or by using dissociable complexes (e.g., crystalline diastereomeric salts). diastereomers have distinct physical properties (e.g., melting points, boiling points, solubility, reactivity, etc.) and are readily separated by taking advantage of these dissimilarities. in certain embodiments, the diastereomers are separated by chromatography, or by separation/resolution techniques based upon differences in solubility. the optically pure enantiomer is then recovered, along with the resolving agent, by any practical means that would not result in racemization. a more detailed description of the techniques applicable to the resolution of stereoisomers of compounds from their racemic mixture can be found in jean jacques, andre collet, samuel h. wilen, "enantiomers, racemates and resolutions," john wiley and sons, inc., 1981.mixtures of isomers obtainable according to the invention can be separated in a manner known to those skilled in the art into the individual isomers diastereoisomers can be separated, for example, by partitioning between polyphasic solvent mixtures, recrystallisation and/or chromatographic separation, for example over silica gel or by e.g. medium pressure liquid chromatography over a reversed phase column, and racemates can be separated, for example, by the formation of salts with optically pure salt-forming reagents and separation of the mixture of diastereoisomers so obtainable, for example by means of fractional crystallisation, or by chromatography over optically active column materials.depending on the choice of the starting materials and procedures, certain embodiments of the compounds of the present invention are present in the form of one of the possible isomers or as mixtures thereof, for example as pure optical isomers, or as isomer mixtures, such as racemates and diastereoisomer mixtures, depending on the number of asymmetric carbon atoms. the present invention is meant to include all such possible isomers, including racemic mixtures, diastereomeric mixtures and optically pure forms. optically active (r)- and (s)-isomers may be prepared using chiral synthons or chiral reagents, or resolved using conventional techniques. if the compound contains a double bond, the substituent may be e or z configuration. if the compound contains a disubstituted cycloalkyl, the cycloalkyl substituent may have a cis- or trans-configuration. all tautomeric forms are also intended to be included.compounds of formula (i) or formula (ii) are made by processes described herein and as illustrated in the examples. intermediates and final products can be worked up and/or purified according to standard methods, e.g. using chromatographic methods, distribution methods, (re-) crystallization, and the like. the invention relates also to those forms of the process in which a compound obtainable as an intermediate at any stage of the process is used as starting material and the remaining process steps are carried out, or in which a starting material is formed under the reaction conditions or is used in the form of a derivative, for example in a protected form or in the form of a salt, or a compound obtainable by the process according to the invention is produced under the process conditions and processed further in situ. all starting materials, building blocks, reagents, acids, bases, dehydrating agents, solvents and catalysts utilized to synthesize the compounds of the present invention are either commercially available or can be produced by organic synthesis methods known to one of ordinary skill in the art.non-limiting examples of synthetic schemes used to make compounds of the invention are illustrated in reaction schemes (i)-(iv). the r₁, r₂₀, r₁₁ and r₂ groups as defined herein.scheme (i) illustrates the synthesis of compounds of formula (i) by coupling the amine with the carboxylic acid in the presence of a base and a coupling reagent. by way of example only, the coupling reagent is hatu and the base is diisopropylethylamine.[ftimg=68000047]scheme (ii) illustrates the synthesis of compounds of formula (ii) by coupling the amine with the carboxylic acid in the presence of a base and a coupling reagent. by way of example only, the coupling reagent is hatu and the base is diisopropylethylamine.[ftimg=68000048]scheme (iii) illustrates the synthesis of compounds of formula (i) by formation of the oxadiazole from the corresponding n'-hydroxyformimidamide and carboxylic acid.[ftimg=68000049]scheme (iv) illustrates the synthesis of compounds of formula (ii) by formation of the oxadiazole from the corresponding n'-hydroxyformimidamide and carboxylic acid.[ftimg=68000050]the examples provided herein are offered to illustrate, but not to limit, the compounds of formula (i) or formula (ii) provided herein, and the preparation of such compounds.pharmacology and utilityprotein tyrosine kinases (ptk) play a central role in the regulation of a wide variety of cellular processes and maintaining control over cellular function. protein kinases catalyze and regulate the process of phosphorylation, whereby the kinases covalently attach phosphate groups to proteins or lipid targets in response to a variety of extracellular signals. examples of such stimuli include hormones, neurotransmitters, growth and differentiation factors, cell cycle events, environmental stresses and nutritional stresses. an extracellular stimulus may affect one or more cellular responses related to cell growth, migration, differentiation, secretion of hormones, activation of transcription factors, muscle contraction, glucose metabolism, control of protein synthesis, and regulation of the cell cycle.many diseases are associated with abnormal cellular responses triggered by protein kinase-mediated events. these diseases include, but are not limited to, autoimmune diseases, inflammatory diseases, bone diseases, metabolic diseases, neurological and neurodegenerative diseases, cancer, cardiovascular diseases, respiratory diseases, allergies and asthma, alzheimer's disease, and hormone-related diseases.examples of protein-tyrosine kinases include, but are not limited to, (a) tyrosine kinases such as irk, igfr-1, zap-70, bmx, btk, chk (csk homologous kinase), csk (c-terminal src kinase), itk-1, src (c-src, lyn, fyn, ick, syk, hck, yes, blk, fgr and frk), tec, txk/rlk, abl, egfr (egfr-1/erb-1, erb-2/neu/her-2, erb-3 and erb-4), fak, fgfr1r (also fgfr1 or fgr-1), fgfr2r (also fgr-2), met (also met-i or c-met), pdgfr (a and beta), tie-1, tie-2 (also tek-1 or tek), vegfr1 (also flt-1), vegfr2 (also kdr), flt-3, flt-4, c-kit, jak1, jak2, jak3, tyk2, lok, ret, trka, pyk2, alk (anaplastic lymphoma kinase), epha (1-8), ephb (1-6), ron, fes, fer or ephb4 (also ephb4-1), and (b) and serine/threonine kinases such as aurora, c-raf, sgk, map kinases (e.g., mkk4, mkk6, etc.), sapk2a, sapk2 beta, ark, atm (1-3), camk (1-iv), camkk, chk1 and 2 (checkpoint kinases), ck1, ck2, erk, ikk-i (also ikk-a or chuk), ikk-2 (also ikk- beta), ilk, jnk (1-3), limk (1 and 2), mlk3raf (a, b, and c), cdk (1-10), pkc (including all pkc subtypes), plk (1-3), nik, pak (1-3), pdk1, pkr, rhok, rip, rip-2, gsk3 (a and beta), pka, p38, erk (1-3), pkb (including all pkb subtypes) (also akt-1, akt-2, akt-3 or akt3-1), irki, frk, sgk, tak1 and tp1-2 (also cot).phosphorylation modulates or regulates a variety of cellular processes such as proliferation, growth, differentiation, metabolism, apoptosis, motility, transcription, translation and other signaling processes. aberrant or excessive ptk activity has been observed in

many disease states including, but not limited to, benign and malignant proliferative disorders, diseases resulting from inappropriate activation of the immune system and diseases resulting from inappropriate activation of the nervous systems. specific diseases and disease conditions include, but are not limited to, autoimmune disorders, allograft rejection, graft vs. host disease, diabetic retinopathy, choroidal neovascularization due to age-related macular degeneration, psoriasis, arthritis, osteoarthritis, rheumatoid arthritis, synovial pannus invasion in arthritis, multiple sclerosis, myasthenia gravis, diabetes mellitus, diabetic angiopathy, retinopathy of prematurity, infantile hemangiomas, non-small cell lung, bladder and head and neck cancers, prostate cancer, breast cancer, ovarian cancer, gastric and pancreatic cancer, psoriasis, fibrosis, rheumatoid arthritis, atherosclerosis, stenosis, auto-immune disease, allergy, respiratory diseases, asthma, transplantation rejection, inflammation, thrombosis, retinal vessel proliferation, inflammatory bowel disease, crohn's disease, ulcerative colitis, bone diseases, transplant or bone marrow transplant rejection, lupus, chronic pancreatitis, cachexia, septic shock, fibroproliferative and differentiative skin diseases or disorders, central nervous system diseases, neurodegenerative diseases, disorders or conditions related to nerve damage and axon degeneration subsequent to brain or spinal cord injury, acute or chronic cancer, ocular diseases, viral infections, heart disease, lung or pulmonary diseases or kidney or renal diseases and bronchitis. tyrosine kinases can be broadly classified as receptor-type (having extracellular, transmembrane and intracellular domains) or the non-receptor type (being wholly intracellular) protein tyrosine kinases. tyrosine kinases transfer the terminal phosphate of atp to tyrosine residues of proteins thereby activating or inactivating signal transduction pathways. inappropriate or uncontrolled activation of many of these kinase (aberrant protein tyrosine kinase activity), for example by over-expression or mutation, results in uncontrolled cell growth. many of the protein tyrosine kinases, whether a receptor or non-receptor tyrosine kinase have been found to be involved in cellular signaling pathways involved in numerous pathogenic conditions, including, but not limited to, immunomodulation, inflammation, or proliferative disorders such as cancer. ckitmast cells are tissue elements derived from a particular subset of hematopoietic stem cells that express cd34, c-kit and cd13 antigens. mast cells are characterized by their heterogeneity, not only regarding tissue location and structure but also at the functional and histochemical levels. immature mast cell progenitors circulate in the bloodstream and differentiate into various tissues. these differentiation and proliferation processes are under the influence of cytokines, one of importance being stem cell factor (scf), also termed c-kit ligand, steel factor or mast cell growth factor. the stem cell factor receptor is encoded by the protooncogene, c-kit, which is expressed in hematopoietic progenitor cells, mast cells, germ cells, interstitial cells of cajal (icc), and some human tumors, and is also expressed by non hematopoietic cells. stem cell factor (scf), also known as c-kit ligand, is the primary regulating factor for human mast cell growth and function. the scf receptor, c-kit receptor, is a type ii transmembrane receptor protein tyrosine kinase which initiates cell growth and proliferation signal transduction cascades in response to scf binding. ligation of c-kit receptor by scf induces its dimerization followed by its transphosphorylation, leading to the recruitment and activation of various intracytoplasmic substrates. these activated substrates induce multiple intracellular signaling pathways responsible for cell proliferation and activation. these proteins are known to be involved in many cellular mechanisms, which in case of disruption, lead to disorders such as abnormal cell proliferation and migration, as well as inflammation. the relationship between mast cells, scf and c-kit receptor is discussed in the following references: huang, e. et al., "the hematopoietic growth factor kl is encoded by the sl locus and is the ligand of the c-kit receptor, the gene product of the w locus", cell, 63, 225-233, 1990 zsebo, k. m. et al., "stem cell factor is encoded at the sl locus of the mouse and is the ligand for the c-kit tyrosine kinase receptor", cell, 63, 213-224, 1990 zhang, s. et al., "cytokine production by cell cultures from bronchial subepithelial myofibroblasts", j. pathol., 180, 95-10, 1996 zhang, s. et al., "human mast cells express stem cell factor", j. pathol., 186, 59-66, 1998 kassel, o. et al., "up and down-regulation by glucocorticoids of the constitutive expression of the mast cell growth factor stem cell factor by human lung fibroblasts in culture", 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cell. biol., 14, 8432-8437, 1994, and ueda. s. et al., "critical roles of c-kit tyrosine residues 567 and 719 in stem cell factor-induced chemotaxis: contribution of src family kinase and pi3-kinase on calcium mobilization and cell migration", blood, 99, 3342-3349, 2002. mast cells are the primary effector cells in allergic inflammation. mast cells are also involved in other pathogenic processes such as acute inflammation and fibrosis. mast cells present in tissues of patients are implicated in or contribute to the genesis of diseases such as autoimmune diseases (multiple sclerosis, rheumatoid arthritis, inflammatory bowel diseases (ibd)), allergic diseases (allergic rhinitis, allergic sinusitis, anaphylactic syndrome, urticaria, angioedema, atopic dermatitis, allergic contact dermatitis, erythema nodosum, erythema multiforme, cutaneous necrotizing venulitis and insect bite skin inflammation and bronchial asthma), tumor angiogenesis, germ cell tumors, mast cell tumors, gastrointestinal stromal tumors, small-cell lung cancer, melanoma, breast cancer, acute myelogenous leukemia, glioblastoma, neuroblastoma and mastocytosis, inflammatory diseases, diabetes, type i diabetes, type ii diabetes, irritable bowel syndrome (ibs), cns disorders and interstitial cystitis. in these diseases, mast cells participate in the destruction of tissues by releasing a cocktail of different proteases and mediators categorized into three groups: preformed granule-associated mediators (histamine, proteoglycans, and neutral proteases), lipid-derived mediators (prostaglandins, thromboxanes and leukotrienes), and various cytokines ((il-1, il-2, il-3, il-4, il-5, il-6, il-8, tnfr-a, gm-csf, mip-la, mip-i beta, mip-2 and ifn-gamma). the liberation by activated mast cells of mediators (tnfr-a, histamine, leukotrienes, prostaglandins etc.) as well as proteases may i) induce inflammation and vasodilatation and ii) participate in the tissue destruction process. in addition, mast cell activation induces diverse effector responses, such as secretion of allergic mediators, proteases, chemokines such as mcp-1 and rantes, leukotrienes, prostaglandins and neurotrophins and induction of cytokine gene transcription (il-4, il-5, il-6, il-13, tnfr-a and gm-csf). these mediators contribute to creating the asthmatic phenotype by their effects on endothelial cells, smooth muscle cells and fibroblasts and on extracellular matrix, and by recruiting other inflammatory cells. asthma is characterized by airflow obstruction, bronchial hyper responsiveness and airway inflammation. airway inflammation is the major factor in the development and perpetuation of asthma. in allergic asthma, allergens are thought to initiate the inflammatory process by inducing a t-lymphocyte mediated response (th2) that results in the production of allergen-specific ige. ige binds to its high-affinity receptor fc epsilon r1 on pulmonary mast cells, triggering a type i (ige-mediated) immediate allergic response. thus, mast cells play a role in asthma. the activation of mast cells by different stimuli such as stress, trauma, infection and neurotransmitters, also participate in the exacerbation of the chemical imbalance causing cns disorders. more specifically, mast cell degranulation is stimulated by common neurotransmitters such as neurotensin, somatostatin, substance p and acetylcholine, by growth or survival factors, notably such as ngf. mast cells involved in the response to such stimulus can be brain mast cells but also other mast cells releasing the content of their granules in the blood stream that ultimately reach sensory, motor or brain neurons. following mast cells activation, released granules liberate various factors capable of modulating and altering neurotransmission and neurons survival. among such factors, serotonin is important since an increase of the level of free serotonin has been observed in depressed patients. alternatively, the sudden burst of serotonin may be followed by a period of serotonin shortage, leading to pain and migraine. as a consequence, it is believed that mast cells exacerbate in autocrine or paracrine manner the deregulation of neurotransmission. for example, anxiety or stress-induced release of neurotransmitters such as serotonin activates mast cells, which in turn release the content of their granules, further contributing to the chemical imbalance in the brain leading to cns disorders. other mediators released by mast cells can be categorized into vasoactive, nociceptive, proinflammatory and other neurotransmitters. taken together, these factors are able to induce disturbance in the activity of neurons, whether they are sensory, motor, or cns neurons. in addition, patients afflicted with mastocytosis are more inclined to develop cns disorders than the normal population. this can be explained by the presence of activating mutations in the c-kit receptor, which induce degranulation of mast cells and a burst of factors contributing to chemical imbalance and neurotransmission alteration. the activation of mast cells by different drugs, including, but not limited to, salicylic derivatives, morphine derivatives, opioids, heroin, amphetamines, alcohol, nicotine, analgesics, anesthetics, and anxiolytics results in the degranulation of mast cells, which participate in the exacerbation of the chemical imbalance responsible for drug habituation and withdrawal syndrome. following mast cells activation, released granules liberate various factors capable of modulating and altering neurotransmission. among such factors is morphine which is bound or stored in mast cells granules. tobacco smoke also induces the release of mediators from canine mast cells and modulates prostaglandin production leading to asthma. in addition, patients afflicted with mastocytosis are more inclined to develop substance use disorders than the normal population. this can be explained by the presence of activating mutations in the c-kit receptor, which induce degranulation of mast cells and a burst of factors contributing to chemical imbalance and neurotransmission alteration. mast cells have also been identified to be involved in or to contribute to drug dependence and withdrawal symptoms. the relationship between mast cells, scf and c-kit kinase in various diseases is discussed in the following references: oliveira et al., "stem cell factor: a hemopoietic cytokine with important targets in asthma", current drug targets, 2: 313-318, 2003 puxeddu et al., "mast cells in allergy and beyond", the international journal of biochemistry and cell biology, 35: 1601-1607, 2003 rottem et al., "mast cells and autoimmunity", autoimmune reviews, 4: 21-27, 2005 woolley, d. e. et al., "the mast cell in inflammatory arthritis", n. engl. j. med., 348:1709-1711, 2003 benoist, c. et al., "mast cells in autoimmune disease", nature, 420:875-878, 2002 nigrovic, p. a. et al., "mast cells in inflammatory arthritis", arthritis res. ther., 7:1-11, 2005 wang, 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cells, and the normal functional activity of this c-kit gene product is important for the maintenance of normal hematopoiesis, melanogenesis, genotogenesis, and growth and differentiation of mast cells. inhibition of c-kit kinase activity reduces the growth and differentiation of mast cells and thereby mediates the diseases and/or conditions associated with mast cells, such as autoimmune diseases, multiple sclerosis, rheumatoid arthritis, inflammatory bowel diseases (ibd), respiratory diseases, allergic diseases, allergic rhinitis, allergic sinusitis, anaphylactic syndrome, urticaria, angioedema, atopic dermatitis, allergic contact dermatitis, erythema nodosum, erythema multiforme, cutaneous necrotizing venulitis and insect bite skin inflammation, bronchial asthma, tumor angiogenesis, germ cell tumors, mast cell tumors, gastrointestinal stromal tumors, small-cell lung cancer, melanoma, breast cancer, acute myelogenous leukemia, glioblastoma, neuroblastoma and mastocytosis, inflammatory diseases, diabetes, type i diabetes, type ii diabetes, irritable bowel syndrome (ibs), cns disorders and interstitial cystitis in addition to its importance in normal cellular physiologic activities, c-kit kinase plays a role in the biological aspects of certain human cancers, and unregulated c-kit kinase activity is implicated in the pathogenesis of human cancers, and in certain tumors types. proliferation of tumor cell growth mediated by c-kit can occur by a specific mutation of the c-kit polypeptide that results in ligand independent activation or by autocrine stimulation of the receptor. in the former case, mutations that cause constitutive activation of c-kit kinase activity in the absence of scf binding are implicated in malignant human cancers, including germ cell tumors, mast cell tumors, gastrointestinal stromal tumors, small-cell lung cancer, melanoma, breast cancer, acute myelogenous leukemia, glioblastoma, neuroblastoma and mastocytosis. a proliferation assay for the evaluation of the efficacy of c-kit inhibitors and pdgfr inhibitors is given in kuriu et al., "proliferation of human myeloid leukemia cell line associated with the tyrosine-phosphorylation and activation of the proto-oncogene c-kit product", blood, 78(11): 2834-2840, 1991 heinrich et al., "inhibition of c-kit receptor tyrosine kinase activity by sti571, a selective tyrosine kinase inhibitor", blood, 96(3): 925-932, 2000 buchdunger et al., "abl protein-tyrosine kinase inhibitor sti571 inhibits in vitro signal transduction mediated by c-kit and platelet-derived growth factor receptors", the journal of pharmacology and experimental therapeutics, 295(1): 139-145,

2000 and simlich et al., "the antiangiogenic protein kinase inhibitors su5416 and su6668 inhibit the sce receptor (c-kit) in a human myeloid leukemia cell line and in acute myeloid leukemia blasts", blood, 97(5): 1413-1421, 2001. this assay use mo7e cells, which are a human promegakaryocytic leukemia cell line that depend on scf for proliferation. these references in combination with berlin et al., ekland et al., and miyachi et al., (cited above) show that that a c-kit kinase inhibitor screened via this proliferation assay was later found to treat rheumatoid arthritis and asthma.in addition, a compound that was initially evaluated for its efficacy as a c-kit inhibit) using a proliferation assay based on ba/f3 cells and ba/f3-derived cells (see wo 2004/01903) was later found to be effective in the treatment of mast cell tumours and asthma (see bellamy f, et al., "pharmacokinetics of mastinib in cats", vet. res. commun., june 16 (epub) 2009 hahn k. a. et al., "mastinib is safe and effective for treatment of canine mast cell tumours, j. vet. intern. med., 22, 1301-1309, 2008 and humbert m. et al., "mastinib, a c-kit/pdgfr receptor tyrosine kinase inhibitor, improves disease control in severe corticosteroid-dependent asthmatics", 64, 1194-1201, 2009. c-kit receptor has a substantial homology to the pdgf receptor and to the csf-1 receptor (c-fms).platelet-derived growth factor (pdgf) receptor familypdgf (platelet-derived growth factor) is commonly occurring growth factor which plays an important role both in normal growth and in pathological cell proliferation. by way of example, such as that observed in carcinogenesis and in diseases of the smooth-muscle cells of blood vessels, for example in atherosclerosis and thrombosis. the pdgf growth factor family consists of pdgf-a, pdgf-b, pdgf-c and pdgf-d, which form either homo- or heterodimers (aa, ab, bb, cc, dd) that bind to the protein tyrosine kinase receptors pdgfr-a and pdgfr- beta. dimerization of the growth factors is a prerequisite for activation of the kinase, as the monomeric forms are inactive. the two receptor isoforms dimerize upon binding resulting in three possible receptor combinations, pdgfr-aa, pdgfr- beta beta and pdgfra beta. growth factor aa binds only to -aa, growth factor bb can bind with -aa, - beta beta and -a beta, growth factors cc and ab specifically interact with -aa and -a beta, and growth factor dd binds to - beta beta pp. the pdgf-receptor plays an important role in the maintenance, growth and development of hematopoietic and non-hematopoietic cells.key downstream mediators of pdgf signaling are ras/mitogen-activated protein kinase (mapk), pi-3 kinase and phospholipase-gamma (plcgamma) pathways. mapk family members regulate various biological functions by phosphorylation of target molecules (transcription factors and other kinases) and thus contribute to regulation of cellular processes such as proliferation, differentiation, apoptosis and immunoresponses. pi-3 kinase activation generated pip3 which functions as a second messenger to activate downstream tyrosine kinases btk and itk, the ser/thr kinases pdk1 and akt (pkb). akt activation is involved in survival, proliferation and cell growth. after activation plc hydrolyses its substrate, ptdlns(4,5)p2, and forms two secondary messengers, diacylglycerol and ins(1,4,5)p3 which stimulates intracellular processes such as proliferation, angiogenesis and cell motility.pdgfr is expressed on early stem cells, mast cells, myeloid cells, mesenchymal cells and smooth muscle cells. only pdgfr- beta is implicated in myeloid leukemias-usually as a translocation partner with tel, huntingtin interacting protein (hip1) or rabaptin5. activation mutations in pdgfr-a kinase domain are associated with gastrointestinal stromal tumors (gist).certain embodiments of compounds of formula (i) and formula (ii) provided herein inhibit pdgf receptor (pdgfra and pdgfrp) activity and c-kit kinase activity, and are useful for the treatment of diseases, which respond to an inhibition of the pdgf receptor kinase. therefore, certain compounds of formula (i) and formula (ii) provided herein are useful for the treatment of tumor diseases, such as gliomas, sarcomas, prostate tumors, small cell lung cancer and tumors of the colon, breast, and ovary. in addition certain embodiments of compounds of formula (i) and formula (ii) provided herein are useful to treat disorders, such as thrombosis, psoriasis, scleroderma, fibrosis, asthma, metabolic diseases and hyper eosinophilia. compounds of formula (i) and formula (ii) provided herein are also effective against diseases associated with vascular smooth-muscle cell migration and proliferation, such as restenosis and atherosclerosis.patients with obliterative bronchiolitis (ob), a chronic rejection of allogenic lung transplants, often show an elevated pdgf concentration in bronchoalveolar lavage fluids. in certain embodiments, compounds of formula (i) and formula (ii) provided herein exhibit useful effects in the treatment of disorders arising as a result of transplantation, for example, allogenic transplantation, especially tissue rejection, such as obliterative bronchiolitis (ob).in certain embodiments, compounds of formula (i) and formula (ii) provided herein are useful for the protection of stem cells, for example to combat the hemotoxic effect of chemotherapeutic agents, such as 5-fluorouracil.the compounds of formula (i) and formula (ii) provided herein, and the pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, are inhibitors of c-kit kinase activity and pdgfr (a and beta) kinase activity. in certain embodiments, the compounds of formula (i) and formula (ii) provided herein, and the pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, are inhibitors of c-kit kinase activity and pdgfr (a and beta) kinase activity. in other embodiments, the compounds of formula (i) and formula (ii) provided herein, and the pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, are inhibitors of either c-kit kinase activity. such compounds of formula (i) and formula (ii) provided herein, and the pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, are useful for treating diseases or disorders in which c-kit kinase, or c-kit and pdgfr (a and/or beta) kinase, contributes to the pathology and/or symptomology of a disease or disorder. such diseases or disorders include, but are not limited to, a mast cell associated disease, inflammatory diseases, respiratory diseases, an allergy disorder, fibrosis diseases, metabolic diseases, autoimmune diseases, a cns related disorder, a neurodegenerative disorder, neurological diseases, dermatological diseases, a graft-versus-host disease, a pain condition, a neoplastic disorder, a cardiovascular disease and cancer.non-limiting examples of such diseases include asthma, allergic rhinitis, allergic sinusitis, bronchial asthma, irritable bowel syndrome (ibs), inflammatory bowel disease (ibd), pulmonary arterial hypertension (pah), idiopathic arterial hypertension (ipah), primary pulmonary hypertension (pph), pulmonary fibrosis, liver fibrosis, cardiac fibrosis, scleroderma, urticaria, dermatoses, atopic dermatitis, allergic contact dermatitis, diabetes, type i diabetes, type ii diabetes, rheumatoid arthritis, multiple sclerosis, cytopenias (by way of example only, anemia, leucopenia, neutropenia, thrombocytopenia, granulocytopenia, pancytopenia and idiopathic thrombocytopenic purpura), systemic lupus erythematosus, chronic obstructive pulmonary disease (copd), adult respiratory distress syndrome (ards), ulcerative colitis, crohns disease, psoriasis, lymphomas (by way of example only, b and t cell lymphomas), myelodysplastic syndrome, breast cancer, pancreatic cancer, papillary thyroid carcinoma, ovarian carcinoma, human adenoid cystic carcinoma, non small cell lung cancer, secretory breast carcinoma, congenital fibrosarcoma, congenital mesoblastic nephroma, acute myelogenous leukemia, chronic myeloid leukemia metastasis, cancer-related pain, neuroblastoma, osteosarcoma, melanoma, bone metastases, a tumor of breast, renal, lung, prostate, pancreas, colon, ovary, thyroid, colorectal tumors, neuronal tumors, uterine tumors, gastrointestinal stromal tumors (gist), gliomas, sarcomas, tumor angiogenesis, germ cell tumors, mast cell tumors, glioblastoma, neuroblastoma, mastocytosis, osteoporosis, hyper eosinophilia, restenosis, atherosclerosis, anaphylactic syndrome, angioedema, erythema nodosum, erythema multiforme, cutaneous necrotizing venulitis, insect bite skin inflammation, cns disorders and interstitial cystitis.in certain embodiments, the compounds of formula (i) and formula (ii) provided herein, and the pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, are useful for treating diseases or disorders in which c-kit kinase contributes to the pathology and/or symptomology of a disease or disorder. non-limiting examples of such diseases include asthma, allergic rhinitis, allergic sinusitis, bronchial asthma, irritable bowel syndrome (ibs), inflammatory bowel disease (ibd), pulmonary arterial hypertension (pah), pulmonary fibrosis, liver fibrosis, cardiac fibrosis, scleroderma, urticaria, dermatoses, atopic dermatitis, allergic contact dermatitis, diabetes, type i diabetes, type ii diabetes, rheumatoid arthritis, multiple sclerosis, cytopenias (by way of example only, anemia, leucopenia, neutropenia, thrombocytopenia, granulocytopenia, pancytopenia and idiopathic thrombocytopenic purpura), systemic lupus erythematosus, chronic obstructive pulmonary disease (copd), adult respiratory distress syndrome (ards), ulcerative colitis, crohns disease, psoriasis, lymphomas (by way of example only, b and t cell lymphomas), myelodysplastic syndrome, breast cancer, pancreatic cancer, papillary thyroid carcinoma, ovarian carcinoma, human adenoid cystic carcinoma, non small cell lung cancer, secretory breast carcinoma, congenital fibrosarcoma, congenital mesoblastic nephroma, acute myelogenous leukemia, chronic myeloid leukemia metastasis, cancer-related pain, neuroblastoma, osteosarcoma, melanoma, bone metastases, a tumor of breast, renal, lung, prostate, pancreas, colon, ovary, thyroid, colorectal tumors, neuronal tumors, uterine tumors, gastrointestinal stromal tumors (gist), gliomas, sarcomas, tumor angiogenesis, germ cell tumors, mast cell tumors, glioblastoma, neuroblastoma, mastocytosis, osteoporosis, hyper eosinophilia, restenosis, atherosclerosis, anaphylactic syndrome, angioedema, erythema nodosum, erythema multiforme, cutaneous necrotizing venulitis, insect bite skin inflammation, cns disorders and interstitial cystitis.in certain embodiments, the compounds of formula (i) and formula (ii) provided herein, and the pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, are useful for treating diseases or disorders in which c-kit kinase and pdgfr (a and/or p) kinase contribute to the pathology and/or symptomology of a disease or disorder. non-limiting examples of such diseases include asthma, allergic rhinitis, allergic sinusitis, bronchial asthma, irritable bowel syndrome (ibs), inflammatory bowel disease (ibd), pulmonary arterial hypertension (pah), pulmonary fibrosis, liver fibrosis, cardiac fibrosis, scleroderma, urticaria, dermatoses, atopic dermatitis, allergic contact dermatitis, diabetes, type i diabetes, type ii diabetes, rheumatoid arthritis, multiple sclerosis, cytopenias (by way of example only, anemia, leucopenia, neutropenia, thrombocytopenia, granulocytopenia, pancytopenia and idiopathic thrombocytopenic purpura), systemic lupus erythematosus, chronic obstructive pulmonary disease (copd), adult respiratory distress syndrome (ards), ulcerative colitis, crohns disease, psoriasis, lymphomas (by way of example only, b and t cell lymphomas), myelodysplastic syndrome, breast cancer, pancreatic cancer, papillary thyroid carcinoma, ovarian carcinoma, human adenoid cystic carcinoma, non small cell lung cancer, secretory breast carcinoma, congenital fibrosarcoma, congenital mesoblastic nephroma, acute myelogenous leukemia, chronic myeloid leukemia metastasis, cancer-related pain, neuroblastoma, osteosarcoma, melanoma, bone metastases, a tumor of breast, renal, lung, prostate, pancreas, colon, ovary, thyroid, colorectal tumors, neuronal tumors, uterine tumors, gastrointestinal stromal tumors (gist), gliomas, sarcomas, tumor angiogenesis, germ cell tumors, mast cell tumors, glioblastoma, neuroblastoma, mastocytosis, osteoporosis, hyper eosinophilia, restenosis, atherosclerosis, anaphylactic syndrome, angioedema, erythema nodosum, erythema multiforme, cutaneous necrotizing venulitis, insect bite skin inflammation, cns disorders and interstitial cystitis.another aspect provided herein includes methods for treating a cell-proliferative disease, comprising administering to a system or subject in need of such treatment an effective amount of a compound of formula (i) and formula (ii), or pharmaceutically acceptable salts or pharmaceutical compositions thereof wherein the cell-proliferative disease is lymphoma, osteosarcoma, melanoma, or a tumor of breast, renal, prostate, colorectal, thyroid, ovarian, pancreatic, neuronal, lung, uterine or gastrointestinal tumor.in certain embodiments, the compounds of formula (i) and formula (ii), pharmaceutically acceptable salts, solvates, n-oxides and isomers thereof, pharmaceutical compositions, and/or combinations provided herein are used in the treatment diseases and/or disorders including, but not limited to, asthma, bronchial asthma, allergic asthma, intrinsic asthma, extrinsic asthma, exercise-induced asthma, drug-induced asthma (including aspirin and nsaid-induced) and dust-induced asthma, chronic obstructive pulmonary disease (copd) bronchitis, including infectious and eosinophilic bronchitis emphysema bronchiectasis cystic fibrosis sarcoidosis farmers lung and related diseases hypersensitivity pneumonitis lung fibrosis, including cryptogenic fibrosing alveolitis, idiopathic interstitial pneumonias, fibrosis complicating anti-neoplastic therapy and chronic infection, including tuberculosis and aspergillosis and other fungal infections complications of lung transplantation vasculitic and thrombotic disorders of the lung vasculature, and pulmonary hypertension antitussive activity including treatment of chronic cough associated with inflammatory and secretory conditions of the airways, and iatrogenic cough acute and chronic rhinitis including rhinitis medicamentosa, and vasomotor rhinitis perennial and seasonal allergic rhinitis including rhinitis nervosa (hay fever) nasal polyposis acute viral infection including the common cold, and infection due to respiratory syncytial virus, influenza, coronavirus (including sars) and adenovirus.in certain embodiments, the compounds of formula (i) and formula (ii), pharmaceutically acceptable salts, solvates, n-oxides and isomers thereof, pharmaceutical compositions, and/or combinations provided herein are used in the treatment of dermatological disorders including, but not limited to, psoriasis, atopic dermatitis, contact dermatitis or other eczematous dermatoses, and delayed-type hypersensitivity reactions phyto- and photodermatitis seborrheic dermatitis, dermatitis herpetiformis, lichen planus, lichen sclerosis et atrophica, pyoderma gangrenosum, skin sarcoid, basal cell carcinoma, actinic keratosis, discoid lupus erythematosus, pemphigus, pemphigoid, epidermolysis bullosa, urticaria, angioedema, vasculitides, toxic erythemas, cutaneous eosinophilias, alopecia areata, male-pattern baldness, sweet's syndrome, weber-christian syndrome, erythema multiforme cellulitis, both infective and non-infective panniculitis cutaneous lymphomas, non-melanoma skin cancer and other dysplastic lesions drug-induced disorders including fixed drug eruptions.in certain embodiments, the compounds of formula (i) and formula (ii), pharmaceutically acceptable salts, solvates, n-oxides and isomers thereof, pharmaceutical compositions, and/or combinations provided herein are used in the treatment of rheumatoid arthritis, irritable bowel syndrome, systemic lupus erythematosus, multiple sclerosis, hashimoto's thyroiditis, crohns disease, inflammatory bowel disease (ibd), graves' disease, addison's disease, diabetes mellitus, idiopathic thrombocytopenic purpura, eosinophilic fasciitis, hyper-ige syndrome, antiphospholipid syndrome and sazary syndrome.in certain embodiments, the compounds of formula (i) and formula (ii), pharmaceutically acceptable salts, solvates, n-oxides and isomers thereof, and pharmaceutical compositions provided herein are used in the treatment of cancer including, but not limited to, prostate, breast, lung, ovarian, pancreatic, bowel and colon, stomach, skin and brain tumors and malignancies affecting the bone marrow (including the leukaemias) and lymphoproliferative systems, such as hodgkin's and non-hodgkin's lymphoma including the prevention and treatment of metastatic disease and tumor recurrences, and paraneoplastic syndromes.provided herein are compounds of formula (i) and formula (ii), pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, and pharmaceutical compositions containing at least one compound of formula (i) or formula (ii), or pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers or mixture of isomers thereof, for use in activating c-kit kinase activity, or c-kit kinase and pdgfr (a and/or p) kinase activity, and thereby are used to in the prevention or treatment of diseases and/or disorders associated with c-kit kinase activity, or c-kit kinase and pdgfr (a and/or p) kinase activity.also provided herein are methods for the treatment of a subject suffering from a disease and/or disorder associated with c-kit kinase activity, wherein the method includes administering to the subject in need thereof, an effective amount of a compound of formula (i) or formula (ii), or pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers or mixture of isomers thereof, either alone or as part of a pharmaceutical composition as described herein.also provided herein are

methods for the treatment of a subject suffering from a disease and/or disorder associated with c-kit kinase activity and pdgfr (a and/or p) kinase activity, wherein the method includes administering to the subject in need thereof, an effective amount of a compound of formula (i) or formula (ii), or pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers or mixture of isomers thereof, either alone or as part of a pharmaceutical composition as described herein, provided herein is the use of a compound of formula (i) or formula (ii), or pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers or mixture of isomers thereof, in the manufacture of a medicament for the treatment of a disease or disorder associated with c-kit kinase activity. also provided herein is the use of a compound of formula (i) or formula (ii), or pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers or mixture of isomers thereof, in the manufacture of a medicament for the treatment of a disease or disorder associated with c-kit kinase activity and pdgfr (a and/or beta) kinase activity. furthermore, provided herein is the use of a compound having formula (i) or formula (ii), or pharmaceutically acceptable salts or pharmaceutical compositions thereof, and optionally in combination with a therapeutically effective amount of a second agent, in the manufacture of a medicament for treating a disease or condition modulated by kinase activity, particularly c-kit, or c-kit and pdgfr (a and beta). in accordance with the foregoing, the present invention further provides a method for preventing or treating any of the diseases or disorders described above in a subject in need of such treatment, which method comprises administering to said subject a therapeutically effective amount of a compound of formula (i) or formula (ii), or a pharmaceutically acceptable salt thereof, for any of the above uses, the required dosage will vary depending on the mode of administration, the particular condition to be treated and the effect desired. (see, "administration and pharmaceutical compositions," *infra*). administration and pharmaceutical compositions for the therapeutic uses of compounds of formula (i) and formula (ii), or pharmaceutically acceptable salts, solvates, n-oxides or isomers thereof, described herein, such compounds are administered in therapeutically effective amounts either alone or as part of a pharmaceutical composition. accordingly, provided herein are pharmaceutical compositions, which comprise at least one compound of formula (i) or formula (ii), or pharmaceutically acceptable salts solvates, n-oxides or isomers thereof, and one or more pharmaceutically acceptable carriers, diluents, or excipients. in addition, such compounds and compositions are administered singly or in combination with one or more additional therapeutic agents. the method of administration of such compounds and compositions include, but are not limited to, oral administration, rectal administration, transdermal administration, parenteral, intravenous administration, intravitreal administration, intramuscular administration, pulmonary administration, inhalation administration, intranasal administration, topical administration, ophthalmic administration or otic administration. in certain embodiments the method of administration of such compounds and compositions is oral administration. in other embodiments the method of administration of such compounds and compositions is pulmonary administration, inhalation administration or intranasal administration. the therapeutically effective amount will vary depending on, among others, the disease indicated, the severity of the disease, the age and relative health of the subject, the potency of the compound administered, the mode of administration and the treatment desired. in certain embodiments, the daily dosage of a compound of formula (i) and formula (ii), satisfactory results are indicated to be obtained systemically at daily dosages of from about 0.03 to 2.5 mg/kg per body weight. in certain embodiments, the daily dosage of a compound of formula (i) and formula (ii), administered by inhalation, is in the range from 0.05 micrograms per kilogram body weight (micro g/kg) to 100 micrograms per kilogram body weight (micro g/kg). in other embodiments, the daily dosage of a compound of formula (i) and formula (ii), administered orally, is in the range from 0.01 micrograms per kilogram body weight (micro g/kg) to 100 milligrams per kilogram body weight (mg/kg). an indicated daily dosage in the larger mammal, e.g. humans, is in the range from about 0.5 mg to about 100 mg of a compound of formula (i) and formula (ii), conveniently administered, e.g. in divided doses up to four times a day or in controlled release form. in certain embodiment, unit dosage forms for oral administration comprise from about 1 to 50 mg of a compound of formula (i) and formula (ii). other aspects provided herein are processes for the preparation of pharmaceutical composition which comprise at least one compound of formula (i) or formula (ii), or pharmaceutically acceptable salts, solvates, n-oxides or isomers thereof. in certain embodiments, such processes include admixing a compound of the formula (i) or formula (ii), or pharmaceutically acceptable salts, solvates, n-oxides or isomers thereof, with one or more pharmaceutically acceptable carriers, diluents or excipients. in certain embodiments, the pharmaceutical compositions comprising a compound of formula (i) or formula (ii) in free form, or in a pharmaceutically acceptable salt, solvate, n-oxide or isomeric form, in association with at least one pharmaceutically acceptable carrier, diluent or excipient are manufactured by mixing, granulating and/or coating methods. in other embodiments, such compositions optionally contain excipients, such as preserving, stabilizing, wetting or emulsifying agents, solution promoters, salts for regulating the osmotic pressure and/or buffers. in other embodiments, such compositions are sterilized. in certain embodiments, the pharmaceutical compositions comprising at least one compound of formula (i) or formula (ii) are adapted for oral administration for the treatment of diseases and/or disorders associated with c-kit kinase activity. in other embodiments, the pharmaceutical compositions comprising at least one compound of formula (i) or formula (ii) are adapted for oral administration for the treatment of diseases and/or disorders associated with c-kit kinase and pdgfr (a and/or p) kinase activity. in certain embodiments, the pharmaceutical compositions comprising at least one compound of formula (i) or formula (ii) are adapted for inhalation administration, including pulmonary administration, inhalation administration or intranasal administration, for the treatment of diseases and/or disorders associated with c-kit kinase activity. in other embodiments, the pharmaceutical compositions comprising at least one compound of formula (i) or formula (ii) are adapted for inhalation administration, including pulmonary administration, inhalation administration or intranasal administration, for the treatment of diseases and/or disorders associated with c-kit kinase and pdgfr (a and/or beta) kinase activity. in certain embodiments, the pharmaceutical compositions comprising at least one compound of formula (i) or formula (ii) are adapted for inhalation administration, including pulmonary administration, inhalation administration or intranasal administration, for the treatment of diseases and/or disorders associated with c-kit kinase activity. in certain embodiments, the respiratory disease is allergic rhinitis or asthma. in certain embodiments, the pharmaceutical compositions comprising at least one compound of formula (i) or formula (ii) are adapted for parenteral or intravenous administration, for the treatment of diseases and/or disorders associated with c-kit kinase activity. in other embodiments, the pharmaceutical compositions comprising at least one compound of formula (i) or formula (ii) are adapted for parenteral or intravenous administration, for the treatment of diseases and/or disorders associated with c-kit kinase and pdgfr (a and/or p) kinase activity. oral dosage forms in certain embodiments, the pharmaceutical compositions containing at least one compound of formula (i) or formula (ii) are administered orally as discrete dosage forms, wherein such dosage forms include, but are not limited to, capsules, gelatin capsules, caplets, tablets, chewable tablets, powders, granules, syrups, flavored syrups, solutions or suspensions in aqueous or non-aqueous liquids, edible foams or whips, and oil-in-water liquid emulsions or water-in-oil liquid emulsions. the capsules, gelatin capsules, caplets, tablets, chewable tablets, powders or granules, used for the oral administration of at least one compound of formula (i) and formula (ii) are prepared by admixing at least one compound of formula (i) and formula (ii) (active ingredient) together with at least one excipient using conventional pharmaceutical compounding techniques. non-limiting examples of excipients used in oral dosage forms described herein include, but are not limited to, binders, fillers, disintegrants, lubricants, absorbents, colorants, flavors, preservatives and sweeteners. non-limiting examples of such binders include, but are not limited to, corn starch, potato starch, starch paste, pre-gelatinized starch, or other starches, sugars, gelatin, natural and synthetic gums such as acacia, sodium alginate, alginic acid, other alginates, tragacanth, guar gum, cellulose and its derivatives (by way of example only, ethyl cellulose, cellulose acetate, carboxymethyl cellulose calcium, sodium carboxymethylcellulose, methyl cellulose, hydroxypropyl methylcellulose and microcrystalline cellulose), magnesium aluminum silicate, polyvinyl pyrrolidone and combinations thereof. non-limiting examples of such fillers include, but are not limited to, talc, calcium carbonate (e.g., granules or powder), microcrystalline cellulose, powdered cellulose, dextrates, kaolin, mannitol, silicic acid, sorbitol, starch, pre-gelatinized starch, and mixtures thereof. in certain embodiments, the binder or filler in pharmaceutical compositions provided herein are present in from about 50 to about 99 weight percent of the pharmaceutical composition or dosage form. non-limiting examples of such disintegrants include, but are not limited to, agar-agar, alginic acid, sodium alginate, calcium carbonate, sodium carbonate, microcrystalline cellulose, croscarmellose sodium, crospovidone, polacrillin potassium, sodium starch glycolate, potato or tapioca starch, pre-gelatinized starch, other starches, clays, other alginates, other celluloses, gums, and combinations thereof. in certain embodiments, the amount of disintegrant used in the pharmaceutical compositions provided herein is from about 0.5 to about 15 weight percent of disintegrant, while in other embodiments the amount is from about 1 to about 5 weight percent of disintegrant. non-limiting examples of such lubricants include, but are not limited to, sodium stearate, calcium stearate, magnesium stearate, stearic acid, mineral oil, light mineral oil, glycerin, sorbitol, mannitol, polyethylene glycol, other glycols, sodium lauryl sulfate, talc, hydrogenated vegetable oil (by way of example only, peanut oil, cottonseed oil, sunflower oil, sesame oil, olive oil, corn oil, and soybean oil), zinc stearate, sodium oleate, ethyl oleate, ethyl laureate, agar, silica, a syloid silica gel (aerosil 200, manufactured by w.r. grace co. of baltimore, md.), a coagulated aerosol of synthetic silica (marketed by degussa co. of plano, tex.), cab-o-sil (a pyrogenic silicon dioxide product sold by cabot co. of boston, mass.) and combinations thereof. in certain embodiments, the amount of lubricants used in the pharmaceutical compositions provided herein is in an amount of less than about 1 weight percent of the pharmaceutical compositions or dosage forms. non-limiting examples of such diluents include, but are not limited to, lactose, dextrose, sucrose, mannitol, sorbitol, cellulose, glycine or combinations thereof. in certain embodiments, tablets and capsules are prepared by uniformly admixing at least one compound of formula (i) or formula (ii) (active ingredients) with liquid carriers, finely divided solid carriers, or both, and then shaping the product into the desired presentation if necessary. in certain embodiments, tablets are prepared by compression. in other embodiments, tablets are prepared by molding. in certain embodiments, at least one compound of formula (i) or formula (ii) is orally administered as a controlled release dosage form. such dosage forms are used to provide slow or controlled-release of one or more compounds of formula (i) or formula (ii). controlled release is obtained using, for example, hydroxypropylmethyl cellulose, other polymer matrices, gels, permeable membranes, osmotic systems, multilayer coatings, microparticles, liposomes, microspheres, or a combination thereof. in certain embodiments, controlled-release dosage forms are used to extend activity of the compound of formula (i) or formula (ii), reduce dosage frequency, and increase patient compliance. administration of compounds of formula (i) or formula (ii) as oral fluids such as solution, syrups and elixirs are prepared in unit dosage forms such that a given quantity of solution, syrups or elixirs contains a predetermined amount of a compound of formula (i) or formula (ii). syrups are prepared by dissolving the compound in a suitably flavored aqueous solution, while elixirs are prepared through the use of a non-toxic alcoholic vehicle. suspensions are formulated by dispersing the compound in a non-toxic vehicle. non-limiting examples of excipients used in oral fluids for oral administration include, but are not limited to, solubilizers, emulsifiers, flavoring agents, preservatives, and coloring agents. non-limiting examples of solubilizers and emulsifiers include, but are not limited to, water, glycols, oils, alcohols, ethoxylated isostearyl alcohols and polyoxy ethylene sorbitol ethers. non-limiting examples of preservatives include, but are not limited to, sodium benzoate. non-limiting examples of flavoring agents include, but are not limited to, peppermint oil or natural sweeteners or saccharin or other artificial sweeteners. parenteral dosage forms in certain embodiments pharmaceutical compositions containing at least one compound of formula (i) or formula (ii) are administered parenterally by various routes including, but not limited to, subcutaneous, intravenous (including bolus injection), intramuscular, and intraarterial. such parenteral dosage forms are administered in the form of sterile or sterilizable injectable solutions, suspensions, dry and/or lyophilized products ready to be dissolved or suspended in a pharmaceutically acceptable vehicle for injection (reconstitutable powders) and emulsions. vehicles used in such dosage forms include, but are not limited to, water for injection up aqueous vehicles such as, but not limited to, sodium chloride injection, ringer's injection, dextrose injection, dextrose and sodium chloride injection, and lactated ringer's injection water-miscible vehicles such as, but not limited to, ethyl alcohol, polyethylene glycol, and polypropylene glycol and non-aqueous vehicles such as, but not limited to, corn oil, cottonseed oil, peanut oil, sesame oil, ethyl oleate, isopropyl myristate, and benzyl benzoate. transdermal dosage forms in certain embodiments pharmaceutical compositions containing at least one compound of formula (i) or formula (ii) are administered transdermally. such transdermal dosage forms include "reservoir type" or "matrix type" patches, which are applied to the skin and worn for a specific period of time to permit the penetration of a desired amount of a compound of formula (i) or formula (ii). by way of example only, such transdermal devices are in the form of a bandage comprising a backing member, a reservoir containing the compound optionally with carriers, optionally a rate controlling barrier to deliver the compound to the skin of the host at a controlled and predetermined rate over a prolonged period of time, and means to secure the device to the skin. in other embodiments, matrix transdermal formulations are used. formulations for transdermal delivery of a compound of formula (i) or formula (ii) include an effective amount of a compound of formula (i) or formula (ii), a carrier and an optional diluent. a carrier includes, but is not limited to, absorbable pharmacologically acceptable solvents to assist passage through the skin of the host, such as water, acetone, ethanol, ethylene glycol, propylene glycol, butane-1,3-diol, isopropyl myristate, isopropyl palmitate, mineral oil, and combinations thereof. in certain embodiments, such transdermal delivery systems include penetration enhancers to assist in delivering one or more compounds of formula (i) or formula (ii) to the tissue. such penetration enhancers include, but are not limited to, acetone various alcohols such as ethanol, oleyl, and tetrahydrofuryl alkyl sulfoxides such as dimethyl sulfoxide dimethyl acetamide dimethyl formamide polyethylene glycol pyrrolidones such as polyvinylpyrrolidone kollidon grades (povidone, polyvidone) urea and various water-soluble or insoluble sugar esters such as tween 80 (polysorbate 80) and span 60 (sorbitan monostearate). in other embodiments, the ph of such a transdermal pharmaceutical composition or dosage form, or of the tissue to which the pharmaceutical composition or dosage form is applied, is adjusted to improve delivery of one or more compounds of formula (i) or formula (ii). in other embodiments, the polarity of a solvent carrier, its ionic strength, or tonicity are adjusted to improve delivery. in other embodiments, compounds such as stearates are added to advantageously alter the hydrophilicity or lipophilicity of one or more compounds of formula (i) or formula (ii) so as to improve delivery. in certain embodiments, such stearates serve as a lipid vehicle for the formulation, as an emulsifying agent or surfactant, and as a delivery-enhancing or penetration-enhancing agent. in other embodiments, different salts, hydrates or solvates of the compounds of formula (i) or formula (ii) are used to further adjust the properties of the resulting composition. in certain embodiments compounds of formula (i) or formula (ii) are transdermally delivered from a patch by iontophoresis. topical dosage forms in certain embodiments at least one

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compound of formula (i) or formula (ii) of the present invention, or a pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, include, but are not limited to antiemetic agents, anti-inflammatory agents, immunomodulatory agents, cytokines, antidepressants, hormones, alkylating agents, antimetabolites, antitumour antibiotics, antimitotic agents, topoisomerase inhibitors, cytostatic agents, anti-invasion agents, antiangiogenic agents, inhibitors of growth factor function, anticancer agents and toll-like receptor modulators.in some embodiments, the compounds of formula (i) or formula (ii), or a pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, are used in combination with a second therapeutic agent for treating asthma. in certain combinations, the second therapeutic agent is a bronchodilator, an anti-inflammatory agent, a leukotriene antagonist, or an ige blocker.the antiemetic agents used in combination with compounds of formula (i) or formula (ii), or a pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, include, but are not limited to, metoclopramide, domperidone, prochlorperazine, promethazine, chlorpromazine, trimethobenzamide, ondansetron, granisetron, hydroxyzine, acetylcholine monoethanolamine, alzapiride, azasetron, benzquinamide, betanautine, bromopride, buclizine, clebopride, cyclizine, dimenhydrinate, diphenidol, dolasetron, meclizine, methallatal, metopimazine, nabilone, oxypemrnyl, pipamazine, scopolamine, sulpiride, tetrahydrocannabinols, thiethylperazine, thiopropazine, tropisetron, and combinations thereof.the anti-inflammatory agents used in combination with compounds of formula (i) or formula (ii), or a pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, include, but are not limited to, non-steroidal anti-inflammatory drugs such as salicylic acid, acetylsalicylic acid, methyl salicylate, diflunisal, salsalate, olsalazine, sulfasalazine, acetaminophen, indomethacin, sulindac, etodolac, mefenamic acid, meclofenamate sodium, tolmetin, ketorolac, dichlofenac, ibuprofen, naproxen, naproxen sodium, fenopofen, ketoprofen, flurbiprofen, oxaprozin, piroxicam, meloxicam, ampiroxicam, droxicam, pivoxicam, tenoxicam, nabumetome, phenylbutazone, oxyphenbutazone, antipyrine, aminopyrine, apazone and nimesulide, leukotriene antagonists including, but not limited to, zileuton, aurothiogluucose, gold sodium thiomalate and auranofin, steroids including, but not limited to, alclometasone dipropionate, amcinonide, beclomethasone dipropionate, betametasone, betamethasone benzoate, betamethasone dipropionate, betamethasone sodium phosphate, betamethasone valerate, clobetasol propionate, clocortolone pivalate, hydrocortisone, hydrocortisone derivatives, desonide, desoximatason, dexamethasone, flunisolide, flucxinolide, flurandrenolide, halcinolide, medrysone, methylprednisolone, methprednisolone acetate, methylprednisolone sodium succinate, mometasone furoate, paramethasone acetate, prednisolone, prednisolone acetate, prednisolone sodium phosphate, prednisolone tebutate, prednisone, triamcinolone, triamcinolone acetonide, triamcinolone diacetate, and triamcinolone hexacetonide and other anti-inflammatory agents including, but not limited to, methotrexate, colchicine, allopurinol, probenecid, thalidomide or a derivative thereof, 5-aminosalicylic acid, retinoid, dithranol or calcipotriol, sulfapyrazone and benzbromarone.the immunomodulatory agents used in combination with compounds of formula (i) or formula (ii), or a pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, include, but are not limited to, azathioprine, tacrolimus, cyclosporin methothrexate, leflunomide, corticosteroids, cyclophosphamide, cyclosporine a, cyclosporin g, mycophenolate mofetil, ascomycin, rapamycin (sirolimus), fk-506, mizoribine, deoxyspergualin, brequinar, mycophenolic acid, malononitriloamindes (such as, by way of example only, leflunamide), t cell receptor modulators, and cytokine receptor modulators, peptide mimetics, and antibodies (such as, by way of example only, human, humanized, chimeric, monoclonal, polyclonal, fvs, scfvs, fab or f(ab)2 fragments or epitope binding fragments), nucleic acid molecules (such as, by way of example only, antisense nucleic acid molecules and triple helices), small molecules, organic compounds, and inorganic compounds. examples of t cell receptor modulators include, but are not limited to, anti-t cell receptor antibodies (such as, by way of example only, anti-cd4 antibodies (such as, by way of example only, cm-t412 (boehringer), idec-ce9.1 (idec and skb), mab 4162w94, orthoclone and oktcd4a (janssen-cilag)), anti-cd3 antibodies (such as, by way of example only, nuvion (product design labs), okt3 (johnson and johnson), or rituxan (idec)), anti-cd5 antibodies (such as, by way of example only, an anti-cd5 ricin-linked immunconjugate), anti-cd7 antibodies (such as, by way of example only, chh-380 (novartis)), anti-cd8 antibodies, anti-cd40 ligand monoclonal antibodies (such as, by way of example only, idec-131 (idec)), anti-cd52 antibodies (such as, by way of example only, campath 1h (llex)), anti-cd2 antibodies, anti-cd11a antibodies (such as, by way of example only, xanelim (genentech)), anti-b7 antibodies (such as, by way of example only, idec-114 (idec)), ctla4-immunoglobulin, and toll receptor-like (tlr) modulators. examples of cytokine receptor modulators include, but are not limited to, soluble cytokine receptors (such as, by way of example only, the extracellular domain of a tnfr-a receptor or a fragment thereof, the extracellular domain of an il-1 beta receptor or a fragment thereof, and the extracellular domain of an il-6 receptor or a fragment thereof), cytokines or fragments thereof (such as, by way of example only, interleukin (il)-2, il-3, il-4, il-5, il-6, il-7, il-8, il-9, il-10, il-11, il-12, il-15, tnfr-a, interferon (ifn)-a, ifn- beta, ifn-gamma, and gm-csf), anti-cytokine receptor antibodies (such as, by way of example only, anti-ifn receptor antibodies, anti-il-2 receptor antibodies (such as, by way of example only, zenapax (protein design labs)), anti-il-4 receptor antibodies, anti-il-6 receptor antibodies, anti-il-10 receptor antibodies, and anti-il-12 receptor antibodies), anti-cytokine antibodies (such as, by way of example only, anti-ifn antibodies, anti-tnfr-a antibodies, anti-il-1 beta antibodies, anti-il-6 antibodies, anti-il-8 antibodies (such as, by way of example only, abx-il-8 (abgenix)), and anti-il-12 antibodies).the alkylating agents used in combination with compounds of formula (i) or formula (ii), or a pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, include, but are not limited to, nitrogen mustards, ethylenimines, methylmelamines, alkyl sulfonates, nitrosoureas, carmustine, lomustine, triazenes, melphalan, mechlorethamine, cis-platin, oxaliplatin, carboplatin, cyclophosphamide, ifosfamide, melphalan, chlorambucil, hexamethylmelaine, thiopeta, busulfan, carmustine, streptozocin, dacarbazine and temozolomide.the antimetabolites used in combination with compounds of formula (i) or formula (ii), or a pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, include, but are not limited to, cytarabine, gemcitabine and antifolates such as, by way of example only, fluoropyrimidines (by way of example only, 5-fluorouracil and tegafur), raltitrexate, methotrexate, cytosine arabinoside, and hydroxyurea.the antitumour antibiotics used in combination with compounds of formula (i) or formula (ii), or a pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, include, but are not limited to, anthracyclines, bleomycin, doxorubicin, daunomycin, epirubicin, idarubicin, mitomycin-c, dactinomycin and mithramycin.the antimitotic agents used in combination with compounds of formula (i) or formula (ii), or a pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, include, but are not limited to, vinca alkaloids (by way of example only, vincristine, vinblastine, vindesine and vinorelbine), taxoids (by way of example only, taxol, paclitaxel and taxotere) and polikinase inhibitors.the topoisomerase inhibitors used in combination with compounds of formula (i) or formula (ii), or a pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, include, but are not limited to, epipodophyllotoxins by way of example only, etoposide and teniposide, amascrine, topotecan, irinotecan and camptothecin.in other embodiments, the combinations described herein include combination of a compound of formula (i) or formula (ii), or a pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, with a leukotriene biosynthesis inhibitor, 5-lipoxygenase (5-lo) inhibitor or 5-lipoxygenase activating protein (flap) antagonist such as zileuton abt-761 fenleuton tepoxalin abbott-79175 abbott-85761 a n-(5-substituted)-thiophene-2-alkylsulfonamide 2,6-di-tert-butylphenolhydrazones a methoxytetrahydropyrans such as zeneca zd-2138 the compound sb-210661 a pyridinyl-substituted 2-cyanonaphthalene compound such as l-739,010 a 2-cyanquinoline compound such as l-746,530 or an indole or quinoline compound such as mk-591, mk-886, and bayx1005.in other embodiments, the combinations described herein include combination of a compound of formula (i) or formula (ii), or a pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, with a receptor antagonist for leukotrienes (ltb4, lt4, ltd4, and lte4) selected from the group consisting of the phenothiazin-3-is such as l-651,392 amidino compounds such as cgs-25019c benzoxalamines such as ontolastol benzenecarboximidamides such as biil 284/260 and compounds such as zafirlukast, ablukast, montelukast, singulair, pranlukast, verlukast (mk-679), rg-12525, ro-245913, iralukast (cgp 45715a), and bayx1795.in other embodiments, the combinations described herein include combination of a compound of formula (i) or formula (ii), or a pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, with a phosphodiesterase (pde) inhibitor such as a methylxanthanine including theophylline and aminophylline a selective pde isoenzyme inhibitor including a pde4 inhibitor, including, but not limited to, cilomilast or roflumilast, an inhibitor of the isoform pde4d, or an inhibitor of pde5.in other embodiments, the combinations described herein include combination of a compound of formula (i) or formula (ii), or a pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, with a histamine type 1 receptor antagonist such as cetirizine, loratadine, desloratadine, fexofenadine, acrivastine, terfenadine, astemizole, azelastine, levocabastine, chlorpheniramine, promethazine, cyclizine, or mizolastine.in other embodiments, the combinations described herein include combination of a compound of formula (i) or formula (ii), or a pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, with a gastroprotective histamine type 2 receptor antagonist. in other embodiments, the combinations described herein include combination of a compound of formula (i) and formula (ii), or a pharmaceutically acceptable salt or solvate thereof, described herein, with an antagonist of the histamine type 4 receptor.in other embodiments, the combinations described herein include combination of a compound of formula (i) or formula (ii), or a pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, with an alpha-i/alpha-2 adrenoceptor agonist vasoconstrictor sympathomimetic agent, such as propylhexedrine, phenylephrine, phenylpropanolamine, ephedrine, pseudoephedrine, naphazoline hydrochloride, oxymetazoline hydrochloride, tetrahydrozoline hydrochloride, xylometazoline hydrochloride, tramazoline hydrochloride or ethylnorepinephrine hydrochloride.in other embodiments, the combinations described herein include combination of a compound of formula (i) or formula (ii), or a pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, with a glucocorticoid, such as flunisolide, triamcinolone acetonide, beclomethasone dipropionate, budesonide, fluticasone propionate, ciclesonide or mometasone furoate.in other embodiments, the combinations described herein include combination of a compound of formula (i) or formula (ii), or a pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, with an immunoglobulin (ig), gamma globulin, ig preparation or an antagonist or antibody modulating ig function such as anti-ige (omalizumab).in other embodiments, the combinations described herein include combination of a compound of formula (i) or formula (ii), or a pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, with a chemotherapeutic agent to treat a cell proliferative disorder, including but not limited to, lymphoma, osteosarcoma, melanoma, or a tumor of breast, renal, prostate, colorectal, thyroid, ovarian, pancreatic, neuronal, lung, uterine or gastrointestinal tumor. non-limiting examples of chemotherapeutic agents used in such combinations are anthracyclines, alkylating agents (e.g., mitomycin c), alkyl sulfonates, aziridines, ethylenimines, methylmelamines, nitrogen mustards, nitrosoureas, antibiotics, antimetabolites, folic acid analogs (e.g., dihydrofolate reductase inhibitors such as methotrexate), purine analogs, pyrimidine analogs, enzymes, podophyllotoxins, platinum-containing agents, interferons, and interleukins. other non-limiting examples of chemotherapeutic agents used in such combinations are busulfan, improfuslan, pipsosulfan, benzodepa, carboquone, meturedapa, uredepa, altretamine, triethylenemelamine, triethylenephosphoramidate, triethylenethiophosphoramidate, trimethylolmelamine, chlorambucil, chlornaphazine, cyclophosphamide, estramustine, ifosfamide, mechlorethamine, mechlorethamine oxide hydrochloride, melphalan, novembichin, phenesterine, prednimustine, trofosfamide, uracil mustard, carmustine, chlorozotacin, fotemustine, lomustine, nimustine, ranimustine, dacarbazine, mannometustine, mitobronitol, mitolactol, pipobroman, acalacinomycins, actinomycin f(1), anthramycin, azaserine, bleomycin, cactinomycin, carubicin, carzinophillin, chromomycin, dactinomycin, daunorubicin, daunomycin, 6-diazo-5-oxo-1-norleucine, doxorubicin, epirubicin, mitomycin c, mycophenolic acid, nogalamycin, olivomycin, peplomycin, plicamycin, porfirimycin, puromycin, streptonigrin, streptozocin, tubercidin, ubenimex, zinostatin, zorubicin, denopoterin, methotrexate, pteropterin, trimetrexate, fludarabine, 6-mercaptopurine, thiampirine, thioguanine, ancitabine, azacitidine, 6-azauridine, camofur, cytarabine, dideoxyuridine, doxifluridine, enocitabine, floxuridine, fluorouracil, tegafur, l-asparaginase, pulmozyme, aceglatone, aldophosphamide glycoside, aminolevulinic acid, amscrine, bestrabucil, bisantrene, carboplatin, cisplatin, defofamide, demecolone, diaziouone, elformithine, elliptinium acetate, etoglugicid, etoposide, flutamide, gallium nitrate, hydroxyurea, interferon-alpha, interferon-beta, interferon-gamma, interleukin-2, lentinan, lonidamine, mitoguazone, mitoxantrone, mopidamol, nitracrine, pentostatin, phenamet, pirarubicin, podophyllinic acid, 2-ethylhydrazide, procarbazine, razoxane, sizofuran, spiropogermanium, paclitaxel, tamoxifen, teniposide, tenuazonic acid, triaziquone, 2,2',27-trichlorotriethylamine, urethane, vinblastine, vincristine, and vindesine.in certain embodiments, the combination treatments provided herein include administration of a compound of formula (i) or formula (ii), or a pharmaceutically acceptable salts, pharmaceutically acceptable solvates (e.g. hydrates), the n-oxide derivatives, protected derivatives, individual isomers and mixture of isomers thereof, or a pharmaceutical composition containing a compound of formula (i) and formula (ii) in combination with one or more additional therapeutic agents, for the treatment of pulmonary arterial hypertension (pah). such additional therapeutic agents include phosphodiesterase-5 inhibitors, prostanoids, endothelin receptor antagonists, calcium channel blockers, oxygen therapy, ilprost, sildenafil, tadalafil, digoxin, furosemide, spirinolactone, warfarin, epoprostenol, treprostini, bosentan and ambrisentan.examples the following examples were offered to illustrate, but not to limit, the compounds of formula (i) or formula (ii) of the present invention, and the preparation of such compounds. synthesis of intermediates synthesis of 3-(imidazo[1,2-a]pyridine-3-carboxamido)-4-methylbenzoic acid (4) [ftimg=68000051]to a suspension of imidazo[1,2-a]pyridine-3-carboxylic acid (1) (4.09 g, 25.3 mmol) in dichloromethane (100 ml) and dmf (0.25 ml) at 0 degrees centigrade was added oxaly chloride (4.15 ml, 48.0 mmol) dropwise over 10 minutes. the reaction was slowly warmed to room temperature and stirred

until complete conversion was detected by lcms. the reaction was subsequently reduced to dryness and suspended in dichloromethane (100 ml) and was added a solution of methyl 3-amino-4-methylbenzoate (2) (4.6 g, 27.9 mmol) in dichloromethane (100 ml) and triethylamine (7.1 ml). contents were stirred at room temperature for 4 hours and diluted with dichloromethane (100 ml). the reaction was washed with water, saturated nahco3, brine, dried over magnesium sulfate, filtered and reduced to dryness. the crude solid was triturated with diethyl ether to remove excess aniline and dried to afford methyl 3-(imidazo[1,2-a]pyridine-3-carboxamido)-4-methylbenzoate (3) as a white solid. ms m/z 310.1 (m+1)+ to a suspension of 3-(imidazo[1,2-a]pyridine-3-carboxamido)-4-methylbenzoate (3) (5.43 g, 17.6 mmol) in thf (225 ml) and meoh (150 ml) was added lioh 3 m (17.5 ml) and water (50 ml). the reaction was stirred at room temperature for 12 hours then reduced in volume on roto-vap to remove thf and meoh. the mixture was diluted with water (75 ml) and neutralized with hcl (17.5 ml of a 3m solution). the resulting precipitate was filtered, washed with water and dried under vacuum to afford 3-(imidazo[1,2-a]pyridine-3-carboxamido)-4-methylbenzoic acid (4) as a white solid. 1h nmr (400 mhz, d6-dms0) delta 10.0 (s, 1h), 9.45 (dt, j=6.8, 1.2 hz, 1h), 8.58 (s, 1h), 7.98 (d, j=2.0 hz, 1h), 7.79 (dt, j=9.2, 1.2 hz, 1h), 7.76 (dd, j=8.0, 1.6 hz, 1h), 7.52 (ddd, j=9.2, 9.2, 1.2 hz, 1h), 7.43 (d, j=8.0 hz, 1h), 7.17 (td, j=6.8, 1.2 hz, 1h), 2.35 (s, 3h). ms m/z 296.1 (m+1)+. synthesis of 2-hydroxy-1-bhenylguanidine (5) [ftimg=68000052] to a solution of brcn (0.11 g, 1.1 mmol) in meoh (10 ml) at 0 degrees centigrade was added solid koac (0.32 g, 3.3 mmol) and a solution of aniline (0.1 ml, 1.1 mmol) in meoh (1 ml). the reaction was stirred for 3 hours then partitioned with water (15 ml) and dichloromethane (25 ml), the organic layer was separated, washed with brine, dried over magnesium sulfate, filtered and reduced to dryness to afford n-phenylcyanamide, which was immediately used without purification. n-phenylcyanamide was dissolved in etoh (7 ml) and treated with h2noh (1.5 eq of a 50 percent aq solution). the mixture was stirred at room temperature for 12 hours then reduced to dryness to afford 2-hydroxy-1-phenylguanidine (5) as a clear yellow oil, which was used without purification. synthesis of n'-hydroxy-6-methylpicolinimidamide (6) [ftimg=68000053] 6-methylpicolinonitrile (12 mg, 0.1 mmol) was dissolved in etoh (0.5 ml) and treated with nh2oh (1.5 eq of a 50 percent aq solution). the mixture was stirred at room temperature for 12 hours then reduced to dryness to afford n'-hydroxy-6-methylpicolinimidamide (6) as a clear yellow oil, which was used without purification. synthesis of n-(5-(n'-hydroxycarbamidimido)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (9) [ftimg=68000054] to a suspension of imidazo[1,2-a]pyridine-3-carboxylic acid (1) (16.6 g, 102 mmol) in dichloromethane (300 ml) and dmf (0.5 ml) at 0 degrees centigrade was added oxalyl chloride (45 ml, 510 mmol) dropwise over 10 minutes. the reaction was slowly warmed to room temperature and stirred until complete conversion was detected by lcms in meoh. the reaction was subsequently reduced to dryness and suspended in dichloroethane (100 ml) and was added to a solution of 3-amino-4-methylbenzonitrile (7) (15 g, 113 mmol) in dichloroethane (200 ml) and pr2net (55 ml) at 0 degrees centigrade after the addition, the cold bath was removed and contents were stirred at room temperature for 1 hour and then heated to 50 degrees centigrade for another 2 hours. after the completion of the reaction, the mixture was cooled and a white precipitate formed. the mixture was filtered and the solid was washed with cold dichloromethane. about 10 g of the desired n-(5-cyano-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (8) was obtained. the filtrate was washed with saturated nh4cl, saturated nahco3, brine, dried over magnesium sulfate, filtered and reduced to dryness. the crude solid was triturated with diethyl ether to remove excess aniline and filtered to afford another crop of n-(5-cyano-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (8) as a white solid. ms m/z 277.1 (m+1) to a stirred and cooled (0 degrees centigrade) suspension of n-(5-cyano-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (8) (10 g, 36.2 mmol) in etoh (225 ml) was added nh2oh (6 ml, 50 percent in water solution). after the addition, the reaction was stirred at room temperature for 2 hours then heated at 50 degrees centigrade for another 2 hours. after cooling to room temperature, the mixture was stored in the fridge overnight. the resulting precipitate was filtered, washed with cold etoh and dried under vacuum to afford n-(5-(n'-hydroxycarbamidimido)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (9) as a white solid. 1h nmr (400 mhz, d6-dms0) delta 9.40 (dt, j=6.8, 1.2 hz, 1h), 8.15 (s, 1h), 7.88 (d, j=2.0 hz, 1h), 7.79 (dt, j=9.2, 1.2 hz, 1h), 7.76 (dd, j=8.0, 1.6 hz, 1h), 7.52 (ddd, j=9.2, 9.2, 1.2 hz, 1h), 7.43 (d, j=8.0 hz, 1h), 7.17 (td, j=6.8, 1.2 hz, 1h), 2.49 (s, 3h). ms m/z 310.1 (m+1)+. synthesis of 5,5-difluorotetrahydro-2h-pyran-2-carboxylic acid (17) [ftimg=68000055] 2-(benzyloxy)acetaldehyde (5 g, 33.3 mmol) in dry thf (10 ml) was added dropwise to a stirred and cooled solution of allylmagnesium chloride (25 ml, 2 m in thf, 50 mmol) in thf (100 ml) at -78 degrees centigrade after the addition, the solution was allowed to warm to 0 degrees centigrade and quenched with saturated nh4cl solution. after standard aqueous work up, the residue was purified over silica using etoac and hexane to give 1-(benzyloxy)pent-4-en-2-ol (11). nah (4.8 g, 120 mmol) was added portion wise to a stirred solution of 1-(benzyloxy)pent-4-en-2-ol (11) (15.3 g, 79.6 mmol) in thf (100 ml) at 0 degrees centigrade after addition, the mixture was warmed to room temperature and stirred for another hour before it was cooled to 0 degrees centigrade allyl bromide (9 ml, 103.5 mmol) was added to the reaction and the resulting mixture was warmed to room temperature and then heated to 50 degrees centigrade overnight. after cooling to room temperature, the mixture was quenched with saturated nh4cl and worked up under standard conditions. the residue was purified over silica using et2o and hexane to give ((2-(allyloxy)pent-4-enyloxy)methyl)benzene (12). benzylidene-bis(tricyclohexylphosphine)dichlororuthenium, bis(tricyclohexylphosphine)benzylidene ruthenium(iv) chloride-grubbs 1 generation catalyst (0.5 g, 0.54 mmol) was added in one portion to a stirred solution of ((2-(allyloxy)pent-4-enyloxy)methyl)benzene (12) (4 g, 17.2 mmol) in toluene (200 ml). the resulting mixture was heated at 50 degrees centigrade under n2 for 2 hours before isopropanol (18 ml) and naoh (0.17 g) were added. the mixture was then heated at 120 degrees centigrade overnight, the solvent was evaporated and the residue was purified over silica gel using et2o and hexane to give 2-(benzyloxyethyl)-3,4-dihydro-2h-pyran (13). bh3.sme2 (17 ml, 1 m in thf) was added slowly to a stirred solution of 2-(benzyloxyethyl)-3,4-dihydro-2h-pyran (2.87 g, 14.06 mmol) (13) in thf (100 ml) at -78 degrees centigrade the resulting mixture was allowed to warm to room temperature overnight. the mixture was quenched by the slow addition of 1m naoh (50 ml) at 0 degrees centigrade followed by h2o2 (13 ml, 30 percent in water). the resulting mixture was stirred for 2 hours at room temperature. after aqueous work up the residue was purified on silica gel using etoac and hexane to give 6-(benzyloxyethyl)tetrahydro-2h-pyran-3-ol (14). dms0 (1.15 ml, 16.2 mmol) was added to a stirred solution of oxalyl chloride (1 ml, 10.8 mmol) in dichloromethane (60 ml) at -78 degrees centigrade after 10 minutes, a dichloromethane solution of 6-(benzyloxyethyl)tetrahydro-2h-pyran-3-ol (14) (1.20 g, 5.40 mmol) was added. stirring was continued for one hour then triethylamine (3.8 ml, 27 mmol) was added and slowly warmed to 0 degrees centigrade the reaction was poured into saturated nh4cl solution and the organic phase was washed with brine and dried (nas04). the residue was purified over silica gel using etoac and hexanes to give 6-(benzyloxyethyl)dihydro-2h-pyran-3(4h)-one (15). deoxo-fluor (4.6 ml, 25 mmol) was added dropwise to a -78 degrees centigrade solution of 6-(benzyloxyethyl)dihydro-2h-pyran-3(4h)-one (15) (1.1 g, 5.06 mmol) in toluene (20 ml) in a plastic container. the mixture was warmed to room temperature overnight and poured into saturated nahco3 solution and extracted with et2o. after washing with brine and drying over mgso4, the residue was purified over silica gel using etoac and hexane to give 2-(benzyloxyethyl)-5,5-difluorotetrahydro-2h-pyran (16). h2 (balloon) was introduced to a stirred mixture of pd(oh)2/c (0.2 g) and 2-(benzyloxyethyl)-5,5-difluorotetrahydro-2h-pyran (16) (1.05 g, 4.3 mmol) in meoh (20 ml). after 2 hours, the mixture was filtered through a pad of celite and the solvent was evaporated to give the crude alcohol product. the oil was azeotroped with toluene to remove residual water and the product was used directly in the following step. dms0 (0.3 ml, 4.11 mmol) was added to a stirred solution of oxalyl chloride (0.28 ml, 3.15 mmol) in dichlorometane (20 ml) at -78 degrees centigrade after 10 minutes, a dichlorometane solution of the alcohol from previous step (0.33 g, 1.37 mmol) was added. the stirring continued for one hour before triethylamine (1.0 ml, 6.85 mmol) was added and after 10 minutes the reaction was warmed to 0 degrees centigrade the reaction was poured into saturated nh4cl solution and the organic phase was washed with brine and dried (nas04). the crude aldehyde was filtration through a pad of silica gel and used directly in the following step. nacio2 (0.74 g, 8.22 mmol) was added in one portion to a stirred mixture of the aldehyde from previous step (1.37 mmol), 3-methyl-2-butene (2 ml) and nah2po4 (2.81 g, 20.5 mmol) in water (10 ml) and t-butoh (10 ml) at 0 degrees centigrade after stirring at room temperature for 2 hours, the mixture was partitioned with etoac and brine. the organic phase was dried (mgso4) and filtered. the residue was purified over silica gel using etoac and hexane to give 5,5-difluorotetrahydro-2h-pyran-2-carboxylic acid (17) as a clear oil. ms m/z 167.1 (m+1)+. synthesis of n-(5-(5-(azetidin-3-yl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (21) [ftimg=68000056] to a vial was added tert-butyl 3-(3-(3-(imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f39) (145 mg, 0.3 mmol) and 4n hcl in 1,4-dioxane (2 ml) and ch3cn (1 ml). the reaction was stirred for 45 minutes. the solvent was concentrated and placed under high vacuum. the solid was taken in water/acetone and the ph was adjusted to neutral with an aqueous solution of ammonium carbonate and lyophilized to afford n-(5-(5-(azetidin-3-yl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (21) which was used directly in the next step. 1h nmr (400 mhz, d6-dms0) delta 10.85 (s, 1 h), 9.66-9.64 (m, 1 h), 9.42 (bs, 1 h), 9.28 (s, 1 h), 8.10-8.08 (m, 2 h), 8.02-7.98 (m, 1 h), 7.89-7.87 (m, 1h), 7.59-7.53 (m, 2 h), 4.53-4.47 (m, 1 h), 4.36-4.29 (m, 4 h), 2.40 (s, 3 h). ms m/z 375.1 (m+1)+. synthesis of 7-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carboxylic acid (24) [ftimg=68000057] ethyl 2-chloroacetate (20 ml, 187 mmol) and ethyl formate (15.1 ml, 187 mmol) were added simultaneously to a stirred and cooled suspension of potassium tert-butoxide (21.4 g, 188 mmol) in dry diisopropylether (300 ml). after the addition, the reaction was warmed to room temperature and stirred overnight. the yellow suspension was filtered and the solid potassium 2-chloro-3-ethoxy-3-oxoprop-1-en-1-olate (22) was vacuum dried and used directly in the following step. to a stirring suspension of 4-(trifluoromethyl)pyridin-2-amine (128 mg, 0.791 mmol) and potassium 2-chloro-3-ethoxy-3-oxoprop-1-en-1-olate (22) (500 mg, 2.64 mmol) in etoh (5 ml) at room temperature was added sulfuric acid (70 micro l, 1.32 mmol) dropwise. the reaction mixture was stirred at room temperature overnight then heated at 78 degrees centigrade for 3 hours. the reaction was cooled to room temperature and the solvent was concentrated. the residue was taken in water and the ph was adjusted between 6-8 with saturated sodium bicarbonate. the crude product was extracted with ethyl acetate. the organic was washed with brine and dried over anhydrous sodium sulfate. the crude product 7-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carboxylate (23) was purified by silica chromatography. ms m/z 259.3 (m+1)+ to a stirring solution of ethyl 7-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carboxylate (23) (100 mg, 0.387 mmol) in thf:meoh (4:1, 1.5 ml) was added 2n lioh (0.25 ml). the reaction was heated at 60 degrees centigrade for 1 hour. then, cooled to room temperature and the ph was adjusted between 4-5 with 1n hcl. the solvent was partially concentrated and the resulting aqueous layer was lyophilized to give 7-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carboxylic acid (24). 1h nmr (400 mhz, d6-dms0) delta 9.44 (d, j=7.2 hz, 1 h), 8.40 (s, 1 h), 8.31-8.30 (m, 1 h), 7.48 (dd, j=2.0, 7.6 hz, 1 h). ms m/z 231.2 (m+1)+. the following compounds were prepared according to the protocol described for 7-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carboxylic acid (24). synthesis of 5,6,7,8-deutero-imidazo[1,2-a]pyridine-3-carboxylic acid (24n) [ftimg=68000058] 2-aminopyridine (d6) (10 g, 99.91 mmol) and potassium 2-chloro-3-ethoxy-3-oxoprop-1-en-1-olate (22) (46.93 g, 250 mmol) were suspended in dry etoh (300 ml) and h2so4 (6.65 ml, 128.8 mmol) was added dropwise at ambient temperature. after the addition, the resulting mixture was heated at reflux for 3 hours before pyridine (20 ml) was added and reflux continued overnight. the reaction was then cooled and solvent evaporated. the residue was partitioned between saturated nahco3 solution and etoac. the aqueous phase was further extracted with etoac and the combined organic phase was washed with brine and dried (mgso4). after filtration and concentration, the residue was purified over silica using etoac/hexane to give ethyl 5,6,7,8-deutero-imidazo[1,2-a]pyridine-3-carboxylate. 1h nmr (400 mhz, cdcl3) delta 8.30 (s, 1 h), 4.42 (q, j=8.4 hz, 2 h), 1.34 (t, j=8.4 hz, 3 h). ms m/z 195.1 (m+1)+. lioh (15.8 g, 377.1 mmol) was added to a stirred solution of ethyl 5,6,7,8-deutero-imidazo[1,2-a]pyridine-3-carboxylate (18.7 g, 95.3 mmol) in thf (100 ml), meoh (100 ml) and h2o (100 ml). after 3 hours, the solvent was evaporated and the solid was resuspended in water. nahso4 (50 g) was added to neutralize the solution and the precipitate was filtered. the solid 5,6,7,8-deutero-imidazo[1,2-a]pyridine-3-carboxylic acid (24 n) was dried in vacuum oven and used without further purification. 1h nmr (400 mhz, d6-dms0) delta 8.22 (s, 1 h). ms m/z 167.0 (m+1)+. intermediate number structure physical data 24a [ftimg=68000059] 1h nmr (400 mhz, d6-dms0) delta 9.64-9.62 (m, 1 h), 8.39 (s, 1 h), 8.01 (d, j = 9.2 hz, 1 h), 7.81 (dd, j = 2.0, 9.2 hz, 1 h). ms m/z 231.2 (m + 1)+. 24b [ftimg=68000060] ms m/z 181.2 (m + 1)+. 24c [ftimg=68000061] ms m/z 181.2 (m + 1)+. 24d [ftimg=68000062] ms m/z 188.1 (m + 1)+. 24e [ftimg=68000063] ms m/z 188.1 (m + 1)+. 24f [ftimg=68000064] ms m/z 241.0 (m + 1)+. 24g [ftimg=68000065] ms m/z 270.0 (m + 1)+. 24h [ftimg=68000066] 1h nmr (400 mhz, d6-dms0) delta 8.94 (d, j = 2.0 hz, 1 h), 8.13 (s, 1 h), 7.70 (d, j = 9.6 hz, 1 h), 7.31 (dd, j = 2.8, 9.8 hz, 1 h), 3.85 (s, 3h). ms m/z 193.1 (m + 1)+. 24i [ftimg=68000067] ms m/z 177.6 (m + 1)+. 24j [ftimg=68000068] ms m/z 177.6 (m + 1)+. 24k [ftimg=68000069] ms m/z 209.06 (m + 1)+. 24l [ftimg=68000070] 1h nmr (400 mhz, d6-dms0) delta 9.21 (s, 1 h), 8.22 (s, 1 h), 7.76 (d, j = 9.2 hz, 1 h), 7.50 (dd, j = 1.6, 9.2 hz, 1 h), 3.72-3.69 (m, 4 h), 3.40-3.28 (m, 2 h), 2.99-2.92 (m, 4 h), 2.88-2.82 (m, 2 h). ms m/z 276.13 (m + 1)+. 24m [ftimg=68000071] 1h nmr (400 mhz, d6-dms0) delta 9.29 (d, j = 1.6 hz, 1 h), 9.15 (dd, j = 1.6, 4.4 hz, 1 h), 8.4 (s, 1 h), 8.20 (d, j = 4.4 hz, 1 h). ms m/z 164.1 (m + 1)+. 24n [ftimg=68000072] ms m/z 167.0 (m + 1)+. 24o [ftimg=68000073] 1h nmr (400 mhz, d6-dms0) delta 8.79 (s, 1 h), 8.49 (s, 1 h), 7.84 (m, 2 h), 3.80 (m, 4 h), 3.16 (m, 4 h). ms m/z 248.1 (m + 1)+. 24p [ftimg=68000074] 1h nmr (400 mhz, d6-dms0) delta 9.69 (dd, j = 0.8, 2.0 hz, 1 h), 9.54 (s, 1 h), 8.42 (s, 1 h), 8.23 (s, 1 h), 8.09 (dd, j = 0.8, 9.6 hz, 1 h), 7.95 (dd, j = 2.0, 9.6 hz, 1 h), 7.87 (s, 1 h). ms m/z 248.1 (m + 1)+. 24q [ftimg=68000075] ms m/z 216.0 (m + 1)+. 24r [ftimg=68000076] /ms m/z 205.0 (m + 1)+. 24s [ftimg=68000077] ms m/z 270.0 (m + 1)+. 24t [ftimg=68000078] ms m/z 207.1 (m + 1)+. 24u [ftimg=68000079] ms m/z 243.1 (m + 1)+. synthesis of 6-(3-cyanopropyl)imidazo[1,2-a]pyridine-3-carboxylic acid (25) [ftimg=68000080] to a stirring suspension of 5-bromopyridin-2-amine (1.2 g, 7.05 mmol) and ethyl 2-chloro-3-hydroxyacrylate potassium salt (6.6 g, 28.19 mmol) (prepared in a similar manner as 22) in etoh (100 ml) at room temperature was added sulfuric acid (751 micro l, 14.10 mmol) dropwise. the reaction mixture was heated at 78 degrees centigrade overnight. the reaction was cooled to room temperature and the solvent was concentrated. the residue was taken in water and the ph was adjusted between 6-8 with saturated sodium bicarbonate. the crude product was extracted with ethyl acetate. the organic was washed with brine and dried over anhydrous sodium sulfate. the crude product was purified by silica chromatography to yield ethyl 6-bromoimidazo[1,2-a]pyridine-3-carboxylate (24s). ms m/z 270.2 (m+1)+. a stirring mixture of ethyl 6-bromoimidazo[1,2-a]pyridine-3-carboxylate (24s) (500 mg, 1.86 mmol), allyl cyanide (224 ul, 2.79 mmol), tris(dibenzylideneacetone)dipalladium(0) (26 mg, 0.028 mmol), [(t-butyl)3ph]bf4 (16 mg, 0.056 mmol), and n-dicyclohexylmethylamine (433 micro l, 2.04 mmol) in anhydrous 1,4-dioxane (6 ml) was heated at 95 degrees centigrade overnight. the reaction was cooled to room temperature and filtered. the solvent was concentrated. the crude product was purified by silica chromatography to give ethyl 6-(3-cyanoprop-1-enyl)imidazo[1,2-a]pyridine-3-carboxylate (24v). ms m/z 256.4 (m+1)+. to a stirring solution of ethyl 6-(3-cyanoprop-1-enyl)imidazo[1,2-a]pyridine-3-carboxylate (24v) (400 mg, 1.57 mmol) in etoh:etoac (1:1, 10 ml) was added catalytic pd/c (10 wt percent, wet basis). the reaction was hydrogenated by balloon overnight then filtered through celite. the crude product ethyl 6-(3-cyanopropyl)imidazo[1,2-a]pyridine-3-carboxylate (24w) was used in the next step without further purification. ms m/z 258.4 (m+1)+. to a stirring

solution of ethyl 6-(3-cyanopropyl)imidazo[1,2-a]pyridine-3-carboxylate (24w) (375 mg, 1.46 mmol) in thf:meoh (4:1, 5 ml) was added 2n lioh (500 micro l). the reaction was heated at 50 degrees centigrade for 45 minutes then cooled to room temperature and the ph was adjusted between 3-4 with 1n hcl. the solvent was partially concentrated and the remaining aqueous was lyophilized to yield 6-(3-cyanopropyl)imidazo[1,2-a]pyridine-3-carboxylic acid (25). 1h nmr (400 mhz, d6-dms) delta 9.21-9.19 (m, 1 h), 8.45 (s, 1 h), 7.85 (dd, j=0.8, 9.2 hz, 1 h), 7.70 (dd, j=1.6, 9.2 hz, 1 h), 2.82 (t, j=7.2 hz, 2 h), 2.55 (t, j=7.2 hz, 2 h), 1.97-1.90 (m, 2 h). ms m/z 230.3 (m+1)+. synthesis of n-(5-(5-(aminomethyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (26) [ftmg=68000081] to a stirring suspension of tert-butyl 3-(3-(imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)methyl(methyl) carbamate (f54) (90 mg, 0.195 mmol) in acetonitrile (1 ml) was added 4n hcl in dioxane (1 ml) and water (0.5 ml). the reaction mixture was stirred at room temperature for 45 minutes. then, the solvent was concentrated and the crude product was dried under high vacuum. the crude product n-(5-(5-(aminomethyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (26) was used in the next step without further purification. 1h nmr (400 mhz, d6-dms) delta 10.04 (s, 1 h), 9.46-9.44 (m, 1 h), 8.74 (s, 2 h), 8.63 (s, 1 h), 8.15 (d, j=2.0 hz, 1 h), 7.86-7.80 (m, 2 h), 7.59-7.54 (m, 1 h), 7.55 (d, j=8.4 hz, 1 h), 7.23-7.20 (m, 1 h), 4.62 (s, 2 h), 2.39 (s, 3 h). ms m/z 349.4 (m+1)+. synthesis of methyl 3-(3-(3-amino-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (31) [ftmg=68000082][ftmg=68000083]a stirring mixture of 4-methyl-3-nitrobenzonitrile (2 g, 12.33 mmol), hydroxylamine hydrogen chloride (1 g, 14.80 mmol) and n-diisopropylethylamine (3.2 ml, 18.50 mmol) in etoh (20 ml) was heated at 78 degrees centigrade for 3 hours. then, the solvent was concentrated and the crude product was dried under high vacuum. the crude product was taken in water and the solid was collected by vacuum filtration. the crude product (27) was used in the next step without further purification. ms m/z 196.3 (m+1)+. to a stirring solution of boc-azetidine-3-carboxylic acid (1.9 g, 9.22 mmol) in anhydrous nmp (12 ml) was added 1,1'-carbonyldiimidazole (cdi) (1.5 g, 9.22 mmol). the reaction was stirred for 5 minutes. then, n'-hydroxy-4-methyl-3-nitrobenzimidamide (27) (1.2 g, 6.1 mmol) was added and the reaction was stirred for 25 minutes. next, the reaction was heated in the microwave at 115 degrees centigrade for 12 minutes. the crude product was extracted with ethyl acetate. the organic was washed with water/brine mixture followed by brine and dried over anhydrous sodium sulfate. the solvent was concentrated and the crude product tert-butyl 3-(3-(4-methyl-3-nitrophenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (28) was taken in dichloromethane and minimal tetrahydrofuran and purified by silica chromatography. ms m/z 361.4 (m+1)+. to stirring suspension of tert-butyl 3-(3-(4-methyl-3-nitrophenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (28) (1 g, 2.78 mmol) in acetonitrile (2 ml) was added 4 n hcl in dioxane (5 ml). the reaction was stirred at room temperature for 1 hour. the solvent was concentrated and the crude product was dried under high vacuum to yield 5-(azetidin-3-yl)-3-(4-methyl-3-nitrophenyl)-1,2,4-oxadiazole hydrochloride (29). ms m/z 261.4 (m+1)+. to a stirring suspension of 5-(azetidin-3-yl)-3-(4-methyl-3-nitrophenyl)-1,2,4-oxadiazole hydrochloride (29) (825 mg, 2.78 mmol) in anhydrous dichloromethane (20 ml) at 0 degrees centigrade was added n,n-diisopropylethylamine (1.2 ml, 6.95 mmol) and methyl chloroformate (215 micro l, 2.78 mmol) dropwise. the reaction was stirred to room temperature for 25 minutes. the crude product was purified by silica chromatography to yield 3-(3-(4-methyl-3-nitrophenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (30). ms m/z 425.39 (m+1)+. to a stirring suspension of methyl 3-(3-(4-methyl-3-nitrophenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (30) (795 mg, 2.50 mmol) in etoh (20 ml) was added stannous chloride dihydrate (2.3 g, 9.99 mmol). the reaction mixture was heated at 78 degrees centigrade for 3 hours. then, the reaction was cooled to room temperature and the solvent was partially concentrated. the ph was adjusted to slightly basic ph with a saturated solution of sodium bicarbonate. the resulting white suspension was filtered and washed with water and ethyl acetate. the aqueous was extracted with ethyl acetate and washed with water, brine and dried over anhydrous sodium sulfate. the solvent was concentrated to give methyl 3-(3-(3-amino-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (31). 1h nmr (400 mhz, d6-dms) delta 7.32 (d, j=1.6 hz, 1 h), 7.12 (dd, j=1.6, 7.6 hz, 1 h), 7.30 (d, j=7.6 hz, 1 h), 5.19 (s, 2 h), 4.38-4.31 (m, 2 h), 4.27-4.20 (m, 1 h), 4.19-4.16 (m, 2 h), 3.60 (s, 3 h), 2.10 (s, 3 h). ms m/z 289.12 (m+1)+. synthesis of n-(5-(5-(chloromethyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (38) [ftmg=68000084]a mixture of n-(5-(n'-hydroxycarbamidoyl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (9) (500 mg, 1.62 mmol) and 2-chloroacetic anhydride (553 mg, 3.23 mmol) in anhydrous nmp (10 ml) was heated in the microwave at 110 degrees centigrade for 12 minutes. the crude was diluted with water and extracted with ethyl acetate. the organic was washed with water/brine mixture and dried over anhydrous sodium sulfate. the solvent was concentrated and the crude product was purified by silica chromatography to yield n-(5-(5-(chloromethyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (38). ms m/z 378.9 (m+1)+. synthesis of (z)-6-fluoro-n-(5-(n'-hydroxycarbamidoyl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (40) [ftmg=68000085]oxalyl chloride (10 ml, 110 mmol) was added dropwise to a stirred suspension of 6-fluoroimidazo[1,2-a]pyridine-3-carboxylic acid (24b) (2 g, 11 mmol) and catalytic amounts of dmf in dichloromethane (20 ml). after 5 hours, the solvent was evaporated and the solid was suspended in dry dce (20 ml) and added to a stirred solution of 3-amino-4-methylbenzonitrile (1.45 g, 11 mmol) and diea (6 mmol) in dce (10 ml) at 0 degrees centigrade after the addition, the reaction was heated at 60 degrees centigrade for 5 hours. the mixture was subjected to standard aqueous work and silica purification to give n-(5-cyano-2-methylphenyl)-6-fluoroimidazo[1,2-a]pyridine-3-carboxamide (39) as a solid. 1h nmr (400 mhz, d6-dms) delta 10.14 (s, 1 h), 9.45 (dd, j=5.2, 2.0 hz, 1 h), 8.62 (s, 1 h), 7.90-7.87 (m, 2 h), 7.68-7.63 (m, 1 h), 7.53 (d, j=8.0 hz, 1 h), 2.37 (s, 3 h). ms m/z 295.1 (m+1)+.nh2oh (5 ml, 16.1 mmol) was added in one portion to a stirred suspension of n-(5-cyano-2-methylphenyl)-6-fluoroimidazo[1,2-a]pyridine-3-carboxamide (39) (0.95 g, 3.23 mmol). the resulting suspension was heated at 60 degrees centigrade overnight and then cooled to 0 degrees centigrade the product, (z)-6-fluoro-n-(5-(n'-hydroxycarbamidoyl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (40) was collected by filtration. ms m/z 328.1 (m+1)+. synthesis of methyl 3-(3-(3-(7-bromoimidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (42) [ftmg=68000086] to a stirring suspension of 7-bromoimidazo[1,2-a]pyridine-3-carboxylic acid (24f) (400 mg, 1.67 mmol), in anhydrous dichloromethane (2 ml) at 0 degrees centigrade under argon was added dropwise oxalyl chloride (325 micro l, 3.72 mmol). then, a drop of anhydrous dmf was added and the reaction mixture was stirred at room temperature for 1.5 hour. the solvent was concentrated and the crude solid was added portion-wise to a stirring solution of methyl 3-(3-(3-amino-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (31) (429 mg, 1.49 mmol) in anhydrous pyridine (1 ml) at 0 degrees centigrade the reaction was stirred to room temperature under argon for 30 minutes. then, the reaction was quenched with water. the solvent was concentrated and the crude product was purified by silica chromatography to yield methyl 3-(3-(3-(7-bromoimidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (42). ms m/z 511.1 (m+1)+.the following compounds were prepared according to the protocol described for methyl 3-(3-(3-(7-bromoimidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (42).intermediatenumberstructurephysical data42g [ftmg=68000087]1h nmr (400 mhz, d6-dms) delta 10.12 (s, 1 h), 9.38 (dd, j= 0.8, 7.2 hz, 1h), 8.59 (s, 1h), 8.14 (dd, j= 0.8, 2.4 hz, 1h), 8.09 (d, j= 1.6 hz, 1h), 7.85 (dd, j= 2.0, 8.0 hz, 1h), 7.51 (d, j= 8.0 hz, 1h), 7.35 (dd, j= 2.0, 7.6 hz, 1h), 4.16-4.42 (m, 5h), 3.60 (s, 3h), 2.37 (s, 3h). ms m/z 511.0, 513.0 (m + 1)+.42j[ftmg=68000088]ms m/z 511.0, 513.0 (m + 1)+. synthesis of 3-(3-(3-(imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)methyl methanesulfonate (44) [ftmg=68000089]carbonyl diimidazole (cdi) (324 mg, 2.0 mmol) was added to a stirred solution of 2-acetoxyacetic acid (236 mg, 2.0 mmol) in nmp. after 20 minutes, n-(5-(n'-hydroxycarbamidoyl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (9) (310 mg, 1.0 mmol) was added in one portion and the resulting solution was stirred for 1 hour before it was heated at 125 degrees centigrade for 15 minutes in a microwave reactor. the reaction solution was subjected to standard aqueous work up to afford a residue which was hydrolyzed by lithium hydroxide monohydrate (252 mg, 6.0 mmol) in thf/meoh/h2o (3:2:1). after removal of all solvents 2m nahco3 (10 ml) was added. the precipitate was filtered and dried in air to afford n-(5-(5-(hydroxymethyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (43). 1h nmr (400 mhz, d6-dms) delta 10.02 (s, 1 h), 9.46 (d, j=6.8 hz, 1 h), 8.59 (s, 1 h), 8.11 (s, 1 h), 7.82 (m, 2 h), 7.53 (m, 2 h), 7.18 (m, 1 h), 6.08 (m, 1 h), 4.80 (d, j=6.0 hz, 2 h), 2.37 (s, 3 h). ms m/z 350.1 (m+1)+. to a solution of n-(5-(5-(hydroxymethyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (43) (210 mg, 0.6 mmol) and diea (0.32 ml, 1.8 mmol) in dcm (5 ml) was added mscl (138 mg, 1.2 mmol). the mixture was stirred at room temperature for 10 minutes then subjected to standard aqueous work up. the crude product was purified by silica chromatography to yield 3-(3-(3-(imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)methyl methanesulfonate (44) (180 mg, 70 percent yield). ms m/z 428.1 (m+1)+.the following compounds were prepared according to the protocol described for 3-(3-(3-(imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)methyl methanesulfonate (44).intermediatenumberstructurephysical data44a [ftmg=68000090]ms m/z 442.1 (m + 1)+.44b[ftmg=68000091]ms m/z 442.1 (m + 1)+.44c[ftmg=68000092]ms m/z 432.1 (m + 1)+.44d[ftmg=68000093]ms m/z 446.1 (m + 1)+. synthesis of n-(5-(5-(3-aminooxetan-3-yl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (47) [ftmg=68000094]a mixture of 3-aminooxetane-3-carboxylic acid (117.0 mg, 1.0 mmol) and nme4oh.5h2o (tmah) (181.0 mg, 1.0 mmol) in ch3cn (10 ml) was stirred at room temperature for 30 minutes. then (boc)2o (327.3 mg, 1.5 mmol) was added and the resulting mixture was stirred overnight. water (10 ml) was added and the mixture was extracted with ether (20 ml). the aqueous layer was acidified to ph=2 by addition of citric acid (solid) and extracted with etoac (2x20 ml). the organic layers were combined, dried over na2so4, filtered and concentrated to yield crude 3-((tert-butoxycarbonyl)amino)oxetane-3-carboxylic acid (45) which was used without further purification. ms m/z 218.1 (m+1)+.carbonyl diimidazole (cdi) (162.2 mg, 1.0 mmol) was added to a stirred solution of 3-((tert-butoxycarbonyl)amino)oxetane-3-carboxylic acid (45) (217.1 mg, 1.0 mmol) in nmp (1.0 ml). after 20 minutes, n-(5-(n'-hydroxycarbamidoyl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (9) (150.0 mg, 0.5 mmol) was added in one portion and the resulting solution was stirred for 1 hour before it was heated at 125 degrees centigrade for 15 minutes in a microwave reactor. the reaction solution was subjected to standard aqueous work up to afford a residue which was purified by silica chromatography to yield tert-butyl 3-(3-(3-(imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)oxetan-3-yl) carbamate (46) (159 mg, 65 percent yield). ms m/z 491.2 (m+1)+.3-(3-(3-(imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl) oxetan-3-yl)carbamate (46) (29.5 mg, 0.06 mmol) was dissolved in tfa (0.5 ml) and stirred at room temperature for 10 minutes. then tfa was removed under vacuum to yield crude n-(5-(5-(3-aminooxetan-3-yl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (47) as a tfa salt which was used without further purification. ms m/z 391.1 (m+1)+. synthesis of n-(2-fluoro-5-(n'-hydroxycarbamidoyl)phenyl)imidazo[1,2-a]pyridine-3-carboxamide (50) [ftmg=68000095]a mixture of 4-fluoro-3-nitrobenzonitrile (5.0 g, 30.1 mmol) and fe powder (5.05 g, 90.3 mmol) in acoh (100 ml) was heated at 80 degrees centigrade for 1 hour under n2. then the solvent was removed under vacuum and water (200 ml) was added to the residue. the solution was adjusted to ph 6 by addition of na2co3 and extracted with dcm (2x200 ml). the organic layers were combined, dried over na2so4, filtered and concentrated to yield 3-amino-4-fluorobenzonitrile (48), which was used without further purification. ms m/z 137.0 (m+1)+. to a stirring suspension of imidazo[1,2-a]pyridine-3-carboxylic acid (1) (3.0 g, 18.5 mmol) in anhydrous dichloromethane (50 ml) at 0 degrees centigrade was added dropwise oxalyl chloride (4.84 ml, 55.5 mmol). then, three drops of anhydrous dmf was added and the reaction mixture was stirred at room temperature for 15 minutes. the solvent was concentrated and the crude solid was added to a stirring solution of 3-amino-4-fluorobenzonitrile (48) (2.5 g, 18.5 mmol) in anhydrous pyridine (50 ml) at room temperature. the reaction was stirred for 20 minutes and quenched with water (200 ml) with stirring for another 10 minutes. then the precipitate was filtered and dried in air to yield n-(5-cyano-2-fluorophenyl)imidazo[1,2-a]pyridine-3-carboxamide (49). 1h nmr (400 mhz, d6-dms) delta 10.40 (s, 1h), 9.43 (td, j=1.2, 6.8 hz, 1h), 8.63 (s, 1h), 8.21 (dd, j=2.0, 7.2 hz, 1h), 7.78-7.84 (m, 2h), 7.54-7.63 (m, 2h), 7.22 (dt, j=1.2, 6.8, 1h). ms m/z 281.1 (m+1)+.nh2oh (10 ml, 32.1 mmol) was added in one portion to a stirred suspension of n-(5-cyano-2-fluorophenyl)imidazo[1,2-a]pyridine-3-carboxamide (49) (3.6 g, 12.85 mmol) in etoh (100 ml). the resulting suspension was heated at 70 degrees centigrade for 3 hours and then the solvent was removed to yield n-(2-fluoro-5-(n'-hydroxycarbamidoyl)phenyl)imidazo[1,2-a]pyridine-3-carboxamide (50). 1h nmr (400 mhz, d6-dms) delta 10.21 (s, 1h), 9.70 (s, 1h), 9.45 (td, j=1.2, 7.2 hz, 1h), 8.61 (s, 1h), 7.95 (dd, j=2.4, 7.6 hz, 1h), 7.79 (td, j=1.2, 8.8 hz, 1h), 7.51-7.60 (m, 2h), 7.31-7.37 (m, 1h), 7.19 (dt, j=1.2, 6.8, 1h), 5.88 (s, 2h). ms m/z 314.1 (m+1)+.the following compounds were prepared according to the protocol described for n-(2-fluoro-5-(n'-hydroxycarbamidoyl)phenyl)imidazo[1,2-a]pyridine-3-carboxamide (50).intermediatenumberstructurephysical data50a[ftmg=68000096]1h nmr (400 mhz, d6-dms) delta 9.96 (s, 1h), 9.65 (s, 1h), 9.44 (td, j= 0.8, 6.8 hz, 1h), 8.55 (s, 1h), 7.78 (td, j= 1.2, 9.2 hz, 1h), 7.52 (m, 2h), 7.21 (d, j= 11.6 hz, 1h), 7.17 (dt, j= 1.2, 6.8 hz, 1h), 5.81 (s, 2h), 2.28 (s, 3h). ms m/z 328.1 (m + 1)+.50b[ftmg=68000097]ms m/z 422.1 (m + 1)+.50c[ftmg=68000098]1h nmr (400 mhz, d6-dms) delta 9.89 (s, 1h), 9.44 (td, j= 6.8, 1.2 hz, 1h), 9.33 (s, 1h), 8.55 (s, 1h), 7.76 (td, j= 9.2, 1.2 hz, 1h), 7.49-7.52 (m, 1h), 7.28 (s, 1h), 7.14-7.18 (m, 2h), 5.72 (s, 2h), 2.34 (s, 3h), 2.24 (s, 3h). ms m/z 324.1 (m + 1)+.50d[ftmg=68000099]1h nmr (400 mhz, d6-dms) delta 9.84 (s, 1h), 9.43 (d, j= 6.8 hz, 1h), 8.59 (s, 1h), 7.78 (d, j= 8.8 hz, 1h), 7.50 (d, j= 8.0 hz, 1h), 7.17 (m, 3h), 5.76 (s, 2h), 2.25 (s, 3h), 2.24 (s, 3h). ms m/z 324.1 (m + 1)+.50e[ftmg=68000100]1h nmr (400 mhz, d6-dms) delta 9.90 (s, 1h), 9.60 (s, 1h), 9.32 (d, j= 7.2 hz, 1h), 8.50 (s, 1h), 7.69 (d, j= 2.20 hz, 1h), 7.56 (m, 1h), 7.50 (dd, j= 1.6, 8.0 hz, 1h), 7.29 (d, j= 8.0 hz, 1h), 7.02 (dd, j= 1.6, 7.2 hz, 1h), 5.80 (s, 2h), 2.42 (s, 3h), 2.27 (s, 3h). ms m/z 324.1 (m + 1)+.50f[ftmg=68000101]1h nmr (400 mhz, d6-dms) delta 10.09 (s, 1h), 9.63 (m, 1h), 9.60 (s, 1h), 8.58 (s, 1h), 7.78 (dd, j= 0.8, 9.6 hz, 1h), 7.69 (d, j= 1.6 hz, 1h), 7.66 (dd, j= 2.0, 9.2 hz, 1h), 7.52 (dd, j= 1.6, 8.0 hz, 1h), 7.31 (d, j= 8.0 hz, 1h), 5.81 (s, 2h), 2.27 (s, 3h). ms m/z 388.0, 390.0 (m + 1)+. synthesis of 5-amino-2-fluoro-4-methylbenzonitrile (51) [ftmg=68000102]a mixture of 5-bromo-4-fluoro-2-methylaniline (2.04 g, 10.0 mmol), cucn (889 mg, 10.0 mmol) and cui (1.9 g, 10.0 mmol) in nmp was purged with n2 for 5 minutes and then sealed and heated at 195 degrees centigrade for 30 minutes under microwave condition. the mixture was subjected to standard aqueous workup to give a residue which was purified by silica chromatography to yield 5-amino-2-fluoro-4-methylbenzonitrile (51) (540 mg, 36 percent yield). ms m/z 151.0 (m+1)+. synthesis of n-(5-(5-(azetidin-3-ylmethyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (55) [ftmg=68000103]carbonyl diimidazole (cdi) (52.0 mg, 0.32 mmol) was added to a stirred solution of 2-(1-(tert-butoxycarbonyl)azetidin-3-yl)acetic acid (69.0 mg, 0.32 mmol) in nmp (1.0 ml). after 20 minutes, n-(5-(n'-hydroxycarbamidoyl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (9) (49.5 mg, 0.16 mmol) was added in one portion and the resulting solution was stirred for 30 minutes before it was heated at 125 degrees centigrade for 15 minutes in a microwave reactor. the reaction mixture was added dropwise to water (20 ml) with stirring. the precipitate was filtered and dried to give tert-butyl 3-(3-(3-(imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)methyl)azetidine-1-carboxylate (54). ms m/z 489.2 (m+1)+.3-(3-(3-(imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)methyl)azetidine-1-carboxylate (54) (29.3 mg, 0.06 mmol) was dissolved in tfa (0.5 ml) and stirred at room temperature for 10 minutes. then tfa was removed under

vacuum to yield crude n-(5-(5-(azetidin-3-ylmethyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (55) which was used without further purification. ms m/z 389.2 (m+1)+. synthesis of 2-(3-(3-difluoropyrrolidin-1-yl)-3-methoxypropanoic acid (58) [ftimg=68000104]a mixture of methyl 2-bromo-3-methoxypropanoate (132.0 mg, 0.66 mmol), 3,3-difluoropyrrolidine (70.6 mg, 0.66 mmol) and k2co3 (91.2 mg, 0.66 mmol) in dmf (2 ml) was heated at 90 degrees centigrade for 3 hours. the mixture was subjected to standard aqueous workup to afford a residue which was dissolved in thf/meoh/h2o (3:2:1, 5 ml). lioh (6n, 3.3 mmol) was added and the resulting mixture was stirred at room temperature for 30 minutes. the solution was acidified to ph5 by addition of 6n hcl. all solvents were removed under vacuum to give a crude 2-(3-(3-difluoropyrrolidin-1-yl)-3-methoxypropanoic acid (58) which was used without purification. ms m/z 210.1 (m+1)+. synthesis of 6-(((triisopropylsilyl)oxy)methyl)imidazo[1,2-a]pyridine-3-carboxylic acid (61) [ftimg=68000105]to a stirring suspension of (6-aminopyridin-3-yl)methanol (1.24 mg, 10.0 mmol) and ethyl 2-chloro-3-hydroxyacrylate, potassium salt (29) (3.76 g, 20.0 mmol) in etoh (10 ml) at room temperature was added conc sulfuric acid (10.0 mmol) dropwise. the reaction mixture was stirred at room temperature for 15 minutes and pyridine (0.92 g, 12.0 mmol) was added. the resulting mixture was heated at 85 degrees centigrade overnight. the reaction was cooled to room temperature and the solvent was concentrated. the residue was taken in water and the solution was adjusted to ph 8 with saturated sodium bicarbonate. the crude product was extracted with ethyl acetate. the organic layer was washed with brine and dried over anhydrous sodium sulfate. the crude product ethyl 6-(hydroxymethyl)imidazo[1,2-a]pyridine-3-carboxylate (59) was purified by silica chromatography. 1h nmr (400 mhz, d6-dmsd) delta 9.16 (d, j=6.8 hz, 1h), 8.26 (s, 1h), 7.67 (s, 1h), 7.19 (dd, j=1.6, 6.8 hz, 1h), 5.57 (t, j=6.4 hz, 1h), 4.63 (d, j=6.0, 2h), 4.36 (q, j=7.2 hz, 2h), 1.35 (t, j=6.8 hz, 3h). ms m/z 221.1 (m+1)+. to a suspension of ethyl 6-(hydroxymethyl)imidazo[1,2-a]pyridine-3-carboxylate (59) (497.0 mg, 2.26 mmol), dmap (12.2 mg, 0.1 mmol) and 1h-imidazole (154.0 mg, 2.26 mmol) in dichloromethane (10 ml), was added tipsci (523.0 mg, 2.71 mmol). the resulting mixture was stirred overnight at room temperature. the solvent was removed under vacuum to yield crude ethyl 6-(((triisopropylsilyl)oxy)methyl)imidazo[1,2-a]pyridine-3-carboxylate (60). ms m/z 377.2 (m+1)+. the crude ethyl 6-(((triisopropylsilyl)oxy)methyl)imidazo[1,2-a]pyridine-3-carboxylate (60) obtained above was dissolved in thf/meoh/h2o (3:2:1, 5 ml). 6n lioh (2.27 ml, 13.6 mmol) was added and the reaction mixture was stirred at room temperature for 2 hours. all solvents were removed and 6n hcl was added until ph 5-6. etoac (5 ml) was added and the mixture was stirred for 1 hour. the precipitate was filtered and dried to give 6-(((triisopropylsilyl)oxy)methyl)imidazo[1,2-a]pyridine-3-carboxylic acid (61). 1h nmr (400 mhz, d6-dmsd) delta 9.37 (s, 1h), 8.21 (s, 1h), 7.76 (dd, j=1.2, 9.2 hz, 1h), 7.46 (dd, j=2.0, 9.2 hz, 1h), 4.94 (s, 2h), 1.20 (m, 3h), 1.08 (d, j=6.8 hz, 18h). ms m/z 349.2 (m+1)+. synthesis of 7-(1h-pyrazol-3-yl)imidazo[1,2-a]pyridine-3-carboxylic acid (63) [ftimg=68000106]to a solution of 5-ethyl 7-bromoimidazo[1,2-a]pyridine-3-carboxylate 24 g (202 mg, 0.75 mmol) in dmf (2 ml) was added (1h-pyrazol-3-yl)boronic acid (101 mg, 0.903 mmol), 1.8 m k2co3 (1.3 ml, 2.26 mmol) and pd(pph3)4 (87 mg, 0.075 mmol). the reaction was evacuated and backfilled with nitrogen twice then heated at 160 degrees centigrade for 10 minutes in a microwave oven. after the reaction mixture was filtered through a pad of celite, the mixture was diluted with a saturated solution of nh4cl and extracted with ethyl acetate. the organic layer was washed with brine, dried over na2so4 and concentrated to give ethyl 7-(1h-pyrazol-3-yl)imidazo[1,2-a]pyridine-3-carboxylate (62). ms (m/z) 257.1 (m+1)+. to a stirring solution of ethyl 7-(1h-pyrazol-3-yl)imidazo[1,2-a]pyridine-3-carboxylate (62) (103 mg, 0.4 mmol) in thf:meoh:h2o (3:2:1, 1.6 ml) was added 6n lioh (0.035 ml). the reaction was stirred at room temperature for 20 minutes. the ph was adjusted between 4-5 with 3n hcl. the resulting mixture was concentrated to yield 7-(1h-pyrazol-3-yl)imidazo[1,2-a]pyridine-3-carboxylic acid (63). ms (m/z) 229.2 (m+1)+. synthesis of n-(5-amino-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (67) [ftimg=68000107]oxaly chloride (10 ml) was added dropwise to a stirred solution of imidazo[1,2-a]pyridine-3-carboxylic acid (1) (3 g, 18.5 mmol) in dry dichloromethane (100 ml) and a few drops of dmf. the resulting solution was stirred at room temperature for 5 hours before it was evaporated to dryness and fresh dichloromethane was added to the resulting acid chloride to make a suspension. in a separate flask, tert-butyl 3-amino-4-methylphenylcarbamate (65) (4.5 g, 20.3 mmol) and diea (10 ml) was dissolved in dichloromethane (100 ml) and the above acid chloride solution was added slowly. the resulting solution was stirred overnight at room temperature. saturated nh4cl was added to the reaction solution and the phases were separated. the organic layer was dried over na2so4 and filtered. after evaporation, the residue was purified over silica gel column using hexane and etoac to give tert-butyl 3-(imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenylcarbamate (66) as a slightly yellow solid. tfa (50 ml) was added to a stirred suspension of tert-butyl 3-(imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenylcarbamate (66) in me2s (5 ml) and dichloromethane (10 ml). after 2 hours the solution was evaporated and partitioned with dichloromethane and saturated nahco3. the aqueous layer was extracted several times with dichloromethane and the combined organic layers were dried over na2so4. n-(5-amino-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (67) was isolated and used without further purification. 1h nmr (400 mhz, cdcl3) delta 9.44 (d, j=6.8 hz, 1 h), 8.05 (s, 1 h), 7.67 (d, j=8.8 hz, 1 h), 7.38-7.33 (m, 2 h), 6.98-6.94 (m, 2 h), 2.19 (s, 3 h). ms m/z 267.1 (m+1)+. synthesis of (e)-n-(5-(2-hydroxyguanidino)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (69) [ftimg=68000108]to n-(5-amino-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (67) (4.53 g, 15 mmol) in meoh (100 ml) was added koac (4.41 g, 45 mmol) and the mixture was stirred at room temperature for 5 minutes then cooled to 0 degrees centigrade before a solution of brcn (1.62 g, 15 mmol) in meoh (30 ml) was added dropwise. the resulting mixture was slowly warmed to room temperature and stirred overnight. the solvent was evaporated and to the residue was added water (150 ml). the mixture was stirred at room temperature for 1 hour, filtered and washed with water (2x20 ml), then air dried to give n-(5-cyanamido-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (68) as a white solid. to a suspension of n-(5-cyanamido-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (68) 3.52 g (12.1 mmol) in 200 ml of etoh was added 0.75 ml nh2oh (50 wt percent in water, 12.1 mmol). the resulting mixture was stirred at room temperature overnight. the precipitate was filtered, washed with etoh (10 ml) and air dried to give n-(5-(2-hydroxyguanidino)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (69) as a white solid, which was used directly in the next step without further purification. 1h nmr (400 mhz, d6-dmsd) delta 9.44 (s, 1 h), 9.46 (dd, j=6.8, 0.8 hz, 1 h), 8.54 (s, 1 h), 8.34 (s, 1 h), 7.76 (dd, j=7.2, 2.2 hz, 1 h), 7.59 (s, 1 h), 7.52-7.43 (m, 2 h), 7.18-7.06 (m, 2 h), 2.13 (s, 3 h). ms m/z 325.1 (m+1)+. synthesis of 6-(3-(tert-butoxy)-3-oxopropyl)imidazo[1,2-a]pyridine-3-carboxylic acid (72) [ftimg=68000109]a stirring mixture of ethyl 6-bromoimidazo[1,2-a]pyridine-3-carboxylate (24s) (500 mg, 1.86 mmol), tert-butyl acrylate (408 ul, 2.79 mmol), tris(dibenzylideneacetone)dipalladium(0) (51 mg, 0.056 mmol), [(t-bu)3ph]bf4 (27 mg, 0.093 mmol) and n,n-dicyclohexylmethylamine (738 ul, 3.48 mmol) in anhydrous 1,4-dioxane (5 ml) was heated at 95 degrees centigrade overnight. the reaction was cooled to room temperature and filtered. the solvent was concentrated and the crude product was purified by silica chromatography to yield ethyl 6-(3-(tert-butoxy)-3-oxoprop-1-en-1-yl)imidazo[1,2-a]pyridine-3-carboxylate (70). ms m/z 317.14 (m+1)+. a stirring mixture of ethyl 6-(3-(tert-butoxy)-3-oxoprop-1-en-1-yl)imidazo[1,2-a]pyridine-3-carboxylate (70) (460 mg, 1.80 mmol) and 10 wt percent pd/c (wet) in ethanol:ethylacetate (1:1, 10 ml) was hydrogenated overnight. the reaction was filtered over celite and the solvent was concentrated. crude ethyl 6-(3-(tert-butoxy)-3-oxopropyl)imidazo[1,2-a]pyridine-3-carboxylate (71) was used in the next step without further purification. ms m/z 319.16 (m+1)+. a stirring mixture of ethyl 6-(3-(tert-butoxy)-3-oxopropyl)imidazo[1,2-a]pyridine-3-carboxylate (71) (400 mg, 1.26 mmol) and 2n lioh (1 ml) in thf:meoh (4:1, 4 ml) was heated at 60 degrees centigrade for 30 minutes. the reaction was cooled to room temperature and the ph was adjusted between 3-5 with 10 percent citric acid. the solvent was partially reduced. the resulting solid was collected by vacuum filtration and washed with excess water. crude 6-(3-(tert-butoxy)-3-oxopropyl)imidazo[1,2-a]pyridine-3-carboxylic acid (72) was dried and used in the next step without further purification. 1h nmr (400 mhz, d6-dmsd) delta 9.11 (s, 1 h), 8.20 (s, 1 h), 7.72 (dd, j=0.8, 9.2 hz, 1 h), 7.50 (dd, j=1.6, 9.2 hz, 1h), 2.91 (t, j=6.8 hz, 2 h), 2.60 (t, j=7.2, 2 h), 1.33 (s, 9 h). ms m/z 291.13 (m+1)+. synthesis of 6(2-cyanoethyl)imidazo[1,2-a]pyridine-3-carboxylic acid (75) [ftimg=68000110]a stirring mixture of ethyl 6-bromoimidazo[1,2-a]pyridine-3-carboxylate (24s) (250 mg, 0.929 mmol), acrylonitrile (92 ul, 1.39 mmol), tris(dibenzylideneacetone)dipalladium(0) (26 mg, 0.0279 mmol), [(t-bu)3ph]bf4 (13 mg, 0.0465 mmol) and n,n-dicyclohexylmethylamine (217 ul, 1.02 mmol) in anhydrous 1,4-dioxane (4 ml) was heated at 95 degrees centigrade overnight. the reaction was cooled to room temperature and filtered. the solvent was concentrated and crude 6-(2-cyanovinyl)imidazo[1,2-a]pyridine-3-carboxylate (73) was purified by silica chromatography. ms m/z 242.09 (m+1)+. a stirring mixture of ethyl 6-(2-cyanovinyl)imidazo[1,2-a]pyridine-3-carboxylate (73) (115 mg, 0.451 mmol) and 10 wt percent pd/c (wet) in ethanol:ethylacetate (1:1, 5 ml) was hydrogenated overnight. the reaction was filtered over celite and the solvent was removed. crude ethyl 6-(2-cyanoethyl)imidazo[1,2-a]pyridine-3-carboxylate (74) was used in the next step without further purification. ms m/z 244.10 (m+1)+. a stirring mixture of ethyl 6-(2-cyanoethyl)imidazo[1,2-a]pyridine-3-carboxylate (74) (100 mg, 0.411 mmol) and 2n lioh (0.2 ml) in thf:meoh (4:1, 3 ml) was heated at 50 degrees centigrade for 45 minutes. the reaction was cooled to room temperature and the ph was adjusted between 3-5 with 10 percent citric acid. the solvent was partially reduced. the resulting solid was collected by vacuum filtration and washed with excess water. crude 6-(2-cyanoethyl)imidazo[1,2-a]pyridine-3-carboxylic acid (75) was dried and used in the next step without further purification. ms m/z 416.07 (m+1)+. synthesis of 6-(3-(oxobutyl)imidazo[1,2-a]pyridine-3-carboxylic acid (78) [ftimg=68000111]a stirring mixture of ethyl 6-bromoimidazo[1,2-a]pyridine-3-carboxylate (24s) (250 mg, 0.929 mmol), methyl vinyl ketone (151 ul, 1.86 mmol), tris(dibenzylideneacetone)dipalladium(0) (26 mg, 0.0279 mmol), [(t-bu)3ph]bf4 (13 mg, 0.0465 mmol) and n,n-dicyclohexylmethylamine (217 ul, 1.02 mmol) in anhydrous 1,4-dioxane (4 ml) was heated at 95 degrees centigrade overnight. the reaction was cooled to room temperature and filtered. the solvent was concentrated and crude 6-(3-oxobut-1-enyl)imidazo[1,2-a]pyridine-3-carboxylate (76) was purified by silica chromatography. ms m/z 259.10 (m+1)+. a stirring mixture of ethyl 6-(3-oxobut-1-enyl)imidazo[1,2-a]pyridine-3-carboxylate (76) (200 mg, 0.774 mmol) and 10 wt percent pd/c (wet) in ethanol:ethylacetate (1:1, 8 ml) was hydrogenated overnight. the reaction was filtered over celite and the solvent was concentrated. crude 6-(3-oxobutyl)imidazo[1,2-a]pyridine-3-carboxylate (77) was used in the next step without further purification. ms m/z 261.12 (m+1)+. a stirring mixture of ethyl 6-(3-oxobutyl)imidazo[1,2-a]pyridine-3-carboxylate (77) (190 mg, 0.730 mmol) and 2n lioh (0.2 ml) in thf:meoh (4:1, 3 ml) was heated at 50 degrees centigrade for 45 minutes. the reaction was cooled to room temperature and the ph was adjusted between 3-5 with 10 percent citric acid. the solvent was partially reduced. the resulting solid was collected by vacuum filtration and washed with excess water. crude 6-(3-oxobutyl)imidazo[1,2-a]pyridine-3-carboxylic acid (78) was dried and used in the next step without further purification. ms m/z 233.08 (m+1)+. synthesis of 6-(3-oxobutyl)imidazo[1,2-a]pyridine-3-carboxylic acid (80) [ftimg=68000112]a mixture of ethyl 7-hydroxyimidazo[1,2-a]pyridine-3-carboxylate (24t) (500 mg, 2.43 mmol) and sodium chlorodifluoroacetate (444 mg, 2.91 mmol) in anhydrous acetonitrile (8 ml) was heated in the microwave at 125 degrees centigrade for 12 minutes. the solvent was concentrated and the crude product ethyl 7-(difluoromethoxy)imidazo[1,2-a]pyridine-3-carboxylate (79) was purified by silica chromatography. ms m/z 257.07 (m+1)+. a stirring mixture of ethyl 7-(difluoromethoxy)imidazo[1,2-a]pyridine-3-carboxylate (79) (150 mg, 0.585 mmol) and 2n lioh (1 ml) in thf:meoh (4:1, 5 ml) was heated at 60 degrees centigrade for 45 minutes. the reaction was cooled to room temperature and the ph was adjusted between 4-5 with 1n hcl. the solvent was partially reduced and the crude product was purified by reverse phase preparative hplc to yield 6-(3-oxobutyl)imidazo[1,2-a]pyridine-3-carboxylic acid (80). ms m/z 229.03 (m+1)+. synthesis of n-(5-(5-(1-(n-hydroxycarbamididoyl)azetidin-3-yl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (83) [ftimg=68000113]to a stirring mixture of n-(5-(5-(azetidin-3-yl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide hydrochloride (21) (200 mg, 0.487 mmol), potassium carbonate (202 mg, 1.46 mmol) and cyanogen bromide (103 mg, 0.974 mmol) in dichloromethane:water (1:1, 15 ml) were heated at 45 degrees centigrade for 1.5 hours. the reaction was cooled to room temperature and the layers were separated. the aqueous layer was washed with 3 times with dcm and dried over anhydrous sodium sulfate. the combined organics were concentrated. the resulting solid was washed with hexanes to give n-(5-(5-(1-cyanoazetidin-3-yl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (82). ms m/z 400.14 (m+1)+. a stirring mixture of n-(5-(5-(1-cyanoazetidin-3-yl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (82) (50 mg, 0.125 mmol), hydroxylamine hcl (13 mg, 0.188 mmol) and diea (44 ul, 0.250 mmol) in ethanol was heated at 78 degrees centigrade for 2 hours. the solvent was concentrated and dried under high vacuum. crude n-(5-(5-(1-(n-hydroxycarbamididoyl)azetidin-3-yl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (83) was used in the next step without further purification. ms m/z 433.17 (m+1)+. synthesis of 7-(3-oxobutyl)imidazo[1,2-a]pyridine-3-carboxylic acid (86) [ftimg=68000114]a stirring mixture of ethyl 7-bromoimidazo[1,2-a]pyridine-3-carboxylate (24g) (500 mg, 1.86 mmol), methyl vinyl ketone (301 ul, 3.72 mmol), tris(dibenzylideneacetone)dipalladium(0) (51 mg, 0.056 mmol), [(t-bu)3ph]bf4 (27 mg, 0.093 mmol) and n,n-dicyclohexylmethylamine (433 ul, 2.04 mmol) in anhydrous 1,4-dioxane (10 ml) was heated at 95 degrees centigrade overnight. the reaction was cooled to room temperature and filtered. the solvent was concentrated and crude ethyl 7-(3-oxobut-1-enyl)imidazo[1,2-a]pyridine-3-carboxylate (84) was purified by silica chromatography. ms m/z 259.10 (m+1)+. a stirring mixture of ethyl 7-(3-oxobut-1-enyl)imidazo[1,2-a]pyridine-3-carboxylate (84) (92 mg, 0.356 mmol) and 10 wt percent pd/c (wet) in ethanol:ethylacetate (1:1, 8 ml) was hydrogenated overnight. the reaction was filtered over celite and the solvent was concentrated. crude ethyl 7-(3-oxobutyl)imidazo[1,2-a]pyridine-3-carboxylate (85) was used in the next step without further purification. ms m/z 261.12 (m+1)+. a stirring mixture of ethyl 7-(3-oxobutyl)imidazo[1,2-a]pyridine-3-carboxylate (85) (90 mg, 0.346 mmol) and 2n lioh (0.5 ml) in thf:meoh (4:1, 3 ml) was heated at 60 degrees centigrade for 45 minutes. the reaction was cooled to room temperature and the ph was adjusted between 3-5 with 10 percent citric acid. the solvent was partially concentrated and the crude product was purified by reverse phase preparative hplc to yield 7-(3-oxobutyl)imidazo[1,2-a]pyridine-3-carboxylic acid (86). ms m/z 233.08 (m+1)+. synthesis of 7-meth-1-d3-imidazo[1,2-a]pyridine-3-carboxylic acid (95) [ftimg=68000115]to a stirring solution of ethyl 7-bromoimidazo[1,2-a]pyridine-3-carboxylate (24g) (500 mg, 1.86 mmol), peppsi (63.2 mg, 0.093 mmol) and 2-iodopropane (928 ul, 9.3 mmol) in anhydrous thf (3 ml) at 0 degrees centigrade under a stream of nitrogen was added methyl-d3-magnesium iodide (5.6 ml, 5.57 mmol). the reaction was stirred to room temperature for 5 hours. then, the reaction was quenched with nh4cl. the crude product was extracted with ether, washed with water and brine and dried over sodium sulfate. the product was purified on silica gel using 10 percent meoh in dichloromethane to yield ethyl 7-methyl-d3-imidazo[1,2-a]pyridine-3-carboxylate (94). 1h nmr (400 mhz, d6-dmsd) delta 8.85 (dd, j=0.4, 7.0 hz, 1h), 7.98 (s, 1h), 7.36 (s, 1h), 6.86 (dd, j=1.6, 7.2 hz, 1h), 4.10 (q, j=7.2 hz, 2h), 1.09 (t, j=7.2 hz, 3h). ms m/z 208.1 (m+1)+. to a stirring suspension of ethyl 7-methyl-d3-imidazo[1,2-a]pyridine-3-carboxylate (94) (142 mg, 0.69 mmol) in thf:meoh: h2o (3:2:1, 3 ml) was added 6n lioh (0.34 ml). the reaction was stirred at room temperature for 2 hours then neutralized with sodium bisulfate monohydrate and concentrated to afford 7-methyl-d3-imidazo[1,2-a]pyridine-3-carboxylic acid (95), which was immediately used without purification. ms (m/z) 180.1 (m+1)+. synthesis of 6(2(2,2-trifluoroethoxy)methyl)imidazo[1,2-a]pyridine-3-carboxylic acid (98) [ftimg=68000116]to a solution of ethyl 6-(hydroxymethyl)imidazo[1,2-a]pyridine-3-carboxylate (59) (460 mg, 2.2 mmol) and diea (0.78 ml, 4.4 mmol) in dcm (5 ml) was added mscl (303 mg, 2.64

mmol). the mixture was stirred at room temperature for 10 minutes then subjected to standard aqueous work up to give a residue. the crude product was dissolved in 2,2,2-trifluoroethanol (2 ml) and was added k2co3 (608 mg, 4.4 mmol). the reaction mixture was heated at 80 degrees centigrade for 2 hours. once complete, the reaction mixture was diluted and extracted with etoac. the organic layers were combined, dried over na2so4, filtered and concentrated to afford a residue which was purified by silica chromatography to yield ethyl 6-((2-(2,2-trifluoroethoxy)methyl)imidazo[1,2-a]pyridine-3-carboxylate (97). 1h nmr (400 mhz, cdcl3) delta 9.33 (m, 1h), 8.32 (s, 1h), 7.76 (dd, j=0.8, 9.2 hz, 1h), 7.47 (dd, j=2.0, 9.2 hz, 1h), 4.76 (s, 2h), 4.44 (q, j=7.2 hz, 2h), 3.92 (q, j=8.4 hz, 2h), 1.45 (t, j=7.2 hz, 3h). ms m/z 303.1 (m+1)+. a solution of ethyl 6-((2,2,2-trifluoroethoxy)methyl)imidazo[1,2-a]pyridine-3-carboxylate (97) (280 mg, 0.92 mmol) in thf/meoh/h2o (3:2:1, 5 ml) was treated with 6n lih (0.92 ml, 5.52 mmol) and stirred at room temperature for 1 hour. all solvents were removed and 6n hcl was added to adjust ph 5-6. then the mixture was purified by hplc to give 6-((2,2,2-trifluoroethoxy)methyl)imidazo[1,2-a]pyridine-3-carboxylic acid (98). 1h nmr (400 mhz, d6-dmsol) delta 9.34 (m, 1h), 8.40 (s, 1h), 7.88 (dd, j=0.8, 9.2 hz, 1h), 7.65 (dd, j=1.6, 9.2 hz, 1h), 4.83 (s, 2h), 4.18 (q, j=9.6 hz, 2h). ms m/z 275.1 (m+1)+. synthesis of 6-(3-(methoxy)methyl)-1h-1,2,4-triazol-5-yl)imidazo[1,2-a]pyridine-3-carboxylic acid (99) [ftimg=68000117]to a solution of ethyl 6-cyanoimidazo[1,2-a]pyridine-3-carboxylate (24q) (265 mg, 1.23 mmol) and 2-methoxyacetylhydrazide (193 mg, 1.85 mmol) in 2-ethoxyethanol (5 ml) was added naome (0.5 m in meoh, 3.7 ml). the mixture was heated at 110 degrees centigrade in a sealed vial overnight. the reaction mixture was purified by hplc to give 6-(3-(methoxy)methyl)-1h-1,2,4-triazol-5-yl)imidazo[1,2-a]pyridine-3-carboxylic acid (99). ms m/z 274.1 (m+1)+. synthesis of 5-(5-(azetidin-1-yl)-1,2,4-oxadiazol-3-yl)-2-methylaniline (109) [ftimg=68000118]to a solution of (z)-n'-hydroxy-4-methyl-3-nitrobenzimidazole (27) (30 g, 153.71 mmol, 1.00 equiv) and diea (39.7 g, 307.18 mmol, 2.00 equiv) in tetrahydrofuran (300 ml) was added dropwise to a solution of triphosgene (18.2 g) in tetrahydrofuran (50 ml). the reaction was stirred for 1 hour at room temperature then heated to reflux for an additional hour. the resulting solution was poured into 500 ml of water and extracted with 3x300 ml of ethyl acetate. the combined organic layers were washed with brine (3x200 ml), dried over anhydrous sodium sulfate, concentrated under vacuum, and purified by flash chromatography (dcm/meoh=20:1) to afford of 3-(4-methyl-3-nitrophenyl)-1,2,4-oxadiazol-5(4h)-one as a pale yellow solid (106). ms m/z 222.1 (m+1)+. to a solution of 3-(4-methyl-3-nitrophenyl)-1,2,4-oxadiazol-5(4h)-one (106) (12 g, 54.26 mmol) in pochl3 (120 ml) was added n,n-dimethylformamide (12 ml). the resulted solution was heated to reflux for 72 hours then concentrated under vacuum. the residue was dissolved in water (250 ml) and extracted with ethyl acetate (3x250 ml). the combined organic layers were washed with brine (3x250 ml), dried over anhydrous sodium sulfate and concentrated under vacuum. the residue was purified by flash chromatography (pe/ea=10:1) to afford 5-chloro-3-(4-methyl-3-nitrophenyl)-1,2,4-oxadiazole (107) as a white solid. 1h nmr (300 mhz, cdcl3) delta 8.64 (dd, j=1.5, 8.4 hz, 1h), 8.18 (dd, j=1.5, 7.8 hz, 1h), 7.56 (d, j=8.1 hz, 1h), 2.70 (s, 3h). ms m/z 240.7 (m+1)+. to a solution of 5-chloro-3-(4-methyl-3-nitrophenyl)-1,2,4-oxadiazole (107) (3.6 g, 15.02 mmol, 1.00 equiv) in ch3cn (40 ml) was added triethylamine (3.03 g, 29.94 mmol) and azetidine hydrochloride (1.68 g, 17.96 mmol). the resulting solution was stirred for 1 hour at room temperature, concentrated under vacuum and purified by prep-hplc to afford 5-(azetidin-1-yl)-3-(4-methyl-3-nitrophenyl)-1,2,4-oxadiazole (108) as a white solid. ms m/z 261.1 (m+1)+. to a stirred solution of 5-(azetidin-1-yl)-3-(4-methyl-3-nitrophenyl)-1,2,4-oxadiazole (108) (1.4 g, 5.38 mmol) in ethanol (25 ml) was added sncl2.2h2o (6.07 g, 26.90 mmol). the resulting solution was stirred for 20 min at reflux then cooled to room temperature and concentrated under vacuum. the residue was poured into saturated sodium hydroxide (50 ml) and extracted with ethyl acetate (3x50 ml). the combined organic layers were washed with brine (3x250 ml), dried over anhydrous sodium sulfate, concentrated under vacuum and purified by flash chromatography (pe/ea=10:1) to afford 5-(5-(azetidin-1-yl)-1,2,4-oxadiazol-3-yl)-2-methylaniline (109) (0.8 g, 65 percent yield) as a white solid. 1h nmr (300 mhz, cdcl3) delta 7.28-7.36 (m, 2h), 7.12 (d, j=7.8 hz, 1h), 4.32 (t, j=7.5 hz, 4h), 3.69 (brs, 2h), 2.47-2.57 (m, 2h), 2.21 (s, 3h). ms m/z 231.1 (m+1)+. synthesis of 6-carbamoylimidazo[1,2-a]pyridine-3-carboxylic acid (110) [ftimg=68000119]to a stirring solution of ethyl 6-cyanoimidazo[1,2-a]pyridine-3-carboxylate (24q) (500 mg, 2.32 mmol) in thf:meoh (4:1, 5 ml) was added 2n lih (4 ml). the reaction was heated at 60 degrees centigrade for 2 h then acidified with 10 percent citric acid. the solvent was partially concentrated and the resulting solid was collected by vacuum filtration and was washed with excess water. the product was purified from the crude solid to afford 6-carbamoylimidazo[1,2-a]pyridine-3-carboxylic acid (110). 1h nmr (400 mhz, d6-dmsol) delta 9.80 (s, 1h), 8.33-8.31 (m, 1h), 8.29 (s, 1h), 7.95 (dd, j=2.0, 9.6 hz, 1h), 7.83 (dd, j=0.8, 9.2 hz, 1h), 7.69 (s, 1h). ms m/z 205.05 (m+1)+. synthesis of 6-(2-(4-methylpiperazin-1-yl)ethyl)imidazo[1,2-a]pyridine-3-carboxylic acid (114) [ftimg=68000120]to a stirring mixture of ethyl 6-bromoimidazo[1,2-a]pyridine-3-carboxylate (24s) (1 g, 3.72 mmol) and tetrakis(triphenylphosphine)palladium(0) (215 mg, 0.19 mmol) in anhydrous toluene (10 ml) under argon was added tributyl[2-ethoxyethyl]stannane (1.7 g, 4.65 mmol). the reaction mixture was heated in a microwave sealed tube overnight at 90 degrees centigrade the reaction was cooled to room temperature and was filtered through celite. the solvent was concentrated and the crude product was purified by silica chromatography to afford (e)-ethyl 6-(2-ethoxyvinyl)imidazo[1,2-a]pyridine-3-carboxylate (111). ms m/z 261.3 (m+1)+. a stirring solution of ethyl 6-(2-ethoxyvinyl)imidazo[1,2-a]pyridine-3-carboxylate (111) (240 mg, 1.15 mmol) in thf:h2o (1:1, 4 ml) was heated at 50 degrees centigrade overnight. the reaction was cooled to room temperature and neutralized with saturated solution of sodium bicarbonate. the crude product was extracted with ethyl acetate. the organic layer was washed with water, brine and dried over anhydrous sodium sulfate. the solvent was concentrated and crude ethyl 6-(2-oxoethyl)imidazo[1,2-a]pyridine-3-carboxylate (112) was used in the next step without further purification. ms m/z 233.3 (m+1)+. to a stirring solution of crude ethyl 6-(2-oxoethyl)imidazo[1,2-a]pyridine-3-carboxylate (112) (214 mg, 0.92 mmol) in dcm (5 ml) and 1-methylpiperazine (231 micro l, 2.30 mmol) at room temperature was added portion-wise sodium triacetoxylborohydride (586 mg, 2.77 mmol). the reaction was stirred at room temperature overnight. the solvent was concentrated. the crude was taken in 10 percent sodium bicarbonate and ethyl acetate. the organic was washed with water, brine and dried over anhydrous sodium sulfate. the solvent was concentrated and the crude product was purified by silica chromatography to afford methyl 6-(2-(4-methylpiperazin-1-yl)ethyl)imidazo[1,2-a]pyridine-3-carboxylate (113). ms m/z 304.4 (m+1)+. to a stirring solution of methyl 6-(2-(4-methylpiperazin-1-yl)ethyl)imidazo[1,2-a]pyridine-3-carboxylate (113) (215 mg, 0.68 mmol) in thf:meoh (4:1, 4 ml) was added 2n lih (3 ml). the reaction was heated at 60 degrees centigrade for 45 minutes. the ph was adjusted between 4-5 with 1n hcl and concentrated. the crude product was purified by preparative hplc to afford 6-(2-(4-methylpiperazin-1-yl)ethyl)imidazo[1,2-a]pyridine-3-carboxylic acid (114). 1h nmr (400 mhz, d6-dmsol) delta 9.25 (s, 1h), 8.35 (s, 1h), 7.83 (d, j=9.2 hz, 1h), 7.61 (dd, j=1.6, 9.2 hz, 1h), 4.65-4.19 (m, 8h), 3.49-3.30 (m, 2h), 3.04-2.99 (m, 2h), 2.81 (s, 3h). ms m/z 316.1 (m+1)+. synthesis of tert-butyl 3-(3-(3-imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidin-1-ylsulfonfylcarbamate (128) [ftimg=68000121]to a stirring solution of n-(5-(5-(azetidin-3-yl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (21) (50 mg, 0.133 mmol) in anhydrous pyridine (1.5 ml) at 0 degrees centigrade was added tert-butyl chlorosulfonfylcarbamate (35 mg, 0.160 mmol). the reaction was stirred to room temperature for 1 hour. the reaction was quenched with water and the solvent was concentrated. the crude product tert-butyl 3-(3-(3-imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidin-1-ylsulfonfylcarbamate (128) was purified by preparative hplc. 1h nmr (400 mhz, d6-dmsol) delta 11.27 (s, 1h), 10.25 (s, 1h), 9.55-9.53 (m, 1h), 8.76 (s, 1h), 8.07 (d, j=1.6 hz, 1h), 7.93-7.90 (m, 1h), 7.84 (dd, j=1.6, 8.0 hz, 1h), 7.75-7.71 (m, 1h), 7.52 (dd, j=8.4 hz, 1h), 7.37-7.34 (m, 1h), 4.37-4.33 (m, 5h), 2.38 (s, 3h), 1.38 (s, 9h). ms m/z 554.17 (m+1)+. synthesis of methyl 3-(3-(4-methyl-3-(6-(((triisopropylsilyl)oxy)methyl)imidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (133) [ftimg=68000122]to a stirring suspension of 6-(((triisopropylsilyl)oxy)methyl)imidazo[1,2-a]pyridine-3-carboxylic acid (61) (70 mg, 0.20 mmol) in anhydrous dichloromethane (5 ml) at room temperature oxalyl chloride was added dropwise (0.05 ml, 2.22 mmol). then, one drop of anhydrous dmf was added and the reaction mixture was stirred at room temperature for 15 minutes. the solvent was concentrated and the crude solid was added to a stirring solution of methyl 3-(3-(3-amino-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (31) (51.1 mg, 0.18 mmol) in anhydrous pyridine (5 ml) at room temperature. the reaction was stirred for 20 minutes. water (20 ml) was added to the reaction mixture and extraction with etoac afforded a residue after removing organic solvents. to the above residue, was added thf (0.5 ml) and tbaif (1m in thf, 0.30 ml) and the resulting mixture was stirred for 30 minutes. thf was removed and the residue was dissolved in etoac (20 ml) and washed with water twice. the organic layers were combined, dried over na2so4, filtered and concentrated to give a crude residue which was dissolved in dcm (1 ml) and followed by addition of diea (52 mg, 0.40 mmol) and mslcl (46 mg, 0.4 mmol). the reaction was stirred for 10 minutes. the mixture was diluted with dcm (10 ml) and washed with water. the organic layers were combined, dried over na2so4, filtered and concentrated to give methyl 3-(3-(4-methyl-3-(6-(((methylsulfonyl)oxy)methyl)imidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (133) which was used without further purification. ms m/z 541.1 (m+1)+. synthesis of 5-(4-methyl-1h-imidazol-1-yl)pyridin-2-amine (134) [ftimg=68000123]to a microwave tube with a magnetic stirring bar was charged cui (382 mg, 2.0 mmol), cs2co3 (6.5 g, 20.0 mmol), 4-methyl-1h-imidazole (1.15 g, 14.0 mmol), 5-bromopyridin-2-amine (1.75 g, 10.0 mmol), and dmf (10 ml) under n2. the system was sealed and then evacuated twice and back filled with n2. the reaction mixture was stirred for 30 min at room temperature, and then heated at 120 degrees centigrade for 48 h. the reaction mixture was then cooled to ambient temperature, diluted with 30 ml of ethyl acetate, washed with water. the combined organic layers were concentrated, and the resulting residue was purified by column chromatography on silica gel to provide 5-(4-methyl-1h-imidazol-1-yl)pyridin-2-amine (134). 1h nmr (400 mhz, d6-dmsol) delta 8.09 (m, 1h), 7.85 (d, j=1.6 hz, 1h), 7.56 (dd, j=2.8, 8.8 hz, 1h), 7.22 (t, j=1.2 hz, 1h), 6.51 (dd, j=0.8, 8.8 hz, 1h), 6.15 (s, 2h), 2.14 (d, j=1.2 hz, 3h). ms m/z 175.1 (m+1)+. synthesis of 6-bromo-n-(5-(5-(3-cyanoazetidin-1-yl)methyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (143) [ftimg=68000124]carbonyl diimidazole (cdi) (2.3 g, 14.24 mmol) was added to a stirred solution of 2-acetoxyacetic acid (1.68 g, 14.24 mmol) in nmp (10 ml). after 30 minutes, 6-bromo-n-(5-(n-hydroxycarbamidoyl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (50f) (1.38 g, 3.56 mmol) was added in one portion and the resulting solution was stirred for 30 minutes before it was heated at 125 degrees centigrade for 15 minutes in a microwave reactor. the reaction solution was subjected to standard aqueous work up to afford a residue which was hydrolyzed by lithium hydroxide monohydrate (897 mg, 21.36 mmol) in thf/meoh/h2o (3:2:1). after removal of all solvents 2n nahco3 (10 ml) was added. the precipitate was filtered and dried in air to afford 6-bromo-n-(5-(5-(hydroxymethyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (142). 1h nmr (400 mhz, d6-dmsol) delta 10.14 (s, 1h), 9.64 (d, j=1.2 hz, 1h), 8.60 (s, 1h), 8.11 (d, j=1.6 hz, 1h), 7.83 (dd, j=1.6, 8.0 hz, 1h), 7.79 (dd, j=0.8, 9.6 hz, 1h), 7.67 (dd, j=2.0, 9.6 hz, 1h), 7.51 (d, j=8.0 hz, 1h), 6.09 (s, 1h), 4.81 (s, 2h), 2.37 (s, 3h). ms m/z 427.9, 429.9 (m+1)+. to a solution of 6-bromo-n-(5-(5-(hydroxymethyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (142) (200 mg, 0.47 mmol) and diea (0.25 ml) in dichloromethane (5 ml) was added mslcl (108.1 mg, 0.94 mmol). the mixture was stirred at room temperature for 10 minutes and then diluted with dichloromethane (10 ml) and washed with water. the organic layers were dried over na2so4, filtered and concentrated to give a residue which was dissolved in dmf (2 ml). then azetidine-3-carbonitrile (116 mg, 1.41 mmol) was added and the reaction mixture was heated at 80 degrees centigrade for 1 hour. the reaction mixture was diluted with water (50 ml) and extracted with etoac. the organic layers were dried over na2so4, filtered and concentrated to give the crude product which was purified by silica chromatography to yield 6-bromo-n-(5-(5-(3-cyanoazetidin-1-yl)methyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (143). 1h nmr (400 mhz, d6-dmsol) delta 10.15 (s, 1h), 9.62 (dd, j=0.8, 2.0 hz, 1h), 8.60 (s, 1h), 8.07 (d, j=1.6 hz, 1h), 7.83 (dd, j=1.6, 8.0 hz, 1h), 7.79 (dd, j=0.8, 9.6 hz, 1h), 7.68 (dd, j=2.0, 9.6 hz, 1h), 7.51 (d, j=8.4 hz, 1h), 4.06 (s, 2h), 3.67 (m, 2h), 3.51-3.60 (m, 3h), 2.37 (s, 3h). ms m/z 492.0, 494.0 (m+1)+. synthesis of 6-(2,4-dimethylthiazol-5-yl)imidazo[1,2-a]pyridine-3-carboxylic acid (146) [ftimg=68000125]a mixture of ethyl 6-bromoimidazo[1,2-a]pyridine-3-carboxylate (24s) (500 mg, 1.86 mmol), bis(pinacolato)diboron (472 mg, 1.86 mmol), dichloro-bis(triphenylphosphine)palladium (65 mg, 0.093 mmol) and potassium acetate (456 mg, 4.65 mmol) in anhydrous dioxane (8 ml) was heated at 95 degrees centigrade for 4 hours. the reaction turned black. the reaction was cooled and filtered through celite. the solvent was concentrated. the oil was taken in etoac. the organic was washed with water/brine mixture, brine and dried over anhydrous sodium sulfate. the crude product was purified by silica chromatography. ms m/z 317 (m+1)+. a mixture of 5-bromo-2,4-dimethylthiazole (171 mg, 0.89 mmol), ethyl 6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[1,2-a]pyridine-3-carboxylate (144) (250 mg, 1.07 mmol), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(11) (39 mg, 0.05 mmol) and a solution of 2m sodium carbonate (300 ul) in anhydrous dioxane (4 ml) was heated in the microwave at 135 degrees centigrade for 25 minutes. the reaction was filtered through celite. the crude product was taken in water and ethylacetate. the organic was washed with water/brine mixture and dried over anhydrous sodium sulfate. the crude product was purified by silica chromatography. ms m/z 302.09 (m+1)+. a mixture of ethyl 6-(2,4-dimethylthiazol-5-yl)imidazo[1,2-a]pyridine-3-carboxylate (145) (190 mg, 0.630 mmol) and 2n lih (1 ml) in thf:meoh (4:1, 4 ml) was heated at 60 degrees centigrade for 30 minutes. the reaction was cooled to room temperature and the ph was adjusted between 4-5 with 10 percent citric acid. the solvent was partially reduced and the resulting solid was collected by vacuum filtration to give 6-(2,4-dimethylthiazol-5-yl)imidazo[1,2-a]pyridine-3-carboxylic acid (146). 1h nmr (400 mhz, d6-dmsol) delta 9.34 (s, 1h), 8.29 (s, 1h), 7.87 (dd, j=0.8, 9.2 hz, 1h), 7.62 (dd, j=2.0, 9.2 hz, 1h), 2.66 (s, 3h), 2.41 (s, 3h). ms m/z 274.06 (m+1)+. synthesis of n-(5-(5-(chloromethyl)-1,2,4-oxadiazol-3-o-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (151) [ftimg=68000126]a mixture of n-(5-(n'-hydroxycarbamidoyl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide 9 (500 mg, 1.62 mmol) and 2-chloroacetic anhydride (553 mg, 3.23 mmol) in anhydrous 1-methyl-2-pyrrolidinone (10 ml) was heated in the microwave at 110 degrees centigrade for 12 minutes. the crude was diluted with water and extracted with ethyl acetate. the organic was washed with water/brine mixture and dried over anhydrous sodium sulfate. the crude product was purified by silica chromatography. ms m/z 368.08 (m+1)+. synthesis of final compounds synthesis of n-(5-(5-(5-difluorotetrahydro-2h-pyran-2-yl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (f10) [ftimg=68000127] hatu (0.134 g, 0.355 mmol) was added in one portion to a stirred solution of 5,5-difluorotetrahydro-2h-pyran-2-carboxylic acid (17) (53 mg, 0.31 mmol) and diea (60 l, 0.355 mmol) in dry dmf (3 ml). after 10 minutes, n-(5-(n'-hydroxycarbamidoyl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (9) (0.1 g, 0.323 mmol) was added in one portion and continued to stir for another 30 minutes, then heated at 110 degrees centigrade for 30 minutes. the reaction was filtered and purified by preparative reverse phase hplc to afford n-(5-(5-(5-difluorotetrahydro-2h-pyran-2-yl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (f10) as a white solid. 1h nmr (400 mhz, d4-meoh) delta 9.73 (d, j=7.2 hz, 1h), 8.74 (s, 1h), 8.17 (m, 1h), 7.98-7.95 (m, 3h), 7.52-7.50 (m, 2h), 5.06 (dd, j=8.4, 2.8 hz, 1h), 4.07-4.00 (m, 1h), 3.91-3.81 (m, 1h), 2.44 (s, 3h), 2.40-2.21 (m, 4h). ms m/z 440.1 (m+1)+. synthesis of tert butyl 3-(3-(3-(imidazo[1,2-a]pyridine-3-carboxamido)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f13) [ftimg=68000128]to a stirring solution of boc-azetidine-3-carboxylic acid (162 mg, 0.8 mmol) in anhydrous nmp (4 ml) was added cdi (131 mg, 0.8 mmol). the reaction was stirred for 2 minutes. n-(5-(n'-

hydroxycarbamimidoyl)-2-methylphenyl]imidazo[1,2-a]pyridine-3-carboxamide (9) (250 mg, 0.8 mmol) was added and the reaction was stirred for 15 minutes, then heated via microwave at 120 degrees centigrade for 15 minutes. the crude was purified by reverse phase hplc to afford tert-butyl 3-(3-(imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f13) as a white solid. 1h nmr (400 mhz, d6-dmsol) delta 10.17 (s, 1h), 9.51 (d, j=6.8 hz, 1h), 8.70 (s, 1h), 8.10 (d, j=2.0 hz, 1h), 7.86 (dt, j=12, 2.0 hz, 2h), 7.68 (t, j=8.0 hz, 1h), 7.51 (d, j=8 hz, 1h), 7.31 (td, j=6.8, 0.8 hz, 1h), 4.06-4.38 (m, 5h) 2.37 (s, 1h), 1.40 (s, 9h). ms m/z 476.2 (m+1)+. synthesis of methyl 3-(3-(3-(imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f15) [ftimg=68000129]to a stirring solution of n-(5-(5-(azetidin-3-yl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (21) (25 mg, 0.0667 mmol) in anhydrous pyridine (1 ml) was added methylchloroformate (5 micro l, 0.667 mmol). the reaction was stirred to room temperature for 10 minutes. the ph was adjusted to neutral with 10 percent citric acid. the crude was purified by reverse phase hplc to afford methyl 3-(3-(3-(imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f15) as a white solid. 1h nmr (400 mhz, d6-dmsol) delta 10.18 (s 1h), 9.52 (d, j=7.2 hz, 1h), 8.71 (s, 1h), 8.10 (s, 1h), 7.82-7.91 (m, 2h), 7.69 (t, j=8.0 hz, 1h), 7.51 (d, j=8.4 hz, 1h), 7.31 (td, j=7.2, 0.8 hz, 1h), 4.15-4.44 (m, 5h) 3.59 (s, 3h), 2.37 (s, 3h). ms m/z 433.3 (m+1)+. synthesis of n-(2-methyl-5-(5-(morpholinomethyl)-1,2,4-oxadiazol-3-yl)phenyl)imidazo[1,2-a]pyridine-3-carboxamide (f22) [ftimg=68000130]a solution of (3-(3-(imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl) methyl methanesulfonate (44) (21.4 mg, 0.05 mmol), diea (13.0 mg, 0.1 mmol) and morpholine (13.0 mg, 0.15 mmol) in dmf (1 ml) was heated at 80 degrees centigrade for 4 hours. the crude product was purified by preparative hplc to yield n-(2-methyl-5-(5-(morpholinomethyl)-1,2,4-oxadiazol-3-yl)phenyl)imidazo[1,2-a]pyridine-3-carboxamide (f22). 1h nmr (400 mhz, cd2cl2) delta 9.60 (d, j=6.8 hz, 1h), 8.60 (d, j=1.6 hz, 1h), 8.45 (s, 1h), 8.06 (s, 1h), 7.89 (dd, j=2.0, 8.0 hz, 1h), 7.80 (d, j=8.8 hz, 1h), 7.54 (m, 1h), 7.43 (d, j=8.0 hz, 1h), 7.15 (m, 1h), 3.93 (s, 2h), 3.75 (m, 4h), 2.67 (m, 4h), 2.48 (s, 3h). ms m/z 419.2 (m+1)+. note: if hcl salt of morpholine (0.15 mmol) was used, agno3 (0.15 mmol) was needed to avoid replacement of oms group by cl. synthesis of n-(2-methyl-5-(5-(1-sulfamoylazetidin-3-yl)-1,2,4-oxadiazol-3-yl)phenyl)imidazo[1,2-a]pyridine-3-carboxamide (f23) [ftimg=68000131]to a stirring solution of tert-butyl 3-(3-(3-(imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidin-1-ylsulfonycarbamate (128) (25 mg, 0.0452 mmol) in ch3cn (0.5 ml) was added hcl (4n in dioxane, 1 ml). the reaction was stirred for 30 minutes. the solvent was concentrated and the crude was purified by preparative hplc to give n-(2-methyl-5-(5-(1-sulfamoylazetidin-3-yl)-1,2,4-oxadiazol-3-yl)phenyl)imidazo[1,2-a]pyridine-3-carboxamide (f23). 1h nmr (400 mhz, d6-dmsol) delta 10.14 (s, 1h), 9.51-9.48 (m, 1h), 8.67 (s, 1h), 8.11 (d, j=1.6 hz, 1h), 7.87-7.84 (m, 2h), 7.66-7.61 (m, 1h), 7.52 (d, j=8.0 hz, 1h), 7.29-7.25 (m, 1h), 7.13 (s, 2h), 4.24-4.18 (m, 1h), 4.16-4.12 (m, 2h), 4.05-4.01 (m, 2h), 2.37 (s, 3h). ms m/z 454.59 (m+1)+. synthesis of (3-(3-(3-(imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)oxetan-3-yl)carbamate (f26) [ftimg=68000132]to a stirring solution of n-(5-(5-(3-aminoxetan-3-yl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (47) (8.0 mg, 0.02 mmol) and diea (5.2 mg, 0.04 mmol) in anhydrous dichloromethane (1 ml) was added methylchloroformate (2.3 mg, 0.024 mmol). the reaction was stirred to room temperature for 10 minutes. the solvent was removed and the crude was purified by preparative hplc to afford methyl methyl (3-(3-(3-(imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)oxetan-3-yl)carbamate (f26). 1h nmr (400 mhz, cdcl3) delta 9.46 (m, 1h), 8.48 (s, 1h), 8.14 (s, 1h), 7.81 (dd, j=1.6, 8.0 hz, 1h), 7.69 (d, j=7.2 hz, 1h), 7.56 (s, 1h), 7.38 (m, 1h), 7.31 (d, j=8.0 hz, 1h), 6.98 (dt, j=0.8, 6.8 hz, 1h), 5.12 (m, 2h), 4.91 (m, 2h), 3.66 (s, 3h), 2.36 (s, 3h). ms m/z 449.1 (m+1)+. synthesis of 3-(3-(4-fluoro-3-(imidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f27) [ftimg=68000133]to a stirring solution of boc-azetidine-3-carboxylic acid (162 mg, 0.8 mmol) in anhydrous nmp (4 ml) was added cdi (131 mg, 0.8 mmol). the reaction was stirred for 10 minutes. n-(2-fluoro-5-(n'-hydroxycarbamimidoyl)phenyl)imidazo[1,2-a]pyridine-3-carboxamide (50) (125 mg, 0.4 mmol) was added and the reaction was stirred for 15 minutes, then heated via microwave at 125 degrees centigrade for 15 minutes. the crude was purified via reverse phase hplc to afford tert-butyl 3-(3-(4-fluoro-3-(imidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f27) as a white solid. ms m/z 479.21 (m+1)+. synthesis of n-(5-(5-(1-(ethylsulfonyl)azetidin-3-yl)-1,2,4-oxadiazol-3-yl)-2-fluorophenyl)imidazo[1,2-a]pyridine-3-carboxamide (f28) [ftimg=68000134]tert-butyl 3-(3-(4-fluoro-3-(imidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f27) (14.4 mg, 0.03 mmol) was dissolved in tfa (0.5 ml) and stirred at room temperature for 10 minutes. then tfa was removed under vacuum. the residue was dissolved in anhydrous dichloromethane (1 ml) and diea (13.0 mg, 0.10 mmol) and ethanesulfonyl chloride (5.8 mg, 0.045 mmol) were added. the reaction was stirred at room temperature for 10 minutes. the solvent was removed and the crude was purified by preparative hplc to afford n-(5-(5-(1-(ethylsulfonyl)azetidin-3-yl)-1,2,4-oxadiazol-3-yl)-2-fluorophenyl)imidazo[1,2-a]pyridine-3-carboxamide (f28). 1h nmr (400 mhz, cdcl3) delta 9.50 (d, j=0.8 hz, 1h), 9.09 (dd, j=2, 7.2 hz, 1h), 8.21 (s, 1h), 7.87 (m, 1h), 7.79 (m, 1h), 7.71 (d, j=9.2 hz, 1h), 7.41 (m, 1h), 7.22 (dd, j=8.8, 10.4 hz, 1h), 7.02 (dt, j=8.8, 6.8 hz, 1h), 4.34 (m, 4h), 4.07 (m, 1h), 3.00 (q, j=7.6 hz, 2h), 1.35 (t, j=7.6 hz, 3h). ms m/z 471.1 (m+1)+. synthesis of methyl 3-(3-(4-methyl-3-(6-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f52) [ftimg=68000135]to a stirring suspension of 6-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carboxylic acid (24a) (50 mg, 0.217 mmol) in anhydrous dichloromethane (2 ml) at 0 degrees centigrade under argon was added dropwise oxalyl chloride (19 micro l, 0.228 mmol). then, a drop of anhydrous dmf was added and the reaction mixture was stirred at room temperature for 1.5 hours. the solvent was concentrated and the crude solid was added portion-wise to a stirring solution of methyl 3-(3-(3-amino-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (31) (47 mg, 0.163 mmol) in anhydrous pyridine (1 ml) at 0 degrees centigrade the reaction was stirred at room temperature under argon for 10 minutes and quenched with water. the crude product was purified by preparative hplc to yield methyl 3-(3-(4-methyl-3-(6-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f52). 1h nmr (400 mhz, d6-dmsol) delta 10.27 (s, 1h), 9.90-9.85 (m, 1h), 8.72 (s, 1h), 8.08 (d, j=1.6 hz, 1h), 8.02-7.99 (m, 1h), 7.86 (dd, j=2.0, 8.0 hz, 1h), 7.79 (dd, j=2.0, 9.2 hz, 1h), 7.52 (d, j=8.0 hz, 1h), 4.37-4.19 (m, 5h), 3.59 (s, 3h), 2.37 (s, 3h). ms m/z 501.43 (m+1)+. synthesis of methyl 3-(3-(4-methyl-3-(7-(1-methyl-1h-pyrazol-3-yl)imidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f56) [ftimg=68000136]methyl 3-(3-(3-(7-bromoimidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (42) (40 mg, 0.078 mmol), 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1h-pyrazole (19.6 mg, 0.094 mmol) and pd(pph3)4 (9 mg, 0.0078 mmol) were added to a flask equipped with a stir bar. the flask was evacuated and backfilled with nitrogen several times. dmf (1 ml) and 1.8 m k2co3 (0.094 mmol) were added by syringe. the flask was sealed and heated at 80 degrees centigrade for 12 hours. the reaction was filtered and directly purified by preparative reverse phase hplc to afford methyl 3-(3-(4-methyl-3-(7-(1-methyl-1h-pyrazol-3-yl)imidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f56). ms m/z 513.2 (m+1)+. synthesis of methyl 3-(3-(4-methyl-3-(7-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f57) [ftimg=68000137]to a stirring suspension of 7-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carboxylic acid (24) (89 mg, 0.387 mmol) in anhydrous dichloromethane (3 ml) at 0 degrees centigrade under argon oxalyl chloride (34 ul, 0.407 mmol) was added dropwise. then, a drop of anhydrous dmf was added and the reaction mixture was stirred at 0 degrees centigrade for 1.5 hours. the solvent was concentrated and the crude solid was added to a stirring solution of methyl 3-(3-(3-amino-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (31) (19 mg, 0.0645 mmol) in anhydrous pyridine (1.5 ml) at 0 degrees centigrade the reaction was stirred at room temperature under argon for 20 minutes. the crude product was filtered and purified by preparative hplc to give methyl 3-(3-(4-methyl-3-(7-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f57). 1h nmr (400 mhz, d6-dmsol) delta 10.25 (s, 1h), 9.4-9.61 (m, 1h), 9.75 (s, 1h), 8.33-8.30 (m, 1h), 8.10 (dd, j=1.6 hz, 1h), 7.86 (dd, j=1.6, 8.0 hz, 1h), 7.52 (d, j=8.4 hz, 1h), 7.46 (dd, j=2.0, 7.6 hz, 1h), 4.40-4.33 (m, 2h), 4.31-4.25 (m, 1h), 4.22-4.18 (m, 2h), 3.59 (s, 3h), 2.38 (s, 3h). ms m/z 501.43 (m+1)+. synthesis of methyl 3-(3-(6-(3-cyanopropyl)imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f59) [ftimg=68000138]to a stirring suspension of 6-(3-cyanopropyl)imidazo[1,2-a]pyridine-3-carboxylic acid (25) (50 mg, 0.218 mmol) in anhydrous dichloromethane (2 ml) at 0 degrees centigrade under argon was added dropwise oxalyl chloride (20 micro l, 0.240 mmol). then, a drop of anhydrous dmf was added and the reaction mixture was stirred at 0 degrees centigrade for 1 hour. the solvent was concentrated and the crude solid was dried under vacuum. to a mixture of the acid chloride and methyl 3-(3-(3-amino-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (31) (31 mg, 0.109 mmol) cooled to degrees centigrade under argon was added anhydrous pyridine (2 ml). the reaction was stirred to room temperature under argon for 20 minutes. the solvent was concentrated. the crude product was purified by silica chromatography. 1h nmr (400 mhz, d6-dmsol) delta 10.13 (s, 1h), 9.38-9.36 (m, 1h), 8.66 (s, 1h), 8.11 (d, j=1.6 hz, 1h), 7.86-7.82 (m, 2h), 7.63-7.60 (m, 1h), 7.51 (d, j=8.0 hz, 1h), 4.39-4.34 (m, 2h), 4.31-4.24 (m, 1h), 4.21-4.18 (m, 2h), 3.59 (s, 3h), 2.81-2.77 (m, 2h), 2.60-2.52 (m, 2h), 2.38 (s, 3h), 1.97-1.90 (m 2h). ms m/z 500.52 (m+1)+. synthesis of methyl 3-(3-(4-methyl-3-(7-methylimidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f61) [ftimg=68000139]to a stirring suspension of 7-methylimidazo[1,2-a]pyridine-3-carboxylic acid (24i) (100 mg, 0.568 mmol) in anhydrous dichloromethane (5 ml) at 0 degrees centigrade under argon was added dropwise oxalyl chloride (53 ul, 0.624 mmol). then, a drop of anhydrous n,n-dimethylformamide was added and the reaction mixture was stirred at 0 degrees centigrade for 1 hour. the solvent was concentrated. a stirring mixture of the acid chloride and methyl 3-(3-(3-amino-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (31) (82 mg, 0.283 mmol) in anhydrous pyridine (2 ml) was stirred at room temperature for 2 hour. the solvent was concentrated and the crude product was purified by silica chromatography to give methyl 3-(3-(4-methyl-3-(7-methylimidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f61). 1h nmr (400 mhz, d6-dmsol) delta 9.97 (s, 1h), 9.33 (d, j=7.2 hz, 1h), 8.52 (s, 1h), 8.09 (d, j=1.6 hz, 1h), 7.83 (dd, j=1.6, 7.6 hz, 1h), 7.58 (s, 1h), 7.50 (d, j=8.0 hz, 1h), 7.03 (dd, j=1.6, 7.2 hz, 1h), 4.39-4.33 (m, 2h), 4.31-4.24 (m, 1h), 4.22-4.16 (m, 2h), 3.59 (s, 3h), 2.43 (s, 3h), 2.36 (s, 3h). ms m/z 447.17 (m+1)+. synthesis of methyl 3-(3-(4-methyl-3-(6-methylimidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f62) [ftimg=68000140]to a stirring suspension of 6-methylimidazo[1,2-a]pyridine-3-carboxylic acid (24j) (35 mg, 0.196 mmol) in anhydrous dichloromethane (2 ml) at 0 degrees centigrade under argon was added dropwise oxalyl chloride (17 ul, 0.206 mmol). then, a drop of anhydrous n,n-dimethylformamide was added and the reaction mixture was stirred at 0 degrees centigrade for 1 hour. the solvent was concentrated. a stirring mixture of the acid chloride and methyl 3-(3-(3-amino-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (31) (28 mg, 0.098 mmol) in anhydrous pyridine (1.5 ml) was stirred at room temperature for 2 hours. the solvent was concentrated and the crude product was purified by silica chromatography to give methyl 3-(3-(4-methyl-3-(6-methylimidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f62). 1h nmr (400 mhz, d6-dmsol) delta 10.15 (s, 1h), 9.36 (s, 1h), 8.67 (s, 1h), 8.11 (d, j=2.0 hz, 1h), 7.85 (dd, j=2.0, 8.0 hz, 1h), 7.81 (d, j=9.2 hz, 1h), 7.57 (dd, j=1.2, 9.2 hz, 1h), 7.51 (d, j=8.0 hz, 1h), 4.39-4.34 (m, 2h), 4.31-4.24 (m, 1h), 4.22-4.17 (m, 2h), 3.59 (s, 3h), 2.41 (s, 3h), 2.37 (s, 3h). ms m/z 447.17 (m+1)+. synthesis of methyl 3-(3-(3-(6-(2-cyanoethyl)imidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f64) [ftimg=68000141]to a stirring suspension of 6-(2-cyanoethyl)imidazo[1,2-a]pyridine-3-carboxylic acid (75) (50 mg, 0.232 mmol) in anhydrous dichloromethane (2 ml) at 0 degrees centigrade under argon was added dropwise oxalyl chloride (22 ul, 0.256 mmol). then, a drop of anhydrous n,n-dimethylformamide was added and the reaction mixture was stirred at 0 degrees centigrade for 1 hour. the solvent was concentrated and the crude solid was dried under vacuo. methyl 3-(3-(3-amino-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (31) (33 mg, 0.116 mmol) and anhydrous pyridine (2 ml) were added to the acid chloride. the reaction was stirred to room temperature under argon for 20 minutes. the crude product was purified by reverse phase preparative hplc to give methyl 3-(3-(3-(6-(2-cyanoethyl)imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f64). 1h nmr (400 mhz, d6-dmsol) delta 10.08 (s, 1h), 9.45 (s, 1h), 8.63 (s, 1h), 8.12 (d, j=1.6 hz, 1h), 7.85 (dd, j=2.0, 5.6 hz, 1h), 7.82 (d, j=6.8 hz, 1h), 7.60 (dd, j=1.6, 9.2 hz, 1h), 7.51 (d, j=8.0 hz, 1h), 4.38-4.33 (m, 2h), 4.31-4.24 (m, 1h), 4.21-4.18 (m, 2h), 3.59 (s, 3h), 3.01 (t, j=7.6 hz, 2h), 2.91 (t, j=6.4 hz, 2h), 2.38 (s, 3h). ms m/z 486.18 (m+1)+. synthesis of methyl 3-(3-(4-methyl-3-(6-(3-oxobutyl)imidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f65) [ftimg=68000142]to a stirring suspension of 6-(3-oxobutyl)imidazo[1,2-a]pyridine-3-carboxylic acid (78) (50 mg, 0.215 mmol) in anhydrous dichloromethane (2 ml) at 0 degrees centigrade under argon was added dropwise oxalyl chloride (20 ul, 0.237 mmol). then, a drop of anhydrous n,n-dimethylformamide was added and the reaction mixture was stirred at 0 degrees centigrade for 1 hour. the solvent was concentrated and the crude solid was dried under vacuo. next, methyl 3-(3-(3-amino-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (31) (27 mg, 0.0796 mmol) and anhydrous pyridine (1 ml) were added to the acid chloride. the reaction was stirred to room temperature under argon for 20 minutes. the crude product was purified by reverse phase preparative hplc to give methyl 3-(3-(4-methyl-3-(6-(3-oxobutyl)imidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f65). 1h nmr (400 mhz, d6-dmsol) delta 10.02 (s, 1h), 9.31 (s, 1h), 8.55 (s, 1h), 8.10 (d, j=1.6 hz, 1h), 7.83 (dd, j=2.0, 8.0 hz, 1h), 7.73 (d, j=9.2 hz, 1h), 7.50 (d, j=8.0 hz, 1h), 7.46 (dd, j=1.6, 9.2 hz, 1h), 4.39-4.34 (m, 2h), 4.31-4.25 (m, 1h), 4.22-4.18 (m, 2h), 3.59 (s, 3h), 2.85 (s, 4h), 2.37 (s, 3h), 2.10 (s, 3h). ms m/z 503.2 (m+1)+. synthesis of methyl 3-(3-(4-methyl-3-(6-(2-morpholinoethyl)imidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f66) [ftimg=68000143]to a stirring suspension of 6-(2-morpholinoethyl)imidazo[1,2-a]pyridine-3-carboxylic acid (24i) (50 mg, 0.182 mmol) in anhydrous dichloromethane (2 ml) at 0 degrees centigrade under argon was added dropwise oxalyl chloride (17 ul, 0.200 mmol). then, a drop of anhydrous n,n-dimethylformamide was added and the reaction mixture was stirred at 0 degrees centigrade for 1 hour. the solvent was concentrated. a stirring mixture of the acid chloride and methyl 3-(3-(3-amino-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (31) (26 mg, 0.0908 mmol) in anhydrous pyridine (1.5 ml) was stirred at room temperature for 2 hours. the crude product was purified by reverse phase preparative hplc to give methyl 3-(3-(4-methyl-3-(6-(2-morpholinoethyl)imidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f66). 1h nmr (400 mhz, d6-dmsol) delta 10.07 (s, 1h), 9.46 (s, 1h), 8.61 (s, 1h), 8.12 (d, j=1.6 hz, 1h), 7.86-7.83 (m, 2h), 7.52-7.49 (m, 2h), 4.39-4.36 (m, 2h), 4.31-4.26 (m, 1h), 4.21-4.17 (m, 2h), 4.03-4.00 (m, 2h), 3.69-3.63 (m, 2h), 3.59 (s, 3h), 3.54-3.44 (m, 4h), 3.14-3.10 (m, 4h), 2.38 (s, 3h). ms m/z 546.24 (m+1)+. synthesis of methyl 3-(3-(6-(3-hydroxy-3-methylbutyl)imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f67) [ftimg=68000144]to a stirring solution of methyl 3-(3-(4-methyl-3-(6-(3-oxobutyl)imidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f65) (10 mg, 0.0199 mmol) in anhydrous thf (1 ml) at -78 degrees centigrade under a stream of argon was added methylmagnesium bromide (27 ul, 0.080 mmol). the reaction was stirred to

room temperature for 15 minutes then cooled to 0 degrees centigrade and quenched with 1n hcl. the crude product was purified by reverse phase preparative hplc to give methyl 3-(3-(6-(3-hydroxy-3-methylbutyl)imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f67). 1h nmr (400 mhz, d6-dmsol) delta 10.10 (s, 1h), 9.34 (s, 1h), 8.63 (s, 1h), 8.10 (d, j=1.6 hz, 1h), 7.84 (dd, j=1.6, 8.0 hz, 1h), 7.78 (d, j=9.2 hz, 1h), 7.56-7.54 (m, 1h), 7.51 (d, j=8.4 hz, 1h), 4.39-4.34 (m, 2h), 4.31-4.25 (m, 1h), 4.22-4.17 (m, 2h), 3.59 (s, 3h), 2.76-2.72 (m, 2h), 2.37 (s, 3h), 1.71-1.67 (m, 2h), 1.15 (s, 6h). ms m/z 519.23 (m+1)+. synthesis of methyl 3-(3-(3-(7-(1h-pyrazol-3-yl)imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f68) [ftimg=68000145]to a stirring solution of 7-(1h-pyrazol-3-yl)imidazo[1,2-a]pyridine-3-carboxylic acid (63) (31.7 mg, 0.14 mmol), and methyl 3-(3-amino-4-methylphenyl)-1,2,4-oxadiazol-5-yl)methylcarbamate (31) (52 mg, 0.18 mmol) in ethyl acetate (0.1 ml) was added propylphosphonic anhydride (50 wt percent in ethyl acetate 0.41 ml). the reaction was heated at 80 degrees centigrade for 12 hours. the resulting mixture was diluted in ethyl acetate and washed with 1n na2co3. after aqueous workup, the residue was purified by reverse phase hplc to afford methyl 3-(3-(3-(7-(1h-pyrazol-3-yl)imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f68). ms (m/z) 499.1 (m+1)+. synthesis of methyl 3-(3-(3-(7-(3-hydroxy-3-methylbutyl)imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f73) [ftimg=68000146]to a stirring suspension of 7-(3-oxobutyl)imidazo[1,2-a]pyridine-3-carboxylic acid (86) (40 mg, 0.172 mmol) in anhydrous dichloromethane (2 ml) at 0 degrees centigrade under argon was added dropwise oxalyl chloride (16 ul, 0.189 mmol). then, a drop of anhydrous n,n-dimethylformamide was added and the reaction mixture was stirred at 0 degrees centigrade for 1 hour. the solvent was concentrated and the crude solid was dried under vacuum. methyl 3-(3-(3-amino-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (31) (25 mg, 0.086 mmol) and anhydrous pyridine (1 ml) were added to the acid chloride. the reaction was stirred to room temperature under argon for 20 minutes. the crude product was purified by reverse phase preparative hplc to give methyl 3-(3-(4-methyl-3-(7-(3-oxobutyl)imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f73). 1h nmr (400 mhz, d6-dmsol) delta 10.24 (s, 1h), 9.44-9.41 (m, 1h), 8.73 (s, 1h), 8.09 (d, j=1.6 hz, 1h), 7.85 (dd, j=1.6, 8.0 hz, 1h), 7.73 (s, 1h), 7.51 (d, j=8.4 hz, 1h), 7.32-7.29 (m, 1h), 4.39-4.35 (m, 2h), 4.31-4.24 (m, 1h), 4.21-4.17 (m, 2h), 3.59 (s, 3h), 2.98-2.91 (m, 4h), 2.37 (s, 3h), 2.13 (s, 3h). ms m/z 503.2 (m+1)+. synthesis of methyl 3-(3-(3-(7-(3-hydroxy-3-methylbutyl)imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f74) [ftimg=68000147]to a stirring solution of methyl 3-(3-(4-methyl-3-(7-(3-oxobutyl)imidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f194) (10 mg, 0.0199 mmol) in anhydrous thf (1 ml) at -78 degrees centigrade under a stream of argon was added methylmagnesium bromide (27 ul, 0.080 mmol). the reaction was stirred to room temperature for 15 minutes and quenched at 0 degrees centigrade with 1n hcl. the crude product was purified by reverse phase preparative hplc to give methyl 3-(3-(3-(6-(3-hydroxy-3-methylbutyl)imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f74). 1h nmr (400 mhz, d6-dmsol) delta 10.11 (s, 1h), 9.41-9.38 (m, 1h), 8.64 (s, 1h), 8.10 (s, 1h), 7.84 (dd, j=1.2, 7.6 hz, 1h), 7.65 (s, 1h), 7.50 (d, j=8.0 hz, 1h), 7.21-7.17 (m, 1h), 4.39-4.35 (m, 2h), 4.31-4.24 (m, 1h), 4.22-4.18 (m, 2h), 3.59 (s, 3h), 2.82-2.77 (m, 2h), 2.37 (s, 3h), 1.74-1.69 (m, 2h), 1.17 (s, 6h). ms m/z 519.23 (m+1)+. synthesis of n-(2-methyl-5-(3-morpholino-1,2,4-oxadiazol-5-yl)phenyl)imidazo[2-a]pyridine-3-carboxamide (f75) [ftimg=68000148]a stirring suspension of 3-(imidazo[1,2-a]pyridine-3-carboxamido)-4-methylbenzoic acid (4) (41 mg, 0.138 mmol) in anhydrous nmp (1 ml) was heated in the microwave at 105 degrees centigrade for 2 minutes to dissolve all solid. then, 1,1'-carbonyldiimidazole (22 mg, 0.138 mmol) was added and the reaction was stirred at room temperature for 15 minutes. n'-hydroxymorpholine-4-carboximidamide (20 mg, 0.138 mmol) was added and the reaction was stirred for 30 minutes. the reaction was heated in the microwave at 130 degrees centigrade for 15 minutes. the crude product was purified by reverse phase preparative hplc to give n-(2-methyl-5-(3-morpholino-1,2,4-oxadiazol-5-yl)phenyl)imidazo[1,2-a]pyridine-3-carboxamide (f75). 1h nmr (400 mhz, d6-dmsol) delta 10.18 (s, 1h), 9.52-9.48 (m, 1h), 8.68 (s, 1h), 8.11 (d, j=2.0 hz, 1h), 7.88-7.83 (m, 2h), 7.68-7.63 (m, 1h), 7.54 (d, j=8.0 hz, 1h), 7.31-7.27 (m, 1h), 3.72-3.69 (m, 4h), 3.41-3.38 (m, 4h), 2.39 (s, 3h). ms m/z 405.16 (m+1)+. synthesis of methyl 3-(3-(4-methyl-3-(5,6,7,8-d4)imidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f76) [ftimg=68000149] oxalyl chloride (6 ml, 69 mmol) was added dropwise to a stirred suspension of 5,6,7,8-deutero-imidazo[1,2-a]pyridine-3-carboxylic acid (24n) (1.91 g, 11.5 mmol) and dmf (0.1 ml). the mixture was stirred overnight and the volatiles were evaporated. methyl 3-(3-(3-amino-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (31) (3.23 g, 11.2 mmol) in dry pyridine (50 ml) was added to the solid acid chloride at 0 degrees centigrade after the addition, the mixture was warmed to room temperature and stirred for 3 hours before it was heated (50 degrees centigrade) for 5 hours. the solvent was evaporated and the residue was stirred in saturated nh4cl and etoac. a precipitate formed and was filtered and washed with water, and etoac to give methyl 3-(3-(3-(4-methyl-3-(5,6,7,8-d4)imidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f76) as a grey solid. 1h nmr (400 mhz, d4-meoh) 8.70 (s, 1h), 8.16 (s, 1h), 7.96 (dd, j=7.6, 1.6 hz, 1h), 7.49 (d, j=7.6 hz, 1h), 4.48-4.44 (m, 2h), 4.32-4.29 (m, 2h), 4.24-4.19 (m, 1h), 3.69 (s, 3h), 2.42 (s, 3h). ms m/z 438.1 (m+1)+. synthesis of n-(5-(5-(azetidin-1-yl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (f77) [ftimg=68000150]to a stirring suspension of imidazo[1,2-a]pyridine-3-carboxylic acid (1) (71 mg, 0.39 mmol) in anhydrous dichloromethane (2 ml) was added dropwise oxalyl chloride (173 ul, 1.98 mmol). then, a drop of anhydrous n,n-dimethylformamide was added and the reaction mixture was stirred at room temperature for 30 minutes. the solvent was concentrated. a stirring mixture of the acid chloride and 5-(azetidin-1-yl)-3-(4-methyl-3-nitrophenyl)-1,2,4-oxadiazole (109) (85 mg, 0.29 mmol) in anhydrous pyridine (2 ml) was stirred at room temperature for 30 minutes. the crude product was purified on silica gel using 10 percent meoh in dichloromethane to give n-(5-(5-(azetidin-1-yl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (f77). 1h nmr (400 mhz, cd2cl2) delta 10.10 (s, 1h), 9.51-9.48 (m, 1h), 8.65 (s, 1h), 7.94 (d, j=1.6 hz, 1h), 7.86-7.83 (m, 1h), 7.71 (dd, j=1.6, 7.6 hz, 1h), 7.64-7.60 (m, 1h), 7.43 (d, j=8.0 hz, 1h), 7.27-7.24 (m, 1h), 4.26-4.22 (m, 4h), 2.48-2.40 (m, 2h), 2.34 (s, 3h). ms m/z 374.15 (m+1)+. synthesis of methyl 3-(3-(5-(imidazo[1,2-a]pyridine-3-carboxamido)-2,4-dimethylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f79) [ftimg=68000151]to a stirring solution of boc-azetidine-3-carboxylic acid (20 mg, 0.1 mmol) in anhydrous nmp (1 ml) was added cdi (16.3 mg, 0.1 mmol). the reaction was stirred for 10 minutes. then, n-(5-(n'-hydroxycarbamidoyl)-2,4-dimethylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (50c) (15 mg, 0.05 mmol) was added and the reaction was stirred for 15 minutes. the reaction was heated in the microwave at 125 degrees centigrade for 15 minutes. the reaction mixture was added dropwise to water (20 ml) and extracted with etoac. the organic layers were combined, dried over na2so4, filtered and concentrated to afford a residue which was dissolved in 0.5 ml of tfa and stirred for 10 minutes. then tfa was removed under vacuum and the residue was dissolved in dcm (1 ml) followed by addition of tea (15 mg, 0.15 mmol) and methyl chloroformate (6 mg, 0.06 mmol). the solvent was removed and the residue was purified by hplc to give methyl 3-(3-(5-(imidazo[1,2-a]pyridine-3-carboxamido)-2,4-dimethylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f79). ms m/z 447.1 (m+1)+. synthesis of methyl 3-(3-(4-methyl-3-(7-methyl-d3-imidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f80) [ftimg=68000152]to a stirring suspension of 7-methyl-d3-imidazo[1,2-a]pyridine-3-carboxylic acid (95) (71 mg, 0.39 mmol) in anhydrous dichloromethane (2 ml) was added dropwise oxalyl chloride (173 ul, 1.98 mmol). then, a drop of anhydrous n,n-dimethylformamide was added and the reaction mixture was stirred at room temperature for 30 minutes. the solvent was concentrated. a stirring mixture of the acid chloride and methyl 3-(3-(3-amino-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (31) (85 mg, 0.29 mmol) in anhydrous pyridine (2 ml) was stirred at room temperature for 30 minutes. the crude product was purified on silica gel using 10 percent meoh in dichloromethane to give methyl 3-(3-(4-methyl-3-(7-methyl-d3-imidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f80). 1h nmr (400 mhz, cd2cl2) delta 9.71 (d, j=7.2 hz, 1h), 9.15 (s, 1h), 9.04 (s, 1h), 8.33 (s, 1h), 7.95 (dd, j=1.2, 8.2 hz, 1h), 7.93 (s, 1h), 7.46 (d, j=8.0 hz, 1h), 7.37 (d, j=7.2 hz, 1h), 4.48 (d, j=9.2 hz, 1h), 4.46 (d, j=8.4 hz, 1h), 4.39 (d, j=6.0 hz, 1h), 4.37 (d, j=6.0 hz, 1h), 4.16 (m, 1h), 3.72 (s, 3h), 2.77 (s, 3h). ms m/z 450.1 (m+1)+. synthesis of n-(5-(5-(azetidin-1-yl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (f77) [ftimg=68000153] to a stirring suspension of imidazo[1,2-a]pyridine-3-carboxylic acid (1) (71 mg, 0.39 mmol) in anhydrous dichloromethane (2 ml) was added dropwise oxalyl chloride (173 ul, 1.98 mmol). then, a drop of anhydrous n,n-dimethylformamide was added and the reaction mixture was stirred at room temperature for 30 minutes. the solvent was concentrated. a stirring mixture of the acid chloride and 5-(azetidin-1-yl)-3-(4-methyl-3-nitrophenyl)-1,2,4-oxadiazole (109) (85 mg, 0.29 mmol) in anhydrous pyridine (2 ml) was stirred at room temperature for 30 minutes. the crude product was purified on silica gel using 10 percent meoh in dichloromethane to give n-(5-(5-(azetidin-1-yl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide (f77). 1h nmr (400 mhz, cd2cl2) delta 10.10 (s, 1h), 9.51-9.48 (m, 1h), 8.65 (s, 1h), 7.94 (d, j=1.6 hz, 1h), 7.86-7.83 (m, 1h), 7.71 (dd, j=1.6, 7.6 hz, 1h), 7.64-7.60 (m, 1h), 7.43 (d, j=8.0 hz, 1h), 7.27-7.24 (m, 1h), 4.26-4.22 (m, 4h), 2.48-2.40 (m, 2h), 2.34 (s, 3h). ms m/z 374.15 (m+1)+. synthesis of methyl 3-(3-(6-(2,2-difluoroethoxy)methyl)imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f95) [ftimg=68000154]methyl 3-(3-(4-methyl-3-(6-(((methylsulfonyl)oxy)methyl)imidazo[1,2-a]pyridine-3-carboxamido)phenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (133) (15.0 mg, 0.028 mmol) and k2co3 (8.3 mg, 0.06 mmol) in 2,2-difluoroethanol (0.5 ml) was heated at 120 degrees centigrade for 5 minutes. the reaction mixture was purified by preparative hplc to afford methyl 3-(3-(3-(6-(((2,2-difluoroethoxy)methyl)imidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f95). ms m/z 527.1 (m+1)+. synthesis of methyl 3-(3-(3-(7-deuteroimidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f97) [ftimg=68000155]method a: a mixture of methyl 3-(3-(3-(7-bromoimidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (42g) (0.185 g, 0.36 mmol) in anhydrous thf (5 ml) was degassed by bubbling argon for few minutes. then, pd(oac)2 (7.9 mg, 0.036 mmol, pph3 (38.0 mg, 0.144 mmol), tmeda (83.4 mg, 0.72 mmol) and finally nabd4 (60.6 mg, 1.44 mmol) were introduced in sequence. the mixture was heated at 65 degrees centigrade under argon for 2 hours. the residue was taken up in brine and extracted with ethyl acetate. the organic phase was separated, dried over na2so4, the solvent was evaporated and the residue was purified by flash chromatography to give methyl 3-(3-(3-(7-deuteroimidazo[1,2-a]pyridine-3-carboxamido)-4-methylphenyl)-1,2,4-oxadiazol-5-yl)azetidine-1-carboxylate (f97). 1h nmr (400 mhz, cd4od) delta 9.53 (dd, j=0.8, 7.2 hz, 1h), 8.49 (s, 1h), 8.16 (d, j=1.6 hz, 1h), 7.94 (dd, j=1.6, 8.0 hz, 1h), 7.75 (m, 1h), 7.49 (d, j=8.0 hz, 1h), 7.18 (dd, j=0.8, 7.2 hz, 1h), 4.47 (m, 2h), 4.33 (m, 2h), 4.24 (m, 1h), 3.70 (s, 3h), 2.43 (s, 3h). ms m/z 434.1 (m+1)+. representative compounds of formula (i) and formula (ii) with ic50 values in the range of 1 nm to 100 nm, and prepared following the procedures described above, are set forth in table 1.table 1c-kitcmpd(mo7e)no.structurephysical data micro mf1(ftimg=68000156)1h nmr (400 mhz, d6-dmsol) delta 10.13 (s, 1h), 9.50-9.48 (m, 1h), 8.66 (s, 1h), 8.10 (d, j = 1.6 hz, 1h), 7.86-7.82 (m, 2h), 7.65-7.61 (m, 1h), 7.53 (d, j = 8.4 hz, 1h), 7.28-7.25 (m, 1h), 4.06-4.02 (m, 4h), 2.44-2.36 (m, 2h), 2.39 (s, 3h). ms m/z 374.1 (m + 1)+.0.049f2[ftimg=68000157]1h nmr (400 mhz, d6-dmsol) delta 10.15 (s, 1h), 9.51-9.48 (m, 1h), 8.68 (s, 1h), 8.13 (d, j = 1.6 hz, 1h), 7.87-7.85 (m, 2h), 7.67-7.63 (m, 1h), 7.55 (d, j = 8.0 hz, 1h), 7.30-7.27 (m, 1h), 4.57-4.50 (m, 4h), 2.40 (s, 3h). ms m/z 410.1 (m + 1)+.0.013f3[ftimg=68000158]ms m/z 417.4 (m + 1)+.0.09f4[ftimg=68000159]1h nmr (400 mhz, d6-dmsol) delta 10.16 (s, 1h), 9.51-9.49 (m, 1h), 8.68 (s, 1h), 8.12 (d, j = 1.2 hz, 1h), 7.87-7.85 (m, 2h), 7.67-7.64 (m, 1h), 7.55 (d, j = 5.9 hz, 1h), 7.30-7.28 (m, 1h), 3.60-3.58 (m, 4h), 2.39 (s, 3h), 2.12-2.06 (m, 4h). ms m/z 438.16 (m + 1)+.0.035f5[ftimg=68000160]1h nmr (400 mhz, d6-dmsol) delta 10.19 (s, 1h), 9.52-9.51 (m, 1h), 8.71 (s, 1h), 8.11 (d, j = 1.2 hz, 1h), 7.90-7.88 (m, 1h), 7.85 (dd, j = 1.2, 5.2 hz, 1h), 7.71-7.68 (m, 1h), 7.55 (d, j = 5.2 hz, 1h), 7.33-7.31 (m, 1h), 4.96-4.85 (m, 1h), 3.61-3.57 (m, 2h), 3.45-3.41 (m, 2h), 2.39 (s, 3h), 2.02-1.93 (m, 2h), 1.81-1.74 (m, 2h). ms m/z 420.17 (m + 1)+.0.034f6[ftimg=68000161]1h nmr (400 mhz, d6-dmsol) delta 10.11 (s, 1h), 9.34 (s, 1h), 8.64 (s, 1h), 7.97 (d, j = 1.6 hz, 1h), 7.80 (d, j = 9.2 hz, 1h), 7.72 (dd, j = 0.36, 8.0 hz, 1h), 7.57-7.54 (m, 1h), 7.45 (d, j = 8.0 hz, 1h), 4.54-4.51 (m, 2h), 4.33-4.30 (m, 2h), 2.40 (s, 3h), 2.35 (s, 3h). ms m/z 472.15 (m + 1)+.0.026f7[ftimg=68000162]ms m/z 390.1 (m + 1)+.0.078f8[ftimg=68000163]1h nmr (400 mhz, d4-meoh) delta 9.73-9.76 (d, j = 7.2 hz, 1h), 8.78 (s, 1h), 8.15-8.13 (m, 1h), 8.06-8.00 (m, 2h), 7.95-7.91 (m, 1h), 7.58-7.48 (m, 2h), 4.72 (dd, j = 12.4, 2.8 hz, 1h), 4.14-4.09 (m, 1h), 3.63-3.57 (m, 1h), 2.35 (s, 3h), 2.06-1.86 (m, 4h), 1.72-1.55 (m, 2h). ms m/z 404.1 (m + 1)+.0.042f9[ftimg=68000164]1h nmr (400 mhz, d4-meoh) delta 9.77 (d, j = 7.2 hz, 1h), 8.78 (s, 1h), 8.14-8.13 (m, 1h), 8.04-8.03 (m, 2h), 7.95-7.93 (m, 1h), 7.57 (ddd, j = 6.8, 6.8, 1.2 hz, 1h), 7.50 (d, j = 8.0, 1h), 5.71 (d, j = 4.4 hz, 1h), 4.15-4.12 (m, 1h), 3.75 (s, 3h), 3.75-3.06 (m, 1h), 2.43 (s, 3h), 2.04-1.94 (m, 2h), 1.80-1.71 (m, 2h), 1.61-1.40 (m, 4h). ms m/z 461.1 (m + 1)+.0.035f10[ftimg=68000165]1h nmr (400 mhz, d4-meoh) delta 9.73 (d, j = 7.2 hz, 1h), 8.74 (s, 1h), 8.17 (m, 1h), 7.98-7.95 (m, 3h), 7.52-7.50 (m, 2h), 5.06 (dd, j = 8.4, 2.8 hz, 1h), 4.07-4.00 (m, 1h), 3.91-3.81 (m, 1h), 2.44 (s, 3h), 2.40-2.21 (m, 4h). ms m/z 440.1 (m + 1)+.0.023f11[ftimg=68000166]1h nmr (400 mhz, d4-meoh) delta 9.73 (d, j = 7.2 hz, 1h), 8.74 (s, 1h), 8.17 (m, 1h), 7.98-7.95 (m, 3h), 7.52-7.50 (m, 2h), 5.06 (dd, j = 8.4, 2.8 hz, 1h), 4.07-4.00 (m, 1h), 3.91-3.81 (m, 1h), 2.44 (s, 3h), 2.40-2.21 (m, 4h). ms m/z 440.1 (m + 1)+.0.023f12[ftimg=68000167]1h nmr (400 mhz, d4-meoh) delta 9.73 (d, j = 7.2 hz, 1h), 8.74 (s, 1h), 8.17 (m, 1h), 7.98-7.95 (m, 3h), 7.52-7.50 (m, 2h), 5.06 (dd, j = 8.4, 2.8 hz, 1h), 4.07-4.00 (m, 1h), 3.91-3.81 (m, 1h), 2.44 (s, 3h), 2.40-2.21 (m, 4h). ms m/z 440.1 (m + 1)+.0.032f13[ftimg=68000168]1h nmr (400 mhz, d6-dmsol) delta 10.17 (s, 1h), 9.51 (d, j = 6.8 hz, 1h), 8.70 (s, 1h), 8.10 (d, j = 2.0 hz, 1h), 7.86 (dd, j = 12, 2.0 hz, 2h), 7.68 (t, j = 8.0 hz, 1h), 7.51 (d, j = 8 hz, 1h), 7.31 (td, j = 6.8, 0.8 hz, 1h), 4.06-4.38 (m, 5h) 2.37 (s, 3h), 1.04 (s, 9h). ms m/z 476.2 (m + 1).0.623f14[ftimg=68000169]1h nmr (400 mhz, d6-dmsol) delta 10.17 (s, 1h), 9.52-9.50 (m, 1h), 8.69 (s, 1h), 8.10 (d, j = 1.6 hz, 1h), 7.88-7.85 (m, 2h), 7.68-7.64 (m, 1h), 7.52 (d, j = 8.0 hz, 1h), 7.31-7.27 (m, 1h), 4.36-4.30 (m, 3h), 4.22-4.19 (m, 2h), 3.11 (s, 3h), 2.37 (s, 3h). ms m/z 453.4 (m + 1)+.0.042f15[ftimg=68000170]1h nmr (400 mhz, d6-dmsol) delta 10.18 (s, 1h), 9.52 (d, j = 7.2 hz, 1h), 8.71 (s, 1h), 8.10 (s, 1h), 7.82-7.91 (m, 2h), 7.69 (t, j = 8.0 hz, 1h), 7.51 (d, j = 8.4 hz, 1h), 7.31 (td, j = 7.2, 0.8 hz, 1h), 4.15-4.44 (m, 5h) 3.59 (s, 3h), 2.37 (s, 3h) ms m/z 433.3 (m + 1).0.021f16[ftimg=68000171]1h nmr (400 mhz, d6-dmsol) delta 1h nmr (400 mhz, d6-dmsol) delta 10.07 (s, 1h), 9.43 (d, j = 7.0, 1h), 8.59 (s, 1h), 8.03 (s, 1h), 7.81-7.71 (m, 2h), 7.56 (s, 1h), 7.45 (d, j = 8.1 hz, 1h), 7.19 (s, 1h), 4.24 (d, j = 3.2 hz, 3h), 4.14 (s, 2h), 3.20-3.07 (m,3h), 2.31 (s,

3h), 1.66 (dd, j = 7.5 hz, 15.2, 2h), 0.92 (d, j = 7.5 hz, 2h). ms m/z 481.5 (m + 1)+0.035f17[ftimg=68000172]1h nmr (400 mhz, d6-dmsol) delta 10.12 (s, 1h), 9.49 (d, j = 6.9 hz, 1h), 8.06 (s, 1h), 7.82 (d, j = 7.8 hz, 2h), 7.63-7.57 (m, 1h), 7.50 (d, j = 8.1 hz, 1h), 7.25 (s, 1h), 3.82 (s, 2h), 3.31 (t, j = 7.1 hz, 2h), 2.98 (d, j = 7.1 hz, 2h), 2.37 (s, 3h), 2.01-2.11 (m, 1h), 1.62 (s, 2h), 1.41-1.25 (m, 2h). ms m/z 418.4 (m + 1)+0.027f18[ftimg=68000173]1h nmr (400 mhz, d6-dmsol) delta 10.15 (s, 1h), 9.51 (d, j = 6.9 hz, 1h), 8.68 (s, 1h), 8.07 (s, 1h), 7.96-7.75 (m, 2h), 7.66 (s, 1h), 7.50 (d, j = 8.1 hz, 1h), 7.29 (s, 1h), 4.30 (d, j = 5.1 hz, 1h), 3.83-3.73 (m, 1h), 3.72-3.51 (m, 1h), 3.09-3.28 (m, 2h), 2.37 (s, 3h), 2.02-2.14 (m, 1h), 1.81-1.91 (m, 2h), 1.61-1.78 (m, 2h). ms m/z 404.4 (m + 1)+0.064f19[ftimg=68000174]1h nmr (400 mhz, d6-dmsol) delta 10.05 (s, 1h), 9.47-9.45 (m, 1h), 8.59 (s, 1h), 8.10-8.09 (d, j = 1.6 hz, 1h), 7.76-7.91 (m, 2h), 7.55-7.49 (m, 2h), 7.20-7.16 (m, 1h), 4.35-4.28 (m, 3h), 4.25-4.20 (m, 2h), 3.22 (q, j = 7.2 hz, 2h), 2.37 (s, 3h), 1.25 (t, j = 7.2 hz, 2h). ms m/z 467.5 (m + 1)+0.033f20[ftimg=68000175]1h nmr (400 mhz, d6-dmsol) delta 10.06 (s, 1h), 9.46 (d, j = 7.0 hz, 1h), 8.63 (s, 1h), 8.09 (s, 1h), 7.82 (d, j = 8.7 hz, 2h), 7.58 (s, 1h), 7.51 (d, j = 8.1 hz, 1h), 7.22 (s, 1h), 3.91-4.01 (m, 2h), 3.53-3.65 (m, 5h), 3.47 (s, 3h), 3.32-3.20 (m, 2h), 3.12 (d, j = 7.4 hz, 4h), 2.37 (s, 3h), 2.21 (s, 2h). ms m/z 446.5 (m + 1)+0.095f21[ftimg=68000176]1h nmr (400 mhz, cdcl3) delta 9.47 (d, j = 7.2 hz, 1h), 8.51 (d, j = 1.2 hz, 1h), 8.13 (s, 1h), 7.81 (dd, j = 1.2, 7.6 hz, 1h), 7.68 (d, j = 9.2 hz, 1h), 7.54 (s, 1h), 7.38 (m, 1h), 7.32 (d, j = 8.0 hz, 1h), 6.99 (t, j = 7.2 hz, 1h), 4.10 (s, 2h), 3.82 (t, j = 12.0 hz, 4h). ms m/z 425.1 (m + 1)+0.044f22[ftimg=68000177]ms m/z 419.2 (m + 1)+0.073f23[ftimg=68000178]1h nmr (400 mhz, d6-dmsol) delta 10.14 (s, 1h), 9.51-9.48 (m, 1h), 8.67 (s, 1h), 8.11 (d, j = 1.6 hz, 1h), 7.87-7.84 (m, 2h), 7.66-7.61 (m, 1h), 7.52 (d, j = 8.0 hz, 1h), 7.29-7.25 (m, 1h), 7.13 (s, 2h), 4.24-4.18 (m, 1h), 4.16-4.12 (m, 2h), 4.05-4.01 (m, 2h), 2.37 (s, 3h). ms m/z 454.5 (m + 1)+0.088f24[ftimg=68000179]1h nmr (400 mhz, d6-dmsol) delta 10.15 (s, 1h), 9.51 (d, j = 6.9 hz, 1h), 8.68 (s, 1h), 8.10 (s, 1h), 7.86 (d, j = 9.0 hz, 2h), 7.65 (s, 1h), 7.52 (d, j = 8.1 hz, 1h), 7.28 (s, 1h), 5.50 (s, 1h), 4.02 (s, 4h), 2.76-2.64 (m, 1h), 2.37 (s, 3h), 1.22 (s, 9h). ms m/z 475.5 (m + 1)+0.08f25[ftimg=68000180]1h nmr (400 mhz, d6-dmsol) delta 10.12 (s, 1h), 9.51-9.49 (m, 1h), 8.66 (s, 1h), 8.12 (d, j = 1.6 hz, 1h), 7.86-7.83 (m, 2h), 7.64-7.60 (m, 1h), 7.52 (d, j = 8.4 hz, 1h), 7.28-7.24 (m, 1h), 5.74 (t, j = 8.0 hz, 1h), 4.13 (q, j = 8.8 hz, 2h), 3.87 (q, j = 7.2 hz, 2h), 3.17 (s, 3h). ms m/z 453.5 (m + 1)+0.046f26[ftimg=68000181]1h nmr (400 mhz, cdcl3) delta 9.46 (m, 1h), 8.48 (s, 1h), 8.14 (s, 1h), 7.81 (dd, j = 1.6, 8.0 hz, 1h), 7.69 (d, j = 7.2 hz, 1h), 7.56 (s, 1h), 7.38 (m, 1h), 7.31 (d, j = 8.0 hz, 1h), 6.98 (dt, j = 0.8, 6.8 hz, 1h), 5.12 (m, 2h), 4.91 (m, 2h), 3.66 (s, 3h), 2.36 (s, 3h). ms m/z 499.0 (m + 1)+0.103f27[ftimg=68000182]ms m/z 479.2 (m + 1)+0.099f28 [ftimg=68000183]1h nmr (400 mhz, cdcl3) delta 9.50 (d, j = 2 hz, 1h), 9.09 (dd, j = 2, 7.2 hz, 1h), 8.21 (s, 1h), 7.87 (m, 1h), 7.79 (m, 1h), 7.71 (d, j = 9.2 hz, 1h), 7.41 (m, 1h), 7.22 (dd, j = 8.8, 10.4 hz, 1h), 7.02 (dt, j = 0.8, 6.8 hz, 1h), 4.34 (m, 4h), 4.07 (m, 1h), 3.00 (q, j = 7.6 hz, 2h), 1.35 (t, j = 7.6 hz, 2h). ms m/z 471.2 (m + 1)+0.12f29[ftimg=68000184]ms m/z 439.2 (m + 1)+0.016f30[ftimg=68000185]1h nmr (400 mhz, cd2cl2) delta = 9.71 (d, j = 6.9 hz, 1h), 9.37 (s, 1h), 9.01 (s, 1h), 8.10 (s, 1h), 8.00 (d, j = 8.8 hz, 1h), 7.89 (d, j = 7.3 hz, 1h), 7.75 (d, j = 7.9 hz, 1h), 7.41 (t, j = 6.9 hz, 1h), 7.29 (d, j = 8.0 hz, 1h), 4.42 (s, 2h), 3.36 (s, 3h), 2.31 (d, j = 9.8 hz, 8h). ms m/z 453.2 (m + 1)+0.02f31[ftimg=68000186]ms m/z 495.2 (m + 1)+0.054f32[ftimg=68000187]1h nmr (400 mhz, d6-dmsol) delta 10.16 (s, 1h), 9.50 (d, j = 6.9 hz, 1h), 8.68 (s, 1h), 8.08 (d, j = 1.7 hz, 1h), 7.84 (dd, j = 5.5, 13.5 hz, 2h), 7.68-7.60 (m, 1h), 7.52 (d, j = 8.1 hz, 1h), 7.28 (t, j = 6.9 hz, 1h), 5.61-5.74 (m, 1h), 4.10 (dd, j = 11.7, 23.8 hz, 1h), 3.95 (dd, j = 11.7, 23.8 hz, 1h), 3.21 (s, 3h), 3.10-3.21 (m, 1h), 2.81-2.87 (m, 1h), 2.37 (s, 3h). ms m/z 503.4 (m + 1)+0.055f33[ftimg=68000188]1h nmr (400 mhz, d6-dmsol) delta 10.17 (s, 1h), 8.69 (s, 1h), 8.06 (d, j = 1.6 hz, 1h), 7.92-7.78 (m, 2h), 7.72-7.61 (m, 1h), 7.50 (d, j = 8.1 hz, 1h), 7.30 (t, j = 6.9 hz, 1h), 3.60 (s, 3h), 3.37 (t, j = 11.0 hz, 1h), 3.05 (br s, 2h), 2.36 (s, 3h), 2.10 (d, j = 10.4 hz, 2h), 1.70 (dd, j = 11.3, 20.4 hz, 2h). ms m/z 461.5 (m + 1)+0.084f34[ftimg=68000189]1h nmr (400 mhz, d6-dmsol) delta 10.12 (s, 1h), 9.48 (d, j = 6.9 hz, 1h), 8.64 (s, 1h), 8.06 (s, 1h), 7.83 (d, j = 8.0 hz, 2h), 7.60 (s, 1h), 2.85-3.15 (m, 4h), 2.36 (s, 3h), 2.22 (d, j = 9.5 hz, 2h), 1.87 (q, j = 9.5 hz, 2h). ms m/z 481.5 (m + 1)+0.095f35[ftimg=68000190]1h nmr (400 mhz, d6-dmsol) delta 10.16 (s, 1h), 9.51 (d, j = 7.0 hz, 1h), 8.68 (s, 1h), 8.11 (d, j = 1.7 hz, 2h), 7.90-7.80 (m, 2h), 7.73-7.57 (m, 1h), 7.53 (d, j = 8.1 hz, 1h), 7.29 (t, j = 6.9 hz, 1h), 5.20 (dd, j = 3.1, 8.9 hz, 1h), 4.06 (d, j = 11.8 hz, 2h), 3.94-3.74 (m, 3h), 3.52-3.31 (m, 2h), 3.00 (s, 3h), 2.38 (s, 3h). ms m/z 483.5 (m + 1)+0.066f36[ftimg=68000191]1h nmr (400 mhz, d6-dmsol) delta 10.16 (s, 1h), 9.51 (d, j = 6.9 hz, 1h), 8.68 (s, 1h), 8.07 (s, 1h), 7.91-7.73 (m, 2h), 7.65 (s, 1h), 7.51 (d, j = 8.1 hz, 1h), 7.28 (s, 1h), 5.32 (dd, j = 3.9, 8.5 hz, 1h), 3.50 (s, 3h), 3.01-3.21 (m, 2h), 2.37 (s, 3h), 2.21-1.87 (m, 4h). ms m/z 467.51 (m + 1)+0.093f37[ftimg=68000192]1h nmr (400 mhz, d6-dmsol) delta 10.15 (s, 1h), 9.50 (d, j = 6.9 hz, 1h), 8.68 (s, 1h), 8.11 (d, j = 1.7 hz, 1h), 7.88-7.83 (m, 2h), 7.68-7.62 (m, 1h), 7.53 (d, j = 8.1 hz, 1h), 7.28 (t, j = 6.5 hz, 1h), 5.15-5.21 (m, 1h), 4.06 (d, j = 11.8 hz, 2h), 3.86-3.78 (m, 2h), 3.43-3.34 (m, 2h), 3.08 (d, j = 9.2 hz, 1h), 3.00 (s, 3h), 2.38 (s, 3h). ms m/z 483.51 (m + 1)+0.06f38 [ftimg=68000193]1h nmr (400 mhz, d6-dmsol) delta 10.21 (s, 1h), 9.52 (d, j = 7.0 hz, 1h), 8.72 (s, 1h), 8.07 (d, j = 1.7 hz, 1h), 7.90 (d, j = 9.0 hz, 1h), 7.84 (dd, j = 1.7, 7.9 hz, 1h), 7.74-7.66 (m, 1h), 7.51 (d, j = 8.1 hz, 1h), 7.33 (t, j = 6.9 hz, 1h), 3.51-3.54 (m, 1h), 3.41-3.33 (m, 1h), 3.30-3.21 (m, 1h), 3.11-3.19 (m, 2h), 3.00-3.08 (m, 1h), 2.91 (s, 3h), 2.70-2.81 (m, 1h), 2.37 (s, 3h), 2.11-2.21 (m, 1h), 1.62-1.74 (m, 1h). ms m/z 481.54 (m + 1)+0.09f39 [ftimg=68000194]1h nmr (400 mhz, d6-dmsol) delta 10.20 (s, 1h), 9.52 (dd, j = 3.5, 4.5 hz, 1h), 8.71 (s, 1h), 8.07 (d, j = 1.7 hz, 1h), 7.92-7.81 (m, 3h), 7.73-7.66 (m, 1h), 7.51 (d, j = 8.1 hz, 1h), 7.32 (dd, j = 5.9, 6.9 hz, 1h), 3.84 (d, j = 11.7 hz, 1h), 3.49-3.41 (m, 2h), 3.18-3.29 (m, 1h), 2.96-2.86 (m, 3h), 2.37 (s, 3h), 2.23-2.13 (m, 1h), 1.70-1.94 (m, 3h). ms m/z 481.54 (m + 1)+0.094f40[ftimg=68000195]1h nmr (400 mhz, d6-dmsol) delta 10.18 (s, 1h), 9.52 (d, j = 6.9 hz, 1h), 8.70 (s, 1h), 8.06 (s, 1h), 7.92-7.76 (m, 2h), 7.72-7.64 (m, 1h), 7.51 (d, j = 8.1 hz, 1h), 7.31 (t, j = 6.9 hz, 1h), 4.27 (s, 2h), 3.34-3.21 (m, 4h), 2.37 (s, 3h), 1.94-2.04 (m, 1h), 1.72-1.88 (m, 3h). ms m/z 461.49 (m + 1)+0.094f41[ftimg=68000196]1h nmr (400 mhz, d6-dmsol) delta 10.18 (s, 1h), 9.52 (d, j = 6.9 hz, 1h), 8.70 (s, 1h), 8.06 (s, 1h), 7.92-7.76 (m, 2h), 7.72-7.64 (m, 1h), 7.51 (d, j = 8.1 hz, 1h), 7.31 (t, j = 6.9 hz, 1h), 4.17 (s, 2h), 3.34-3.21 (m, 4h), 2.37 (s, 3h), 1.94-2.04 (m, 1h), 1.72-1.88 (m, 3h). ms m/z 481.54 (m + 1)+0.092f42[ftimg=68000197]ms m/z 475.2 (m + 1)+0.013f43[ftimg=68000198]1h nmr (400 mhz, d6-dmsol) delta 10.18 (s, 1h), 9.52 (d, j = 6.8 hz, 1h), 8.70 (s, 1h), 8.10 (d, j = 2.5 hz, 1h), 7.88 (m, 1h), 7.67 (m, 1h), 7.53 (d, j = 8.4 hz, 1h), 7.30 (t, j = 7.2 hz, 1h), 7.26 (t, j = 5.2 hz, 1h), 4.59 (m, 2h), 4.47 (m, 3h), 2.38 (s, 3h). ms m/z 489.2 (m + 1)+0.024f44[ftimg=68000199]1h nmr (400 mhz, d6-dmsol) delta 10.03 (s, 1h), 9.46 (d, j = 6.9 hz, 1h), 8.59 (s, 1h), 8.07 (d, j = 1.6 hz, 1h), 7.84-7.76 (m, 2h), 7.55-7.46 (m, 2h), 7.17-1.15 (m, 3h), 3.07-3.37 (m, 5h), 2.37 (s, 3h), 1.68-1.80 (m, 3h), 1.23-1.59 (m, 6h) ms m/z 418.46 (m + 1)+0.017f45[ftimg=68000200]1h nmr (400 mhz, cdcl3) delta 9.48 (d, j = 7.2 hz, 1h), 9.08 (dd, j = 2.0, 7.6 hz, 1h), 8.19 (s, 1h), 7.81 (m, 2h), 7.70 (d, j = 8.8 hz, 1h), 7.40 (m, 1h), 7.22 (m, 1h), 7.01 (m, 1h), 4.00 (s, 2h), 3.11 (t, j = 13.2 hz, 2h), 2.94 (t, j = 7.2 hz, 2h), 2.29 (m, 2h). ms m/z 443.1 (m + 1)+0.09f46[ftimg=68000201]1h nmr (400 mhz, cdcl3) delta 9.49 (m, 1h), 9.07 (dd, j = 2.0, 7.6 hz, 1h), 8.18 (s, 1h), 7.81 (m, 2h), 7.70 (m, 1h), 7.40 (m, 1h), 7.22 (m, 1h), 7.01 (m, 1h), 3.91 (s, 4h), 2.02 (m, 4h). ms m/z 457.1 (m + 1)+0.073f47 [ftimg=68000202]ms m/z 481.54 (m + 1)+0.047f48[ftimg=68000203]1h nmr (400 mhz, cdcl3) delta 8.54 (d, j = 6.5 hz, 1h), 8.53 (s, 1h), 8.36 (m, 2h), 7.81 (d, j = 7.9 hz, 1h), 7.76 (s, 1h), 7.41 (dd, j = 8.9, 6.9 hz, 1h), 7.35 (d, j = 7.9 hz, 1h), 6.99 (t, j = 6.1 hz, 1h), 4.41 (m, 4h), 4.12 (m, 1h), 3.71 (s, 3h), 2.41 (s, 3h). ms m/z 433.2 (m + 1)+0.08f49[ftimg=68000204]1h nmr (400 mhz, d6-dmsol) delta 10.19 (s, 1h), 9.54-9.50 (m, 1h), 8.71 (s, 1h), 8.06 (d, j = 1.7 hz, 1h), 7.89 (d, j = 9.0 hz, 1h), 7.83 (dd, j = 1.8, 7.9 hz, 1h), 7.73-7.66 (m, 1h), 7.50 (d, j = 8.1 hz, 1h), 7.32 (td, j = 1.1, 6.9 hz, 1h), 3.83 (dd, j = 2.3, 11.1 hz, 1h), 3.73 (dt, j = 3.6, 10.9 hz, 1h), 3.34 (td, j = 3.0, 10.8 hz, 1h), 3.18 (dd, j = 9.3, 11.1 hz, 1h), 2.93 (qd, j = 7.2, 15.6 hz, 2h), 2.36 (s, 3h), 2.15-2.05 (m, 1h), 1.88-1.78 (m, 1h), 1.64-1.44 (m, 2h), 1.30-1.41 (m, 1h). ms m/z 418.46 (m + 1)+0.045f50[ftimg=68000205]ms m/z 439.0 (m + 1)+0.077f51[ftimg=68000206]ms m/z 453.2 (m + 1)+0.043f52[ftimg=68000207]1h nmr (400 mhz, d6-dmsol) delta 10.27 (s, 1h), 9.88 (s, 1h), 8.72 (s, 1h), 8.08 (d, j = 1.6 hz, 1h), 8.01 (d, j = 9.5 hz, 1h), 7.86 (dd, j = 1.7, 7.9 hz, 1h), 7.79 (dd, j = 1.9, 9.5 hz, 1h), 7.52 (d, j = 8.1 hz, 1h), 4.39-4.10 (m, 6h), 3.59 (s, 3h), 2.37 (s, 3h). ms m/z 501.43 (m + 1)+0.218f53[ftimg=68000208]1h nmr (400 mhz, d6-dmsol) delta 10.16 (s, 1h), 9.51 (d, j = 6.9 hz, 1h), 8.69 (s, 1h), 8.10 (d, j = 1.7 hz, 1h), 7.86 (dd, j = 5.4, 11.7 hz, 2h), 7.69-7.63 (m, 1h), 7.51 (d, j = 8.1 hz, 1h), 7.29 (t, j = 6.9 hz, 1h), 4.37 (s, 3h), 4.27 (dd, j = 5.4, 8.6 hz, 2h), 4.18 (s, 3h), 4.04 (q, j = 7.1 hz, 3h), 2.37 (s, 3h), 1.17 (t, j = 7.1 hz, 3h) ms m/z 447.46 (m + 1)+0.093f54[ftimg=68000209]1h nmr (400 mhz, d6-dmsol) delta 10.15 (s, 1h), 9.49 (dd, j = 2.5, 5.0 hz, 1h), 8.66 (s, 1h), 8.09 (d, j = 1.6 hz, 1h), 7.88 (ddd, j = 3.4, 8.9, 9.6 hz, 2h), 7.72-7.63 (m, 1h), 7.52 (d, j = 8.1 hz, 1h), 4.38 (s, 2h), 4.34-4.24 (m, 1h), 4.23 (d, j = 19.4 hz, 2h), 3.60 (s, 3h), 2.35 (d, j = 15.0 hz, 3h) ms m/z 451.1 (m + 1)+0.037f55[ftimg=68000210]1h nmr (400 mhz, d6-dmsol) delta 10.13 (s, 1h), 9.48-9.46 (m, 1h), 8.64 (s, 1h), 8.08 (d, j = 1.6 hz, 1h), 7.90-7.87 (m, 1h), 7.85 (dd, j = 2.0, 8.0 hz, 1h), 7.67-7.62 (m, 1h), 7.51 (d, j = 8.4 hz, 1h), 4.42-4.33 (m, 2h), 4.31-4.24 (m, 1h), 4.27-4.15 (m, 2h), 3.59 (s, 3h), 2.36 (s, 3h). ms m/z 451.42 (m + 1)+0.054f56[ftimg=68000211]ms m/z 513.2 (m + 1)+0.006f57[ftimg=68000212]1h nmr (400 mhz, d6-dmsol) delta 10.25 (s, 1h), 9.64-9.61 (m, 1h), 9.75 (s, 1h), 8.33-8.30 (m, 1h), 8.10 (dd, j = 1.6 hz, 1h), 7.86 (dd, j = 1.6, 8.0 hz, 1h), 7.52 (d, j = 8.4 hz, 1h), 7.46 (dd, j = 2.0, 7.6 hz, 1h), 4.40-4.33 (m, 2h), 4.31-4.25 (m, 1h), 4.22-4.18 (m, 2h), 3.59 (s, 3h), 2.38 (s, 3h). ms m/z 501.43 (m + 1)+0.135f8[ftimg=68000213]ms m/z 467.1 (m + 1)+0.089f59[ftimg=68000214]1h nmr (400 mhz, d6-dmsol) delta 10.13 (s, 1h), 9.38-9.36 (m, 1h), 8.66 (s, 1h), 8.11 (d, j = 1.6 hz, 1h), 7.86-7.82 (m, 2h), 7.63-7.60 (m, 1h), 7.51 (d, j = 8.0 hz, 1h), 4.39-4.34 (m, 2h), 4.31-4.24 (m, 1h), 4.21-4.18 (m, 2h), 3.59 (s, 3h), 2.81-2.77 (m, 2h), 2.60-2.52 (m, 2h), 2.38 (s, 3h), 1.97-1.90 (m, 2h). ms m/z 500.52 (m + 1)+0.033f60[ftimg=68000215]1h nmr (400 mhz, d6-dmsol) delta 10.01 (s, 1h), 9.12 (d, j = 2.4 hz, 1h), 8.54 (s, 1h), 8.09 (d, j = 1.6 hz, 1h), 7.85 (dd, j = 1.6, 7.8 hz, 1h), 7.72 (d, j = 9.6 hz, 1h), 7.51 (d, j = 8.0 hz, 1h), 7.32 (dd, j = 2.4, 9.6 hz, 1h), 4.38 (bs, 2h), 4.32-4.25 (m, 1h), 4.20 (bs, 2h), 3.83 (s, 3h), 3.59 (s, 3h), 2.37 (s, 3h). ms m/z 463.1 (m + 1)+0.028f61[ftimg=68000216]1h nmr (400 mhz, d6-dmsol) delta 9.97 (s, 1h), 9.33 (d, j = 7.2 hz, 1h), 8.52 (s, 1h), 8.09 (d, j = 1.6 hz, 1h), 7.83 (dd, j = 1.6, 7.6 hz, 1h), 7.58 (s, 1h), 7.50 (d, j = 8.0 hz, 1h), 7.03 (dd, j = 1.6, 7.2 hz, 1h), 4.39-4.33 (m, 2h), 4.31-4.24 (m, 1h), 4.22-4.16 (m, 2h), 3.59 (s, 3h), 2.43 (s, 3h), 2.36 (s, 3h). ms m/z 447.17 (m + 1)+0.026f62[ftimg=68000217]1h nmr (400 mhz, d6-dmsol) delta 10.15 (s, 1h), 9.36 (s, 1h), 8.67 (s, 1h), 8.11 (d, j = 2.0 hz, 1h), 7.85 (dd, j = 2.0, 8.0 hz, 1h), 7.81 (d, j = 9.2 hz, 1h), 7.57 (dd, j = 1.2, 9.2 hz, 1h), 7.51 (d, j = 8.0 hz, 1h), 4.39-4.34 (m, 2h), 4.31-4.24 (m, 1h), 4.22-4.17 (m, 2h), 3.59 (s, 3h), 2.41 (s, 3h), 2.37 (s, 3h). ms m/z 447.17 (m + 1)+0.036f63[ftimg=68000218]ms m/z 612.2 (m + 1)+0.013f64 [ftimg=68000219]1h nmr (400 mhz, d6-dmsol) delta 10.08 (s, 1h), 9.45 (s, 1h), 8.63 (s, 1h), 8.12 (d, j = 1.6 hz, 1h), 7.85 (dd, j = 2.0, 5.6 hz, 1h), 7.82 (d, j = 6.8 hz, 1h), 7.60 (dd, j = 1.6, 9.2 hz, 1h), 7.51 (d, j = 8.0 hz, 1h), 4.38-4.33 (m, 2h), 4.31-4.24 (m, 1h), 4.21-4.18 (m, 2h), 3.59 (s, 3h), 3.01 (t, j = 7.6 hz, 2h), 2.91 (t, j = 6.4 hz, 2h), 2.38 (s, 3h). ms m/z 486.18 (m + 1)+0.064f65[ftimg=68000220]1h nmr (400 mhz, d6-dmsol) delta 10.02 (s, 1h), 9.31 (s, 1h), 8.55 (s, 1h), 8.10 (d, j = 1.6 hz, 1h), 7.83 (dd, j = 2.0, 8.0 hz, 1h), 7.73 (d, j = 9.2 hz, 1h), 7.50 (d, j = 8.0 hz, 1h), 7.46 (dd, j = 1.6, 9.2 hz, 1h), 4.39-4.34 (m, 2h), 4.31-4.25 (m, 1h), 4.22-4.18 (m, 2h), 3.59 (s, 3h), 2.85 (s, 4h), 2.37 (s, 3h), 2.10 (s, 3h). ms m/z 503.2 (m + 1)+0.033f66[ftimg=68000221]1h nmr (400 mhz, d6-dmsol) delta 10.07 (s, 1h), 9.46 (s, 1h), 8.61 (s, 1h), 8.12 (d, j = 1.6 hz, 1h), 7.86-7.83 (m, 2h), 7.52-7.49 (m, 2h), 4.39-4.36 (m, 2h), 4.31-4.26 (m, 1h), 4.21-4.17 (m, 2h), 4.03-4.00 (m, 2h), 3.69-3.63 (m, 2h), 3.59 (s, 3h), 3.54-3.44 (m, 4h), 3.14-3.10 (m, 4h), 2.38 (s, 3h). ms m/z 546.24 (m + 1)+0.05f67[ftimg=68000222]1h nmr (400 mhz, d6-dmsol) delta 10.10 (s, 1h), 9.34 (s, 1h), 8.63 (s, 1h), 8.10 (d, j = 1.6 hz, 1h), 7.84 (dd, j = 1.6, 8.0 hz, 1h), 7.78 (d, j = 9.2 hz, 1h), 7.56-7.54 (m, 1h), 7.51 (d, j = 8.4 hz, 1h), 4.39-4.34 (m, 2h), 4.31-4.25 (m, 1h), 4.22-4.17 (m, 2h), 3.59 (s, 3h), 2.76-2.72 (m, 2h), 2.37 (s, 3h), 1.71-1.67 (m, 2h), 1.15 (s, 6h). ms m/z 519.23 (m + 1)+0.029f68[ftimg=68000223]ms m/z 499.1 (m + 1)+0.013f69[ftimg=68000224]ms m/z 419.1 (m + 1)+0.039f70[ftimg=68000225]ms m/z 419.1 (m + 1)+0.006f71[ftimg=68000226]ms m/z 405.2 (m + 1)+0.011f72[ftimg=68000227]ms m/z 405.2 (m + 1)+0.006f73[ftimg=68000228]1h nmr (400 mhz, d-dmsol) delta 10.24 (s, 1h), 9.44-9.41 (m, 1h), 8.73 (s, 1h), 8.09 (d, j = 1.6 hz, 1h), 7.85 (dd, j = 1.6, 8.0 hz, 1h), 7.73 (s, 1h), 7.51 (d, j = 8.4 hz, 1h), 7.32-7.29 (m, 1h), 4.39-4.35 (m, 2h), 4.31-4.24 (m, 1h), 4.21-4.17 (m, 2h), 3.59 (s, 3h), 2.98-2.91 (m, 4h), 2.37 (s, 3h), 2.13 (s, 3h). ms m/z 503.2 (m + 1)+0.037f4[ftimg=68000229]1h nmr (400 mhz, d6-dmsol) delta 10.11 (s, 1h), 9.41-9.38 (m, 1h), 8.64 (s, 1h), 8.10 (s, 1h

(dd, j = 2.0, 8.0 hz, 1h), 7.57 (s, 1h), 7.42 (d, j = 8.0 hz, 1h), 7.02 (dd, j = 1.6, 7.2 hz, 1h), 5.89 (s, 1h), 4.12-4.07 (m, 4h), 2.42 (s, 3h), 2.33 (s, 3h), 1.45 (s, 3h). ms m/z 418.18 (m + 1)+.0.062f89[ftimg=68000244]1h nmr (400 mhz, d6-dmso) delta 9.95 (s, 1h), 9.33-9.31 (m, 1h), 8.51 (s, 1h), 7.95 (d, j = 1.6 hz, 1h). 7.71 (dd, j = 1.6, 7.6 hz, 1h), 7.57 (s, 1h), 7.43 (d, j = 8.4 hz, 1h), 7.03 (dd, j = 1.6, 7.2 hz, 1h), 3.77-3.74 (m, 4h), 2.42 (s, 3h), 2.33 (s, 3h), 2.20-2.10 (m, 4h). ms m/z 452.18 (m + 1)+.0.031f90[ftimg=68000245]1h nmr (400 mhz, d6-dmso) delta 9.95 (s, 1h), 9.33-9.31 (m, 1h), 8.51 (s, 1h), 7.93 (d, j = 2.0 hz, 1h), 7.70 (dd, j = 1.6, 8.0 hz, 1h), 7.57 (s, 1h), 7.42 (d, j = 8.0 hz, 1h), 7.03 (dd, j = 2.0, 7.2 hz, 1h), 5.02-4.86 (m, 1h), 3.72-3.62 (m, 4h), 2.42 (s, 3h), 2.33 (s, 3h), 2.06-1.94 (m, 2h), 1.87-1.81 (m, 2h). ms m/z 434.19 (m + 1)+.0.033f91[ftimg=68000246]1h nmr (400 mhz, d6-dmso) delta 9.95 (s, 1h), 9.33-9.31 (m, 1h), 8.51 (s, 1h), 7.94 (d, j = 1.6 hz, 1h), 7.71 (dd, j = 2.0, 8.0 hz, 1h), 7.57 (s, 1h), 7.43 (d, j = 8.4 hz, 1h), 7.02 (dd, j = 2.0, 7.2 hz, 1h), 3.73-3.71 (m, 4h), 3.61-3.58 (m, 4h), 2.42 (s, 3h), 2.33 (s, 3h). ms m/z 418.18 (m + 1)+.0.064f92[ftimg=68000247]1h nmr (400 mhz, d6-dmso) delta 9.96 (s, 1h), 9.93-9.91 (m, 1h), 8.51 (s, 1h), 7.94 (d, j = 2.0 hz, 1h), 7.71 (dd, j = 1.6, 8.0 hz, 1h), 7.57 (s, 1h), 7.43 (d, j = 8.0 hz, 1h), 7.02 (dd, j = 1.6, 7.2 hz, 1h), 4.05-3.99 (m, 2h), 3.85-3.81 (m, 2h), 2.64-2.54 (m, 2h), 2.42 (s, 3h), 2.33 (s, 3h). ms m/z 438.16 (m + 1)+.0.021f93[ftimg=68000248]1h nmr (400 mhz, d6-dmso) delta 9.96 (s, 1h), 9.33-9.31 (m, 1h), 8.50 (s, 1h), 7.92 (d, j = 1.6 hz, 1h), 7.71 (dd, j = 1.6, 7.6 hz, 1h), 7.57 (s, 1h), 7.43 (d, j = 8.0 hz, 1h), 7.02 (dd, j = 1.6, 7.2 hz, 1h), 4.17-4.13 (m, 1h), 4.01-3.96 (m, 1h), 3.30-3.21 (m, 2h), 2.82-2.74 (m, 1h), 2.42 (s, 3h), 2.33 (s, 3h), 2.00-1.97 (m, 1h), 1.84-1.81 (m, 1h), 1.64-1.56 (m, 2h). ms m/z 484.18 (m + 1)+.0.048f94[ftimg=68000249]1h nmr (400 mhz, d6-dmso) delta 10.21 (s, 1h), 9.53-9.51 (m, 1h), 8.71 (s, 1h), 8.10 (d, j = 1.2 hz, 1h), 7.91-7.88 (m, 1h), 7.85 (dd, j = 1.2, 5.6 hz, 1h), 7.72-7.69 (m, 1h), 7.54 (d, j = 5.2 hz, 1h), 7.34-7.32 (m, 1h), 4.66 (s, 1h), 4.54 (s, 1h), 3.77-3.74 (m, 2h), 3.48-3.46 (m, 1h), 3.29-3.27 (m, 1h), 2.39 (s, 3h), 1.96-1.94 (m, 1h), 1.88-1.86 (m, 1h). ms m/z 416.16 (m + 1)+.0.092f95[ftimg=68000250]ms m/z 527.1 (m + 1)+.0.019f96[ftimg=68000251]ms m/z 509.1 (m + 1)+.0.026f97[ftimg=68000252]1h nmr (400 mhz, d4-meod) delta 9.53 (dd, j = 0.8, 7.2 hz, 1h), 8.49 (s, 1h), 8.16 (d, j = 1.6 hz, 1h), 7.94 (dd, j = 1.6, 8.0 hz, 1h), 7.75 (m, 1h), 7.49 (d, j = 8.0 hz, 1h), 7.18 (dd, j = 0.8, 7.2 hz, 1h), 4.47 (m, 2h), 4.33 (m, 2h), 4.24 (m, 1h), 3.70 (s, 3h), 2.43 (s, 3h) ms m/z 434.1 (m + 1)+.0.044f98[ftimg=68000253]1h nmr (400 mhz, d4-meod) delta 9.53 (s, 1h), 8.49 (s, 1h), 8.16 (d, j = 1.6 hz, 1h), 7.94 (dd, j = 2.0, 8.0 hz, 1h), 7.75 (dd, j = 0.8, 8.8 hz, 1h), 7.58 (dd, j = 1.2, 8.8 hz, 1h), 7.49 (d, j = 8.0 hz, 1h), 4.47 (m, 2h), 4.33 (m, 2h), 4.24 (m, 1h), 3.70 (s, 3h), 2.43 (s, 3h) ms m/z 434.1 (m + 1)+.0.043f99[ftimg=68000254]ms m/z 525.1 (m + 1)+.0.049*20 percent fbs, otherwise 1 percent fbsrepresentative compounds of formula (i) and formula (ii) with c-kit inhibition ic50 values greater than 100 nm and prepared following the procedures described above, are set forth in table 2c-kitcmpd(mo7e)no.structurephysical data micro mf100[ftimg=68000255]ms m/z 537.2 (m + 1)+.0.198f101[ftimg=68000256]ms m/z 433.2 (m + 1)+.0.332f102[ftimg=68000257]1h nmr (400 mhz, d4-meoh) delta 9.73 (d, j = 7.2 hz, 1h), 8.74 (s, 1h), 8.15-8.14 (m, 1h), 7.98-7.92 (m, 3h), 7.53-7.49 (m, 2h), 4.03 (ddd, j = 12, 4, 4 hz, 2 h), 3.61 (ddd, j = 12, 12, 4 hz, 2 h), 3.40-3.30 (m, 1h), 2.46 (s, 3h), 2.11-2.07 (m, 2h), 2.02-1.96 (m, 2h). ms m/z 404.1 (m + 1)+.0.286f103[ftimg=68000258]1h nmr (400 mhz, d4-meoh) delta 9.77 (d, j = 7.1 hz, 1h), 8.79 (d, j = 2.4 hz, 1h), 8.16-8.15 (m, 1 h), 8.07-8.03 (m, 2h), 7.95-7.93 (m, 1h), 7.59-7.55 (m, 1h), 7.50 (d, j = 8 hz, 1h), 4.85 (dd, j = 10.4, 2.8 hz, 1h), 4.08 (d, j = 11.6, 1h), 3.70 (ddd, j = 11.6, 3.2, 3.2 hz, 1h), 2.43 (s, 3 h), 2.11-2.07 (m, 1h), 2.01-1.87 (m, 1h), 1.82-1.63 (m, 2h), ms m/z 390.1 (m + 1)+.0.229*f104[ftimg=68000259]1h nmr (400 mhz, d4-meoh) delta 9.77 (d, j = 7.1 hz, 1h), 8.79 (d, j = 2.4 hz, 1h), 8.16-8.15 (m, 1 h), 8.07-8.03 (m, 2h), 7.95-7.93 (m, 1h), 7.59-7.55 (m, 1h), 7.50 (d, j = 8 hz, 1h), 4.85 (dd, j = 10.4, 2.8 hz, 1h), 4.08 (d, j = 11.6, 1h), 3.70 (ddd, j = 11.6, 3.2, 3.2 hz, 1h), 2.43 (s, 3 h), 2.11-2.07 (m, 1h), 2.01-1.87 (m, 1h), 1.82-1.63 (m, 2h), ms m/z 390.1 (m + 1)+.0.224*f105[ftimg=68000260]1h nmr (400 mhz, d4-meoh) delta 9.73-9.68 (m, 1h), 8.73-8.70 (m, 1h), 8.16-8.14 (m, 1h), 7.97-7.87 (m, 3h), 7.51-7.39 (m, 2h), 4.12-4.07 (m, 1h), 3.54-3.50 (m, 2h), 3.23-3.20 (m, 2h), 2.57 (s, 3h), 2.20-2.04 (m, 2h), 1.86-1.79 (m, 2h), 1.48 (s, 9h). ms m/z 503.1 (m + 1)+.0.505f106[ftimg=68000261]1h nmr (400 mhz, d4-meoh) delta 9.73-9.76 (d, j = 7.2 hz, 1h), 8.78 (s, 1h), 8.15-8.13 (m, 1 h), 8.06-8.00 (m, 2h), 7.95-7.91 (m, 2h), 7.58-7.48 (m, 2 h), 5.12 (dd, j = 8.0, 4.0 hz, 1 h), 3.63-3.60 (m, 1h), 3.48-3.45 (m, 1h), 2.49-2.35 (m, 1 h), 2.41 (s, 3h), 2.10-2.05 (m, 3h). ms m/z 489.2 (m + 1)+.0.648*f109[ftimg=68000264]1h nmr (400 mhz, d4-meoh) delta 9.78 (d, j = 7.2 hz, 1h), 8.79-8.70 (m, 1h), 8.15 (d, j = 2.0 hz, 1h), 8.03-7.94 (m, 3h), 7.60-7.50 (m, 2h), 5.58 (m, 1h), 3.98-3.90 (m, 2h), 2.43 (s, 3h), 2.01-1.95 (m, 2h), 1.75-1.68 (m, 2h), 1.50-1.30 (m, 2h). ms m/z 403.2 (m + 1)+.0.215f110[ftimg=68000265]1h nmr (400 mhz, d4-meoh) delta 9.77 (d, j = 7.2 hz, 1h), 8.78 (s, 1h), 8.14-8.13 (m, 1h), 8.04-8.03 (m, 2h), 7.95-7.93 (m, 1h), 7.57 (ddd, j = 6.8, 6.8, 1.2 hz, 1h), 7.50 (d, j = 8.0, 1h), 5.54 (d, j = 4.4 hz, 1h), 3.83-3.80 (m, 1h), 3.65-3.55 (m, 1 h), 3.07 (s, 3h), 2.43 (s, 3h), 2.04-1.94 (m, 2h), 1.80-1.71 (m, 2h), 1.61-1.40 (m, 4h). ms m/z 481.2 (m + 1)+.0.227*f111[ftimg=68000266]1h nmr (400 mhz, d4-meoh) delta 9.76 (d, j = 7.2 hz, 1h), 8.77 (s, 1h), 8.14-8.13 (m, 1h), 8.04-8.03 (m, 2h), 7.95-7.93 (m, 1 h), 7.57 (ddd, j = 6.8, 6.8, 1.2 hz, 1h), 7.52 (ddd, j = 6.8, 6.8, 1.2 hz, 1h), 7.52 (d, j = 8.0, 1h), 5.01-4.98 (m, 1h), 3.75-3.72 (m, 1h), 3.37-3.30 (m, 1h), 2.96 (s, 3h), 2.46 (s, 3h), 2.46-2.38 (m, 1h), 2.21-2.16 (m, 1 h), 2.07-1.90 (m, 2h), 1.82-1.74 (m, 1h). ms m/z 417.2 (m + 1)+.0.243f112[ftimg=68000267]1h nmr (400 mhz, d4-meoh) delta 9.76 (d, j = 7.2 hz, 1h), 8.78 (s, 1h), 8.14-8.13 (m, 1h), 8.04-8.03 (m, 2h), 7.95-7.93 (m, 1 h), 7.57 (ddd, j = 6.8, 6.8, 1.2 hz, 1h), 7.52 (d, j = 8.0, 1h), 4.79 (dd, j = 10.4, 2.4 hz, 1h), 4.10-4.05 (m, 1h), 3.75-3.70 (m, 1h), 3.38-3.31 (m, 1h), 2.43 (s, 3h), 2.28-2.19 (m, 2 h), 2.04-1.95 (m, 1h), 1.70-1.60 (m, 1h). ms m/z 420.1 (m + 1)+.0.227f113[ftimg=68000268]1h nmr (400 mhz, d6-dmso) delta 10.17 (s, 1h), 9.51 (d, j = 6.8 hz, 1h), 8.70 (s, 1h), 8.10 (d, j = 2.0 hz, 1h), 7.86 (dt, j = 12, 2.0 hz, 1h), 7.68 (t, j = 8.0 hz, 1h), 7.51 (d, j = 8 hz, 1h), 7.31 (t, d, j = 6.8, 0.8 hz, 1h), 4.06-4.38 (m, 5h) 2.37 (s, 3h), 1.40 (s, 9h) ms m/z 476.2 (m + 1)+.0.623f114[ftimg=68000269]0.183f115[ftimg=68000270]1h nmr (400 mhz, d6-dmso) delta 10.14 (s, 1h), 9.51-9.49 (m, 1 h), 8.67 (s, 1h), 8.10 (d, j = 1.6, hz, 1h), 7.86-7.84 (m, 2h), 7.66-7.61 (m, 1h), 7.51 (d, j = 8.0 hz, 1h), 7.29-7.25 (m, 1 h), 4.60-4.56 (m, 1h), 4.43-4.40 (m, 1h), 4.31-4.25 (m, 2 h), 4.12-4.10 (m, 1h), 2.37 (s, 3h), 1.80 (s, 3h). ms m/z 417.43 (m + 1)+.0.464f116[ftimg=68000271]1h nmr (400 mhz, d6-dmso) delta 10.19 (s, 1h), 9.52-9.49 (m, 1 h), 8.69 (s, 1h), 8.06 (s, 1h), 7.89-7.85 (m, 1h), 7.82 (dd, j = 1.2, 7.6 hz, 1h), 7.69-7.64 (m, 1h), 7.52 (d, j = 8.0 hz, 1h), 7.32-7.27 (m, 1h), 5.44-5.41 (m, 1h), 4.35-4.32 (m, 2h), 3.87-3.82 (m, 2h), 3.74-3.70 (m, 1h), 3.53-3.48 (m, 2h), 2.37 (s, 3h), 1.45 (s, 9h). ms m/z 505.54 (m + 1)+.0.792f117[ftimg=68000272]1h nmr (400 mhz, d6-dmso) delta 10.19 (s, 1h), 9.52-9.48 (m, 1 h), 8.69 (s, 1h), 8.06 (s, 1h), 7.89-7.85 (m, 1h), 7.82 (dd, j = 1.2, 7.6 hz, 1h), 7.68-7.64 (m, 1h), 7.52 (d, j = 8.4 hz, 1h), 7.32-7.28 (m, 1h), 5.44-5.41 (m, 1h), 4.35-4.31 (m, 2h), 3.87-3.83 (m, 2h), 3.74-3.70 (m, 1h), 3.53-3.47 (m, 1), 2.37 (s, 3h), 1.44 (s, 9h). ms m/z 505.54 (m + 1)+.0.629f118[ftimg=68000273]ms m/z 405.42 (m + 1)+.0.936f119[ftimg=68000274]ms m/z 417.43 (m + 1)+.0.434f120[ftimg=68000275]1h nmr (400 mhz, d6-dmso) delta 10.16 (s, 1h), 9.51-9.48 (m, 1 h), 8.67 (s, 1h), 8.06 (s, 1h), 7.87-7.82 (m, 2h), 7.67-7.63 (m, 1h), 7.51 (d, j = 8.0 hz, 1 h), 7.30-7.27 (m, 1h), 5.48-5.43 (m, 1h), 3.96-3.90 (m, 3 h), 3.18-3.06 (m, 1h), 2.37 (s, 3h), 1.30 (s, 9h). ms m/z 525.40 (m + 1)+.0.311f121[ftimg=68000276]1h nmr (400 mhz, d6-dmso) delta 10.11 (s, 1h), 9.49-9.47 (m, 1 h), 8.65 (s, 1h), 8.09 (d, j = 4.0 hz, 1h), 7.85-7.82 (m, 2h), 7.61-7.57 (m, 1h), 7.51 (d, j = 8.0 hz, 1h), 7.25-7.22 (m, 1 h), 4.97-4.93 (m, 1h), 3.40-3.34 (m, 2h), 2.94-2.68 (m, 2h), 2.37 (s, 3h). ms m/z 425.40 (m + 1)+.0.205f122[ftimg=68000277]1h nmr (400 mhz, d6-dmso) delta 10.16 (s, 1h), 9.52- (m, 1h), 8.69 (s, 1h), 8.10 (d, j = 2.0 hz, 1h), 7.88-7.83 (m, 2h), 7.68-7.63 (m, 1h), 7.52 (d, j = 8.4 hz, 1h), 7.31-7.27 (m, 1h), 5.08-5.05 (m, 1h), 3.94-3.89 (m, 2h), 3.71-3.60 (m, 3h), 3.26-3.19 (m, 1h), 2.38 (s, 3h), 1.40 (s, 9h). ms m/z 505.54 (m + 1)+.0.296f123[ftimg=68000278]ms m/z 405.42 (m + 1)+.0.527f124[ftimg=68000279]1h nmr (400 mhz, d6-dmso) delta 10.14 (s, 1h), 9.46 (d, j = 7.2 hz, 1h), 8.66 (s, 1h), 7.99 (s, 1h), 7.83 (d, j = 9.2 hz, 1h), 7.75 (dd, j = 7.6, 1.6 hz, 1h), 7.75 (dt, j = 7.6, 1.6 hz, 1h), 7.43 (d, j = 8 hz, 1h), 7.28 (t, j = 7.2 hz, 1h), 3.53 (t, j = 4.4, hz, 1h), 3.46 (t, j = 4.4, hz, 2h), 3.43 (t, j = 4.4, hz, 2h), 3.35 (t, j = 4.4, hz, 2h), 2.30 (s, 3h). ms m/z 461.49 (m + 1)+.0.426f125[ftimg=68000280]1h nmr (400 mhz, d6-dmso) delta 10.15 (s, 1h), 9.50 (d, j = 7.2 hz, 1h), 8.68 (s, 1h), 8.05 (s, 1h), 7.68 (d, j = 8.8 hz, 1h), 7.80 (dd, j = 8.0, 1.6 hz, 1h), 7.65 (t, j = 8.8 hz, 1h), 7.50 (d, j = 8 hz, 1h), 7.29 (t, j = 6.8 hz, 1h), 3.95-4.05 (m, 3h), 3.25-3.63 (m, 4h), 3.50 (t, j = 7.6 hz, 2h), 3.15 (t, j = 7.2 hz, 2h), 2.68 (t, j = 7.2 hz, 2h), 2.36 (s, 3h). ms m/z 481.47 (m + 1)+.0.426f126[ftimg=68000281]1h nmr (400 mhz, d6-dmso) delta 11 nmr (400 mhz, d6-dmso) delta 10.16 (s, 1h), 9.52 (dt, j = 7.2, 1.2 hz, 1h), 8.69 (s, 1h), 8.09 (d, j = 1.2 hz, 1h), 7.84-7.89 (m, 2h), 7.67 (t, j = 8.0, 1h), 7.51 (d, j = 8.0 hz, 1h), 7.30 (t, d, j = 7.2, 0.8 hz, 1h), 4.11-4.34 (m, 5h), 2.37 (s, 3h), 1.46 (s, 3h), 0.76-0.81 (m, 2h), 0.57-0.62 (m, 2h). ms m/z 473.50 (m + 1).0.891f127[ftimg=68000282]1h nmr (400 mhz, d6-dmso) delta 10.19 (s, 1h), 9.52 (d, j = 6.9, 1h), 8.71 (s, 1h), 8.09 (s, 1h), 7.76-7.91 (m, 2h), 7.72-7.62 (m, 1h), 7.51 (d, j = 8.1, 1h), 7.30 (d, j = 6.9, 1h), 4.32-4.23 (m, 10h), 4.14-4.08 (m, 3h), 3.53-3.46 (m, 2h), 3.24 (s, 3h), 2.37 (s, 4h). ms m/z 477.48 (m + 1)+.0.517f128[ftimg=68000283]1h nmr (400 mhz, dmso) delta 10.24 (s, 1h), 9.52 (dd, j = 7.5, 1.1 hz, 1h), 8.73 (s, 1h), 8.05 (s, 1h), 7.86 (m, 2h), 7.69 (m, 1h), 7.51 (dd, j = 6.3, 1.6 hz, 1h), 7.31 (m, 1h), 4.12 (d, j = 10.8 hz, 1h), 3.98 (d, j = 10.7 hz, 1h), 3.76 (m, 2h), 2.37 (s, 3h), 1.5 (s, 3h). ms m/z 390.2 (m + 1)+.0.141f129[ftimg=68000284]ms m/z 414.1 (m + 1)+.0.313f130[ftimg=68000285]ms m/z 407.1 (m + 1)+.0.127f131[ftimg=68000286]ms m/z 405.2 (m + 1)+.0.738f132[ftimg=68000287]ms m/z 419.1 (m + 1)+.0.283f133[ftimg=68000288]1h nmr (400 mhz, d6-dmso) delta 11.27 (s, 1h), 10.25 (s, 1h), 9.55-9.51 (m, 1h), 8.76 (s, 1h), 8.07 (d, j = 1.6 hz, 1h), 7.93-7.89 (m, 1h), 7.85 (dd, j = 1.6, 8.0 hz, 1h), 7.75-7.71 (m, 1h), 7.52 (d, j = 8.4 hz, 1h), 7.37-7.34 (m, 1h), 4.37-4.32 (m, 5h), 2.38 (s, 3h), 1.38 (s, 9h). ms m/z 554.59 (m + 1)+.0.138f134[ftimg=68000289]1h nmr (400 mhz, d6-dmso) delta 10.08 (s, 1h), 9.48 (d, j = 6.9, 1h), 8.64 (s, 1h), 8.11 (s, 1h), 7.87-7.79 (m, 2h), 7.59 (s, 1h), 7.52 (d, j = 8.2, 1h), 7.23 (s, 1h), 4.24-4.18 (m, 1h), 4.16-4.12 (m, 2h), 4.05-4.01 (m, 2 h), 3.31-3.38 (m, 2h), 2.37 (s, 3h). ms m/z 532.56 (m + 1)+.0.892f135[ftimg=68000290]1h nmr (400 mhz, d6-dmso) delta 10.12 (s, 1h), 9.46 (d, j = 7.0, 1h), 8.66 (s, 1h), 8.07 (d, j = 1.6, 1h), 7.93-7.83 (m, 2h), 7.67-7.57 (m, 1h), 7.48 (d, j = 8.1, 1h), 7.24 (t, j = 6.9, 1h), 4.24-4.18 (m, 1h), 4.16-4.12 (m, 2h), 4.05-4.01 (m, 2h), 3.31-3.38 (m, 14h), 2.37 (s, 3h) 1.98-1.88 (m, 2h). ms m/z 546.59 (m + 1)+.0.751f136[ftimg=68000291]1h nmr (400 mhz, d6-dmso) delta 10.48 (s, 1h), 9.57 (d, j = 7.0, 1h), 8.96 (s, 1h), 8.13 (s, 1h), 7.97 (d, j = 9.0, 1h), 7.94-7.87 (m, 1h), 7.81 (s, 1h), 7.56 (d, j = 8.1, 1h), 7.42 (s, 1h), 5.96-5.80 (m, 1h), 4.19-4.02 (m, 3h), 3.00 (s, 1h), 2.88 (s, 1h), 2.40 (s, 3h). ms m/z 375.40 (m + 1)+.0.543f137[ftimg=68000292]ms m/z 462.2 (m + 1)+.0.792f138[ftimg=68000293]ms m/z 463.1 (m + 1)+.0.271f139[ftimg=68000294]ms m/z 491.2 (m + 1)+.0.139f140[ftimg=68000295]1h nmr (400 mhz, cdcl3) delta 9.46 (m, 1h), 8.48 (s, 1h), 8.14 (s, 1h), 7.81 (dd, j = 1.6, 8.0 hz, 1h), 7.69 (d, j = 7.2 hz, 1h), 7.56 (s, 1h), 7.38 (m, 1h), 7.31 (d, j = 8.0 hz, 1h), 6.98 (dt, j = 0.8, 6.8 hz, 1h), 5.12 (m, 2h), 4.91 (m, 2h), 3.66 (s, 3h), 2.36 (s, 3h). ms m/z 449.0 (m + 1)+.0.103f141[ftimg=68000296]ms m/z 463.1 (m + 1)+.0.714f142[ftimg=68000297]ms m/z 419.41 (m + 1)+.0.578f143[ftimg=68000298]ms m/z 417.43 (m + 1)+.0.314f144[ftimg=68000299]1h nmr (400 mhz, d6-dmso) delta 10.05 (s, 1h), 9.46 (d, j = 6.9, 2h), 8.63 (s, 1h), 8.07 (s, 1h), 7.88-7.73 (m, 2h), 7.51 (d, j = 8.2, 2h), 7.22 (s, 1h), 4.77 (d, j = 5.7, 2h), 4.17-4.08 (m, 2h), 3.4-3.98 (m, 10h), 2.37 (s, 3h) ms m/z 476.50 (m + 1)+.0.963f145[ftimg=68000300]ms m/z 461.49 (m + 1)+.0.447f146[ftimg=68000301]1h nmr (400 mhz, d6-dmso) delta 10.15 (s, 1h), 9.51 (d, j = 6.9 1h), 8.68 (s, 2h), 8.07 (s, 1h), 7.88-7.73 (m, 2h), 7.69-7.60 (m, 1h), 7.51 (d, j = 8.1, 1h), 7.29 (t, j = 6.9, 1h), 4.62 (d, j = 5.9, 2h), 4.32 (m, 2h), 3.94 (m, 2h), 3.80 (m, 2h), 2.37 (s, 3h), 2.10-2.15 (m, 1h), 1.96-1.76 (m, 3h). ms m/z 447.46 (m + 1)+.0.187f147[ftimg=68000302]1h nmr (400 mhz, d6-dmso) delta 10.15 (s, 1h), 9.51 (d, j = 6.9, 1h), 8.68 (s, 2h), 8.07 (s, 1h), 7.88-7.73 (m, 2h), 7.69-7.60 (m, 1h), 7.51 (d, j = 8.1, 1h), 7.29 (t, j = 6.9, 1h), 4.62 (d, j = 8.1, 1h), 7.29 (t, j = 6.9, 1h), 4.62 (d, j = 5.9, 2h), 4.32 (m, 2h), 3.94 (m, 2h), 3.80 (m, 2h), 2.37 (s, 3h), 2.10-2.15 (m, 1h), 1.96-1.76 (m, 3h). ms m/z 447.46 (m + 1)+.0.232f148[ftimg=68000303]1h nmr (400 mhz, d6-dmso) delta 10.14 (s, 1h), 9.50 (d, j = 7.0, 1h), 8.81 (t, j = 5.7, 1h), 8.67 (s, 1h), 8.08 (d, j = 1.7, 1h), 7.87-7.77 (m, 2h), 7.68-7.60 (m, 1h), 7.51 (d, j = 8.1, 1h), 7.28 (t, j = 6.9, 1h), 4.75 (d, j = 5.9, 2h), 4.66 (d, j = 5.9, 2h), 4.27-4.34 (m, 3h), 2.37 (s, 3h), 1.54 (s, 3h). ms m/z 447.46 (m + 1)+.0.151f149[ftimg=68000304]1h nmr (400 mhz, d6-dmso) delta 10.13 (s, 1h), 8.73 (s, 1h), 8.67 (s, 1h), 8.07 (s, 1h), 7.87-7.77 (m, 2h), 7.65 (s, 1h), 7.51 (d, j = 8.1, 1h), 7.28 (s, 1h), 4.61 (d, j = 5.7, 2h), 3.85 (t, j = 5.7, 2h), 3.32 (t, j = 5.7, 2h), 2.37 (s, 3h), 2.07 (s, 1h), 1.60-1.71 (m, 4h). ms m/z 461.49 (m + 1)+.0.684f150[ftimg=68000305]1h nmr (400 mhz, d6-dmso) delta 10.10 (s, 1h), 9.49 (d, j = 6.9, 1h), 8.71 (s, 1h), 8.65 (s, 1h), 8.07 (s, 1h), 7.87-7.77 (m, 2h), 7.68-7.58 (m, 1h), 7.51 (d, j = 8.1, 1h), 7.25 (s, 1h), 4.63 (d, j = 5.7, 2h), 2.37 (s, 3h), 2.31 (s, 2h), 1.19 (s, 6h). ms m/z 4

3.93- 3.76 (m, 3h), 3.60-3.39 (m, 2h), 2.36 (s, 3h), 2.14 (s, 3h). ms m/z 447.46 (m + 1)+0.358f169[ftimg=68000324]1h nmr (400 mhz, d6-dmso) delta 10.18 (s, 1h), 9.51 (d, j = 6.9, 1h), 8.69 (s, 1h), 8.06 (d, j = 1.7, 1h), 7.90-7.79 (m, 2h), 7.70-7.64 (m, 1h), 7.51 (d, j = 8.1, 1h), 7.30 (t, j = 6.5, 1h), 3.88-3.94 (m, 1h), 3.74-3.85 (m, 1h), 3.64- 3.71 (m, 1h), 3.54-3.63 (m, 3h), 3.52-3.42 (m, 3h), 2.36 (s, 3h). ms m/z 447.46 (m + 1)+0.132f170[ftimg=68000325]1h nmr (400 mhz, d6-dmso) delta 10.14 (s, 1h), 9.50 (d, j = 6.9, 1h), 8.67 (s, 1h), 8.08 (d, j = 1.7, 1h), 7.89-7.84 (m, 2h), 7.67-7.61 (m, 1h), 7.51 (d, j = 8.1, 1h), 7.28 (t, j = 6.9, 1h), 4.02- 3.93 (m, 2h), 3.74-3.85 (m, 1h), 3.51-3.55 (m, 1h), 3.41-3.45 (m, 2h), 2.98 (s, 3h), 2.37 (s, 3h), 2.33-2.22 (m, 1h), 1.96 (m, 1h). ms m/z 467.51 (m + 1)+0.137f171[ftimg=68000326]1h nmr (400 mhz, d6-dmso) delta 10.21 (s, 1h), 9.52 (d, j = 6.9, 1h), 8.71 (s, 1h), 8.06 (d, j = 1.6, 1h), 7.87 (dd, j = 8.4, 24.5, 2h), 7.71 (t, j = 8.0, 1h), 7.51 (d, j = 7.9, 1h), 7.33 (t, j = 6.9, 1h), 3.34-4.02 (m, 6h), 2.37 (s, 4h), 1.97 (s, 3h). ms m/z 431.46 (m + 1)+0.24f172 [ftimg=68000327]1h nmr (400 mhz, d6-dmso) delta 10.18 (s, 1h), 9.51 (d, j = 6.9, 1h), 8.68 (s, 1h), 8.05 (d, j = 1.6, 1h), 7.89-7.84 (m, 2h), 7.70-7.63 (m, 1h), 7.52 (d, j = 8.1, 1h), 7.29 (t, j = 6.9, 1h), 5.54 (s, 1h), 3.90- 4.10 (m, 2h), 3.61-3.71 (m, 2h), 3.22-3.01 (m, 1h), 2.88-2.76 (m, 1h), 2.37 (s, 3h). ms m/z 483.44 (m + 1)+0.122f173[ftimg=68000328]1h nmr (400 mhz, d6-dmso) delta 10.19 (d, j = 11.4, 1h), 9.50 (d, j = 6.9, 1h), 8.68 (s, 1h), 8.04 (s, 1h), 7.91- 7.77 (m, 2h), 7.71- 7.61 (m, 1h), 7.51 (d, j = 8.1, 1h), 7.29 (t, j = 6.6, 1h), 5.51-5.60 (m, 1h), 4.20-4.29 (m, 2h), 3.01-3.08 (m, 1h), 2.71-2.91 (m, 1h), 2.37 (s, 3h), 2.01-2.09 (m, 3h). ms m/z 467.44 (m + 1)+0.212f174[ftimg=68000329]1h nmr (400 mhz, d6-dmso) delta 10.13 (s, 1h), 9.50 (d, j = 6.9, 1h), 8.66 (s, 1h), 8.09 (s, 1h), 7.85 (d, j = 9.3, 2h), 7.62 (s, 1h), 7.51 (d, j = 8.1, 1h), 7.26 (s, 1h), 4.32 (t, j = 7.9, 2h), 4.16 (d, j = 5.6, 2h), 2.78 (s, 6h), 2.38 (s, 3h). ms m/z 446.47 (m + 1)+0.831f175[ftimg=68000330]1h nmr (400 mhz, d6-dmso) delta 10.15 (s, 1h), 9.51 (d, j = 6.9, 1h), 8.68 (s, 1h), 8.10 (s, 1h), 7.85 (t, j = 8.1, 2h), 7.65 (s, 1h), 7.52 (d, j = 8.1, 1h), 7.28 (s, 1h), 5.03- 5.10 (m, 1h), 3.28-3.84 (m, 6h), 2.37 (s, 3h), 1.40 (s, 9h). ms m/z 505.54 (m + 1)+0.728f176 [ftimg=68000331]ms m/z 489.54 (m + 1)+0.452f177[ftimg=68000332]ms m/z 447.1 (m + 1)+0.398f178[ftimg=68000333]ms m/z 467.1 (m + 1)+0.476f179 [ftimg=68000334]ms m/z 439.2 (m + 1)+0.119f180[ftimg=68000335]ms m/z 433.1 (m + 1)+0.169f181[ftimg=68000336]ms m/z 419.1 (m + 1)+0.337f182 [ftimg=68000337]ms m/z 433.1 (m + 1)+0.259f183[ftimg=68000338]1h nmr (400 mhz, d6-dmso) delta 10.15 (s, 1h), 9.51-9.348 (m, 1 h), 8.66 (s, 1h), 8.03 (d, j = 1.6 hz, 1h), 7.91-7.88 (m, 1h), 7.87-7.84 (m, 1h), 7.81-7.79 (m, 1h), 7.66-7.62 (m, 1h), 7.50 (d, j = 8.4 hz, 1h), 5.32- 5.27 (m, 1h), 4.71-4.65 (m, 2 h), 4.51-4.44 (m, 2h), 3.58- 3.52 (m, 1h), 2.36 (s, 3h), 1.41 (s, 9h). ms m/z 505.54 (m + 1)+0.454f184[ftimg=68000339]1h nmr (400 mhz, d6-dmso) delta 10.19 (s, 1h), 9.53-9.51 (m, 1 h), 8.72 (s, 1h), 8.07-8.06 (m, 1h), 7.89 (d, j = 8.8 hz, 1h), 7.84-7.82 (m, 1h), 7.73-7.68 (m, 1h), 7.51 (d, j = 8.0 hz, 1 h), 7.35-7.31 (m, 1h), 3.56- 3.52 (m, 1h), 3.40-3.34 (m, 1 h), 3.26-3.17 (m, 1h), 3.14- 3.12 (m, 2h), 3.04-2.98 (m, 2 h), 2.37 (s, 3h), 2.09-2.01 (m, 1h), 1.70-1.61 (m, 1h), 1.38 (s, 9h). ms m/z 503.56 (m + 1)+0.496f185[ftimg=68000340]1h nmr (400 mhz, d6-dmso) delta 10.19 (s, 1h), 9.53-9.51 (m, 1 h), 8.71 (s, 1h), 8.07-8.06 (m, 1h), 7.89 (d, j = 8.8 hz, 1h), 7.84-7.82 (m, 1h), 7.72-7.67 (m, 1h), 7.51 (d, j = 8.0 hz, 1 h), 7.34-7.30 (m, 1h), 3.56- 3.52 (m, 1h), 3.40-3.34 (m, 1 h), 3.26-3.17 (m, 1h), 3.14- 3.12 (m, 2h), 3.04-2.98 (m, 1 h), 2.71-2.62 (m, 1h), 2.37 (s, 3h), 2.08-2.02 (m, 1h), 1.70- 1.61 (m, 1h), 1.38 (s, 9h). ms m/z 503.56 (m + 1)+0.452f186[ftimg=68000341]1h nmr (400 mhz, d6-dmso) delta 10.19 (s, 1h), 9.53-9.51 (m, 1 h), 8.70 (s, 1h), 8.06 (d, j = 1.2 hz, 1h), 7.90-7.87 (m, 1h), 7.83 (dd, j = 1.6, 8.0 hz, 1h), 7.71-7.67 (m, 1h), 7.50 (d, j = 8.0 hz, 1h), 7.33-7.30 (m, 1 h), 3.72-3.62 (m, 1h), 3.29- 3.21 (m, 2h), 2.36 (s, 3h), 2.15- 2.07 (m, 1h), 1.98-1.87 (m, 1 h), 1.79-1.75 (m, 1h), 1.55- 1.48 (m, 1h), 1.35 (s, 9h). ms m/z 503.56 (m + 1)+0.291f187[ftimg=68000342]1h nmr (400 mhz, d6-dmso) delta 10.20 (s, 1h), 9.53-9.50 (m, 1 h), 8.70 (s, 1h), 8.06 (d, j = 1.6 hz, 1h), 7.90-7.87 (m, 1h), 7.83 (dd, j = 2.0, 8.0 hz, 1h), 7.71-7.67 (m, 1h), 7.50 (d, j = 8.0 hz, 1h), 7.34-7.30 (m, 1 h), 3.67-3.46 (m, 1h), 3.30- 3.27 (m, 2h), 2.36 (s, 3h), 2.18- 2.09 (m, 1h), 1.98-1.87 (m, 1 h), 1.79-1.75 (m, 1h), 1.55- 1.49 (m, 1h), 1.35 (s, 9h). ms m/z 503.56 (m + 1)+0.32f188[ftimg=68000343]1h nmr (400 mhz, d6-dmso) delta 10.10 (s, 1h), 9.48 (d, j = 7.0, 1h), 9.25 (s, 2h), 8.65 (s, 1h), 8.11 (s, 1h), 7.84 (d, j = 7.9, 2h), 7.73- 7.56 (m, 1h), 7.53 (d, j = 8.1, 1h), 7.25 (d, j = 6.9, 1h), 5.33 (t, j = 7.0, 1h), 4.10-4.15 (m, 2h), 3.91-4.01 (m, 2h), 3.79-3.69 (m, 2h), 3.30 (br s, 2h), 2.38 (s, 3h). ms m/z 405.42 (m + 1)+0.399f189[ftimg=68000344]1h nmr (400 mhz, d6-dmso) delta 10.13 (s, 1h), 9.49 (d, j = 6.9, 1h), 9.29 (s, 1h), 8.68 (s, 1h), 8.11 (d, j = 1.7, 1h), 7.93-7.81 (m, 2h), 7.69-7.57 (m, 1h), 7.53 (d, j = 8.2, 1h), 7.27 (t, j = 6.9, 1h), 5.37-5.26 (m, 1h), 4.15 (d, j = 12.9, 1h), 3.96 (s, 1h), 3.73 (s, 1h), 3.60-3.38 (m, 1h), 3.30 (br s, 2h), 2.38 (s, 3h). ms m/z 405.42 (m + 1)+0.824f190 [ftimg=68000345]1h nmr (400 mhz, d6-dmso) delta 10.10 (s, 1h), 9.46 (d, j = 6.9, 1h), 8.65 (s, 1h), 8.12 (s, 1h), 7.85 (t, j = 9.1, 2h), 7.65-7.49 (m, 2h), 7.25 (d, j = 7.0, 1h), 5.17 (s, 1h), 3.41 (m, 2h), 2.39 (s, 3h), 2.35- 2.26 (m, 2h), 2.01-2.15 (m, 2h). ms m/z 389.42 (m + 1)+0.476f191[ftimg=68000346]1h nmr (400 mhz, d6-dmso) delta 10.15 (s, 1h), 9.50 (d, j = 7.0, 1h), 8.40 (s, 1h), 8.09 (s, 1h), 7.85 (t, j = 9.1, 2h), 7.65 (s, 1h), 7.51 (d, j = 8.1, 1h), 7.28 (s, 1h), 5.23- 5.03 (m, 1h), 2.64-2.52 (m, 1h), 2.37 (s, 3h), 2.21-2.38 (m, 3h). ms m/z 403.41 (m + 1)+0.465f192[ftimg=68000347]1h nmr (400 mhz, d6-dmso) delta 10.17 (s, 1h), 9.51 (d, j = 7.0, 1h), 8.69 (s, 1h), 8.40 (s, 1h), 8.09 (s, 1h), 7.89-7.84 (m, 2h), 7.67 (s, 1h), 7.52 (d, j = 8.1, 1h), 7.30 (s, 1h), 5.12 (s, 1h), 2.72- 2.52 (m, 1h), 2.37 (s, 3h), 2.33-2.20 (m, 2h). ms m/z 403.41 (m + 1)+0.672f193[ftimg=68000348]1h nmr (400 mhz, d6-dmso) delta 10.18 (s, 1h), 9.51 (d, j = 7.0, 1h), 8.69 (s, 1h), 8.06 (s, 1h), 7.89- 7.84 (m, 2h), 7.68 (s, 1h), 7.50 (d, j = 8.1, 1h), 7.30 (s, 1h), 4.35- 4.25 (m, 1h), 3.36-3.41 (m, 1h), 3.24 (s, 1h), 2.96-2.78 (m, 1h), 2.36 (s, 3h), 2.01-2.15 (m, 2h), 2.02 (s, 3h), 1.86-1.71 (m, 1h), 1.68-1.55 (m, 1h). ms m/z 445.49 (m + 1)+0.354f194[ftimg=68000349]1h nmr (400 mhz, d6-dmso) delta 10.13 (s, 1h), 9.50 (d, j = 6.9, 1h), 8.66 (s, 1h), 8.10 (s, 1h), 7.89- 7.84 (m, 2h), 7.64 (d, j = 7.0, 2h), 7.52 (d, j = 8.1, 1h), 7.26 (t, j = 7.2, 1h), 5.01-5.11 (m, 1h), 3.94-4.19 (m, 6h), 3.65 (s, 3h), 2.37 (s, 3h). ms m/z 463.46 (m + 1)+0.105f195[ftimg=68000350]1h nmr (400 mhz, d6-dmso) delta 10.12 (s, 1h), 9.57-9.44 (m, 1h), 8.66 (s, 1h), 8.11 (s, 1h), 7.85 (d, j = 9.0, 2h), 7.69-7.56 (m, 1h), 7.54-7.46 (m, 1h), 7.26 (s, 1h), 5.19-4.96 (m, 1h), 3.94-4.19 (m, 6h), 3.34-3.10 (m, 3h), 2.38 (s, 3h). ms m/z 447.46 (m + 1)+0.566f196[ftimg=68000351]1h nmr (400 mhz, d6-dmso) delta 10.13 (s, 1h), 9.49 (d, j = 6.9, 1h), 8.64 (s, 1h), 8.04 (s, 1h), 7.83 (t, j = 7.6, 2h), 5.31-5.15 (m, 1h), 3.61 (s, 3h), 2.67 (s, 1h), 2.36 (s, 3h), 2.33 (s, 1h), 1.99 (br s, 3h). ms m/z 447.46 (m + 1)+0.475f197[ftimg=68000352]1h nmr (400 mhz, d6-dmso) delta 10.14 (s, 1h), 9.49 (d, j = 6.9, 1h), 8.65 (s, 1h), 8.03 (s, 1h), 7.89- 7.84 (m, 2h), 7.69-7.57 (m, 1h), 7.50 (d, j = 8.1, 1h), 7.26 (s, 1h), 5.24-5.16 (m, 1h), 2.36 (s, 3h), 2.21-1.87 (m, 6h). ms m/z 431.46 (m + 1)+0.46f198 [ftimg=68000353]1h nmr (400 mhz, d6-dmso) delta 10.13 (s, 1h), 9.50 (d, j = 6.9, 1h), 8.66 (s, 1h), 8.10 (s, 1h), 7.89- 7.84 (m, 2h), 7.64 (d, j = 7.2, 1h), 7.52 (d, j = 8.1, 1h), 7.26 (t, j = 7.2, 1h), 5.01-5.11 (m, 1h), 3.94-4.19 (m, 6h), 3.65 (s, 3h), 2.37 (s, 3h). ms m/z 463.46 (m + 1)+0.142f199[ftimg=68000354]1h nmr (400 mhz, d6-dmso) delta 10.12 (s, 1h), 9.57-9.44 (m, 1h), 8.66 (s, 1h), 8.11 (s, 1h), 7.85 (d, j = 9.0, 2h), 7.69-7.56 (m, 1h), 7.54-7.46 (m, 1h), 7.26 (s, 1h), 5.19-4.96 (m, 1h), 3.94-4.19 (m, 6h), 3.34-3.10 (m, 3h), 2.38 (s, 3h). ms m/z 447.46 (m + 1)+0.509f200[ftimg=68000355]1h nmr (400 mhz, d6-dmso) delta 10.09 (s, 1h), 9.46 (d, j = 6.9, 2h), 8.65 (s, 1h), 8.13 (s, 1h), 7.85 (t, j = 9.1, 2h), 7.63-7.53 (m, 2h), 7.53 (s, 1h), 7.24 (s, 1h), 5.25- 5.10 (m, 1h), 3.49- 3.30 (m, 3h), 2.39 (s, 3h), 2.35-2.28 (m, 2h), 2.01-2.14 (m, 2h). ms m/z 389.42 (m + 1)+0.395f201[ftimg=68000356]ms m/z 437.2 (m + 1)+0.443f202 [ftimg=68000357]1h nmr (400 mhz, d6-dmso) delta 10.17 (s, 1h), 9.51 (d, j = 6.9, 1h), 8.69 (s, 1h), 8.10 (s, 1h), 7.64- 7.77 (m, 2h), 7.20-7.61 (m, 1h), 7.53 (d, j = 8.1, 1h), 7.29 (t, j = 6.9, 1h), 5.51-5.63 (m, 1h), 4.03 (s, 3h), 2.80-2.67 (m, 1h), 2.38 (s, 3h), 1.38 (s, 3h), 0.91- 0.70 (m, 1h), 0.56 (s, 3h). ms m/z 473.50 (m + 1)+0.208f203[ftimg=68000358]1h nmr (400 mhz, d6-dmso) delta 10.11 (s, 1h), 9.48 (d, j = 7.0, 1h), 8.66 (s, 1h), 8.09 (d, j = 1.6, 1h), 7.86-7.80 (m, 2h), 7.64-7.58 (m, 1h), 7.52 (d, j = 8.1, 1h), 7.25 (t, j = 6.4, 1h), 3.61-3.74 (m, 1h), 3.51-3.58 (m, 1h), 3.29-3.38 (m, 2h), 2.37 (s, 3h), 1.81-1.92 (m, 4h). ms m/z 403.45 (m + 1)+0.826f204[ftimg=68000359]1h nmr (400 mhz, d6-dmso) delta 10.22 (s, 1h), 9.53 (d, j = 6.9, 1h), 8.72 (s, 1h), 8.06 (s, 1h), 7.90 (d, j = 9.0, 1h), 7.83 (d, j = 7.9, 1h), 7.75-7.67 (m, 1h), 7.51 (d, j = 8.1, 1h), 7.34 (t, j = 6.9, 1h), 3.61-3.53 (m, 4h), 3.40- 3.45 (m, 1h), 3.33-3.21 (m, 1h), 3.10- 3.21 (m, 2h), 3.08 (t, j = 7.2, 1h), 2.76-2.59 (m, 1h), 2.37 (s, 3h), 2.07 (s, 1h), 1.69 (s, 1h). ms m/z 461.49 (m + 1)+0.2f205[ftimg=68000360]1h nmr (400 mhz, d6-dmso) delta 10.22 (s, 1h), 9.53 (d, j = 6.9, 1h), 8.72 (s, 1h), 8.06 (s, 1h), 7.90 (d, j = 9.0, 1h), 7.83 (d, j = 7.9, 1h), 7.75-7.67 (m, 1h), 7.51 (d, j = 8.1, 1h), 7.34 (t, j = 6.9, 1h), 3.61-3.53 (m, 4h), 3.40- 3.45 (m, 1h), 3.33-3.21 (m, 2h), 3.08 (t, j = 7.2, 1h), 2.76-2.59 (m, 1h), 2.37 (s, 3h), 2.07 (s, 1h), 1.69 (s, 1h). ms m/z 461.49 (m + 1)+0.284f206[ftimg=68000361]1h nmr (400 mhz, d6-dmso) delta 10.21 (s, 1h), 9.52 (d, j = 7.0, 1h), 8.72 (s, 1h), 8.07 (d, j = 1.7, 1h), 7.90 (d, j = 9.0, 1h), 7.84 (dd, j = 1.7, 7.9, 1h), 7.74-7.66 (m, 1h), 7.51 (d, j = 8.1, 1h), 7.33 (t, j = 6.9, 1h), 3.51-3.54 (m, 1h), 3.41- 3.33 (m, 1h), 3.30-3.21 (m, 1h), 3.11-3.19 (m, 2h), 3.00- 3.08 (m, 1h) = 8.0, 10.0, 1h), 2.91 (s, 3h), 2.70-2.81 (m, 1h), 2.37 (s, 3h), 2.11-2.21 (m, 1h), 1.62- 1.74 (m, 1h). ms m/z 481.54 (m + 1)+0.169f207[ftimg=68000362]1h nmr (400 mhz, d6-dmso) delta 10.17 (s, 1h), 9.51 (d, j = 6.9, 1h), 8.69 (s, 1h), 8.06 (s, 1h), 7.86- 7.80 (m, 2h), 7.66 (s, 1h), 7.51 (d, j = 8.1, 1h), 7.29 (s, 1h), 5.12 (s, 1h), 2.72- 2.52 (m, 1h), 2.37 (s, 3h), 2.33-2.20 (m, 2h). ms m/z 403.41 (m + 1)+0.159f208[ftimg=68000363]1h nmr (400 mhz, d6-dmso) delta 10.17 (s, 1h), 9.51 (d, j = 6.9, 1h), 8.69 (s, 1h), 8.06 (s, 1h), 7.86- 7.80 (m, 2h), 7.66 (s, 1h), 7.51 (d, j = 8.1, 1h), 7.29 (s, 1h), 3.81- 3.71 (m, 2h), 3.59 (s, 3h), 3.36- 3.23 (m, 2h), 3.12-3.03 (m, 1h), 2.36 (s, 3h), 2.25-2.15 (m, 1h), 1.94-1.80 (m, 1h), 1.79- 1.69 (m, 1h), 1.59-1.43 (m, 1h). ms m/z 461.49 (m + 1)+0.141f208[ftimg=68000363]1h nmr (400 mhz, d6-dmso) delta 10.17 (s, 1h), 9.51 (d, j = 6.9, 1h), 8.69 (s, 1h), 8.06 (s, 1h), 7.86- 7.80 (m, 2h), 7.66 (s, 1h), 7.51 (d, j = 8.1, 1h), 7.29 (s, 1h), 3.81- 3.71 (m, 2h), 3.59 (s, 3h), 3.36- 3.23 (m, 2h), 3.12-3.03 (m, 1h), 2.36 (s, 3h), 2.25-2.15 (m, 1h), 1.94-1.80 (m, 1h), 1.79- 1.69 (m, 1h), 1.59-1.43 (m, 1h). ms m/z 461.49 (m + 1)+0.134f209[ftimg=68000364]1h nmr (400 mhz, d6-dmso) delta 10.20 (s, 1h), 9.52 (dd, j = 3.5, 4.5, 1h), 8.71 (s, 1h), 8.07 (d, j = 1.7, 1h), 7.92-7.81 (m, 2h), 7.73-7.66 (m, 1h), 7.51 (d, j = 8.1, 1h), 7.32 (dd, j = 5.9, 6.9, 1h), 3.84 (d, j = 11.7, 1h), 3.49-3.41 (m, 2h), 3.18-3.29 (m, 1h), 2.96- 2.86 (m, 3h), 2.37 (s, 3h), 2.23- 2.13 (m, 1h), 1.70-1.94 (m, 3h). ms m/z 481.54 (m + 1)+0.148f210[ftimg=68000365]1h nmr (400 mhz, d6-dmso) delta 10.13 (s, 1h), 9.46 (d, j = 7.0, 1h), 8.65 (s, 1h), 7.99 (d, j = 1.7, 1h), 7.83 (d, j = 9.0, 1h), 7.76 (dd, j = 1.7, 7.9, 1h), 7.66-7.60 (m, 1h), 7.44 (d, j = 8.1, 1h), 7.26 (t, j = 6.9, 1h), 3.84 (s, 2h), 2.91 (d, j = 7.0, 2h), 2.63 (s, 2h), 2.30 (s, 3h), 1.88-2.01 (m, 1h), 1.61 (d, j = 11.1, 2h), 1.31 (s, 9h), 1.02- 1.15 (m, 2h). ms m/z 517.59 (m + 1)+0.71f211[ftimg=68000366]1h nmr (400 mhz, d6-dmso) delta 10.21 (s, 1h), 9.53 (d, j = 6.9, 1h), 8.73 (s, 1h), 8.07 (s, 1h), 7.90 (d, j = 9.1, 1h), 7.83 (d, j = 7.8, 1h), 7.75-7.68 (m, 1h), 7.50 (d, j = 8.0, 1h), 7.33 (t, j = 6.6, 1h), 4.16 (br s, 1h), 3.33-3.11 (m, 4h), 2.37 (s, 3h), 2.01 br (s, 1h), 1.81 (br s, 3h), 1.33 (s, 9h). ms m/z 503.56 (m + 1)+0.106f212[ftimg=68000367]1h nmr (400 mhz, d6-dmso) delta 10.16 (s, 1h), 9.50 (d, j = 6.9, 1h), 8.67 (s, 1h), 8.03 (s, 1h), 7.91- 7.83 (m, 2h), 7.66-7.56 (m, 1h), 7.50 (d, j = 8.1, 1h), 7.28 (s, 1h), 5.26-5.19 (m, 1h), 3.65-3.89 (m, 5h), 2.36 (s, 4h), 2.03 (s, 3h), 1.81-1.85 (m, 1h). ms m/z 447.46 (m + 1)+0.172f13[ftimg=68000368]1h nmr (400 mhz, d6-dmso) delta 10.10 (s, 1h), 9.48 (d, j = 6.9, 1h), 8.63 (s, 1h), 8.07 (d, j = 1.7, 1h), 7.93-7.79 (m, 2h), 7.64-7.46 (m, 1h), 7.22 (t, j = 6.9, 1h), 5.21-5.42 (m, 1h), 3.08 (s, 3h), 2.38 (s, 3h), 2.21-1.96 (m, 3h), 1.25 (q, j = 6.7, 4h). ms m/z 467.51 (m + 1)+0.137f214[ftimg=68000369]1h nmr (400 mhz, d6-dmso) delta 10.19 (s, 1h), 9.52 (d, j = 7.0, 1h), 8.70 (s, 1h), 8.06 (d, j = 1.7, 1h), 7.94-7.77 (m, 2h), 7.72- 7.66 (m, 1h), 7.50 (d, j = 8.1, 1h), 7.32 (t, j = 6.4, 1h), 3.95 (br s, 2h), 3.57 (s, 3h), 2.98 (d, j = 7.1, 2h), 2.81 (s, 2h), 2.36 (s, 3h), 2.06 (br s, 1h), 1.70 (d, j = 12.1, 2h), 1.19 (q, j = 12.1, 2h). ms m/z 475.51 (m + 1)+0.142f215[ftimg=68000370]1h nmr (400 mhz, d6-dmso) delta 10.17 (s, 1h), 9.51 (d, j = 6.9, 1h), 8.69 (s, 1h), 8.06 (d, j = 1.7, 1h), 7.88 (d, j = 9.0, 1h), 7.83 (dd, j = 1.7, 7.9, 1h), 7.70-7.64 (m, 1h), 7.51 (d, j = 8.1, 1h), 7.31 (t, j = 6.5, 1h), 3.55 (d, j = 11.9, 2h), 3.03 (d, j = 7.1, 2h), 2.84 (s, 3h), 2.45-2.59 (m, 2h), 2.37 (s, 3h), 2.00 (br s, 1h), 1.81 (d, j = 10.9, 2h), 1.29 (q, j = 10.9, 2h). ms m/z 495.57 (m + 1)+0.175f216[ftimg=68000371]ms m/z 403.45 (m + 1)+0.519f217[ftimg=68000372]ms m/z 519.2 (m + 1)+0.173f218[ftimg=68000373]ms m/z 505.1 (m + 1)+0.155f219[ftimg=68000374]ms m/z 499.2 (m + 1)+0.158f220[ftimg=68000375]ms m/z 520.2 (m + 1)+0.69f221[ftimg=68000376]ms m/z 523.0 (m + 1)+0.851f222[ftimg=68000377]ms m/z 501.0 (m + 1)+0.376f223[ftimg=68000378]ms m/z 493.1 (m + 1)+0.151f224[ftimg=68000379]ms m/z 523.2 (m + 1)+0.854f225[ftimg=68000380]1h nmr (400 mhz, d6-dmso) delta 10.18 (s, 1h), 9.52 (d, j = 6.9, 1h), 8.70 (s, 1h), 8.06 (s, 1h), 7.92-7.76 (m, 2h), 7.72-7.64 (m, 1h), 7.51 (d, j = 8.1, 1h), 7.31 (t, j = 6.9

490.20 (m + 1)+.0.317f247[ftimg=68000402]ms m/z 505.1 (m + 1)+.0.328f248[ftimg=68000403]1h nmr (400 mhz, d6-dmso) delta 10.10 (s, 1h), 9.51-9.48 (m, 1h), 8.65 (s, 1h), 7.94 (d, j = 1.6 hz, 1h), 7.86-7.83 (m, 1h), 7.71 (dd, j = 1.6, 7.6 hz, 1h), 7.64-7.60 (m, 1h), 7.43 (d, j = 8.0 hz, 1h), 7.27-7.24 (m, 1h), 4.26-4.22 (m, 4h), 2.48-2.40 (m, 2h), 2.34 (s, 3h). ms m/z 374.15 (m + 1)+.0.132f249[ftimg=68000404]ms m/z 447.1 (m + 1)+.0.426f250[ftimg=68000405]ms m/z 518.1 (m + 1)+.0.114f251[ftimg=68000406]1h nmr (400 mhz, d6-dmso) delta 10.15 (s, 1h), 9.51-9.48 (m, 1h), 8.67 (s, 1h), 8.09 (d, j = 1.6 hz, 1h), 7.87-7.82 (m, 2h), 7.66- 7.62 (m, 1h), 7.53 (d, j = 8.4 hz, 1h), 7.30-7.26 (m, 1h), 3.90 (s, 4h), 2.39 (s, 3h), 1.44 (s, 3h). ms m/z 404.16 (m + 1)+.0.157f252[ftimg=68000407]ms m/z 498.7 (m + 1)+.0.421f253[ftimg=68000408]ms m/z 543.7 (m + 1)+.0.215f254[ftimg=68000409]1h nmr (400 mhz, d6-dmso) delta 9.93 (s, 1h), 9.33-9.31 (m, 1h), 8.50 (s, 1h), 7.93 (d, j = 1.6 hz, 1h), 7.69 (dd, j = 1.6, 7.6 hz, 1h), 7.57 (s, 1h), 7.42 (d, j = 8.0 hz, 1h), 7.02 (dd, j = 1.6, 7.2 hz, 1h), 4.45-4.38 (m, 3h), 4.10- 4.06 (m, 2h), 3.25 (s, 3h), 2.42 (s, 3h), 2.33 (s, 3h). ms m/z 418.18 (m + 1)+.0.111f255[ftimg=68000410]1h nmr (400 mhz, d6-dmso) delta 9.94 (s, 1h), 9.32-9.31 (m, 1h), 8.51 (s, 1h), 7.95 (d, j = 1.6 hz, 1h), 7.71 (dd, j = 1.6, 8.0 hz, 1h), 7.57 (s, 1h), 7.43 (d, j = 8.0 hz, 1h), 7.03 (dd, j = 1.6, 7.2 hz, 1h), 4.43-4.38 (m, 1h), 4.25- 4.21 (m, 1h), 4.06-4.00 (m, 3h), 3.70-3.67 (m, 1h), 3.23-3.16 (m, 3h), 2.42 (s, 3h), 2.34 (s, 3h). ms m/z 473.18 (m + 1)+.0.129f256[ftimg=68000411]ms m/z 494.2 (m + 1)+.0.106f257[ftimg=68000412]ms m/z 501.14 (m + 1)+.0.137f258[ftimg=68000413]ms m/z 552.24 (m + 1)+.0.146f259[ftimg=68000414]ms m/z 483.15 (m + 1)+.0.177f260[ftimg=68000415]ms m/z 420.17 (m + 1)+.0.205f261[ftimg=68000416]ms m/z 489.22 (m + 1)+.0.291f262[ftimg=68000417]ms m/z 447.17 (m + 1)+.0.309f263[ftimg=68000418]ms m/z 376.13 (m + 1)+.0.357f264[ftimg=68000419]ms m/z 501.14 (m + 1)+.0.438f265[ftimg=68000420]ms m/z 503.24 (m + 1)+.0.505f266[ftimg=68000421]ms m/z 463.16 (m + 1)+.0.523f267[ftimg=68000422]ms m/z 519.23 (m + 1)+.0.65f268[ftimg=68000423]ms m/z 489.22 (m + 1)+.0.912f269[ftimg=68000424]ms m/z 431.17 (m + 1)+.1.012f270[ftimg=68000425]ms m/z 475.2 (m + 1)+.1.038f271[ftimg=68000426]ms m/z 403.18 (m + 1)+.1.12f272[ftimg=68000427]ms m/z 501.13 (m + 1)+.1.139f273[ftimg=68000428]ms m/z 501.13 (m + 1)+.1.168f274[ftimg=68000429]ms m/z 403.18 (m + 1)+.1.204f275[ftimg=68000430]ms m/z 447.18 (m + 1)+.1.233f276[ftimg=68000431]ms m/z 405.17 (m + 1)+.1.243f277[ftimg=68000432]ms m/z 505.21 (m + 1)+.1.247f278[ftimg=68000433]ms m/z 489.22 (m + 1)+.1.278f279[ftimg=68000434]ms m/z 493.19 (m + 1)+.1.284f280[ftimg=68000435]ms m/z 389.15 (m + 1)+.1.309f281[ftimg=68000436]ms m/z 467.15 (m + 1)+.1.373f282[ftimg=68000437]ms m/z 503.24 (m + 1)+.1.6*f283[ftimg=68000438]ms m/z 489.22 (m + 1)+.1.633f284[ftimg=68000439]ms m/z 403.18 (m + 1)+.1.649f285[ftimg=68000440]ms m/z 403.18 (m + 1)+.1.673f286[ftimg=68000441]ms m/z 391.14 (m + 1)+.1.681f287[ftimg=68000442]ms m/z 501.13 (m + 1)+.1.681f288[ftimg=68000443]ms m/z 503.24 (m + 1)+.1.78*f289[ftimg=68000444]ms m/z 417.19 (m + 1)+.1.884f290[ftimg=68000445]ms m/z 403.19 (m + 1)+.1.887f291[ftimg=68000446]ms m/z 467.15 (m + 1)+.1.921f292[ftimg=68000447]ms m/z 462.18 (m + 1)+.1.934f293[ftimg=68000448]ms m/z 419.17 (m + 1)+.2.153f294[ftimg=68000449]ms m/z 417.17 (m + 1)+.2.201f295[ftimg=68000450]ms m/z 389.17 (m + 1)+.2.203f296[ftimg=68000451]ms m/z 389.17 (m + 1)+.2.443f297[ftimg=68000452]ms m/z 390.15 (m + 1)+.2.79f298[ftimg=68000453]ms m/z 375.16 (m + 1)+.2.857f299[ftimg=68000454]ms m/z 505.14 (m + 1)+.3.52f300[ftimg=68000455]ms m/z 475.2 (m + 1)+.3.56f301[ftimg=68000456]ms m/z 519.16 (m + 1)+.3.97f302[ftimg=68000457]ms m/z 423.15 (m + 1)+.4.33f303[ftimg=68000458]ms m/z 474.21 (m + 1)+.4.64f304[ftimg=68000459]ms m/z 403.18 (m + 1)+.5.23f305[ftimg=68000460]ms m/z 423.15 (m + 1)+.8.08f306[ftimg=68000461]ms m/z 423.15 (m + 1)+.8.37f307[ftimg=68000462]ms m/z 505.17 (m + 1)+.10f308[ftimg=68000463]ms m/z 529.21 (m + 1)+.10f309[ftimg=68000464]ms m/z 511.14 (m + 1)+.10f310[ftimg=68000465]ms m/z 543.21 (m + 1)+.10*20 percent fbs instead of 1 percent fbs assays compounds of formula (i) and formula (ii) provided herein were assayed to measure their capacity to inhibit c-kit and pdgfr kinases using the appropriate assay described below: c-kit inhibition was evaluated using the mo7e cell proliferation assay, and pdgfr inhibition was evaluated using the rat a10 cell proliferation assay and the human tg/ha-vsmc cell proliferation assay.mo7e cell proliferation assaythe compounds of table 1 and table 2 were tested for inhibition of scf dependent proliferation using human mo7e cells which endogenously express c-kit in a 384 well format. three-fold serially diluted test compounds (cmax=10 nm) were evaluated for their antiproliferative activity of mo7e cells stimulated with human recombinant scf. after 48 hours of incubation at 37 degrees centigrade, cell viability was measured by adding 25 ul of celltiter glo (promega) to the cells and the luminescence was measured by a clipr ccd camera (molecular devices).rat a10 cell proliferation assayrat a10 cells (atcc) were resuspended in dmem supplemented with 1 percent fbs or 20 percent fbs and 10 ng/ml recombinant rat pdgfr-bb at 20,000 cells/ml. the cells were aliquoted into 384 well plates at 50 micro l/well and incubated for 4 hours at 37 degrees centigrade 0.5 micro l of test compound 3-fold serially diluted in dmso was added to each well. the plates were returned to the incubator for a further 68 hours. 25 micro l of celltiter-glo (promega) was added to each well and the plates were incubated on the bench for 15 minutes. luminescence was then read using a clipr ccd camera (molecular devices).human tg/ha-vsmc cell proliferation assayhuman tg/ha-vsmc cells (atcc) were resuspended in dmem supplemented with 1 percent fbs and 30 ng/ml recombinant human pdgfr-bb at 60,000 cells/ml. the cells were aliquoted into 384 well plates at 50 micro l/well and incubated for 4 hours at 37 degrees centigrade 0.5 micro l of test compound 3-fold serially diluted in dmso was added to each well. the plates were returned to the incubator for a further 68 hours. 25 micro l of celltiter-glo (promega) was added to each well and the plates were incubated on the bench for 15 minutes. luminescence was then read using a clipr ccd camera (molecular devices).certain assay resultsvarious compounds of formula (i) and formula (ii) in free form or in pharmaceutically acceptable salt form, exhibit pharmacological properties, for example, as indicated by the tests described herein and presented in table 1 and table 2. the ic50 value is given as that concentration of the test compound in question that provoke a response halfway between the baseline and maximum responses. certain compounds of formula (i) or formula (ii) having specific ic50 for c-kit inhibition values of less than or equal to 100 nm are listed in table 1, while certain compounds of formula (i) or formula (ii) having specific ic50 for c-kit inhibition values greater than 100 nm are listed in table 2.in other embodiments, compounds of formula (i) or formula (ii) have ic50 values for c-kit inhibition in the range from 1 nm to 1 micro m. in other embodiments, compounds of formula (i) or formula (ii) have ic50 values for c-kit inhibition in the range from 1 nm to 500 nm. in other embodiments, compounds of formula (i) or formula (ii) have ic50 values for c-kit inhibition in the range from 1 nm to 200 nm. in other embodiments, compounds of formula (i) or formula (ii) have ic50 values for c-kit inhibition in the range from 1 nm to 100 nm. in other embodiments, compounds of formula (i) or formula (ii) have ic50 values for c-kit inhibition in the range from 1 nm to 50 nm. in other embodiments, compounds of formula (i) or formula (ii) have ic50 values for c-kit inhibition in the range from 1 nm to 25 nm. in other embodiments, compounds of formula (i) or formula (ii) have ic50 values for c-kit inhibition in the range from 1 nm to 10 nm. in other embodiments, compounds of formula (i) or formula (ii) have ic50 values for c-kit inhibition in the range from 1 nm to 5 nm. in other embodiments, compounds of formula (i) or formula (ii) have ic50 values for c-kit inhibition in the range from 1 nm to 2.5 nm.it is understood that the examples and embodiments described herein are for illustrative purposes only and that various modifications or changes in light thereof will be suggested to persons skilled in the art and are to be included within the spirit and purview of this application and scope of the appended claims. (Results 0)

Search 23: PN=(WO2013033228) (Results 1)

Search 24: TAC=(hexahydrocyclopenta[c]pyrrol) and PN=(WO2013033228) and IC=(A61K31/473) (Results 1)

Search 25: TAC=(hexahydrocyclopenta[c]pyrrol) and IC=(A61K31/473) (Results 2)

Search 26: TAC=(antibacterial) and IC=(A61K31/473) (Results 71)

Search 27: TAC=(antibacterial) and CPC=(C07D495/04) (Results 84)

Search 28: TAC=(antibacterial) and IC=(A61K31/473) and CPC=(C07D495/04 or C07D491/14) (Results 2)

Search 29: (26) AND PD=(2005 OR 2004 OR 2009 OR 2001 OR 2002 OR 2003 OR 2006 OR 2008 OR 2010 OR 2000 OR 2007 OR 2011) (Results 53)

Search 30: (27) AND PD=(2003 OR 2004 OR 2002 OR 2005 OR 2000 OR 2006 OR 2010) (Results 35)

Abstract: Source: US5292892A The present invention relates to a novel **antibacterial** compound obtainable from the genus *Alteromonas* and which shares structural similarity with the pseudomonic acids.

International (IPC 8-9): A61K31/40 A61K39/40 A61K45/00 A61P31/04 C07D339/02 C07D419/14 C07D495/04 C07D495/06 C07H7/06 C12N1/20 C12P1/06 C12P17/18 C12P19/26 (Advanced/Invention); A61K31/40 A61K39/40 A61K45/00 C12R1/01 (Advanced/Non-invention); A61K31/40 A61K39/40 A61K45/00 A61P31/00 C07D339/00 C07D419/00 C07D495/00 C12N1/20 C12P1/06 C12P17/18 (Core/Invention)

International (IPC 1-7): A61K31/40 A61K31/71 A61K39/40 A61K45/00 C07D209/00
C07D339/00 C07D339/02 C07D419/14 C07D495/04 C07D495/06 C07G11/00 C07H7/06
C12N1/20 C12P1/04 C12P1/06 C12P17/16 C12P17/18 C12P19/26 C12R1/01

US: 435/118 435/252.1 548/453

[illegible]

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Designated states: AT BE CH DE DK ES FR GB GR IT LI LU MC NL PT SE

Title: Thiomarinol compounds

Abstract: Source: US5399711A Two thiomarinol derivatives, which have **antibacterial** and anti-mycoplasmal properties, are obtainable from microorganisms of the genus *Alteromonas* and are named "thiomarinol B" and "thiomarinol C". Thiomarinol B can also be prepared by the oxidation of thiomarinol.

Classifications:

International (IPC 8-9): A61K31/33 A61K31/35 A61K31/385 A61K31/40 A61K31/407 A61K35/60 A61K35/74 A61P31/04 C07D209/02 C07D209/34 C07D339/02 C07D339/04 C07D401/12 C07D405/12 C07D407/12 C07D495/04 C07G11/00 C07H7/02 C12P1/04 C12P1/06 C12P17/18 C12P19/26 (Advanced/Invention):

A61K31/40 C07D209/34 C07D339/02 C07D339/04 C12P17/18 C12R1/00

C12R1/01 (Advanced/Non-invention);

A61K31/35 A61K31/385 A61K31/40 A61K31/407 A61K35/66 A61P31/00 C07D209/00
C07D339/00 C07D401/00 C07D405/00 C07D495/00 C07G11/00 C12P1/04 C12P1/06

C12P17/18 (Core/Invention);

C07D209/00 C07D339/00 (Core/Non-ir

A61K C07D C12N (Subclass/Invention)

International (IPC 1-7): A61K A61K31/35 A61K31/385 A61K31/40 A61K31/42

A61K31/44 A61K31/70 A61K31/71 A61K35/74 A61K39/002 A61P31/04 C07D

C07D209/00 C07D339/00 C07D401/12 C07D405/12 C07D495/02 C07D495/04

C07D513/04 C07G11/00 C07H7/02 C12N C12N1/20 C12P1/04 C12P1/06 C12P17/18

C12P19/02 C12P19/26 C12R1/01

CPC: C07D495/04

European: C07D495/04

US: 435/119 548/453

С-ароматизация	-	С-ароматизация	-
С-активация	-	С-активация	+
С-деактивация	-	С-деактивация	-
магнитная	+	магнитная	-
термическая	+	термическая	-
механическая	-	механическая	-
осветлительная	-	осветлительная	-
защитная	+	защитная	+

Table 1

Microorganism in faecal flora	MIC (µg/ml)	
	S	P
<i>Staphylococcus aureus</i> 209E	≤0.01	≤0.01
<i>Staphylococcus aureus</i> 502	≤0.01	≤0.01
<i>Staphylococcus aureus</i> 103 (MRSA)	≤0.01	0.2
<i>Enterococcus faecalis</i> 51	0.02	0.05
<i>Enterococcus faecalis</i> 102	0.4	1.0
<i>Enterococcus faecalis</i> 500	0.5	0.3
<i>Streptococcus faecalis</i>	0.5	0.4
<i>Streptococcus pneumoniae</i>	0.5	0.4
<i>Streptococcus pneumoniae</i> 542 (S)	0.2	0.2
<i>Enterobacter cloacae</i>	0.5	>100
<i>Enterobacter cloacae</i> 1196	3.1	>100
<i>Proteus mirabilis</i> 1425	0.05	0.6
<i>Morganella morganii</i> 1510	0.2	>100
<i>Pseudomonas aeruginosa</i> 1501	0.3	0.2
<i>Pseudomonas aeruginosa</i> No. 7	0.4	>100
<i>Pseudomonas aeruginosa</i> 1510	0.2	>100

TABLE 1

Исследуемый в тесте штамм микоплазмы	MFC (клетки)		
	A	B	P
Микоплазма <i>novae</i> Donelle	0,0708	0,050	20,206
Микоплазма <i>reisseri</i> PG-31	0,06	0,1	8,25
Микоплазма <i>reisseri</i> K-1	0,05	0,1	0,95
Микоплазма <i>reisseri</i> K-16	0,025	-	-
Микоплазма <i>burnetii</i> B757	-	0,75	0,75

Tadokura

Family:

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JP2532199 B2	19960911	JP19930231332	19930917
JP3123864 B2	20010115	JP19930273355	19931101
JP6199865 A2	19940719	JP19930273355	19931101
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KR0177839 B1	19990320	KR19930018972	19930918
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NO933328 A	19940321	NO19930003328	19930917
NO933328 A0	19930917	NO19930003328	19930917
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RU95107329 A	19970210	RU19950107329	19950511
RU95107329 A1	19970210	RU19950107329	19950511
TH15928 A	19950526	TH19931001672	19930917
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Priority:

JP19920248970 19920918 JP19920294170 19921102 CA19932106443 19930917
 JP19930231332 19930917 JP19930273355 19931101 JP19920295695 19921105
 BR19971100615 19970513 JP19930275108 19931104

Probable Assignee: SANKYO CO LTD

Assignee(s): (std): SANKYO CO ; SANKIO KOMPANI LTD

Assignee(s): SAKAIDA YOSHIHARU ; OGAWA KANEO ; KODAMA KENTARO ; KAGASAKI TAKESHI ; SANKYO COMPANY LIMITED ; SHIOZAWA HIDEYUKI ; TORIKATA AKIO ; TAKAHASHI SHUJI ; SANKYO CO LTD ; SANKIO KOMPANI LIMITED ; SANKYO CO LTD TOKIO TOKYO JP ; SANKYO CO LTD JP ; DAIICHI SANKYO CO LTD ; FUJIMOTO KATSUMI ; HIRAI KOICHI ; ISHII AKIRA ; IWANO YUJI

Inventor(s): (std): AKIO TORIKATA ; AKIRA ISIJ ; AKIRO ISIJ ; ESIKHARA SAKAJDA ; ESIKHARU SAKAJDA ; FUJIMOTO KATSUI ; FUJIMOTO MASAHICO ; FUSIMOTO KATSUMI ; HIDEYUKI SHIOZAWA ; HIDEYUKI SHIOZAWA C O SANKYO C ; HIRAI KOICHI ; HIRAI KOICHI C O SANKYO COMPAN ; ISHII AKIRA ; ISHII AKIRA C O SANKYO COMPANY ; IWANO YUJI ; IWANO YUJI C O SANKYO COMPANY ; FUJIMOTO KATSUMI ; FUJIMOTO KATSUMI C O SANKYO CO ; JUDZI IVANO ; KAGASAKI TAKESHI ; KAGASAKI TAKESHI C O SANKYO CO ; KANEO OGAWA ; KATSUMI FUDZIMOTO ; KENTARO KODAMA ; KHIDEJUKI SIOZAVA ; KHIDEYUKI SIOZAVA ; KODAMA KENTARO ; KODAMA KENTARO C O SANKYO COMP ; OGAWA KANEO ; OGAWA KANEO C O SANKYO COMPANY ; SAKAIDA YOSHIKI ; SAKAIDA YOSHIHARU ; SAKAIDA YOSHIHARU C O SANKYO C ; KOJTI KHIRAJ ; SHIOZAWA HIDEYUKI ; SHUJI TAKAHASHI ; SHUJI TAKAHASHI C O SANKYO COM ; SUDZI TAKAKHASI ; TAKAHASHI HIDEJI ; TAKAHASHI SHUJI ; TAKASHI SHUJI ; TORIGATA AKIO ; TORIKATA AKIO ; TORIKATA AKIO C O SANKYO COMPA ; TAKESI KAGASAKI ; YUDZI IVANO

Inventor(s): YUJI IWANO ; TAKESI KAGASAKI[JP] ; TORIKATA AKIO C O SANKYO COMPANY LTD ; TORIKATA AKIO JP ; YOSHIHARU SAKAIDA ; TAKASHI SHUJI JP ; TAKESHI KAGASAKI ; TAKESI KAGASAK ; SUDZI TAKAKHASI[JP] ; SHUJI TAKAHASHI C O SANKYO COMPANY LTD ; SHIOZAWA HIDEYUKI JP ; KOJTI KHIRAJ[JP] ; SAKAIDA YOSHIHARU C O SANKYO CY LTD ; SAKAIDA YOSHIHARU JP ; OGAWA KANEO C O SANKYO COMPANY LTD ; OGAWA KANEO JP ; KODAMA KENTARO C O SANKYO COMPANY LTD ; KODAMA KENTARO JP ; KOICHI HIRAI ; KHIDEJUKI SIOZAVA[JP] ; KENTARO KODAMA[JP] ; KATSUMI FUDZIMOTO[JP] ; KATSUMI FUJIMOTO ; KANEO OGAWA[JP] ; KANEO OGAWA ; KAGASAKI TAKESHI C O SANKYO COMPANY LTD ; KAGASAKI TAKESHI JP ; JUDZI IVANO[JP] ; FUJIMOTO KATSUMI C O SANKYO COMPANY LTD ; IWANO YUJI C O SANKYO COMPANY LTD ; IWANO YUJI JP ; ISHII AKIRA C O SANKYO COMPANY LTD ; ISHII AKIRA JP ; HIRAI KOICHI C O SANKYO COMPANY LTD ; HIRAI KOICHI JP ; HIDEYUKI SHIOZAWA C O SANKYO COMPANY LTD ; FUJIMOTO KATSUI JP ; ESIKHARU SAKAJDA[JP] ; ESIKHARA SAKAJDA[JP] ; AKIRO ISIJ[JP] ; AKIRA ISIJ[JP] ; AKIO TORIKATA[JP] ; AKIRA ISHII

Designated states: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE

Title: Condensed-ring thiophene derivatives, their production and use

Abstract: Source: US5817819A PCT No. PCT/JP95/00728 Sec. 371 Date Jun. 16, 1995 Sec. 102(e) Date Jun. 16, 1995 PCT Filed Apr. 14, 1995 PCT Pub. No. WO95/28405 PCT Pub. Date Oct. 26, 1995A gonadotropin-releasing hormone antagonistic composition, which comprises an optionally substituted condensed-bicyclic compound consisting of a homo or hetero 5 to 7 membered ring and a homo or hetero 5 to 7 membered ring is effective as a prophylactic or therapeutic agent for the prevention or treatment of several hormone dependent diseases, for example, a sex hormone dependent cancer (e.g. prostatic cancer, cancer of uterine cervix, breast cancer, pituitary adenoma), benign prostatic hypertrophy, myoma of the uterus, endometriosis, precocious puberty, amenorrhea, premenstrual syndrome, polycystic ovary syndrome and acne vulgaris; is effective as a fertility controlling agent in both sexes (e.g. a pregnancy controlling agent and a menstrual cycle controlling agent); can be used as a contraceptive of male or female, as an ovulation-inducing agent of female; can be used as an infertility treating agent by using a rebound effect owing to a stoppage of administration thereof; is useful as modulating estrous cycles in animals in the field of animal husbandry, as an agent for improving the quality of edible meat or promoting the growth of animals; is useful as an agent of spawning promotion in fish.

Classifications:

International (IPC 8-9): A61K31/38 A61K31/43 A61K31/435 A61K31/4365 A61K31/44 A61K31/4406 A61K31/445 A61K31/4453 A61K31/47 A61K31/4725 A61K31/475 A61K31/49 A61K31/495 A61K31/496 A61K31/50 A61K31/505 A61K31/53 A61K31/535 A61K31/54 A61K31/55 A61P13/02 A61P13/08 A61P15/00 A61P15/18 A61P25/00 A61P35/00 A61P43/00 A61P5/00 A61P5/04 A61P5/24 C07D239/00 C07D333/00 C07D401/06 C07D405/04 C07D495/04 C07D495/06 C07D513/02 C07D513/04 C07D519/00 C07F5/02 C07F7/10 C07F9/6561 (Advanced/Invention); A61K31/505 C07D221/00 C07D239/00 C07D333/00 C07D495/04 (Advanced/Non-invention); A61K31/38 A61K31/43 A61K31/435 A61K31/4353 A61K31/44 A61K31/4406 A61K31/445 A61K31/4453 A61K31/47 A61K31/472 A61K31/475 A61K31/49 A61K31/495 A61K31/496 A61K31/50 A61K31/505 A61K31/53 A61K31/535 A61K31/54 A61K31/55 A61P13/00 A61P15/00 A61P25/00 A61P35/00 A61P43/00 C07D239/00 C07D333/00 C07D401/00 C07D405/00 C07D495/00 C07D513/00 C07D519/00 (Core/Invention); C07D221/00 C07D239/00 C07D333/00 (Core/Non-invention); A61K (Subclass/Invention)

International (IPC 1-7):

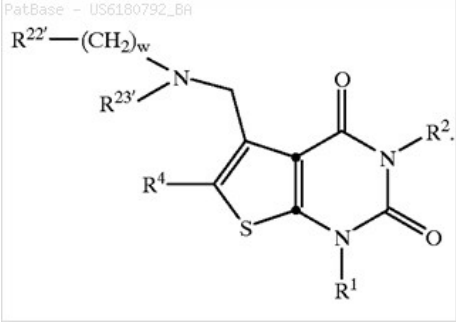
A61D5/04 A61K A61K3/504 A61K31/38 A61K31/395 A61K31/435 A61K31/4365 A61K31/437 A61K31/44 A61K31/445 A61K31/47 A61K31/475 A61K31/495 A61K31/496 A61K31/505 A61K31/53 A61K31/54 A61K31/55 A61P5/24 C07D221/00 C07D239/00 C07D333/00 C07D401/06 C07D405/04 C07D419/00 C07D494/04 C07D495/04 C07D495/06 C07D513/02 C07D513/04 C07D519/00 C07F5/02 C07F7/10 C07F9/547 C07F9/6561 **CPC:** C07D495/04

European: C07D495/04

US: 514/226.8 514/228.2 514/233.8 514/234.2 514/241 514/242 514/249 514/252.04 514/252.1 514/252.16 514/253.04 514/256 514/260.1 514/263.2 514/263.22 514/266.21 514/297 514/298 514/301 544/127 544/238 544/257 544/264 544/278 544/284 544/333 544/353 544/362 544/61 546/102 546/108 546/114

Family:

Publication number	Publication date	Application number	Application date
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CN1146206 A	19970326	CN19951092628	19950414
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WO9624597 A1	19960815	WO1996JP00263	19960207	

Priority:

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Probable Assignee: TAKEDA CHEMICAL INDUSTRIES LIMITED

- Assignee(s):** (std): CHOH NOBUO ; FURUYA SHUICHI ; HINUMA SHUJI ; KATO KOICHI ; TAKEDA CHEMICAL IND LTD ; TAKEDA CHEMICAL INDUSTRIES ; TAKEDA CHEMICAL INDUSTRIES LIMITED ; TAKEDA KEMIKAL INDASTRIZ LTD
- Assignee(s):** TAKEDA PHARMACEUTICAL COMPANY LIMITED ; CHO NOBUO ; TAKEDA PHARMACEUTICAL CO LTD ; TAKEDA CHEM IND LTD ; TAKEDA CHEMICAL IND
- Inventor(s):** (std): CHOH N ; CHOH NOBUO ; FURUYA S ; FURUYA SHIUCHI ; FURUYA SHUICHI ; HINUMA KUNIIJI ; HINUMA SHUJ ; HINUMA SHUJI ; KATO K ; KATO KOICHI ; KINUMA S ; CHO NOBUO ; KOICHI KATO ; KOITI KATO ; NOBUO CHOH ; NOBUO TOKH ; SHIUCHI FURUYA ; SHUICHI FURUYA ; SHUJI HINUMA ; SUDZI KHINUMA ; SUITI FURUJA
- Inventor(s):** Suichi ; Shuichi ; Nobuo ; Choh ; Koichi ; Kato ; etc. ; Furuya
- Designated states:** AL AM AT AU AZ BB BE BF BG BJ BR BY CA CF CG CH CI CM CN CZ DE DK EE ES FI FR GA GB GE GN GR HU IE IS IT KE KG KR KZ LI LK LR LS LT LU LV MC MD MG MK ML MN MR MW MX NE NL NO NZ PL PT RO RU SD SE SG SI SK SN SZ TD TG TJ TM TR TT UA UG US UZ VN

Title: Conjugated terthiophene and furan compounds with photoenhanced biocidal properties

Abstract: Source: US5869051A PCT No. PCT/EP95/01938 Sec. 371 Date Nov. 22, 1996 Sec. 102(e) Date Nov. 22, 1996 PCT Filed May 22, 1995 PCT Pub. No. WO95/32001 PCT Pub. Date Nov. 30, 1995Conjugates of a carrier molecule and an organic molecule producing singlet oxygen after irradiation are useful in diagnostic and therapeutic applications. The organic molecule is a terthienyl or terfuranyl compound derivatized to react with amino, thiol, or saccharide groups of the carrier molecule. Suitable carrier molecules include antibodies, peptides, haptamers, sugars, and other analogous molecules which direct the organic molecule to a biological target.

Classifications:
International (IPC 8-9): A61K41/00 A61K47/48 C07D333/20 C07D333/22 C07D333/24 C07D409/14 C07D495/04 (Advanced/Invention)
International (IPC 1-7): A61K39/395 A61K39/40 A61K41/00 A61K41/00 A61K47/48 C07H11/00 C07K16/00
CPC: A61K41/0057 A61K47/48007 C07D333/20 C07D333/22 C07D333/24 C07D409/14 C07D495/04
European: A61K41/00W A61K47/48H C07D333/20 C07D333/22 C07D333/24 C07D409/14 C07D409/14R C07D495/04
US: 424/1.53 424/179.1 424/181.1 435/7.21 530/391.7 536/115 536/118 540/1

Family:

Publication number	Publication date	Application number	Application date	
AT191852 E	20000515	AT19950920073T	19950522	
AU199525662 A1	19951218	AU19950025662	19950522	
CA2191195 AA	19961125	CA19952191195	19950522	
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EP0760679 A1	19970312	EP19950920073	19950522	
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ES2147288 T3	20000901	ES19950920073T	19950522	
ITFI940095 A0	19940523	IT1994FI00095	19940523	
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US5869051 A	19990209	US19960750021	19961122	
WO9532001 A1	19951130	WO1995EP01938	19950522	

Priority:
IT1994FI00095 19940523 WO1995EP01938 19950522

Probable Assignee: NERI GIOVANNI

Assignee(s): (std): GIOVANNI NERI ; MOLteni AND C ; NERI GIOVANNI ; MOLteni AND C DEI ALITT FLLI ; RONCUCCI GABRIO ; MOLENTI AND C DEI FRATELLI ALITT ; MOLteni AND C DEI FRATELLI ALITT

Assignee(s): L MOLteni AND C DEI FRATELLI ALITT SOCIETA'... ; L MOLteni AND C DEI FRATELLI ALITT SOCIETA DI ES ; L MOLteni AND C DEI FRATELLI ALITT SOCIETA DI ESERCIZIO SOCIETA PER AZIONI ; L MOLteni AND C DEI FRATELLI ALITT SOCIETA DI ESERCIZIO SOCIETA ; L MOLteni AND C DEI FRATELLI ALITT SOCIETA DI ESERCIZIO S P A SCANDICCI ; L MOLteni AND C DEI F LLI ALITT SOCIETA DI ESERCIZIO ; MOLENTI AND C DEI ALITT FLLI ; L MOLteni AND C DEI FLLI ; L MOLENTI AND C DEI FRATELLI ALITT SOCIETA DI ESERCIZIO SOCIETA PER AZIONI ; L MOLteni AND C DEI ALITT SOCIETA DI ES FLLI ; L MOLteni AND C DEI ALITT SOCIETA DI ESERCIZIO FL ; L MOLteni AND C DEI ALITT SOCIETA DI ESERCIZIO SO ; L MOLteni AND C DEI ALITT SOCIETA DI ESERCIZIO SOCIETA PER AZIONI FLLI ; L MOLteni AND C DEI ALLITT SOCIETA DI ESERCIZIO S

Inventor(s): (std): RONCUCCI GABRIO ; NERI GIOVANNI

Inventor(s): GIOVANNI NERI ; GABRIO RONCUCCI

Designated states: AM AT AU BB BE BF BG BJ BR BY CA CF CG CH CI CM CN CZ DE DK EE ES FI FR GA GB GE GN GR HU IE IS IT JP KE KG KP KR KZ LI LK LR LT LU LV MC MD MG ML MN MR MW MX NE NL NO NZ PL PT RO RU SD SE SG SI SK SN SZ TD TG TJ TM TT UA UG US UZ VN

Title: Heterocyclic compounds with **antibacterial** and antimycotic properties

Abstract: Source: US6316476B The invention is drawn to novel antibiotics, XENORXIDES of formula shown below, wherein R₁, R₂=hydrogen, substituted or unsubstituted alkyl, cycloalkyl, acyl, aryl, aralkyl, or heterocyclyl group; R₃=hydrogen, alkyl cycloalkyl, aralkyl or aryl group, produced by bacterial symbiont *Xenorhabdus bovienii* and/or other *Xenorhabdus* species, and/or by oxidation of the corresponding dithiopyrrolone derivatives with oxygen and *Xenorhabdus* species, and/or its cell-free filtrate, the additional salts thereof, the compositions thereof and their use as medicaments and/or agrochemicals, particularly in the treatment of infectious diseases involving microorganisms susceptible to them, including drug-resistant *Staphylococcus*.

Classifications:

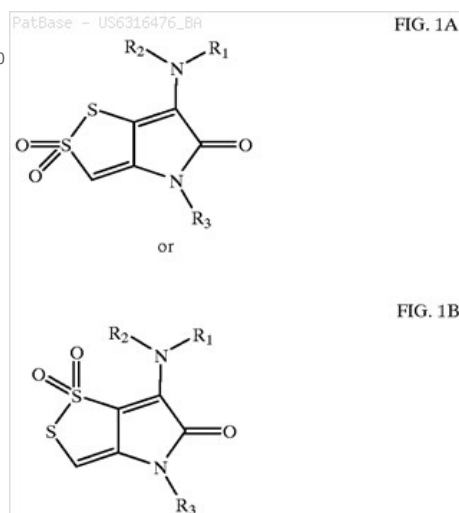
International (IPC 8-9): A61K31/40 C07D495/04 C12P17/18 (Advanced/Invention)

International (IPC 1-7): A01N43/82 A61K31/40 C07D209/00 C07D285/01 C07D339/00 C07D495/04 C12P17/18

CPC: C07D495/04 C12P17/185

European: C07D495/04 C12P17/18D

US: 435/119 514/360 548/123



Family:

Publication number	Publication date	Application number	Application date
AU199652647 A1	19961030	AU19960052647	19960410
AU752376 B2	20020919	AU19960052647	19960410
CA2217957 AA	19971009	CA19962217957	19960410
US6316476 BA	20011113	US19960685211	19960723
WO9632396 A1	19961017	WO1996CA00217	19960410

Priority:

US19950420307 19950411 WO1996CA00217 19960410 US19960685211 19960723

Probable Assignee: WELICHEM BIOTECH INC

Assignee(s): (std): CHEN GENHUI ; GENHUI CHEN ; JIANXIONG LI ; JOHN MALCOLM WEBSTER ; LI JIANXIONG ; WEBSTER JOHN MALCOLM ; WELICHEM BIOTECH INC

Assignee(s): WELICHEM BIOTECH INC SUITE 316 WAYBURNE DRI VEB

Inventor(s): (std): CHEN GENHUI ; LI JIANXIONG ; WEBSTER JOHN M ; WEBSTER JOHN MALCOLM

Inventor(s): GENHUI CHEN ; JIANXIONG LI ; JOHN MALCOLM WEBSTER

Designated states: AT AU BE BF BG BJ BR BY CA CF CG CH CI CM CN CZ DE DK ES FI FR GA GB GN GR HU IE IT JP KE KP KR LS LU MC ML MR MW MX NE NL NO NZ PL PT RO RU SD SE SG SI SK SN SZ TD TG TJ TM UA UG US UZ VN

Title: Amide derivatives

Abstract: Source: US6166016A PCT No. PCT/JP97/01875 Sec. 371 Date Dec. 2, 1998 Sec. 102(e) Date Dec. 2, 1998 PCT Filed Jun. 2, 1997 PCT Pub. No. WO97/46560 PCT Pub. Date Nov. 12, 1997 The invention provides amide derivatives which are useful as analgesics, anti-inflammatory agents, antimicrobial drugs, hypoglycemic agents, hypolipidemic agents, antihypertensive agents, anti-cancer agents, etc., the derivatives being represented by the formula wherein ring A represents a benzene ring, a naphthalene ring, a pyridine ring or a furan ring; R⁴ represents a heterocyclic group selected from the group consisting of a lower alkyl-substituted thieno[3,2-d]pyrimidin-4-yl group, an optionally substituted pyrazolo[1,5-a]-1,3,5-triazin-4-yl group, a pyrazolo[3,4-d]pyrimidin-4-yl group substituted at the 6-position and a purin-6-yl group substituted at the 2-position; and R⁵ represents a hydrogen atom or a group represented by

Classifications:

International (IPC 8-9): A61K31/165 A61K31/505 A61K31/519 A61K31/52 A61K31/53 A61P25/04 A61P25/06 C07C233/11 C07D473/00 C07D473/34 C07D487/04

C07D495/04 (Advanced/Invention);

A61K31/505 A61P29/00 A61P3/06 A61P3/10 A61P31/04 A61P35/00

C07D473/00 (Advanced/Non-invention)

International (IPC 1-7): A61K31/165 A61K31/166 A61K31/505 A61K31/52 A61K31/53

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C07D495/04

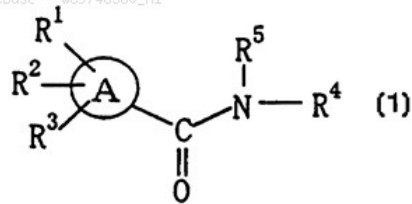
CPC: C07D473/34 C07D487/04 C07D495/04

European: C07D473/34 C07D487/04 C07D495/04

US: 514/245 514/246 514/260.1 514/262.1 514/263.1 544/211 544/262 544/277

544/278

PatBase - W09746560_r1

**Family:**

Publication number	Publication date	Application number	Application date
AT228518 E	20021215	AT19970924299T	19970602
AU199729778 A1	19980105	AU19970029778	19970602
AU716633 B2	20000302	AU19970029778	19970602
CA2257222 AA	19981204	CA19972257222	19970602
CA2257222 C	20020820	CA19972257222	19970602
CN1066448 C	20010530	CN19971095345	19970602
CN1221419 A	19990630	CN19971095345	19970602
DE69717453 D1	20030109	DE19976017453	19970602
DE69717453 T2	20030710	DE19976017453T	19970602
EP0915093 A1	19990512	EP19970924299	19970602
EP0915093 A4	19990818	EP19970924299	19970602
EP0915093 B1	20021127	EP19970924299	19970602
JP3870298 B2	20070117	JP19980500408T	19970602
KR20000016395 A	20000325	KR19987009969	19981205
TW470736 B	20020101	TW19970107762	19970606
US6166016 A	20001226	US19980194727	19981202
WO9746560 A1	19971211	WO1997JP01875	19970602

Priority:

JP19960144099 19960606 JP19970073116 19970326 WO1997JP01875 19970602

Probable Assignee: OTSUKA PHARMACEUTICAL FACTORY INC

Assignee(s): (std): IWAMOTO TAKESHI ; OKAMURA TAKASHI ; OTSUKA PHARMA CO LTD ; SHIBUTANI TADAO ; SHOJI YASUO ; YASUDA TSUNEO

Assignee(s): OTSUKA PHARMACEUTICAL CO ; OTSUKA PHARMACEUTICAL CO LTD ; OTSUKA PHARMACEUTICAL FACTORY INC

Inventor(s): (std): KOMATSUSHIMA SHI ; MINAMIHAMA MUYA CHO ; NAOHIRO SHIBUTANI ; NARUTO SHI ; OKAMURA TAKASHI ; SHIBUTANI TADAO ; SHOJI ; SHOJI YASUO ; TADAO SHIBUTANI ; TAKASHI OKAMURA ; IWAMOTO TAKESHI ; YASUDA TSUNEO ; YASUO ; YASUO SHOJI

Inventor(s): IWAMOTO TAKESHI KENTOPARESU TOKUSHIM ; TAKESHI IWAMOTO ; TSUNEO YASUDA ; OKAMURA TAKASHI EDITAUN GOMAIHAMA D ; SHIBUTANI NAOHIRO

Designated states: AT AU BE CA CH CN DE DK ES FI FR GB GR IE IT JP KR LI LU MC NL PT SE US

Title: Quinoline and naphthyridine carboxylic acid **antibacterials**

Abstract: Source: US2002049223A Compounds having formula (I) or pharmaceutically acceptable salts or prodrugs thereof, are useful as **antibacterial** agents.

Classifications:

International (IPC 8-9): A61K31/4375 A61K31/4436 A61K31/444 A61K31/4725 A61K31/496 A61K31/542 A61P31/04 A61P43/00 C07B61/00 C07D405/04 C07D409/04 C07D409/14 C07D413/14 C07D417/14 C07D471/04 C07D495/04 C07D513/04 C07D519/00 (Advanced/Invention); A61K31/496 A61K31/542 A61P43/00 C07B61/00 (Advanced/Non-invention); A61K31/4353 A61K31/4427 A61K31/472 A61K31/496 A61K31/542 A61P31/00 A61P43/00 C07B61/00 C07D405/00 C07D409/00 C07D413/00 C07D417/00 C07D471/00 C07D495/00 C07D513/00 C07D519/00 (Core/Invention); A61K A61P C07D (Subclass/Invention)

International (IPC 1-7): A61K A61K31/381 A61K31/423 A61K31/428 A61K31/4375 A61K31/4436 A61K31/444 A61K31/47 A61K31/4709 A61K31/4725 A61K31/4745 A61K31/496 A61K31/542 A61P A61P31/04 A61P43/00 C0741/02 C07B61/00 C07D221/00 C07D279/00 C07D333/00 C07D335/00 C07D405/04 C07D405/10 C07D409/00 C07D409/04 C07D409/10 C07D409/14 C07D413/04 C07D413/14 C07D417/04 C07D417/10 C07D417/14 C07D471/02 C07D471/04 C07D487/04 C07D495/04 C07D495/10 C07D513/04 C07D519/00

CPC: C07D405/04 C07D409/04 C07D409/14 C07D413/14 C07D417/14 C07D471/04 C07D495/04 C07D513/04

European: C07D405/04 C07D409/04 C07D409/14 C07D413/14 C07D417/14 C07D471/04 C07D495/04 C07D513/04 C07D519/00

US: 514/300 514/312 514/312S 546/123 546/123S 546/156 546/156S

Family:

Publication number	Publication date	Application number	Application date	
AR030537 AA	20030827	AR2000P105819	20001103	
AU200114689 A5	20010514	AU20010014689	20001106	
BG106679 A	20030131	BG20020106679	20020509	
BRPI0010728 A	20040217	BR2000PI10728	20001106	
CZ20021531 A3	20020911	CZ20020001531	20001106	
EP1226146 A2	20020731	EP20000976992	20001106	
IL148738 A0	20020912	IL20000148738	20001106	
JP2003524633 T2	20030819	JP20010535357T	20001106	
MXPA02004474 A1	20021107	MX2002PA04474	20020503	
NO20022156 A	20020704	NO20020002156	20020506	
NO20022156 A0	20020506	NO20020002156	20020506	
US2002049223 AA	20020425	US20010850664	20010507	
WO0132655 A2	20010510	WO2000US30551	20001106	
WO0132655 A3	20020124	WO2000US30551	20001106	
ZA200202187 A	20041117	ZA20020002187	20020318	

Priority:

US19990163920P 19991105

US19990435297 19991105

US20000705332 20001103

WO2000US30551 20001106

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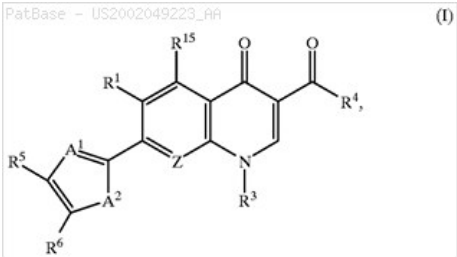
Probable Assignee: ABBOTT LABORATORIES

Assignee(s): (std): ABBOTT LAB ; ABBOTT LABORATORIES ; ANDERSON DAVID D ; COOPER CURT S ; DINGES JURGEN ; DONNER PAMELA L ; ELMORE STEVEN W ; GREEN BRIAN E ; SCHULTZ COLLEEN C ; HUTCHINSON DOUGLAS K ; LYNCH LINDA M ; PRATT JOHN K ; XIE QINGHUA

Inventor(s): (std): ANDERSON DAVID D ; BRIAN E GREEN ; COLLEEN C SCHULTZ ; COOPER CURT S ; CURT S COOPER ; DAVID D ANDERSON ; DINGES JURGEN ; DONNER PAMELA L ; DOUGLAS K HUTCHINSON ; ELMORE STEVEN W ; GREEN BRIAN E ; HUTCHINSON DOUGLAS K ; JURGEN DINGES ; LINDA M LYNCH ; LYNCH LINDA M ; PAMELA L DONNER ; PRATT JOHN K ; QINGHUA XIE ; SCHULTZ COLLEEN C ; STEVEN W ELMORE ; XIE QINGHUA ; XIE QINGHUA

Inventor(s): QUINGHUA XIE

Designated states: AE AG AL AM AT AU AZ BA BB BE BF BG BJ BR BY BZ CA CF CG CH CI CM CN CR CU CY CZ DE DK DM DZ EE ES FI FR GA GB GD GE GH GM GN GR GW HR HU ID IE IL IN IS IT JP KE KG KP KR KZ LC LI LK LR LS LT LU LV MA MC MD MG MK ML MN MR MW MX MZ NE NL NO NZ PL PT RO RU SD SE SG SI SK SL SN SZ TD TG TJ TM TR TT TZ UA UG UZ VN YU ZA ZW



Title: **ANTIBACTERIAL** AGENTS

Abstract: Source: US2003114666A The present invention provides compounds of formula (I): wherein R1-R6 and J and K have any of the values defined in the specification, and pharmaceutically acceptable salt thereof, that are useful as **antibacterial** agents. Also disclosed are pharmaceutical compositions comprising one or more compounds of formula I, processes for preparing compounds of formula I, and intermediates useful for preparing compounds of formula I.

Classifications:

International (IPC 8-9): A61K31/517 A61K31/519 A61K31/5383 A61P31/04 C07D221/00 C07D235/00 C07D239/95 C07D239/96 C07D307/04 C07D401/04 C07D403/04 C07D409/04 C07D413/04 C07D413/14 C07D471/04 C07D471/06 C07D487/04 C07D487/06 C07D491/04 C07D491/048 C07D493/10 C07D495/04 C07D498/06 C07D498/08 C07F9/6561 (Advanced/Invention); C07D401/00 C07D403/00 C07D409/00 C07D413/00 C07D471/00 C07D487/00 C07D491/00 C07D493/00 C07D495/00 C07F9/00 (Core/Invention)
International (IPC 1-7): A61K31/517 A61K31/519 A61K31/5383 A61P31/04 C0743/02 C07D221/00 C07D235/00 C07D239/72 C07D239/95 C07D239/96 C07D307/04 C07D403/04 C07D409/04 C07D409/04 C07D413/04 C07D413/04 C07D471/04 C07D471/04 C07D471/06 C07D471/06 C07D487/02 C07D487/04 C07D487/04 C07D487/06 C07D487/06 C07D491/04 C07D491/04 C07D491/048 C07D495/04 C07D498/06 C07D498/08

CPC: C07D401/04 C07D403/04 C07D409/04 C07D413/14 C07D471/04 C07D487/04 C07D487/06 C07D491/04 C07D493/10 C07D495/04 C07F9/6561

European: C07D401/04 C07D403/04 C07D409/04 C07D413/14 C07D471/04 C07D487/04 C07D487/06 C07D491/04 C07D493/10 C07D495/04 C07F9/6561

US: 540/600 540/600P 544/256 544/256S 544/279 544/279S 544/285 544/285S

Family:

Publication number	Publication date	Application number	Application date
AU2002302894 AA	20030102	AU20020302894	20020513
BRPI0210028 A	20040622	BR2002PI10028	20020513
CA2446963 AA	20031110	CA20022446963	20020513
DOP20020422 A	20021230	DO20020000422	20020619
EP1401830 A2	20040331	EP20020730582	20020513
GT200200104 A	20030211	GT20020000104	20020531
HN2002000150 A	20020913	HN20020000150	20020618
JP2005501021 T2	20050113	JP20030506266T	20020513
MXPA03009894 A1	20040217	MX2003PA09894	20031028
PA8548401 A1	20030514	PA20020085484	20020619
PE02722003 A1	20030321	PE20020000523	20020618
SV2003001089 A	20030318	SV20020001089	20020618
US2003114666 AA	20030619	US20020174302	20020618
WO02102793 A2	20021227	WO2002IB01768	20020513
WO02102793 A3	20030410	WO2002IB01768	20020513

Priority:

US20010299249P 20010619 US20020369332P 20020403 US20020174302 20020618
WO2002IB01768 20020513

Probable Assignee: WARNER LAMBERT CO

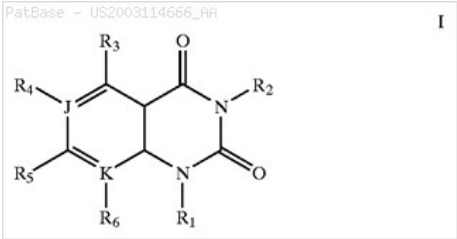
Assignee(s): (std): ELLSWORTH EDMUND LEE ; KERSCHEN JAMES ALAN ; WARNER LAMBERT CO ; SHOWALTER HOWARD DANIEL HOLLIS ; POWELL SHARON ANNE ; STIER MICHAEL ANDREW ; TRAN TUAN PHONG ; SANCHEZ JOSEPH PETER ; WARNER LAMBERT CO LLC

Assignee(s): WARNER LAMBERT COMPANY LLC ; WARNER LAMBERT COMPANY ; WARNER LAMBERT COMPANYLLC

Inventor(s): (std): ELISWORTH EDMUND LEE ; ELLSORTH EDMUND ; ELLSWORTH EDMUN LEE ; ELLSWORTH EDMUND LEE ; HOLLIS HOWARD DANIEL ; HOLLIS SHOWALTER HOWARD DANIEL ; KERSCHEN JAMES ALAN ; KRZYZANIAK JOSEPH FRANCIS ; LEE ELLSWORTH EDMUND ; POWELL SHARON ALAN ; POWELL SHARON ANNE ; SANCHEZ JOSEPH PETER ; SHOWALTER HOWARD DANIEL H ; SHOWALTER HOWARD DANIEL HOLLIS ; SHOWALTER HOWARD DANIEL HOLLIS ; STIER MICHAEL ANDREW ; TRAN TUAN PHONG ; TUAN PHONG TRAN

Inventor(s): EDMUN LEE ELLSWORTH ; EDMUND LEE ELLSWORTH ; EDMUND LEE ELLSWORTH ; SHARON ANNE POWELL ; MICHAEL ANDREW STIER ; HOWARD DANIEL HOLLIS ; HOWARD DANIEL HOLLIS SHOWALTER ; HOWARD DANIEL HOLLIS SHOWALTER ; JAMES ALAN KERSCHEN ; JOSEPH FRANCIS KRZYZANIAK ; JOSEPH PETER SANCHEZ

Designated states: AE AG AL AM AT AU AZ BA BB BE BF BG BJ BR BY BZ CA CF CG CH CI CM CN CO CR CU CY CZ DE DK DM DZ EC EE ES FI FR GA GB GD GE GH GM GN GQ GR GW HR HU ID IE IL IN IS IT JP KE KG KP KR KZ LC LI LK LR LS LT LU LV MA MC MD MG MK ML MN MR MW MX MZ NE NL NO NZ OM PH PL PT RO RU SD SE SG SI SK SL SN SZ TD TG TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW



Title: **ANTIBACTERIAL** AGENT HAVING THIOPHENE SKELETON

Abstract: A compound having a thiophene skeleton which has excellent **antibacterial** activity against gram-positive bacteria and resistant gram-positive bacteria. The compound having a thiophene skeleton is represented by the following formula: (I) wherein X is =CH-R8, =C(R8)2, =CO, =C=N-R11, -O-, -S-, or =N-R11; R1, R2, R3, R4, and R5 each independently is hydrogen, halogeno, amino, nitro, lower alkyl, or lower alkoxy; R6, R7, R8, and R9 each independently is hydrogen, hydroxy, lower alkyl, lower alkoxy, or phenyl, provided that when two R6, R7, R8, or R9 substituents are present on the same carbon atom, these substituents may be the same or different; R10 is halogenated lower alkyl; R11 is hydrogen, hydroxy, lower alkyl, lower alkoxy, alkanoyl, benzoyl, (lower alkyloxy)carbonyl, (lower alkyl)sulfonyl, benzenesulfonyl, or benzyloxycarbonyl; and n is 1 or 2.

Classifications:

International (IPC 8-9): A61K31/381 A61K31/382 A61K31/4365 A61P31/04 C07D333/68 C07D495/04 (Advanced/Invention)

International (IPC 1-7): A61K31/381 A61K31/382 A61K31/4365 A61P31/04 C07D333/68 C07D495/04

CPC: A61K31/381 A61K31/4365 C07D333/68 C07D495/04

European: A61K31/381 A61K31/4365 C07D333/68 C07D495/04



Family:

Publication number	Publication date	Application number	Application date
JP2002308870 A2	20021023	JP20010113137	20010411
WO04031169 A1	20040415	WO2002JP10366	20021004

Priority:

JP20010113137 20010411 WO2002JP10366 20021004

Probable Assignee: RRF KENKYUSHO KK

Assignee(s): (std): HARA HIROTO ; IKESUE KOICHI ; MAEDA YUTAKA ; NAKASHIMA MIHOKO ; RRF KENKYUSHO KK ; RRF RES INC ; YOSHIDA TOSHIO ; YASUDA MINORU ; YOKOSE KAZUTERU

Assignee(s): RRF RESEARCH INC

Inventor(s): (std): HARA HIROTO ; IKESUE KOICHI ; MAEDA YUTAKA ; NAKAJIMA MIHOKO ; NAKASHIMA MIHOKO ; YASUDA MINORU ; YOKOSE KAZUTERU ; YOSHIDA TOSHIO

Designated states: AT BE BG CH CN CY CZ DE DK EE ES FI FR GB GR IE IT LU MC NL PT SE SK TR US

Title: Novel heterocyclic compounds, method for preparing same and use thereof as medicines, in particular as **antibacterial** agents

Abstract: Source: US2005245505A The invention relates to new heterocyclic compounds of general formula (I), and their salts with a base or an acid: The invention also relates to a process for the preparation of these compounds, as well as their use as medicaments, in particular as anti-bacterial agents.

Classifications:

International (IPC 8-9): A61K31/44 A61K31/47 A61K31/551 A61K31/675 A61P31/04 A61P43/00 C07D215/00 C07D215/38 C07D217/22 C07D217/26 C07D223/16 C07D243/04 C07D243/10 C07D401/06 C07D401/12 C07D471/04 C07D471/08 C07D471/18 C07D487/04 C07D491/04 C07D491/048 C07D491/18 C07D495/04 C07D495/18 C07D498/04 C07D498/18 C07D513/00 C07D513/02 C07D513/04 C07D513/18 C07F9/645 (Advanced/Invention)

International (IPC 1-7): A61K31/55 A61K31/551 A61K31/675 A61P31/04 C07D215/38 C07D217/22 C07D217/26 C07D223/14 C07D231/12 C07D233/64 C07D243/04 C07D243/10 C07D243/38 C07D249/04 C07D307/38 C07D401/12 C07D453/04 C07D471/04 C07D471/08 C07D471/08 C07D471/18 C07D487/04 C07D491/04 C07D491/048 C07D491/18 C07D495/04 C07D495/18 C07D498/04 C07D498/18 C07D513/04 C07D513/18 C07F9/645

CPC: C07D215/38 C07D217/22 C07D217/26 C07D471/04 C07D471/08 C07D491/04 C07D495/04 C07D513/04

European: C07D215/38 C07D217/22 C07D217/26 C07D471/04 C07D471/08 C07D471/18 C07D491/04 C07D491/18 C07D495/04 C07D495/18 C07D498/04 C07D498/18 C07D513/04 C07D513/18

US: 514/214.03 514/214.030P 514/292 514/293 514/305 514/305S 514/311 540/576 540/576S 540/593 546/114 546/134 546/134S 546/152 546/152S 546/82 546/83 546/84 548/153



Family:

Publication number	Publication date	Application number	Application date	
AR036091 AA	20040811	AR2002P102156	20020607	
AT359286 E	20070515	AT20020778894T	20020604	
AU2002345861 AA	20021223	AU20020345861	20020604	
CA2449830 AA	20031201	CA20022449830	20020604	
CA2449830 C	20121127	CA20022449830	20020604	
DE60219469 D1	20070524	DE20026019469	20020604	
DE60219469 T2	20071129	DE20026019469T	20020604	
DK1399444 T3	20070604	DK20020778894T	20020604	
EP1399444 A2	20040324	EP20020778894	20020604	
EP1399444 B1	20070411	EP20020778894	20020604	
EP1798231 A2	20070620	EP20070007308	20020604	
EP1798231 A3	20080227	EP20070007308	20020604	
ES2284938 T3	20071116	ES20020778894T	20020604	
FR2825705 A1	20021213	FR20010007520	20010608	
FR2825705 B1	20050520	FR20010007520	20010608	
IL158756 A0	20040512	IL20020158756	20020604	
JP2005518333 T2	20050623	JP20030503627T	20020604	
JP4509551 B2	20100721	JP20030503627T	20020604	
MXPA03011039 A1	20040319	MX2003PA11039	20031201	
PT1399444 T	20070531	PT20020778894T	20020604	
US2005245505 AA	20051103	US20040480019	20040414	
US2007299108 AA	20071227	US20070810981	20070607	
US7288549 BB	20071030	US20040480019	20040414	
US8148540 BB	20120403	US20070810981	20070607	
WO02100860 A2	20021219	WO2002FR01877	20020604	
WO02100860 A3	20031120	WO2002FR01877	20020604	

Priority:

FR20010007520 20010608	EP20020778894 20020604	US20020480019 20020604
US20040480019 20040414	US20070810981 20070607	WO2002FR01877 20020604

Probable Assignee: ASTRAZENECA

Assignee(s): (std): ASTRAZENECA ; ASZODI JOSEPH ; AVENTIS PHARMA S A ; AVENTIS PHARMA SA ; COLETTE PASCAL ; COLLETTE PASCAL ; LAMPILAS MAXIME ; MUSICKI BRANISLAV ; ROWLANDS DAVID ALAN ; MUSICKI BRANISLAY ; ROWLANDS DAVID ALAN ; NOVEXEL

Inventor(s): (std): ASZODI JOSEPH ; ASZODI JOSEF ; COLETTE PASCAL ; COLLETTE PASCAL ; MUSICKI BRANISLAV ; MUSICKI BRANISLAY ; JOSEPH ASZODI ; LAMPILAS MAXIME ; ROWLANDS DAVID A ; ROWLANDS DAVID ALAN

Inventor(s): MAXIME LAMPILAS ; PASCAL COLLETTE ; ROWLANDS DAVID ; DAVID ALAN ROWLANDS ; BRANISLAV MUSICKI

Agent(s): HIRSCH AND ASSOCIES; HEDMAN AND COSTIGAN PC; CHARLES A MUSERLIAN C O HEDMAN AND COSTIGAN; CHARLES A

Designated states: AE AG AL AM AT AU AZ BA BB BE BF BG BJ BR BY BZ CA CF CG CH CI CM CN CO CR CU CY CZ DE DK DM DZ EC EE ES FI FR GA GB GD GE GH GM GN GQ GR GW HR HU ID IE IL IN IS IT JP KE KG KP KR KZ LC LI LK LR LS LT LU LV MA MC MD MG MK ML MN MR MW MX MZ NE NL NO NZ OM PH PL PT RO RU SD SE SG SI SK SL SN SZ TD TG TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

Title: COMPOUNDS AND METHODS FOR THE TREATMENT OR PREVENTION OF FLAVIVIRUS INFECTIONS

Abstract: Source: US2004116509A The present invention provides novel compounds represented by formula I: or pharmaceutically acceptable salts thereof useful for treating flaviviridae viral infection.

Classifications:

International (IPC 8-9): A61K31/20 A61K31/341 A61K31/343 A61K31/35 A61K31/38 A61K31/381 A61K31/382 A61K31/4025 A61K31/4035 A61K31/404 A61K31/41 A61K31/4155 A61K31/42 A61K31/422 A61K31/426 A61K31/427 A61K31/433 A61K31/437 A61K31/438 A61K31/4436 A61K31/4535 A61K31/454 A61K31/4709 A61K31/4725 A61K31/496 A61K31/55 A61K31/7056 A61K38/13 A61K38/20 A61K38/21 A61K45/00 A61K45/06 A61P1/16 A61P31/12 A61P31/14 C07D211/00 C07D233/00 C07D333/00 C07D333/36 C07D333/38 C07D333/40 C07D333/42 C07D333/54 C07D333/62 C07D335/00 C07D409/00 C07D409/02 C07D409/04 C07D409/06 C07D409/10 C07D409/12 C07D409/14 C07D413/02 C07D413/04 C07D413/12 C07D417/04 C07D417/12 C07D417/14 C07D419/14 C07D471/10 C07D495/04 C07F7/10 (Advanced/Invention); A61P31/14 C07D211/00 C07D233/00 C07D333/40 (Advanced/Non-invention); A61K31/00 A61P31/00 C07D333/00 C07D409/00 C07D413/00 C07D417/00 C07D471/00 C07D495/00 (Core/Invention)

International (IPC 1-7): A61K31/20 A61K31/38 A61K31/381 A61K31/382 A61K31/4025 A61K31/4035 A61K31/404 A61K31/41 A61K31/4155 A61K31/42 A61K31/427 A61K31/433 A61K31/437 A61K31/44 A61K31/4436 A61K31/4535 A61K31/454 A61K31/4709 A61K31/4725 A61K31/496 A61K31/55 A61K45/00 A61P1/16 A61P31/00 A61P31/12 C07D211/00 C07D211/70 C07D233/00 C07D333/00 C07D333/36 C07D333/40 C07D333/62 C07D335/00 C07D401/00 C07D409/04 C07D409/12 C07D409/14 C07D413/04 C07D413/12 C07D417/04 C07D417/12 C07D417/14 C07D419/14 C07D471/10 C07D495/04

CPC: A61K31/20 A61K31/341 A61K31/343 A61K31/426 C07D333/40 A61K31/381 A61K45/06 C07D333/38 C07D409/04 C07D409/06 C07D409/10 C07D409/12 C07D409/14 C07D417/04 C07D417/12 C07D417/14 C07D419/14 C07D471/10 C07D495/04

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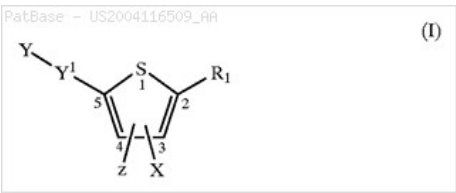
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Family:

Publication number	Publication date	Application number	Application date
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AT438637 E	20090815	AT20020742563T	20020611
AU2002344854 AA	20021223	AU20020344854	20020611
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WO02100851 A2	20021219	WO2002CA00876	20020611
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Priority:

US20010296731P 20010611	WO2002CA00876 20020611	US20020166031 20020611
EP20020742563 20020611	JP20030503618 20020611	AU20020344854 20020611



Probable Assignee: VERTEX PHARMACEUTICALS CANADA INC

Assignee(s): (std): BEDARD JEAN ; CHAN CHUN KONG LAVAL ; DAS SANJOY ; DAS SANJOY KUMAR ; NGUYEN BA NGHE ; SHIRE BIOCHEM INC ; SIDDIQUI MOHAMMAD A ; REDDY THUMKUNTA J ; PEREIRA OSWY Z ; REDDY THUMKUNTA JAGADEESWAR ; SIDDIQUI M ARSHAD ; VERTEX PHARMA ; SIDDIQUI MOHAMMAD ARSHAD ; WANG WUYI ; YANNOPOULOS CONSTANIN ; VIROCHEM PHARMA INC ; VIRUS CHEM PHARMA INC ; VERTEX PHARMACEUTICALS CANADA INC ; YANNOPOULOS CONSTANTIN ; YANNOPOULOS CONSTANTIN G

Assignee(s): VERTEX PHARMACEUTICALS (CANADA) INC ; VERTEX PHARMACEUTICALS INC ; SIDDIQUI M

Inventor(s): (std): ARSHAD SIDDIQUI M ; ARSHAD SIDDIQUI MOHAMMAD ; BA NGHE NGUYEN ; BEDARD JEAN ; CHAN CHUN ; CHAN CHUN KONG ; CHAN CHUN KONG LAVAL ; CHAN CHUNG KONG LAVAL ; CONSTANIN YANNOPOULOS ; CONSTANTIN YANNOPOULOS ; DAS SANJOY ; DAS SANJOY KUMAR ; JAGADEESWAR REDDY THUMKUNTA ; JEAN BEDARD ; KONG LAVAL CHAN CHUN ; KUMAR DAS SANJOY ; KUMAR SANJOY ; LAVAL CHAN CHUN KONG ; M ARSHAD SIDDIQUI ; NGHE NGUYEN BA ; NGUYEN BA NGHE ; PEREIRA OSWY ; PEREIRA OSWY Z ; PEREIRA OSYW Z ; REDDY THUMKUNTA ; REDDY THUMKUNTA J ; REDDY THUMKUNTA JAGADEESWAR ; SIDDIQUI ARSHAD M ; SIDDIQUI M ; SIDDIQUI M ARSHAD ; SIDDIQUI MOHAMMAD A ; SIDDIQUI MOHAMMAD ARSHAD ; SIDDIQUI MOHAMMED ARSHAD ; THUMKUNTA JAGADEESWAR REDDY ; WANG WAYI ; WANG WUYI ; WUYI WANG ; YANNOPOULOS CONSTANIN ; YANNOPOULOS CONSTANIN G ; YANNOPOULOS CONSTANTIN ; YANNOPOULOS CONSTANTIN G

Inventor(s): SIDDIQUI MOHAMMAD ; SANJOY KUMAR DAS ; OSWY Z PEREIRA ; CHUN KONG LAVAL CHAN

Agent(s): HOFFMANN EITLE; MILLEN WHITE ZELANO AND BRANIGAN PC; MILLEN WHITE ZELANO BRANIGAN PC; HONIGMAN MILLER SCHWARTZ AND COHN; KATHRYN D; JONATHAN P

Designated states: AE AG AL AM AT AU AZ BA BB BE BF BG BJ BR BY BZ CA CF CG CH CI CM CN CO CR CU CY CZ DE DK DM DZ EC EE ES FI FR GA GB GD GE GH GM GN GQ GR GW HR HU ID IE IL IN IS IT JP KE KG KP KR KZ LC LI LK LR LS LT LU LV MA MC MD MG MK ML MN MR MW MX MZ NE NL NO NZ OM PH PL PT RO RU SD SE SG SI SK SL SN SZ TD TG TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

Title: ISOQUINOLINE COMPOUNDS HAVING ANTIINFECTIVE ACTIVITY

Abstract: Source: US2003083268A Isoquinoline compounds having the formula where R1, R2, Y, m, n, and Z are as defined herein, bind to the minor groove of DNA and have antifungal and **antibacterial** activity.

Classifications:

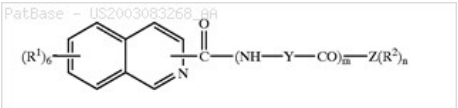
International (IPC 8-9): A61K31/38 A61K31/385 A61K31/40 A61K31/4025 A61K31/409 A61K31/427 A61K31/4453 A61K31/454 A61K31/47 A61K31/4725 A61K31/4741 A61K31/496 A61K31/497 A61K31/501 A61K31/506 A61K31/535 A61K31/5355 A61K31/5377 A61K31/54 A61K31/541 A61K31/55 A61K31/551 A61K38/04 A61K38/05 A61K38/06 A61P31/04 A61P33/02 C07D207/00 C07D207/42 C07D217/12 C07D217/26 C07D333/00 C07D333/56 C07D401/12 C07D401/14 C07D403/04 C07D403/14 C07D405/00 C07D409/04 C07D409/14 C07D413/00 C07D413/14 C07D417/04 C07D417/14 C07D491/056 C07D495/04 (Advanced/Invention); A61P31/12 A61P33/02 (Advanced/Non-invention)

International (IPC 1-7): A61K31/38 A61K31/385 A61K31/40 A61K31/4025 A61K31/418 A61K31/4184 A61K31/4196 A61K31/422 A61K31/427 A61K31/44 A61K31/453 A61K31/454 A61K31/47 A61K31/4725 A61K31/4741 A61K31/535 A61K31/5377 A61K31/541 A61K38/04 A61K38/05 A61P31/04 C0743/02 C0749/02 C07D207/30 C07D217/02 C07D217/12 C07D333/56 C07D401/14 C07D403/14 C07D405/00 C07D409/00 C07D409/14 C07D41/02 C07D411/00 C07D413/00 C07D413/02 C07D413/14 C07D417/02 C07D417/12 C07D417/14 C07D491/056 C07D495/04 C07K5/04 C12N C12Q

CPC: C07D401/14 C07D207/42 C07D217/26 C07D401/12 C07D403/04 C07D403/14 C07D409/04 C07D409/14 C07D413/14 C07D417/04 C07D417/14 C07D495/04

European: C07D207/42 C07D217/26 C07D401/12 C07D401/14 C07D401/14R C07D403/04 C07D403/14 C07D403/14R C07D409/04 C07D409/14 C07D409/14R C07D413/14 C07D417/04 C07D417/14 C07D417/14R C07D495/04

US: 514/17 514/18 514/19 514/2.4 514/2.400S 514/2.7 514/2.700S 514/217.09 514/217.090S 514/218 514/218S 514/227.5 514/227.500S 514/227.8 514/227.800P 514/231.8 514/232.5 514/232.500P 514/232.500S 514/232.8 514/233.5 514/233.500S 514/235.8 514/236.8 514/237.2 514/237.200P 514/237.200S 514/252.01 514/252.010S 514/254.07 514/254.070S 514/255.05 514/255.050S 514/256 514/256S 514/3.3 514/3.300S 514/307 514/320 514/326 514/326S 514/331 514/331S 514/337 514/337S 514/357 514/357S 514/371 514/372 514/372S 514/38 514/380 514/380S 514/383 514/383S 514/387 514/394 514/394S 514/397 514/397S 514/408 514/408S 514/422 514/422S 514/443 514/443S 514/444 514/534 514/534S 544/111 544/133 544/133P 544/134 544/137 544/138 544/139 544/140 544/141 546/146 546/146S 546/202 546/202S 546/336 546/336S 548/181 548/181S 548/233 548/233S 548/264.8 548/264.800S 548/304.7 548/305.4 548/305.400S 548/518 548/518S 548/525 548/525S 548/527 548/541 548/541P 548/567 548/567S 549/57 549/57P 549/59 560/41 560/41S 564/152 564/152S



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US20080020186 20080125

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WO2002US17952 20020606

US20040001237 20041130

US20080020256 20080125

Probable Assignee: GENESOF PHARMACEUTICALS INC

Assignee(s): (std): BAIRD ELDON E ; BURLI ROLAND W ; GENESOF INC ; GENESOF PHARMACEUTICALS INC ; JONES PETER ; KAIZERMAN JACOB A ; HU WENHAO ; TAYLOR MATTHEW J ; MCMINN DUSTIN L

Inventor(s): (std): BAIRD ELDON E ; BUERLI ROLAND W ; BURLI ROLAND W ; JONES PETER ; KAIZERMAN JACOB ; KAIZERMAN JACOB A ; MCMINN DUSTIN L ; HU WENHAO ; TAYLOR MATTHEW J

Inventor(s): BAIRD ELDON ; JACOB A KAIZERMAN ; PETER JONES ; ROLAND W BURLI ; TAYLOR MATTHEW ; MATTHEW J TAYLOR ; DUSTIN L MCMINN ; ELDON E BAIRD ; BURLI ROLAND

Agent(s): TOWNSEND AND TOWNSEND AND CREW LLP

Designated states: AE AG AL AM AT AU AZ BA BB BE BF BG BJ BR BY BZ CA CF CG CH CI CM CN CO CR CU CY CZ DE DK DM DZ EC EE ES FI FR GA GB GD GE GH GM GN GQ GR GW HR HU ID IE IL IN IS IT JP KE KG KP KR KZ LC LI LK LR LS LT LU LV MA MC MD MG MK ML MN MR MW MX MZ NE NL NO NZ OM PH PL PT RO RU SD SE SG SI SK SL SN SZ TD TG TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

Title: **ANTIBACTERIAL** BENZOIC ACID DERIVATIVES

Abstract: Source: US2004110802A The invention provides antimicrobial agents and methods of using the agents for sterilization, sanitation, antisepsis, disinfection, and treatment of infections in mammals.

Classifications:

International (IPC 8-9): A61P31/00 C07D209/42 C07D213/82 C07D231/14 C07D241/24 C07D261/08 C07D261/10 C07D261/20 C07D277/68 C07D279/02 C07D333/38 C07D401/12 C07D405/12 C07D409/12 C07D413/04 C07D413/12 C07D417/12 C07D471/04 C07D487/08 C07D495/04 (Advanced/Invention)

International (IPC 1-7): A61K31/415 A61K31/44 A61K31/4745 A61P31/00 C07D209/42 C07D213/46 C07D213/57 C07D213/82 C07D231/14 C07D241/24 C07D261/08 C07D261/10 C07D261/20 C07D277/68 C07D279/02 C07D333/38 C07D401/12 C07D405/12 C07D409/12 C07D413/04 C07D413/12 C07D417/12 C07D471/04 C07D487/08 C07D495/04

CPC: C07D209/42 C07D213/82 C07D231/14 C07D241/24 C07D261/08 C07D261/10 C07D261/20 C07D277/68 C07D279/02 C07D333/38 C07D401/12 C07D405/12 C07D409/12 C07D413/04 C07D413/12 C07D417/12 C07D471/04 C07D487/08 C07D495/04

European: C07D209/42 C07D213/82 C07D231/14 C07D241/24 C07D261/08 C07D261/10 C07D261/20 C07D277/68 C07D279/02 C07D333/38 C07D401/12 C07D405/12 C07D409/12 C07D413/04 C07D413/12 C07D417/12 C07D471/04 C07D487/08 C07D495/04

US: 514/355 514/357 514/357S 546/313 546/313S 546/315 546/315S 546/33 546/330 546/330S

Family:

Publication number	Publication date	Application number	Application date	
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US2004110802 AA	20040610	US20030645802	20030820	
WO04018428 A1	20040304	WO2003US24796	20030822	

Priority:

US20020405429P 20020823 US20020430592P 20021203 US20030645802 20030820

WO2003US24796 20030822

Probable Assignee: PHARMACIA AND UPJOHN CO

Assignee(s): (std): BEAUCHAMP THOMAS J ; FISHER JED F ; NORTHUIS JILL M ; ROMERO DONNA L ; UPJOHN CO ; THORARENSEN ATLI ; RUBLE CRAIG J

Assignee(s): ROMERO DONNA LEE ; RUBLE J CRAIG ; PHARMACIA AND UPJOHN CO ; PHARMACIA AND UPJOHN CO LLC ; PHARMACIA AND UPJOHN COMPANY

Inventor(s): (std): THORARENSEN ATLI ; RUBLE CRAIG J ; ROMERO DONNA L ; NORTHUIS JILL M ; FISHER JED F ; BEAUCHAMP THOMAS J ; ROMERO DONNA LEE ; RUBLE J CRAIG

Inventor(s): THOMAS J BEAUCHAMP ; ATLI THORARENSEN ; CRAIG J RUBLE ; DONNA L ROMERO ; JED F FISHER ; JILL M NORTHUIS

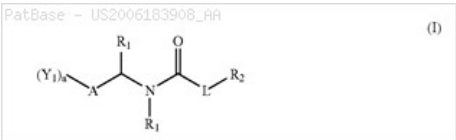
Designated states: AE AG AL AM AT AU AZ BA BB BE BF BG BJ BR BY BZ CA CF CG CH CI CM CN CO CR CU CY CZ DE DK DM DZ EC EE ES FI FR GA GB GD GE GH GM GN GQ GR GW HR HU ID IE IL IN IS IT JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MC MD MG MK ML MN MR MW MX MZ NE NL NO NZ OM PG PH PL PT RO RU SC SD SE SG SI SK SL SN SY SZ TD TG TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

Title: HETEROCYCLIC COMPOUNDS, METHODS OF MAKING THEM AND THEIR USE IN THERAPY

Abstract: Source: US2006183908A In part, the present invention is directed to **antibacterial** compounds of formula (I) wherein A is a bicyclic heteroaryl ring or a tricyclic ring and R₂ is an heterocyclic residue; L is a bond, or L is alkyl, alkenyl or cycloalkyl.

Classifications:

International (IPC 8-9): A01N43/00 A01N43/62 A61K31/4353 A61K31/437 A61K31/4375 A61K31/44 A61K31/4427 A61K31/443 A61K31/4436 A61K31/4439 A61K31/444 A61K31/4545 A61K31/4709 A61K31/496 A61K31/4985 A61K31/519 A61K31/5377 A61K31/55 A61K31/551 A61K31/5517 A61K9/02 A61K9/20 A61L2/16 A61P31/04 A61P43/00 C07D213/54 C07D213/73 C07D213/74 C07D243/00 C07D401/00 C07D401/06 C07D401/12 C07D401/14 C07D405/12 C07D409/12 C07D413/00 C07D413/06 C07D413/12 C07D471/02 C07D471/04 C07D471/14 C07D487/00 C07D487/22 C07D491/00 C07D495/04 C07D498/00 C07D498/04 C07D519/00 (Advanced/Invention); A61K31/551 A61K9/02 A61K9/20 A61L2/16 A61P43/00 (Advanced/Non-invention); A01N43/00 A01N43/48 A61K31/00 A61K31/4353 A61K31/4427 A61K31/4523 A61K31/4709 A61K31/496 A61K31/519 A61K31/5375 A61K31/55 A61K31/551 A61K9/02 A61K9/20 A61L2/16 A61P31/00 A61P43/00 C07D213/00 C07D243/00 C07D401/00 C07D405/00 C07D409/00 C07D471/00 C07D487/00 C07D491/00 C07D495/00 C07D498/00 C07D519/00 (Core/Invention)
International (IPC 1-7): A61K31/4427 A61P31/04 C07D213/73 C07D401/12 C07D405/12 C07D409/12 C07D471/04 C07D495/04
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European: C07D213/73 C07D401/12 C07D405/12 C07D409/12 C07D471/04 C07D495/04
US: 514/213.01 514/220 514/221 514/221S 514/234.2 514/234.200S 514/235.5 514/235.500S 514/237.2 514/237.200S 514/253.01 514/253.010S 514/300 514/300S 514/318 514/318S 514/343 514/343S 540/555 540/557 540/557S 540/568 540/568S 540/577 544/117 544/117S 544/131 544/131S 544/360 544/360S 546/122 546/122P 546/122S 546/193 546/193S 546/276.4 546/276.400S



Family:

Publication number	Publication date	Application number	Application date
AU2003298937 AA	20040630	AU20030298937	20031205
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EP1575951 B1	20140625	EP20030796699	20031205
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JP2006513262 T2	20060420	JP20050508475T	20031205
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US2006183908 AA	20060817	US20030537747	20031205
US2011124633 AA	20110526	US20100844403	20100727
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Priority:

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US20030537747	20031205	US20060537747	20060327	US20100844403	20100727
JP20050508475	20031205	EP20030796699	20031205		

Probable Assignee: DEBIOPHARM INT SA

Assignee(s): (std): BERMAN JUDD ; DEBIOPHARM INT FORUM APRES DEMAÏN SA ; DEBIOPHARM INT SA ; DECORNEZ HELENE YVONNE ; MANNING DAVID DOUGLAS ; SAMPSON PETER ; PAULS HEINZ W ; RAMNAUTH JAILALL ; SURMAN MATTHEW DAVID ; XIE DEJIAN ; AFFINIUM PHARM INC

Assignee(s): AFFINIUM PHARMACEUTICALS INC

Inventor(s): (std): BERMAN JUDD ; BERMAN JUDD M ; DOUGLAS DAVID ; DECORNEZ HELENE Y ; DECORNEZ HELENE YVONNE ; MANNING DAVID DOUGLAS ; PAULS HEINZ W ; RAMNAUTH JAILALL ; SAMPSON PETER ; SURMAN MATTHEW D ; SURMAN MATTHEW DAVID ; XIE DEJIAN

Inventor(s): SURMAN MATTHEW ; PETER SAMPSON ; MATTHEW DAVID SURMAN ; PAULS HEINZ ; DEJIAN XIE ; HEINZ W PAULS ; HELENE YVONNE DECORNEZ ; JAILALL RAMNAUTH ; JUDD BERMAN ; DAVID DOUGLAS MANNING ; DECORNEZ HELENE

Agent(s): SIMPSON TOBIAS RUTGER; FOLEY HOAG LLP, PATENT GROUP WORLD TRADE CENTER WEST; FOLEY HOAG LLP PATENT GROUP WORLD TRADE CENTER WEST; GOODWIN PROCTER LLP

Designated states: AE AG AL AM AT AU AZ BA BB BE BF BG BJ BR BW BY BZ CA CF CG CH CI CM CN CO CR CU CY CZ DE DK DM DZ EC EE ES FI FR GA GB GD GE GH GM GN GQ GR GW HR HU ID IE IL IN IS IT JP KE KG KP KR KZ LC LI LK LR LS LT LU LV MA MC MD MG MK ML MN MR MW MX MZ NE NI NL NO NZ OM PG PH PL PT RO RU SC SD SE SG SI SK SL SN SY SZ TD TG TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

Title: 2-NH-heteroarylimidazoles with **antibacterial** activity

Abstract: Source: US2004147548A Compounds of formula (I): are inhibitors of bacterial methionyl tRNA synthetase and are of use in treating bacterial infections.

Classifications:

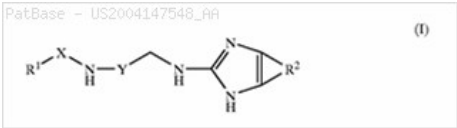
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International (IPC 1-7): A61K31/4188 A61K31/437 A61K31/4745 A61K31/4985 A61K31/5025 A61K31/52 A61P31/04 C07D471/02 C07D471/04 C07D473/00 C07D487/04 C07D495/04

CPC: C07D471/04 A61K31/4164 A61K31/44 C07D473/00 C07D487/04 C07D495/04

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US: 514/248 514/249 514/249S 514/261 514/263.4 514/266.2 514/266.200S 514/303 514/303S 514/393 514/393S 544/236 544/236S 544/264 544/277 544/277S 544/350 544/350S 546/118 546/118S 548/303.7



Family:

Publication number	Publication date	Application number	Application date	
AU2003293420 AA	20040630	AU20030293420	20031205	
CA2508147 AA	20050603	CA20032508147	20031205	
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GB200228545 A0	20030115	GB20020028545	20021206	
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US2004147548 AA	20040729	US20030729416	20031205	
US2006014748 AA	20060119	US20050223327	20050909	
US2007213362 AA	20070913	US20070751451	20070521	
US6943175 BB	20050913	US20030729416	20031205	
US7220757 BB	20070522	US20050223327	20050909	
WO04052288 A2	20040624	WO2003US38729	20031205	
WO04052288 A3	20040826	WO2003US38729	20031205	

Priority:

GB20020028545	20021206	WO2003US38729	20031205	US20030729416	20031205
US20050223327	20050909	US20030729146	20031205	US20070751451	20070521

Probable Assignee: REPLIDYNE INC

Assignee(s): (std): GLAXO GROUP LTD ; HAMPRECHT DIETER ; JARVEST RICHARD ; REPLIDYNE INC ; BERGE JOHN ; FORREST ANDREW

Assignee(s): GLAXO GROUP LIMITED ; SMITHKLINE BEECHAM PLC

Inventor(s): (std): ANDREW FORREST ; BERGE JOHN ; DIETER HAMPRECHT ; FORREST ANDREW ; HAMPRECHT DIETER ; JARVEST RICHARD ; JOHN BERGE ; RICHARD JARVEST

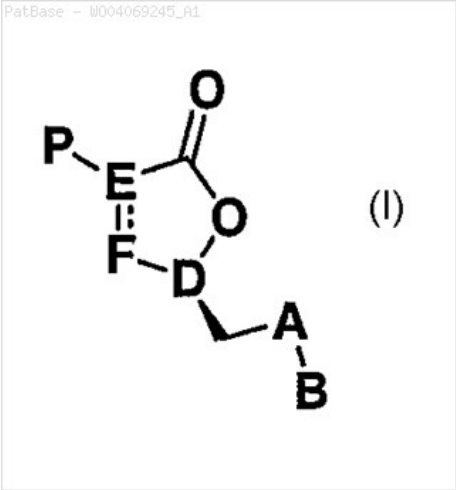
Agent(s): SWANSON AND BRATSCHUN LLC

Designated states: AE AG AL AM AT AU AZ BA BB BE BF BG BJ BR BW BY BZ CA CF CG CH CI CM CN CO CR CU CY CZ DE DK DM DZ EC EE EG ES FI FR GA GB GD GE GH GM GN GQ GR GW HR HU ID IE IL IN IS IT JP KE KG KP KR KZ LC LI LK LR LS LT LU LV MA MC MD MG MK ML MN MR MW MX MZ NE NI NL NO NZ OM PG PH PL PT RO RU SC SD SE SG SI SK SL SN SY SZ TD TG TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW

Title: **Antibacterial** agents

Abstract: Source: US2005277630A Compounds of formula I and methods for their preparation are disclosed. Further disclosed are methods of making biologically active compounds of formula I as well as pharmaceutically acceptable compositions comprising compounds of formula I. Compounds of formula I as disclosed herein can be used in a variety of applications including use as **antibacterial** agents.

Classifications:
International (IPC 8-9): A61K31/422 A61K31/429 A61K31/4439 A61K31/496 A61K31/519 A61K31/5377 A61K31/55 A61K31/551 A61P31/04 C07D413/04 C07D413/14 C07D491/04 C07D491/044 C07D495/04 C07D498/04 C07D513/04 (Advanced/Invention)
International (IPC 1-7): A61K31/422 A61K31/551 A61P31/04 C07D413/04 C07D413/14 C07D491/04 C07D491/14 C07D495/04 C07D498/04 C07D513/04
CPC: C07D413/04 C07D413/14 C07D491/04 C07D495/04 C07D513/04
European: C07D413/04 C07D413/14 C07D491/04 C07D495/04 C07D498/04 C07D513/04
US: 514/220 540/560 540/560S



Family:

Publication number	Publication date	Application number	Application date
BRPI0407335 A	20060110	BR2004PI07335	20040127
CA2514241 AA	20050722	CA20042514241	20040127
EP1594495 A1	20051116	EP20040705475	20040127
JP2006516990 T2	20060713	JP20060502378T	20040127
MXPA05008400 A1	20051005	MX2005PA08400	20050808
US2005277630 AA	20051215	US20040772860	20040206
WO04069245 A1	20040819	WO2004IB00231	20040127

Priority:
US20030445909P 20030207 WO2004IB00231 20040127 US20040772860 20040206

Probable Assignee: WARNER LAMBERT CO
Assignee(s): (std): CHUPAK LOUIS S ; CHUPAK LOUIS STANLEY ; JIAO WENHUA ; JOSYULA ; JOSYULA VARA PRASAD VENKATA NA ; JOSYULA VERA PRASAD V N ; KANEKO TAKUSHI ; WARNER LAMBERT CO
Assignee(s): WARNER LAMBERT CO LLC ; WARNER LAMBERT COMPANY LLC ; JOSYULA VARA PRASAD VENKATA NAGENDRA
Inventor(s): (std): CHUPAK LOUIS S ; CHUPAK LOUIS STANLEY ; JIAO WENHUA ; JOSYULA ; JOSYULA VARA P V N ; JOSYULA VARA PRASAD VENKATA NA ; KANEKO TAKUSHI ; JOSYULA VERA PRASAD V N
Inventor(s): JOSYULA VERA PRASAD VENKATA NAGENDRA ; JOSYULA VERA PRASAD VN ; LOUIS STANLEY CHUPAK ; TAKUSHI KANEKO ; VARA PRASAD VENKATA NAGENDRA JOSYULA ; WENHUA JIAO ; JOSYULA VARA PRASAD VENKATA NAGENDRA ; JOSYULA VARA PVN
Agent(s): HEIDI M BERVEN WARNER LAMBERT CO LLC
Designated states: AE AG AL AM AT AU AZ BA BB BE BF BG BJ BR BW BY BZ CA CF CG CH CI CM CN CO CR CU CY CZ DE DK DM DZ EC EE EG ES FI FR GA GB GD GE GH GM GN GQ GR GW HR HU ID IE IL IN IS IT JP KE KG KP KR KZ LC LI LK LR LS LT LU LV MA MC MD MG MK ML MN MR MW MX MZ NA NE NI NL NO NZ OM PG PH PL PT RO RU SC SD SE SG SI SK SL SN SY SZ TD TG TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

Title: SUBSTITUTED THIOPHENES WITH **ANTIBACTERIAL** ACTIVITY

Abstract: Source: US2005009833A Novel substituted thiophenes that are inhibitors of bacterial methionyl t-RNA synthetase (MRS) are disclosed. Also disclosed are method for their preparation and their use in therapy as anti-bacterial agents.

Classifications:

International (IPC 8-9): A61K31/415 A61K31/4178 A61K31/4184 A61K31/4188 A61K31/437 A61K31/4436 A61K31/47 A61K31/4709 A61K31/501 A61K31/5025 A61K31/505 A61K31/506 A61K31/513 A61K31/519 A61P31/00 A61P31/04 C07D215/233 C07D215/38 C07D235/22 C07D409/02 C07D409/12 C07D471/04 C07D487/04 C07D495/04 (Advanced/Invention); A61K31/415 A61K31/4427 A61K31/47 A61K31/505 A61K31/506 C07D215/00 C07D235/00 C07D409/00 C07D495/00 (Core/Invention); A61K (Subclass/Invention)

International (IPC 1-7): A61K A61K31/415 A61K31/47 A61K31/4709 A61K31/501 A61K31/505 A61K31/513 C07D215/233 C07D235/22 C07D409/12 C07D49/02 C07D495/04

CPC: C07D409/12 C07D401/04 C07D403/04 C07D495/04

European: C07D401/04 C07D403/04 C07D409/12 C07D495/04

US: 514/252.01 514/255.05 514/269 514/275 514/312 514/313 514/342 514/397 544/238 544/31 544/310 544/329 544/405 546/153 546/159 546/280.4 546/280.400 548/311.1 548/311.100 548/315.1

Family:

Publication number	Publication date	Application number	Application date	
AU2004218481 AA	20040916	AU20040218481	20040227	
AU2011201854 AA	20110519	AU20110201854	20110421	
CA2517523 AA	20050830	CA20042517523	20040227	
EP1603881 A2	20051214	EP20040715720	20040227	
EP1603881 A4	20100707	EP20040715720	20040227	
GB200304809 A0	20030409	GB20030004809	20030303	
JP2006519261 T2	20060824	JP20060508886T	20040227	
US2005009833 AA	20050113	US20040789811	20040227	
US2006128735 AA	20060615	US20060343378	20060130	
US7030137 BB	20060418	US20040789811	20040227	
WO04078119 A2	20040916	WO2004US05930	20040227	
WO04078119 A3	20041229	WO2004US05930	20040227	

Priority:

GB20030004809 20030303	US20030527229P 20031205	WO2004US05930 20040227
US20060343378 20060130	US20040789811 20040227	AU20040218481 20040227
AU20110201854 20110421		

Probable Assignee: REPLIDYNE INC

Assignee(s): (std): BERGE JOHN ; FRYDRYCH CATHERINE SIMONE VICT ; GLAXO GROUP LTD ; REPLIDYNE INC ; JARVEST RICHARD ; GUILLES JOSEPH ; QIU JIAN ; TARASOW THEODORE M

Assignee(s): JIAN QIU ; FRYDRYCH CATHERINE SIMONE VICTOIRE ; GLAXO GROUP LIMITED

Inventor(s): (std): BERGE JOHN ; FRYDRYCH CATHERINE S V ; FRYDRYCH CATHERINE SIMONE VICT ; GUILLES JOSEPH ; JARVEST RICHARD ; QIU JIAN ; TARASOW THEODORE M ; THEODORE M TARASOW ; RICHARD JARVEST ; JOSEPH GUILLES ; JOHN BERGE ; JIAN QIU ; FRYDRYCH CATHERINE SIMONE VICTOIRE ; CATHERINE SIMONE VICTOIRE FRYDRYCH

Inventor(s): TARASOW THEODORE ; FRYDRYCH CATHERINE SV ; FRYDRYCH CATHERINE ; FRYDRYCH CATHERINE S

Agent(s): SWANSON AND BRATSCHUN LLC

Designated states: AE AG AL AM AT AU AZ BA BB BE BF BG BJ BR BW BY BZ CA CF CG CH CI CM CN CO CR CU CY CZ DE DK DM DZ EC EE EG ES FI FR GA GB GD GE GH GM GN GQ GR GW HR HU ID IE IL IN IS IT JP KE KG KP KR KZ LC LI LK LR LS LT LU LV MA MC MD MG MK ML MN MR MW MX MZ NA NE NI NL NO NZ OM PG PH PL PT RO RU SC SD SE SG SI SK SL SN SY SZ TD TG TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

Title: DERIVATIVES OF 1-PIPERAZINE-AND 1-HOMOPIPERAZINE-CARBOXYLATES, PREPARATION METHOD THEREOF AND USE OF SAME AS INHIBITORS OF THE FAAH ENZYME

Abstract: Source: US2006293310A The invention relates to a compound having general formula (I): Wherein m, R₁ and R₂ are as defined herein. The invention also relates to the use of the compound in therapeutics. More specifically, the compounds of the invention are inhibitors of the FAAH enzyme, and therefore, can be used for the treatment of various disorders associated with FAAH enzyme, which include in a non-limiting manner, pain, eating disorders, neurological and psychiatric pathologies, among other disorders.

Classifications:

International (IPC 8-9): A61K31/49 A61K31/495 A61K31/496 A61K31/4965 A61K31/497 A61K31/50 A61K31/501 A61K31/506 A61K31/53 A61K31/55 A61K31/551 A61P1/00 A61P1/08 A61P11/00 A61P13/00 A61P13/02 A61P13/12 A61P19/10 A61P25/00 A61P25/04 A61P25/08 A61P25/20 A61P25/28 A61P27/02 A61P29/00 A61P31/00 A61P31/04 A61P31/12 A61P33/00 A61P35/00 A61P37/00 A61P37/02 A61P37/08 A61P43/00 A61P9/00 A61P9/10 C07C235/06 C07D213/24 C07D213/74 C07D213/75 C07D215/16 C07D215/38 C07D215/46 C07D217/22 C07D231/38 C07D237/20 C07D239/28 C07D239/42 C07D241/20 C07D243/08 C07D261/20 C07D285/08 C07D295/033 C07D295/16 C07D295/18 C07D295/185 C07D295/20 C07D295/205 C07D307/81 C07D311/04 C07D311/58 C07D317/58 C07D401/00 C07D401/04 C07D403/02 C07D403/04 C07D405/00 C07D405/04 C07D405/10 C07D409/00 C07D411/00 C07D413/02 C07D413/04 C07D417/02 C07D417/04 C07D495/04 (Advanced/Invention); A61P11/00 A61P19/10 A61P27/02 A61P33/00 C07D295/185 C07D295/205 C07D401/04 C07D405/04 (Advanced/Non-invention); A61K31/49 A61K31/495 A61K31/496 A61K31/4965 A61K31/50 A61K31/501 A61K31/506 A61K31/53 A61K31/55 A61K31/551 A61P1/00 A61P11/00 A61P13/00 A61P19/00 A61P25/00 A61P27/00 A61P29/00 A61P31/00 A61P33/00 A61P35/00 A61P37/00 A61P43/00 A61P9/00 C07C235/00 C07D213/00 C07D215/00 C07D217/00 C07D231/00 C07D237/00 C07D239/00 C07D241/00 C07D261/00 C07D285/00 C07D295/00 C07D307/00 C07D311/00 C07D317/00 C07D401/00 C07D403/00 C07D405/00 C07D409/00 C07D411/00 C07D413/00 C07D417/00 C07D495/00 (Core/Invention); A61K A61P C07C C07D (Subclass/Invention)

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CPC: C07D213/74 C07D215/46 C07D231/38 C07D239/42 C07D295/185 C07D295/205 C07D311/04 C07D317/58 C07D495/04

European: C07D213/74 C07D215/46 C07D231/38 C07D239/42 C07D295/185 C07D295/205 C07D311/04 C07D317/58 C07D495/04

US: 514/218 514/241 514/241S 514/248 514/248S 514/252.02 514/252.020P 514/252.020S 514/252.11 514/252.110S 514/252.14 514/252.140S 514/252.17 514/252.170S 514/253.01 514/253.010S 514/253.04 514/253.040S 514/253.05 514/253.050S 514/253.06 514/253.060S 514/254.02 514/254.020S 514/254.03 514/254.030S 514/254.04 514/254.040S 514/254.05 514/254.050S 514/254.06 514/254.060S 514/254.11 514/254.110S 514/255.01 514/255.010S 514/284 514/284S 514/295 514/295S 540/575 540/575S 544/209 544/209S 544/237 544/237S 544/238 544/238S 544/268 544/295 544/295S 544/353 544/353S 544/357 544/357S 544/360 544/360S 544/362 544/362S 544/363 544/363S 544/368 544/368S 544/369 544/369S 544/376 544/376S 544/377 544/377S 544/381 544/389 544/389S

PatBase - US2006293310_AA

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Family:

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AR046982 AA	20060104	AR2004P104843	20041222	
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AU2004314287 AA	20050804	AU20040314287	20041217	
AU2004314287 BB	20110407	AU20040314287	20041217	
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CN101538254 A	20090923	CN200910132126	20041217	
CN101538254 B	20110727	CN200910132126	20041217	
CN1922161 A	20070228	CN200480040912	20041217	
CY1107902 T1	20130904	CY20081100272T	20080307	
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EP1701946 B1	20071219	EP20040816424	20041217	
ES2297533 T3	20080501	ES20040816424T	20041217	
FR2864080 A1	20050624	FR20030015248	20031223	
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HK1099552 A1	20100319	HK20070106691	20070622	
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HR20080078 T3	20080331	HR20080000078	20080222	
IL176478 A0	20061005	IL20060176478	20060621	
IL176478 A1	20100531	IL20060176478	20060621	
IN01735KN2006 A	20070511	IN2006KN01735	20060622	
IN235693 B	20090814	IN2006KN01735	20060622	
JP2007519628 T2	20070719	JP20060546236T	20041217	
JP4833080 B2	20111207	JP20060546236T	20041217	
KR101276427 B1	20130619	KR20067014698	20041217	
KR20060130126 A	20061218	KR20067014698	20041217	
MA28234 A1	20061002	MA20060029120	20060619	
NO20063229 A	20060831	NO20060003229	20060711	
NZ548194 A	20091224	NZ20040548194	20041217	
PT1701946 T	20080211	PT20040816424T	20041217	
RS50544 B	20100507	RS20080000062	20041217	
RS50544 B	20100507	YU20080000062	20041217	
RU2006126710 A	20080127	RU20060126710	20041217	
RU2356890 C2	20090527	RU20060126710	20041217	
SI1701946 T1	20080430	SI20040030595T	20041217	
TH104646 A	20101029	TH20041005109	20041221	
TW200530199 A	20050916	TW20040140162	20041222	
TWI339121 B	20110321	TW20040140162	20041222	
US2006293310 AA	20061228	US20060473284	20060622	
US2010137329 AA	20100603	US20100701897	20100208	
US7687503 BB	20100330	US20060473284	20060622	
US8114866 BB	20120214	US20100701897	20100208	
WO05070910 A2	20050804	WO2004FR03289	20041217	
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ZA200505522 A	20071128	ZA20050005522	20041217	

Priority:

FR20030015248 20031223 WO2004FR03289 20041217 EP20040816424 20041217
US20060473284 20060622 US20100701897 20100208 HK20070106691 20070622

Probable Assignee:

SANOFI

Assignee(s):

(std): ABOUABDELLAH AHMED ; ALMARIO GARCIA ANTONIO ; HOORNAERT CHRISTIAN ; LI ADRIEN TAK ; SANOFI AVENTIS ; SANOFI SYNTHELABO ; SANOFI EVENTIS ; SANOFI SA

Assignee(s):

SANOFI

Inventor(s):

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Inventor(s):

ABOUABDELLAH AHMED ALMARIO GARCIA ANTONIO HOORNAERT CHRISTIAN LI ADRIEN TAK ; AL'MARIO GARSIIA ANTONIO ; ABOUABDELLAH AHMED ALMARIO GARCIA ANTONIO ; ABOUABDELLAH AHMED ALMARIO GARCIA ANTONIO HOORNAER

Agent(s):

ROSS J OEHLER SANOFI AVENTIS US LLC; ANDREA Q RYAN SANOFI AVENTIS US LLC; BALARAM; KELLY L

Designated states:

AE AG AL AM AT AU AZ BA BB BE BF BG BJ BR BW BY BZ CA CF CG CH CI CM CN CO CR CU CY CZ DE DK DM DZ EC EE EG ES FI FR GA GB GD GE GH GM GN GQ GR GW HR HU ID IE IL IN IS IT JP KE KG KP KR KZ LC LI LK LR LS LT LU LV MA MC MD MG MK ML MN MR MW MX MZ NA NE NI NL NO NZ OM PG PH PL PT RO RU SC SD SE SG SI SK SL SM SN SY SZ TD TG TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

Title: Selected CGRP - antagonists, process for preparing them and their use as pharmaceutical compositions

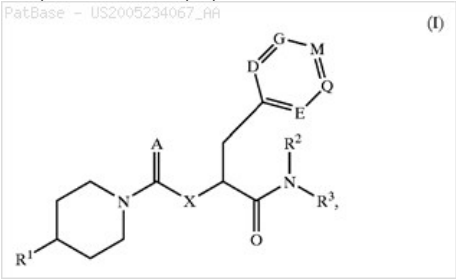
Abstract: Source: US2005234067A The present invention relates to the CGRP antagonists of general formula wherein A, X, D, E, G, M, Q and R¹>1 </SUP>>1 </SUP>>3 </SUP>>are defined as in claim 1, the tautomers, the diastereomers, the enantiomers, the hydrates thereof, the mixtures thereof and the salts thereof and the hydrates of the salts, particularly the physiologically acceptable salts thereof with inorganic or organic acids, pharmaceutical compositions containing these compounds, the use thereof and processes for the preparation thereof.

Classifications:

International (IPC 8-9): A61K31/445 A61K31/45 A61K31/4523 A61K31/454 A61K31/4545 A61K31/4709 A61K31/4745 A61K31/496 A61K31/497 A61K31/501 A61K31/517 A61K31/519 A61K31/537 A61K31/5377 A61K31/541 A61K31/55 A61K31/551 A61K31/5513 A61K31/554 A61P1/00 A61P1/02 A61P1/04 A61P1/10 A61P1/12 A61P11/00 A61P11/02 A61P11/06 A61P13/08 A61P15/08 A61P15/12 A61P17/00 A61P17/02 A61P17/04 A61P19/02 A61P25/00 A61P25/02 A61P25/04 A61P25/06 A61P25/36 A61P27/16 A61P29/00 A61P3/00 A61P3/10 A61P31/00 A61P31/04 A61P35/00 A61P37/08 A61P39/02 A61P43/00 A61P5/50 A61P9/00 A61P9/02 A61P9/08 A61P9/10 C07B57/00 C07D207/12 C07D211/00 C07D211/36 C07D211/56 C07D239/72 C07D243/04 C07D243/10 C07D243/14 C07D265/04 C07D295/12 C07D295/26 C07D401/00 C07D401/04 C07D401/12 C07D401/14 C07D403/02 C07D403/14 C07D405/12 C07D405/14 C07D413/04 C07D413/14 C07D417/04 C07D451/02 C07D453/02 C07D471/04 C07D487/08 C07D487/10 C07D491/10 C07D495/04 C07D495/14 C07D498/02 C07D498/10 (Advanced/Invention); A61K31/551 A61P11/00 A61P11/06 A61P13/08 A61P15/08 A61P17/00 A61P17/02 A61P19/02 A61P25/36 A61P29/00 A61P3/10 A61P31/04 A61P37/08 A61P39/02 A61P9/10 C07B57/00 C07B61/00 C07D401/14 C07D405/12 C07D405/14 C07D413/14 (Advanced/Non-invention); A61K31/00 A61K31/445 A61K31/4523 A61K31/454 A61K31/4545 A61K31/4709 A61K31/4738 A61K31/4745 A61K31/4965 A61K31/501 A61K31/517 A61K31/537 A61K31/5375 A61K31/551 A61P1/00 A61P11/00 A61P13/00 A61P15/00 A61P17/00 A61P19/00 A61P25/00 A61P27/00 A61P29/00 A61P3/00 A61P31/00 A61P37/00 A61P39/00 A61P43/00 A61P9/00 C07B57/00 C07D211/00 C07D243/00 C07D401/00 C07D403/00 C07D405/00 C07D413/00 C07D451/00 C07D453/00 C07D471/00 C07D487/00 C07D495/00 C07D498/00 (Core/Invention); C07B57/00 C07B61/00 (Core/Non-invention); A61K A61P C07D (Subclass/Invention)
International (IPC 1-7): A61K31/4155 A61K31/4162 A61K31/435 A61K31/4418 A61K31/4427 A61K31/4433 A61K31/4439 A61K31/445 A61K31/454 A61K31/4545 A61K31/4745 A61K31/497 A61K31/501 A61K31/541 A61K31/551 A61K31/554 A61P1/12 A61P11/00 A61P11/06 A61P17/00 A61P17/02 A61P19/02 A61P25/06 A61P29/00 A61P29/03 A61P3/08 A61P3/10 A61P9/00 C07D211/00 C07D243/10 C07D401/02 C07D401/04 C07D401/14 C07D403/02 C07D403/14 C07D405/12 C07D405/14 C07D41/02 C07D413/14 C07D417/04 C07D43/02 C07D471/04 C07D495/04 C07D498/10
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European: C07D401/04 C07D401/12 C07D401/14 C07D405/12 C07D405/14 C07D413/14 C07D471/04 C07D495/04 C07D498/10
US: 514/211.15 514/211.150P 514/218 514/218S 514/221 514/227.5 514/227.500S 514/229.8 514/229.800S 514/252.03 514/252.030P 514/252.13 514/252.16 514/252.160S 514/252.17 514/252.170S 514/253.03 514/253.030S 514/253.09 514/253.090S 514/255.05 514/255.050S 514/260.1 514/260.100S 514/266.22 514/266.220S 514/293 514/293S 514/316 514/316S 514/318 514/318S 514/319 514/319S 514/326 514/326S 540/488 540/488S 540/500 540/500S 540/502 540/502P 540/570 540/570S 540/575 540/575S 544/231 544/231S 544/238 544/238S 544/278 544/278S 544/284 544/284S 544/286 544/286S 544/361 544/361S 544/364 544/364S 544/365 544/405 544/405S 544/60 544/60S 544/71 544/71S 546/158 546/158S 546/187 546/187S 546/194 546/194S 546/207 546/207S 546/208 546/208S 546/210 546/210S 546/82 546/82S

Family:

Publication number	Publication date	Application number	Application date	
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AR049625 AA	20060823	AR2005P101139	20050323	
AR053344 AA	20070502	AR2006P101117	20060322	
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Priority:

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Probable Assignee: BOEHRINGER INGELHEIM INT

Assignee(s): (std): BOEHRINGER INGELHEIM GMBH ; BOEHRINGER INGELHEIM INT ; DREYER ALEXANDER ; DOODS HENRI ; BOEHRINGER INGELHEIM PHARMA ; MUELLER STEPHAN GEORG ; RUDOLF KLAUS ; LUSTENBERGER PHILIPP ; STENKAMP DIRK ; SCHAENZLE GERHARD ; SANTAGOSTINO MARCO ; PALEARI FABIO ; ARNDT KIRSTEN

Assignee(s): BOEHRINGER INGELEHIM INT ; BOEHRINGER INGELEHIM INT GMBH ; BOEHRINGER INGELHEIM INT GMBH CO KG ; BOEHRINGER INGELHEIM INTERNATL GMBH ; BOEHRINGER INGELHEIM PHARMA GMBH ; BOEHRINGER INGELHEIM INTERNACIONAL GMBH ; BOEHRINGER INGELHEIM INTERNATIONAL GMBH ; BOEHRINGER INGELHEIM PHARMA GMBH AND CO KG ; BOEHRINGER INGELHEIM INT GMBH

Inventor(s): (std): ARDNT KIRSTEN ; ARNDT KIRSTEN ; CHAENZLE GERHARD ; DOODS HENRI ; DOODS HENRI NICO ; DREYER ALEXANDER ; MUELLER STEPHAN GEORG ; MULLER STEPHAN G ; PALEARI FABIO ; RODOLF KLAUS ; RUDOLF KLAUS ; SANTAGOSTINO MARCO ; SCHAEENZLE GERHARD ; SCHANZLE GERHARD ; SHAENZLE GERHARD ; STENCAMP DIRK ; STENKAMP DIRK ; PHILIPP LUSTENBERGER ; MARCO SANTAGOSTINO ; KLAUS RUDOLF ; KIRSTEN ARNDT ; HENRI DOODS ; GERHARD SCHAEENZLE ; GEORG MUELLER STEPHAN ; FABIO PALEARI ; DIRK STENKAMP ; ALEXANDER DREYER ; LUSTENBERGER PHILIPP ; MUELLER STEPHAN ; USTENBERGER PHILIPP ; SANAGOSTINO MARCO ; MULLER STEPHAN GEORG ; LUSTEBERGER PHILLIP ; ARNDT KRISTEN ; MUELLER STEPHAN G ; RUDLOF KLAUS ; MUELLER

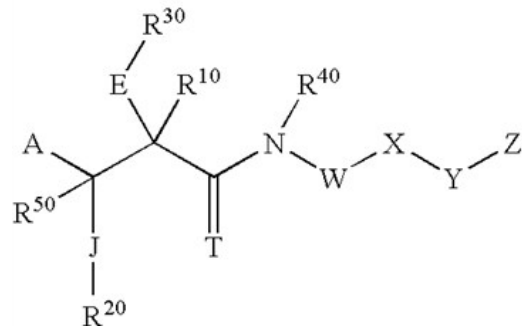
Inventor(s): PHILLIPP LUSTENBERGER ; DIE ERFINDERNENNUNG LIEGT NOCH NICHT VOR ; MARCO SANAGOSTINO ; MUELLER STEPHAN G RUDOLF KLAUS LUSTENBERGER PHILIP ; PELEARI FABIO ; STEPHAN GEORG MUELLER ; GERHARD SHAENZLE ; KIRSTEN ARDNT ; KLAUS RODOLF

Agent(s): HAMMANN HEINZ; HAMMANN HEINZ ET AL; SIMON ELKE ANNA MARIA; MICHAEL P MORRIS BOEHRINGER INGELHEIM CORP; MICHAEL P MORRIS BOEHRINGER INGELHEIM USA CORP; MORRIS MICHAEL P; DEVLIN MARY ELLEN M; STEMPEL ALAN R; MICHAEL P; MARY ELLEN M; ALAN R

Designated states: AE AG AL AM AT AU AZ BA BB BE BF BG BJ BR BW BY BZ CA CF CG CH CI CM CN CO CR CU CY CZ DE DK DM DZ EC EE EG ES FI FR GA GB GD GE GH GM GN GQ GR GW HR HU ID IE IL IN IS IT JP KE KG KM KN KP KR KZ LC LI LK LR LS LT LU LV LY MA MC MD MG MK ML MN MR MW MX MZ NA NE NG NI NL NO NZ OM PG PH PL PT RO RU SC SD SE SG SI SK SL SM SN SY SZ TD TG TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

Title: COMPOUNDS FOR THE TREATMENT OF INFLAMMATORY DISORDERS

Abstract: Source: US2006178366A This invention relates to compounds of the Formula (I):



isomer thereof, which can be useful for the treatment of diseases or conditions mediated by MMPs, aggrecanase, ADMP, LpxC, ADAMS, TACE, or a pharmaceutically acceptable salt, solvate or

Classifications:

International (IPC 8-9): A61K31/16 A61K31/165 A61K31/167 A61K31/381 A61K31/40 A61K31/4025 A61K31/403 A61K31/4035 A61K31/404 A61K31/415 A61K31/4155 A61K31/417 A61K31/4184 A61K31/421 A61K31/422 A61K31/4245 A61K31/426 A61K31/427 A61K31/428 A61K31/43 A61K31/4355 A61K31/437 A61K31/438 A61K31/44 A61K31/4402 A61K31/4409 A61K31/4427 A61K31/4439 A61K31/445 A61K31/4468 A61K31/451 A61K31/452 A61K31/4525 A61K31/454 A61K31/47 A61K31/4709 A61K31/472 A61K31/4725 A61K31/4747 A61K31/495 A61K31/496 A61K31/4995 A61K31/506 A61K31/519 A61K31/529 A61K31/537 A61K31/5375 A61K31/5377 A61K31/551 A61P1/02 A61P1/04 A61P1/16 A61P11/00 A61P11/06 A61P13/02 A61P13/12 A61P17/00 A61P17/06 A61P19/02 A61P19/08 A61P19/10 A61P25/00 A61P25/18 A61P25/32 A61P27/02 A61P27/06 A61P29/00 A61P3/04 A61P3/10 A61P37/06 A61P37/08 A61P39/00 A61P43/00 A61P7/02 A61P7/04 A61P7/08 A61P9/00 A61P9/10 C07C233/18 C07C235/06 C07C235/08 C07C235/10 C07D205/00 C07D207/00 C07D207/06 C07D207/08 C07D207/09 C07D207/14 C07D207/20 C07D207/26 C07D209/04 C07D209/08 C07D209/44 C07D211/10 C07D211/18 C07D211/32 C07D211/46 C07D211/54 C07D211/58 C07D211/62 C07D211/64 C07D213/30 C07D213/40 C07D213/74 C07D215/14 C07D217/06 C07D217/14 C07D231/12 C07D233/64 C07D235/00 C07D239/42 C07D241/36 C07D261/06 C07D263/30 C07D263/32 C07D265/30 C07D277/22 C07D277/28 C07D277/62 C07D295/00 C07D295/12 C07D295/18 C07D295/185 C07D307/00 C07D307/52 C07D307/68 C07D317/64 C07D333/20 C07D401/00 C07D401/04 C07D401/12 C07D401/14 C07D403/12 C07D405/12 C07D409/00 C07D409/12 C07D409/14 C07D413/00 C07D413/10 C07D413/12 C07D413/14 C07D417/04 C07D417/12 C07D417/14 C07D471/00 C07D471/02 C07D471/04 C07D471/10 C07D471/18 C07D471/20 C07D487/04 C07D487/08 C07D487/18 C07D495/04 C07D498/02 C07D498/04 C07D513/00 C07D513/04 (Advanced/Invention);

C07D295/18 C07D333/20 C07D403/12 C07D471/10 (Advanced/Non-invention); A61K31/16 A61K31/165 A61K31/167 A61K31/381 A61K31/40 A61K31/4025 A61K31/403 A61K31/415 A61K31/4155 A61K31/416 A61K31/421 A61K31/422 A61K31/4245 A61K31/426 A61K31/427 A61K31/428 A61K31/429 A61K31/4353 A61K31/438 A61K31/44 A61K31/4402 A61K31/4409 A61K31/4427 A61K31/445 A61K31/4468 A61K31/451 A61K31/4523 A61K31/47 A61K31/4709 A61K31/472 A61K31/4747 A61K31/495 A61K31/496 A61K31/4995 A61K31/519 A61K31/529 A61K31/5375 A61K31/551 A61P1/00 A61P11/00 A61P13/00 A61P17/00 A61P19/00 A61P25/00 A61P27/00 A61P29/00 A61P3/00 A61P33/00 A61P35/00 A61P37/00 A61P39/00 A61P43/00 A61P7/00 A61P9/00 C07C233/00 C07C235/00 C07D205/00 C07D207/00 C07D209/00 C07D211/00 C07D213/00 C07D215/00 C07D217/00 C07D233/00 C07D235/00 C07D239/00 C07D241/00 C07D261/00 C07D263/00 C07D265/00 C07D277/00 C07D295/00 C07D307/00 C07D317/00 C07D333/00 C07D401/00 C07D403/00 C07D405/00 C07D409/00 C07D413/00 C07D417/00 C07D471/00 C07D487/00 C07D495/00 C07D498/00 C07D513/00 (Core/Invention);

A61K C07C C07D (Subclass/Invention)

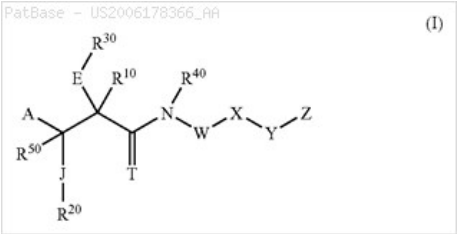
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Publication number	Publication date	Application number	Application date
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Priority:

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Probable Assignee: MERCK SHARP AND DOHME CORP

Assignee(s): (std): BELANGER DAVID B ; CHAN TIN YAU ; DAI CHAOYANG ; GIRIJAVALLABHAN VINAY M ; GUO ZHUYAN ; KOZLOWSKI JOSEPH A ; ORTH PETER ; MAZZOLA ROBERT D ; MC KITTRICK BRIAN ; LAVEY BRIAN J ; PALIWAL SUNIL ; LI DANSU ; POPOVICI MULLER JANETA ; MCKITTRICK BRIAN ; MANSOOR UMAR FARUK ; REDDY PANDURANGA A ; MADISON VINCENT S ; ZHU ZHAONING ; VACCARO HENRY A ; ZHOU GUOWEI ; WONG SHING CHUN ; SHIH NENG YANG ; TING PAULINE C ; ROSNER KRISTIN E ; SHIPPS GERALD W JR ; SIDDIQUI M ARSHAD ; YU WENSHENG ; ZHAO LIANYUN ; SIDDIQUI M A ; SCHERING CORP ; SCHERING AG

Assignee(s): SHIPPS GERALD W ; SIDDIQUI M ; MERCK SHARP AND DOHME CORP

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Inventor(s): UMAR FARUK MANSOOR ; VACCARO HENRY ; VINAY M GIRIJAVALLABHAN ; VINCENT S MADISON ; W JR ; W JR SIDDIQUI M ARSHAD BELANGER DAVID B ; ZHU ZHAO NING ; TIN YAU CHAN ; TING PAULINE ; SIDDIQUI M ; SHIPPS GERALD WJR ; SHIPPS GERALD ; SHIPPS GERALD W ; REDDY PANDURANGA ADULLA P ; ROBERT D MAZZOLA ; ROSNER KRISTIN ; REDDY PANDURANGA ; MAZZOLA ROBERT ; MANSOOR UMAR ; KRISTIN E ROSNER ; PANDURANGA A REDDY ; PAULINE C TING ; M ARSHAD SIDDIQUI ; MADISON VINCENT ; KOZLOWSKI JOSEPH ; JOSEPH A KOZLOWSKI ; HENRY A VACCARO ; GUO ZHUYAN ORTH PETER ZHU ZHAONING MAZZOLA ROBERTD ; GUO ZHU YAN ; BELANGER DAVID ; GERALD W JR SHIPPS ; GIRIJAVALLABHAN VINAY ; BRIAN J LAVEY ; BRIAN MC KITTRICK ; DAVID B BELANGER

Agent(s): HOFFMANN EITLE; SCHERING PLOUGH PATENT DEPARTMENT K 6 1 1990 CORP; MERCK PATENT DEPARTMENT K 6 1 1990; JEREMY; KRISHNA G; ERIC A; VALERIE J

Designated states: AE AG AL AM AT AU AZ BA BB BE BF BG BJ BR BW BY BZ CA CF CG CH CI CM CN CO CR CU CY CZ DE DK DM DZ EC EE EG ES FI FR GA GB GD GE GH GM GN GQ GR GT GW HN HR HU ID IE IL IN IS IT JP KE KG KM KN KP KR KZ LA LC LI LK LR LS LT LU LV LY MA MC MD MG MK ML MN MR MW MX MY MZ NA NE NG NI NL NO NZ OM PG PH PL PT RO RS RU SC SD SE SG SI SK SL SM SN SV SY SZ TD TG TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

Title: 3-AMINO-6-ARYL-THIENO[2,3-B]PYRIDIN-2-CARBOXAMIDES, PHARMACEUTICAL PREPARATIONS CONTAINING THE SAME AND THEIR USE AS TNFa INHIBITORS

Abstract: The invention relates to the novel 3-amino-6-aryl-thieno[2,3-b]pyridin-2-carboxamides of general formula (1), to methods for producing them, to pharmaceutical preparations containing said compounds and/or the tautomers and optionally the physiologically acceptable salts obtained therefrom and/or the solvates thereof. The invention also relates to the use of said compounds, their tautomers, salts or solvates as inhibitors of TNFa release.

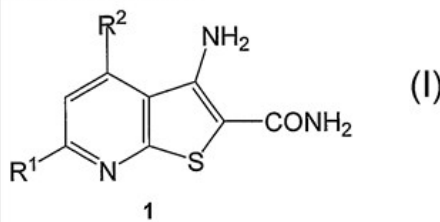
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International (IPC 8-9): A61K31/4365 A61P37/00 C07D495/04 (Advanced/Invention); A61K31/4353 A61P37/00 C07D495/00 (Core/Invention)

CPC: C07D495/04

European: C07D495/04

PatBase - W006074919_A2



Family:

Publication number	Publication date	Application number	Application date
EP1681292 A1	20060719	EP20050000521	20050112
EP1683799 A1	20060726	EP20050000522	20050112
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Priority:

EP20050000521 20050112 EP20050000522 20050112

Probable Assignee: IBFB PHARMA GMBH

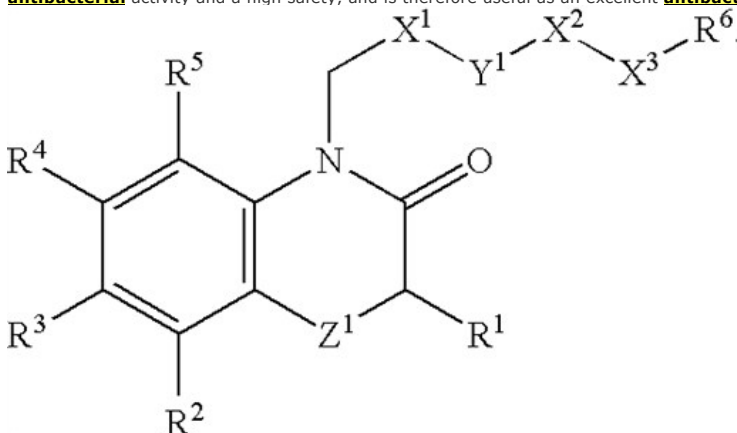
Assignee(s): (std): CURACYTE DISCOVERY GMBH ; DAGHISH MOHAMMED ; HEINICKE JOCHEN ; IBFB PHARMA GMBH ; KROEDEL ANDREAS ; LEISTNER SIEGFRIED ; REICHELTA CLAUDIA ; LUDWIG ALEXANDER ; SCHULZE ALEXANDER

Inventor(s): (std): DAGHISH MOHAMMED ; HEINICKE JOCHEN ; KROEDEL ANDREAS ; LEISTNER SIEGFRIED ; LUDWIG ALEXANDER ; REICHELTA CLAUDIA ; SCHULZE ALEXANDER

Designated states: AE AG AL AM AT AU AZ BA BB BE BF BG BJ BR BW BY BZ CA CF CG CH CI CM CN CO CR CU CY CZ DE DK DM DZ EC EE EG ES FI FR GA GB GD GE GH GM GN GQ GR GW HR HU ID IE IL IN IS IT JP KE KG KM KN KP KR KZ LC LI LK LR LS LT LU LV LY MA MC MD MG MK ML MN MR MW MX MZ NA NE NG NI NL NO NZ OM PG PH PL PT RO RU SC SD SE SG SI SK SL SM SN SY SZ TD TG TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

Title: NOVEL NITROGENATED HETEROCYCLIC COMPOUND AND SALT THEREOF

Abstract: Source: US2010168418A A nitrogen-containing heterocyclic compound represented by the general formula: wherein the dashed line represents a single bond or a double bond; R^1 , R^2 , R^3 , R^4 and R^5 independently represent a hydrogen atom, halogen atom, a lower alkyl, aryl, lower alkoxy or monocyclic heterocyclic group which may be substituted or the like; R^6 represents a lower alkyl, aryl, monocyclic heterocyclic, bicyclic heterocyclic or tricyclic heterocyclic group which may be substituted; X^1 represents a lower alkylene group or the like; X^2 represents a lower alkylene, lower alkenylene or lower alkynylene group which may be substituted; X^3 represents an oxygen atom, sulfur atom, a sulfinyl group, sulfonyl group or the like; Y^1 represents a bivalent cyclic group, containing a nitrogen, which may be substituted or the like; and Z^1 represents a nitrogen atom, a carbon atom which may be substituted or the like, or a salt thereof. The compound or salt has a potent **antibacterial** activity and a high safety, and is therefore useful as an excellent **antibacterial** agent.



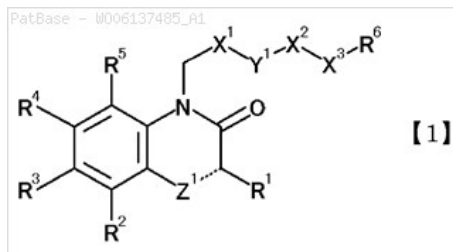
Classifications:

International (IPC 8-9): A61K31/47 A61K31/4709 A61K31/49 A61K31/495 A61K31/496 A61K31/497 A61K31/498 A61K31/538 A61K31/5415 A61K31/542 A61P31/04 C07D215/22 C07D401/06 C07D401/14 C07D405/12 C07D405/14 C07D409/14 C07D413/14 C07D417/14 C07D455/04 C07D471/04 C07D471/06 C07D491/05 C07D491/056 C07D493/04 C07D495/04 C07D498/04 C07D513/04 C07D513/06 (Advanced/Invention); A61K31/47 A61K31/4709 A61K31/49 A61K31/496 A61P31/00 C07D401/00 C07D405/00 C07D409/00 C07D491/00 (Core/Invention)

CPC: C07D401/14 C07D405/14 C07D215/227 C07D401/06 C07D405/12 C07D409/14 C07D413/14 C07D471/04 C07D491/04 C07D495/04 C07D513/04 C07D519/00

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Family:

Publication number	Publication date	Application number	Application date
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EP2468743 A1	20120627	EP20120000147	20060622
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US2010168418 AA	20100701	US20060993652	20060622
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US8329694 BB	20121211	US20060993652	20060622
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Priority:

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WO2006JP312515	20060622	EP20060767173	20060622	JP20070522363	20060622
US20070993652	20071221	US20120463434	20120503		

Probable Assignee: TOYAMA CHEMICAL CO LTD

Assignee(s): (std): USHIYAMA FUMIHITO ; USHIKI YASUNOBU ; TSUTSUI YASUHIRO ; URABE HIROKI ; TAISHO PHARMA CO LTD ; TOYAMA CHEMICAL CO LTD ; TANAKA TADASHI ; ANDO JUNICHI ; KAWAGUCHI YASUKO ; KIYOTO TARO ; MOTONO MAI ; NOGUCHI TOSHIYA

Assignee(s): TAISHO PHARMACEUTICAL CO LTD ; TAISHO PHARMACEUTICAL CO ; TOYAMA CHEMICAL CO

Inventor(s): (std): ANDO JUNICHI ; KAWAGUCHI YASUKO ; KIYOTO TARO ; MOTONO MAI ; NOGUCHI TOSHIYA ; TANAKA TADASHI ; TSUTSUI YASUHIRO ; URABE HIROKI ; USHIKI YASUNOBU ; USHIYAMA FUMIHITO

Agent(s): HARTZ NIKOLAI ; BLODIG WOLFGANG; OBLON SPIVAK MCCLELLAND MAIER AND NEUSTADT LLP

Designated states: AE AG AL AM AT AU AZ BA BB BE BF BG BJ BR BW BY BZ CA CF CG CH CI CM CN CO CR CU CY CZ DE DK DM DZ EC EE EG ES FI FR GA GB GD GE GH GM GN GQ GR GW HN HR HU ID IE IL IN IS IT JP KE KG KM KN KP KR KZ LA LC LI LK LR LS LT LU LV LY MA MC MD MG MK ML MN MR MW MX MZ NA NE NG NI NL NO NZ OM PG PH PL PT RO RS RU SC SD SE SG SI SK SL SM SN SY SZ TD TG TJ TM TN TR TT TZ UA UG US UZ VC VN ZA ZM ZW

Title: ENANTIOMERIC COMPOUNDS WITH **ANTIBACTERIAL** ACTIVITY

Abstract: Source: US2008108651A Novel compounds in enantiomeric excess that are inhibitors of bacterial methionyl synthetase (MetRS) are disclosed. Also disclosed are methods for their preparation and their use in therapy as **antibacterial** agents, and in particular their use in therapy for *Clostridium difficile* infection.

Classifications:
International (IPC 8-9): A01N43/02 A01N43/42 A01N43/90 A01P3/00 A61K31/38 A61K31/41 A61K31/415 A61K31/4365 A61K31/44 A61K31/47 A61K31/4709 A61K31/4743 A61P1/04 A61P1/12 A61P11/00 A61P15/00 A61P17/00 A61P25/00 A61P27/16 A61P31/04 A61P43/00 A61P9/00 C07D215/00 C07D215/18 C07D221/04 C07D405/12 C07D409/12 C07D471/02 C07D471/04 C07D491/02 C07D495/04 C07D498/02 C07D513/02 C07D513/04 C07D515/02 (Advanced/Invention);
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WO08039641 A3	20081204	WO2007US78161	20070911
WO08039642 A2	20080403	WO2007US78173	20070911
WO08039642 A3	20081224	WO2007US78173	20070911

Priority:

US20060826940P 20060926	US20060826957P 20060926	US20060826945P 20060926
US20060826954P 20060926	US20070853477 20070911	US20070853314 20070911
US20070853589 20070911	WO2007US78144 20070911	US20070853636 20070911
WO2007US78124 20070911	EP20070814797 20070911	

Probable Assignee: CRESTONE INC

Assignee(s): (std): GUILLES JOSEPH ; JANJIC NEBOJSA ; GYORKOS ALBERT CHARLES ; STRONG SARAH ; REPLIDYNE INC ; SUN XICHENG ; REPLIDYNE INC US ; CRESTONE INC

Assignee(s): CRESTONE INC6973 CARTER TRAILBOULDERCO80301US ; CARDIOVASCULAR SYSTEMS INC

Inventor(s): (std): GUILLES JOSEPH ; GYORKOS ALBERT CHARLES ; JANJIC NEBOJSA ; STRONG SARAH ; SUN XICHENG ; XICHENG SUN ; SARAH STRONG ; NEBOJSA JANJIC ; JOSEPH GUILLES ; CHARLES GYORKOS ALBERT ; GYORKOS ALBERT C

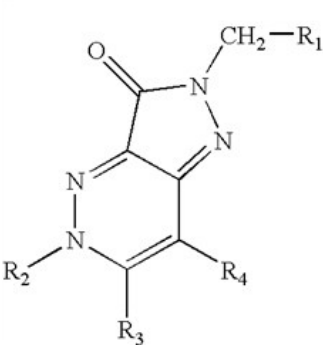
Inventor(s): GYORKOS ALBERT ; GUILLES JOSEPHUS ; ALBERT CHARLES GYORKOS ; SUN XICHENGUS ; STRONG SARAHUS ; JANJIC NEBOJSAUS ; GYORKOS ALBERT CHARLESUS

Agent(s): DOERRIES HANS ULRICH; SWANSON AND BRATSCHUN LLC; SWANSON BARRY J ET AL; SWANSON AND BRATSCHUN LLC ET AL

Designated states: AE AG AL AM AT AU AZ BA BB BE BF BG BH BJ BR BW BY BZ CA CF CG CH CI CM CN CO CR CU CY CZ DE DK DM DO DZ EC EE EG ES FI FR GA GB GD GE GH GM GN GQ GR GT GW HN HR HU ID IE IL IN IS IT JP KE KG KM KN KP KR KZ LA LC LI LK LR LS LT LU LV LY MA MC MD ME MG MK ML MN MR MT MW MX MY MZ NA NE NG NI NL NO NZ OM PG PH PL PT RO RS RU SC SD SE SG SI SK SL SM SN SV SY SZ TD TG TJ TM TN TR TT TZ UA UG US UZ VC VN ZA ZM ZW

Title: SUBSTITUTED 2,5-DIHYDRO-3H-PYRAZOLO[4,3-C]PYRIDAZIN-3-ONE DERIVATIVES, PREPARATION THEREOF AND THERAPEUTIC USE OF THE SAME

Abstract: Source: US2009281107A The invention relates to compounds having the formula (I):



Also disclosed are the method of preparation and their use in therapy.

Classifications:

International (IPC 8-9): A61K31/4985 A61K31/5025 A61P1/00 A61P1/04 A61P1/06 A61P1/08 A61P1/12 A61P1/16 A61P19/02 A61P23/00 A61P25/00 A61P25/04 A61P25/06 A61P25/16 A61P25/18 A61P25/22 A61P25/24 A61P25/28 A61P25/30 A61P25/34 A61P29/00 A61P3/00 A61P3/04 A61P3/06 A61P3/10 A61P37/00 A61P43/00 A61P9/12 C07D231/20 C07D237/06 C07D249/08 C07D285/06 C07D333/06 C07D487/04 C07D495/04 C07D519/00 (Advanced/Invention); A61K31/5025 A61P1/00 A61P19/00 A61P25/00 A61P29/00 A61P3/00 A61P37/00 A61P43/00 A61P9/00 C07D231/00 C07D237/00 C07D249/00 C07D285/00 C07D333/00 C07D487/00 C07D495/00 C07D519/00 (Core/Invention); C07D (Subclass/Invention)

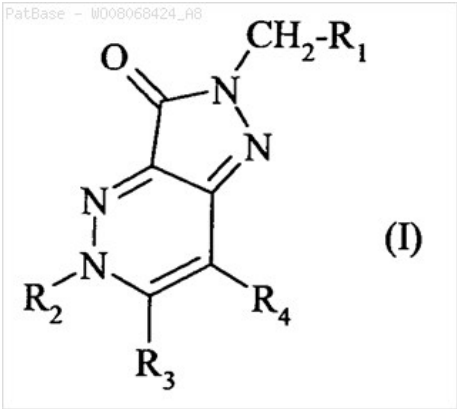
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CPC: C07D231/20 C07D237/06 C07D249/08 C07D285/06 C07D333/06 C07D487/04 C07D495/04

European: C07D231/20 C07D237/06 C07D249/08 C07D285/06 C07D333/06 C07D487/04 C07D495/04

US: 514/248 544/236 544/236S

Wherein R₁, R₂, R₃ and R₄ are as described herein.



Family:

Publication number	Publication date	Application number	Application date
AR063898 AA	20090225	AR2007P105186	20071122
AT494290 E	20110115	AT20070870295T	20071119
AU2007330652 AA	20080612	AU20070330652	20071119
BRPI0719291 A2	20140225	BR2007PI19291	20071119
CA2668196 AA	20090501	CA20072668196	20071119
CL2007003346 A1	20080704	CL20070003346	20071122
CL33462007 A1	20080704	CL20070003346	20071122
CN101541802 A	20090923	CN200780043189	20071119
DE602007011815 D1	20110217	DE200760011815T	20071119
EP2094706 A2	20090902	EP20070870295	20071119
EP2094706 B1	20110105	EP20070870295	20071119
FR2909090 A1	20080530	FR20060010371	20061123
FR2909090 B1	20090109	FR20060010371	20061123
IL198523 A0	20100217	IL20090198523	20090503
INO1665KN2009 A	20090612	IN2009KN01665	20090504
JP2010510297 T2	20100402	JP20090537670T	20071119
KR20090092774 A	20090901	KR20097010476	20071119
MX2009005447 A1	20090807	MX20090005447	20090522
PE14962008 A1	20090104	PE20070001610	20071120
RU2009123841 A	20101227	RU20090123841	20071119
US2009281107 AA	20091112	US20090468294	20090519
US7915258 BB	20110329	US20090468294	20090519
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WO08068424 A3	20080724	WO2007FR01889	20071119
WO08068424 A8	20090702	WO2007FR01889	20071119

Priority:

FR20060010371 20061123 WO2007FR01889 20071119

Probable Assignee: SANOFI AVENTIS

Assignee(s): (std): CONGY CHRISTIAN ; DOS SANTOS VICTOR ; RINALDI CARMONA MURIELLE ; ROUQUETTE ARNAUD ; SANOFI AVENTIS SA ; SANOFI AVENTIS ; VAN BROECK DIDIER ; SANOFI SA

Assignee(s): SANOFI AVENTIS SOC ANONYME ; SANOFI ; SANOFI AVENTIS SOCIETE ANONYME

Inventor(s): (std): MURIELLE RINALDI CARMONA ; SANTOS VICTOR DOS ; VICTOR DOS SANTOS ; VAN BROECK DIDIER ; ROUQUETTE ARNAUD ; RINALDI CARMONA MURIELLE ; DOS SANTOS VICTOR ; DIDIER BROECK VAN ; BROECK DIDIER VAN ; BROEK DIDIER VAN ; CONGY CHRISTIAN DOS SANTOS VIC ; CONGY CHRISTIAN ; CHRISTIAN CONGY ; ARNAUD ROUQUETTE

Inventor(s): DIDIER VAN BROECK ; DIDIER VAN BROEK ; CONGY CHRISTIAN DOS SANTOS VICTOR RINALDI... ; CONGY CHRISTIAN DOS SANTOS VICTOR RINALDI CARMONA MURIELLE ROUQUETTE ARNAUD VAN BROECK DIDIER

Agent(s): WERNER ALAIN HENRI; ANDREA Q RYAN SANOFI AVENTIS US LLC; SERENA; SCULLY SCOTT MURPHY AND PRESSER PC; KUGEL DOMINIQUE ET AL

Designated states: AE AG AL AM AT AU AZ BA BB BE BF BG BH BJ BR BW BY BZ CA CF CG CH CI CM CN CO CR CU CY CZ DE DK DM DO DZ EC EE EG ES FI FR GA GB GD GE GH GM GN GQ GR GT GW HN HR HU ID IE IL IN IS IT JP KE KG KM KN KP KR KZ LA LC LI LK LR LS LT LU LV LY MA MC MD ME MG MK ML MN MR MT MW MX MY MZ NA NE NG NI NL NO NZ OM PG PH PL PT RO RS RU SC SD SE SG SI SK SL SM SN SV SY SZ TD TG TJ TM TN TR TT TZ UA UG US UZ VC VN ZA ZM ZW

Title: SUBSTITUTED PYRROLIDINE AMIDES, THE PRODUCTION THEREOF, AND THE USE THEREOF AS MEDICATIONS

Abstract: Source: US2010099664A The object of the present invention is novel substituted pyrrolidine amides of the general formula (I) in which D, L, E, G, J, M, L¹, L², R⁴, and R⁵ are defined as in the specification, the tautomers, enantiomers, diastereomers, mixtures, and salts thereof, particularly physiologically tolerated salts with inorganic or organic acids or bases having valuable properties.

Classifications:

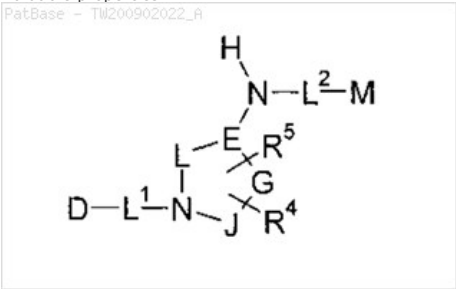
International (IPC 8-9): A61K31/404 A61K31/42 A61K31/4365 A61K31/4535 A61K31/4725 A61K31/4985 A61K31/55 A61K31/551 A61P11/00 A61P19/02 A61P25/16 A61P25/28 A61P29/00 A61P35/00 A61P43/00 A61P7/00 A61P7/02 A61P9/00 C07D207/00 C07D209/00 C07D223/00 C07D223/16 C07D401/00 C07D401/06 C07D401/14 C07D403/06 C07D405/12 C07D405/14 C07D409/14 C07D413/14 C07D417/00 C07D417/14 C07D419/00 C07D419/14 C07D471/04 C07D487/02 C07D487/04 C07D495/00 C07D495/02 C07D495/04 C07D513/02 C07D513/04 (Advanced/Invention); A61K31/404 A61K31/4365 A61K31/4725 A61K31/4985 A61K31/55 A61K31/551 A61P11/00 A61P19/02 A61P25/16 A61P25/28 A61P29/00 A61P35/00 A61P43/00 A61P7/02 A61P9/00 C07D403/06 (Advanced/Non-invention); A61K31/403 A61K31/42 A61K31/4353 A61K31/472 A61K31/4985 A61K31/55 A61K31/551 A61P11/00 A61P19/00 A61P25/00 A61P29/00 A61P35/00 A61P43/00 A61P7/00 A61P9/00 C07D401/00 C07D403/00 C07D405/00 C07D409/00 C07D417/00 C07D419/00 C07D487/00 C07D495/00 C07D513/00 (Core/Invention)

International (IPC 1-7): A61K31/4725 A61K31/5377 A61K31/55 A61P7/02 C07D409/14 C07D413/14 C07D495/04 C07D513/04

CPC: C07D419/14 C07D401/06 C07D401/14 C07D495/04 C07D417/14

European: C07D401/06 C07D401/14 C07D417/14 C07D419/14 C07D495/04

US: 514/213.01 514/213.010S 514/215 514/301 514/301S 540/593 540/593S 540/594 540/594S 546/114 546/114S



Family:

Publication number	Publication date	Application number	Application date
AR065852 AA	20090708	AR2008P101240	20080326
CA2682012 AA	20081002	CA20082682012	20080326
EP1975165 A1	20081001	EP20070105053	20070327
EP2132193 A1	20091216	EP20080718234	20080326
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US2010099664 AA	20100422	US20080531343	20080326
US8309542 BB	20121113	US20080531343	20080326
UY30979 A1	20081031	UY20080030979	20080325
WO08116881 A1	20081002	WO2008EP53568	20080326

Priority:

EP20070105053 20070327 WO2008EP53568 20080326 EP20080718234 20080326

Probable Assignee: BOEHRINGER INGELHEIM INT GMBH

Assignee(s): (std): BOEHRINGER INGELHEIM INT ; BOEHRINGER INGELHEIM PHARMA ; DAHMANN GEORG ; PRIEPKE HENNING ; SCHULER METZ ANNETTE ; GERLACH KAI ; WIENEN WOLFGANG ; NAR HERBERT

Assignee(s): BOEHRINGER INGELHEIM PHARMA GMBH AND CO KG ; BOEHRINGER INGELHEIM INT GMBH ; BOEHRINGER INGELHEIM INTERNATIONAL GMBH

Inventor(s): (std): DAHMANN GEORGE ; GERLACH KAI ; DAHMANN GEORG ; NAR HERBERT ; PRIEPKE HENNING ; SCHULER METZ ANNETTE ; WIENEN WOLFGANG

Inventor(s): WOLFGANG WIENEN ; ANNETTE SCHULER METZ ; SCHULER-METZ, ANNETTE ; DAHMANN GEORG AND ; HENNING PRIEPKE ; HERBERT NAR ; KAI GERLACH ; DIE ERFINDERNENNUNG LIEGT NOCH NICHT VOR ; GEORG DAHMANN

Agent(s): HAMMANN HEINZ ET AL; HAMMANN HEINZ; SIMON ELKE ANNA MARIA; MICHAEL P MORRIS BOEHRINGER INGELHEIM USA CORP; MICHAEL P; EDOUARD G; USHA R

Designated states: AE AG AL AM AO AT AU AZ BA BB BE BF BG BH BJ BR BW BY BZ CA CF CG CH CI CM CN CO CR CU CY CZ DE DK DM DO DZ EC EE EG ES FI FR GA GB GD GE GH GM GN GQ GR GT GW HN HR HU ID IE IL IN IS IT JP KE KG KM KN KP KR KZ LA LC LI LK LR LS LT LU LV LY MA MC MD ME MG MK ML MN MR MT MW MX MY MZ NA NE NG NI NL NO NZ OM PG PH PL PT RO RS RU SC SD SE SG SI SK SL SM SN SV SY SZ TD TG TJ TM TN TR TT TZ UA UG US UZ VC VN ZA ZM ZW

Title: **ANTIBACTERIAL** AMIDE AND SULFONAMIDE SUBSTITUTED HETEROCYCLIC UREA COMPOUNDS

Abstract: Source: US2012015941A The present invention provides novel amide and sulfonamide substituted heterocyclic urea compounds having useful **antibacterial** activity. Use of these compounds as pharmaceutical compositions and method of their production are also provided.

Classifications:

International (IPC 8-9): A01N43/78 A61K31/425 A61K31/426 A61K31/427 A61K31/433 A61K31/437 A61K31/4375 A61K31/4439 A61K31/497 A61K31/498 A61K31/501 A61K31/506 A61K31/513 A61K31/519 A61K31/5377 A61K31/675 A61P31/04 C07D239/47 C07D277/20 C07D277/28 C07D277/48 C07D285/08 C07D417/04 C07D417/06 C07D417/12 C07D417/14 C07D471/04 C07D487/04 C07D491/048 C07D495/04 C07D498/04 C07D513/04 C07F9/6539 (Advanced/Invention); A01N43/72 A61K31/425 (Core/Invention)
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US: 514/232.2 514/232.200P 514/236.2 514/236.200S 514/236.8 514/236.800S 514/249 514/249S 514/252.05 514/252.050S 514/255.05 514/255.050S 514/256 514/256S 514/259.3 514/259.300S 514/272 514/274 514/300 514/300S 514/301 514/301S 514/342 514/342S 514/361 514/361S 514/364 514/364S 514/371 514/371S 514/92 514/92S 544/133 544/133S 544/134 544/134S 544/238 544/238S 544/281 544/281S 544/298 544/316 544/333 544/333S 544/355 544/355S 544/405 544/405S 544/82 544/82S 546/114 546/114S 546/121 546/121S 546/268.7 546/268.700S 546/270.7 546/270.700S 548/119 548/119S 548/125 548/125S 548/127 548/127S 548/128 548/128S 548/196 548/196S

Family:

Publication number	Publication date	Application number	Application date
EP2200440 A1	20100630	EP20080782264	20080723
EP2200440 A4	20120104	EP20080782264	20080723
JP2010534673 T2	20101111	JP20100518355T	20080723
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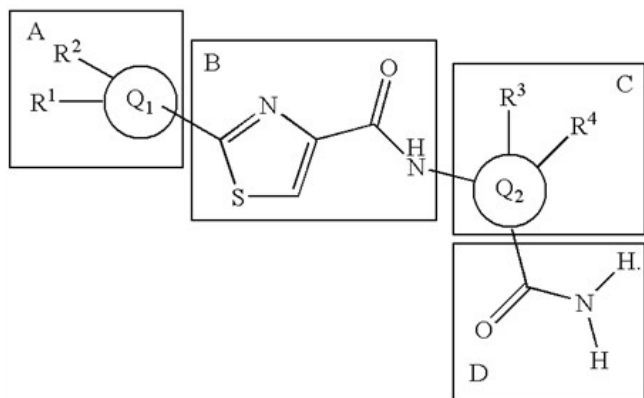
Priority:
US20070961634P 20070723 US20080022725P 20080122 US20080022725 20080122
WO2008US70893 20080723 US20080669634 20080723

Probable Assignee: CRESTONE INC
Assignee(s): (std): CRESTONE INC ; GUILLES JOSEPH ; JARVIS THALE ; REPLIDYNE INC ; SUN XICHENG ; STRONG SARAH ; JARVIS THALE CROSS ; ROHLOFF JOHN C ; QIU JIAN
Assignee(s): CARDIOVASCULAR SYSTEMS INC
Inventor(s): (std): JARVIS THALE ; SUN XICHENG ; STRONG SARAH ; ROHLOFF JOHN C ; QIU JIAN ; JARVIS THALE CROSS ; GUILLES JOSEPH
Agent(s): DOERRIES HANS ULRICH; SWANSON AND BRATSCHUN LLC; SWANSON AND BRATSCHUN LLC ET AL
Designated states: AE AG AL AM AO AT AU AZ BA BB BE BF BG BH BJ BR BW BY BZ CA CF CG CH CI CM CN CO CR CU CY CZ DE DK DM DO DZ EC EE EG ES FI FR GA GB GD GE GH GM GN GQ GR GT GW HN HR HU ID IE IL IN IS IT JP KE KG KM KN KP KR KZ LA LC LI LK LR LS LT LU LV LY MA MC MD ME MG MK ML MN MR MT MW MX MY MZ NA NE NG NI NL NO NZ OM PG PH PL PT RO RS RU SC SD SE SG SI SK SL SM SN ST SV SY SZ TD TG TJ TM TN TR TT TZ UA UG US UZ VC VN ZA ZM ZW

Title: NOVEL 2-ARYLTHIAZOLE-4-CARBOXAMIDE DERIVATIVES, THEIR PREPARATION AND USE AS PHARMACEUTICALS

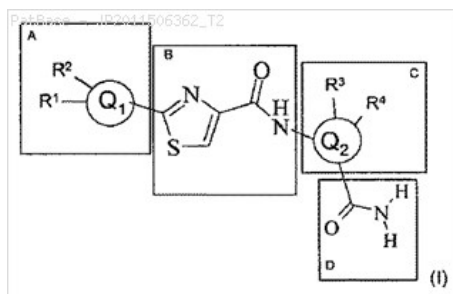
Abstract: Source: US2009163486A The present invention relates to 2-arylthiazole-4-carboxamide derivatives of the formula (I), the use thereof as medicament for the treatment of various disorders, and processes for the preparation thereof

(I)



Classifications:

International (IPC 8-9): A61K31/425 A61K31/426 A61K31/427 A61K31/535 A61K31/538 A61P1/00 A61P1/16 A61P11/00 A61P11/06 A61P13/12 A61P15/08 A61P17/00 A61P17/04 A61P17/06 A61P17/14 A61P19/02 A61P21/00 A61P25/00 A61P27/02 A61P27/16 A61P29/00 A61P3/10 A61P35/00 A61P35/02 A61P37/02 A61P37/06 A61P37/08 A61P43/00 A61P5/00 A61P5/14 A61P7/00 A61P7/04 A61P7/06 A61P9/00 C07D277/20 C07D277/32 C07D277/56 C07D413/04 C07D417/04 C07D417/10 C07D417/12 C07D417/14 C07D495/04 (Advanced/Invention); A61P1/00 A61P1/16 A61P11/00 A61P11/06 A61P13/12 A61P15/08 A61P17/00 A61P17/04 A61P17/06 A61P17/14 A61P19/02 A61P21/00 A61P25/00 A61P27/02 A61P27/16 A61P3/10 A61P35/00 A61P35/02 A61P37/02 A61P37/06 A61P5/00 A61P5/14 A61P7/00 A61P7/04 A61P7/06 A61P9/00 C07B61/00 (Advanced/Non-invention); A61K31/425 A61P37/00 C07D277/00 C07D417/00 C07D495/00 (Core/Invention)
CPC: C07D277/56 C07D417/04 C07D417/12 C07D417/14 C07D495/04
European: C07D277/56 C07D417/04 C07D417/12 C07D417/14 C07D495/04
US: 514/230.5 514/230.500P 514/365 514/365S 544/105 544/105S 548/200 548/200S



Family:

Publication number	Publication date	Application number	Application date
AT509013 E	20110515	AT20080877913T	20081202
CA2706813 AA	20100526	CA20082706813	20081202
EP2070916 A1	20090617	EP20070076069	20071210
EP2240457 A1	20101020	EP20080877913	20081202
EP2240457 B1	20110511	EP20080877913	20081202
ES2364530 T3	20110906	ES20080877913T	20081202
JP2011506362 T2	20110303	JP20100537291T	20081202
JP5348705 B2	20131120	JP20100537291T	20081202
US2009163486 AA	20090625	US20080331775	20081210
US8163739 BB	20120424	US20080331775	20081210
WO09074247 A1	20090618	WO2008EP10188	20081202
WO09074247 A8	20100715	WO2008EP10188	20081202

Priority:

EP20070076069 20071210 US20080022686P 20080122 US20080331775 20081210
 WO2008EP10188 20081202 EP20080877913 20081202

Probable Assignee: BAYER INTELLECTUAL PROPERTY GMBH

Assignee(s): (std): NGUYEN DUY ; BOTHE ULRICH ; VON BONIN ARNE ; BOEMER ULF ; GUENTHER JUDITH ; ULF BOMER ; DUY NGUYEN ; JUDITH GUENTHER ; ULRICH BOTHE ; BAYER SCHERING PHARMA AG ; BOMER ULF ; ARNE VON BONIN ; BAYER PHARMA AG

Assignee(s): BAYER SCHERING PHARMA AKTIENGESELLSCHAFT ; BAYER PHARMA AKTIENGESELLSCHAFT ; BAYER INTELLECTUAL PROPERTY GMBH

Inventor(s): (std): ARNE VON BONIN ; BOEMER ULF ; BOMER ULF ; BOTHE ULRICH ; DUY NGUYEN ; GUENTHER GUDITH ; GUENTHER JUDITH ; JUDITH GUENTHER ; NGUYEN DUY ; ULF BOMER ; ULRICH BOTHE ; VON BONIN ARNE

Agent(s): MILLEN WHITE ZELANO AND BRANIGAN PC; BAYER SCHERING PHARMA AKTIENGESELLSCHAFT

Designated states: AE AG AL AM AO AT AU AZ BA BB BE BF BG BH BJ BR BW BY BZ CA CF CG CH CI CM CN CO CR CU CY CZ DE DK DM DO DZ EC EE EG ES FI FR GA GB GD GE GH GM GN GQ GR GT GW HN HR HU ID IE IL IN IS IT JP KE KG KM KN KP KR KZ LA LC LI LK LR LS LT LU LV LY MA MC MD ME MG MK ML MN MR MT MW MX MY MZ NA NE NG NI NL NO NZ OM PG PH PL PT RO RS RU SC SD SE SG SI SK SL SM SN ST SZ TD TG TJ TM TN TR TT TZ UA UG US UZ VC VN ZA ZM ZW

Title: IMIDAZOLE CARBONYL COMPOUND

Abstract: Source: US2010311966A An antibiotic compound having a novel mechanism of action, weak cytotoxicity, high solubility in water, effective in inhibiting both DNA gyrase GyrB and topoisomerase IV ParE subunits, and having **antibacterial** activity.

Classifications:

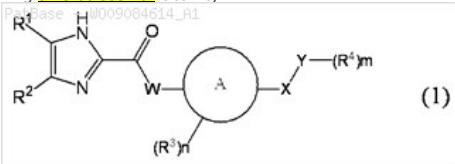
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European: C07D233/66 C07D401/12 C07D401/14 C07D403/12 C07D409/14 C07D413/12 C07D417/12 C07D417/14 C07D487/06 C07D487/12 C07D495/04 C07D498/04 C07D513/04 C07D519/00

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Family:

Publication number	Publication date	Application number	Application date
BRPI0821855 A2	20150616	BR2008PI21855	20081226
CA2710959 AA	20090709	CA20082710959	20081226
CA2710959 C	20131001	CA20082710959	20081226
CN101959882 A	20110126	CN200880127756	20081226
CN101959882 B	20130911	CN200880127756	20081226
EP2226322 A1	20100908	EP20080867971	20081226
EP2226322 A4	20110608	EP20080867971	20081226
EP2226322 B1	20150121	EP20080867971	20081226
ES2535085 T3	20150505	ES20080867971T	20081226
IN04669CN2010 A	20110211	IN2010CN04669	20100726
JP2014196369 A2	20141016	JP20140149113	20140722
JP5586234 B1	20140910	JP20090548077T	20081226
KR20100098657 A	20100908	KR20107013997	20081226
TW200932221 A	20090801	TW20080150632	20081225
US2010311966 AA	20101209	US20080811004	20081226
US2014073622 AA	20140313	US20130027077	20130913
US8536197 BB	20130917	US20080811004	20081226
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Priority:

JP20070337693	20071227	WO2008JP73686	20081226	US20100811004	20100628
US20130027077	20130913	JP20090548077	20081226	EP20080867971	20081226
JP20140149113	20140722				

Probable Assignee: DAIICHI SANKYO CO LTD

Assignee(s): (std): FUJISAWA TETSUNORI ; MASUDA NOBUHISA ; TAKESHITA HIROSHI ; YOKOMIZO AKI ; KAGOSHIMA YOSHIKO ; SONEDA TSUYOSHI ; YAMAMOTO YUKO ; HOSOKAWA TAKAFUMI ; KONOSU TOSHIYUKI ; NOGUCHI TETSUJI ; KUROYANAGI JUNICHI ; UCHIDA TAKUYA ; ACHIWA ISSEI ; DAIICHI SANKYO CO LTD

Assignee(s): DAIICHI SANKYO COMPANY LIMITED ; DAIICHI SANKYO CO

Inventor(s): (std): ACHIWA ISSEI ; AKI YOKOMIZO ; FUJISAWA TETSUNORI ; HIROSHI TAKESHITA ; HOSOKAWA TAKAFUMI ; ISSEI ACHIWA ; JUNICHI KUROYANAGI ; KAGOSHIMA YOSHIKO ; KONOSU TOSHIYUKI ; KUROYANAGI JUNICHI ; MASUDA NOBUHISA ; NOBUHISA MASUDA ; NOGUCHI TETSUJI ; SONEDA TSUYOSHI ; TAKAFUMI HOSOKAWA ; TAKESHITA HIROSHI ; TAKUYA UCHIDA ; TETSUJI NOGUCHI ; TETSUNORI FUJISAWA ; TOSHIYUKI KONOSU ; TSUYOSHI SONEDA ; UCHIDA TAKUYA ; YAMAMOTO YUKO ; YOKOMIZO AKI ; YOSHIKO KAGOSHIMA ; YUKO YAMAMOTO ; TAKESHITA YUTAKA ; SONEDA GO ; MIKOJIMA YOSHIKO ; HOSOKAWA TAKASHI ; ACHIWA KAZUNARI

Agent(s): FAIRBAIRN ANGUS CHISHOLM; CHRISTENSEN OCONNOR JOHNSON KINDNESS PLLC; ISHIBASHI KOKI ET AL

Designated states: AE AG AL AM AO AT AU AZ BA BB BE BF BG BH BJ BR BW BY BZ CA CF CG CH CI CM CN CO CR CU CY CZ DE DK DM DO DZ EC EE EG ES FI FR GA GB GD GE GH GM GN GQ GR GT GW HN HR HU ID IE IL IN IS IT JP KE KG KM KN KP KR KZ LA LC LI LR LS LT LU LV LY MA MC MD ME MG MK ML MN MR MT MW MX MY MZ NA NE NG NI NL NO NZ OM PG PH PL PT RO RS RU SC SD SE SG SI SK SL SM SN ST SV SY SZ TD TG TJ TM TN TR TT TZ UA UG US UZ VC VN ZA ZM ZW

Title: COMPOUNDS AND COMPOSITIONS AS TLR ACTIVITY MODULATORS

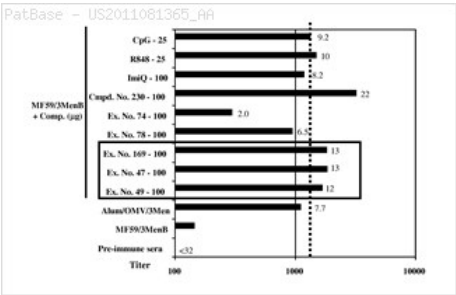
Abstract: Source: US2011081365A The invention provides a novel class of compounds, pharmaceutical compositions comprising such compounds and methods of using such compounds to treat or prevent diseases or disorders associated with Toll-Like Receptors, including TLR7 and TLR8. In one aspect, the compounds are useful as adjuvants for enhancing the effectiveness of a vaccine (formula I) wherein: X3 is N; X4 is N Or CR3; X5 is -CR4-CR5.

Classifications:

International (IPC 8-9): A61K31/4353 A61K31/4375 A61K31/438 A61K31/44 A61K31/4745 A61K31/496 A61K31/4985 A61K31/519 A61K31/5377 A61K31/675 A61K39/00 A61K39/02 A61K39/095 A61K39/12 A61K39/39 A61P1/04 A61P11/00 A61P11/02 A61P11/06 A61P17/00 A61P17/04 A61P17/06 A61P19/02 A61P25/00 A61P29/00 A61P31/04 A61P31/18 A61P35/00 A61P35/02 A61P37/00 A61P37/02 A61P37/04 A61P37/06 A61P37/08 A61P43/00 C07D C07D221/12 C07D239/70 C07D413/14 C07D471/00 C07D471/04 C07D471/12 C07D471/14 C07D491/056 C07D491/12 C07D491/147 C07D495/04 C07F9/40 (Advanced/Invention); A61K31/4375 A61P11/06 A61P37/02 C07D471/04 C07D471/12 C07K14/22 (Advanced/Non-invention); A61K31/4353 A61P37/00 C07D221/00 C07D471/00 C07D491/00 C07D495/00 (Core/Invention); A61K31/4375 A61P37/02 C07D471/04 (Core/Non-invention); C07D (Subclass/Invention)

International (IPC 1-7): A61K31/4375 A61K31/4985 A61P1/04 A61P1/12 A61P11/00 A61P11/06 A61P29/00 A61P31/00 A61P35/00 A61P37/04 C07D221/12 C07D471/04 C07D471/12 C07D491/056 C07D491/12 C07D495/04 **CPC:** C07D471 C07D221 C07D491 C07D495 C07D471/14 C07D471/04 C07D221/12 C07D491/056 C07D495/04 **European:** C07D221/12 C07D471/04 C07D491/056 C07D495/04

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Family:

Publication number	Publication date	Application number	Application date
AR071281 AA	20100609	AR2009P100743	20090303
AU2009222105 AA	20090911	AU20090222105	20090227
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CA2716706 AA	20100823	CA20092716706	20090227
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EP2268618 A1	20110105	EP20090718298	20090227
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HN2010001759 A	20121210	HN20100001759	20100903
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US895577 BB	20141125	US20130867752	20130422
VN12681 A1	20140625	VN20100002633	20090227
WO09111337 A1	20090911	WO2009US35563	20090227

Priority:

US20080033139P 20080303	US20090148336P 20090129	WO2009US35563 20090227
US20090921129 20090227	US20130867752 20130422	US20100921129 20101206

Probable Assignee: NOVARTIS AG

Assignee(s): (std): IRM LLC ; LI YONGKAI ; MISHRA PRANAB ; SINGH MANMOHAN ; NOVARTIS AG ; NOVARTIS 35 ; NOVARTIS INT AG ; ZHANG XIAOYUE ; WU TOM YAO HSIANG ; ZOU YEFEN ; SKIBINSKI DAVID ; VALIANTE NICHOLAS ; CORTEZ ALEX

Assignee(s): DEFENSE THREAT REDUCTION AGENCY DEPT OF DEFENSE US GOV ; NOVARTIS A G ; NOVARTIS AG IRM LLC ; NOVARTIS INT PHARMACEUTICAL LTD ; NOVARTIS VACCINES AND DIAGNOSTICS INC ; NOVARTIS VACCINES AND DIAGNOSTICS SRL

Inventor(s): (std): ALEX CORTEZ ; DAVID SKIBINSKI ; LI YONG KAI ; NICHOLAS VALIANTE ; PRANAB MISHRA ; MANMOHAN SINGH ; WO TOM YAO HSIANG ; XIAOYUE ZHANG ; YAO HSIANG WU TOM ; YEFEN ZOU ; YONGKAI LI ; ZHANG XIAO YUE ; ZOU YEFEN ; ZHANG XIAOYUE ; WU TOM YAO HSIANG ; VALIANTE NICHOLAS ; SKIBINSKI DAVID ; SINGH MANMOHAN ; MISHRA PRANAB ; LI YONGKAI ; CORTEZ ALEX ; ZOU YE FEN

Inventor(s): ZOU, Yefen ; ZHANG, Xiaoyue ; WU, Tom Yao-Hsiang ; MISHRA, Pranab ; SINGH, Manmohan ; SKIBINSKI, David ; TOM YAO HSIANG WU ; VALIANTE, Nicholas ; LI, Yongkai ; CORTEZ, Alex

Agent(s): KIDDLE SIMON JOHN; DANIEL E; GENOMICS INSTITUTE OF THE NOVARTIS RESEARCH FOUNDATION; GENOMICS INST OF NOVARTIS RESEARCH FOUNDATION; RAYMOND DANIEL E ET AL

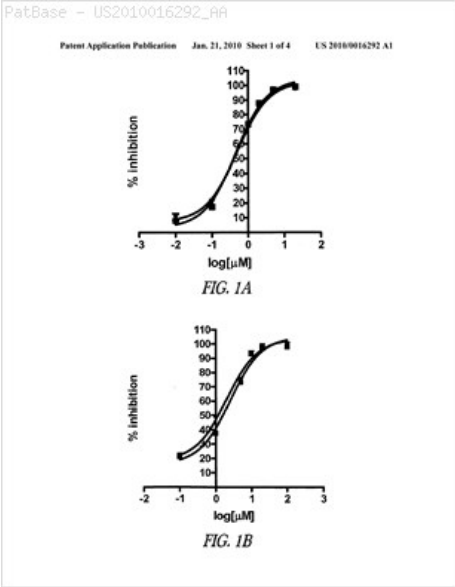
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Title: INHIBITORS OF LETHAL FACTOR PROTEASE

Abstract: Source: US2010016292A The invention provides compounds that can efficiently and specifically inhibit bacterial toxins, such as inhibit the lethal factor (LF) protease activity of anthrax toxin and/or botulinum neurotoxin type A. The invention also provides methods for inhibiting proteases, such as lethal factor protease, as well as methods for treating bacterial infections, such as anthrax and botulinum.

Classifications:

International (IPC 8-9): A61K31/427 A61K31/4427 A61K31/5377 A61K31/551 C07D277/04 C07D413/06 C07D417/06 (Advanced/Invention)
CPC: A61K31/427 A61K31/4427 A61K31/5377 A61K31/551 C07D417/06 C07D417/14 C07D491/04 C07D495/04
European: A61K31/427 A61K31/4427 A61K31/5377 A61K31/551 C07D417/06 C07D417/14 C07D491/04 C07D495/04
US: 514/218 514/236.5 514/236.500S 514/341 514/341S 514/365 514/365S 514/369 544/133 544/133S 546/269.7 546/269.700S 548/183 548/183S



Family:

Publication number	Publication date	Application number	Application date
US2010016292 AA	20100121	US20080176058	20080718
US7947717 BB	20110524	US20080176058	20080718

Priority:

US20080176058 20080718

Probable Assignee: BURNHAM INST FOR MEDICAL RESEARCH

Assignee(s): (std): BURNHAM INST ; BURNHAM INST MEDICAL RESEARCH

Assignee(s): BURNHAM INSTITUTE FOR MEDICAL RESEARCH ; THE BURNHAM INSTITUTE ; BURNHAM INST FOR MEDICAL RESEARCH

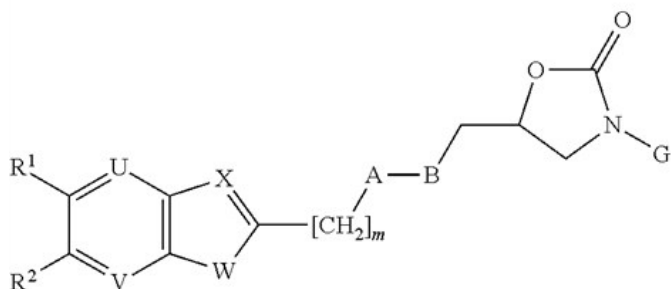
Inventor(s): (std): PELLECCIA MAURIZIO

Agent(s): SCHWEGMAN LUNDBERG AND WOESSNER PA

Title: 2-BENZOTHIOPHENYL- AND 2-NAPHTHYL-OXAZOLIDINONES AND THEIR AZAISOSTERE ANALOGUES AS **ANTIBACTERIAL** AGENTS

Abstract: Source: US2011195949A The invention relates to **antibacterial** compounds of formula (I)

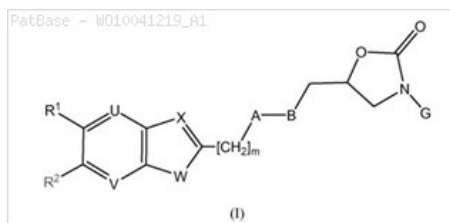
(I)



wherein U, V, W, X, R¹, R², m, A, B and G are as defined in the description, to pharmaceutically acceptable salts of such compounds and to the use of these compounds in the manufacture of a medicament.

Classifications:

International (IPC 8-9): A61K31/422 A61K31/498 A61K31/538 A61K31/5415
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C07D495/04 (Advanced/Invention);
A61K31/422 A61P31/00 C07D413/00 C07D417/00 C07D495/00 (Core/Invention)
CPC: C07D413/14 C07D417/04 C07D417/14 C07D495/04
European: C07D413/14 C07D417/04 C07D417/14 C07D495/04
US: 514/210.21 514/210.210P 514/224.2 514/224.200S 514/230.5 514/230.500S
544/105 544/105S 544/52 544/52S



Family:

Publication number	Publication date	Application number	Application date
CA2738775 AA	20100415	CA20092738775	20091009
CN102164915 A	20110824	CN200980138040	20091009
EP2346862 A1	20110727	EP20090737476	20091009
EP2346862 B1	20120912	EP20090737476	20091009
ES2395491 T3	20130213	ES20090737476T	20091009
JP2012505201 T2	20120301	JP20110530619T	20091009
US2011195949 AA	20110811	US20090123707	20091009
WO10041219 A1	20100415	WO2009IB54434	20091009

Priority:

WO2008IB54168 20081010 WO2009IB54434 20091009

Probable Assignee: ACTELION PHARMACEUTICALS LTD

Assignee(s): (std): ACTELION PHARMACEUTICALS LTD ; EGGER VERENA ; GUDE MARKUS ; HUBSCHWERLEN CHRISTIAN ; SURIVET JEAN PHILIPPE ; ZUMBRUNN ACKLIN CORNELIA ; RUEEDI GEORG

Assignee(s): KAEGI EGGER VERENA

Inventor(s): (std): CHRISTIAN HUBSCHWERLEN ; CORNELIA ZUMBRUNN ACKLIN ; EGGER VERENA ; GEORG RUEEDI ; GUDE MARKUS ; HUBSCHWERLEN CGRISTEN ; HUBSCHWERLEN CHRISTIAN ; JEAN PHILIPPE SURIVET ; KAEGI EGGER VERENA ; MARKUS GUDE ; RUEEDI GEORG ; SURIVET JEAN PHILIPPE ; VERENA EGGER ; ZUMBRUNN ACKLIN CORNELIA

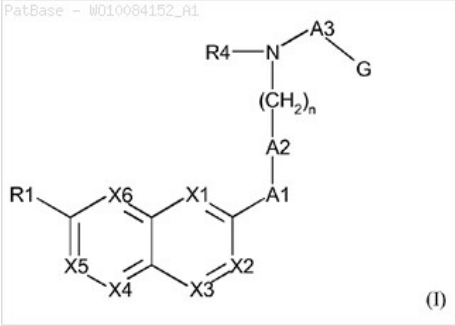
Agent(s): RUHLMANN ERIC

Designated states: AE AG AL AM AO AT AU AZ BA BB BE BF BG BH BJ BR BW BY BZ CA CF CG CH CI CL CM CN CO CR CU CY CZ DE DK DM DO DZ EC EE EG ES FI FR GA GB GD GE GH GM GN GQ GR GT GW HN HR HU ID IE IL IN IS IT JP KE KG KM KN KP KR KZ LA LC LI LK LR LS LT LU LV LY MA MC MD ME MG MK ML MN MR MT MW MX MY MZ NA NE NG NI NL NO NZ OM PE PG PH PL PT RO RS RU SC SD SE SG SI SK SL SM SN ST SV SY SZ TD TG TJ TM TN TR TT TZ UA UG US UZ VC VN ZA ZM ZW

Title: NOVEL BICYCLIC ANTIBIOTICS

Abstract: Source: US2012040957A Compounds of formula (I) wherein X1, X3; X4 and X6, each independently of the others, represents a nitrogen atom or CR2, with the proviso that at least one of X1, X3; X4 and X6 represents a nitrogen atom; X2 represents C-H, C-(C1-C6alkyl), C-(C1-C6alkoxy), C-halogen, C-COOH; X5 represents C-H or C-(C1-C6alkyl), C-halogen; R1 and R2, independently of one another, represent hydrogen or a substituent selected from hydroxy, halogen, carboxy, amino, C1-C6alkylamino, di(C1-C6alkyl)amino, mercapto, cyano, nitro, C1-C6alkyl, C1-C6alkoxy, C1-C6alkylthio, C1-C6alkylamino-carbonyloxy, C2-C6alkenyl, C2-C6alkynyl, C1-C6alkylcarbonyloxy, C1-C6alkyl-sulfonyloxy, C1-C6heteroalkylcarbonyloxy, C5-C6heterocyclyl-carbonyloxy, C1-C6heteroalkyl, C1-C6heteroalkoxy, wherein heteroalkyl, heteroalkoxy groups or heterocyclyl comprise 1, 2 or 3 heteroatoms selected from nitrogen, oxygen and sulphur, in which substituents the alkyl moieties are unsubstituted or further substituted by halogeno, cyano, hydroxy, C1-C4alkoxy, C1-C4alkylcarbonyl, C1-C4alkoxycarbonyl, unsubstituted or substituted phenoxy or phenylcarbonyl, unsubstituted or substituted C5-C6heterocyclyl or carboxy; A1 represents a divalent group of one of the formulae -O-(CH2)m-(CH2)-, -S-(CH2)m-(CH2)- or -(C-O)-(CH2)m-(CH2)-, wherein the (CH2)m moiety is optionally substituted by C1-C4alkyl, C2-C4alkenyl, C3-C6cycloalkyl, C3-C6cycloalkylmethyl, morpholinomethyl, halogen, carboxy, hydroxy, C1-C4alkoxy; C1-C4alkoxyC1-C4alkyl, C1-C4alkoxy(C1-C4alkylenoxy)C1-C4alkyl, benzyloxyC1-C4alkyl, amino, mono- or di-(C1-C4alkyl)amino or acylamino, in which substituents the alkyl moieties can be further substituted by 1 or more fluoro atoms m is 0, 1 or 2, provided that the number of atoms in the direct chain between the two terminal valencies of A1 is at least 3, which group A1 is linked to A2 via the terminal (CH2)- moiety; A2 is a group selected from C3-C8 cycloalkylene; saturated and unsaturated 4 to 8-membered heterocyclodiyl with 1, 2 or 3 heteroatoms selected from nitrogen, oxygen and sulphur, which group A2 is unsubstituted or substituted; R4 represents hydrogen or C1-C4 alkyl; A3 represents C1-C4 alkylene, C2-C4 alkenylene, >C=O, -C(O)C1-C3 alkylene-, -C(O)NH-, or a group selected from -C2H4NH-, -C2H4O-, and -C2H4S- being linked to the adjacent NR4-group via the carbon atom; and G represents aryl or heteroaryl, which is unsubstituted or substituted and n is 0, 1 or 2; or a pharmaceutically acceptable salts, hydrates or solvates thereof are valuable **antibacterial** agents.

Classifications:
International (IPC 8-9): A61K31/4375 A61K31/47 A61K31/4709 A61K31/498 A61K31/536 A61K31/5365 A61K31/538 A61K31/5383 A61K31/5415 A61K31/542 A61P31/04 A61P33/00 C07D215/20 C07D215/54 C07D265/36 C07D279/16 C07D333/34 C07D401/12 C07D405/12 C07D405/14 C07D409/12 C07D409/14 C07D413/04 C07D413/12 C07D413/14 C07D417/12 C07D417/14 C07D471/04 C07D495/04 C07D498/04 C07D513/04 C07D519/00 (Advanced/Invention); A61K31/4353 A61K31/47 A61P33/00 C07D405/00 C07D409/00 C07D413/00 C07D417/00 (Core/Invention)
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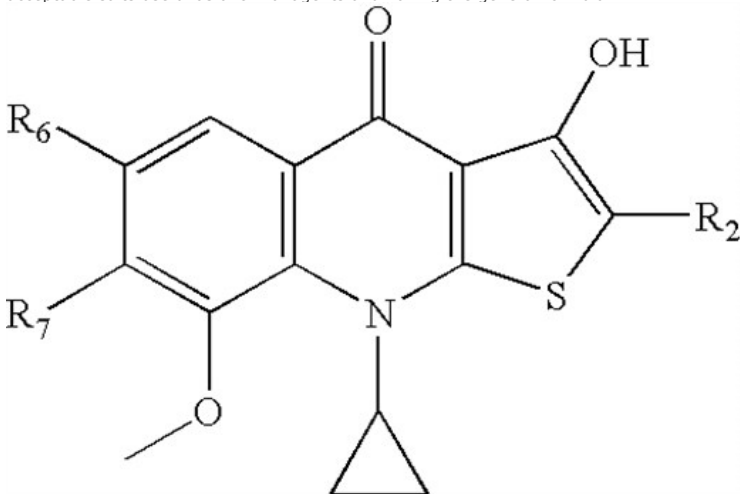
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EP2389376 A1	20111130	EP20100700583	20100121
IN05934CN2011 A	20130405	IN2011CN05934	20110818
JP2012515745 T2	20120712	JP20110546788T	20100121
JP5662346 B2	20150128	JP20110546788T	20100121
US2012040957 AA	20120216	US20100145323	20100121
US2014221348 AA	20140807	US20140216486	20140317
US2015080373 AA	20150319	US20140552853	20141125
US8716280 BB	20140506	US20100145323	20100121
US8927542 BB	20150106	US20140216486	20140317
WO10084152 A1	20100729	WO2010EP50684	20100121

Priority:
EP20090151027 20090121 WO2010EP50684 20100121 EP20100700583 20100121
US20110145323 20110804 US20140216486 20140317 US20140552853 20141125

Probable Assignee: BASILEA PHARMACEUTICA AG
Assignee(s): (std): BASILEA PHARMACEUTICA AG ; BASILIEA PHARMACEUTICA AG ; DANEL FRANCK HUBERT ; GAUCHER BERANGERE ; ROUSSEL PATRICK
Inventor(s): (std): BERANGERE GAUCHER ; DANEL FRANCK HUBERT ; GAUCHER BERANGERE ; HUBERT DANEL FRANCK ; PATRICK ROUSSEL ; ROUSSEL PATRICK
Agent(s): BOHEST AG
Designated states: AE AG AL AM AO AT AU AZ BA BB BE BF BG BH BJ BR BW BY BZ CA CF CG CH CI CL CM CN CO CR CU CY CZ DE DK DM DO DZ EC EE EG ES FI FR GA GB GD GE GH GM GN GQ GR GT GW HN HR HU ID IE IL IN IS IT JP KE KG KM KN KP KR KZ LA LC LI LK LR LS LT LU LV MA MC MD ME MG MK ML MN MR MT MW MX MY MZ NA NE NG NI NL NO NZ OM PE PG PH PL PT RO RS RU SC SD SE SG SI SK SL SM SN ST SV SY SZ TD TG TH TJ TM TN TR TT TZ UA UG US UZ VC VN ZA ZM ZW

Title: HYDROXYTHIENOQUINOLONES AND RELATED COMPOUNDS AS ANTI-INFECTIVE AGENTS

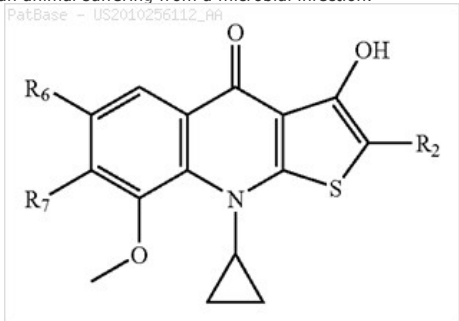
Abstract: Source: US2010256112A Disclosed herein are hydroxylthienoquinolones and related compounds and their pharmaceutically acceptable salts useful as antiviral agents and having the general formula



in which the variables R₂, R₆, and R₇ are defined herein. Certain compounds provided herein possess potent **antibacterial**, antiprotzoal, or antifungal activity and are particularly efficacious for the treatment of MRSA infections. The invention also provides pharmaceutical compositions, pharmaceutical compositions containing a hydroxylthienoquinolone in combination with one or more other active agent, and methods of treating microbial infections in animals by administering an effective amount of a hydroxylthienoquinolone or related compound to an animal suffering from a microbial infection.

Classifications:

International (IPC 8-9): A61K31/4365 A61K31/4743 A61K31/496 A61P29/00 A61P31/00 A61P31/04 C07D495/04 C07D495/14 C07D495/16 C07D498/16 C07D519/00 (Advanced/Invention); A61P C07D (Subclass/Invention)
CPC: A61K31/4743 A61K31/496 C07D495/04 C07D498/16 C07D519/00
European: A61K31/4743 A61K31/496 C07D495/04 C07D498/16 C07D519/00
US: 514/210.21 514/210.210P 514/253.03 514/253.030S 514/291 514/291S 544/361 544/361S 546/80 546/80S



Family:

Publication number	Publication date	Application number	Application date
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CA2756701 AA	20101007	CA20102756701	20100405
CN102388053 A	20120321	CN201080015154	20100405
EA201101451 A1	20120330	EA20110001451	20100405
EP2414368 A2	20120208	EP20100759532	20100405
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EP2414368 B1	20131127	EP20100759532	20100405
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IN07000DN2011 A	20130208	IN2011DN07000	20110913
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US2010256112 AA	20101007	US20100754057	20100405
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WO10115184 A2	20101007	WO2010US29938	20100405
WO10115184 A3	20110324	WO2010US29938	20100405

Priority:

US20090166371P 20090403 US20100754057 20100405 WO2010US29938 20100405

Probable Assignee: ACHILLION PHARMACEUTICALS INC

Assignee(s): (std): ACHILLION PHARMACEUTICALS INC ; BRADBURY BARTON JAMES ; DESHPANDE MILIND ; HASHIMOTO AKIHIRO ; KIM HA YOUNG ; PHADKE AVINASH ; WILES JASON ALLAN ; LUCIEN EDLAINE ; PUCCI MICHAEL ; PAIS GODWIN ; WANG QIUPING

Inventor(s): (std): AKIHIRO HASHIMOTO ; ALLAN WILES JASON ; AVINASH PHADKE ; BRADBURY BARTON JAMES ; DESHPANDE MILIND ; EDLAINE LUCIEN ; GODWIN PAIS ; KIM HA YOUNG ; LUCIEN EDLAINE ; MICHAEL PUCCI ; MILIND DESHPANDE ; PAIS GODWIN ; PHADKE AVINASH ; PUCCI MICHAEL ; QIUPING WANG ; WANG QIUPING ; WILES JASON ALLAN ; YOUNG KIM HA ; HASHIMOTO AKIHIRO ; JAMES BRADBURY BARTON

Inventor(s): JASON ALLAN WILES ; HA YOUNG KIM ; BARTON JAMES BRADBURY

Agent(s): SMAGGASGALE GILLIAN HELEN; CANTOR COLBURN LLP; MAXWELL LESLIE ANNE

Designated states: AE AG AL AM AO AT AU AZ BA BB BE BF BG BH BJ BR BW BY BZ CA CF CG CH CI CL CM CN CO CR CU CY CZ DE DK DM DO DZ EC EE EG ES FI FR GA GB GD GE GH GM GN GQ GR GT GW HN HR HU ID IE IL IN IS IT JP KE KG KM KN KP KR KZ LA LC LI LK LR LS LT LU LV LY MA MC MD ME MG MK ML MN MR MT MW MX MY MZ NA NE NG NI NL NO NZ OM PE PG PH PL PT RO RS RU SC SD SE SG SI SK SL SM SN ST SV SY SZ TD TG TH TJ TM TN TR TT TZ UA UG US UZ VC VN ZA ZM ZW

Title: PREPARATION AND APPLICATION OF NOVEL **ANTIBACTERIAL** AND ANTICANCER COMPOUNDS AND THEIR DERIVATIVES

Abstract: Source: US2012035206A Novel antibiotic and anticancer compounds of formula I, II, III, IV, derivatives, ostereoisomer, racemic and noracemic mixture of ostereoisomer, or the pharmaceutically acceptable salts or solvates of these compounds are disclosed. The preparation, pharmaceutical composition and biological activity of these compounds are disclosed.

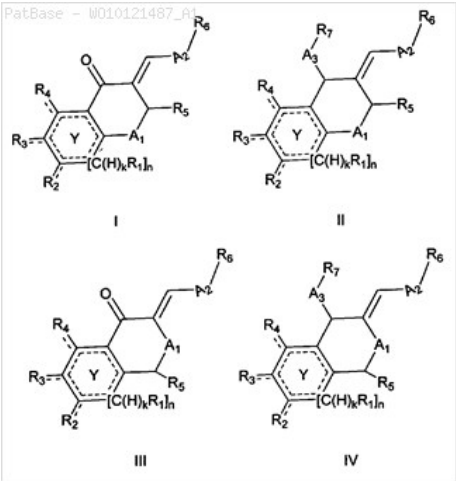
Classifications:

International (IPC 8-9): A61K31/382 A61K31/4162 A61K31/4365 A61K31/4743 A61K9/00 A61K9/02 A61K9/06 A61K9/08 A61K9/10 A61K9/107 A61K9/12 A61K9/20 A61K9/48 A61P31/00 A61P31/04 A61P31/10 A61P35/00 A61P35/02 C07D335/04 C07D335/06 C07D471/04 C07D495/04 (Advanced/Invention)

CPC: A61K31/382 A61K31/4365 C07D335/04 C07D335/06 C07D495/04

European: C07D335/04 C07D335/06 C07D495/04

US: 514/301 514/432 514/432S 546/114 546/114S 549/23 549/23S



Family:

Publication number	Publication date	Application number	Application date
CA2759793 AA	20101028	CA20102759793	20100409
CN101870689 A	20101027	CN200910137455	20090423
CN101870689 B	20130828	CN200910137455	20090423
CN101906094 A	20101208	CN200910203152	20090606
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EP2423213 B1	20140108	EP20100766578	20100409
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JP5489026 B2	20140514	JP20120506310T	20100409
US2012035206 AA	20120209	US20100265864	20100409
WO10121487 A1	20101028	WO2010CN00471	20100409

Priority:

CN200910137455 20090423 CN200910203152 20090606 WO2010CN00471 20100409
EP20100766578 20100409

Probable Assignee: YANG GENGLIANG

Assignee(s): (std): BAI LIGAI ; FANG BAOLING ; GENGLIANG YANG ; LI LINBO ; YANG GENGLIANG ; WANG GE ; TIAN WEI ; YANG CHUNLIU ; MA ZHENGYUE

Inventor(s): (std): BAI LIGAI ; BAOLING FANG ; CHUNLIU YANG ; FANG BAOLING ; GE WANG ; GENGLIANG YANG ; LI LINBO ; LINBO LI ; MA ZHENGYUE ; TIAN WEI ; WANG GE ; WEI TIAN ; YANG CHUNLIU ; YANG GENGLIANG ; ZHENGYUE MA ; LIGAI BAI

Agent(s): PLUCKER GUY

Designated states: AE AG AL AM AO AT AU AZ BA BB BE BF BG BH BJ BR BW BY BZ CA CF CG CH CI CL CM CN CO CR CU CY CZ DE DK DM DO DZ EC EE EG ES FI FR GA GB GD GE GH GM GN GQ GR GT GW HN HR HU ID IE IL IN IS IT JP KE KG KM KN KP KR KZ LA LC LI LK LR LS LT LU LV LY MA MC MD ME MG MK ML MN MR MT MW MX MY MZ NA NE NG NI NL NO NZ OM PE PG PH PL PT RO RS RU SC SD SE SG SI SK SL SM SN ST SV SY SZ TD TG TH TJ TM TN TR TT TZ UA UG US UZ VC VN ZA ZM ZW