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DIVISION DE NUEVAS CREACIONES

CONTESTACION A REPAROS - OBSERVACIONES
APORTACION DE NUEVA DOCUMENTACION A
UNA SOLICITUD DE PATENTE DE INVENCION O
MODELO DE UTILIDAD O DISEÑO INDUSTRIAL

6.

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Observaciones ____ ☐
Otros ____ ☐
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☒ PATENTE ☐ MODELO DE UTILIDAD ☐ DISEÑO INDUSTRIAL

TITULO **COMPUESTOS DE DIHIDROPIRIMIDINA HETEROCICLICOS**

SOLICITANTE **BRISTOL - MYERS SQUIBB COMPANY**

INDICE DE DOCUMENTOS QUE SE ACOMPAÑAN

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dos Unidos de la solicitud USSNo.60/169,091	☐	
sentada para la misma invención, de la cual	☐	
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THE UNITED STATES OF AMERICA

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THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM THE RECORDS OF THE UNITED STATES PATENT AND TRADEMARK OFFICE OF THOSE PAPERS OF THE BELOW IDENTIFIED PATENT APPLICATION THAT MET THE REQUIREMENTS TO BE GRANTED A FILING DATE UNDER 35 USC 111

APPLICATION NUMBER. ***60/169,091***
FILING DATE ***December 06, 1999***

By Authority of the
COMMISSIONER OF PATENTS AND TRADEMARKS

T` LAWRENCE
Certifying Officer

12-07-99 A/Prov 8

Attorney Docket No. HA726*

PTO/SB/16 (6-95)

PROVISIONAL APPLICATION COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION under 37 CFR 1.53(c)

Docket Number HA726*		Type a plus sign(+) inside this box →	+

INVENTOR(S)/APPLICANT(S)

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TITLE OF THE INVENTION (280 CHARACTERS MAX)

Heterocyclic Dihydropyrimidine Compounds

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ENCLOSED APPLICATION PARTS (check all that apply)

☒ Specification — 208 *Number of Pages* — ☐ Small Entity Statement

☐ Drawing(s) — ☐ *Number of Sheets* — ☐ Other(specify)

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METHOD OF PAYMENT

☒ The Commissioner is hereby authorized to charge filing fees and credit Deposit Account Number 19-3880. The Provisional Filing Fee Amount is ($)150.00. The Commissioner is hereby authorized to charge any additional fees which may be required except the Issue Fee, or credit any overpayment to Deposit Account 19-3880.

The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

☒ No.

Attorney Docket No HA726*

☐ Yes, the name of the U.S. Government agency and the Government contract number are: _____

Respectfully submitted,

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☐ Additional inventors are being named on separately numbered sheets attached hereto.

1 10

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	Karnail Atwal, Wayne Vaccaro, John Lloyd, Heather Finlay & Lin Yan
Serial No	Unassigned
Filed	Concurrently Herewith
For	Heterocyclic Dihydropyrimidine Compounds

Princeton, New Jersey 08543-4000

December 6, 1999

Express Mail Certificate

Assistant Commissioner for Patents
Washington, D C 20231

"Express Mail" mailing label number EM260263971US

Date of Deposit December 6, 1999

I hereby certify that the above-captioned provisional application, attached hereto, including a 208 page specification, including claims and abstract, and cover sheet with the inventors' names thereon, are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1 10 on the date indicated above and are addressed to the Assistant Commissioner for Patents, Washington, D C 20231

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HETEROCYCLIC DIHYDROPYRIMIDINE COMPOUNDS

Field of the Invention

The present invention relates to heterocyclic dihydropyrimidine compounds, to methods of using such compounds in the treatment of arrhythmia and I_{Kur}-associated disorders, and to pharmaceutical compositions containing such compounds

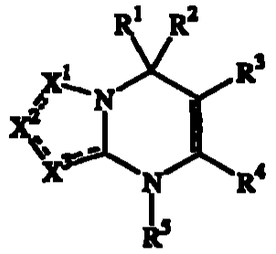
Background of the Invention

Atrial fibrillation and flutter are the most common arrhythmias encountered in clinical practice. Although some presently available antiarrhythmic drugs can convert sustained fibrillation to sinus rhythm, they are only effective in acute atrial fibrillation and even then their efficacy is low Furthermore, these drugs are of limited use because of a variety of potentially adverse effects, including ventricular proarrhythmia. Thus, there is presently an unmet medical need for safe and efficacious treatment of atrial fibrillation and other supraventricular arrhythmias.

The ultrarapid delayed rectifier potassium current (I_{Kur}) is a rapidly activating sustained current that has been identified in human atrial myocytes but is apparently absent from human ventricular myocytes (Konarzewska et al., *Circulation J Physiol*, *491*, 13 (1996)) Considerable molecular biological, pharmacological and biophysical data indicates that I_{Kur} is encoded by the potassium channel gene Kv1.5 I_{Kur} plays a significant role in the repolarization of the atrial action potential and selective inhibition of this current in human atrial myocytes prolongs action potential duration by greater than 50% (Wang et al., *Circ. Res*, *73*, 1061 (1993)). Prolongation of the action potential consequently prolongs atrial effective refractory period, that is, inhibition of I_{Kur} produces a class III antiarrhythmic effect. Importantly, an inhibitor of I_{Kur} may have utility against atrial fibrillation without having the attendant ventricular proarrhythmic risk associated with other class III agents that have potassium channel targets expressed in both atrium and ventricle.

Summary of the Invention

The present invention provides heterocyclic dihydropyrimidine compounds of the following formula I, including enantiomers, diastereomers, and salts thereof, for the treatment of arrhythmia and I_{Kur} -associated disorders



(I)

where

X^1, X^2 and X^3 are independently selected from N, NR^6, $(CR^7)_q$, $(CHR^7)_q$, or C=O, wherein the bonds connecting X^1, X^2 and X^3 to adjacent atoms may be single or double bonds forming a 5 to 7-membered saturated, partially unsaturated or aromatic ring;

R^1, R^2, R^3, R^4, R^5, R^6 and R^7 are the same or different and are independently selected from groups of the formula $-(CH_2)_n-(Z^1)_m-(CH_2)_p-Z^2$; or

R^1, R^2, R^3, R^4 and R^5 may, in one or more pairs of two (such as R^1 and R^2, R^1 and R^3, R^2 and R^3, R^3 and R^4 or R^4 and R^5), together with the atoms to which they are bonded, form a carbocyclic, substituted carbocyclic, heterocyclic or substituted heterocyclic group; or

R^6 and R^7 may, in one or more pairs of two (such as R^6 and R^7, R^6 and R^6, or R^7 and R^7), together with the atoms to which they are bonded, form a carbocyclic, substituted carbocyclic, heterocyclic or substituted heterocyclic group;

Z^1 is $-CZ^3Z^4-$, -O-, $-NZ^3-$, -S-, -SO-, $-SO_2-$, -C(O)-, $-C(O)Z^3-$, $-C(O)NZ^4$; -C(S)-, $-C(=NOZ^3)-$, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, carbocyclo, substituted carbocyclo, aryl, substituted aryl, heterocyclo; or substituted heterocyclo;

Z^2 is hydrogen, $-OZ^5$, $-OC(O)Z^5$, $-NZ^5-C(O)-Z^6$, $-NZ^5-CO_2-Z^6$, $-NZ^5(C=O)-NZ^6Z^7$, $-NZ^5Z^6$, $-NO_2$, halo, -CN, $-C(O)Z^5$, $-CO_2Z^5$, $-C(S)Z^5$, $-(C=NOZ^5)Z^6$,

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$-C(O)NZ^5Z^6$, $-C(S)NZ^5Z^6$; $-SZ^5$, $-SOZ^5$, $-SO_2Z^5$, $-SO_2NZ^5Z^6$, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, carbocyclo; substituted carbocyclo, aryl, substituted aryl, heterocyclo (such as heteroaryl); or substituted heterocyclo;

Z^3, Z^4, Z^5, Z^6 and Z^7 are independently hydrogen, halo, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, carbocyclo, substituted carbocyclo; aryl, substituted aryl, heterocyclo, or substituted heterocyclo; or

Z^3, Z^4, Z^5, Z^6 and Z^7 may, in one or more pairs of two (such as Z^3 and Z^4, Z^5 and Z^6 or Z^6 and Z^7), together with the atoms to which they are bonded, form a carbocyclic, substituted carbocyclic, heterocyclic or substituted heterocyclic group;

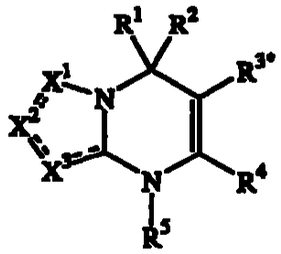
n and p are independently selected from integers from 0 to 10 wherein, when m is 0, p is also 0;

m is an integer selected from 0 or 1, and

q is an integer selected from 1 to 3

The present invention provides novel methods for the prevention and treatment of arrhythmia and I_{Kur} -associated disorders employing one or more compounds of the formula I, enantiomers, diastereomers or pharmaceutically acceptable salts thereof In particular the present invention provides a novel method for the selective prevention and treatment of supraventricular arrhythmias.

In addition, compounds within the formula I, as well as enantiomers, diastereomers and salts thereof are novel compounds, including compounds of formula I* and salts thereof



(I*)

where

X^1, X^2, X^3, R^1, R^2, R^4 and R^5 are as defined above;

R^{3*} is $-OZ^5$, $-OC(O)-Z^5$, $-NZ^5-C(O)_2-Z^6$, $-NZ^5(C=O)-NZ^6Z^7$, $-NZ^5Z^6$, $-(C=NOZ^5)Z^6$, $-C(O)NZ^{5*}Z^{6*}$, $-C(S)NZ^{5*}Z^{6*}$, $-SZ^5$, $-SOZ^5$, $-SO^2Z^5$, $-SO_2NZ^5Z^6$, $-C(O)Z^{3*}-Z^{2*}$, halo, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, carbocyclo; substituted carbocyclo, aryl, substituted aryl, heterocyclo or substituted heterocylco;

Z^{2*} is other than hydrogen when Z^{3*} is heterocyclo;

Z^{3*} is heterocyclo or substituted heterocyclo;

Z^{5*} is substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, carbocyclo; substituted carbocyclo; aryl, substituted aryl, heterocyclo, or substituted heterocyclo; and

Z^{6*} is hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, carbocyclo; substituted carbocyclo, aryl, substituted aryl, heterocyclo; or substituted heterocyclo, provided that Z^{6*} is not hydrogen when Z^{5*} is unsubstituted cycloalkyl, unsubstituted aryl, or unsubstituted benzyl,

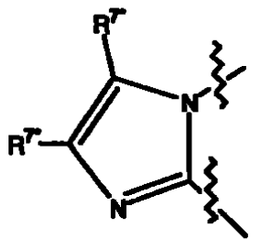
or Z^{5*} and Z^{6*} may together with the nitrogen atom to which they are bonded form a heterocyclic group or substituted heterocyclic group, provided that Z^{5*} and Z^{6*} do not together form unsubstituted piperidinyl, unsubstituted pyrrolidinyl, or unsubstituted morpholinyl, and further provided that when

(i) R^1 and R^5 are each hydrogen, and

(ii) R^2 is aryl or substituted aryl, and

(iii) R^4 is heterocyclo-substituted aryl, and

(iv) X^1, X^2 and X^3 form the ring



where R^{7*} is H or alkyl

Z^{5*} and Z^{6*} do not together form unsubstituted piperazinyl or N-alkyl-substituted piperazinyl,

Preferred Compounds

Compounds of the formula I and salts thereof wherein one or more, and especially all, of X^1, X^2, X^3, R^1, R^2, R^3, R^4 and R^5 are selected from the following definitions, are preferred compounds of the present invention.

R^1 is hydrogen,

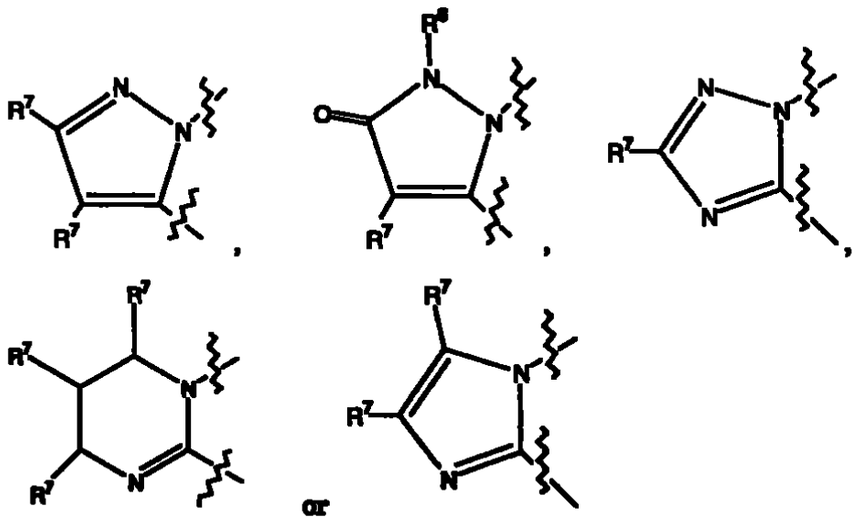
R^2 is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo, carbocyclo or substituted carbocyclo;

R^3 is $-(CH_2)_n-Z^2$, $-(CH_2)_n-C(O)Z^3-(CH_2)_p-Z^2$, or $-(CH_2)_n-C(O)NZ^4-(CH_2)_p-Z^2$;

R^4 is alkyl or substituted alkyl, and

R^5 is hydrogen, or $-(CH_2)_n-Z^2$; and

X^1, X^2 and X^3, together with the atoms to which they are bonded, form a ring selected from.



where R^6 and/or R^7 are the same or different, as defined above.

Compounds of the formula I and salts thereof wherein one or more, and especially all, of X^1, X^2, X^3, R^1, R^2, R^3, R^4 and R^5 are selected from the following definitions, are more preferred compounds of the present invention

R^1 is hydrogen,

R^2 is aryl (especially where aryl is phenyl), substituted aryl, heterocyclo, substituted heterocyclo, carbocyclo or substituted carbocyclo;

R^3 is $-(CH_2)_n-Z^2$, $-(CH_2)_n-C(O)Z^3-(CH_2)_p-Z^2$, or $-(CH_2)_n-C(O)NZ^4-(CH_2)_p-Z^2$ wherein

Z^2 is selected from $-C(O)NZ^5Z^6$, $-CO_2Z^5$, $-SO_2Z^5$, $-NZ^5Z^6$, $-NZ^5CO_2Z^6$, $-NZ^5C(O)Z^6$, $-OZ^5$, aryl, substituted aryl, heterocyclo, substituted heterocyclo, alkyl or substituted alkyl,

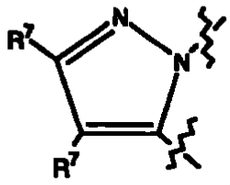
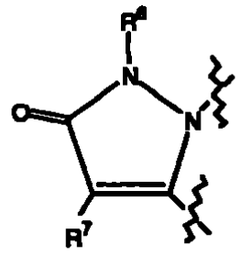
Z^3 is heterocyclo or substituted heterocyclo; and

n and p are independently selected from integers 0 to 3,

R^4 is alkyl, or substituted alkyl,

R^5 is hydrogen, or $-(CH_2)_n-Z^2$ wherein Z^2 is selected from $-C(O)NZ^5Z^6$, $-CO_2Z^5$, $-NZ^5Z^6$, aryl, substituted aryl, alkyl, or substituted alkyl, and

X^1, X^2 and X^3, together with the atoms to which they are bonded, form a ring selected from.

Compounds of the formula I and salts thereof wherein one or more, and especially all, of X^1, X^2, X^3, R^1, R^2, R^3, R^4 and R^5 are selected from the following definitions, are most preferred compounds of the present invention.

R^1 is hydrogen,

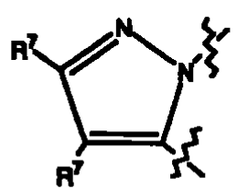
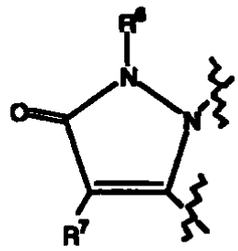
R^2 is aryl (especially where aryl is phenyl), substituted aryl, heterocyclo, substituted heterocyclo, carbocyclo or substituted carbocyclo;

R^3 is heterocyclo or substituted heterocyclo, $-C(O)NZ^5Z^6$, $-C(O)Z^3$-$CONZ^5Z^6$, $-C(O)Z^3$-Z^2, or $-C(O)Z^3$-CO_2Z^5, wherein Z^3 is heterocyclo or substituted heterocyclo, and Z^2 is aryl or substituted aryl,

R^4 is alkyl (especially lower alkyl) or substituted alkyl (especially halo-substituted alkyl),

R^5 is hydrogen, alkyl or substituted alkyl, and

X^1, X^2 and X^3, together with the atoms to which they are bonded, form a ring selected from.

wherein

R^6 is H or $C(O)Z^5$, where Z^5 is alkyl or carbocyclo; and

R^7 is independently selected from H, alkyl, substituted alkyl (especially halo-substituted), halo, or CN

Detailed Description of the Invention

The following are definitions of terms used in this specification. The initial definition provided for a group or term herein applies to that group or term throughout the present specification, individually or as part of another group, unless otherwise indicated.

The terms "alk" or "alkyl" refer to straight or branched chain hydrocarbon groups having 1 to 12 carbon atoms, preferably 1 to 8 carbon atoms, such as methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, t-butyl, pentyl, hexyl, heptyl, octyl, etc. Lower alkyl groups, that is, alkyl groups of 1 to 6 carbon atoms, are generally most preferred. The term "substituted alkyl" refers to alkyl groups substituted with one or more groups (such as by groups described above in the definition of R^1), preferably selected from aryl, substituted aryl, heterocyclo, substituted heterocyclo, carbocyclo, substituted carbocyclo, halo, hydroxy, alkoxy (optionally substituted), aryloxy (optionally substituted), alkylester (optionally substituted), arylester (optionally substituted), alkanoyl (optionally substituted), aryol (optionally substituted), cyano, nitro, amino, substituted amino, amido, lactam, urea, urethane, sulfonyl, etc.

The term "alkenyl" refers to straight or branched chain hydrocarbon groups having 2 to 12 carbon atoms, preferably 2 to 4 carbon atoms, and at least one double carbon to carbon bond (either cis or trans), such as ethenyl. The term "substituted alkenyl" refers to alkenyl groups substituted with one or more groups (such as by groups described above in the definition of R^1), preferably selected from aryl, substituted aryl, heterocyclo, substituted heterocyclo, carbocyclo, substituted carbocyclo, halo, hydroxy, alkoxy (optionally substituted), aryloxy (optionally substituted), alkylester (optionally substituted), arylester (optionally substituted), alkanoyl (optionally substituted), aryol (optionally substituted), cyano, nitro, amino, substituted amino, amido, lactam, urea, urethane, sulfonyl, etc.

The term "alkynyl" refers to straight or branched chain hydrocarbon groups having 2 to 12 carbon atoms, preferably 2 to 4 carbon atoms, and at least one triple carbon to carbon bond, such as ethynyl. The term "substituted alkynyl" refers to alkynyl groups substituted with one or more groups (such as by groups described above in the definition of R^1), preferably selected from aryl, substituted aryl, heterocyclo, substituted heterocyclo, carbocyclo, substituted carbocyclo, halo,

hydroxy, alkoxy (optionally substituted), aryloxy (optionally substituted), alkylester (optionally substituted), arylester (optionally substituted), alkanoyl (optionally substituted), aryol (optionally substituted), cyano, nitro, amino, substituted amino, amido, lactam, urea, urethane, sulfonyl, etc.

The terms "ar" or "aryl" refer to aromatic homocyclic (i.e., hydrocarbon) mono-, bi- or tricyclic ring-containing groups preferably having 6 to 12 members such as phenyl, naphthyl and biphenyl. Phenyl is a preferred aryl group. The term "substituted aryl" refers to aryl groups substituted with one or more groups (such as by groups described above in the definition of R^1), preferably selected from alkyl, substituted alkyl, alkenyl (optionally substituted), aryl (optionally substituted), heterocyclo (optionally substituted), halo, hydroxy, alkoxy (optionally substituted), aryloxy (optionally substituted), alkanoyl (optionally substituted), aroyl, (optionally substituted), alkylester (optionally substituted), arylester (optionally substituted), cyano, nitro, amino, substituted amino, amido, lactam, urea, urethane, sulfonyl, etc., where optionally one or more pair of substituents together with the atoms to which they are bonded form a 3 to 7 member ring.

The terms "cycloalkyl" and "cycloalkenyl" refer to mono-, bi- or tri homocyclic ring groups of 3 to 15 carbon atoms which are, respectively, fully saturated and partially unsaturated. The term "cycloalkenyl" includes bi- and tricyclic ring systems that are not aromatic as a whole, but contain aromatic portions (e.g. fluorene, tetrahydronapthalene, dihydroindene, and the like). The terms "substituted cycloalkyl" and "substituted cycloalkenyl" refer, respectively, to cycloalkyl and cycloalkenyl groups substituted with one or more groups (such as by groups described above in the definition of R^1), preferably selected from aryl, substituted aryl, heterocyclo, substituted heterocyclo, carbocyclo, substituted carbocyclo, halo, hydroxy, alkoxy (optionally substituted), aryloxy (optionally substituted), alkylester (optionally substituted), arylester (optionally substituted), alkanoyl (optionally substituted), aryol (optionally substituted), cyano, nitro, amino, substituted amino, amido, lactam, urea, urethane, sulfonyl, etc.

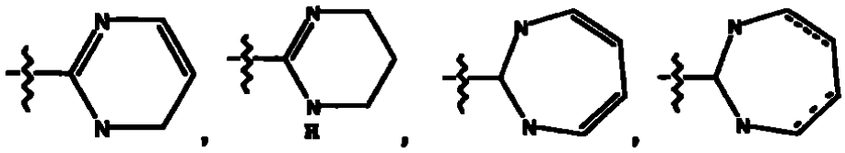
The terms "carbocyclo", "carbocyclic" or "carbocyclic group" refer to both cycloalkyl and cycloalkenyl groups. The terms "substituted carbocyclo", "substituted carbocyclic" or "substituted carbocyclic group" refer to carbocyclo or carbocyclic

groups substituted with one or more groups as described in the definition of cycloalkyl and cycloalkenyl

The terms "halogen" and "halo" refer to fluorine, chlorine, bromine and iodine.

The terms "heterocycle", "heterocyclic", "heterocyclic group" or "heterocyclo" refer to fully saturated or partially or completely unsaturated, including aromatic ("heteroaryl") or nonaromatic cyclic groups (for example, 3 to 13 member monocyclic, 7 to 17 member bicyclic, or 10 to 20 member tricyclic ring systems, preferably containing a total of 3 to 10 ring atoms) which have at least one heteroatom in at least one carbon atom-containing ring. Each ring of the heterocyclic group containing a heteroatom may have 1, 2, 3 or 4 heteroatoms selected from nitrogen atoms, oxygen atoms and/or sulfur atoms, where the nitrogen and sulfur heteroatoms may optionally be oxidized and the nitrogen heteroatoms may optionally be quaternized. The heterocyclic group may be attached at any heteroatom or carbon atom of the ring or ring system. The rings of multi-ring heterocycles may be either fused, bridged and/or joined through one or more spiro unions.

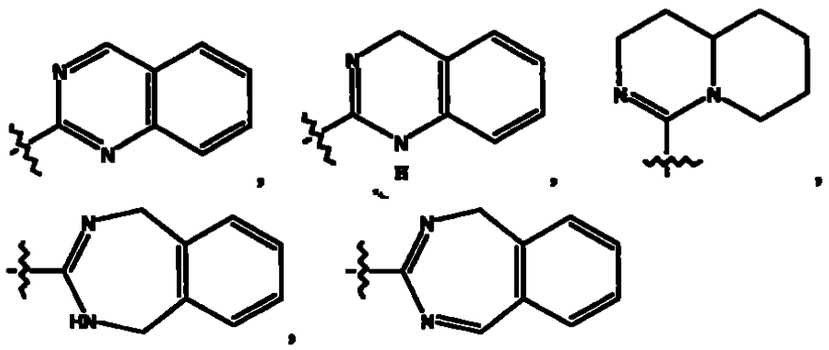
Exemplary monocyclic heterocyclic groups include azetidinyl, pyrrolidinyl, pyrrolyl, pyrazolyl, oxetanyl, pyrazolinyl, imidazolyl imidazolinyl, imidazolidinyl, oxazolyl, oxazolidinyl, isoxazolinyl, isoxazolyl, thiazolyl, thiadiazolyl, thiazolidinyl, isothiazolyl, isothiazolidinyl, furyl, tetrahydrofuryl, thienyl, oxadiazolyl, piperidinyl, piperazinyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolodinyl, 2-oxoazepinyl, azepinyl, 4-piperidonyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl, tetrahydropyranyl, tetrazoyl, triazolyl, morpholinyl, thiamorpholinyl, thiamorpholinyl sulfoxide, thiamorpholinyl sulfone, 1,3-dioxolane and tetrahydro-1,1-dioxothienyl,



and the like.

Exemplary bicyclic heterocyclic groups include indolyl, benzothiazolyl, benzoxazolyl, benzothienyl, quinuclidinyl, quinolinyl, tetra-hydroisoquinolinyl, isoquinolinyl, benzimidazolyl, benzopyranyl, indolizinyl, benzofuryl, benzofuranly, dihydrobenzofuranyl, chromonyl, coumarinyl, benzodioxolyl, dihydrobenzodioxolyl,

benzodioxinyl, cinnolinyl, quinoxalinyl, indazolyl, pyrrolopyridyl, furopyridinyl (such as furo[2,3-c]pyridinyl, furo[3,2-b]pyridinyl] or furo[2,3-b]pyridinyl), dihydroisoindolyl, dihydroquinazolinyl (such as 3,4-dihydro-4-oxo-quinazolinyl), tetrahydroquinolinyl, azabicycloalkyls (such as 6-azabicyclo[3.2.1]octane), azaspiroalkyls (such as 1,4 dioxa-8-azaspiro[4.5]decane), imidazopyridinyl (such as imidazo[1,5-a]pyridin-3-yl), triazolopyridinyl (such as 1,2,4-triazolo[4,3-a]pyridin-3-yl), and hexahydroimidazopyridinyl (such as 1,5,6,7,8,8a-hexahydroimidazo[1,5-a]pyridin-3-yl),



and the like.

Exemplary tricyclic heterocyclic groups include carbazolyl, benzidolyl, phenanthrolinyl, acridinyl, phenanthridinyl, xanthenyl and the like.

The terms "substituted heterocycle", "substituted heterocyclic", "substituted heterocyclic group" and "substituted heterocyclo" refer to heterocycle, heterocyclic and heterocyclo groups substituted with one or more groups (such as by groups described above in the definition of R^1), preferably selected from alkyl, substituted alkyl, alkenyl, oxo, aryl, substituted aryl, heterocyclo, substituted heterocyclo, carbocyclo (optionally substituted), halo, hydroxy, alkoxy (optionally substituted), aryloxy (optionally substituted), alkanoyl (optionally substituted), aroyl (optionally substituted), alkylester (optionally substituted), arylester (optionally substituted), cyano, nitro, amido, amino, substituted amino, lactam, urea, urethane, sulfonyl, etc., where optionally one or more pair of substituents together with the atoms to which they are bonded form a 3 to 7 member ring.

The term "alkanoyl" refers to alkyl group (which may be optionally substituted as described above) linked to a carbonyl group (i.e. –C(O)-alkyl). Similarly, the term

"aroyl" refers to an aryl group (which may be optionally substituted as described above) linked to a carbonyl group (i.e., -C(O)-aryl)

Throughout the specification, groups and substituents thereof may be chosen to provide stable moieties and compounds.

The compounds of formula I form salts which are also within the scope of this invention. Reference to a compound of the formula I herein is understood to include reference to salts thereof, unless otherwise indicated. The term "salt(s)", as employed herein, denotes acidic and/or basic salts formed with inorganic and/or organic acids and bases In addition, when a compound of formula I contains both a basic moiety and an acidic moiety, zwitterions ("inner salts") may be formed and are included within the term "salt(s)" as used herein. Pharmaceutically acceptable (i.e., non-toxic, physiologically acceptable) salts are preferred, although other salts are also useful, e.g., in isolation or purification steps which may be employed during preparation. Salts of the compounds of the formula I may be formed, for example, by reacting a compound I with an amount of acid or base, such as an equivalent amount, in a medium such as one in which the salt precipitates or in an aqueous medium followed by lyophilization.

The compounds of formula I which contain a basic moiety may form salts with a variety of organic and inorganic acids. Exemplary acid addition salts include acetates (such as those formed with acetic acid or trihaloacetic acid, for example, trifluoroacetic acid), adipates, alginates, ascorbates, aspartates, benzoates, benzenesulfonates, bisulfates, borates, butyrates, citrates, camphorates, camphorsulfonates, cyclopentanepropionates, digluconates, dodecylsulfates, ethanesulfonates, fumarates, glucoheptanoates, glycerophosphates, hemisulfates, heptanoates, hexanoates, hydrochlorides (formed with hydrochloric acid), hydrobromides (formed with hydrogen bromide), hydroiodides, 2-hydroxyethanesulfonates, lactates, maleates (formed with maleic acid), methanesulfonates (formed with methanesulfonic acid), 2-naphthalenesulfonates, nicotinates, nitrates, oxalates, pectinates, persulfates, 3-phenylpropionates, phosphates, picrates, pivalates, propionates, salicylates, succinates, sulfates (such as those formed with sulfuric acid), sulfonates (such as those mentioned herein), tartrates, thiocyanates, toluenesulfonates such as tosylates, undecanoates, and the like.

The compounds of formula I which contain an acidic moiety may form salts with a variety of organic and inorganic bases. Exemplary basic salts include ammonium salts, alkali metal salts such as sodium, lithium, and potassium salts, alkaline earth metal salts such as calcium and magnesium salts, salts with organic bases (for example, organic amines) such as benzathines, dicyclohexylamines, hydrabamines (formed with N,N-bis(dehydroabietyl)ethylenediamine), N-methyl-D-glucamines, N-methyl-D-glucamides, t-butyl amines, and salts with amino acids such as arginine, lysine and the like.

Basic nitrogen-containing groups may be quaternized with agents such as lower alkyl halides (e.g. methyl, ethyl, propyl, and butyl chlorides, bromides and iodides), dialkyl sulfates (e.g. dimethyl, diethyl, dibutyl, and diamyl sulfates), long chain halides (e.g. decyl, lauryl, myristyl and stearyl chlorides, bromides and iodides), aralkyl halides (e.g. benzyl and phenethyl bromides), and others.

Prodrugs and solvates of the compounds of the invention are also contemplated herein. The term "prodrug", as employed herein, denotes a compound which, upon administration to a subject, undergoes chemical conversion by metabolic or chemical processes to yield a compound of the formula I, or a salt and/or solvate thereof. Solvates of the compounds of formula I are preferably hydrates.

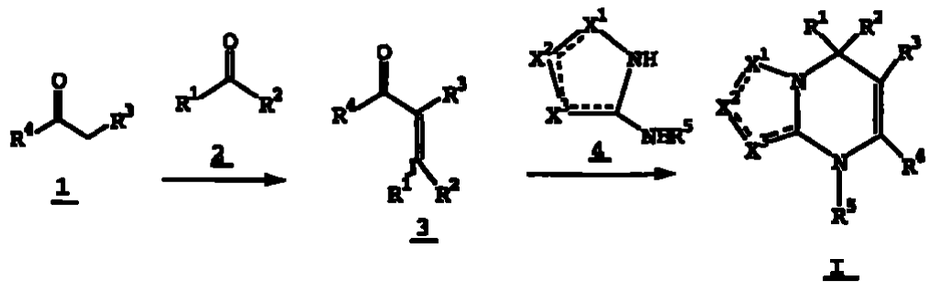
To the extent that compounds of the formula I, and salts thereof, may exist in their tautomeric form, all such tautomeric forms are contemplated herein as part of the present invention.

All stereoisomers of the present compounds, such as those which may exist due to asymmetric carbons on the various R and Z substituents, including enantiomeric forms (which may exist even in the absence of asymmetric carbons) and diastereomeric forms, are contemplated within the scope of this invention. Individual stereoisomers of the compounds of the invention may, for example, be substantially free of other isomers, or may be admixed, for example, as racemates or with all other, or other selected, stereoisomers. The chiral centers of the present invention can have the S or R configuration as defined by the IUPAC 1974 Recommendations.

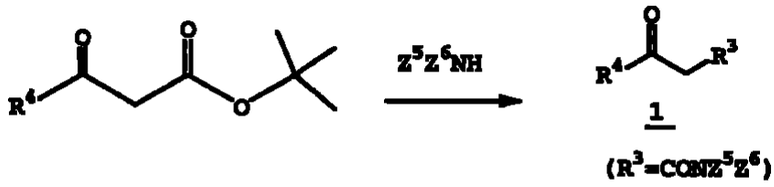
The terms "including", "such as", "for example" and the like are intended to refer to exemplary embodiments and not to limit the scope of the present invention.

Schemes

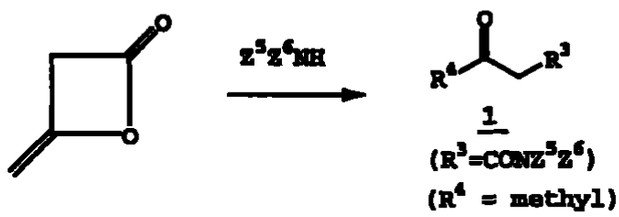
Compounds of formula I may be prepared using the sequence of steps outlined below



Compounds 1, 2 and 4 used in this preparation are commercially available or are readily prepared by methods well known to those skilled in the art. For example compounds of formula 1 where $R^3 = CONZ^5Z^6$ can be prepared by the method of Witzeman (JOC 1991, 56(5), 1713) which involves warming an amine and a t-butoxy-β-ketoester neat or in a suitable solvent (xylenes, toluene, etc.)

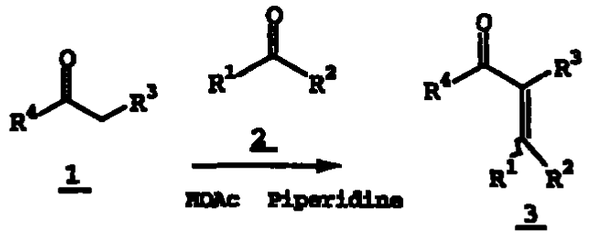


Alternately compounds of formula 1 where R^4 = methyl and $R^3 = CONZ^5Z^6$ may be prepared by reaction of an amine with diketene in a suitable solvent such as dichloromethane at temperatures between –100 –22 °C.



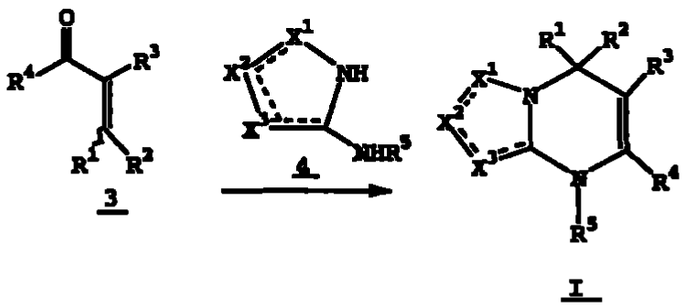
Compounds of formula 3 can be prepared by modification of the Knovenagel condensation For example condensation of a compound of formula 1 and a

compound of formula 2 at temperatures between 22-170 °C in solvents such as toluene or dimethylformamide in the presence of an acid such as acetic acid and an a base such as piperidine with removal of water generated during the reaction by the use of 4Å dry molecular sieves or a Dean-Stark trap affords compounds of formula 3 as a mixture of cis and trans stereoisomers.



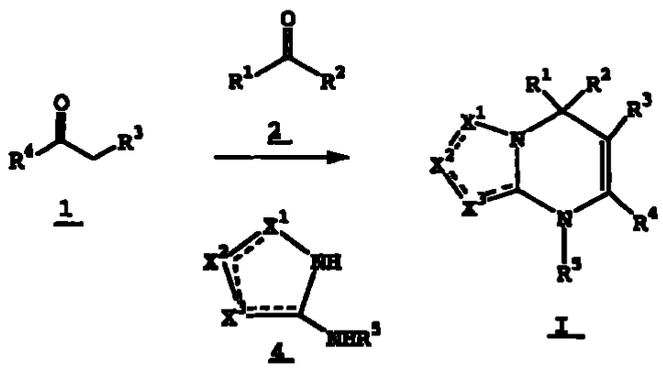
1 2 3

Compounds of formula I may also be prepared by condensation of compounds of formula 3 with compounds of formula 4 by warming at temperatures between 30-150 °C in alcoholic solvents such as ethanol or propanol or by warming between 30-150 °C in a solvent such as dimethylformamide and in the presence of a base such as sodium acetate.

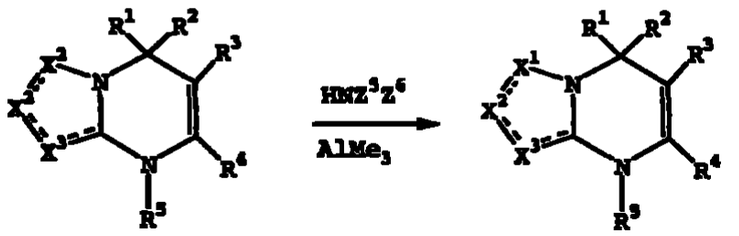


3 4 I

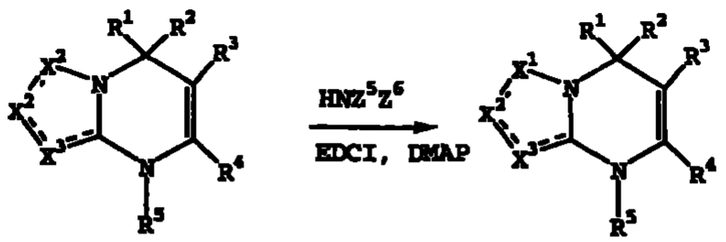
Compounds of formula I where R^3 = ester may be prepared by condensation of compounds of formula 1, formula 2 and heterocycles of formula 4 by warming between temperatures of 30 – 150 °C in the presence of a base such as sodium carbonate or sodium bicarbonate in a suitable solvent such as dimethylformamide.



Compounds of formula I where R^3 = amide maybe prepared by treating compounds of formula I where R^3 = ester with a suitable amine and trimethylaluminium in a solvent such as toluene at temperatures between 0-150 °C



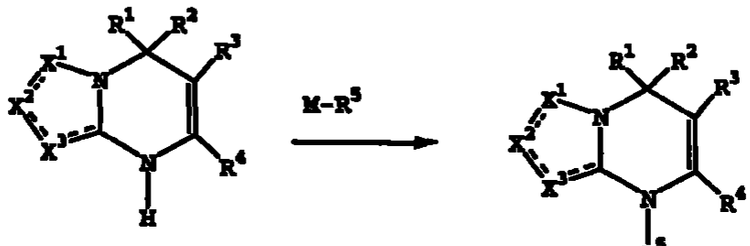
Compounds of formula I where R^3 = amide may also be prepared by condensing compounds of formula I where R^3 = COOH with a suitable amine by amidation methods well known to those skilled in the art. For example treatment of a compound of formula I where R^3 = COOH with 1-[3-(dimethylammo)propyl]-3-ethylcarbodiimide hydrochloride (EDCI) and dimethylaminopyridine (DMAP) in a solvent such as dichloromethane affords compounds of formula I where R^3 = amide.



I
(R^3 = COOH)

I
(R^3 = $CONZ^5Z^6$)

Compounds of formula I where R^5 is a substituent other than hydrogen may be formed by reacting a compound of formula 5 with a reactive species M-R^5 such that a compound of formula Ia is obtained, where M is Cl, Br, OR etc., and R^5 is as defined above (other than hydrogen).



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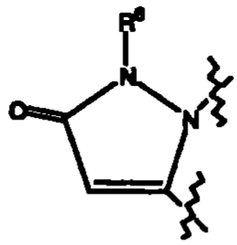
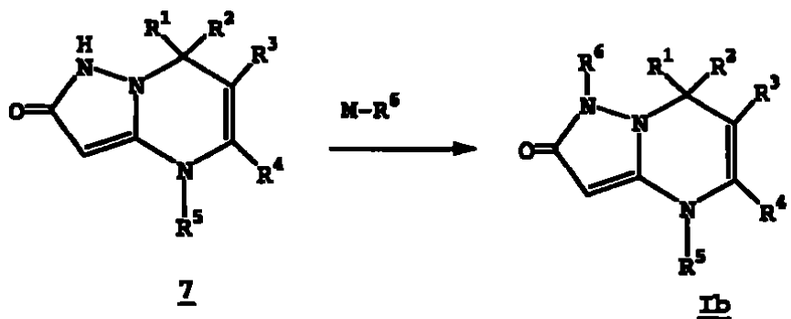
Ia

Compounds of formula I where X^1, X^2 and X^3 form a ring of the structure

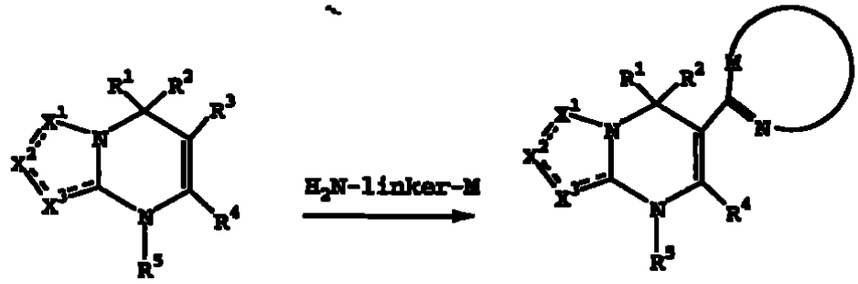


where R^6 is a substituent other than hydrogen may be formed by reacting a compound of formula 7 with a reactive species M-R^6 such that a compound of formula Ib is obtained where M is Cl, Br, OR, etc. and R^6 is as defined above.



7 Ib

Compounds of formula Ic where R^3 is a amino containing heterocycle may be formed by condensing compounds of formula I where R^3 is an acid or ester with an amine which is attached through a linker to M. M may be NH_2, NHR, SH, or OH. The linker unit may be selected such that unsubstituted, substituted or fused heterocycles are formed.



I Ic

R^3 = Ester or Acid

Additional compounds within the scope of the present invention can be prepared from the compounds obtained by the above described methods through conversion of the substituent groups to other functionality by the usual methods of chemical syntheses, as illustrated in the following examples.

Compounds of formula I that contain chiral centers maybe obtained in non-racemic form by non-racemic syntheses or resolution by methods well known to those skilled in the art. Compounds that are non-racemic are designated as "chiral" in the examples.

In the examples described below it may be necessary to protect reactive functionality such as hydroxy, amino, thio or carboxy groups, where these are desired in the final product, to avoid their unwanted participation in reactions. The

introduction and removal of protecting groups are well known to those skilled in the art, for example see (Green, T W in "Protective Groups in Organic Synthesis", John Wiley and Sons, 1991)

Utility

The compounds of the present invention are antiarrhythmic agents which are useful in the prevention and treatment (including partial alleviation or cure) of arrhythmias. The present compounds are particularly useful in the selective prevention and treatment of supraventricular arrhythmias such as atrial fibrillation, and atrial flutter By "selective prevention and treatment of supraventricular arrhythmias" is meant the prevention or treatment of supraventricular arrhythmias wherein the ratio of the prolongation of the atrial effective refractory period to the prolongation of the ventricular effective refractory period is greater than 1 1 This ratio is preferably greater than 4 1, more preferably greater than 10·1, and most preferably such that prolongation of the atrial effective refractory response period is achieved without significantly detectable prolongation of the ventricular effective refractory period.

In addition, the present compounds can block I_{Kur}, and thus may be useful in the prevention and treatment of all I_{Kur}-associated conditions. An "I_{Kur}-associated condition" is a disorder which may be prevented, partially alleviated or cured by the administration of an I_{Kur} blocker The Kv1 5 gene is known to be expressed in stomach tissue, intestinal/colon tissue, the pulmonary artery, and pancreatic beta cells. Thus, administration of an I_{Kur} blocker could provide useful treatment for disorders such as reflux esauphagitis, functional dispepsia, constipation, asthma, and diabetes. Additionally, Kv1.5 is known to be expressed in the anterior pituitary Thus, administration of an I_{Kur} blocker could stimulate growth hormone secretion. I_{Kur} inhibitors can additionally be useful in cell poliferative disorders such as leukemia, and autoimmune diseases such as rheumatoid arthritis and transplant rejection.

The present invention thus provides methods for the prevention or treatment of one or more of the aforementioned disorders, comprising the step of administering to a subject in need thereof an effective amount of at least one compound of the formula I. Other therapeutic agents such as those described below may be employed with the inventive compounds in the present methods. In the

methods of the present invention, such other therapeutic agent(s) may be administered prior to, simultaneously with or following the administration of the compound(s) of the present invention.

The present invention also provides pharmaceutical compositions comprising at least one of the compounds of the formula I or salts thereof capable of preventing or treating one or more of the aforementioned disorders in an amount effective therefor, and a pharmaceutically acceptable vehicle or diluent. The compositions of the present invention may contain other therapeutic agents as described below, and may be formulated, for example, by employing conventional solid or liquid vehicles or diluents, as well as pharmaceutical additives of a type appropriate to the mode of desired administration (for example, excipients, binders, preservatives, stabilizers, flavors, etc.) according to techniques such as those well known in the art of pharmaceutical formulation.

The compounds of the formula I may be administered by any suitable means, for example, orally, such as in the form of tablets, capsules, granules or powders, sublingually; bucally; parenterally, such as by subcutaneous, intravenous, intramuscular, or intrasternal injection or infusion techniques (e.g., as sterile injectable aqueous or non-aqueous solutions or suspensions), nasally such as by inhalation spray; topically, such as in the form of a cream or ointment; or rectally such as in the form of suppositories, in dosage unit formulations containing non-toxic, pharmaceutically acceptable vehicles or diluents. The present compounds may, for example, be administered in a form suitable for immediate release or extended release. Immediate release or extended release may be achieved by the use of suitable pharmaceutical compositions comprising the present compounds, or, particularly in the case of extended release, by the use of devices such as subcutaneous implants or osmotic pumps. In the case where the compounds of formula I are being administered to prevent or treat arrhythmias, the compounds may be administered to achieve chemical conversion to normal sinus rhythm, or may optionally be used in conjunction with electrical cardioconversion

Exemplary compositions for oral administration include suspensions which may contain, for example, microcrystalline cellulose for imparting bulk, alginic acid or sodium alginate as a suspending agent, methylcellulose as a viscosity enhancer, and

sweeteners or flavoring agents such as those known in the art, and immediate release tablets which may contain, for example, microcrystalline cellulose, dicalcium phosphate, starch, magnesium stearate and/or lactose and/or other excipients, binders, extenders, disintegrants, diluents and lubricants such as those known in the art. The compounds of formula I may also be delivered through the oral cavity by sublingual and/or buccal administration. Molded tablets, compressed tablets or freeze-dried tablets are exemplary forms which may be used. Exemplary compositions include those formulating the present compound(s) with fast dissolving diluents such as mannitol, lactose, sucrose and/or cyclodextrins. Also included in such formulations may be high molecular weight excipients such as celluloses (avicel) or polyethylene glycols (PEG). Such formulations may also include an excipient to aid mucosal adhesion such as hydroxy propyl cellulose (HPC), hydroxy propyl methyl cellulose (HPMC), sodium carboxy methyl cellulose (SCMC), maleic anhydride copolymer (e.g., Gantrez), and agents to control release such as polyacrylic copolymer (e.g., Carbopol 934). Lubricants, glidants, flavors, coloring agents and stabilizers may also be added for ease of fabrication and use.

Exemplary compositions for nasal aerosol or inhalation administration include solutions in saline which may contain, for example, benzyl alcohol or other suitable preservatives, absorption promoters to enhance bioavailability, and/or other solubilizing or dispersing agents such as those known in the art.

Exemplary compositions for parenteral administration include injectable solutions or suspensions which may contain, for example, suitable non-toxic, parenterally acceptable diluents or solvents, such as mannitol, 1,3-butanediol, water, Ringer's solution, an isotonic sodium chloride solution, or other suitable dispersing or wetting and suspending agents, including synthetic mono- or diglycerides, and fatty acids, including oleic acid.

Exemplary compositions for rectal administration include suppositories which may contain, for example, a suitable non-irritating excipient, such as cocoa butter, synthetic glyceride esters or polyethylene glycols, which are solid at ordinary temperatures, but liquify and/or dissolve in the rectal cavity to release the drug.

Exemplary compositions for topical administration include a topical carrier such as Plastibase (mineral oil gelled with polyethylene)

The effective amount of a compound of the present invention may be determined by one of ordinary skill in the art, and includes exemplary dosage amounts for an adult human of from about 0.001 to 100 mg/kg of body weight of active compound per day, which may be administered in a single dose or in the form of individual divided doses, such as from 1 to 4 times per day It will be understood that the specific dose level and frequency of dosage for any particular subject may be varied and will depend upon a variety of factors including the activity of the specific compound employed, the metabolic stability and length of action of that compound, the species, age, body weight, general health, sex and diet of the subject, the mode and time of administration, rate of excretion, drug combination, and severity of the particular condition. Preferred subjects for treatment include animals, most preferably mammalian species such as humans, and domestic animals such as dogs, cats and the like, subject to the aforementioned disorders.

The compounds of the present invention may be employed alone or in combination with each other and/or other suitable therapeutic agents useful in the treatment of the aforementioned disorders, such as other antiarrhythmic agents, calcium channel blockers, cyclooxygenase inhibitors, platelet aggregation inhibitors, fibrinogen antagonists, diuretics, angiotensin converting enzyme inhibitors, angiotensin II antagonists, thrombolytic agents, thromboxane receptor antagonists, prostacyclin mimetics, or phospodiesterase inhibitors Exemplary other antiarrhythmic agents include Class I agents (such as propafenone and quinidine), Class II agents (such as sotalol), and Class III agents (such as dofetilide and amiodarone). Exemplary calcium channel blockers include diltiazem, verapamil, nifedipine, and amlodipine. Exemplary cyclooxygenase inhibitors include aspirin or indomethacin. Exemplary platelet aggregation inhibitors include clopidogrel, ticlopidene or aspirin. Exemplary diuretics include chlorothiazide, hydrochlorothiazide, flumethiazide, hydroflumethiazide, bendroflumethiazide, methylchlorothiazide, trichloromethiazide, polythiazide, benzthiazide, ethacrynic acid tricrynafen, chlorthalidone, furosemide, musolimine, bumetanide, triamterene, amiloride or spironolactone. Exemplary angiotensin converting enzyme inhibitors include captopril, zofenopril, fosinopril, enalapril, ceranopril, cilazopril, delapril, pentopril, quinapril, ramipril, lisinopril or salts of such compounds Exemplary

angiotensin II antagonists include losartan, irbesartan or valsartan Exemplary thrombolytic agents include tissue plasminogen activator (tPA), recombinant tPA, streptokinase, urokinase, prourokinase, anisoylated plasminogen streptokinase activator complex (APSAC, Eminase, Beecham Laboratories) or animal salivary gland plasminogen activators Exemplary thromboxane receptor antagonists include ifetroban

The above other therapeutic agents, when employed in combination with the compounds of the present invention, may be used, for example, in those amounts indicated in the Physicians' Desk Reference (PDR) or as otherwise determined by one of ordinary skill in the art.

All documents cited in the present specification are incorporated herein by reference in their entirety

The following examples and preparations describe the manner and process of making and using the invention and are illustrative rather than limiting It is to be understood that there may be other embodiments which fall within the spirit and scope of the invention as defined by the claims appended hereto. Abbreviations employed herein are defined below

DCM = dichloromethane

DMAP = dimethylaminopyridine

DMF = dimethylformamide

DMPU = 1,3-Dimethyl-3,4,5,6-tetrahydro-2(1 *H*)-pyrimidinone

EDCI (or EDC) = 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride

M+H = monoisotopic mass plus one proton

Et = ethyl

h = hours

HPLC = high performance liquid chromatography

HOBT = hydroxybenzotriazole

LC/MS = liquid chromatography/mass spectrometry

Me = methyl

min = minutes

MS = mass spectrometry

NaOAc = sodium acetate

Ph = phenyl

PPA = phosphoric acid

Pr = propyl

Py = pyridine

PyBrOP = bromo-tris-pyrrolidino-phosphonium hexafluorophosphate

RT = room temperature

Rt = retention time

TEA = triethylamine

TFA = trifluoroacetic acid

TLC = thin layer chromatography

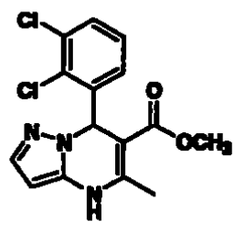
THF = tetrahydrofuran

TMSOTf = trimethylsilyl trifluoromethanesulfonate

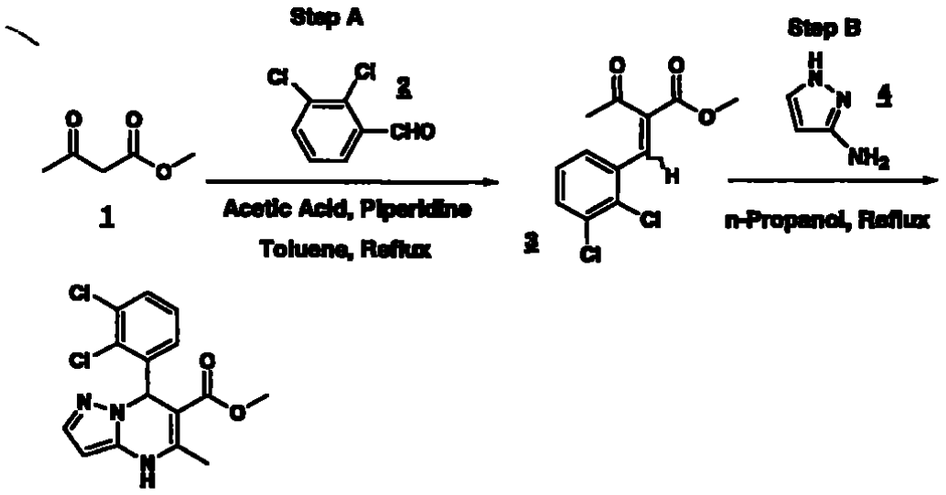
35

Example 1

7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid methyl ester



Method



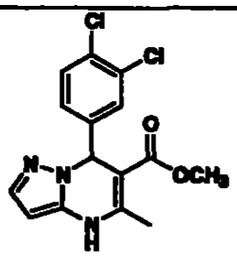
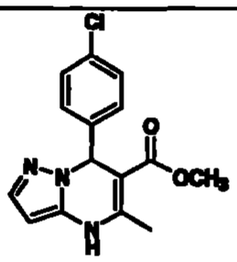
Step A. A mixture of methyl acetoacetate 1 (5 mL, 46 mmol), 2,3-dichlorobenzaldehyde 2 (8 1 g, 46 mmol), piperidine (1 1 ml, 12 mmol), and acetic acid (0.6 mL, 11 mmol) in toluene (200 mL) was refluxed overnight with azeotropic removal of water via a Dean-Stark trap. The mixture was cooled to room temperature, quenched with water, transferred to a separatory funnel, diluted with ethyl acetate, washed with aqueous NaOH (1M), aqueous HCl (1M), water and brine and concentrated in vacuo. The residue was purified by flash chromatography (silica gel, 33% Ethyl acetate/hexanes) to afford 10.8 g (85% yield) of compound 3 as a mixture of diasteromers Reverse Phase LC/MS YMC S5 ODS 4.6 x 50 mm Ballistic column, UV detection at 220λ, 4 min. gradient (10% MeOH/H_2O with 0 1% TFA-90%

MeOH/H_2O with 0 1% TFA), 4 mL/min. Diastereomer A, Rt = 3.51 min,(53%) Diastereomer B, Rt=3 70 min (45%) MS (M+H 273)

Step B A mixture of compound 3 (5 g, 18.3 mmol), 3-aminopyrazole 4 (1.5 g, 18 3 mmol) in 1-propanol (60 mL) was refluxed for 6 h The mixture was cooled to room temperature and concentrated and recrystallized from ethyl acetate/hexanes to give 1 25 g (20%) of the title compound as a yellow solid. The mother liquor was concentrated and purified by flash chromatography (silica gel, 5% methanol/dichloromethane) to give an additional 1 62 g (26%) of the title compound. Combined yield 2.87g (46%) Reverse Phase LC/MS YMC S5 ODS 4 6 x 50 mm Ballistic column, UV detection at 220λ, 4 min. gradient (10% MeOH/H_2O with 0 1% TFA-90% MeOH/H_2O with 0 1% TFA), 4 mL/min. Rt = 3.38 min, (96% pure) MS (M+H 338) HMR ($CDCl_3$, 400 MHz) 7 98(1H, app s), 7 15(3H, m) 6 91(1H,s), 5.52(1H, app. s),.3 61(3H, s), 2.39(3H,s)

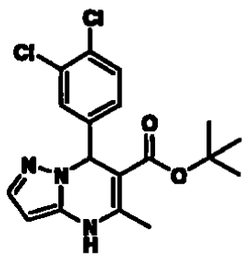
Examples 2 and 3

The compounds of Examples 2 and 3, shown in the table provided below, were prepared in a manner similar to that described in Example 1

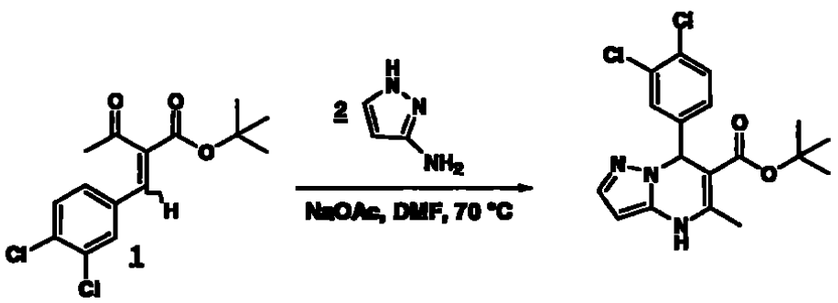
Example	Structure	Name	(M+H)
2		7 (3,4-Dichlorophenyl)-4,7 dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid methyl ester	338
3		7-(4-Chlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid methyl ester	303

Example 4

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1 1-dimethylethyl ester



Method 1

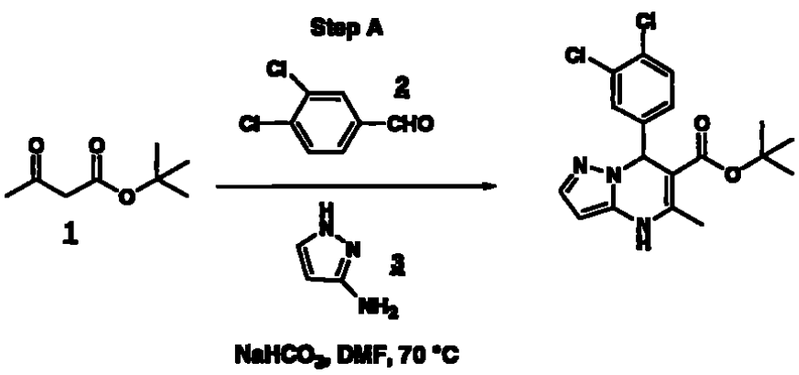


Compound 1 Compound 1 was prepared by condensing t-butoxyacetoacetate and 2,4-dichlorobenzaldehyde as described in Example 1 step A.

Title Compound. A mixture of compound 1 (44.4 g, 141 mmol), 3-aminopyrazole 2 (17.6 g 212 mmol) and sodium acetate (46.3 g, 564 mmol) in dimethylformamide (300 mL) was stirred at 70 °C overnight (17 h). The mixture was cooled to room temperature, transferred to a separatory funnel, diluted with water and ethyl acetate, washed with water (a small amount of methanol was added to breakup emulsions that formed) and brine, dried over anhydrous sodium sulfate and concentrated. A precipitate formed. The precipitate was collected and washed with ethyl acetate, ethyl ether and hexanes and dried to give 8 93g. The mother liquor was concentrated to give a second crop of precipitate 9.32 g. LC/MS analysis indicated the precipitates

were not pure. The precipitates were combined, dissolved in dichloromethane and concentrated onto enough silica gel such that a free flowing powder was obtained. The resulting powder was loaded onto a chromatography column prepacked with silica gel and dichloromethane. Elution with 100% dichloromethane followed by 3% methanol/dichloromethane gave 15 1 g (29% yield) of the title compound. Reverse Phase LC/MS YMC S5 ODS 4.6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min gradient (10% MeOH/H20 with 0 1% TFA-90% MeOH/H_2O with 0 1% TFA), 4 mL/min. Rt = 4.63min, (97% pure) MS (M+H 380) HMR (CD_3OD, 400 MHz) 7 41(2H, m), 7 33(1H, d, J=2 Hz), 7 08(1H, m), 6 21(1H,s), 5 68(1H, d, J=2 Hz), 2.43(3H, s), 1 37(9H,s)

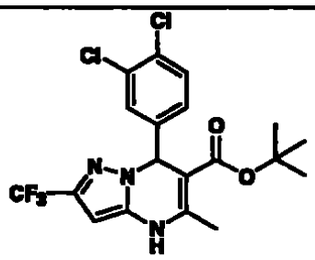
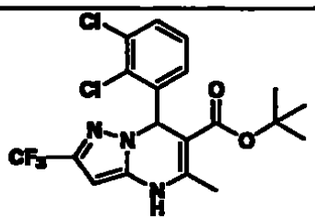
Method 2



A mixture of t-butoxyacetoacetate 1 (22.6 g, 143 mmol), 3,4-dichlorobenzaldehyde 2 (25.0 g, 143 mmol), 3-aminopyrazole 3 (15 4 g, 185 mmol) and sodium bicarbonate (36 g, 428 mmol) in dimethylformamide (250 mL) was stirred at 70 °C overnight (18 h) The mixture was cooled to room temperature, quenched with ethyl acetate and water, transferred to a separatory funnel, washed with water and brine, dried over sodium sulfate, filtered and concentrated. The residue was recrystallized from ethyl acetate/hexanes to give 16 8g (31% yield) of the title compound as a white solid. Data for the title compound is given in method 1

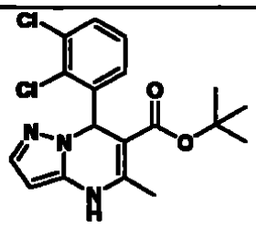
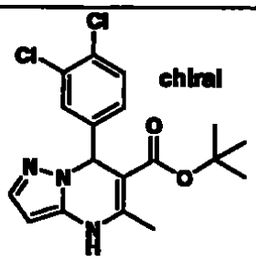
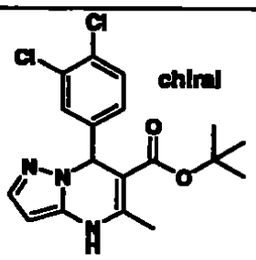
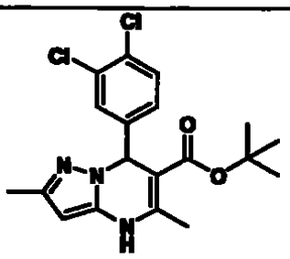
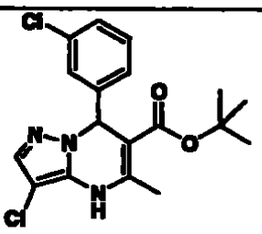
Examples 5 and 6

The compounds of Examples 5 and 6, shown in the table provided below, were prepared in a manner similar to that described in Example 4, Method 1

Example	Structure	Name	(M+H)
5		7 (3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1 1-dimethylethyl ester	448
6		7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-2 (trifluoromethyl)pyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1 1-dimethylethyl ester	448

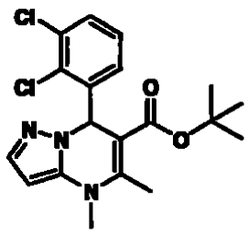
Examples 7-11

The compounds of Examples 7-11, shown in the table provided below, were prepared in a manner similar to that described in Example 4, Method 2. The compound of Example 4, method 2 could be resolved into the corresponding enantiomers A (Example 8) and B (Example 9) by preparative chiral HPLC (Chiralcel OD column (50 X 500 mm), eluting with 7% isopropanol/hexanes containing 0 1 % triethylamine amine at 50 mL/min), UV detection at 254λ. Analytical HPLC (Chiralcel OD column (4.6 X 250 mm) eluting with 10% isopropanol/hexanes containing 0 1 % triethylamine amine at 1 mL/min), UV detection at 254λ, enantiomer A (Rt= 6.98 min, 98% ee) enantiomer B (Rt= 9.22 min, 98% ee)

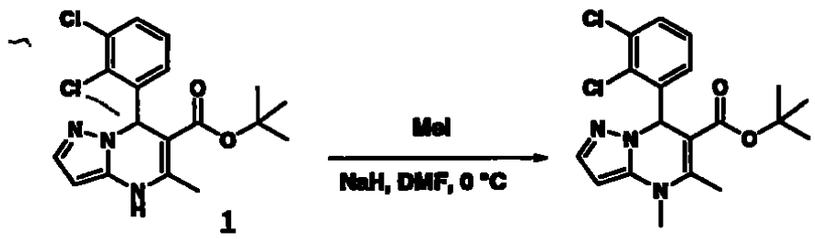
Example	Structure	Name	(M+H)
7		7-(2,3-Dichlorophenyl)-4,7 dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1,1-dimethylethyl ester	380
8		7-(3,4-Dichlorophenyl)-4 7 dihydro-5-methylpyrazolo[1 5 a]pyrimidine-6-carboxylic acid 1,1-dimethylethylester enantiomer A	380
9		7-(3,4-Dichlorophenyl)-4,7 dihydro-5-methylpyrazolo[1 5-a]pyrimidine-6-carboxylic acid 1,1-dimethylethylester enantiomer B	380
10		7-(3,4-Dichlorophenyl)-4,7 dihydro-2,5-dimethylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1,1-dimethylethyl ester	394
11		3-Chloro-7-(3-chlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1 1-dimethylethyl ester	380

Example 12

7-(2,3-Dichlorophenyl)-4,7-dihydro-4,5-dimethylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1 1-dimethylethyl ester



Method



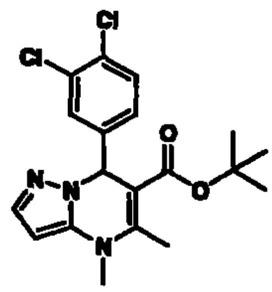
1

Compound 1 Compound 1 was prepared as described in Example 4, method 1

Title Compound. Sodium hydride (0.186 g, 7.76 mmol) was added to a 0 °C solution of 1 (2.27 g, 5.97 mmol) in dimethylformamide (30 mL). After 10 min., methyl iodide (0.41 mL, 6.57 mmol) was added. After an additional 85 min, the mixture was quenched with saturated ammonium chloride solution, diluted with ethyl acetate, transferred to a separatory funnel, washed with saturated ammonium chloride, water and brine, dried over anhydrous sodium sulfate and concentrated onto enough silica gel such that a free flowing powder was obtained. The resulting powder was loaded onto a chromatography column prepacked with 100% dichloromethane. Elution with 0-10% ethyl acetate/dichloromethane gave 1.16 g (49%) of the title compound as a slightly yellow solid. Reverse Phase LC/MS: YMC S5 ODS 4.6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 40-100% Solvent B/A (Solvent A: 10% MeOH/H20 with 0.1% TFA, Solvent B: 90% MeOH/H_2O with 0.1% TFA), 4 mL/min. Rt = 3.46 min, (96% pure). MS (M+H): 394). HMR (CD_3Cl, 400 MHz) 7.39(1H, d, J=2 Hz), 7.35(1H, m), 7.23(1H, m), 7.11(1H, m), 6.91(1H,s), 5.58(1H, d, J=2 Hz), 2.38(3H, s), 2.62(3H, s), 1.27(9H,s).

Example 13

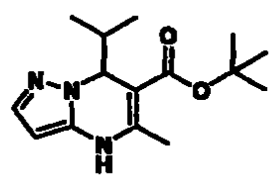
7 (3,4-Dichlorophenyl)-4,7-dihydro-4,5-dimethylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1,1-dimethylethyl ester



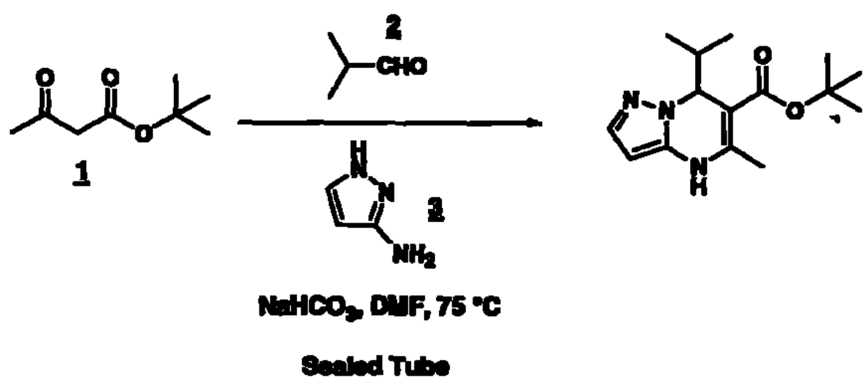
The title compound was prepared in a similar manner to that provided in Example 12 yielding a compound with (M+H) 394.

Example 14

4,7-Dihydro-5-methyl-7-(1-methylethyl)pyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1,1-dimethylethyl ester



Method.

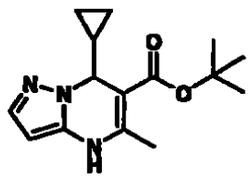


A pressure tube was dried with a heat gun under nitrogen. The pressure tube was charged in the following order with isobutyraldehyde 2 (0.262 g, 3.63 mmol),

dimethylformamide (3 mL), t-butylacetoacetate 1 (0.574 g, 3 63 mmol), 3-aminopyrazole 3 (0.362 g, 4.36 mmol) and sodium acetate (1 22 g, 14 5 mmol) The mixture was flushed with nitrogen. The tube was sealed and warmed to 75 °C and stirred overnight. The mixture was cooled to room temperature, diluted with ethyl acetate to a volume of 20 mL, washed with lithium chloride (2.4M, 10 mL) and brine, dried over anhydrous sodium sulfate, filtered and concentrated to give 1 02 of a yellow oil. The oil was purified by flash chromatography (silica, 45% ethyl acetate/heptane) to give 0.42 g (41% yield) of the title compound. Reverse Phase HPLC YMC S5 ODS 4 6 x 50mm Ballistic column, UV detection at 220 λ, 4 min. gradient 0-100% Solvent B/A (Solvent A. 10% MeOH/H_2O with 0.2% PPA, Solvent B 90% MeOH/H_2O with 0.2% PPA), 4mL/min. Rt = 3 83 min, (100% pure) Reverse Phase LC/MS YMC S5 ODS 4.6 x 50mm Ballistic column, UV detection at 220 λ, 4 mm. gradient 0-100% Solvent B/A (Solvent A. 10% MeOH/H_2O with 0 1% TFA, Solvent B 90% MeOH/H_2O with 0 1% TFA), 4mL/min. Rt = 3 06mm MS (EM, M+1 278) HMR ($CDCl_3$, 400MHz) 7 37(1H,d,J=2.2Hz), 6 35(1H,s), 5 55(1H,d,J=1 8Hz), 5.29(1H,d,J=2.2Hz), 2.41(3H,s), 1.50(9H,s), 1.28-1 19(1H,m), 1 07(3H,d,J=7 0Hz), 0 60(3H,d,J=7.0Hz)

Example 15

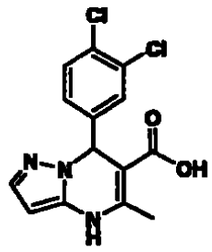
7-Cyclopropyl-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1,1-dimethylethyl ester



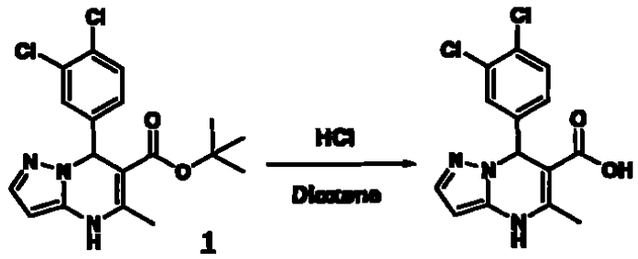
The title compound was prepared in a similar manner to that provided in Example 14 yielding a compound with (M+H) 275

Example 16

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid



Method.



1

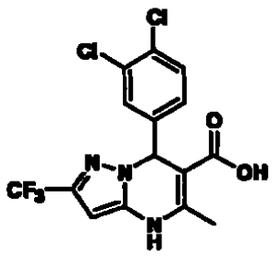
Compound 1 Compound 1 was prepared as described in Example 4.

Title Compound HCl (4M in dioxane) was added to solid compound 1 (1 13 g, 2.97 mmol) at room temperature. The solid dissolves and a precipitate forms. The resulting thick reaction mixture was allowed to stir overnight and was concentrated in

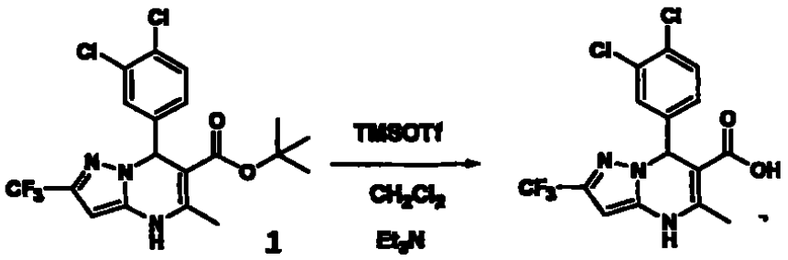
vacuo to give 1 14 g (120% contains dioxane) of the title compound as a white solid Reverse Phase LC/MS YMC S5 ODS 4 6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 0-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0 1% TFA, Solvent B 90% MeOH/H_2O with 0.1% TFA), 4 mL/min Rt = 3.54 min, (93% pure) MS (M+H 324) HMR (CD_3OD, 400 MHz) 7 96(1H, d, J=3 Hz), 7.51(2H, m), 7 21(1H, m), 6.49(1H,s), 6 11(1H, d, J=3 Hz), 2.51(3H, s). The title compound was used in subsequent reactions without further purification.

Example 17

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-6-carboxylic acid



Method.



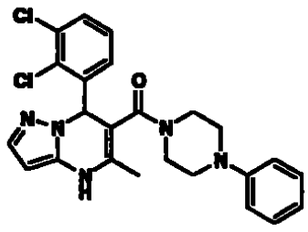
Compound 1 Compound 1 (the compound of Example 5) was prepared in a manner similar to that described in Example 4

Title Compound Trimethylsilyl trifluoromethanesulfonate (0.873 mL, 4.82 mmol) was added to a room temperature solution of compound 1 (1.08 g, 2.41 mmol) in dichloromethane (50 mL). After 2h triethylamine (0.672 ml, 4.82 mmol) was added

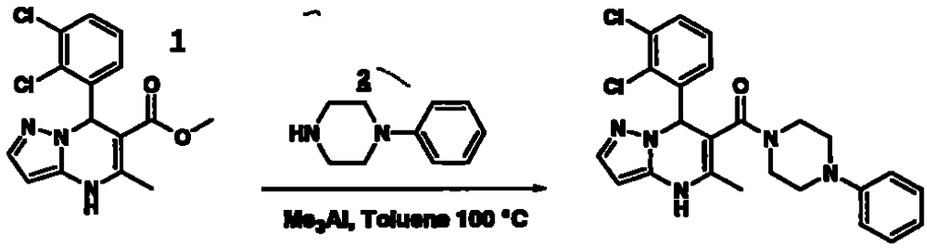
and the reaction mixture was poured into water The organic layer was separated and dried over Na_2SO_4, concentrated, and purified by flash chromatography (50% ethylacetate/hexane → 100% ethyl acetate) to give 0 71 g (75% yield) of the title compound as a white solid. MS (M+H 392)

Example 18

1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine



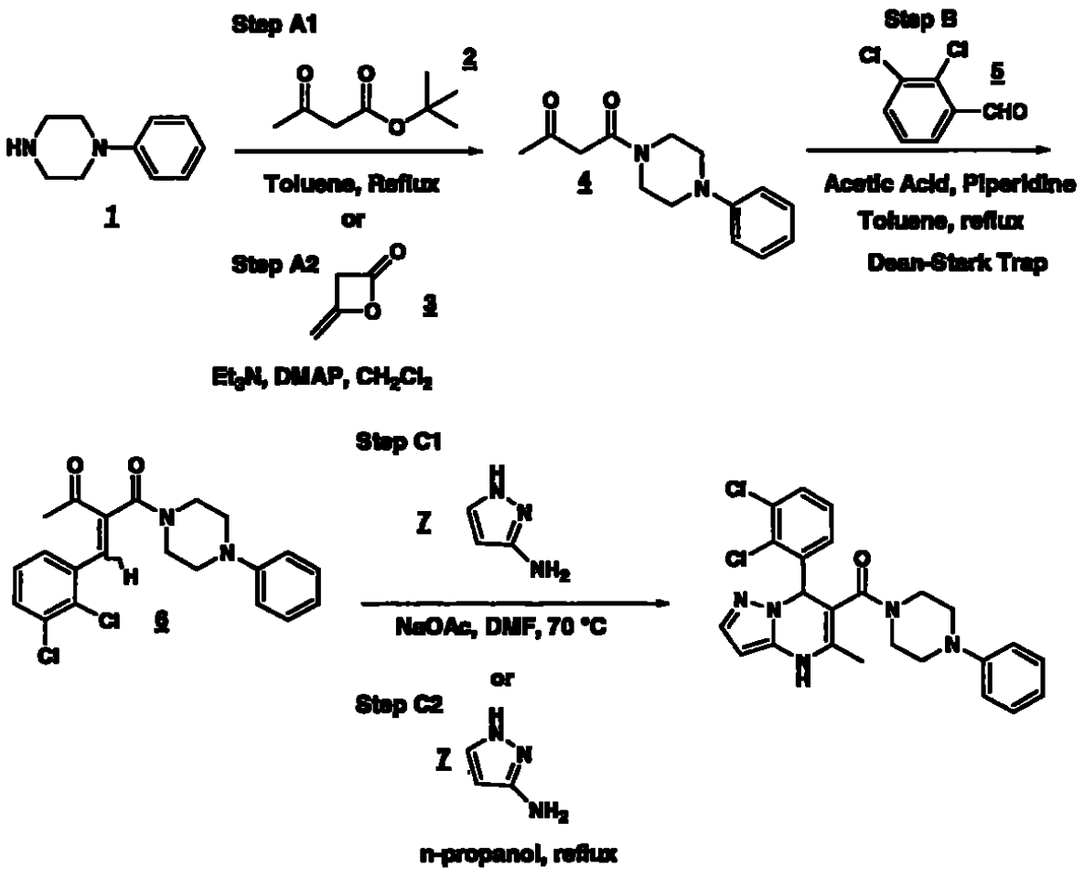
Method 1



Compound 1 Compound 1 was prepared as described in Example 1

Title Compound Trimethylaluminium (1 1 mL, 2.2 mmol, 2 M in toluene) was dropwise added to a room temperature solution of 1-phenylpiperazine 2 (0.4 mL, 2.2 mmol) in toluene (7 mL) After one hour compound 1 (0 50 g, 1.5 mmol) was added and the resulting mixture was stirred at 100 °C for 18 h. The mixture was cooled to room temperature, quenched with water, diluted with ethyl acetate, transferred to a separatory funnel, washed with aqueous HCl (1M), water and brine, dried over anhydrous sodium sulfate and concentrated in vacuo. The residue was purified by flash chromatography (silica gel, 50% ethyl acetate/hexanes followed by 5% methanol/dichloromethane to provide 0.22 g (32%) of a solid which was further purified by recrystallization from methanol/ethyl ether to give 0 15 g (22%) of the title compound. Reverse Phase LC/MS YMC S5 ODS 4.6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min gradient 0-100% Solvent B/A (Solvent A 10% MeOH/H20 with 0.1% TFA, SolventB 90% MeOH/H_2O with 0 1% TFA), 4 mL/min. Rt = 3.58 min, (92% pure) MS (M+H. 468) Additional Data for the title compound is reported in Method 2, step C variation 1

Method 2



Step A Variation 1 A mixture of N-phenylpiperazine 1 (6 7 mL, 41 mmol) and t-butoxyacetoacetate 2 (6.8 mL, 45 mmol) in toluene (50 mL) was refluxed overnight. The mixture was cooled to room temperature, transferred to a separatory funnel, diluted with ethyl ether and extracted (3X) with aqueous HCl (1M) The HCl extracts were combined and washed with ethyl ether (2X), made basic (pH 9) with aqueous NaOH (50% w/w) and extracted with ethyl acetate. The ethyl acetate extracts were combined, washed with water and brine, dried over anhydrous sodium sulfate, filtered and concentrated to give 9 76 g (97.6%) of compound 4 as a thick amber oil. Reverse Phase LC/MS YMC S5 ODS 4 6 x 50 mm Ballistic column, UV

detection at 220 λ, 4 min. gradient 0-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0 1% TFA, SolventB 90% MeOH/H_2O with 0 1% TFA), 4 mL/min. Rt = 1 65 min, (100% pure). MS (M+H 247) HMR ($CDCl_3$, 400 MHz) 7 28(2H, m), 6 91(3H, m), 3 80(2H, m), 3 78(2H, m), 3 59(4H, m), 3 19(4H, m), 2.30(3H, s)

Step A Variation 2 Diketene 3 (5.50 g, 65 5 mmol) was slowly added over 15 min. to a 0 °C solution of 4-phenylpiperazine 1 (5.31 g, 32 7 mmol) in dichloromethane (50 mL) TLC after 4 h indicated compound 1 was not completely consumed. Additional diketene (5.50 g, 65 5 mmol) was added. After an additional 1 5h the reaction was quenched with 1N NaOH, transferred to a separatory funnel, washed with 1H NaOH and brine, dried over sodium sulfate, concentrated onto enough silica gel such that a free flowing powder was obtained. The resulting powder was loaded onto a chromatography column prepacked with silica and 50% ethyl acetate/hexanes Elution with 50-100% ethylacetate/hexanes gave 8.2 g (100%) of compound 4 as a thick yellow oil. Data for compound 4 is given above in step A variation 1

Step B A mixture of compound 4 (9 76 g, 40 mmol), 2,3-dichlorobenzaldehyde 6 (7 89 g, 45 mmol), piperidine (1 0 ml, 10 mmol), acetic acid (0 59 mL, 10 mmol) in toluene (100 mL) was refluxed overnight with azeotropic removal of water via a Dean-Stark trap The mixture was cooled to room temperature and concentrated in vacuo and was typically used in subsequent reactions without purification. Compound 6 may be Purified by silica gel chromatography (30-40% ethyl acetate/hexanes). Reverse Phase LC/MS YMC S5 ODS 4.6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 0-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0 1% TFA, SolventB 90% MeOH/H_2O with 0 1% TFA), 4 mL/mm Rt = 3.83 mm, (96% pure). MS (M+H. 404) HMR ($CDCl_3$, 400 MHz) 7 82(1H, s), 7.55(1H, dd, J=1, 8 Hz), 7.48(1H, dd, J=1, 8 Hz), 7.23(3H, m), 6 89(1H, app. t, 7 Hz), 6.81(2H, d, J=8 Hz), 3 78(2H, m), 3.34(1H, m), 3 23(2H, m), 2 96(1H, m), 2.85(1H, m), 2.50(3H, s), 2.42(1H, M)

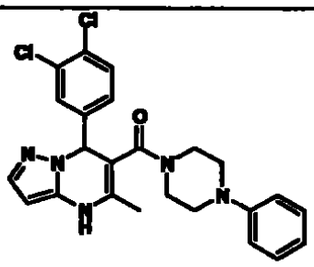
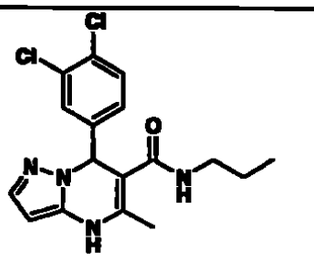
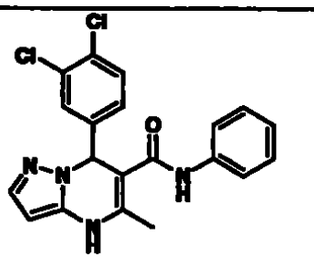
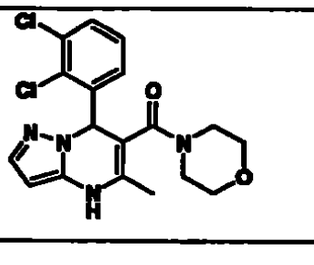
Step C Variation 1 A mixture of compound 6 (16 g, 40 mmol), 3-aminopyrazole 7 (5 1 g 62 mmol) and sodium acetate (10.1 g, 123 mmol) in dimethylformamide (100

mL) was stirred at 70 °C overnight (17 h) The mixture was cooled to room temperature, transferred to a separatory funnel, diluted with water and ethyl acetate, washed with water (a small amount of methanol was added to breakup emulsions that formed) and brine, dried over anhydrous sodium sulfate and concentrated. The resulting residue was purified by silica gel chromatography Elution with 50% ethyl acetate/hexanes followed by 100% ethyl acetate afforded 6 2 g (33% yield from compound 1) of the title compound. The title compound could be resolved into the corresponding enantiomers A (Example 28) and B (Example 29) by preparative chiral HPLC (Chiracel OD column (50 X 500 mm), eluting with 30% isopropanol/hexanes containing 0 1 % triethylamine amine at 50 mL/min), UV detection at 254λ, enantiomer A Rt= 42 min, enantiomer B Rt= 54 min Analytical HPLC (Chiracel OD column (4 6 X 250 mm) eluting with 30% isopropanol/hexanes containing 0 1 % triethylamine amine at 1 mL/min), UV detection at 254λ, enantiomer A Rt= 11 7 min, enantiomer B Rt= 17 6 min. Data given for enantiomer A. Reverse Phase LC/MS YMC S5 ODS 4 6 x 50 mm Ballistic column, UV detection at 220λ, 4 min. gradient 0-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0 1% TFA, Solvent B 90% MeOH/H_2O with 0.1% TFA), 4 mL/min Rt = 3 54min (91% pure) MS (M+H 468) HMR (HCl salt of 8a, CD_3OD, 400 MHz) 7 94(1H, d, J=3 Hz), 7 56(8H, m), 7 38(1H, m), 6 05(1H, d, J=3 Hz), 4 23(1H,m), 3 57(7H, m), 2.01(3H, s)

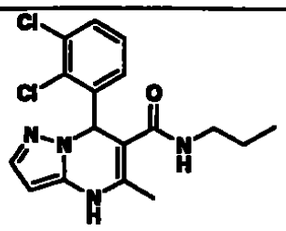
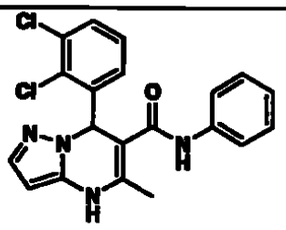
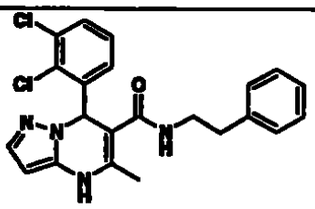
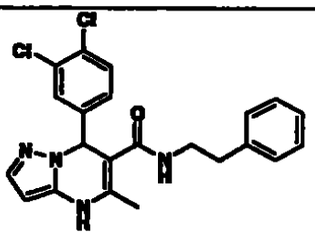
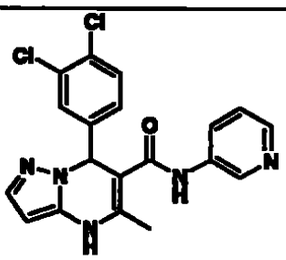
Step C Variation 2. A mixture of compound 5 (6.0 g, 15 mmol), 3-aminopyrazole 7 (1 24 g, 15 mmol) in n-propanol (50 mL) was refluxed overnight (19 h) The mixture was cooled to room temperature, transferred to a separatory funnel, diluted with ethyl acetate. An attempt to wash the solution with saturated ammonium chloride resulted in the formation of a precipitate. The precipitate was dissolved with water and methanol. The resulting mixture was washed with water and brine, dried over anhydrous sodium sulfate and concentrated. The resulting residue was purified by silica gel chromatography Elution with 70% ethyl acetate/hexanes followed by 100% ethyl acetate afforded 2 7 g (39% yield) of the title compound as a white solid. The title compound could be resolved into the corresponding enantiomers A and B as described in Step C variation 1

Examples 19-27

The compounds of Examples 19-27, shown in the table provided below, were prepared in a manner similar to that described in Example 18, Method 1

Example	Structure	Name	(M+H)
19		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine	468
20		7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-propylpyrazolo[1,5-a]pyrimidine-6-carboxamide	365
21		7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-phenyl-pyrazolo[1,5-a]pyrimidine-6-carboxamide	399
22		4-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]morpholine	393

52

23		7 (2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-N-propylpyrazolo[1 5-a]pyrimidine-6-carboxamide	365
24		7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-N-phenylpyrazolo[1,5-a]pyrimidine-6-carboxamide	399
25		7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-N-(2-phenylethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	427
26		7-(3 4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-(2-phenylethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	427
27		7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-3-pyridinylpyrazolo[1,5-a]pyrimidine-6-carboxamide	400

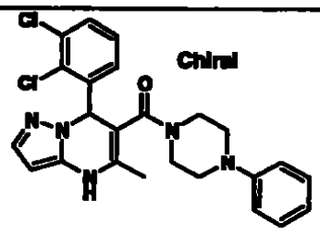
Examples 28-82

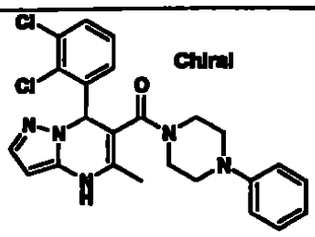
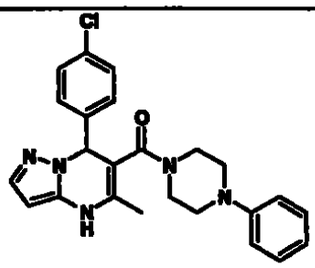
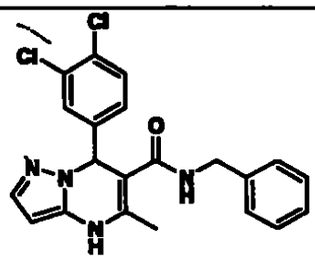
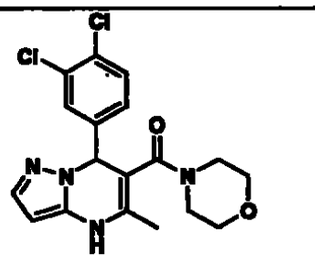
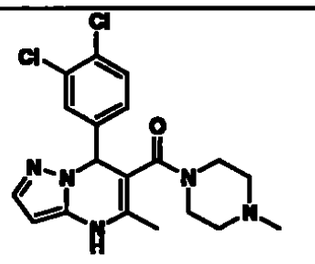
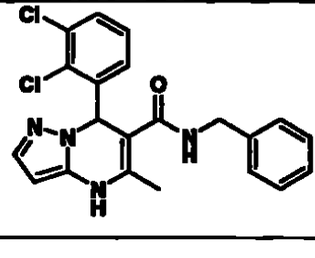
The compounds of Examples 28-82, shown in the table provided below, were prepared in a manner similar to that described in Example 18, Method 2.

HPLC resolution of Example 47, Chiralcel OD column (50 X 500 mm), eluting with 30% isopropanol/hexanes containing 0 1 % triethylamine at 50 mL/min), UV detection at 254λ, provided enantiomers A (Example 50) and B (Example 51) Chiralcel OD column (4 6 X 250 mm) eluting with 30% isopropanol/hexanes containing 0 1 % triethylamine at 1 mL/min), UV detection at 254 λ, enantiomer A Rt = 9.8 min, >99% ee. Enantiomer B Rt = 14 2 min, >99% ee.

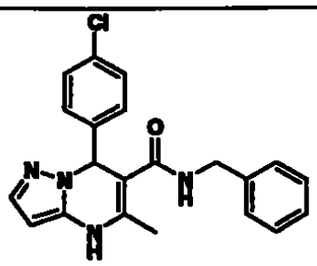
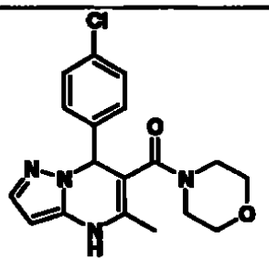
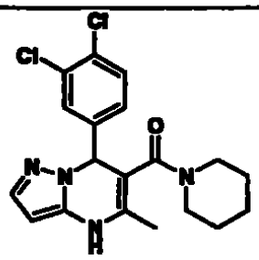
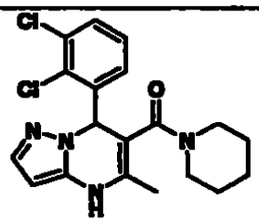
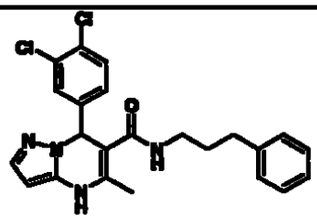
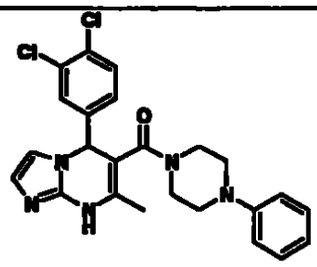
HPLC resolution of Example 70, Chiralpak AD column (50 X 500 mm), eluting with 15% ethanol/hexanes containing 0 1 % triethylamine at 50 mL/min), UV detection at 254 λ, provided enantiomers A (Example 72) and B (Example 71) Chiralpak AD column (4 6 X 250 mm) eluting with 15% ethanol/hexanes containing 0 1 % triethylamine at 1 mL/min), UV detection at 254 λ, enantiomer A Rt = 6 9 min, >99% ee. Enantiomer B Rt= 13.4 min, >99% ee.

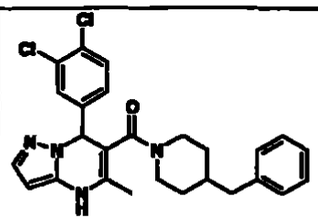
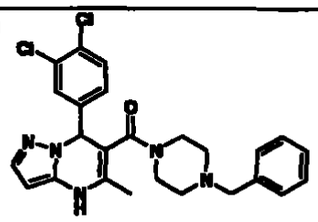
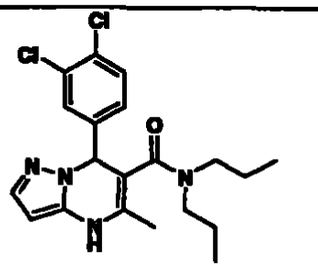
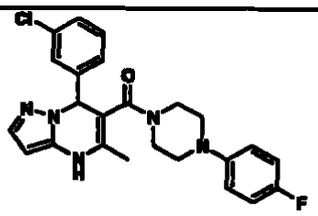
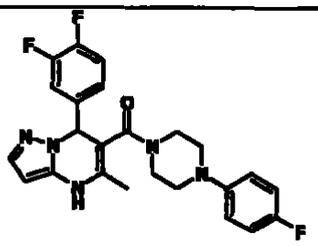
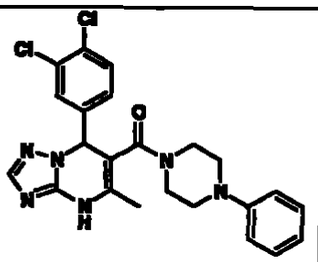
HPLC resolution of Example 80, Chiralpak AD column (50 X 500 mm), eluting with 25% isopropanol/hexanes containing 0 1 % triethylamine at 50 mL/mm), UV detection at 254 λ, provided enantiomers A (Example 81) and B (Example 82) Chiralpak AD column (4 6 X 250 mm) eluting with 30% isopropanol/hexanes containing 0 1 % triethylamine at 1 mL/min), UV detection at 254 λ, enantiomer A Rt = 5.3 min, >99% ee. Enantiomer B Rt = 7 1 min, >99% ee.

Example	Structure	Name	(M+H)
28		1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenyl-piperazine, enantiomer A	468

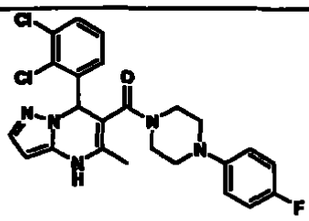
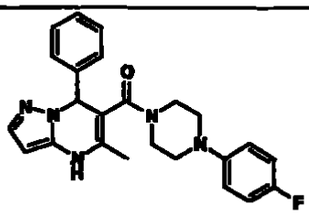
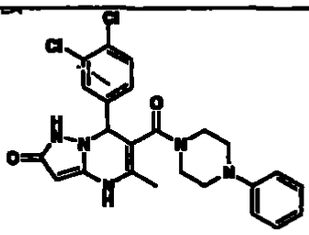
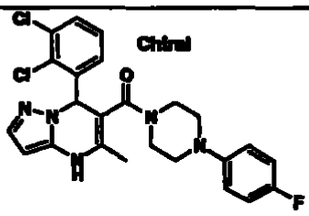
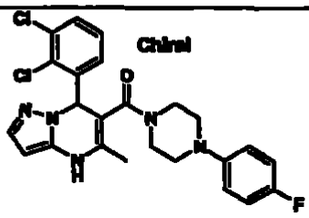
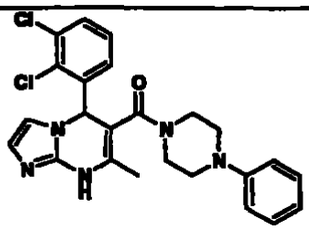
29	 Chiral	1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl pyrazolo[1 5-a]pyrimidin-6-yl]carbonyl]-4-phenyl piperazine enantiomer B	468
30		1-[[7-(4-Chlorophenyl)-4,7 dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine	433
31		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-(phenylmethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	413
32		4-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]morpholine	393
33		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-methyl-piperazine	406
34		7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-N-(phenylmethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	413

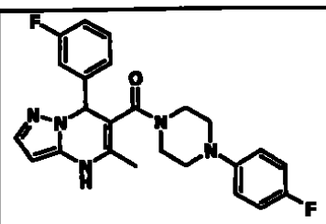
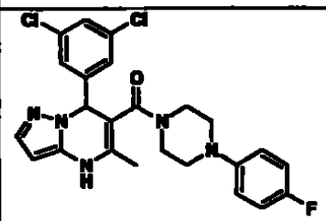
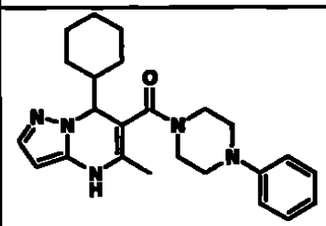
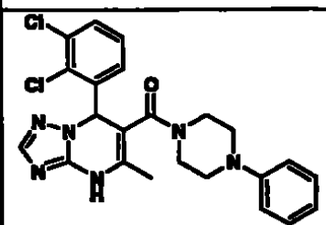
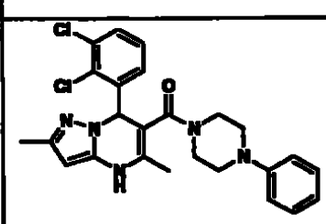
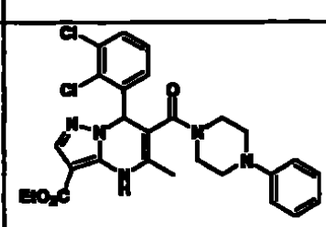
55

35		7-(4-Chlorophenyl)-4,7-dihydro-5-methyl-N-(phenylmethyl)pyrazolo[1 5-a]pyrimidine-6-carboxamide	378
36		4-[[7-(4-Chlorophenyl)-4,7 dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]morpholine	358
37		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperidine	391
38		1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperidine	391
39		7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-(3-phenylpropyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	441
40		1-[[5-(3,4-Dichlorophenyl)-5,8-dihydro-7-methyl-imidazo[1,2-a]pyrimidin-6-yl]carbonyl]-4-phenyl-piperazine	468

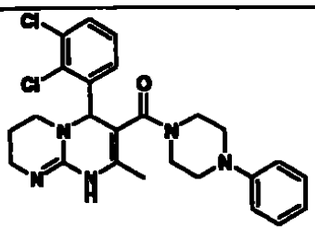
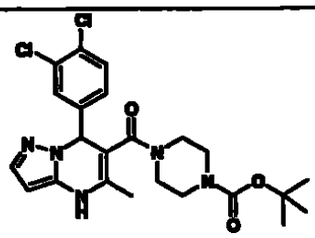
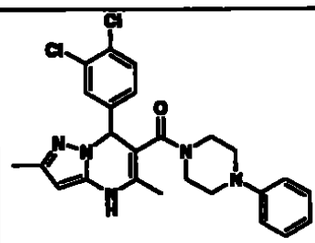
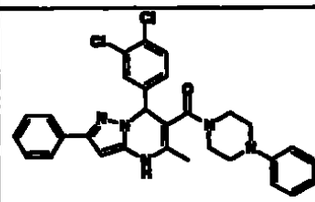
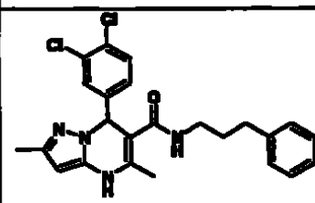
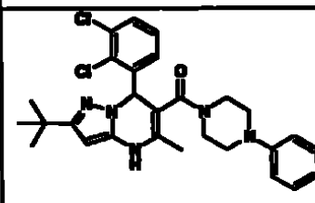
41		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1 5-a]pyrimidin-6-yl]carbonyl]-4-(phenyl-methyl)piperidine	481
42		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6 yl]carbonyl]-4-(phenyl-methyl)piperazine	482
43		7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N,N-dipropylpyrazolo[1,5-a]pyrimidine-6-carboxamide	407
44		1-[[7-(3-Chlorophenyl)-4,7 dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	451
45		1 [[7 (3,4-Difluorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	453
46		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl[1,2,4]triazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine	469

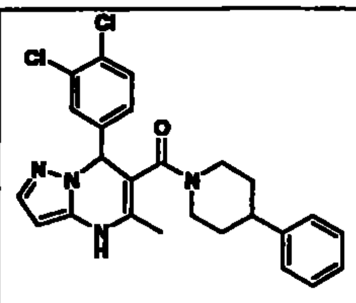
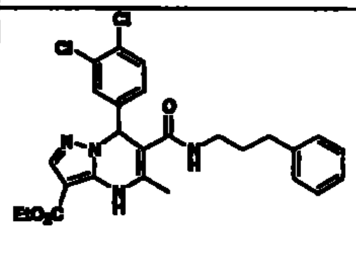
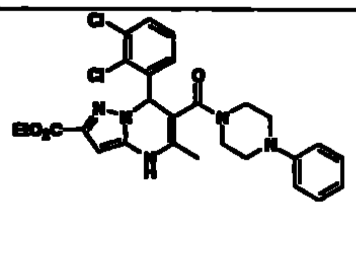
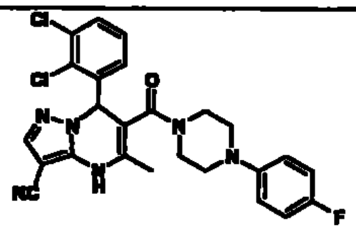
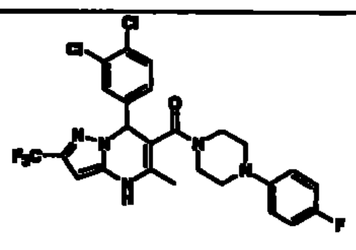
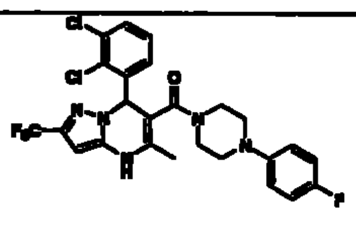
57

47		1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine	486
48		1-(4-Fluorophenyl)-4-[[4,7-dihydro-5-methyl-7 phenylpyrazolo[1 5-a]pyrimidin-6-yl)carbonyl]piperazine	417
49		1-[[7-(3,4-Dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine	484
50		1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine, enantiomer A	486
51		1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine, enantiomer B	486
52		1-[[5-(2,3-Dichlorophenyl)-5,8-dihydro-7-methyl-imidazo[1,2-a]pyrimidin-8-yl]carbonyl]-4-phenyl-piperazine	468

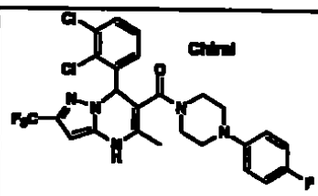
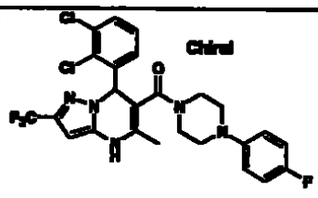
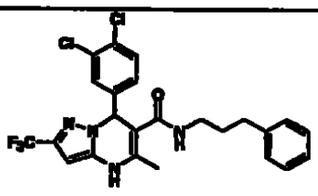
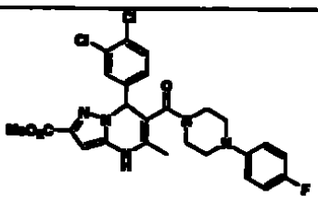
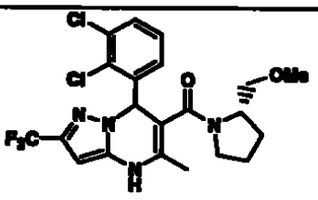
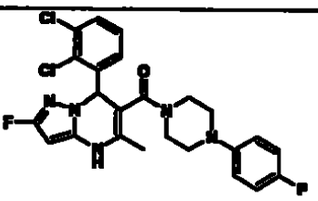
53		1-(4-Fluorophenyl)-4-[[7-(3-fluorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-piperazine	435
54		1-[[7-(3,5-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine	486
55		1-[(7-Cyclohexyl-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl)carbonyl]-4-phenylpiperazine	405
56		1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)carbonyl]-4-phenyl-piperazine	469
57		1-[[7-(2,3-Dichlorophenyl)-4,7 dihydro-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenyl-piperazine	482
58		7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-6-[(4-phenyl-1-piperazinyl)-carbonyl]pyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester	540

59

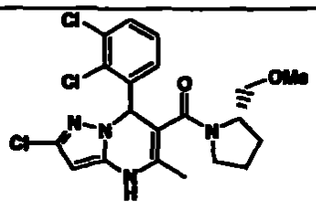
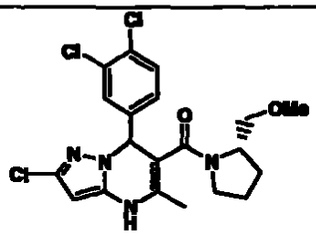
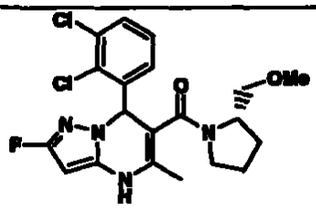
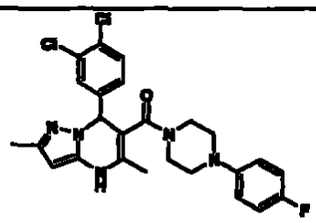
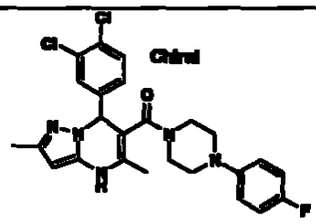
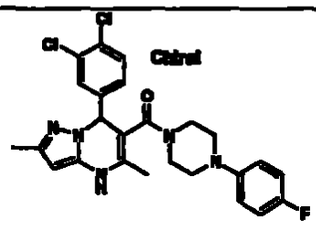
59		1-[[4-(2 3-Dichlorophenyl)-4,6 7,8-tetrahydro-2-methyl-1H-pyrimido[1,2-a]pyrimidin-3-yl]carbonyl]-4-phenyl-piperazine	484
60		4-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1-pipera-zinecarboxylic acid 1,1-dimethylethyl ester	492
61		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-2,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine	482
62		1-[[7-(3,4-Dichlorophenyl)-4,7 dihydro-5-methyl-2-phenylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine	544
63		7-(3,4-Dichlorophenyl)-4,7-dihydro-2,5-dimethyl-N-(3-phenylpropyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	455
64		1-[[7-(2,3-Dichlorophenyl)-2-(1,1-dimethylethyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine	524

65		1 [[7 (3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenyl-piperidine	467
66		7 (3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-6-[[(3-phenylpropyl)amino]carbonyl] pyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester	513
67		7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-6-[(4-phenyl-1-piperazinyl)-carbonyl]pyrazolo[1,5-a]pyrimidine-2-carboxylic acid ethyl ester	540
68		1 [[3-Cyano-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	511
69		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	554
70		1-[[7 (2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	554

61

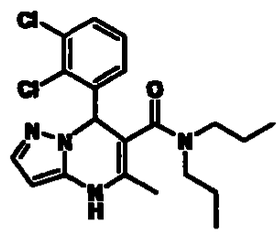
71		1 [[7-(2,3-Dichlorophenyl)-4,7dihydro-5-methyl 2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine, enantiomer B	554
72		1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine, enantiomer B	554
73		7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-(3-phenylpropyl)-2-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	509
74		7-(3,4-Dichlorophenyl)-6-[[4-(4-fluorophenyl)-1-pipera-zinyl]carbonyl]-4,7-dihydro-5-methylpyrazolo[1,5-a]pyri-midine-2-carboxylic acid methyl ester	544
75		(2S)-1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-2-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxymethyl)pyrrolidine	489
76		1-[[7-(2,3-Dichlorophenyl)-2-fluoro-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	504

62

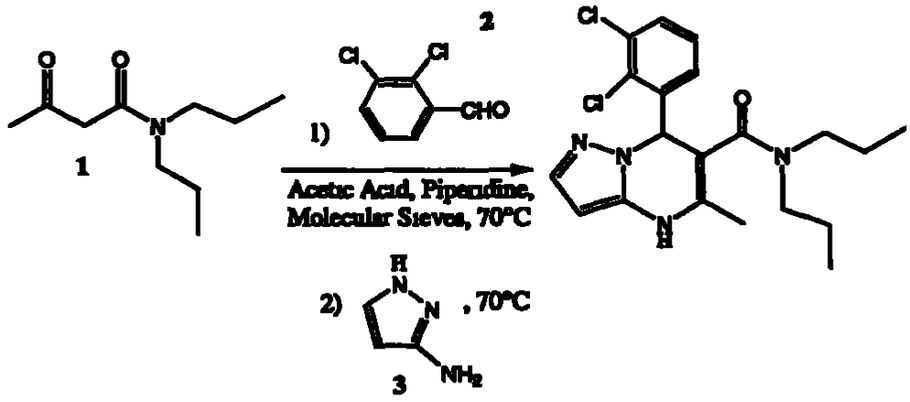
77		(2S)-1-[[2-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxymethyl)pyrrolidine	455
78		(2S)-1-[[2-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxymethyl)pyrrolidine	455
79		(2S)-1-[[7-(2,3-Dichloro-phenyl)-2-fluoro-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxy-methyl)pyrrolidine	439
80		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-2,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	500
81		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-2,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine, enantiomer A	500
82		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine, enantiomer B	500

Example 83

7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-N,N-dipropylpyrazolo[1,5-a]pyrimidine-6-carboxamide



Method



Compound 1: Compound 1 was prepared as described in Example 18, Method 2 Step A1 from t-butoxyacetoacetate and dipropylamine.

Title Compound. A mixture of compound 1 (0.2 g, 1.1 mmol), 2,3-dichlorobenzaldehyde 2 (0.23 g, 1.3 mmol), piperidine (0.015 ml, 0.27 mmol), acetic acid (0.027 mL, 0.27 mmol) and 4A Molecular Sieves (spatula tip) in

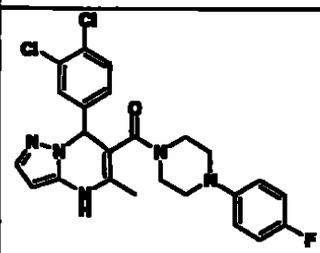
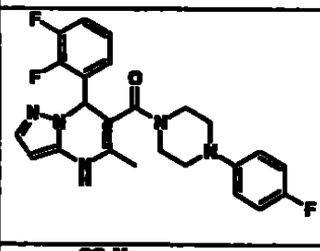
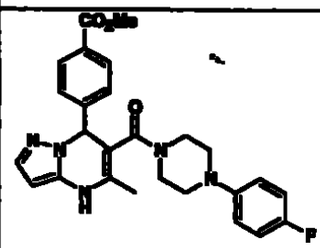
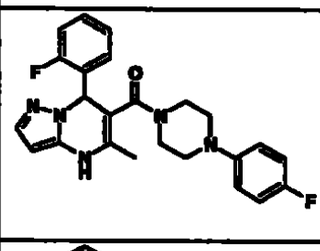
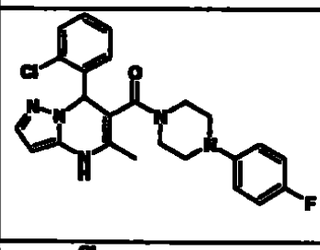
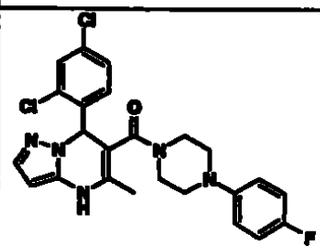
dimethylformamide (1 mL) was stirred at 70 °C overnight. The mixture was cooled to room temperature. 3-aminopyrazole 3 (0 13 g, 1 6 mmol) and sodium acetate (0.28 g, 3 5 mmol) were added and the mixture was stirred overnight at 70 °C. The mixture was cooled to room temperature, transferred to a separatory funnel, diluted with water and ethyl acetate, washed with water (a small amount of methanol was added to breakup emulsions that formed) and brine, dried over anhydrous sodium sulfate and concentrated. The resulting residue was purified by silica gel chromatography (50% ethyl acetate/hexanes followed by 100% ethyl acetate) to afford 0 10 g (23% yield from compound 1) of the title compound. Reverse Phase LC/MS YMC S5 ODS 4.6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 40-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0.1% TFA, Solvent B 90% MeOH/H_2O with 0 1% TFA), 4 mL/mn. Rt = 2.94 min, (96% pure). MS (M+H. 407).

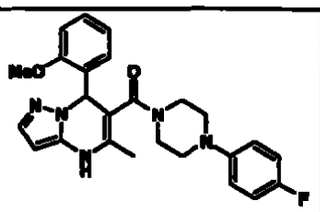
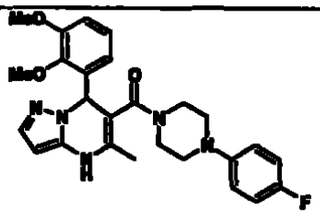
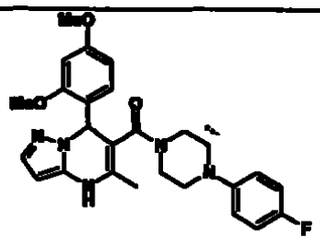
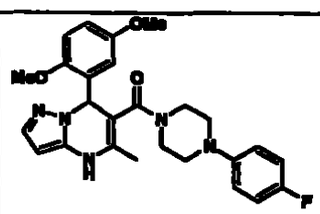
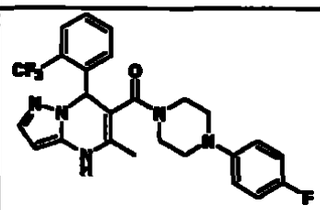
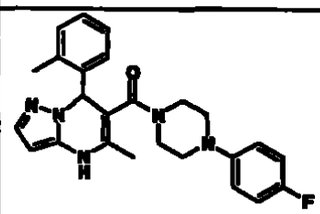
Examples 84-169

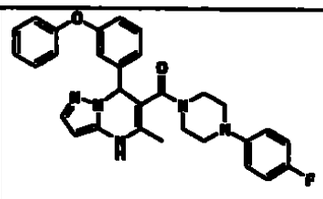
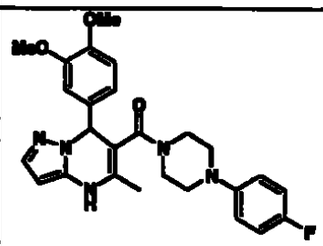
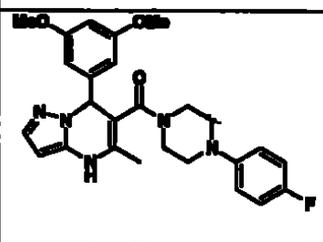
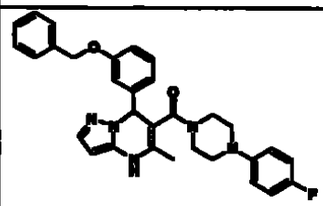
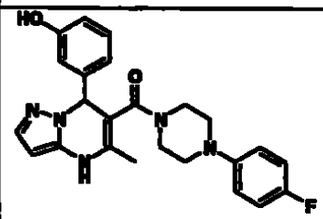
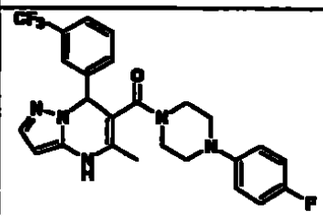
The compounds of Examples 84-169, shown in the table provided below, were prepared in a manner similar to that described in Example 83

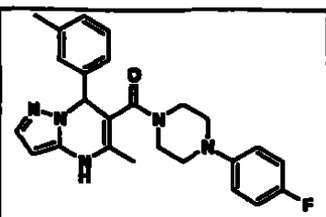
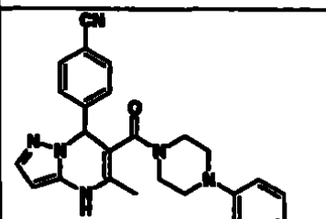
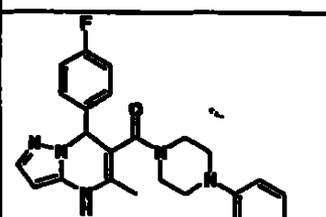
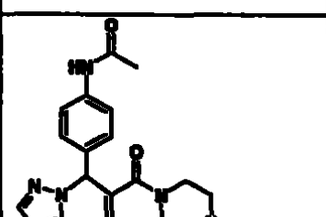
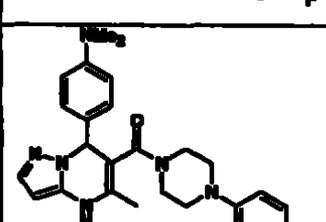
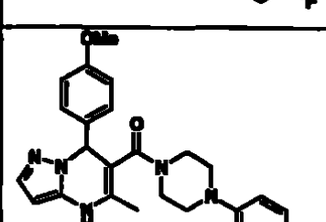
HPLC resolution of Example 84, Chiralpak AS column (50 X 500 mm), eluting with 30% isopropanol/hexanes containing 0 1 % triethylamine at 50 mL/mn), UV detection at 254 λ, provided enantiomers A (Example 166) and B (Example 167) Chiralpak AS column (4.6 X 250 mm) eluting with 40% isopropanol/hexanes containing 0 1 % triethylamine at 1 mL/min), UV detection at 254 λ, enantiomer A Rt = 5.53 min, >99% ee. Enantiomer B Rt = 12.0 min, 98% ee.

HPLC resolution of Example 165, Chiralpak AD column (50 X 500 mm), eluting with 20% isopropanol/hexanes containing 0.1 % triethylamine at 50 mL/mn), UV detection at 254 λ provided enantiomers A (Example 169) and B (Example 168). Chiralpak AD column (4.6 X 250 mm) eluting with 20% isopropanol/hexanes containing 0.1 % triethylamine at 1 mL/min), UV detection at 254 λ, enantiomer A Rt = 8.3 min, >99% ee. Enantiomer B Rt = 12.8 min, 98% ee.

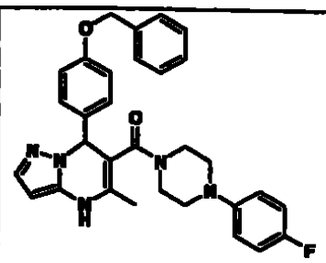
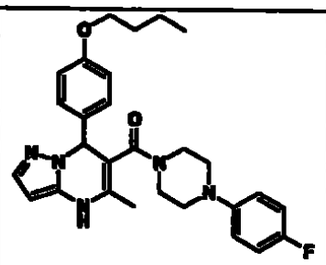
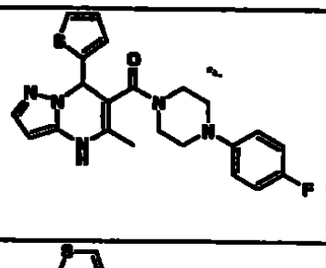
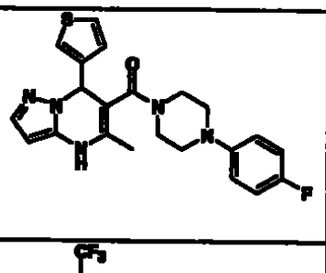
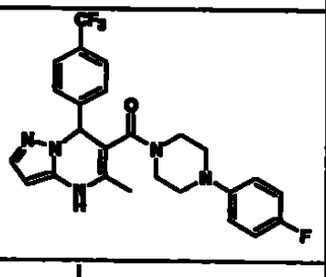
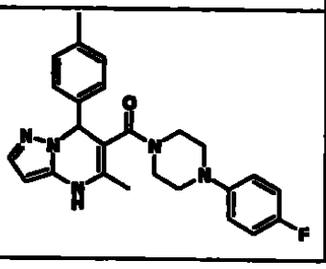
Example	Structure	Name	(M+H)
84		1-[[7 (3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	486
85		1-[[7-(2,3-Difluorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	453
86		4-[6-[[4-(4-Fluorophenyl)-1-piperazinyl]carbonyl]-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-7-yl]benzoic acid methyl ester	475
87		1-(4-Fluorophenyl)-4-[[7-(2-fluorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-piperazine	435
88		1-[[7-(2-Chlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	451
89		1-[[7-(2,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine	486

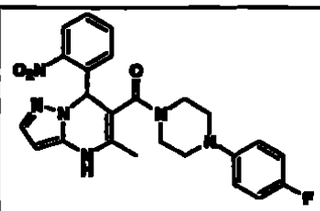
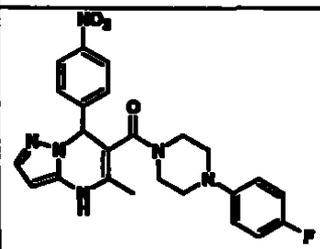
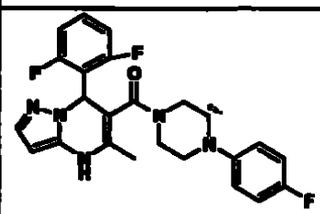
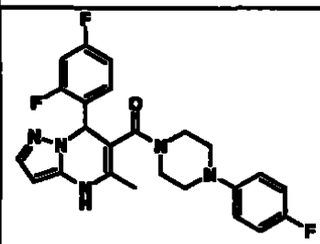
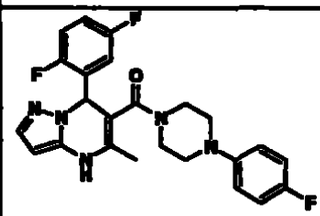
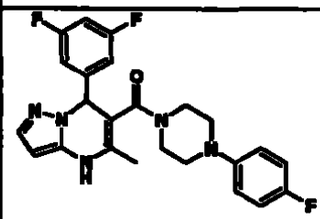
90		1-[[4,7-Dihydro-7-(2-methoxyphenyl)-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	447
91		1-[[7-(2,3-Dimethoxyphenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine	477
92		1-[[7-(2,4-Dimethoxyphenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine	477
93		1-[[7-(2,5-Dimethoxyphenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine	477
94		1-[[4,7-Dihydro-5-methyl-7-[2-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	485
95		1-[[4,7-Dihydro-5-methyl-7-(2-methylphenyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	431

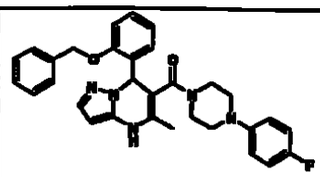
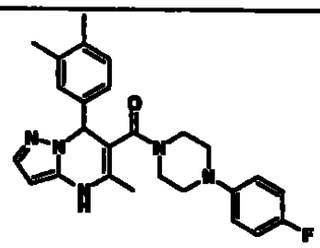
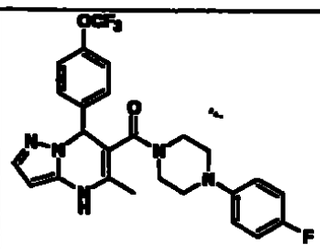
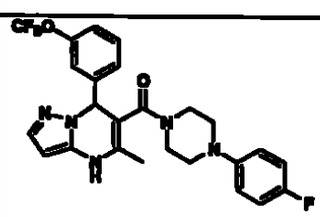
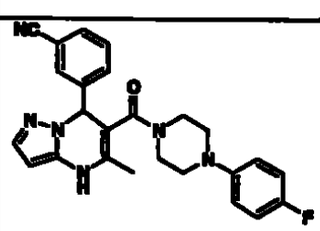
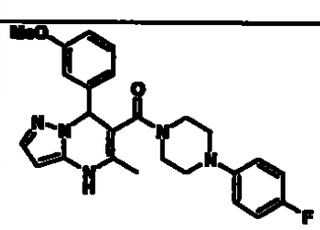
96		1-[[4,7-Dihydro-5-methyl-7-(3-phenoxyphenyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	509
97		1-[[7-(3,4-Dimethoxyphenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine	477
98		1-[[7-(3,5-Dimethoxyphenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine	477
99		1-[[4,7-Dihydro-5-methyl-7-[3-(phenylmethoxy)phenyl]pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine	523
100		1-[[4,7-Dihydro-7-(3-hydroxyphenyl)-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine	433
101		1-[[4,7-Dihydro-5-methyl-7-[3-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine	485

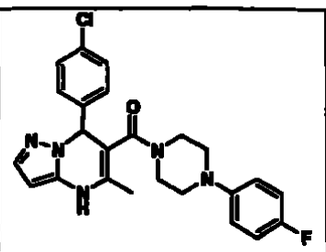
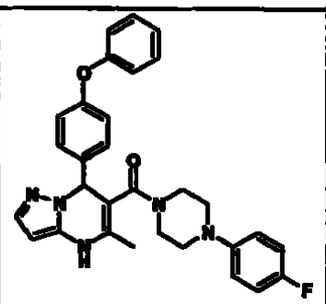
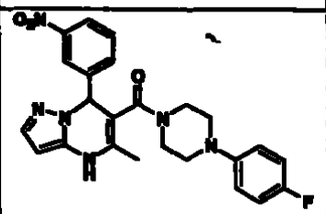
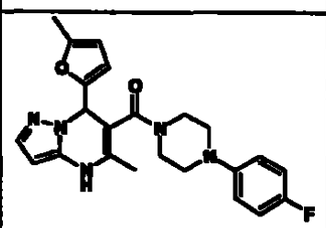
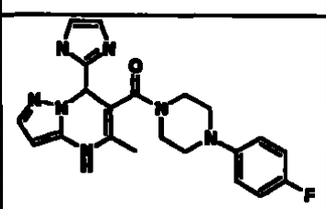
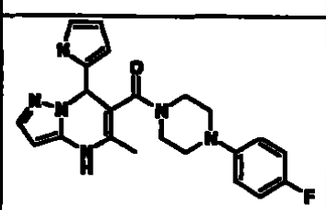
102		1-[[4,7-Dihydro-5-methyl-7-(3-methylphenyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	431
103		1-[[7-(4-Cyanophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	442
104		1-(4-Fluorophenyl)-4-[[7-(4-fluorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-piperazine	435
105		N-[4-[6-[[4-(4-Fluorophenyl)-1-piperazinyl]carbonyl]-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-7-yl]phenyl]acetamide	474
106		1-[[7-[4-(Dimethyl-amino)phenyl]-4,7-dihydro-5-methylpyrazolo[1,5-a]pyri-midin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	460
107		1-[[4,7-Dihydro-7-(4-methoxyphenyl)-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	447

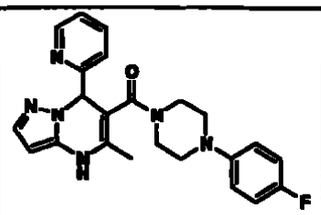
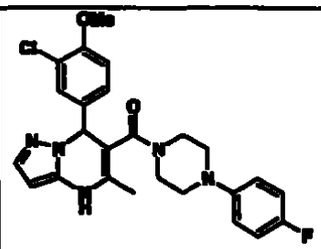
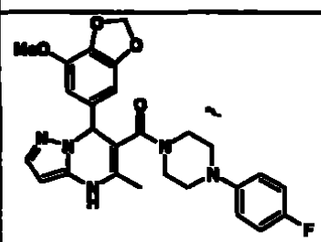
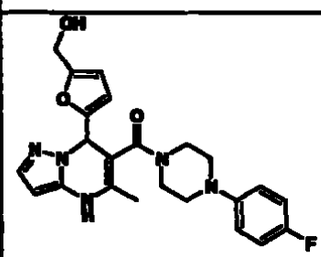
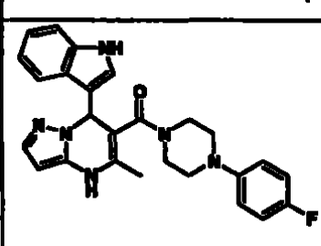
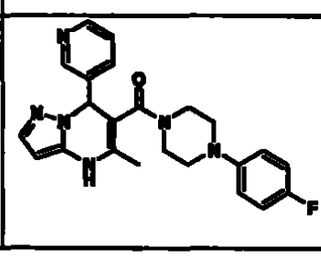
HA726

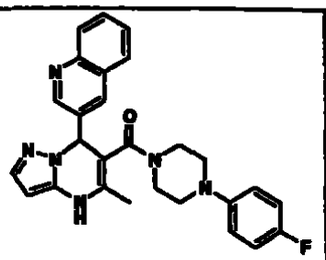
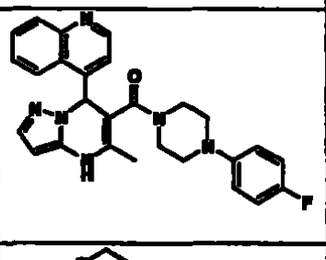
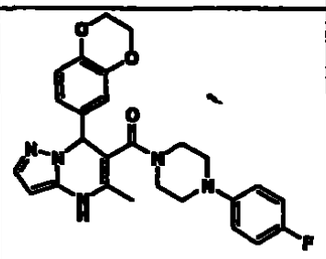
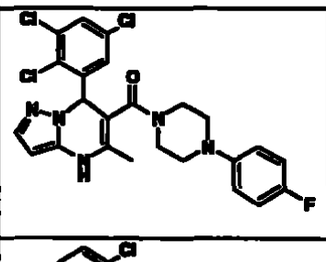
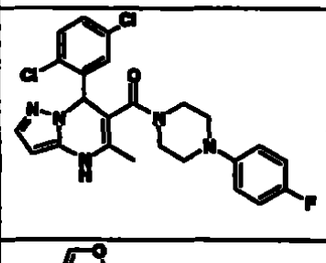
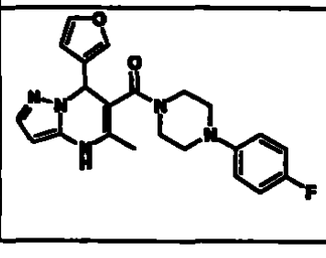
108		1-[[4,7-Dihydro-5-methyl-7-[4-(phenylmethoxy)phenyl]pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	523
109		1-[[7-(4-Butoxyphenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	489
110		1-[[4,7-Dihydro-5-methyl-7-(2-thienyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	423
111		1-[[4,7-Dihydro-5-methyl-7-(3-thienyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	423
112		1-[[4,7-Dihydro-5-methyl-7-[4-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	485
113		1-[[4,7-Dihydro-5-methyl-7-(4-methylphenyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	431

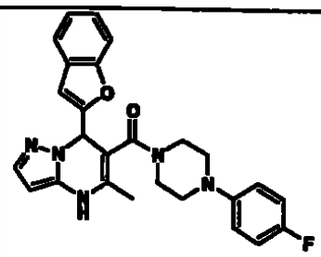
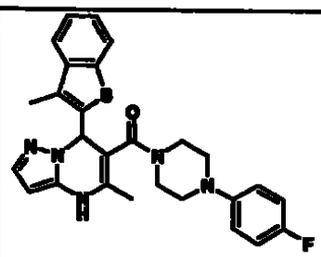
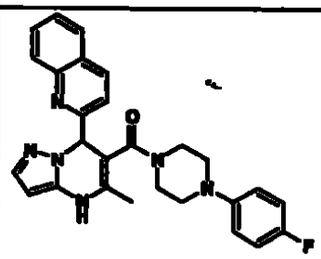
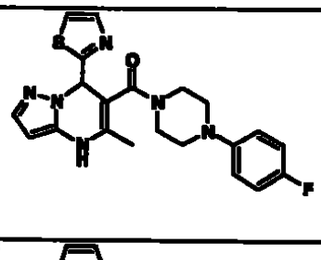
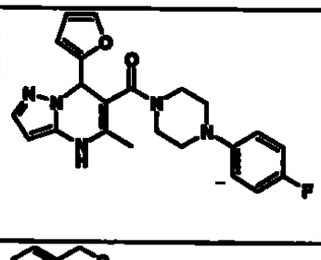
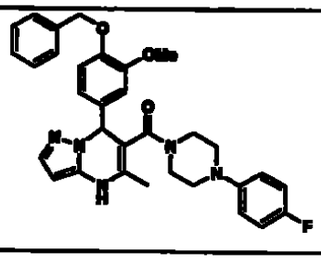
114		1-[[4,7-Dihydro-5-methyl-7-(2-nitrophenyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	462
115		1-[[4,7-Dihydro-5-methyl-7-(4-nitrophenyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	462
116		1-[[7-(2,6-Difluorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	453
117		1-[[7-(2,4-Difluorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	453
118		1-[[7-(2,5-Difluorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	453
119		1-[[7-(3,5-Difluorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	453

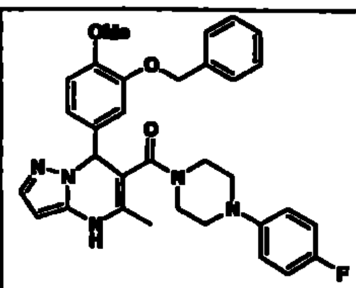
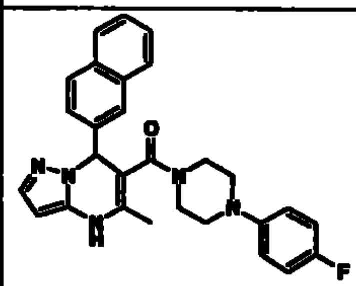
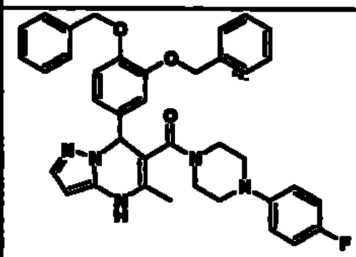
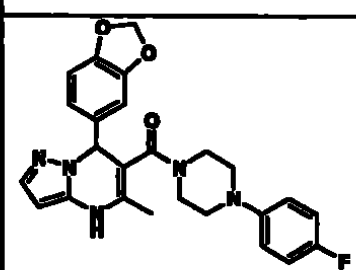
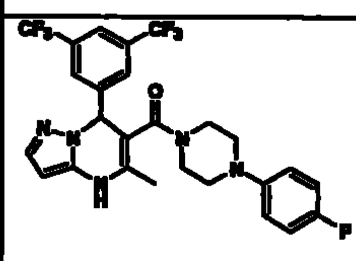
120		1-[[4,7-Dihydro-5-methyl-7-[2-(phenylmethoxy)phenyl]pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	523
121		1-[[7-(3,4-Dimethylphenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	445
122		1-[[4,7-Dihydro-5-methyl-7-[4-(trifluoromethoxy)phenyl]pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	501
123		1-[[4,7-Dihydro-5-methyl-7-[3-(trifluoromethoxy)phenyl]pyrazolo[1 5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	501
124		1-[[7-(3-Cyanophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	442
125		1-[[4,7-Dihydro-7-(3-methoxyphenyl)-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	447

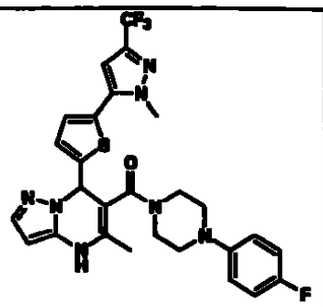
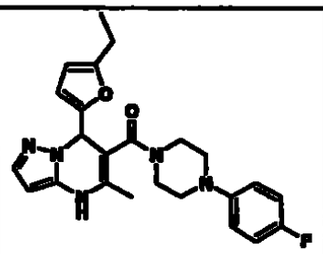
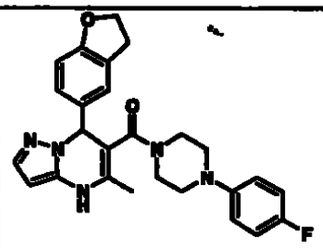
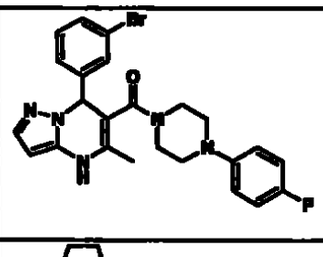
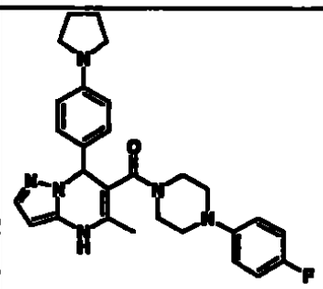
126		1-[[7-(4-Chlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	451
127		1-[[4,7-Dihydro-5-methyl-7-(4-phenoxyphenyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	509
128		1-[[4,7-Dihydro-5-methyl-7-(3-nitrophenyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	462
129		1-[[4,7-Dihydro-5-methyl-7-(5-methyl-2-furanyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	421
130		1-[[4,7-Dihydro-7 (1H-Imidazol-2-yl)-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	407
131		1-[[4,7-Dihydro-5-methyl-7-(1H-pyrrol-2-yl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	406

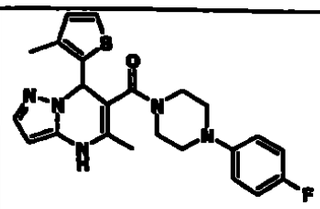
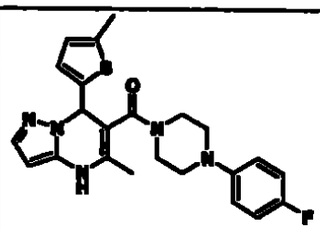
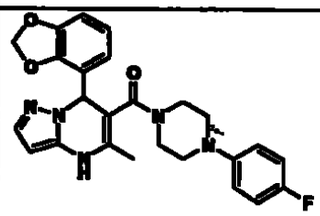
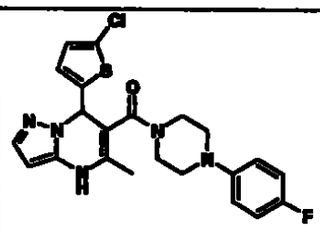
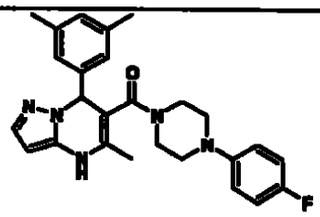
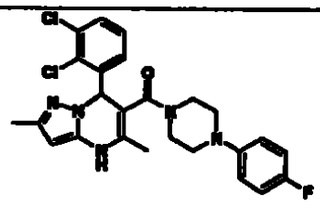
132		1-[[4,7-Dihydro-5-methyl-7-(2-pyridinyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	418
133		1-[[7-(3-Chloro-4-methoxyphenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	481
134		1-[[4,7-Dihydro-7-(4-methoxy-1,3-benzodioxol-6-yl)-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	491
135		1-[[4,7-Dihydro-7-[5-(hydroxymethyl)-2-furanyl]-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	437
136		1-[[4,7-Dihydro-7-(1H-indol-3-yl)-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	456
137		1-[[4,7-Dihydro-5-methyl-7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	418

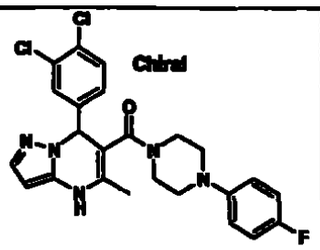
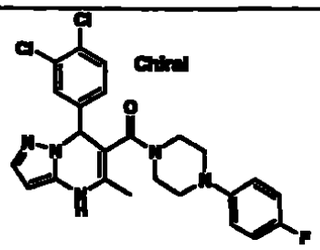
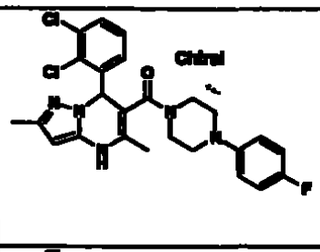
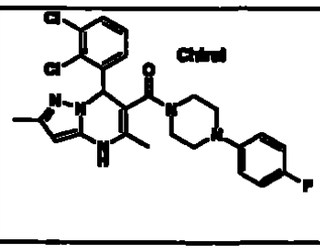
138		1-[[4,7-Dihydro-5-methyl-7-(3-quinolinyl)pyrazolo[1 5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	468
139		1-[[4,7-Dihydro-5-methyl-7-(4-quinolinyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	468
140		1-[[7-(2,3-Dihydro-1,4-benzodioxin-6-yl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	475
141		1-[[4,7-Dihydro-5-methyl-7-(2,3,5-trichloro-phenyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	520
142		1-[[7-(2,5-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	486
143		1-(4-Fluorophenyl)-4-[[7-(3-furanyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-piperazine	407

144		1-[[7-(2-Benzofuranyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	457
145		1-[[4,7-Dihydro-5-methyl-7 (3-methylbenzo[b]thiophen-2-yl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	487
146		1-[[4,7-Dihydro-5-methyl-7-(2-quinolinyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	468
147		1 [[4,7-Dihydro-5-methyl-7-(2-thiazolyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	424
148		1-(4-Fluorophenyl)-4-[[7-(2-furanyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-piperazine	407
149		1-[[4,7-Dihydro-7-[3-methoxy-4-(phenylmethoxy)phenyl]-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	553

150		1-[[4,7-Dihydro-7-[4-methoxy-3-(phenylmethoxy)phenyl]-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	553
151		1-[[4,7-Dihydro-5-methyl-7-(2-naphthalenyl)pyrazolo[1,5 a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	467
152		1-[[7-[3,4-Bis(phenyl-methoxy)phenyl]-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	629
153		1-[[7-(1,3-Benzodioxol-5-yl) 4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine	461
154		1-[[7-[3,5-Bis(trifluoro-methyl)phenyl]-4,7-dihydro-5-methylpyrazolo[1,5-a]pyri-midin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	553

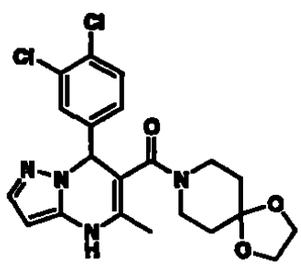
155		1-[[4,7-Dihydro-5-methyl-7-[5-[1-methyl-3-(trifluoromethyl) 1H-pyrazol-5-yl]-2-thienyl]pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	571
156		1-[[7-(5-Ethyl-2-furanyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	435
157		1-[[7-(2,3-Dihydro-5-benzofuranyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	459
158		1-[[7-(3-Bromophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	496
159		1-[[4,7-Dihydro-5-methyl-7-[4-(1-pyrrolidinyl)-phenyl]pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	486

160		1-[[4,7-Dihydro-5-methyl-7-(3-methyl-2-thienyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	437
161		1-[[4,7-Dihydro-5-methyl-7-(5-methyl-2-thienyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	437
162		1-[[7-(1,3-Benzodioxol-4-yl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	461
163		1-[[7-(5-Chloro-2-thienyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	457
164		1-[[7-(3,5-Dimethylphenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine	445
165		1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-2,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	500

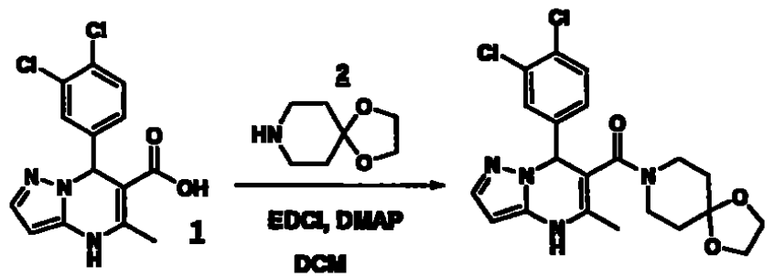
166		1 [[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine, enantiomer A	486
167		1 [[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine, enantiomer B	486
168		1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine, enantiomer B	500
169		1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine, enantiomer A	500

Example 170

8-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,4-dioxa-8-azaspiro[4.5]decane



Method



Compound 1 Compound 1 was prepared as described in Example 16.

Title Compound Compound 2 (0.068 g, 0.47 mmol) was added to a suspension of compound 1 (0.10 g, 0.32 mmol), EDCI (0.09 g, 0.47 mmol), DMAP(0.004g, 0.03 mmol) in dichloromethane (1 mL) When LC/MS indicated the reaction was complete the mixture was loaded directly onto a Worldwide Monitoring CLEAN-UP CARTRIDGE (silica gel, CUSIL12M6) which had been equilibrated with 100% hexanes Elution with 100% hexanes (40 mL), followed by 50% Ethyl acetate/hexanes (40 mL) and 100% ethyl acetate (70 mL) The purest fractions (TLC analysis) were combined to give 0.043 g (30% yield) of the title compound as a white solid. Reverse Phase LC/MS YMC S5 ODS 4.6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 40-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0 1% TFA, Solvent B 90% MeOH/H_2O with 0.1% TFA), 4 mL/min. Rt = 2.12 min, (97% pure) MS (M+H. 449). HMR (DMSO-d_6, 400 MHz, 100 ^{0}C) 9.02(1H, bs), 7.49(1H, d, J= 8Hz), 7.26(1H, d, J=2 Hz), 7 14(1H, d, J=2 Hz), 6.95(1H, d, J=8 Hz), 6.08(1H, s), 5.55(1H, d, J=2 Hz), 3.84(4H, m), 3.55(2H,m), 3 20(2H, m), 1 86(3H, s), 1.37(2H, m), 1.26(2H, m).

Examples 171-377

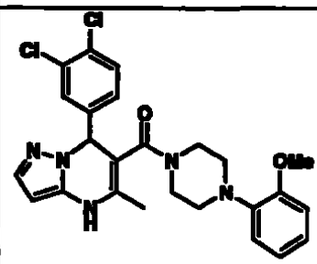
The compounds of Examples 171-377, shown in the table provided below, were prepared in a manner similar to that described in Example 170

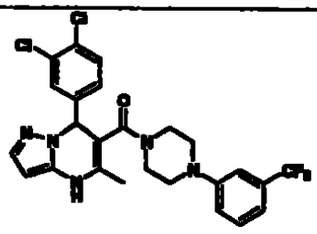
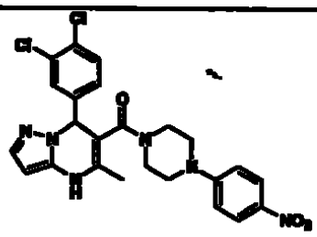
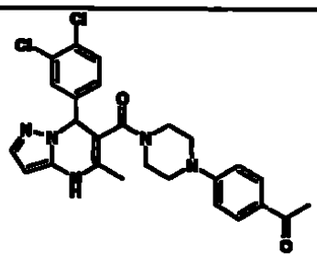
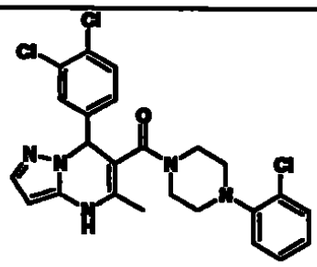
HPLC resolution of Example 194, Chiralpak AD column (50 X 500 mm), eluting with 30% isopropanol/hexanes containing 0 1 % triethylamine at 50 mL/min), UV detection at 254 λ, provided enantiomers A (Example 250)and B (Example 251) Chiralpak AD column (4.6 X 250 mm) eluting with 30% isopropanol/hexanes containing 0 1 % triethylamine at 1 mL/min), UV detection at 254 λ, enantiomer A Rt = 5.32 min, 99% ee. Enantiomer B Rt = 8.59 min, 98% ee.

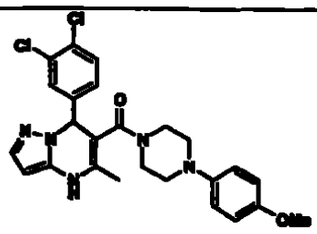
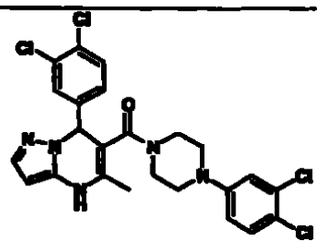
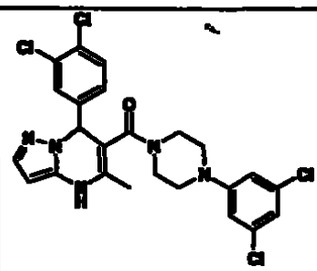
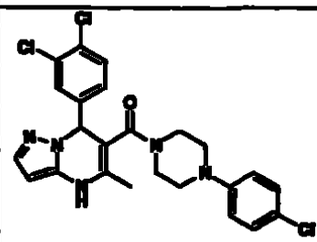
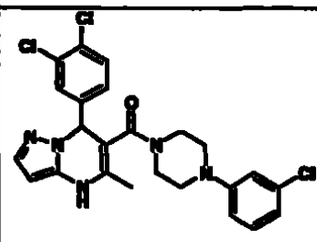
HPLC resolution of Example 221, Chiralpak AS column (50 X 500 mm), eluting with 50% isopropanol/hexanes containing 0 1 % triethylamine at 42 mL/min), UV detection at 254 λ provided enantiomers A (Example 328) and B (Example 329). Chiralpak AS column (4.6 X 250 mm) eluting with 30% isopropanol/hexanes containing 0 1 % triethylamine amine at 1 mL/min), UV detection at 254 λ, enantiomer A Rt = 5 12 min, >99% ee. Enantiomer B Rt = 8.70 min, >99% ee.

HPLC resolution of Example 288, Chiralpak AD column (50 X 500 mm), eluting with 30% isopropanol/hexanes containing 0 1 % triethylamine at 50 mL/min), UV detection at 254 λ provided enantiomers A (Example 376) and B (Example 377). Chiralpak AD column (4.6 X 250 mm) eluting with 30% isopropanol/hexanes containing 0 1 % triethylamine at 1 mL/min), UV detection at 254 λ, enantiomer A Rt = 3.8 min, >99% ee. Enantiomer B Rt = 5 6 min, >99% ee.

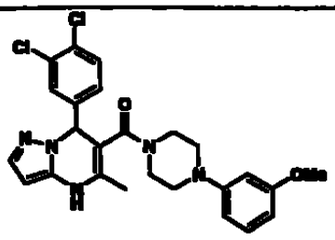
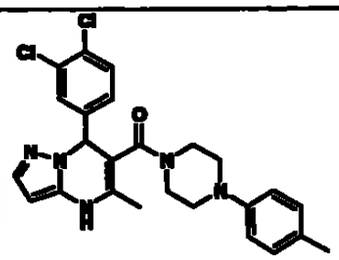
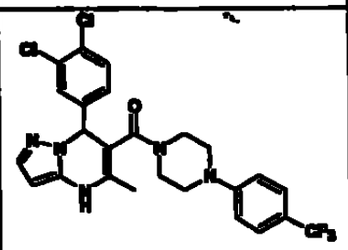
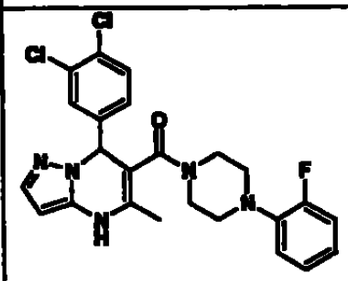
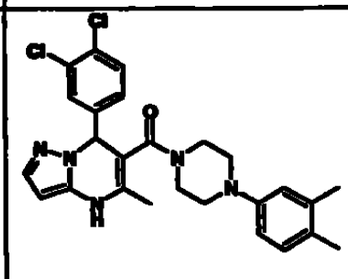
HPLC resolution of Example 333, Chiralpak AD column (50 X 500 mm), eluting with 40% isopropanol/hexanes containing 0.1 % triethylamine at 50 mL/min), UV detection at 254 λ, provided enantiomers A (Example 364) and B (Example 365). Chiralpak AD column (4.6 X 250 mm) eluting with 40% isopropanol/hexanes containing 0 1 % triethylamine at 1 mL/min), UV detection at 254 λ, enantiomer A Rt = 4.92 min, >99% ee. Enantiomer B Rt = 8.0 min, >97% ee.

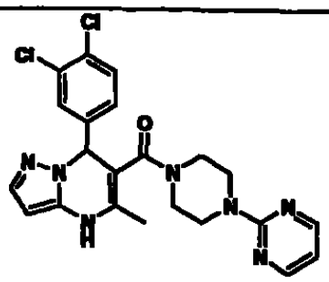
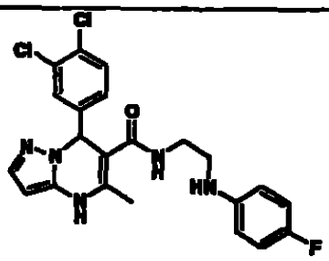
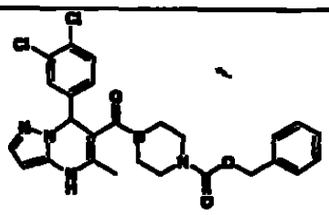
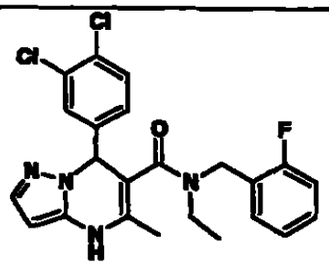
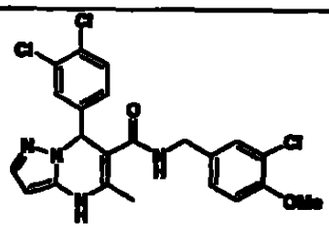
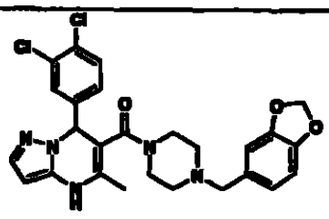
Example	Structure	Name	(M+H)
171		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-(2-methoxy-	498

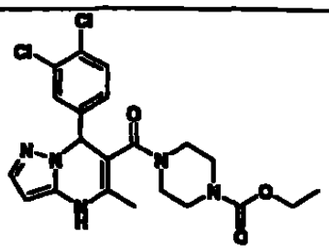
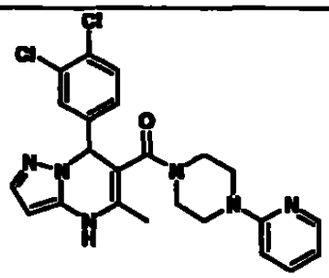
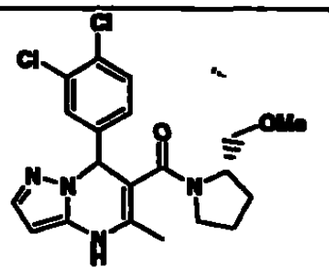
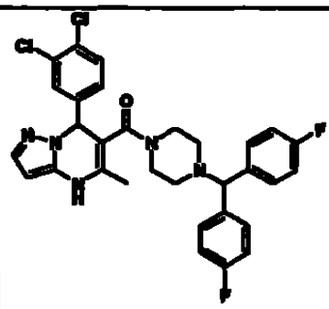
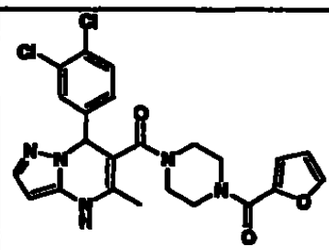
		phenyl)piperazine	
172		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]-pyrimidin-6-yl]carbonyl]-4-[3-(trifluoromethyl)-phenyl]piperazine	536
173		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-nitrophenyl)piperazine	513
174		1-(4-Acetylphenyl)-4-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperazine	510
175		1-(2-Chlorophenyl)-4-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperazine	502

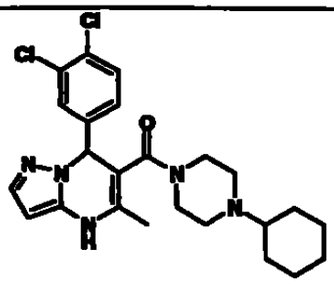
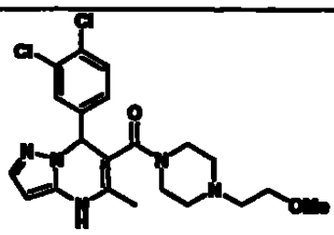
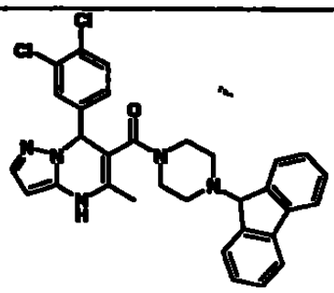
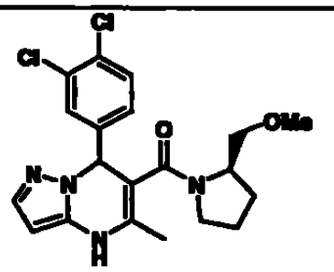
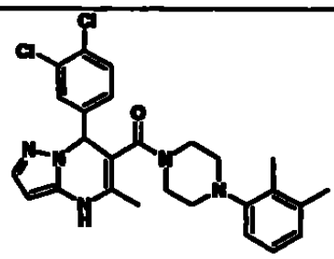
176		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]-carbonyl]-4-(4-methoxy-phenyl)piperazine	498
177		1-(3,4-Dichlorophenyl)-4-[[7-(3,4-dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]-carbonyl]piperazine	537
178		1-(3,5-Dichlorophenyl)-4-[[7-(3,4-dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]-carbonyl]piperazine	537
179		1-(4-Chlorophenyl)-4-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperazine	502
180		1-(3-Chlorophenyl)-4-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyra-zolo[1,5-a]pyrimidin-6-yl]carbonyl]piperazine	502

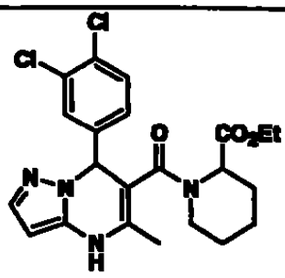
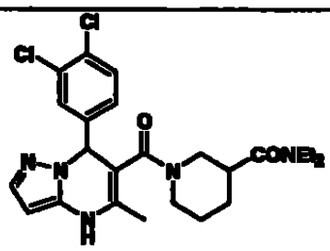
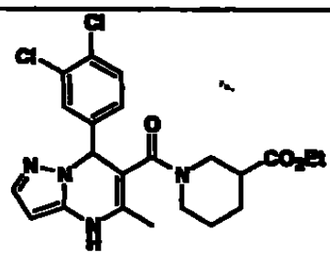
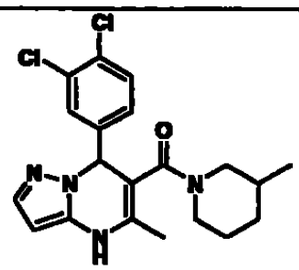
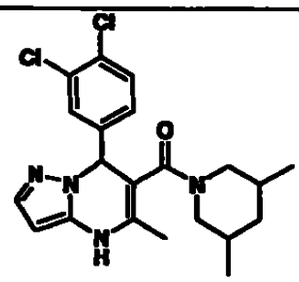
84

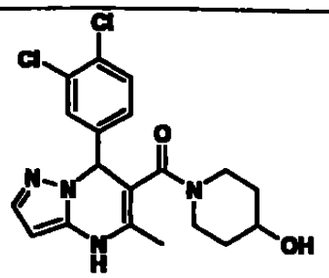
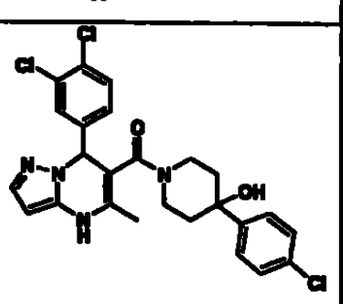
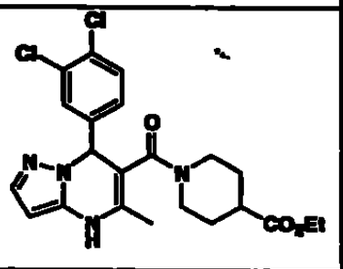
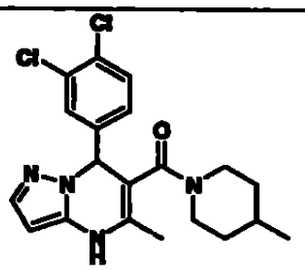
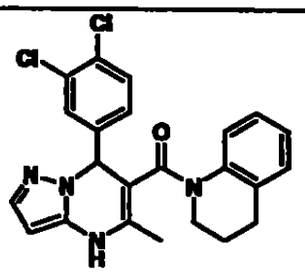
181		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-(3-methoxy-phenyl)piperazine	498
182		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-(4-methyl-phenyl)piperazine	482
183		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5a]-pyrimidin-6-yl]car-bonyl]-4-[4-(trifluoromethyl)-phenyl]piperazine	536
184		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-(2-fluoro-phenyl)piperazine	486
185		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-(3,4-dimethyl-phenyl)piperazine	496

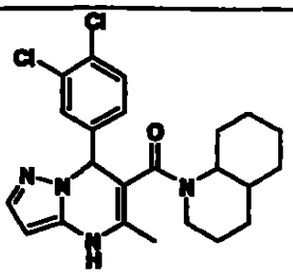
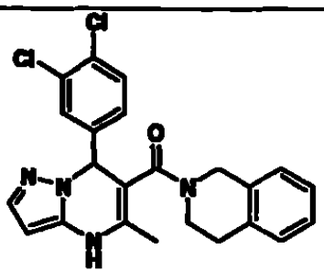
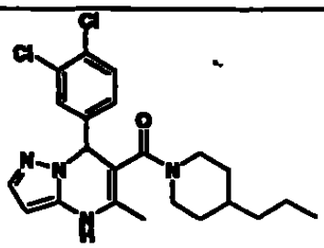
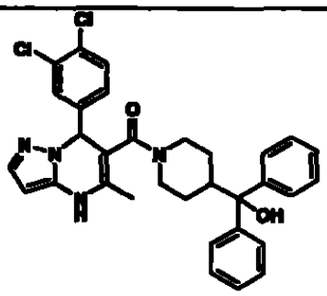
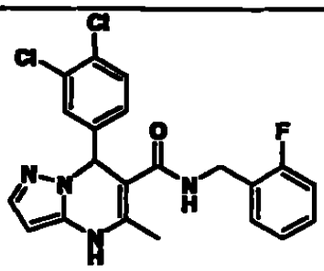
186		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(2-pyrimidinyl)piperazine	470
187		7-(3,4-Dichlorophenyl)-N-[2-[(4-fluorophenyl)amino]ethyl]-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidine-6-carboxamide	460
188		4-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1-piperazinecarboxylic acid phenylmethyl ester	526
189		7-(3,4-Dichlorophenyl)-N-ethyl-N-[(2-fluorophenyl)methyl]-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidine-6-carboxamide	459
190		N-[(3-Chloro-4-methoxyphenyl)methyl]-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidine-6-carboxamide	477
191		1-(1,3-Benzodioxol-5-ylmethyl)-4-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperazine	526

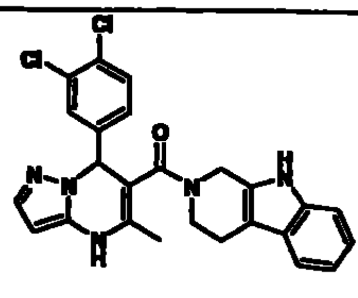
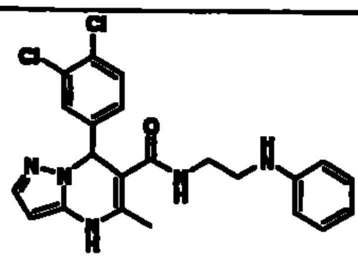
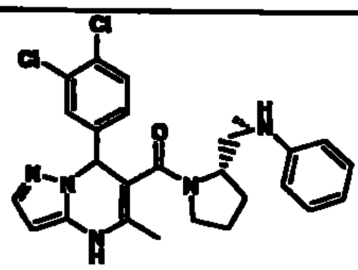
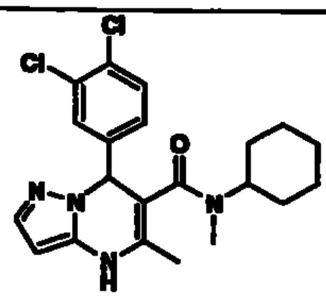
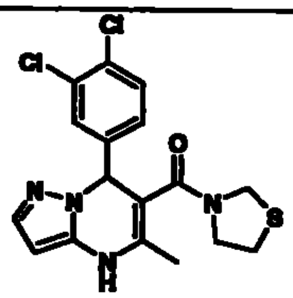
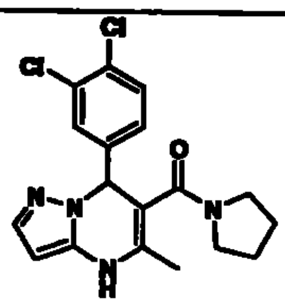
192		4-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1-piperazinecarboxylic acid ethyl ester	464
193		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(2-pyridinyl)piperazine	469
194		(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxymethyl)pyrrolidine	421
195		1-[Bis(4-fluorophenyl)-methyl]-4-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperazine	594
196		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(2-furanyl-carbonyl)piperazine	486

197		1-Cyclohexyl-4-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperazine	474
198		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(2-methoxyethyl)piperazine	450
199		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(9H-fluoren-9-yl)piperazine	556
200		(2R)-1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxy-methyl)pyrrolidine	421
201		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(2,3-dimethyl-phenyl)piperazine	496

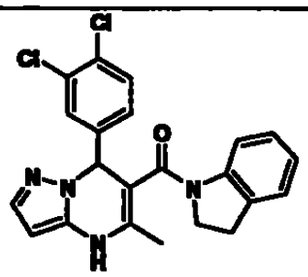
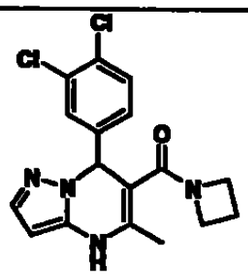
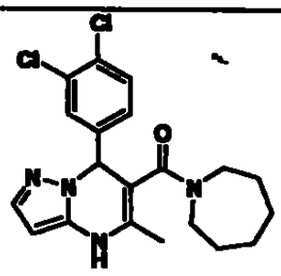
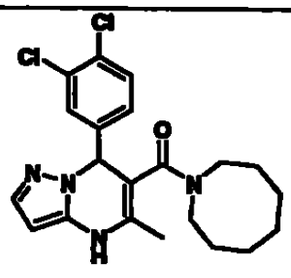
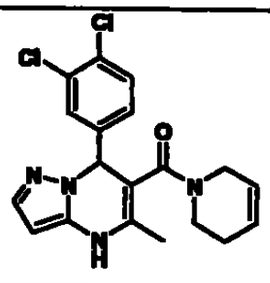
202		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-2-piperidine-carboxylic acid ethyl ester	463
203		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-N,N-diethyl-3-piperidinecarboxamide	490
204		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-3-piperidine-carboxylic acid ethyl ester	463
205		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-3-methyl-piperidine	405
206		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-3,5-dimethyl-piperidine	419

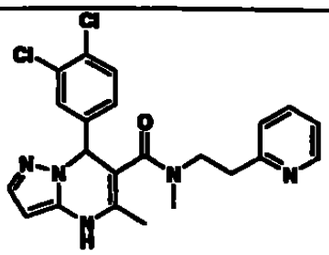
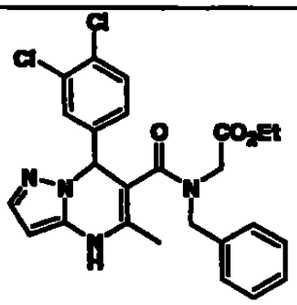
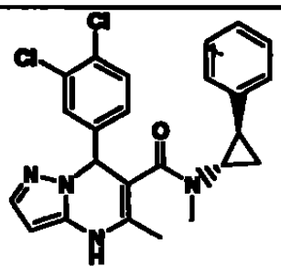
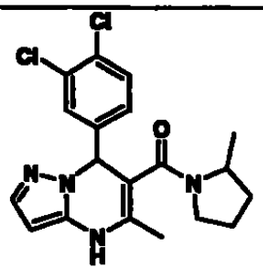
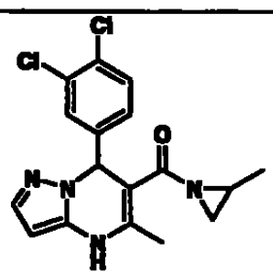
207		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-hydroxy-piperidine	407
208		4-(4-Chlorophenyl)-1-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyri-midin-6-yl]carbonyl]-4-hydroxypiperidine	517
209		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-piperidine-carboxylic acid ethyl ester	463
210		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-methylpiperidine	405
211		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,4-tetrahydroquinoline	439

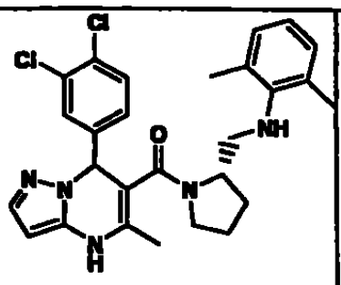
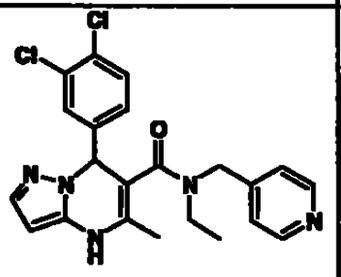
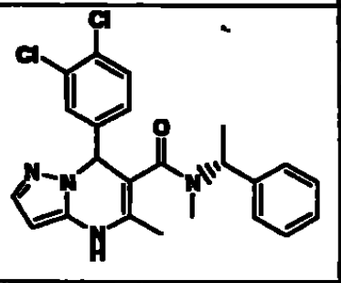
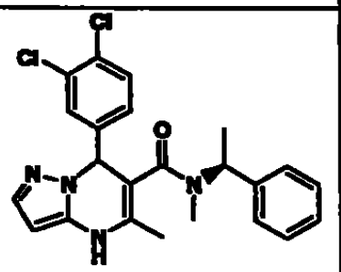
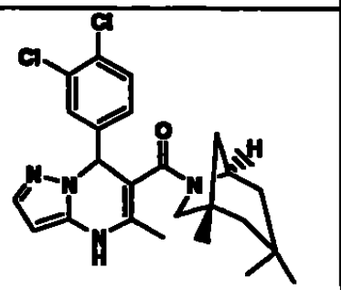
212		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]-pyrimidin-6-yl]carbonyl]-decahydroquinoline	445
213		2-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,4-tetrahydroisoquinoline	439
214		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-propylpiperidine	433
215		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(hydroxydiphenylmethyl) piperidine	573
216		7-(3,4-Dichlorophenyl)-N-[(2-fluoro-phenyl)methyl]-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyri-midine-6-carboxamide	431

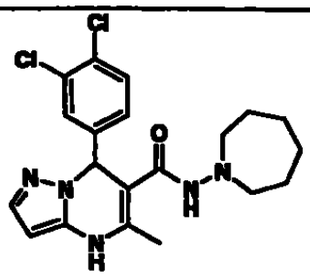
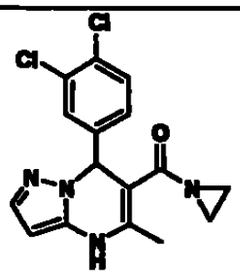
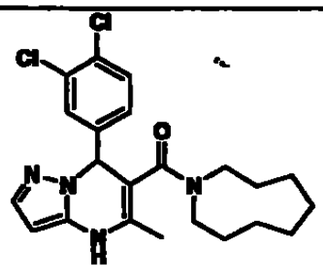
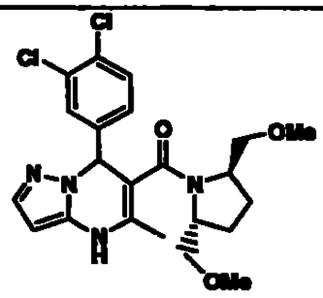
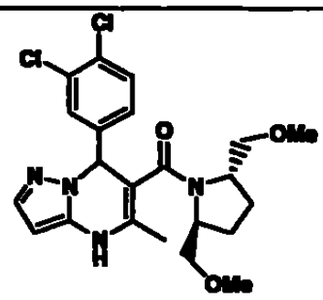
217		2-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole	478
218		7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-[2-(phenylamino)-ethyl]pyrazolo[1,5-a]pyrimidine-6-carboxamide	442
219		(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-[(phenyl-amino)methyl]pyrrolidine	482
220		N-Cyclohexyl-7-(3,4-dichlorophenyl)-4,7-dihydro-N,5-dimethyl-pyrazolo[1,5-a]pyrimidine-6-carboxamide	419
221		3-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]thiazole	395
222		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]pyrrolidine	377

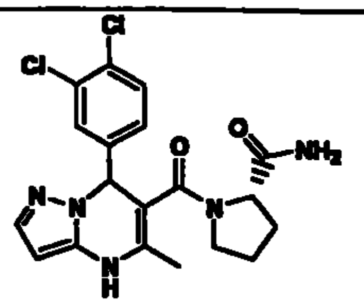
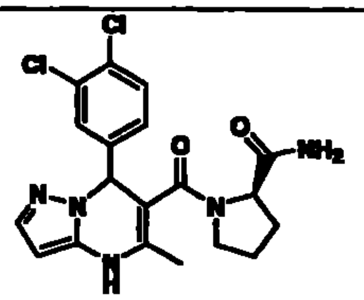
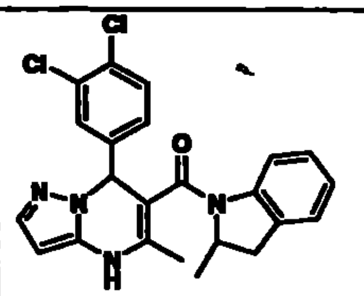
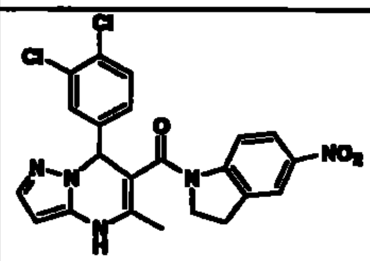
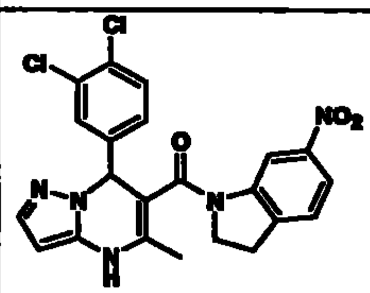
92

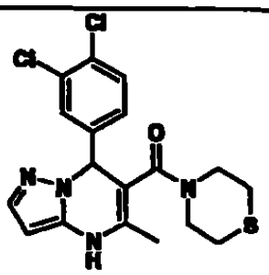
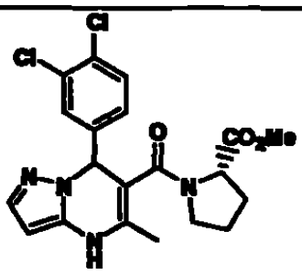
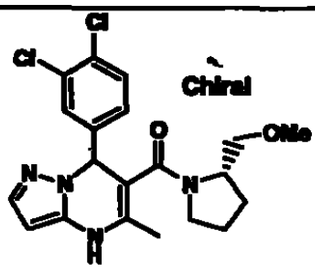
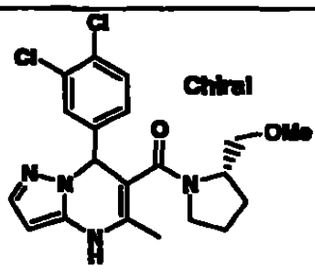
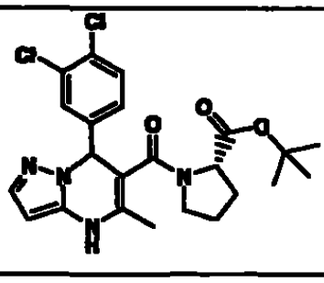
223		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-3,4-dihydro-1H-indole	425
224		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]azetidine	363
225		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]hexahydro-1H-azepine	405
226		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]octahydroazocine	419
227		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,6-tetrahydropyridine	389

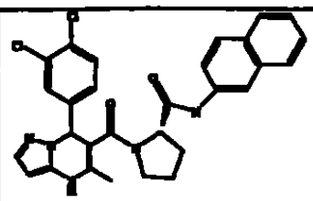
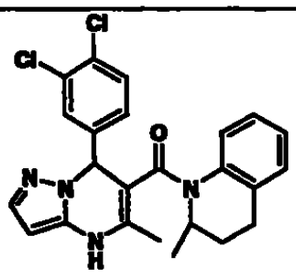
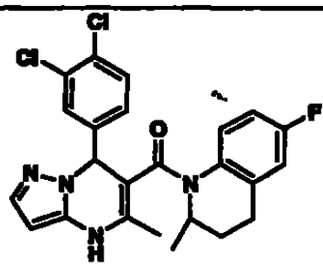
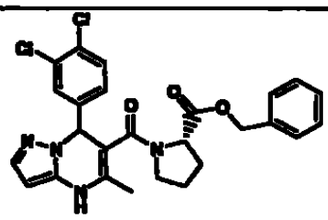
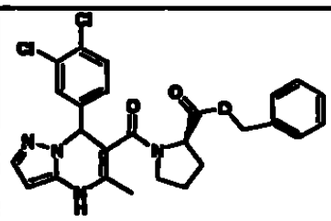
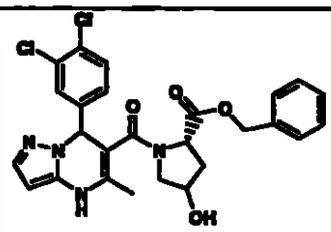
228		7-(3,4-Dichlorophenyl)-4,7dihydro-N,5-dimethyl-N-[2-(2-pyridinyl)-ethyl]pyrazolo[1,5-a]pyrimidine-6-carboxamide	442
229		N-[[7-(3,4-Dichlorophenyl)-4,7dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-N-(phenylmethyl)glycine ethyl ester	499
230		trans-7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-(2-phenylcyclopropyl)pyrazolo[1,5-a]pyrimidine-6-carboxamde	439
231		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-methylpyrrolidine	391
232		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-methylazıridine	363

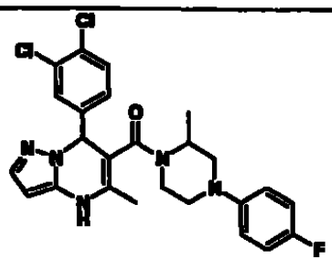
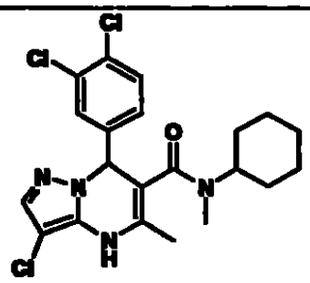
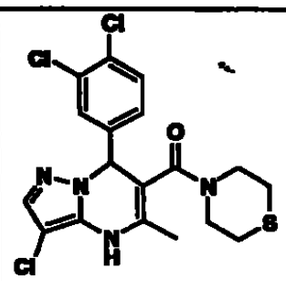
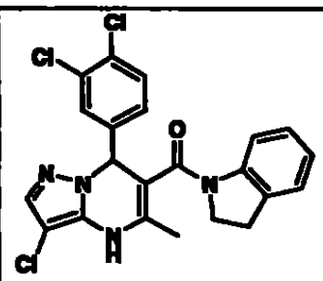
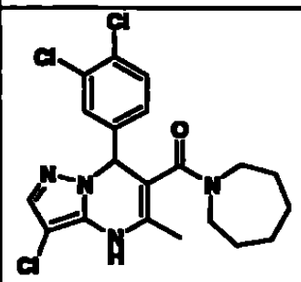
233		(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-[[(2,6-dimethylphenyl)amino]methyl]pyrrolidine	510
234		7-(3,4-Dichlorophenyl)-N-ethyl-4,7-dihydro-5-methyl-N-(4-pyridinylmethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	442
235		7-(3,4-Dichlorophenyl)-4,7-dihydro-N,5-dimethyl-N-[(1R)-1-phenylethyl]pyrazolo[1,5-a]pyrimidine-6-carboxamide	441
236		7-(3,4-Dichlorophenyl)-4,7-dihydro-N,5-dimethyl-N-[(1S)-1-phenylethyl]pyrazolo[1,5-a]pyrimidine-6-carboxamide	441
237		6-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,3,3-trimethyl-6-azabicyclo[3.2.1]octane	459

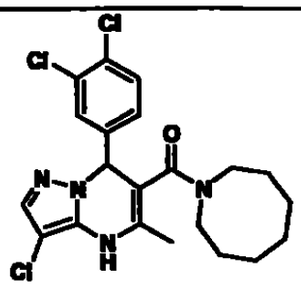
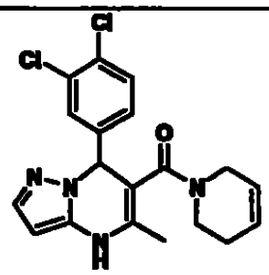
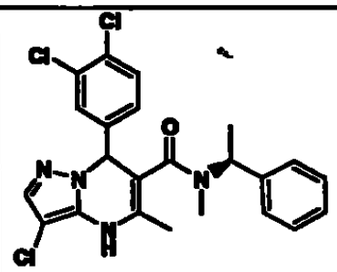
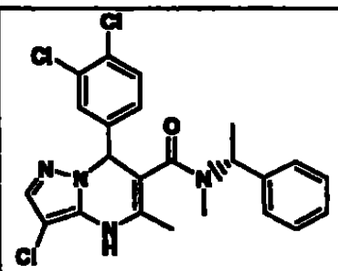
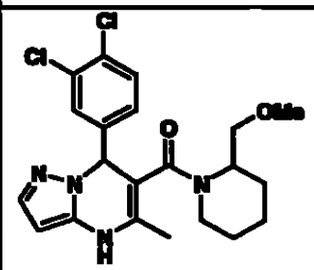
238		7-(3,4-Dichlorophenyl)-N-(hexahydro-1H-azepin-1-yl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxamide	420
239		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]aziridine	349
240		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]octahydro-1H-azonine	433
241		(2R-trans)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2,5-bis(methoxymethyl)-pyrrolidine	465
242		(2S-trans)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2,5-bis-(methoxymethyl)pyrrolidine	465

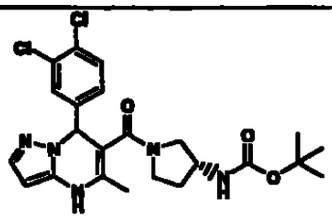
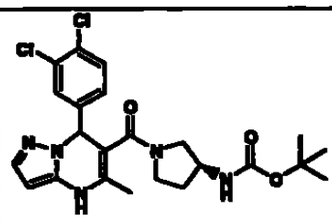
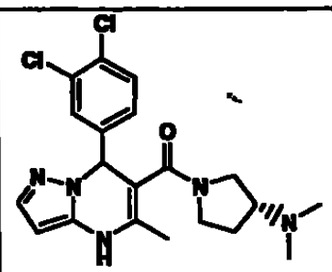
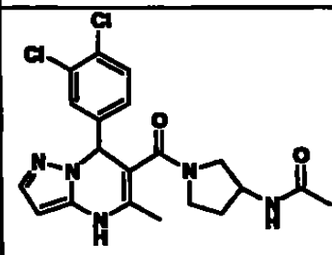
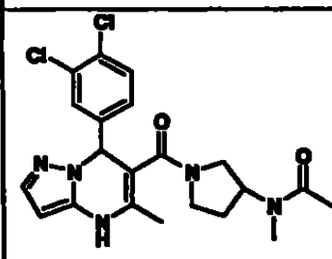
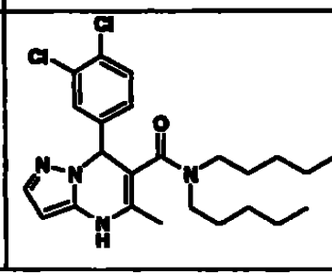
243		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-L-prolinamide	420
244		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-D-prolinamide	420
245		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2,3-dihydro-2-methyl-1H-indole	439
246		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2,3-dihydro-5-nitro-1H-indole	470
247		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2,3-dihydro-6-nitro-1H-indole	470

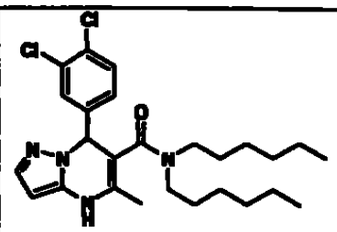
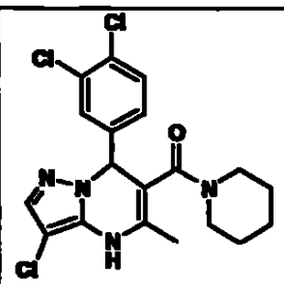
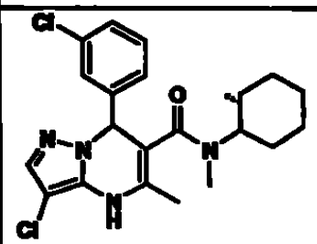
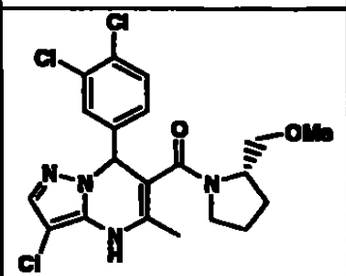
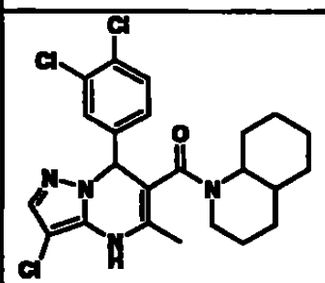
248		4-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-thiomorpholine	409
249		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-L-proline methyl ester	435
250		(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxymethyl)pyrrolidine, enantiomer A	421
251		(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxymethyl)pyrrolidine, enantiomer B	421
252		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-L-proline 1,1-dimethylethyl ester	477

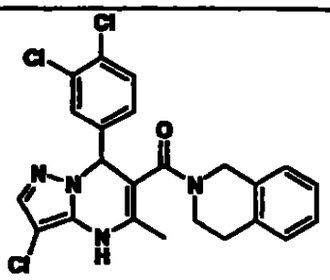
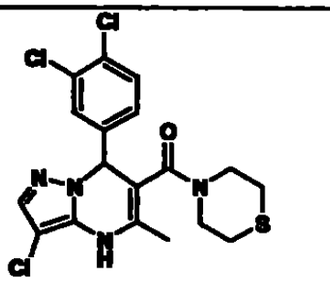
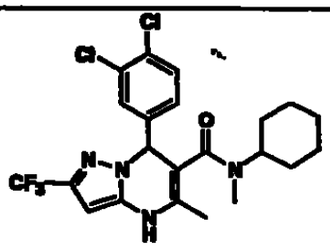
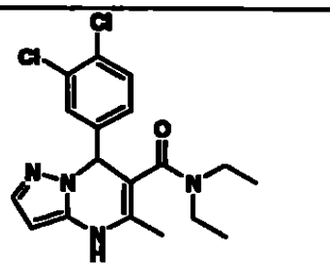
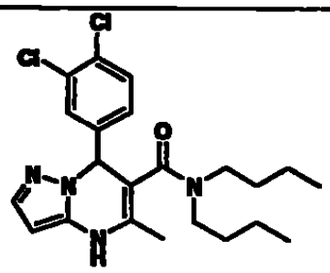
253		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-N-(2-naphthalenyl)-L-prolinamide	560
254		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,4-tetrahydro-2-methylquinoline	453
255		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-6-fluoro-1,2,3,4-tetrahydro-2-methylquinoline	471
256		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-L-proline phenylmethyl ester	511
257		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-D-proline phenylmethyl ester	511
258		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-hydroxy-L-proline phenylmethyl ester	527

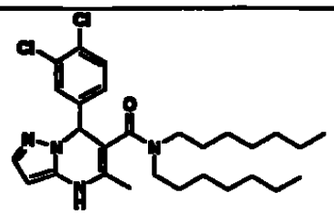
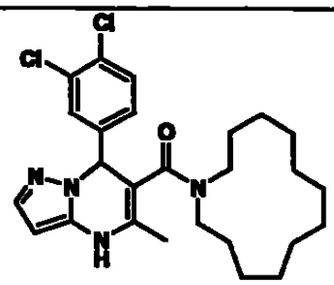
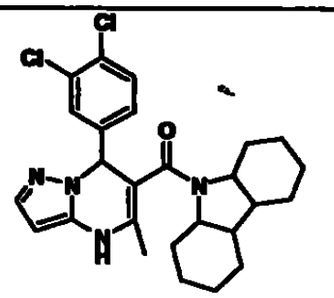
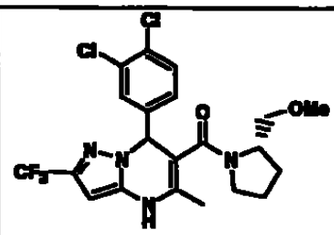
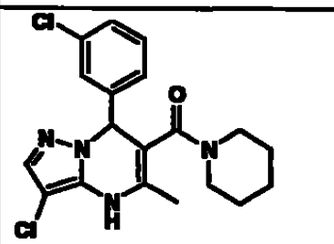
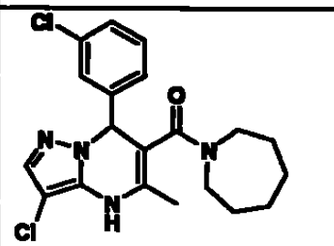
259		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)-2-methylpiperazine	500
260		3-Chloro-N-cyclohexyl-7-(3,4-dichlorophenyl)-4,7-dihydro-N,5-dimethyl-pyrazolo[1,5-a]pyrimidine-6-carboxamide	453
261		4-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-thiomorpholine	443
262		1-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2,3-dihydro-1H-indole	459
263		1-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]hexahydro-1H-azepine	439

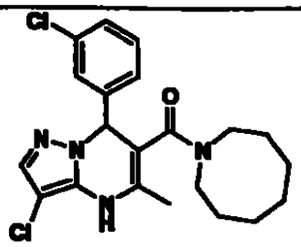
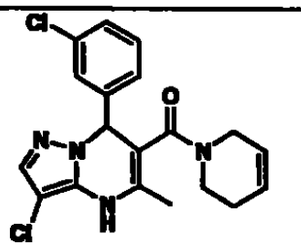
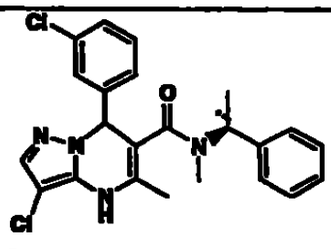
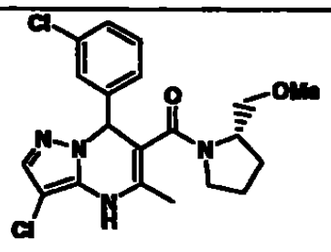
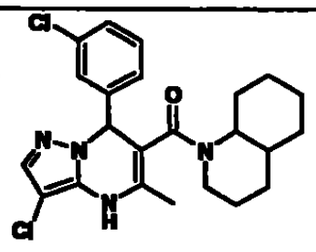
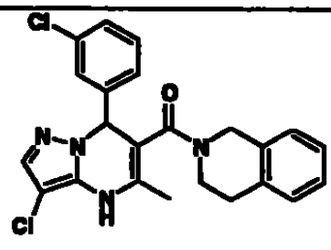
264		1-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-octahydroazocine	453
265		1-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,6-tetrahydropyridine	423
266		3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-N,5-dimethyl-N-[(1S)-1-phenylethyl]-pyrazolo[1,5-a]pyrimidine-6-carboxamide	475
267		3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-N,5-dimethyl-N-[(1R)-1-phenylethyl]-pyrazolo[1,5-a]pyrimidine-6-carboxamide	475
268		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]-carbonyl]-2-(methoxy-methyl)piperidine	435

269		[(3R)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-3-pyrrolidinyl]carbamic acid 1,1-dimethylethyl ester	492
270		[(3S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-3-pyrrolidinyl]carbamic acid 1,1-dimethylethyl ester	492
271		(3R)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-3-(dimethylamino)pyrrolidine	420
272		N-[1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-3-pyrrolidinyl]acetamide	434
273		N-[1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-3-pyrrolidinyl]-N-methylacetamide	448
274		7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N,N-dipentyl-pyrazolo[1,5-a]pyrimidine-6-carboxamide	463

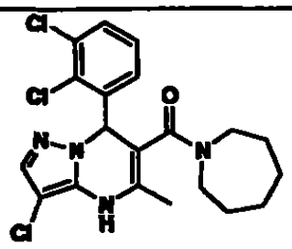
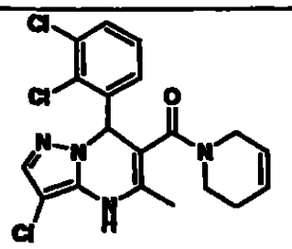
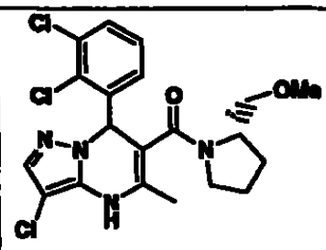
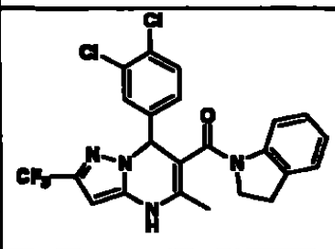
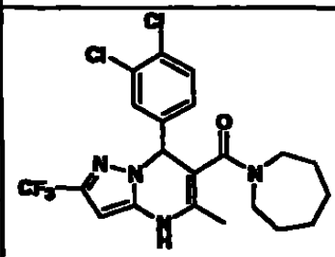
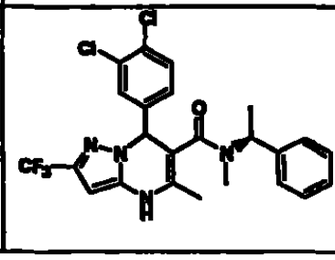
275		7-(3,4-Dichlorophenyl)-N,N-dihexyl-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxamide	491
276		1-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperidine	425
277		3-Chloro-7-(3-chlorophenyl)-N-cyclohexyl-4,7-dihydro-N,5-dimethyl-pyrazolo[1,5-a]pyrimidine-6-carboxamide	419
278		(2S)-1-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxymethyl)pyrrolidine	455
279		1-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-decahydroquinoline	479

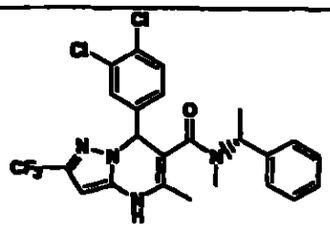
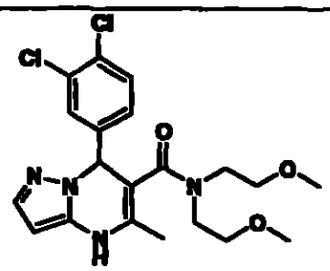
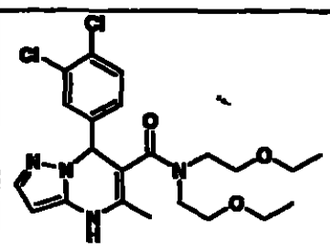
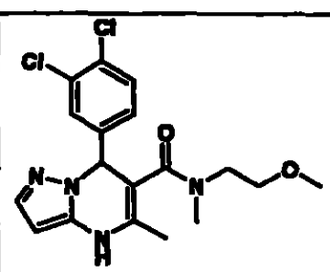
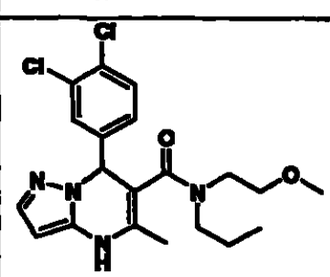
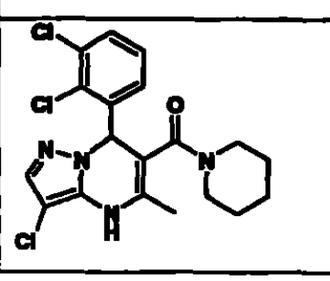
280		2-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,4-tetrahydroisoquinoline	473
281		4-[[3-Chloro-7-(3-chlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-thiomorpholine	409
282		N-Cyclohexyl-7-(3,4-dichlorophenyl)-4,7-dihydro-N,5-dimethyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	487
283		7-(3,4-Dichlorophenyl)-N,N-diethyl-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxamide	379
284		N,N-Dibutyl-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidine-6-carboxamide	435

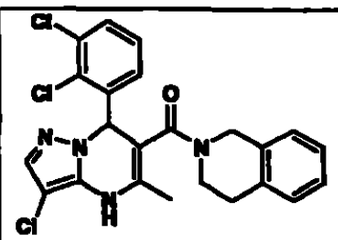
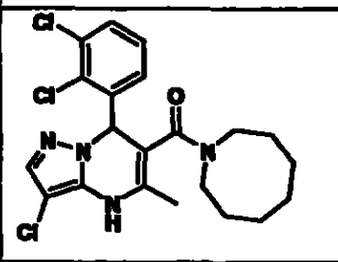
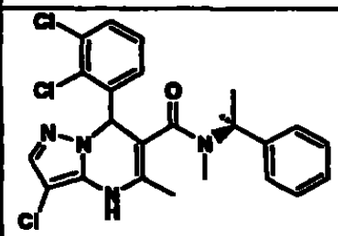
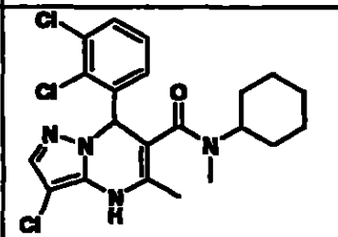
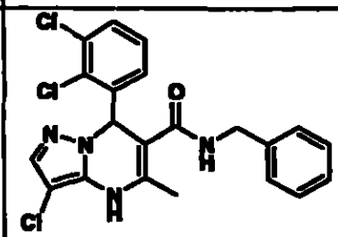
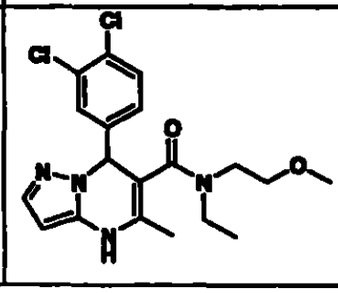
285		7-(3,4-Dichlorophenyl)-N,N-diheptyl-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidine-6-carboxamide	519
286		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-azacyclotridecane	489
287		9-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-dodecahydro-1H-fluorene	485
288		(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-2-(trifluoromethyl)pyrazolo-[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxymethyl)pyrrolidine	489
289		1-[[3-Chloro-7-(3-chlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperidine	391
290		1-[[3-Chloro-7-(3-chlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]hexahydro-1H-azepine	405

291		1-[[3-Chloro-7-(3-chlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-octahydroazocine	419
292		1-[[3-Chloro-7-(3-chlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,6-tetrahydropyridine	389
293		3-Chloro-7-(3-chlorophenyl)-4,7-dihydro-N,5-dimethyl-N-[(1S)-1-phenyl-ethyl]pyrazolo[1,5-a]pyrimidine-6-carboxa-mide	441
294		(2S)-1-[[3-Chloro-7-(3-chlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxymethyl)pyrro-lidine	421
295		1-[[3-Chloro-7-(3-chlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-decahydroquinoline	445
296		2-[[3-Chloro-7-(3-chlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,4-tetrahydroisoquinoline	439

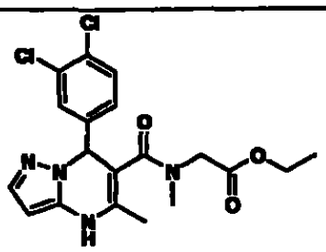
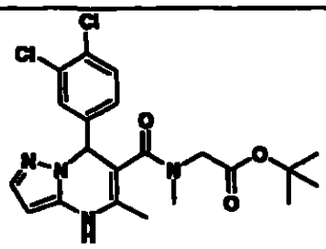
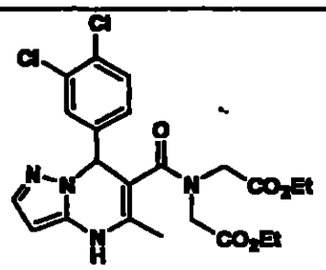
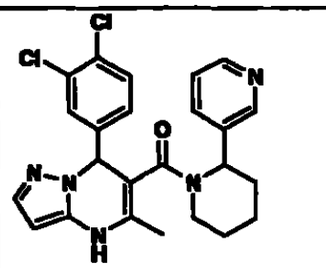
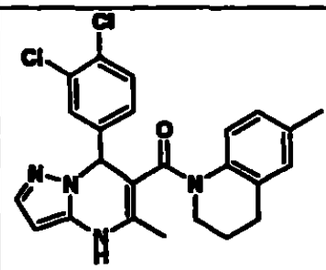
106

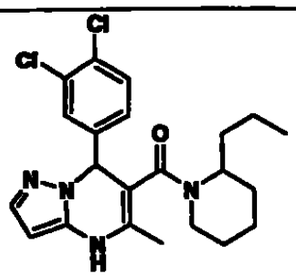
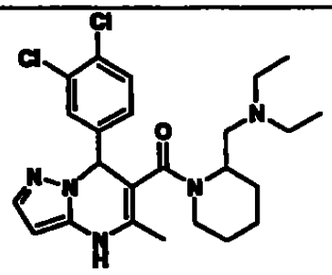
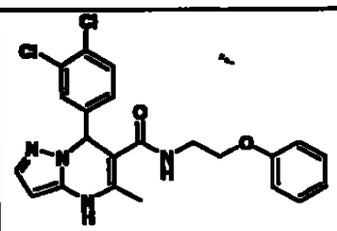
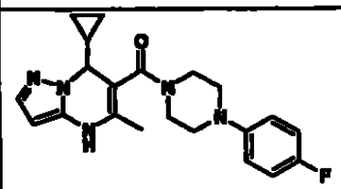
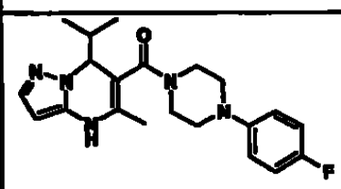
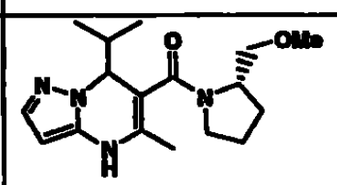
297		1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pynmidin-6-yl]carbonyl]hexahydro-1H-azepine	439
298		1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,6-tetrahydropyridine	423
299		(2S)-1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimi-din-6-yl]carbonyl]-2-(methoxymethyl)pyrroli-dine	455
300		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methyl-2-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2,3-dihydro-1H-indole	493
301		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methyl-2-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]hexahydro-1H-azepine	473
302		7-(3,4-Dichlorophenyl)-4,7-dihydro-N,5-di-methyl-N-[(1S)-1-phenylethyl]-2-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	509

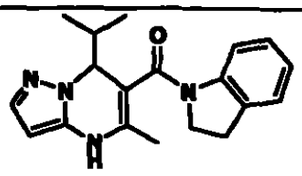
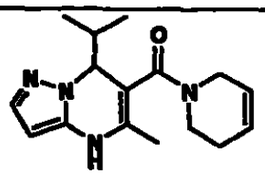
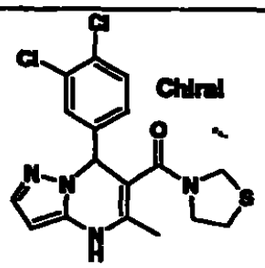
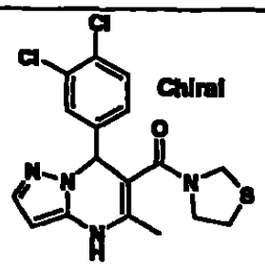
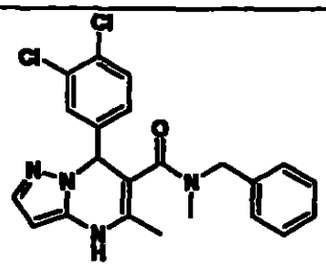
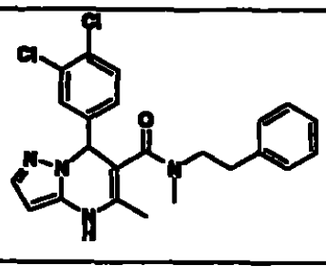
303		7-(3,4-Dichlorophenyl)-4,7-dihydro-N,5-dimethyl-N-[(1R)-1-phenylethyl]-2-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	509
304		7-(3,4-Dichlorophenyl)-4,7-dihydro-N,N-bis(2-methoxyethyl)-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxamide	439
305		7-(3,4-Dichlorophenyl)-N,N-bis(2-ethoxyethyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxamide	467
306		7-(3,4-Dichlorophenyl)-4,7-dihydro-N-(2-methoxyethyl)-N,5-dimethylpyrazolo[1,5-a]pyrimidine-6-carboxamide	395
307		7-(3,4-Dichlorophenyl)-4,7-dihydro-N-(2-methoxyethyl)-5-methyl-N-propylpyrazolo[1,5-a]pyrimidine-6-carboxamide	423
308		1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperidine	425

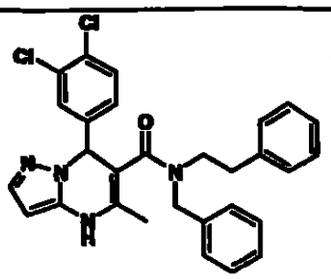
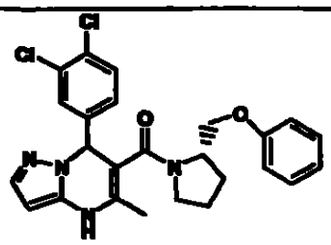
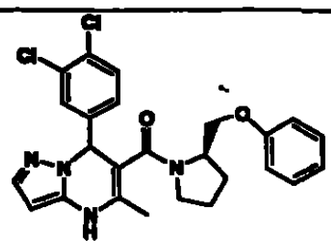
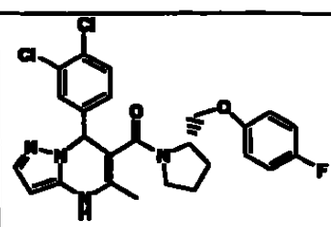
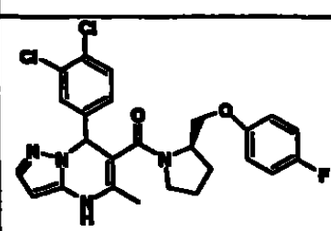
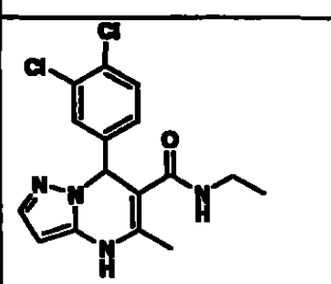
309		2-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,4-tetrahydroisoquinoline	473
310		1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-octahydroazocine	453
311		3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-N,5-dimethyl-N-[(1S)-1-phenylethyl]-pyrazolo[1,5-a]pyrimidine-6-carboxamide	475
312		3-Chloro-N-cyclohexyl-7-(2,3-dichlorophenyl)-4,7-dihydro-N,5-dimethyl-pyrazolo[1,5-a]pyrimidine-6-carboxamide	453
313		3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methyl-N-(phenylmethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	447
314		7-(3,4-Dichlorophenyl)-N-ethyl-4,7-dihydro-N-(2-methoxyethyl)-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxamide	409

109

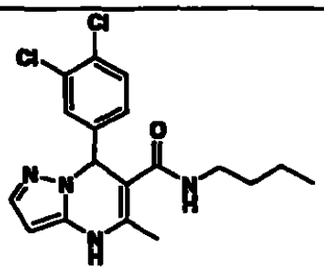
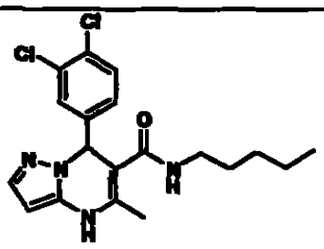
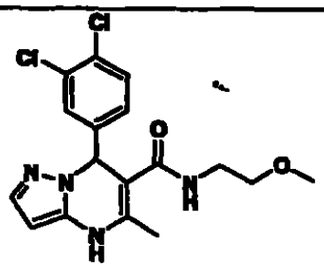
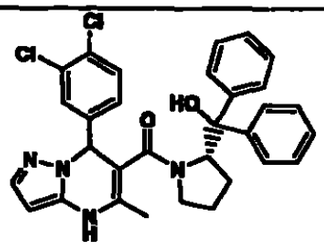
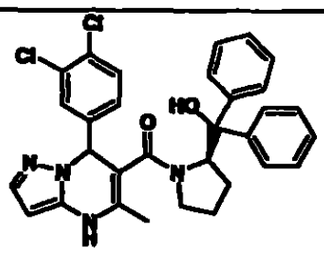
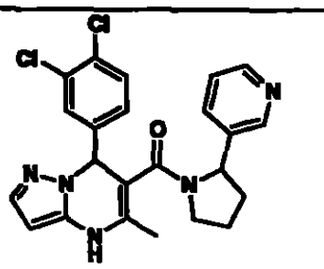
315		N-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-N-methylglycine ethyl ester	423
316		N-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-N-methylglycine 1,1-dimethylethyl ester	451
317		N-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-N-(2-ethoxy-2-oxoethyl)glycine ethyl ester	495
318		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(3-pyridinyl)piperidine	468
319		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,4-tetrahydro-6-methylquinoline	453

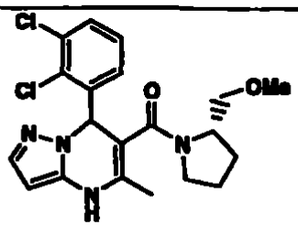
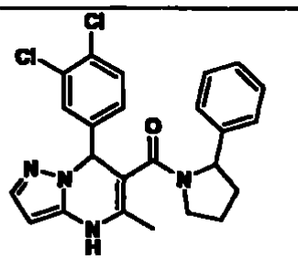
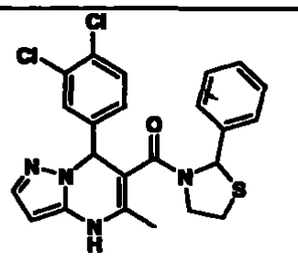
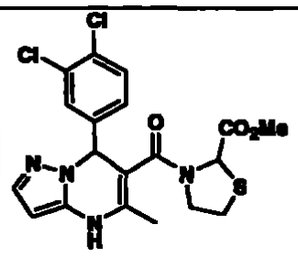
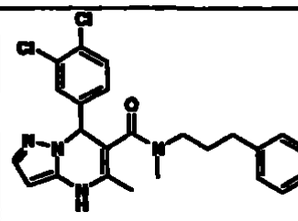
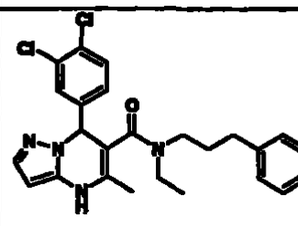
320		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-propylpiperidine	433
321		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-[(diethylamino)methyl]piperidine	476
322		7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-(2-phenoxyethyl)-pyrazolo[1,5-a]pyrimidine-6-carboxamide	443
323		1-[(7-Cyclopropyl-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl)carbonyl]-4-(4-fluorophenyl)piperazine	381
324		1-[[4,7-Dihydro-5-methyl-7-(1-methyl-ethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	383
325		(2S)-1-[[4,7-Dihydro-5-methyl-7-(1-methyl-ethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxy-methyl)pyrrolidine	318

326		1-[[4,7-Dihydro-5-methyl-7-(1-methyl-ethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2,3-dihydro-1H-indole	322
327		1-[[4,7-Dihydro-5-methyl-7-(1-methylethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,6-tetrahydropyridine	286
328		3-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]thiazolidine, enantiomer A	395
329		3-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]thiazolidine, enantiomer B	395
330		7-(3,4-Dichlorophenyl)-4,7-dihydro-N,5-dimethyl-N-(phenyl-methyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	427
331		7-(3,4-Dichlorophenyl)-4,7-dihydro-N,5-dimethyl-N-(2-phenylethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	441

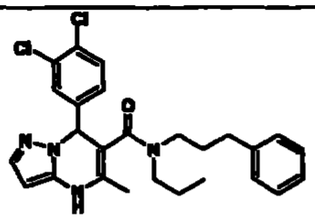
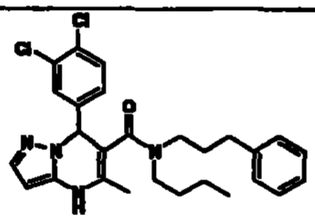
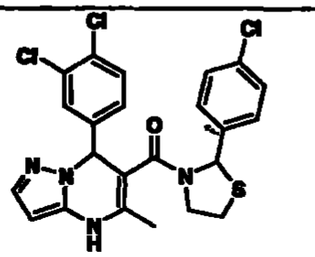
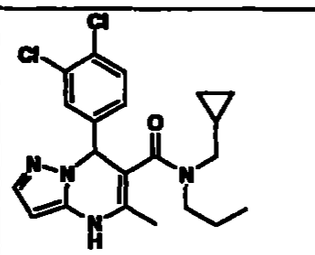
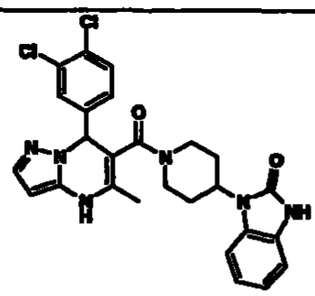
332		7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-(2-phenylethyl)-N-(phenylmethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	517
333		(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(phenoxymethyl)pyrrolidine	483
334		(2R)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(phenoxymethyl)pyrrolidine	483
335		(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-[(4-fluorophenoxy)methyl]-pyrrolidine	501
336		(2R)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-[(4-fluorophenoxy)methyl]-pyrrolidine	501
337		7-(3,4-Dichlorophenyl)-N-ethyl-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxamide	351

113

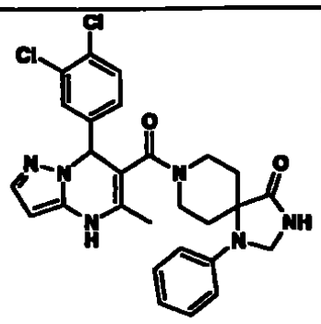
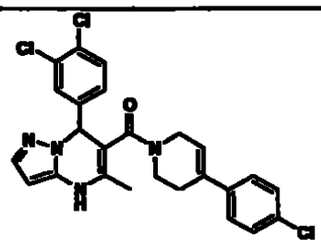
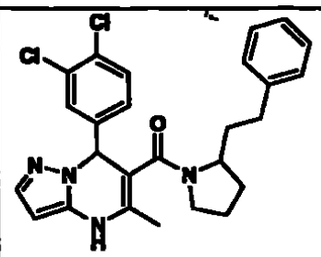
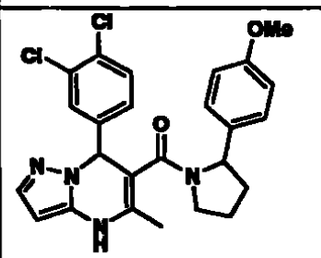
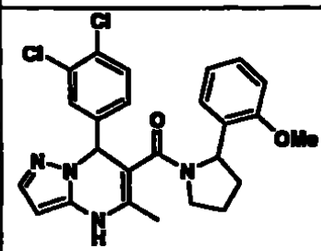
338		N-Butyl-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidine-6-carboxamide	379
339		7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-pentylpyrazolo[1,5-a]pyrimidine-6-carboxamide	393
340		7-(3,4-Dichlorophenyl)-4,7-dihydro-N-(2-methoxyethyl)-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxamide	381
341		(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(hydroxydiphenylmethyl) pyrrolidine	559
342		(2R)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(hydroxydiphenylmethyl) pyrrolidine	559
343		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(3-pyridinyl)pyrrolidine	454

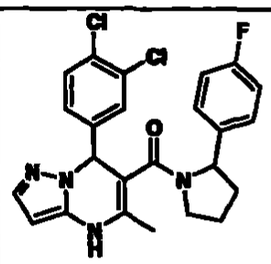
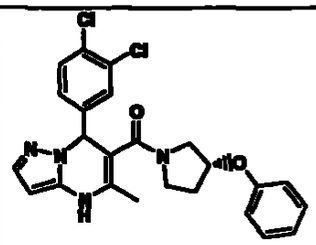
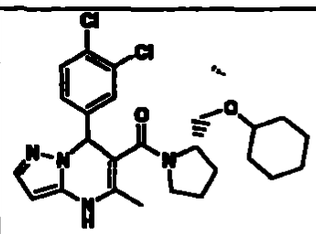
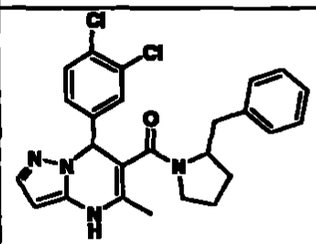
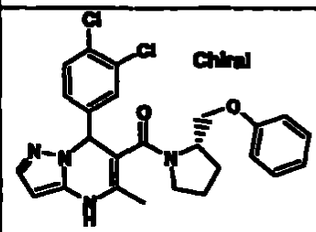
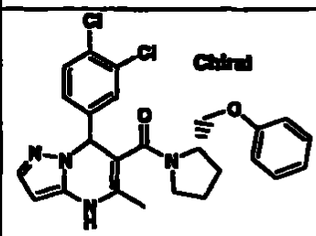
344		(2S)-1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxymethyl)pyrrolidine	421
345		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-phenylpyrrolidine	453
346		3-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-phenylthiazolidine	471
347		3-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-thiazolidinecarboxylic acid methyl ester	453
348		7-(3,4-Dichlorophenyl)-4,7-dihydro-N,5-dimethyl-N-(3-phenylpropyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	455
349		7-(3,4-Dichlorophenyl)-N-ethyl-4,7-dihydro-5-methyl-N-(3-phenylpropyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	469

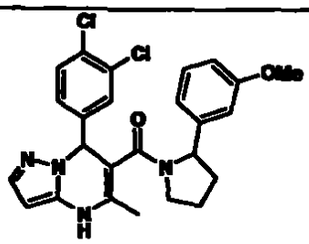
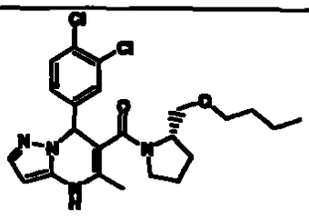
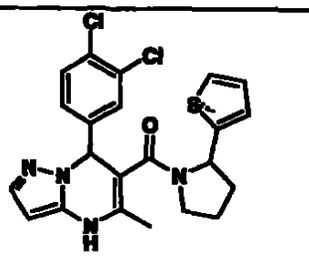
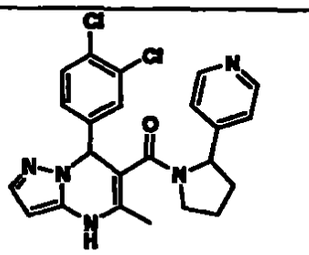
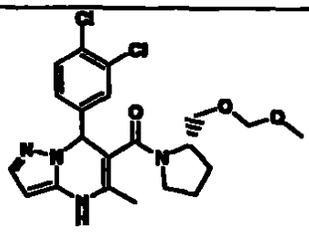
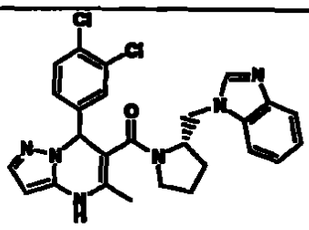
115

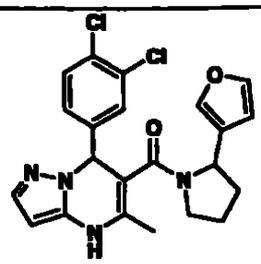
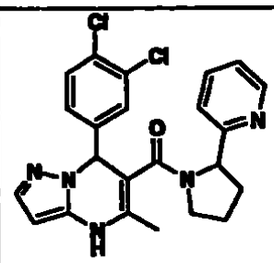
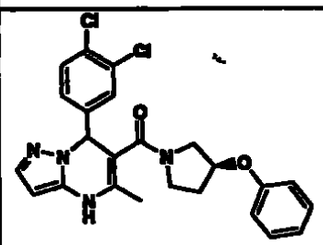
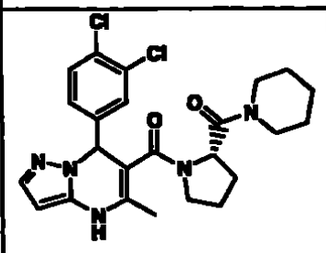
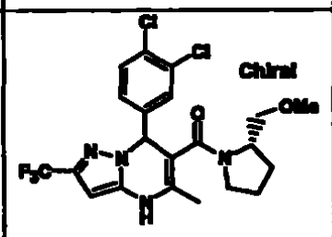
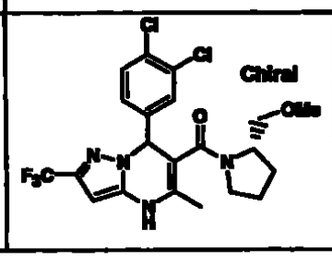
350		7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-(3-phenylpropyl)-N-propylpyrazolo[1,5-a]pyrimidine-6-carboxamide	483
351		N-Butyl-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-N-(3-phenylpropyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	497
352		2-(4-Chlorophenyl)-3-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]thiazolidine	505
353		N-(Cyclopropylmethyl)-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-N-propylpyrazolo[1,5-a]pyrimidine-6-carboxamide	419
354		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(2,3-dihydro-2-oxo-1H-benzimidazol-1-yl)piperidine	523

716

355		8-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one	537
356		4-(4-Chlorophenyl)-1-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,6-tetrahydropyridine	499
357		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(2-phenylethyl)pyrrolidine	481
358		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(4-methoxyphenyl)pyrrolidine	483
359		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(2-methoxyphenyl)pyrrolidine	483

360		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-2-(4-fluoro-phenyl)pyrrolidine	471
361		(3R)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-3-phenoxypyrrolidine	469
362		(2S)-2-[(Cyclohexyl-oxy)methyl]-1-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]pyrrolidine	489
363		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-2-(phenyl-methyl)pyrrolidine	467
364		(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(phenoxymethyl)pyrro-lidine, diastereomer A	483
365		(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(phenoxymethyl)pyrro-lidine, diastereomer B	483

366		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-2-(3-methoxy-phenyl)pyrrolidine	483
367		(2S)-2-(Butoxymethyl)-1-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]pyrrolidine	463
368		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(2-thienyl)pyrrolidine	459
369		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(4-pyridinyl)pyrrolidine	454
370		(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-[(methoxymethoxy)-methyl]pyrrolidine	451
371		(2S)-2-(1H-Benzimidazol-1-ylmethyl)-1-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]pyrrolidine	507

372		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(3-furanyl)pyrrolidine	443
373		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(2-pyridinyl)pyrrolidine	454
374		(3S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-3-phenoxypyrrolidine	469
375		(3S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-3-phenoxypyrrolidine	488
376		(2S)-1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methyl-2-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxymethyl)pyrrolidine, enantiomer A	489
377		(2S)-1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methyl-2-(trifluoro-methyl)pyrazolo[1,5-a]-pyrimidin-6-yl]carbonyl]-2-(methoxymethyl)pyrro-lidine, enantiomer B	489

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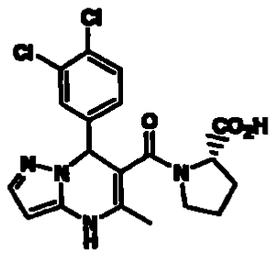
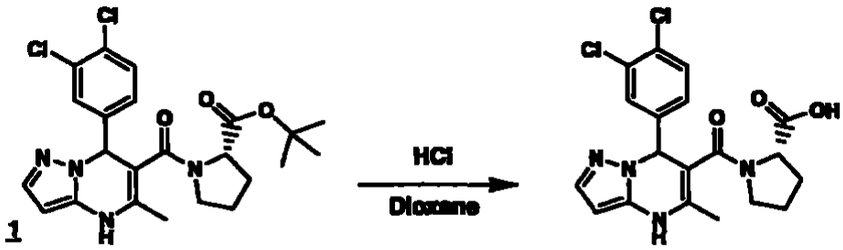
Example 378

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-L-proline



Method.



Compound 1 Compound 1 (the compound of Example 252) was prepared in a manner similar to that described in Example 170.

Title Compound. Hydrochloric acid (5 mL, 4M in Dioxane) was added to compound 1 (0.05 g, 0.1 mmol). The resulting mixture was stirred at room temperature. After 3 h the mixture was concentrated in vacuo. LC/MS analysis of the residue indicated that starting material remained. Additional Hydrochloric acid (5 mL, 4M in Dioxane) was added. The resulting mixture was stirred at room temperature for 7 h. TLC analysis indicated that compound 1 was consumed. The mixture was concentrated in vacuo. The residue was purified by preparative reverse phase HPLC to give the title compound as a mixture of diastereomers. LC/MS indicated that the compound was still impure (50% pure) Reverse Phase LC/MS, YMC S5 ODS 4.6 x 50 mm Ballistic

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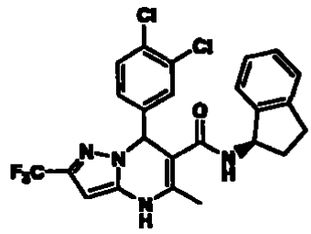
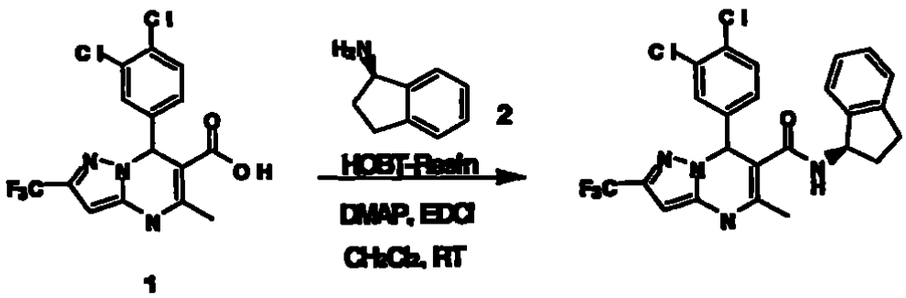
UV detection at 220 λ, 4 min. gradient, 0-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0 1% TFA, Solvent B 90% MeOH/H_2O with 0.1% TFA), 4 mL/min. Diastereomer A Rt = 3 34, Diastereomer B Rt = 3.49 min. MS (M+H. 421). The product was triturated with dichloromethane to give 0.014 g (32 % yield) of the title compound (85% pure by HPLC) Reverse Phase LC/MS YMC S5 4 6 x 50 mm combiscreen, UV detection at 220 λ, 4 min. gradient, 0-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0.2% H_3PO_4, Solvent B 90% MeOH/H_2O with 0.2% H_3PO_4), 4 mL/min. Diastereomer A Rt = 2.82, Diastereomer B Rt = 2.97 min.

Example 379

7-(3,4-Dichlorophenyl)-4,7-dihydro-N-[(1R)-2,3-dihydro-1H-inden-1-yl]-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide



Method.



1

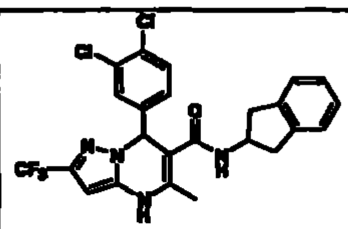
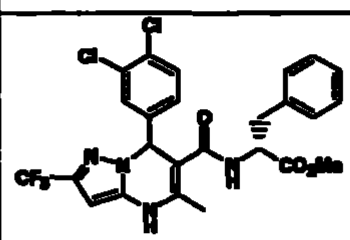
Compound 1. Compound 1 was prepared as described in Example 17

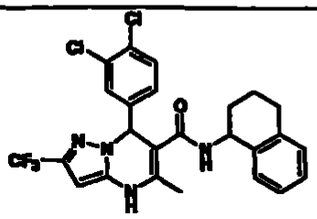
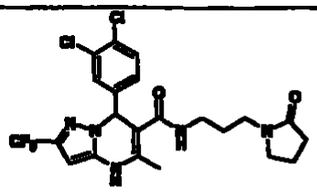
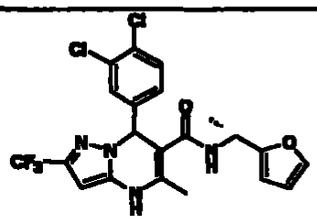
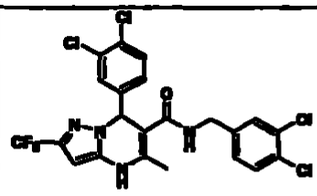
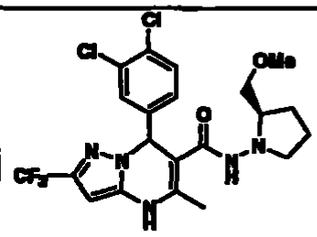
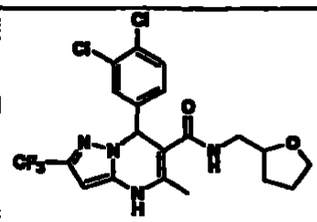
Title Compound: To a suspension of polystyrene-supported HOBt resin (NovaBiochem, >1 2 mmol/g, 50 mg, 1 0 eq) in anhydrous CH_2Cl_2 (1.0 mL) was added Compound 1 (47 mg, 2.0 eq), EDCI (23 mg, 2.0 eq), and DMAP (0 7 mg, 0 1

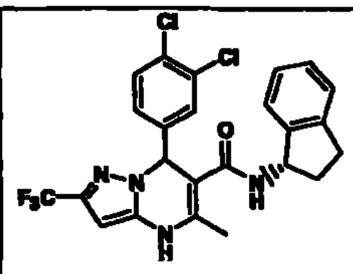
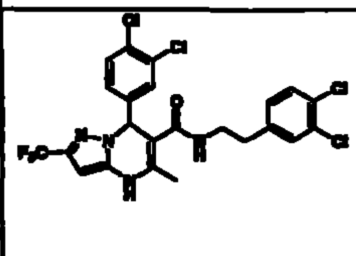
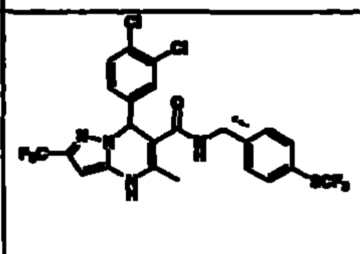
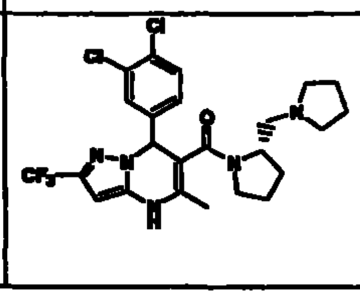
eq). The suspension was shaken vigorously using a VORTEX-GENIE2 for 1 hr. Solvent was then drained and the resin was washed sequentially with DMF (3x2 mL), THF (3x2 mL), and CH_2Cl_2 (3x2 mL) with vigorous shaking. The resin was resuspended in CH_2Cl_2 (1 mL) and to which was added (R)-(-)-Aminoindan 2 (0.006 mL, 0.8 eq). The mixture was shaken for 2 hr. Solvent was drained and the resin was washed with CH_2Cl_2 (3x1 mL) with vigorous shaking. All the washing solutions were combined and the solvent was removed under reduced pressure. The residue was purified through a silica gel cartridge eluting with 100 % EtOAc to give the title compound as a white solid. Reverse Phase LC/MS YMC S5 ODS 4.6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 0-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0.2% H_3PO_4, Solvent B 90% MeOH/H_2O with 0.2% H_3PO_4), 4 mL/min. Rt = 2.96 min, (diastereomers, 96% pure). MS (M+H): 507

Examples 380-391

The compounds of Examples 380-391, shown in the table provided below, were prepared in a manner similar to that described in Example 379.

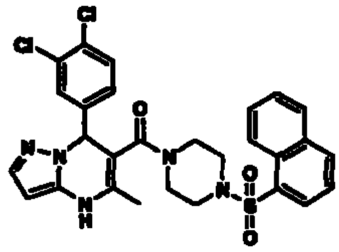
Example	Structure	Name	(M+H)
380		7-(3,4-Dichlorophenyl)-N-(2,3-dihydro-1H-inden-2-yl)-4,7-dihydro-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	507
381		N-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-D-phenylalanine methyl ester	553

382		7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-(1,2,3,4-tetrahydro-1-naphthalenyl)-2-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	521
383		7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-[3-(2-oxo-1-pyrrolidinyl)propyl]-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	516
384		7-(3,4-Dichlorophenyl)-N-(2-furanylmethyl)-4,7-dihydro-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	471
385		7-(3,4-Dichlorophenyl)-N-[(3,4-dichlorophenyl)methyl]-4,7-dihydro-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	550
386		7-(3,4-Dichlorophenyl)-4,7-dihydro-N-[(2R)-2-(methoxymethyl)-1-pyrrolidinyl]-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	504
387		7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-[(tetrahydro-2-furanyl)-methyl]-2-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidine-6-carbo-xamide	475

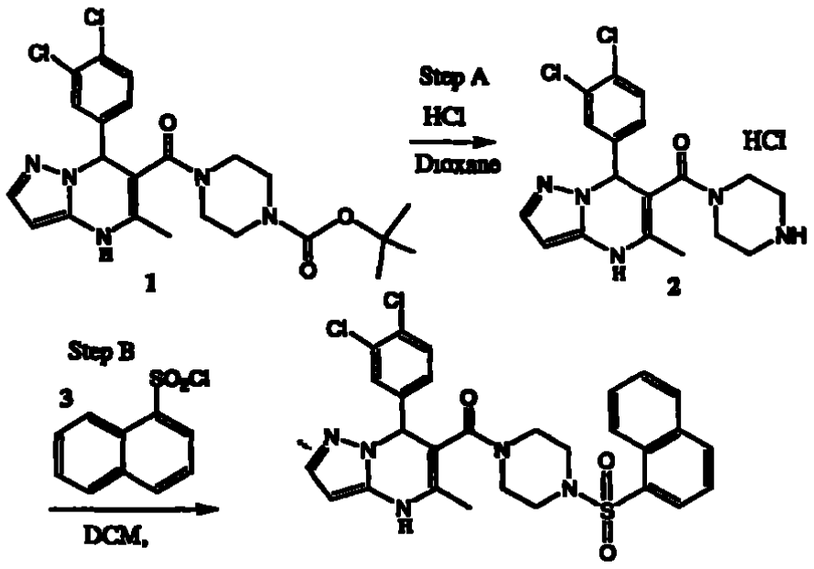
388		7-(3,4-Dichlorophenyl)-4,7-dihydro-N-[(1S)-2,3-dihydro-1H-inden-1-yl]-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	507
389		7-(3,4-Dichlorophenyl)-N-[2-(3,4-dichlorophenyl)ethyl]-4,7-dihydro-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide	564
390		7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-2-(trifluoromethyl)-N-[[4-[(trifluoromethyl)thio]phenyl]methyl]pyrazolo-[1,5-a]pyrimidine-6-carboxamide	581
391		(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7dihydro-5-methyl-2-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(1-pyrrolidinylmethyl)pyrrolidine	666

Example 392

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(1-naphthalenylsulfonyl)piperazine



Method.



Compound 1: Compound 1 (the compound of Example 60) was prepared in a manner similar to that described in Example 18, Method 2.

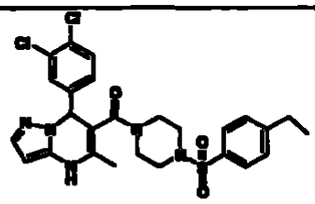
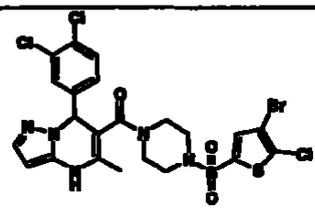
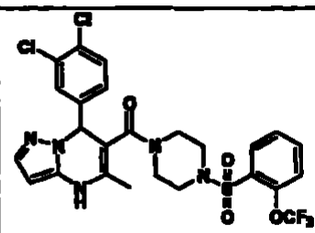
Step A: HCl (4M in dioxane) was added to solid compound 1 (0.53 g, 1.1 mmol). A gummy precipitate forms immediately. Dichloromethane was added, the gummy precipitate remained. The solvent was decanted and the residue was triturated with ethyl acetate (3X), concentrated to give 0.63 g (130 % contains residual dioxane) of the hydrochloride salt compound 2 as a light yellow powder. Reverse Phase LC/MS. YMC S5 ODS 4.6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 40-100% Solvent B/A (Solvent A: 10% MeOH/H20 with 0.1% TFA, Solvent B: 90% MeOH/H_2O with 0.1% TFA), 4 mL/min. Rt = 0.57 min, (92% pure). MS (M+H): 392. Compound 2 was used without purification.

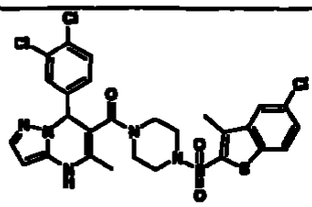
Step B. Compound 2 (0.077 g, 0.18 mmol) and compound 3 (0.049 g, 0.22 mmol) were suspended in dichloromethane (1 mL). Triethylamine (0.05 mL, 0.36 mmol) was added. A clear solution results. TLC after 30 min indicated consumption of starting material. The mixture was loaded directly onto a Worldwide Monitoring CLEAN-UP

CARTRIDGE (silica, CUSIL12M6) which had been equilibrated with 100% hexanes. Elution with 100% hexanes (40 mL), followed by 50% Ethyl acetate/hexanes (40 mL) and 100% ethyl acetate (40 mL) The purest fractions (TLC analysis) were combined to give 0 068 g (65% yield) of the title compound as a white solid. Reverse Phase LC/MS YMC S5 ODS 4 6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 40-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0.1% TFA, Solvent B 90% MeOH/H_2O with 0.1% TFA), 4 mL/min. Rt = 3.46 min, (90% pure). MS (M+H. 582). HMR ($CDCl_3$, 400 MHz) 8.60(1H, d, J=8), 8.05(2H, m), 7 95(1H, m), 7.62(4H, m), 7.35(1H, d, J=2 Hz), 7 17(1H, d, J=8 Hz), 7.06(1H, d, J=2 Hz), 6.81(1H, d, J=6 Hz), 6.17(1H, m), 5.54(1H, d, J=2 Hz), 3.23(8H,m), 1.86(3H, s).

Examples 393-396

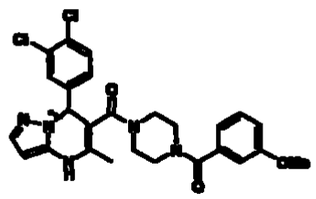
The compounds of Examples 393-396, shown in the table provided below, were prepared in a manner similar to that described in Example 392.

Example	Structure	Name	(M+H)
393		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-[(4-ethylphenyl)sulfonyl]-piperazine	560
394		1-[(4-Bromo-5-chloro-2-thienyl)sulfonyl]-4-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimi-din-6-yl]carbonyl]-piperazine	651
395		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-[[2-(trifluoro-methoxy)phenyl]sul-fonyl]piperazine	616

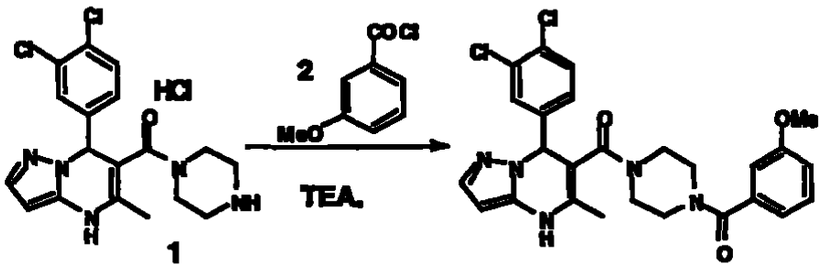
396		1-[(5-Chloro-3-methyl-benzo[b]thiophen-2-yl)sulfonyl]-4-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperazine	637

Example 397

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-[(3-methoxyphenyl)carbonyl]piperazine



Method.



Compound 1- Compound 1 was prepared as described in Step A of Example 392.

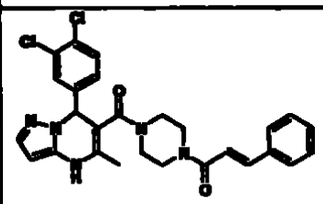
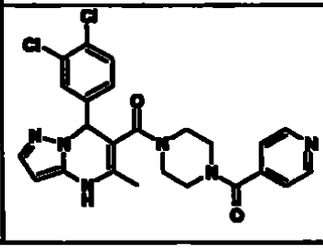
Title Compound Compound 1 (0.062 g, 0.15 mmol) and compound 2 (0.025 mL, 0.17 mmol) were suspended in dichloromethane (1 mL). Triethylamine (0.040, 0.29 mmol) was added. A clear solution results TLC after 30 min indicated consumption of starting material The mixture was loaded directly onto a Worldwide Monitoring CLEAN-UP CARTRIDGE (CUSIL12M6) which had been equilibrated with 100%

128

hexanes. Elution with 100% hexanes (40 mL), followed by 50% Ethyl acetate/hexanes (100 mL) and 100% ethyl acetate (100 mL). The purest fractions (TLC analysis) were combined to give 0 022 g (29% yield) of the title compound as a white solid. Reverse Phase LC/MS YMC S5 ODS 4 6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 40-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0.1% TFA, Solvent B 90% MeOH/H_2O with 0.1% TFA), 4 mL/min. Rt = 2.69 min, (90% pure) MS (M+H 526).

Examples 398 and 399

The compounds of Examples 398 and 399, shown in the table provided below, were prepared in a manner similar to that described in Example 397

Example	Structure	Name	(M+H)
398		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-(1-oxo-3-phenyl-2-propenyl)-piperazine	522
399		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-(4-pyridinylcar-bonyl)piperazine	497

Example 400

1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-4,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine

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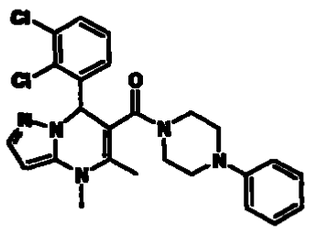

Method.

Compound 1 Compound 1 was prepared as described in Example 18.

Title Compound Compound 1 (0 08g, 0 17 mmol) was dissolved in dimethylformamide (1 0 mL) NaH (0 005g, 0.22 mmol, 60% in oil) was added and the mixture was stirred for 5 min Iodomethane (0.012 mL, 0 18 mmol) was added. When TLC (5% methanol/dichloromethane) analysis indicated consumption of starting material the reaction was quenched with water, diluted with ethyl acetate, transferred to a separatory funnel, washed with saturated water and brine, dried over anhydrous sodium sulfate and concentrated. The residue was purified by silica gel chromatography eluting with 100% dichloromethane followed by 3% methanol/dichloromethane to provide 0.06g (75%) of the title compound as a amber oil. Reverse Phase LC/MS YMC S5 ODS 4.6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 40-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0.1% TFA, Solvent B 90% MeOH/H_2O with 0.1% TFA), 4 mL/min. Rt = 2 99 min, (96% pure) MS (M+H 482)

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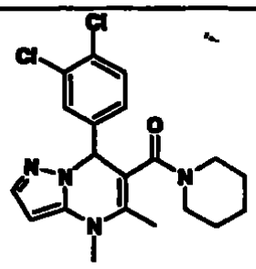
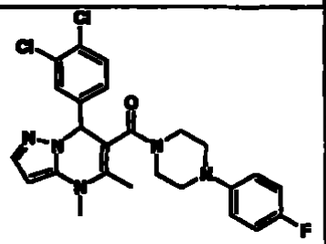
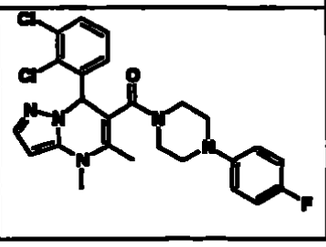
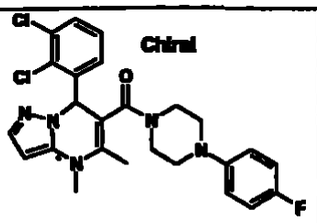
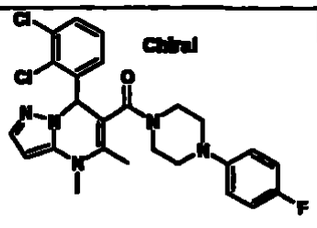
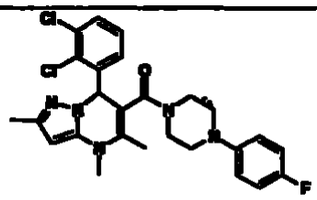
Examples 401-406

The compounds of Examples 401-406, shown in the table provided below, were prepared in a manner similar to that described in Example 400

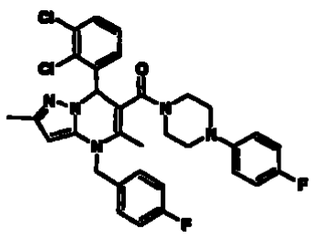
HPLC resolution of Example 403, Chiralpak AD column (50 X 500 mm), eluting with 35% isopropanol/hexanes containing 0 1 % triethylamine at 50 mL/min), UV detection at 254 λ provided enantiomers A (Example 405) and B (Example 404) Chiralpak AD column (4.6 X 250 mm) eluting with 30% isopropanol/hexanes containing 0 1 % triethylamine at 1 mL/min), UV detection at 254 λ, enantiomer A Rt = 14.4 min, >99% ee. Enantiomer B Rt = 28.7 min, >99% ee.

Example	Structure	Name	(M+H)
401		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-4,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperidine	405
402		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-4,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	500
403		1-[[7-(2,3-Dichloro-phenyl)-4,7-dihydro-4,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	500

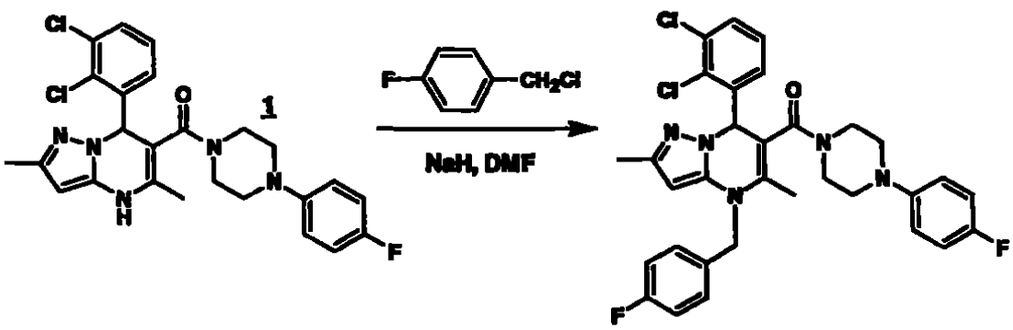
404	 Chiral	1-[[7-(2,3-Dichloro-phenyl)-4,7-dihydro-4,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine, enantiomer B	500
405	 Chiral	1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-4,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine, enantiomer A	500
406		1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-2,4,5-trimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	514

Example 407

1-[[7-(2,3-Dichlorophenyl)-4-[(4-fluorophenyl)methyl]-4,7dihydro-2,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine



Method.

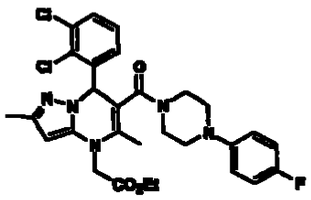


Compound 1 Compound 1 was prepared in a manner similar to that described in Example 18, Method 2.

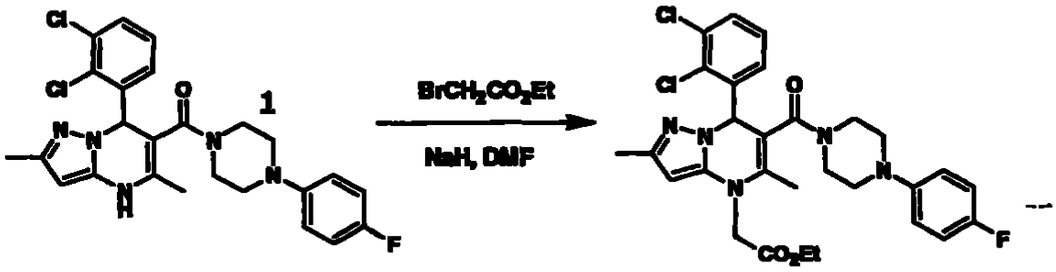
Title Compound. Compound 1 (0.10g, 0.21 mmol) was dissolved in dimethylformamide (1.0 mL). NaH (0.007g, 0.27 mmol, 60% in oil) was added and the mixture was stirred for 5 min. 4-Fluorobenzyl chloride (0.028 mL, 0.23 mmol) was added. When TLC (5% methanol/ dichloromethane) analysis indicated consumption of starting material the reaction was quenched with water, diluted with ethyl acetate, transferred to a separatory funnel, washed with saturated water and brine, dried over anhydrous sodium sulfate and concentrated. The residue was purified by silica gel chromatography eluting with 100% dichloromethane followed by 3% methanol/dichloromethane to provide 0.09g (69%) of the title compound as a amber oil Reverse Phase LC/MS YMC S5 ODS 4 6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 40-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0 1% TFA, Solvent B 90% MeOH/H_2O with 0.1% TFA), 4 mL/min. Rt = 3.20 min, (93% pure) MS (M+H. 608).

Example 408

7-(2,3-Dichlorophenyl)-6-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-2,5-dimethylpyrazolo[1,5-a]pyrimidine-4(7H)-acetic acid ethyl ester



Method.

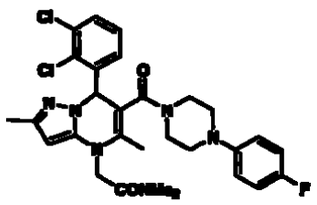


Compound 1: Compound 1 was prepared in a manner similar to that described in Example 18, Method 2.

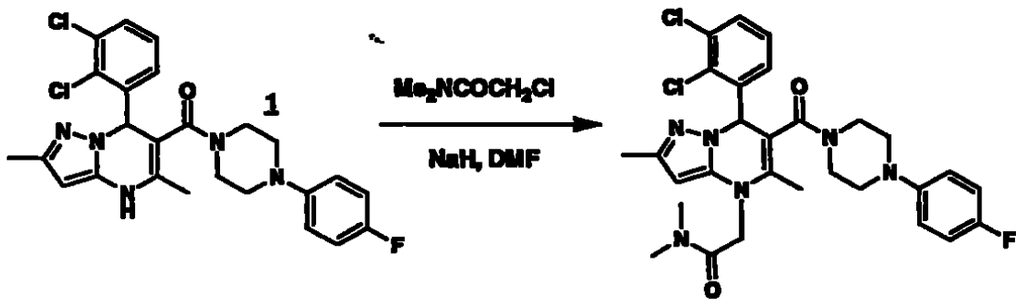
Title Compound. Compound 1 (0.10g, 0.21 mmol) was dissolved in dimethylformamide (1.0 mL). NaH (0.006g, 0.24 mmol, 60% in oil) was added and the mixture was stirred for 5 min. Ethyl bromoacetate (0.029 mL, 0.26 mmol) was added. When TLC (5% methanol/dichloromethane) analysis indicated consumption of starting material the reaction was quenched with water, diluted with ethyl acetate, transferred to a separatory funnel, washed with saturated water and brine, dried over anhydrous sodium sulfate and concentrated. The residue was purified by silica gel chromatography eluting with 100% dichloromethane followed by 3% methanol/dichloromethane to provide 0.086g (74%) of the title compound as a yellow glass. Reverse Phase LC/MS: YMC S5 ODS 4.6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 40-100% Solvent B/A (Solvent A: 10% MeOH/H20 with 0.1% TFA, Solvent B: 90% MeOH/H_2O with 0.1% TFA), 4 mL/min. Rt = 3.22 min, (97% pure). MS (M+H: 586)

Example 409

7-(2,3-Dichlorophenyl)-6-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-N,N,2,5-tetramethylpyrazolo[1,5-a]pyrimidine-4(7H)-acetamide



Method.



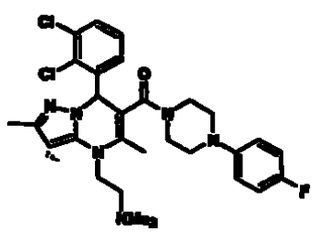
Compound 1 Compound 1 was prepared in a manner similar to that described in Example 18, Method 2.

Title Compound Compound 1 (0.08g, 0.16 mmol) was dissolved in dimethylformamide (0.8 mL). NaH (0.005g, 0.19 mmol, 60% in oil) was added and the mixture was stirred for 5 min. 2-chloro-N,N-dimethylacetamide (0.021 mL, 0.21 mmol) was added. When TLC (5% methanol/dichloromethane) analysis indicated consumption of starting material the reaction was quenched with water, diluted with ethyl acetate, transferred to a separatory funnel, washed with water and saturated brine, dried over anhydrous sodium sulfate and concentrated. The residue was purified by silica gel chromatography eluting with 100% dichloromethane followed by 3% methanol/dichloromethane to provide 0.058g (62%) of the title compound as a yellow

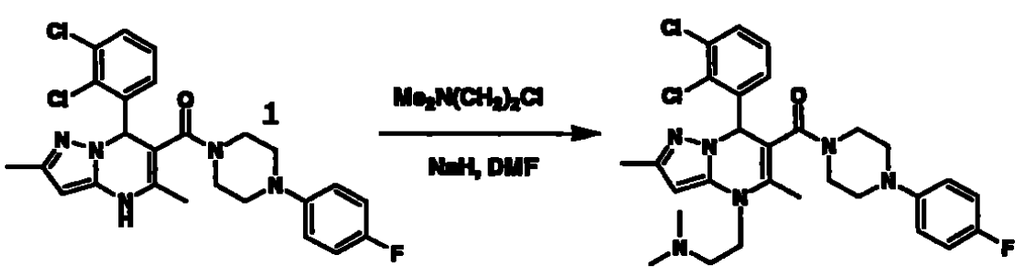
oil. Reverse Phase LC/MS YMC S5 ODS 4 6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 40-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0.1% TFA, Solvent B 90% MeOH/H_2O with 0 1% TFA), 4 mL/min. Rt = 2.63 min, (93% pure) MS (M+H 585)

Example 410

1-[[7-(2,3-Dichlorophenyl)-4-[2-(dimethylamino)ethyl]-4,7-dihydro-2,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine



Method



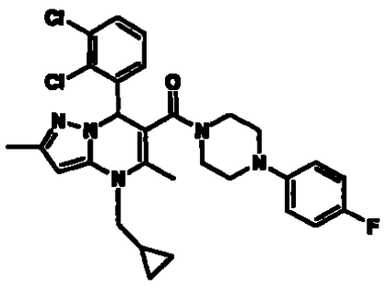
Compound 1. Compound 1 was prepared in a manner similar to that described in Example 18, Method 2.

Title Compound. Compound 1 (0.11g, 0.21 mmol) was dissolved in dimethylformamide (1.0 mL). Sodium hydride (0.054g, 0.47 mmol, 60% in oil) was added and the mixture was stirred for 5 min. 1-Chloro-2-dimethylaminoethane hydrochloride (0.040 g, 0 27 mmol) was added After 25 min the reaction was quenched with water, diluted with ethyl acetate, transferred to a separatory funnel,

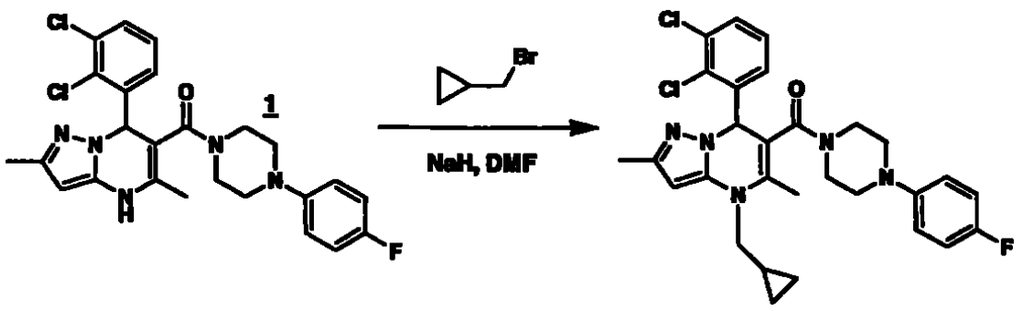
washed with saturated water and brine, dried over anhydrous sodium sulfate and concentrated. LC/MS analysis of the residue indicated mostly unreacted starting material The residue was redissolved in dimethylformamide (1 0 mL), Sodium hydride (0 10 g, 4.2 mmol) was added and the mixture was stirred for 5 min. 1-Chloro-2-dimethylaminoethane hydrochloride (0 15 g, 1 05 mmol) was added. When TLC (5% methanol/dichloromethane) analysis indicated consumption of starting material the reaction was quenched with water, diluted with ethyl acetate, transferred to a separatory funnel, washed with saturated water and brine, dried over anhydrous sodium sulfate and concentrated. The residue was purified by silica gel chromatography eluting with 100% dichloromethane followed by 3% methanol/dichloromethane to provide 0.030g (25%) of the title compound as a yellow glass. Reverse Phase LC/MS YMC S5 ODS 4.6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 40-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0 1% TFA, Solvent B 90% MeOH/H_2O with 0.1% TFA), 4 mL/min. Rt = 1 72 min, (92% pure). MS (M+H 571)

Example 411

1-[[4-(Cyclopropylmethyl)-7-(2,3-dichlorophenyl)-4,7-dihydro-2,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine



Method

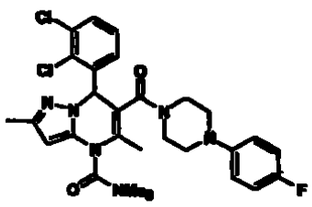


Compound 1· Compound 1 was prepared in a manner similar to that described in Example 18, Method 2.

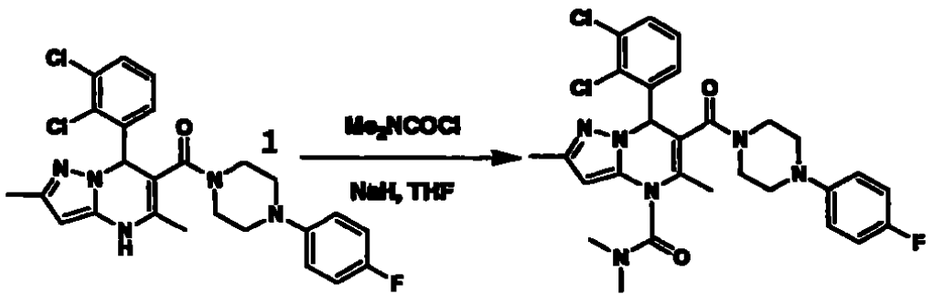
Title Compound. Compound 1 (0.11g, 0.21 mmol) was dissolved in dimethylformamide (1.0 mL). Sodium hydride (0.006g, 0.25 mmol, 60% in oil) was added and the mixture was stirred for 5 min (Bromomethyl)cylcopropane(0.0251 mL, 0.27 mmol) was added. When TLC (5% methanol/dichloromethane) analysis indicated consumption of starting material the reaction was quenched with water, diluted with ethyl acetate, transferred to a separatory funnel, washed with saturated water and brine, dried over anhydrous sodium sulfate and concentrated. The residue was purified by silica gel chromatography eluting with 100% dichloromethane followed by 3% methanol/dichloromethane to provide 0.104g (89%) of the title compound as a yellow glass. Reverse Phase LC/MS YMC S5 ODS 4.6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 40-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0.1% TFA, Solvent B 90% MeOH/H_2O with 0 1% TFA), 4 mL/min. Rt = 2.99 min, (95% pure). MS (M+H. 554)

Example 412

7-(2,3-Dichlorophenyl)-6-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-N,N,2,5-tetramethylpyrazolo[1,5-a]pyrimidine-4(7H)-carboxamide



Method



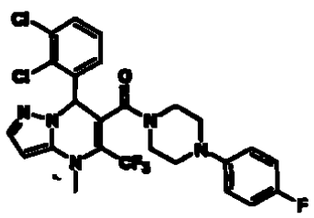
Compound 1. Compound 1 was prepared in a manner similar to that described in Example 18, Method 2.

Title Compound Compound 1 (0.22 g, 0.44 mmol) was dissolved in tetrahydrofuran (3.0 mL) Sodium hydride (0 106g, 4.44 mmol, 60% in oil) was added and the mixture was stirred for 5 min. N,N-Dimethylcarbamoyl chloride (0.12 mL, 1 33 mmol) was added. The mixture was stirred overnight. TLC (5% methanol/dichloromethane) analysis indicated consumption of starting material the reaction was quenched with water, diluted with ethyl acetate, transferred to a separatory funnel, washed with saturated water and brine, dried over anhydrous sodium sulfate and concentrated. The residue was purified by silica gel chromatography eluting with 100% dichloromethane followed by 3% methanol/dichloromethane to provide 0.22 g (87% yield) of the title compound. LC/MS indicated that the compound was impure. The title compound was further purified by silica gel chromatography eluting with 10% ethyl acetate/hexanes, followed by 50% ethyl acetate/hexanes and 100% ethyl acetate to afford 0.118 g (47%

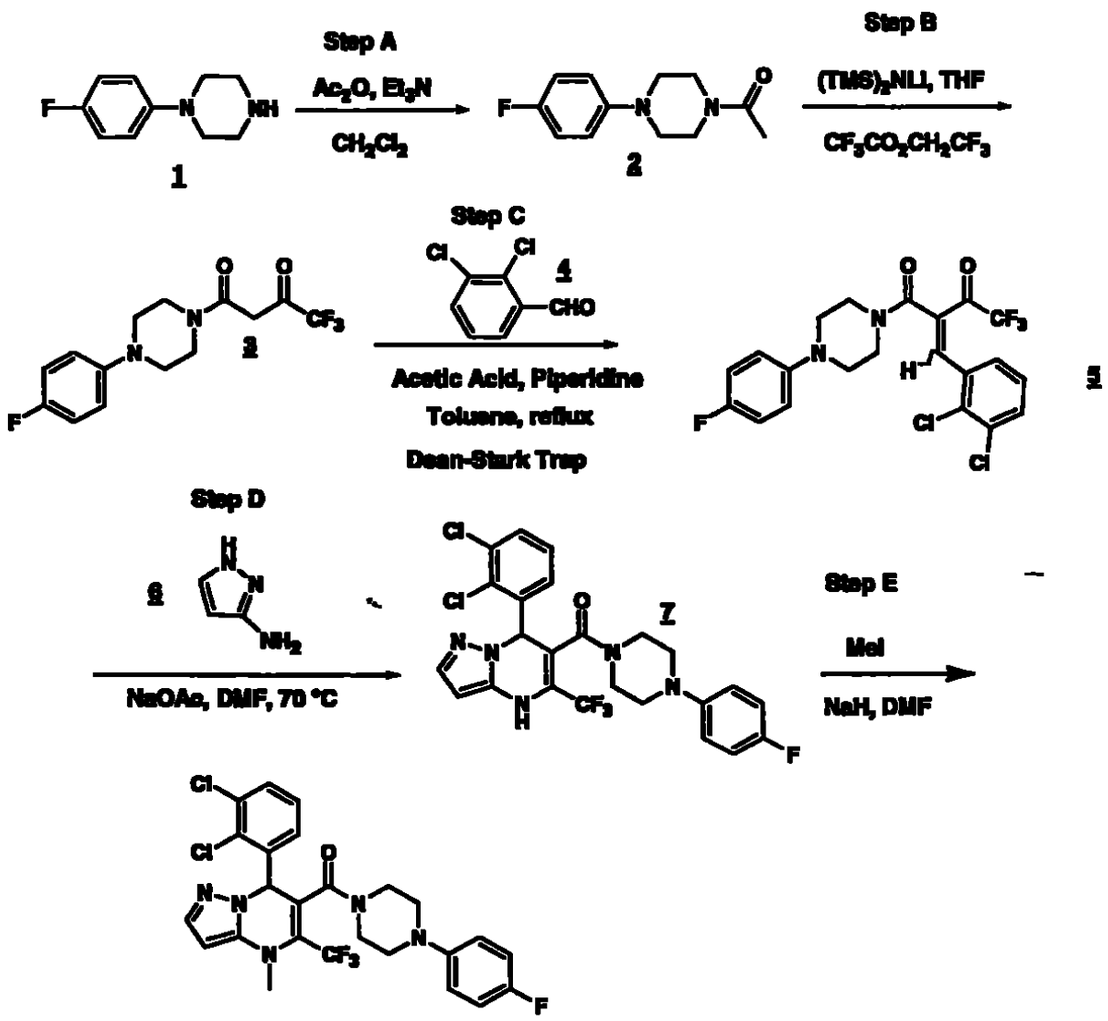
yield) of the title compound as a white glass. Reverse Phase LC/MS YMC S5 ODS 4 6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 40-100% Solvent B/A (Solvent A 10% MeOH/H20 with 0.1% TFA, Solvent B 90% MeOH/H_2O with 0 1% TFA), 4 mL/min. Rt = 2.45 min, (95% pure) MS (M+H 571)

Example 413

1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-4-methyl-5-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine



Method



Step A. Acetic anhydride (0 77 mL, 8.14 mmol) was dropwise added to a solution of 4-(4-fluorophenyl)piperazine 1 (1 17 g, 6.49 mmol) in dichloromethane (10 mL). TLC after 30 min. indicated reaction was complete. The mixture was transferred to a separatory funnel, washed with water and brine, dried over anhydrous sodium sulfate and concentrated to give 1.28 g (89% yield) of compound 2 as a clear solid. Reverse Phase LC/MS YMC S5 ODS 4 6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 0-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0.1% TFA, Solvent B 90% MeOH/H_2O with 0 1% TFA), 4 mL/min. Rt = 1.58 min, (92% pure) MS (M+H. 223). HMR ($CDCl_3$, 400 MHz): 6.96(2H, m), 6.89(2H, m), 3 77(2H, m),

3 62(2H m), 3 07(4H, m), 2.14(3H, s) Compound 2 was used without further purification in the next step.

Step B Lithium hexamethyldisilylazide (6.1 mL, 6 1 mmol, 1M in tetrahydrofuran) was dropwise added to a –78 °C solution of compound 2 (1.22 g, 5.5 mmol) in tetrahydrofuran (25 mL) After 40 min. 2,2,2-trifluoroethyl trifluoroacetate (0.9 mL, 6.6 mmol) was added to the yellow solution. The reaction turned from yellow to clear After an additional 10 min. the cooling bath was removed and the mixture was allowed to warm to room temperature. After 30 min. more the reaction was quenched with saturated ammonium chloride, diluted with ethyl acetate, transfered to a separatory funnel, washed with saturated ammonium chloride, water and brine, dried over anhydrous sodium sulfate and concentrated onto enough silica gel such that a free flowing powder was obtained. The resulting powder was loaded onto a chromatography column prepacked with silica gel and 30% ethylacetate/hexanes. Elution with 30% ethyl acetate/hexanes gave 0.998 g (57% yield) of compound 3 as a yellow solid. Reverse Phase LC/MS YMC S5 ODS 4.6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 40-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0 1% TFA, Solvent B 90% MeOH/H_2O with 0.1% TFA), 4 mL/min. Rt = 2.87 min, (90% pure). MS (M+H. 319). HMR ($CDCl_3$, 400 MHz) (note compound exists in the enol form) 7.00(2H, m), 6.90(2H, m), 5.80(1H, s), 3 79(4H, m), 3 13(4H, m)

Step C Compound 3 and compound 4 were condensed as described in Example 18, Method 2 Step B, to provide compound 5. Compound 5 was used in the next step without further purification.

Step D Compound 5 and compound 6 were condensed as described in Example 18, Method 2 Step C1, to afford compound 7 Reverse Phase LC/MS of crude 6: YMC S5 ODS 4.6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 0-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0.1% TFA, Solvent B 90% MeOH/H_2O with 0 1% TFA), 4 mL/min Rt = 4.12 min, (58% pure). MS (M+H. 540) Compound 7 was purified by silica gel chromatography eluting with 20-50% ethyl

acetate/hexanes followed by recrystallization from ethyl acetate/hexanes to give 0.084 g (6% yield) of compound 7 as a white solid. Reverse Phase LC: YMC S5 ODS 4.6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 0-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0.2% H_3PO_4, Solvent B 90% MeOH/H_2O with 0 2% H_3PO_4), 4 mL/mm Rt = 4.15 mm, (92% pure)

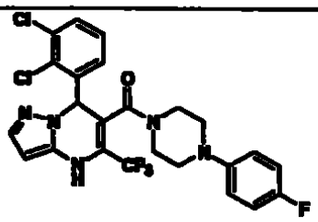
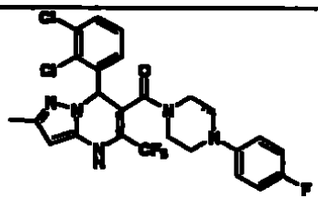
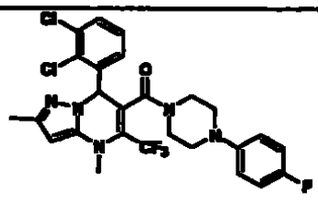
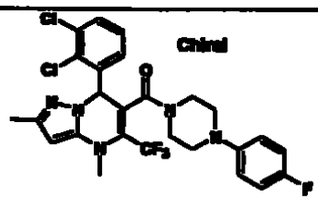
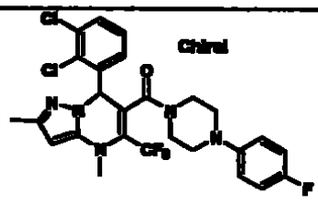
Step E. Compound 7 (0.08g, 0 14 mmol) was dissolved in dimethylformamide (1 0 mL). NaH (0.005g, 0.19 mmol, 60% in oil) was added and the mixture was stirred for 305 mm. Iodomethane (0.010 mL, 0 16 mmol) was added. The mixture was stirred for 2h and then quenched with saturated ammonium chloride, diluted with ethyl acetate, transferred to a separatory funnel, washed with saturated water and brine, dried over anhydrous sodium sulfate and concentrated. The residue was purified by preparative reverse phase HPLC YMC S5 ODS 20 x 100 mm Ballistic column, UV detection at 220 λ, 10 mm. gradient 30-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0.1% TFA, Solvent B 90% MeOH/H_2O with 0.1% TFA), 20 mL/min. Rt = 10.6 mm,. to provide 0 037g (45%) of the title compound. Reverse Phase LC/MS YMC S5 ODS 4 6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 0-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0.1% TFA, Solvent B 90% MeOH/H_2O with 0.1% TFA), 4 mL/min. Rt = 3.83 min. MS (M+H 568). Reverse Phase LC: YMC S5 ODS 4 6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 0-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0.2% H_3PO_4, Solvent B 90% MeOH/H_2O with 0 2% H_3PO_4), 4 mL/min. Rt = 4.37 mm., 89% pure.

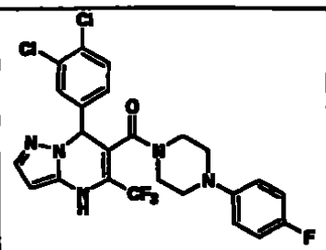
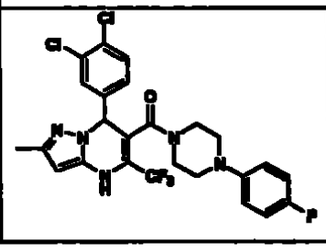
<u>Examples 414-421</u>

The compounds of Examples 414-421, shown in the table provided below, were prepared in a manner similar to that described in Example 413

HPLC resolution of Example 416, Chiralpak AD column (50 X 500 mm), eluting with 50% isopropanol/hexanes containing 0.1 % triethylamine at 50 mL/mm), UV detection at 254 λ, provided enantiomers A (Example 418) and B (Example 417) Chiralpak AD column (4 6 X 250 mm) eluting with 50% isopropanol/hexanes

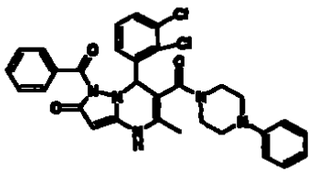
containing 0.1 % triethylamine at 1 mL/mm), UV detection at 254 λ, enantiomer A Rt = 14.4 min, 89% ee. Enantiomer B Rt = 28 7 min, 87% ee.

Example	Structure	Name	(M+H)
414		1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	554
415		1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-2-methyl-5-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	554
416		1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-2,4-dimethyl-5-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	568
417		1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-2,4-dimethyl-5-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine, enantiomer B	568
418		1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-2,4-dimethyl-5-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine, enantiomer A	568

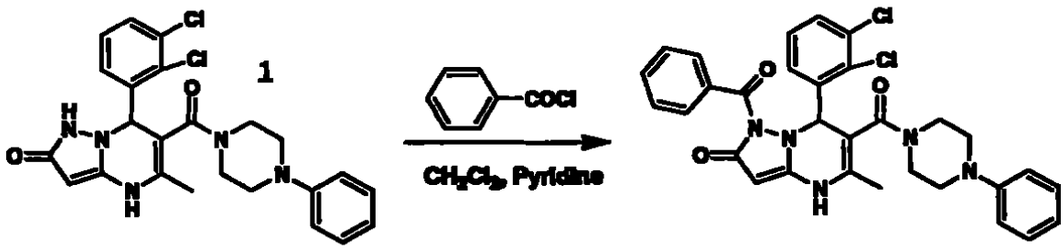
419		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	540
420		1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-2-methyl-5-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	554

Example 421

1-[[1-Benzoyl-7-(2,3-dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine



Method.

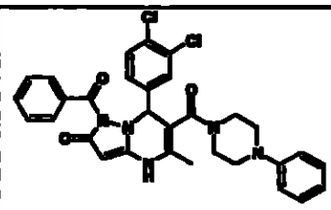
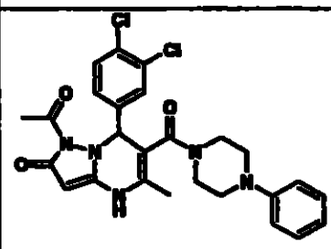
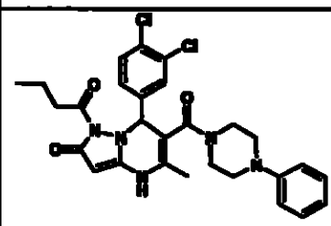


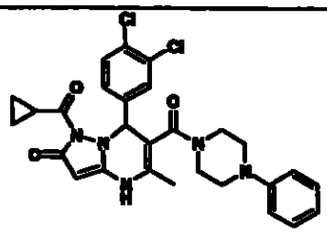
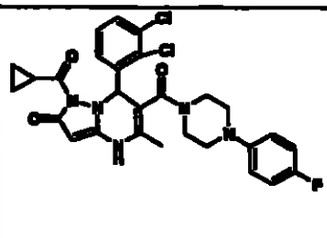
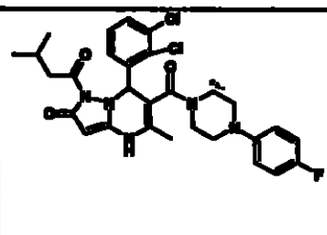
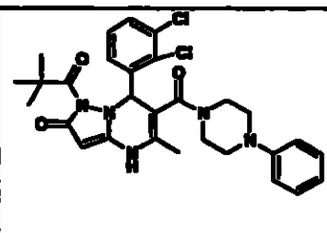
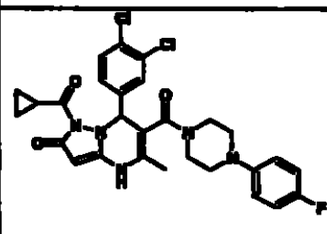
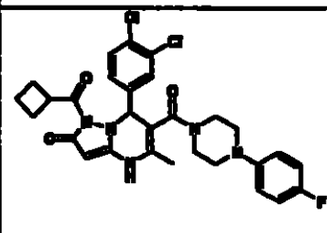
Compound 1 Compound 1 was prepared in manner similar to that described in Example 18, Method 2.

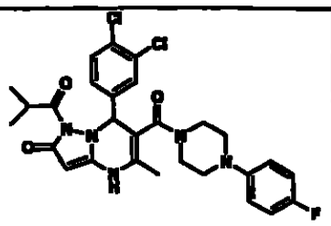
Title Compound Benzoyl chloride (0 007 mL, 0 06 mmol) and pyridine (0.008 mL, 0.10 mmol) were added to a 0 °C solution of compound 1 (0.08g, 0.17 mmol) in dichloromethane (5 mL) After 1h, TLC indicated the reaction was complete. The reaction was quenched with methanol and concentrated. The residue was purified by silica gel chromatography eluting with 80% ethyl acetate/hexanes to afford 0.024 g (81%) of the title compound as a white solid. Reverse Phase LC/MS YMC S5 ODS 4 6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 0-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0 1% TFA, Solvent B 90% MeOH/H_2O with 0.1% TFA), 4 mL/min. Rt = 4.05 min, (86% pure). (M+H. 588). HMR ($CDCl_3$, 400 MHz). 8.08(1H, s), 8.06(1H, s), 7.51(1H, m), 7.37(2H, t, J=8 Hz), 7.28(1H, m), 7 18(2H, m), 7.08(1H, m), 6 9-6.7(3H, m), 6.45 (1H, bs), 5 60(1H, bs), 4.15-2 8 (6H, m), 2.20(1H, bs), 1.88(3H, s), 1.45(1H, bs)

Examples 422-431

The compounds of Examples 422-431, shown in the table provided below, were prepared in a manner similar to that described in Example 421

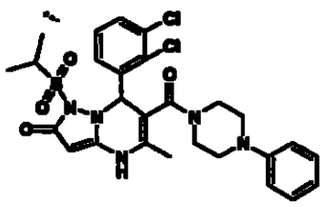
Example	Structure	Name	(M+H)
422		1-[[1-Benzoyl-7-(3,4-dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine	588
423		1-[[1-Acetyl-7-(3,4-dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine	526
424		1-[[7-(3,4-Dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-2-oxo-1-(1-oxobutyl)-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine	554

425		1-[[1-(Cyclopropyl-carbonyl)-7-(3,4-dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-phenyl-piperazine	552
426		1-[[1-(Cyclopropyl-carbonyl)-7-(2,3-dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-(4-fluoro-phenyl)piperazine	570
427		1-[[7-(2,3-Dichloro-phenyl)-1,2,4,7-tetra-hydro-5-methyl-1-(3-methyl-1-oxobutyl)-2-oxopyra-zolo[1,5-a]pyri-midin-6-yl]carbonyl]-4-(4-fluorophenyl)-piperazine	586
428		1-[[7-(2,3-Dichloro-phenyl)-(2,2-dimethyl-1-oxopropyl)-1,2,4,7-tetrahydro-5-methyl-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-phenyl-piperazine	568
429		1-[[1-(Cyclopropyl-carbonyl)-7-(3,4-dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-(4-fluoro-phenyl)piperazine	570
430		1-[[1-(Cyclobutyl-carbonyl)-7-(3,4-dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-(4-fluoro-phenyl)piperazine	584

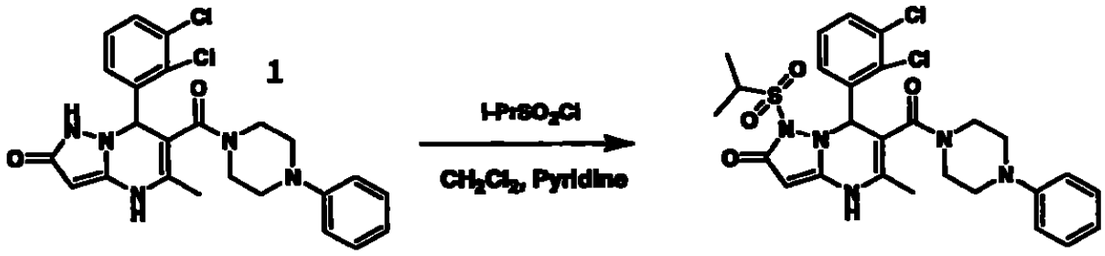
431		1-[[7-(3,4-Dichloro-phenyl)-1,2,4,7-tetrahydro-5-methyl-1-(2-methyl-1-oxopropyl)-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-(4-fluoro-phenyl)piperazine	572

Example 432

1-[[7-(2,3-Dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-1-[(1-methylethyl)sulfonyl]-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine



Method.



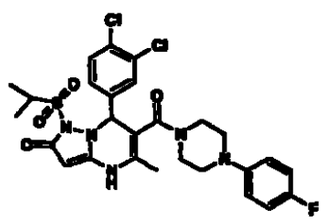
Compound 1 Compound 1 was prepared in a manner similar to that described in Example 18, Method 2.

Title Compound Isopropylsulfonyl chloride (0.11 mL, 0.97 mmol) and pyridine (0.12 mL, 1.46 mmol) were added to a 0 °C solution of compound 1 (0.234 g, 0.487 mmol) in dichloromethane (10 mL). The resulting mixture was allowed to warm to

room temperature. After 5h, TLC indicated the reaction was complete. The reaction was quenched with methanol and concentrated. The residue was purified by silica gel chromatography eluting with 5% methanol/ethyl acetate to afford 0.095 g (33%) of the title compound as a pale yellow solid. Reverse Phase LC/MS YMC S5 ODS 4.6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 0-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0 1% TFA, Solvent B 90% MeOH/H_2O with 0.1% TFA), 4 mL/min. Rt = 3.57 min, (92% pure) (M+H. 590)

Example 433

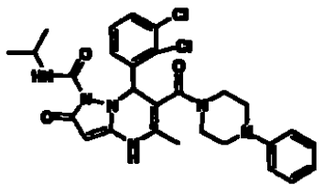
1-[[7-(3,4-Dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-1-[(1-methylethyl)sulfonyl]-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine



The title compound was prepared in a manner similar to that described in Example 432. (M+H) 608.

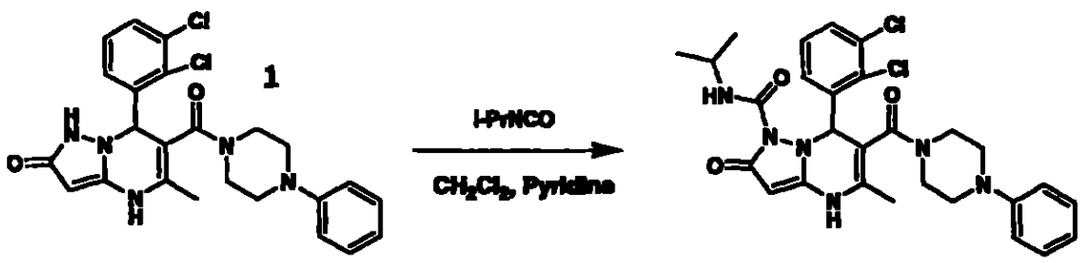
Example 434

7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-N-(1-methylethyl)-2-oxo-6-[(4-phenyl-1-piperazinyl)carbonyl]pyrazolo[1,5-a]pyrimidine-1(2H)-carboxamide



Method.

HA726

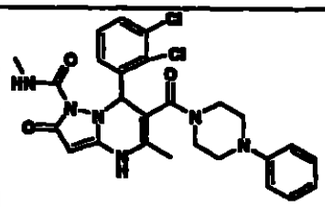


Compound 1 Compound 1 was prepared in a manner similar to that described in Example 18, *Method 2*

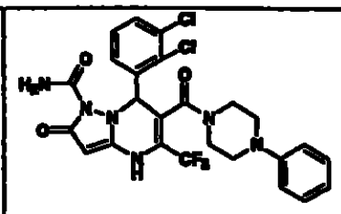
Title Compound. Isopropyl isocyanate (0.034 mL, 0.35 mmol) and pyridine (0.057 mL, 0.706 mmol) were added to a 0 °C solution of compound 1 (0 170 g, 0.350 mmol) in dichloromethane (50 mL). The resulting mixture was allowed to warm to room temperature. After 5h, TLC indicated the reaction was complete. The reaction was quenched with methanol and concentrated. The residue was purified by silica gel chromatography eluting with 75% ethyl acetate/hexanes to afford 0.027 g (13%) of the title compound as a white solid Reverse Phase LC/MS YMC S5 ODS 4.6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 0-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0 1% TFA, Solvent B 90% MeOH/H_2O with 0.1% TFA), 4 mL/min. Rt = 3 68 min, (95% pure) (M+H. 569)

Examples 435 and 436

The compounds of Examples 435 and 436, shown in the table provided below, were prepared in a manner similar to that described in Example 434

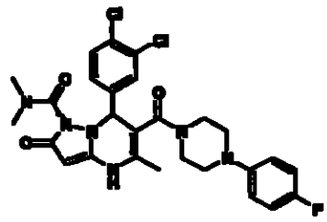
Example	Structure	Name	(M+H)
435		7-(2,3-Dichlorophenyl)-4,7-dihydro-N,5-dimethyl-2-oxo-6-[(4-phenyl-1-piperazinyl)-carbonyl]pyrazolo[1,5-a]pyrimidine-1(2H)-carboxamide	541

150

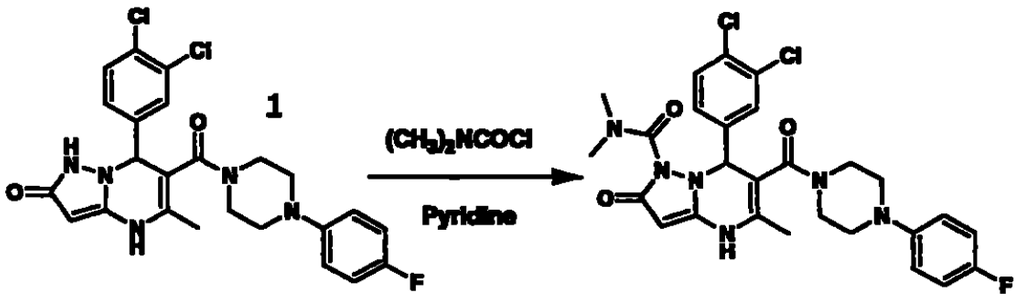
436		7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-2-oxo-6-[(4-phenyl-1-piperazinyl)carbonyl]-pyrazolo[1,5-a]pyrimidine-1(2H)-carboxamide	527

Example 437

7-(3,4-Dichlorophenyl)-6-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-4,7-dihydro-N,N,5-trimethyl-2-oxopyrazolo[1,5-a]pyrimidine-1(2H)-carboxamide



Method



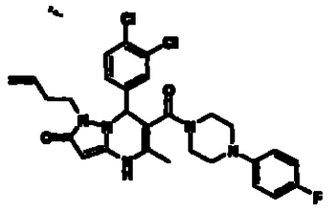
Compound 1 Compound 1 was prepared in a manner similar to that described in Example 18, Method 2.

Title Compound. Dimethylcarbamoyl chloride (0.10 mL, 1.1 mmol) was added to a 0 °C solution of compound 1 (0.52 g, 1.0 mmol) in pyridine (5 mL). The resulting mixture was stirred at 0 °C for 30 min., the cooling bath was removed, and the mixture was concentrated. The residue was dissolved in ethyl acetate and washed with water and brine, dried over anhydrous sodium sulfate and concentrated. The residue

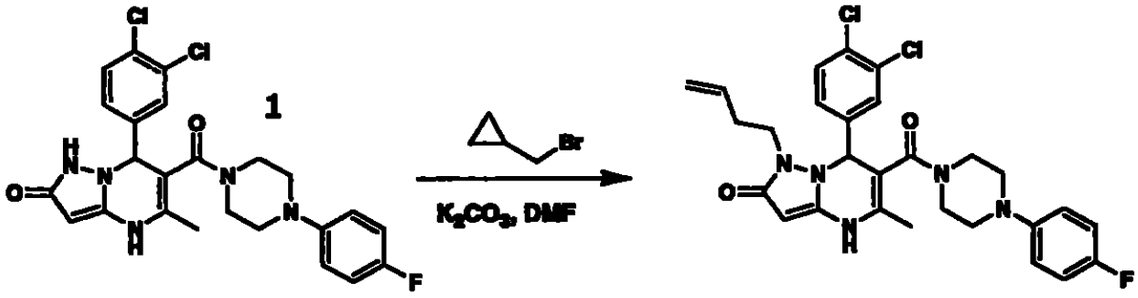
was purified by silica gel chromatography eluting with 5% methanol/ethyl acetate to afford 0 038 g (6%) of the title compound as a white solid. Reverse phase LC/MS YMC S5 TurboPack Pro 4 6 x 33 column, UV detection at 220 λ, 2 min gradient 0 – 100 % Solvent B/A (Solvent A. 10 % MeOH/H_2O with 0.1 % TFA, Solvent B 90 % MeOH/H_2O with 0 1 % TFA), 4 mL/min. Rt = 1.97 min, 92 % pure) MS (M+H. 573).

Example 438

1-[[1-(3-Butenyl)-7-(3,4-dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine



Method.

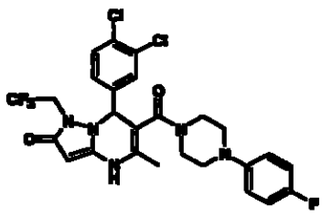
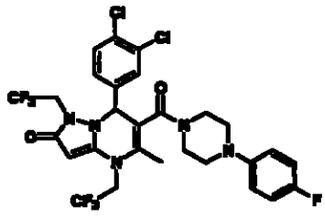


Compound 1. Compound 1 was prepared in a manner similar to that described in Example 18, Method 2.

Title Compound (Bromomethyl)cyclopropane (0.246 mL, 1.82 mmol) was added to a mixture of compound 1 (0.831 g, 1 66 mmol) and potassium carbonate (g, mmol)

in dimethylformamide (10 mL) The resulting mixture was allowed to stir at room temperature for 4h. The reaction was diluted with ethyl acetate, transferred to a separatory funnel, washed with water and brine, dried over anhydrous sodium sulfate and concentrated. The residue was purified by silica gel chromatography eluting with 5% methanol/ethyl acetate to afford 0.030 g (3%) of the title compound. Reverse Phase LC/MS YMC S5 ODS 4 6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 0-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0.1% TFA, Solvent B 90% MeOH/H_2O with 0 1% TFA), 4 mL/min. Rt = 2.99 min, (87% pure) (M+H. 556)

Examples 439 and 440

1-[[7-(3,4-Dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-2-oxo-1-(2,2,2-trifluoroethyl)pyrazolo-[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	1-[[7-(3,4-Dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-2-oxo-1,4-bis(2,2,2-trifluoroethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine
	
Example 439	Example 440

Method

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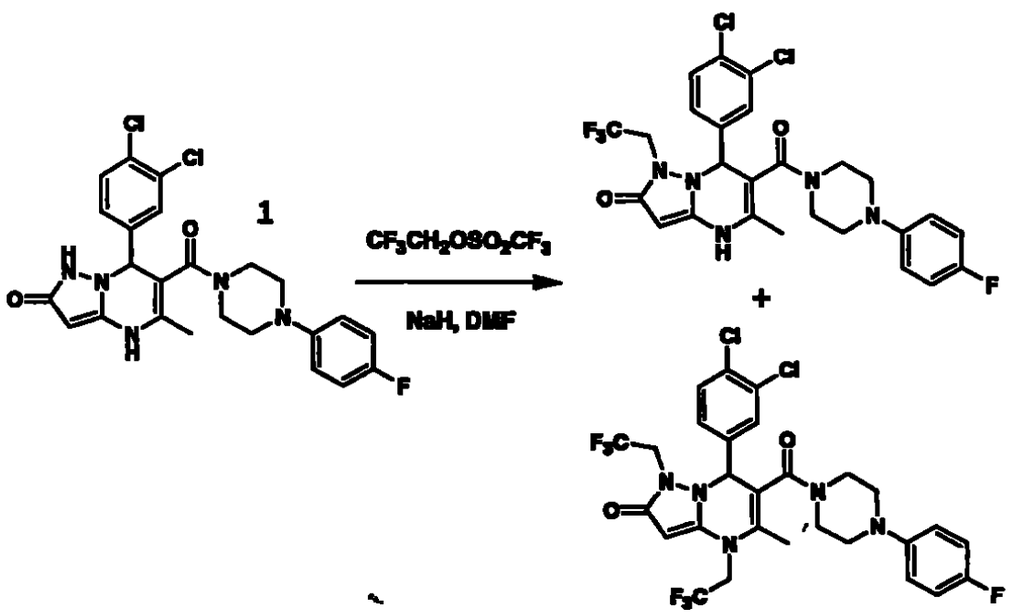


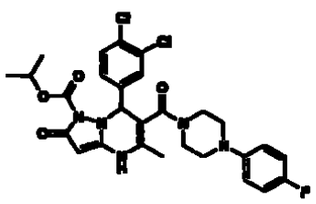
Compound 1 Compound 1 was prepared in a manner similar to that described in Example 18, Method 2

Title Compounds 2,2,2-trifluoroethyl trifluormethanesulfonate (0.49 g, 2.1 mmol) was added to a solution of compound 1 (0 967 g, 1 93 mmol) in dimethylformamide (10 mL) Sodium hydride (0.12 g, 2.89 mmol) was added. TLC (10% methanol/ethyl acetate) indicated consumption of compound 1 The resulting mixture was was diluted with ethyl acetate, transferred to a separatory funnel, washed with water and brine, dried over anhydrous sodium sulfate and concentrated. The residue was purified by silica gel chromatography eluting with 100% ethyl acetate followed by10% methanol/ethyl acetate to give a mixture of the title compounds. The title compounds were separated by preparative reverse phase HPLC YMC S5 ODS 20 X 100 mm column, 25 mL/min, 15 minute gradient eluting with 50%-100% solvent B/A (Solvent A. 10% MeOH/H20 with 0.1% TFA, Solvent B 90% MeOH/H_2O with 0 1% TFA) Compound of Example 439 Rt = 11.05 min, Compound of Example 440 Rt = 11.88 min. Compound of Example 439 Reverse phase LC/MS YMC S5 4.6 x 50 Ballistic column, UV detection at 220 λ, 4 min gradient 0 – 100 % Solvent B/A

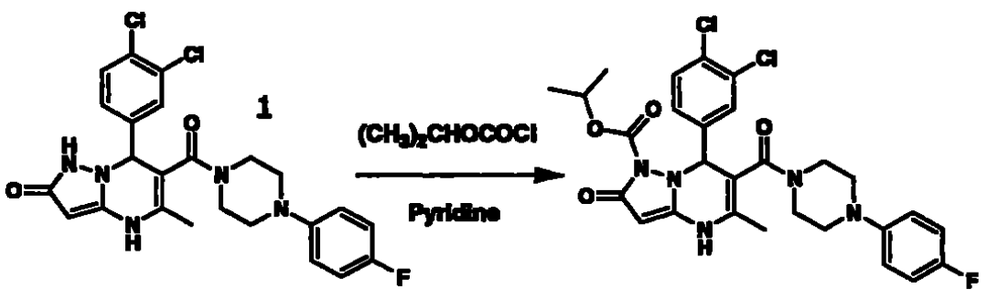
(Solvent A. 10 % MeOH/H_2O with 0 1 % TFA, Solvent B 90 % MeOH/H_2O with 0.1 % TFA), 4 mL/min. Rt = 2.87 min, 95 % pure) MS (M+H 584) Compound of Example 440 Reverse phase LC/MS YMC S5 4 6 x 50 Ballistic column, UV detection at 220 λ, 4 min gradient 0 – 100 % Solvent B/A (Solvent A. 10 % MeOH/H_2O with 0.1 % TFA, Solvent B 90 % MeOH/H_2O with 0 1 % TFA), 4 mL/min. Rt = 3.25 min, 85 % pure) MS (M+H. 666)

Example 441

7-(3,4-Dichlorophenyl)-6-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-4,7-dihydro-5-methyl-2-oxopyrazolo[1,5-a]pyrimidine-1(2H)-carboxylic acid 1-methylethyl ester



Method



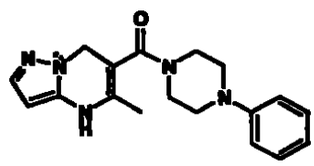
Compound 1 Compound 1 was prepared in a manner similar to that described in Example 18, Method 2.

Title Compound: Isopropyl chloroformate (1.0 mL, 1.0 mmol, 1M in toluene) was added to a 0 °C solution of compound 1 (0 46 g, 0 92 mmol) in pyridine (5 mL) The resulting mixture was stirred at 0 °C for 30 min , the cooling bath was removed. After

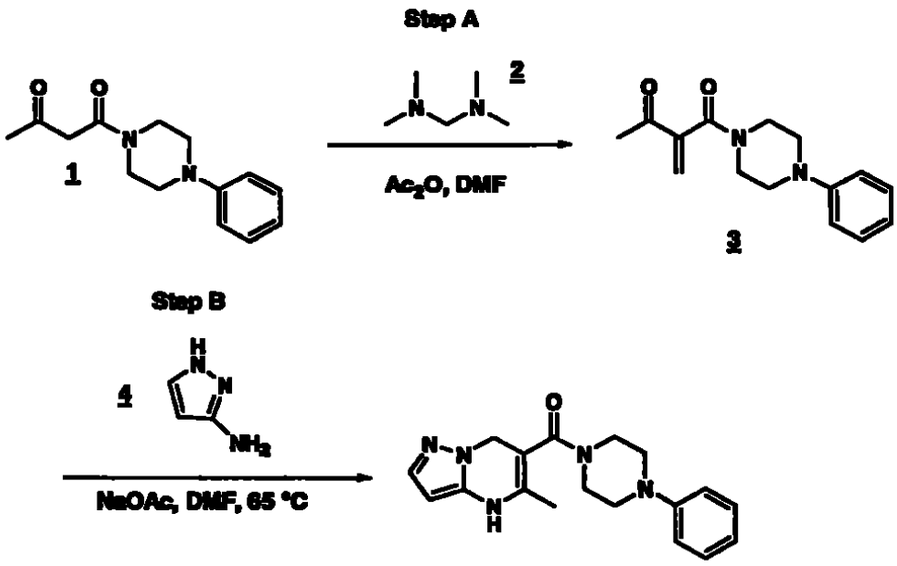
2h methanol was added to quench the reaction and the mixture was concentrated. The residue was purified by silica gel chromatography eluting with 5% methanol/ethyl acetate to afford 0.057 g (11%) of the title compound as a light pink solid. Reverse phase LC/MS YMC S5 ODS 4 6 x 50 column, UV detection at 220 λ, 4 min gradient 0 – 100 % Solvent B/A (Solvent A. 10 % MeOH/H_2O with 0.1 % TFA, Solvent B 90 % MeOH/H_2O with 0.1 % TFA), 4 mL/min. Rt = 3 67 min, 95 % pure) (M+H. 573)

Example 442

1-[(4,7-Dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl)carbonyl]-4-phenylpiperazine



Method



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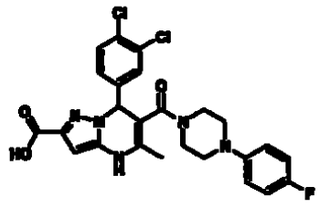
Compound 1 Compound 1 was prepared in a manner similar to that described in Example 18, Method 2.

Step A Compound 2 (0 6 mL, 4.4 mmol) and acetic anhydride (0.83 mL, 8.8 mmol) were added to a solution of compound 1 (0 72 g, 2.9 mmol) in dimethylformamide (10 mL) The mixture was allowed to stir overnight, poured into water, extracted with dichloromethane. The extracts were combined, dried over anhydrous sodium sulfate and concentrated. The residue was purified by silica gel chromatography eluting with 50% ethyl acetate/hexanes to 100% ethyl acetate/hexanes to give 0.290 g (38% yield) of compound 3 as a colorless syrup (M+H. 259)

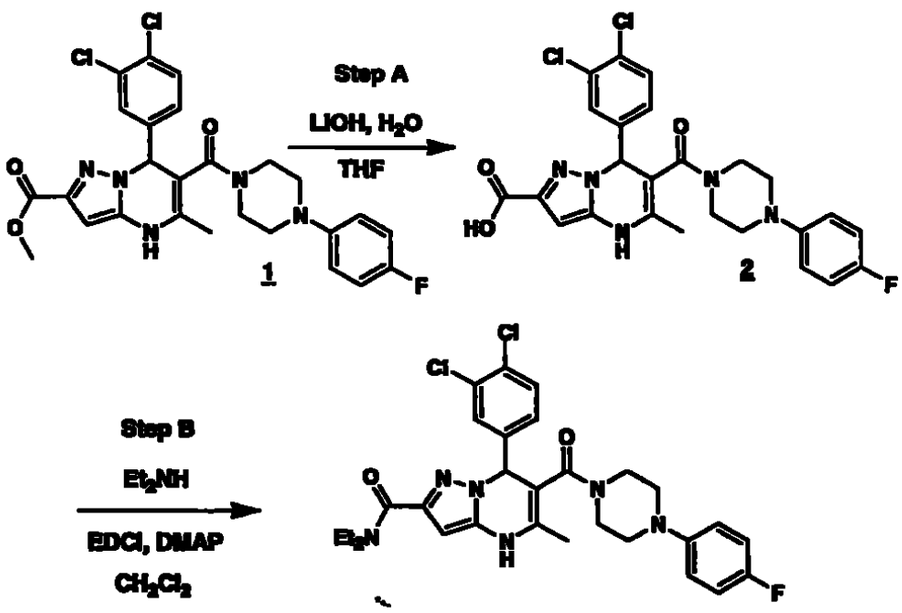
Step B Condensation of compound 3 and compound 4 as described in Example 18, Method 2 Step C provided the title compound. Reverse Phase LC/MS YMC S5 ODS 4 6 x 50 mm Ballistic column, UV detection at 220 λ, 4 min. gradient 0-100% Solvent B/A (Solvent A. 10% MeOH/H20 with 0.1% TFA, Solvent B 90% MeOH/H_2O with 0 1% TFA), 4 mL/min. Rt = 1 96 min, (87% pure). (M+H 323)

Example 443

7-(3,4-Dichlorophenyl)-6-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-2-carboxylic acid



Method.



Compound 1 Compound 1 was prepared in a manner similar to that described in Example 18, Method 2.

Step A. Lithium hydroxide (0.43 g, 1.8 mmol) was dissolved in water (3 mL) and added slowly to a room temperature solution of compound 1 in tetrahydofuran (9 mL). The resulting mixture was stirred at room temperature for 3h. TLC indicated that all of compound 1 had been consumed. The mixture was quenched by the addition of acidic Dowex resin. The resin was filtered off The filtrate was diluted with ethyl acetate, washed with water and brine, dried over anhydrous sodium sulfate and concentrated to give 0.41 g (86% yield) of compound 2 as a light yellow solid. Reverse phase LC/MS YMC S5 ODS 4.6 x 50 column, UV detection at 220 λ, 4 min gradient 0 – 100 % Solvent B/A (Solvent A. 10 % MeOH/H_2O with 0.1 % TFA, Solvent B 90 % MeOH/H_2O with 0 1 % TFA), 4 mL/min. Rt = 3.37 min, 96 % pure). MS (M+H. 530)

Step B EDCI (0.025 g, 0 13 mmol), DMAP (0 003g, 0.02 mmol) were added to a solution of compound 2 (0.0508 g, 0 1 mmol) and diethylamine (0.014 mL, 0 13 mmol) in dichloromethane (3 mL) The mixture was stirred overnight. TLC indicated

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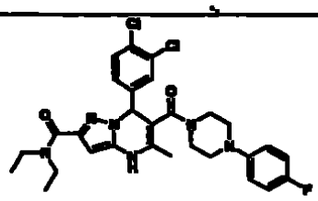
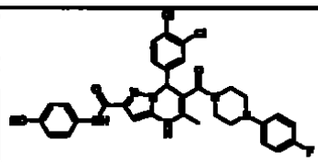
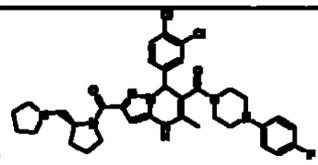
some starting material remained. The solvent was removed under reduced pressure. The resulting residue was purified by silica gel chromatography eluting with 5% methanol/ethyl acetate to give the title compound as a white solid Reverse phase LC/MS YMC S5 4.6 x 50 Ballistic column, UV detection at 220 λ, 4 min gradient 0 – 100 % Solvent B/A (Solvent A 10 % MeOH/H_2O with 0 1 % TFA, Solvent B 90 % MeOH/H_2O with 0 1 % TFA), 4 mL/min. Rt = 3 74 min, 91 % pure). MS (M+H. 585)

Examples 444-449

The compounds of Examples 445-450, shown in the table provided below, were prepared in a manner similar to that described in Example 443

Example	Structure	Name	(M+H)
444		7-(3,4-Dichlorophenyl)-N,N-diethyl-6-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-2-carboxamide	585
445		7-(3,4-Dichlorophenyl)-6-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-4,7-dihydro-N-(4-hydroxyphenyl)-5-methylpyrazolo[1,5-a]pyrimidine-2-carboxamide	621
446		1-[[7-(3,4-Dichloro-phenyl)-4,7dihydro-5-methyl-2-[[(2S)-2-(1-pyrrolidinylmethyl)-1-pyrrolidinyl]carbonyl]-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	666

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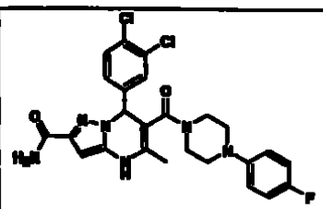
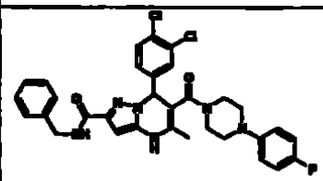
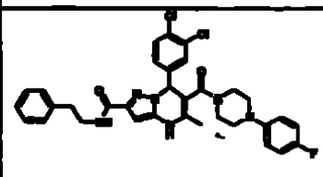
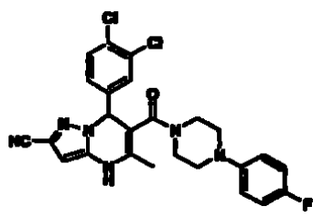
447		7-(3,4-Dichlorophenyl)-6-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-2-carboxamide	529
448		7-(3,4-Dichlorophenyl)-6-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-4,7-dihydro-5-methyl-N-(phenylmethyl)pyrazolo-[1,5-a]pyrimidine-2-carboxamide	619
449		7-(3,4-Dichlorophenyl)-6-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-4,7-dihydro-5-methyl-N-(2-phenylethyl)-pyrazolo[1,5-a]pyri-midine-2-carboxamide	633

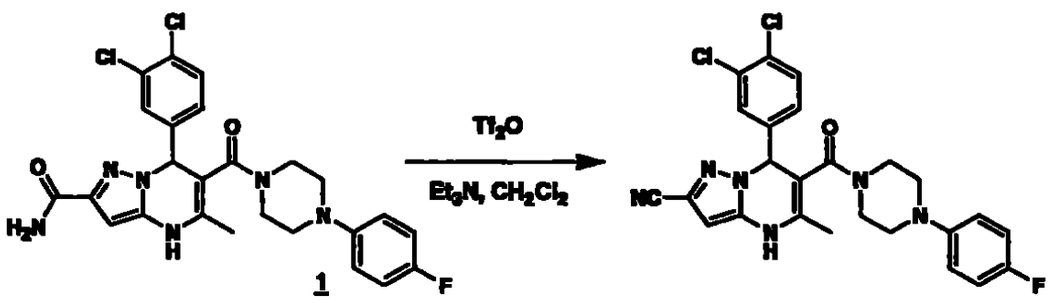
Example 450

1-[[2-Cyano-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine



Method

160

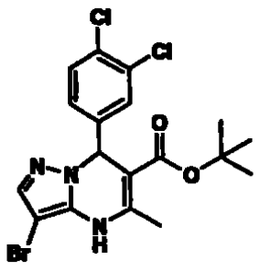


Compound 1 Compound 1 (the compound of Example 447) was prepared in a manner similar to that described in Example 443

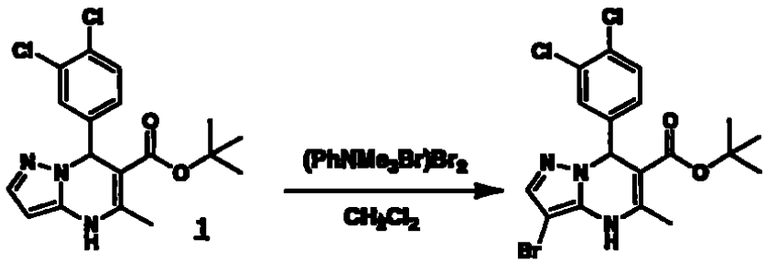
Title Compound. Triflic anhydride (0 036 mL, 0.21 mmol) was added to a 0 °C solution of compound 1 (0 103 g, 0 19 mmol) and triethylamine (0.054 mL, 0.39 mmol) in dichloromethane (5 mL) After 10 mm., TLC (5% methanol/ethyl acetate) indicated that compound 1 remained. Additional Triflic anhydride (0.036 mL, 0.21 mmol) and triethylamine (0 054 mL, 0.39 mmol) were added. After 10 mm., TLC (5% methanol/ethyl acetate) indicated that compound 1 remained. The mixture was warmed to room temperature and stirred for an additional 30 mm The reaction was poured into saturated sodium bicarbonate, extracted with dichloromethane. The extracts were combined, dried over anhydrous sodium sulfate and concentrated. The resulting residue was purified by silica gel chromatography eluting with 2% methanol/ethyl acetate to 0.018 g (19 % yield) of the title compound as a white solid. Reverse phase LC/MS YMC S5 4.6 x 33 column, UV detection at 220 λ, 2 min gradient 0 – 100 % Solvent B/A (Solvent A. 10 % MeOH/H_2O with 0.1 % TFA, Solvent B 90 % MeOH/H_2O with 0 1 % TFA), 4 mL/min. Rt = 3.60 mm, 81 % pure) MS (M+H. 511)

Example 451

3-Bromo-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1,1-dimethylethyl ester



Method.

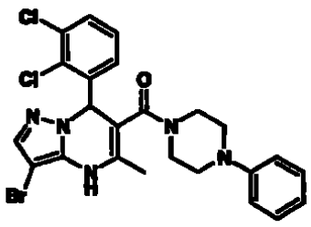


Compound 1. Compound 1 was prepared as described in Example 4

Title Compound. Phenyltrimethylammonium tribromide (0.057 g, 0 14 mmol) was added to a 0 °C solution of compound 1 (0 05 g, 0.13 mmol) in dichloromethane (2 mL). The mixture was allowed to warm to room temperature over 4h. The solvent was removed under reduced pressure. The resulting residue was purified by preparative TLC (Analtech, silica gel, 20 X 20 cm, 1000μ) Elution with 25% acetone/hexane provided 0.047 g (79% yield) of the title compound as a white solid. Reverse Phase HPLC: YMC S5 ODS 4 6 x 50mm Ballistic column, UV detection at 220 λ, 4mm. gradient 0-100% Solvent B/A (Solvent A. 10% MeOH/H_2O with 0.2% H_3PO_4, Solvent B 90% MeOH/H_2O with 0.2% H_3PO_4), 4mL/min. Rt = 4.67 min, (95% pure). Reverse Phase LC/MS YMC S5 ODS 4.6 x 50 mm Ballistic column, UV detection at 220 λ, 4mm. gradient 0-100% Solvent B/A (Solvent A. 10% MeOH/H_2O with 0 1% TFA, Solvent B. 90% MeOH/H_2O with 0.1% TFA), 4mL/min. Rt = 4.19 min. MS (EM, M+1 458) HMR ($CDCl_3$, 400MHz) 7.37(1H,d,J=2.0Hz), 7 36(1H,d,J=8.0Hz), 7.33(1H,s), 7 12(1H,dd,J=2.2 and 8.4Hz), 6.38(1H,s), 6 27(1H,s), 2.53(3H,s), 1 36(9H,s)

Example 452

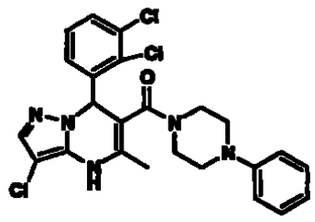
1-[[3-Bromo-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine



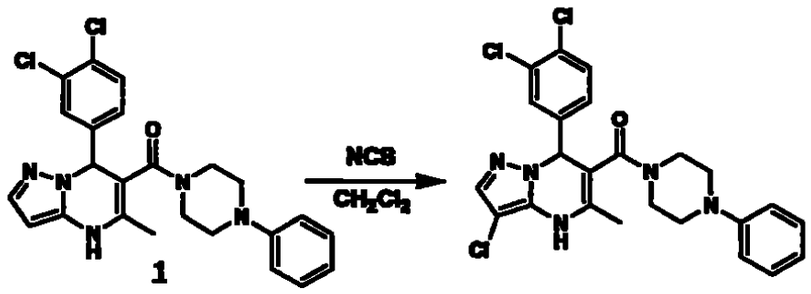
The compound of Example 452 was prepared in a manner similar to that described in Example 451 (M+H) 547

Example 453

1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine



Method.



1

Compound 1 Compound 1 was prepared in a manner similar to that described in Example 18, Method 2

Title Compound N-chlorosuccinimide (0 0102 g, 0 076 mmol) was added to a 0 °C solution of compound 1 (0.0343 g, 0 073 mmol) in dichloromethane (4 mL) The mixture was allowed to warm to room temperature over 2h. The solvent was removed under reduced pressure. The resulting residue was purified by preparative TLC (Analtech, silica gel, 20 X 20 cm, 1000μ). Elution with 50% acetone/hexane provided 0 0287g (77% yield) of the title compound as a yellow oil which solidified upon standing Reverse Phase HPLC. YMC S5 ODS 4.6 x 50mm Ballistic column, UV detection at 220 λ, 4 min. gradient 0-100% Solvent B/A (Solvent A. 10% MeOH/H_2O with 0.2% PPA, Solvent B 90% MeOH/H_2O with 0.2% PPA), 4mL/min. Rt = 4.21 min, (91% pure) Reverse Phase LC/MS YMC S5 ODS 4 6 x 50mm Ballistic column, UV detection at 220 λ, 4mm. gradient 0-100% Solvent B/A (Solvent A. 10% MeOH/H_2O with 0 1% TFA, Solvent B 90% MeOH/H_2O with 0 1% TFA), 4mL/min. Rt = 3 72min. MS (EM, M+1 501)

Examples 454-463

The compounds of Examples 454-463, shown in the table provided below, were prepared in a manner similar to that described in Example 453

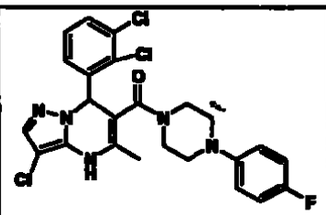
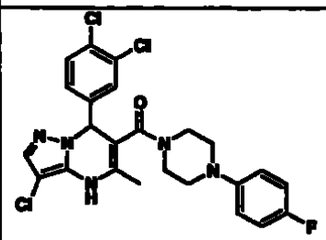
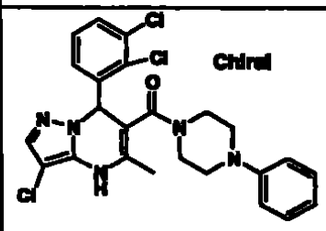
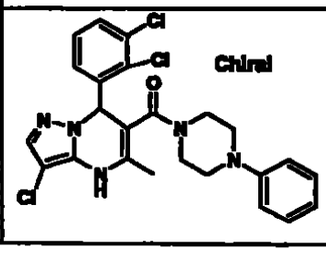
Example 456 was obtained from the single enantiomer B of Example 30, and Example 457 was obtained from the single enantiomer A of Example 29 Chiralpak AD column (4 6 X 250 mm) eluting with 30% isopropanol/hexanes containing 0.1 % triethylamine at 1 mL/min), UV detection at 254λ, Example 456 Rt = 5 9 min, >99% ee Example 457 Rt = 6.3 min, >99% ee.

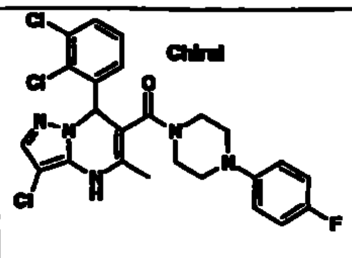
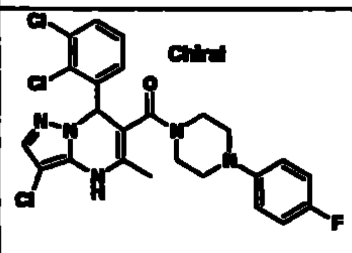
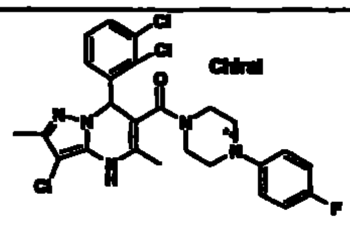
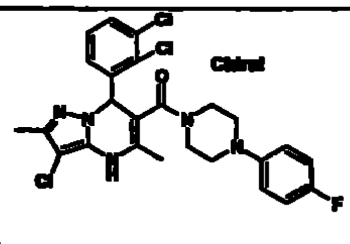
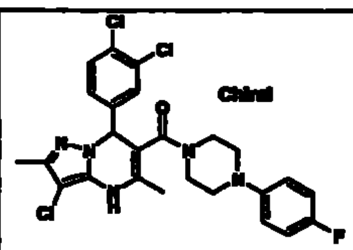
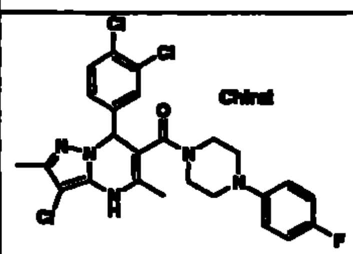
Example 458 was obtained from the single enantiomer A of Example 51, and Example 459 was obtained from the single enantiomer B of Example 52. Chiralcel OD column (4.6 X 250 mm) eluting with 30% isopropanol/hexanes containing 0 1 % triethylamine at 1 mL/min), UV detection at 254λ, Example 458 Rt = 7.8 min, >99% ee. Example 459 Rt = 8.4 min, >99% ee.

Example 460 was obtained from the single enantiomer A of Example 169, and Example 461 was obtained from the single enantiomer B of Example 168. Chiralpak

AD column (4 6 X 250 mm) eluting with 20% isopropanol/hexanes containing 0.1 % triethylamine at 1 mL/min), UV detection at 254λ, Example 461 Rt = 9 2 min, >99% ee. Example 460 Rt = 9.4 min, >99% ee.

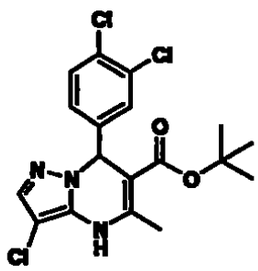
Example 462 was obtained from the single enantiomer A of Example 81, and Example 463 was obtained from the single enantiomer B of Example 82. Chiralpak AD column (4 6 X 250 mm) eluting with 20% isopropanol/hexanes containing 0 1 % triethylamine at 1 mL/min), UV detection at 254λ, Example 462 Rt= 8.25 min, >99% ee. Example 463 Rt = 8 28 min, >99% ee.

Example	Structure	Name	(M+H)
454		1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	520
455		1-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine	520
456		1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine, enantiomer B	502
457		1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenyl-piperazine, enantiomer A	502

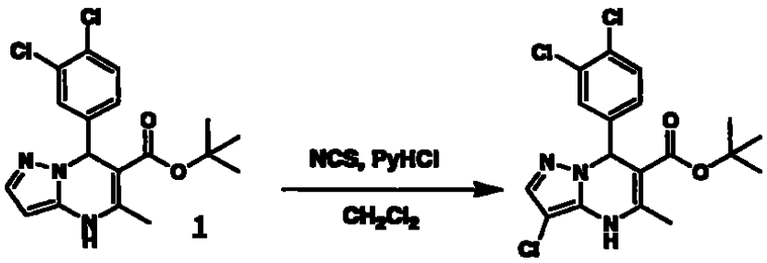
458		1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine, enantiomer A	520
459		1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine, enantiomer B	520
460		1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine, enantiomer A	534
461		1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine, enantiomer B	534
462		1-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine, enantiomer A	534
463		1-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine, enantiomer B	534

Example 464

3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1,1-dimethylethyl ester



Method.



1

Compound 1 Compound 1 was prepared as described in Example 4

Title Compound. Pyridine hydrochloride (0.020 g, 0.173 mmol) was added to a 0 °C solution of compound 1 (0.060 g, 0.158 mmol) in dichloromethane (4 mL). After 2 min, N-chlorosuccinimide (0.0231 g, 0.174 mmol) was added. The mixture was allowed to warm to room temperature and was stirred for 13h. The solvent was removed under reduced pressure. The resulting residue was purified by preparative TLC (Analtech, silica gel, 20 X 20 cm, 1000μ). Elution with 20% acetone/hexane provided 0.0092g (14% yield) of the title compound as a yellow oil. Reverse Phase HPLC: YMC S5 ODS 4.6 x 50mm Ballistic column, UV detection at 220 λ, 4mm. gradient 0-100% Solvent B/A (Solvent A: 10% MeOH/H_2O with 0.2% PPA, Solvent B: 90% MeOH/H_2O with 0.2% PPA), 4mL/min. Rt = 4.61 min, (94% pure). Reverse

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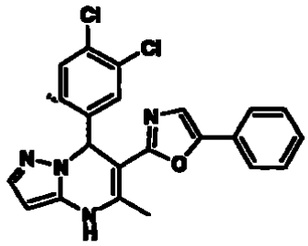
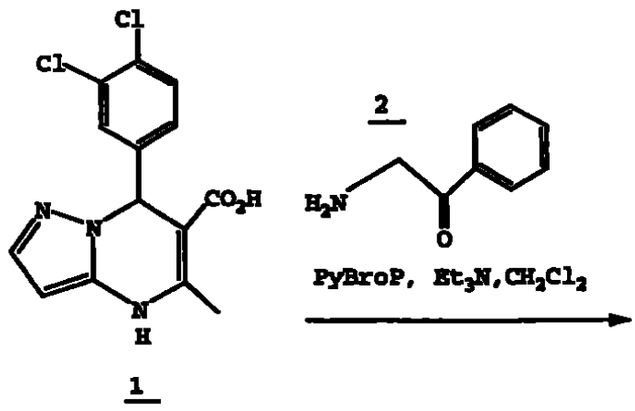
Phase LC/MS YMC S5 ODS 4 6 x 50mm Ballistic column, UV detection at 220 λ, 4min gradient 0-100% Solvent B/A (Solvent A. 10% MeOH/H_2O with 0.1% TFA, Solvent B 90% MeOH/H_2O with 0 1% TFA), 4mL/min. Rt = 4.71min MS (EM, M+1 414) HMR ($CDCl_3$, 400MHz) 7 37(1H,s), 7 36(1H,d,J=1 7Hz), 7 36(1H,d,J=8.4Hz), 7 12(1H,dd,J=2.0 and 8.4Hz), 6.45(1H,brs), 6.24(1H,s), 2.52(3H,s), 1 36(9H,s)

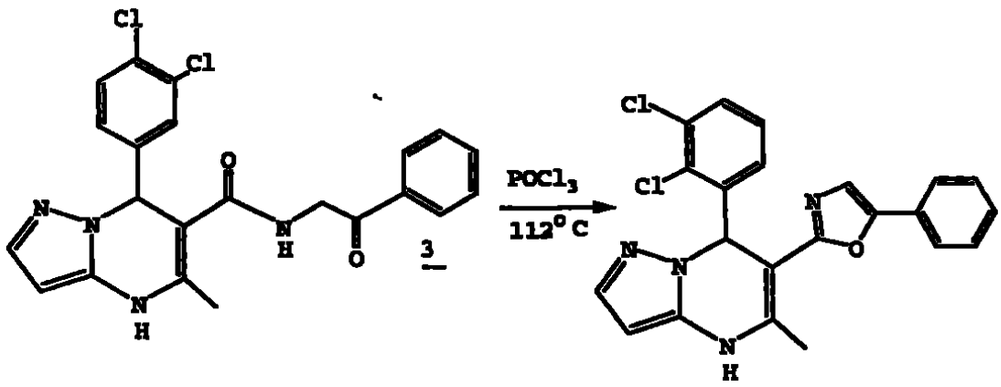
Example 465

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-6-(5-phenyl-2-oxazolyl)pyrazolo[1,5-a]pyrimidine



Method.





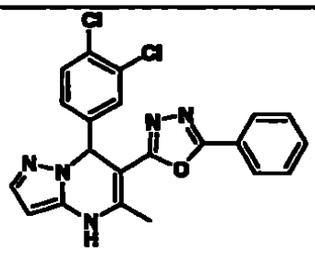
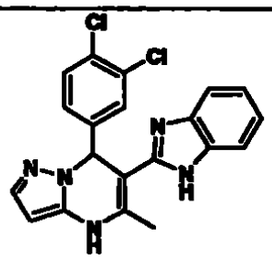
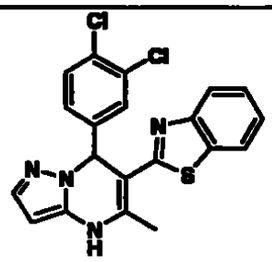
Compound 1 Compound 1 was synthesized as described in Example 16

Compound 3 Compound 1 (200 mg, 0 62 mmol) was suspended in 2 mL of dichloromethane. Triethylamine (300 µL, 2.2 mmol) and 2-aminoacetophenone 2 (116 mg, 0.68 mmol) were added followed by bromo-tris-pyrrolidino-phosphonium hexafluorophosphate (PyBrOP) (312 mg, 0.68 mmol) All the solid dissolved upon addition of PyBrOP and the reaction was stirred for 4 hrs The mixture was loaded onto silica gel and purified by flash chromatography on silica gel eluted with 40% acetone, hexane to yield 106 mg (39%) of a pink solid. ^{1}H NMR (400 MHz, CDCl3) 44180-148-16,^{1}H COSY (400 MHz, CD3OD), ^{13}C NMR (100 MHz, $CDCl_3$), HPLC >99% at 4 0 min (YMC S5 ODS 4.6 x 50 mm column,10-90% methanol, water with 0.2% phosphoric acid gradient over 4 min., 4 mL/ min , uv detection at 220 nm)

Title Compound The amide 3 (100 mg, 0.22 mmol) was dissolved in 2 mL phosphorus oxychloride and heated to 112° for 2 h. The mixture was then quenched onto ice and extracted with ethylacetate. The extracts were dried over magnesium sulfate, filtered and the solvent removed to provide 339 mg of a brown oil. The oil was purified by flash chromatography on silica gel eluted with 20-40% acetone, hexane to yield 50 mg (51%) of the title compound as a white powder mp 229-231°, ^{1}H NMR (400 MHz, CD3OD), MS (ESI) *m/z* 423 (MH^+); HPLC >99% at 4.7 min (YMC S5 ODS 4.6 x 50 mm column, 10-90% methanol, water with 0.2% phosphoric acid gradient over 4 min. then hold at 90% methanol, water; 4 mL/ min , uv detection at 220 nm).

Examples 466-469

The compounds of Examples 466-473, shown in the table provided below, were prepared in a manner similar to that described in Example 465

Example	Structure	Name	(M+H)
466		7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-6-(5-phenyl-1,3,4-oxadiazol-2-yl)pyrazolo[1,5-a]pyrimidine	424
467		6-(1H-Benzimidazol-2-yl)-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine	396
468		6-(2-Benzothiazolyl)-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidine	413

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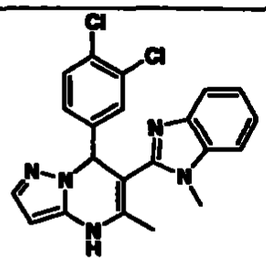
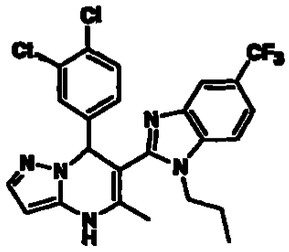
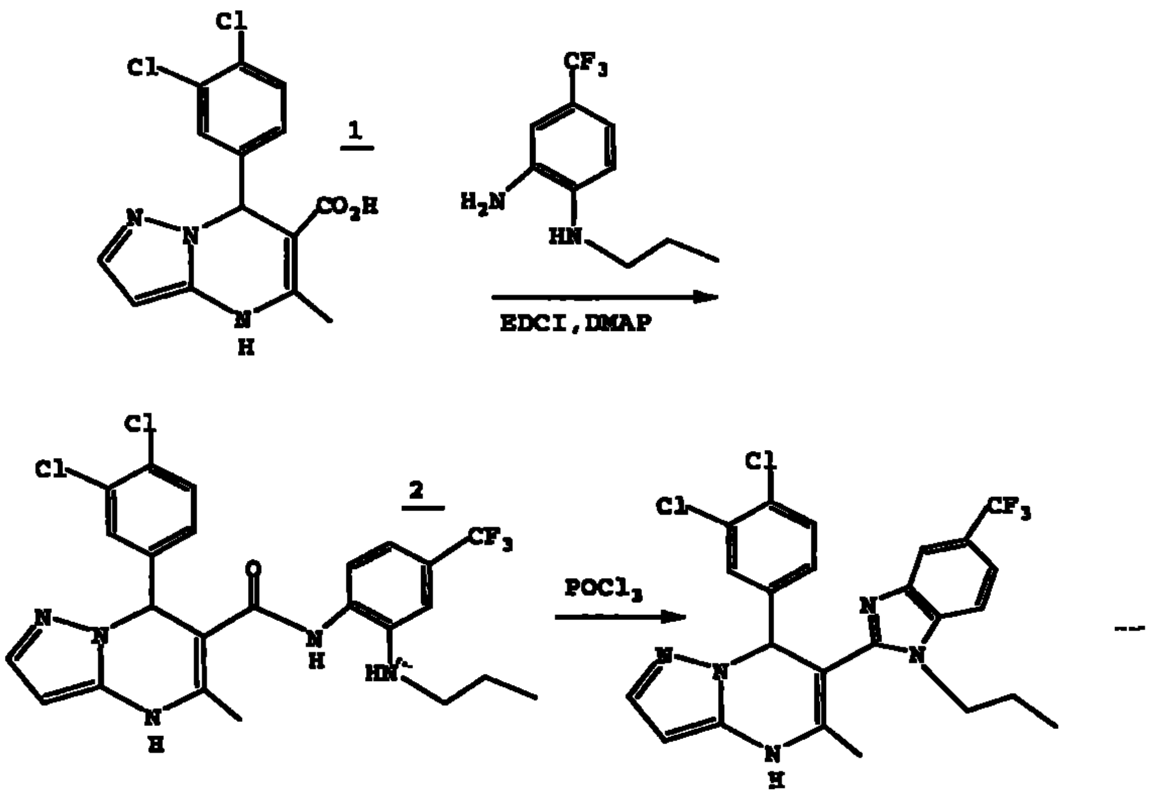
469		7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-6-(1-methyl-1H-benzimidazol-2-yl)pyrazolo[1,5-a]pyrimidine	410

Example 470

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-6-[5-(trifluoromethyl)-1-propyl-1H-benzimidazol-2-yl]pyrazolo[1,5-a]pyrimidine



Method



Compound 2. To a solution of acid **1**, prepared as described in Example 16, (0 15g, 0.463 mmol), 2-(n-propylamino)-5-trifluromethylaniline (0.141g, 0.648 mmol) and DMAP (5mg, cat.) EDCI (0.124g, 0.0648 mmol) was added and the solution was stirred at room temperature for 2 hours. The reaction was treated with saturated sodium bicarbonate, the organic solution was dried with magnesium sulfate and the solvent was evaporated. The crude product **2** was used without further purification.

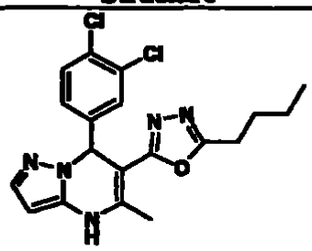
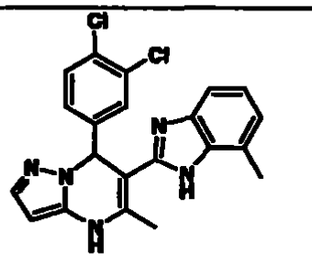
Title Compound Compound **2** was dissolved in phosphorus oxychloride (4 mL) and heated to 80 °C for 4 h. TLC indicated the reaction was not complete. Additional phosphorus oxychloride (2 mL) was added and the mixture was heated for 2h and then left to stand at room temperature overnight. The mixture was then quenched onto ice, made basic with ammonium hydroxide, and extracted with ethyl acetate. The extracts were dried over magnesium sulfate and concentrated. The crude product was purified by preparative reversed phase chromatography (YMC PACK ODSA S3 20x 100 mm column 50-100 methanol, water with 0 1% TFA gradient over 10 min., 20 mL/min., uv detection at 220 nm.) The appropriate fractions were evaporated, the residue was partitioned between saturated sodium bicarbonate

and ethyl acetate, the organic solution was dried and the solvent was removed under vacuum giving the product (27 mg, 11 5%) as a tan glass. $[M+H]^+$ *m/z* 506, HPLC 91 1% at 4.6 mm (YMC S5 ODS 4 6 x 50 mm column,10-90% methanol, water with 0.2% phosphoric acid gradient over 4 mm., 4 mL/ min , uv detection at 220 nm)

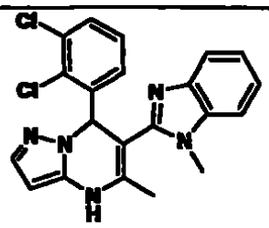
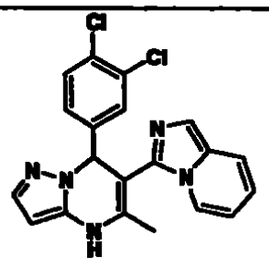
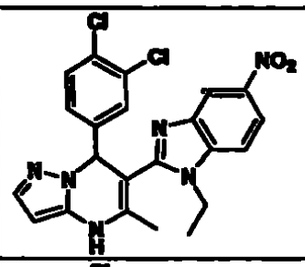
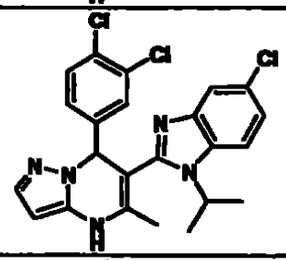
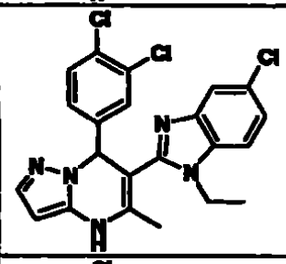
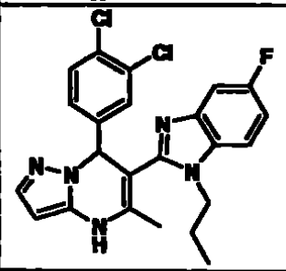
Examples 471-482

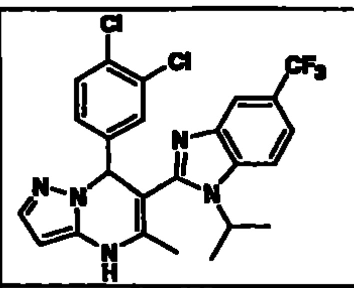
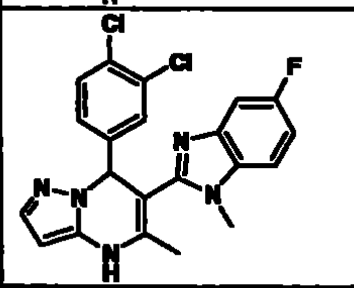
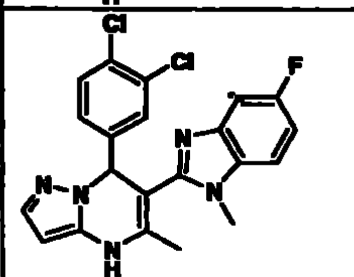
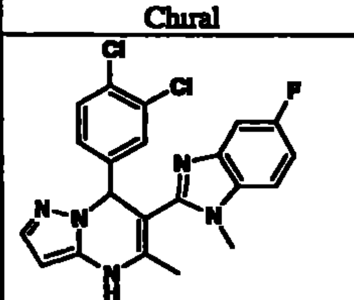
The compounds of Examples 471-482, shown in the table provided below, were prepared in a manner similar to that described in Example 470

HPLC resolution of Example 480, Chiralcel OD column (50 X 500 mm), eluting with 25% isopropanol/hexanes containing 0 1 % triethylamine at 50 mL/min), UV detection at 254 λ provided enantiomers A (Example 481) and B (Example 482). Analytical Chiralcel OD column (4 6 X 250 mm) eluting with 25% isopropanol/hexanes containing 0 1 % triethylamine at 1 mL/min), UV detection at 254 λ, enantiomer A Rt = 7.2 min, >99% ee. Enantiomer B Rt = 10.0 min, >99% ee.

Example	Structure	Name	(M+H)
471		6-(5-Butyl-1,3,4-oxadiazol-2-yl)-7-(3,4-dichlorophenyl)-4,7dihydro-5-methylpyrazolo[1,5-a]pyrimidine	404
472		1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methyl-6-(4-methyl-1H-benzimidazol-2-yl)pyra-zolo[1,5-a]pyrimidine	410

173

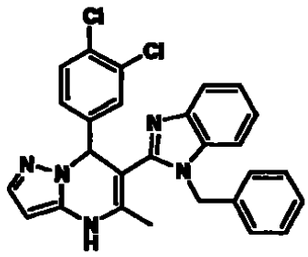
473		1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-6-(1-methyl-1H-benzimidazol-2-yl)pyrazolo[1,5-a]pyrimidine	410
474		7-(3,4-Dichlorophenyl)-4,7-dihydro-6-(imidazo[1,5-a]pyridin-3-yl)-5-methylpyrazolo[1,5-a]pyrimidine	510
475		7-(3,4-Dichlorophenyl)-6-(1-ethyl-5-nitro-1H-benzimidazol-2-yl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidine	469
476		6-[5-Chloro-1-(1-methylethyl)-1H-benzimidazol-2-yl]-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidine	472
477		6-(5-Chloro-1-ethyl-1H-benzimidazol-2-yl)-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidine	458
478		7-(3,4-Dichlorophenyl)-6-(5-fluoro-1-propyl-1H-benzimidazol-2-yl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine	456.35

479		7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-6-[1-(1-methylethyl)-5-(trifluoromethyl)-1H-benzimidazol-2-yl]pyrazolo[1,5-a]pyrimidine	506
480		7-(3,4-Dichlorophenyl)-6-(5-fluoro-1-methyl-1H-benzimidazol-2-yl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidine	428
481	 Chiral	7-(3,4-Dichlorophenyl)-6-(5-fluoro-1-methyl-1H-benzimidazol-2-yl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidine, enantiomer A	428
482	 Chiral	7-(3,4-Dichlorophenyl)-6-(5-fluoro-1-methyl-1H-benzimidazol-2-yl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidine, enantiomer B	428

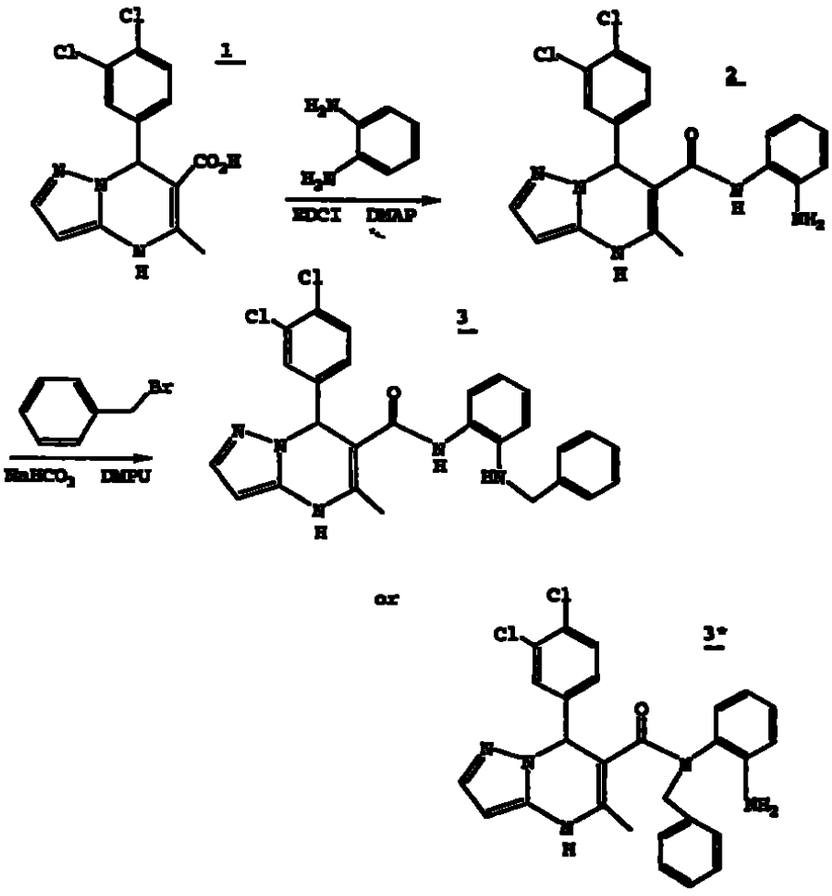
<u>Example 483</u>

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-6-[1-(phenylmethyl)-1H-benzimidazol-2-yl]pyrazolo[1,5-a]pyrimidine

175



Method.



Compound 1 Prepared as described in Example 16.

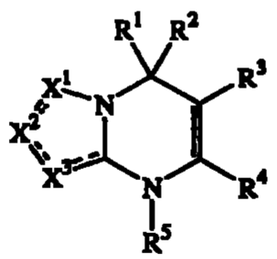
Compound 2. Prepared from compound 1 and phenylenediamine in a manner similar to that described in Example 470.

Compound 3. A suspension of 2 (50 mg 0.121mmol), $NaHCO_3$ (50 mg, 0.6 mmol) and benzyl bromide (20 mg, 0 121 mmol) in DMPU (0.5 mL) was stirred at room temp overnight. Another equivalent of benzyl bromide was added completing the reaction. The suspension was partitioned between water and ethyl acetate, the organic phase was dried ($MgSO_4$), and the solvent was evaporated. The residue was flash chromatographed through silica eluting with hexane-acetone 2.1 to provide either or both of compounds 3 and 3* (exact structure was not determined) (24.8 mg, 41%) as a white solid. Mp 135-140, $[M+H]^+$ *m/z* 504, HPLC 100% at 4 4 min (YMC S5 ODS 4.6 x 50 mm column,10-90% methanol, water with 0.2% phosphoric acid gradient over 4 min., 4 mL/ mn., uv detection at 220 nm)

Title Compound Compound(s) 3/3* was dissolved in phosphorus oxychloride (1.5 mL) and heated to 80 °C for 5 h. Heating was discontinued and the mixture was left to stand at room temperature overnight. The mixture was quenched onto ice, made basic with ammonium hydroxide, and extracted with ethyl acetate. The extracts were dried over magnesium sulfate and concentrated. The residue was purified by flash chromatography (silica gel, 50% acetone/hexanes) to give 6.6 mg of the title compound as a tan solid. Mp 225-230; $[M+H]^+$ *m/z* 486, HPLC 100% at 3.8 min (YMC S5 ODS 4 6 x 50 mm column,10-90% methanol, water with 0.2% phosphoric acid gradient over 4 min., 4 mL/ min., uv detection at 220 nm).

We claim.

1 A method of treating atrial arrhythmias comprising administering to a patient in need thereof an effective amount of at least one compound of formula I



(I)

enantiomers, diastereomers and pharmaceutically acceptable salts thereof, wherein

X^1, X^2 and X^3 are independently selected from N, NR^6, $(CR^7)_q$, $(CHR^7)_q$, or C=O, wherein the bonds connecting X^1, X^2 and X^3 to adjacent atoms may be single or double bonds forming a 5 to 7-membered saturated, partially unsaturated or aromatic ring;

R^1, R^2, R^3, R^4, R^5, R^6 and R^7 are independently selected from groups of the formula $-(CH_2)_n-(Z^1)_m-(CH_2)_p-Z^2$; or

R^1, R^2, R^3 R^4 and R^5 may, in one or more pairs of two, together with the atoms to which they are bonded, form a carbocyclic, substituted carbocyclic, heterocyclic or substituted heterocyclic group; or

R^6 and R^7 may, in one or more pairs of two, together with the atoms to which they are bonded, form a carbocyclic, substituted carbocyclic, heterocyclic or substituted heterocyclic group,

Z^1 is $-CZ^3Z^4-$, -O-, $-NZ^3-$; -S-, -SO-, $-SO_2-$, -C(O)-, $-C(O)Z^3-$, $-C(O)NZ^4$, -C(S)-, $-C(=NOZ^3)-$, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, carbocyclo; substituted carbocyclo; aryl, substituted aryl, heterocyclo; or substituted heterocyclo,

Z^2 is hydrogen, $-OZ^5$, $-OC(O)Z^5$, $-NZ^5-C(O)-Z^6$, $-NZ^5-CO_2-Z^6$, $-NZ^5(C=O)-NZ^6Z^7$, $-NZ^5Z^6$, $-NO_2$, halo, $-CN$, $-C(O)Z^5$, $-CO_2Z^5$, $-C(S)Z^5$, $-(C=NOZ^5)Z^6$, $-C(O)NZ^5Z^6$, $-C(S)NZ^5Z^6$, $-SZ^5$, $-SOZ^5$, $-SO_2Z^5$, $-SO_2NZ^5Z^6$, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, carbocyclo; substituted carbocyclo, aryl, substituted aryl, heterocyclo, or substituted heterocyclo,

Z^3, Z^4, Z^5, Z^6 and Z^7 are independently hydrogen, halo, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, carbocyclo; substituted carbocyclo; aryl, substituted aryl, heterocyclo; or substituted heterocyclo, or

Z^3, Z^4, Z^5, Z^6 and Z^7 may, in one or more pairs of two, together with the atoms to which they are bonded, form a carbocyclic, substituted carbocyclic, heterocyclic or substituted heterocyclic group;

n and p are independently selected from integers from 0 to 10 wherein, when m is 0, p is also 0;

m is an integer selected from 0 or 1, and

q is an integer selected from 1 to 3

2. A method of treating atrial fibrillation comprising administering to a patient in need thereof an effective amount of at least one compound of claim 1

3 A method of treating atrial flutter comprising administering to a patient in need thereof an effective amount of at least one compound of claim 1

4. A method of selectively treating supraventricular arrhythmias comprising administering to a patient in need thereof an effective amount of at least one compound of claim 1

5 A method of treating I_{Kur}-associated conditions comprising administering to a patient in need thereof an effective amount of at least one compound of claim 1

6. A method of treating reflux esauphagitis comprising administering to a patient in need thereof an effective amount of at least one compound of claim 1

7 A method of treating functional dispepsia comprising administering to a patient in need thereof an effective amount of at least one compound of claim 1

8. A method of treating constipation comprising administering to a patient in need thereof an effective amount of at least one compound of claim 1

9 A method of treating asthma comprising administering to a patient in need thereof an effective amount of at least one compound of claim 1

10 A method of treating diabetes comprising administering to a patient in need thereof an effective amount of at least one compound of claim 1

11 A method stimulating the secretion of growth hormone comprising administering to a patient in need thereof an effective amount of at least one compound of claim 1

12. A method of treating cell proliferative disorders comprising administering to a patient in need thereof an effective amount of at least one compound of claim 1

13 A method of treating autoimmune diseases comprising administering to a patient in need thereof an effective amount of at least one compound of claim 1

14. The method of claim 1 where in formula I

R^1 is hydrogen

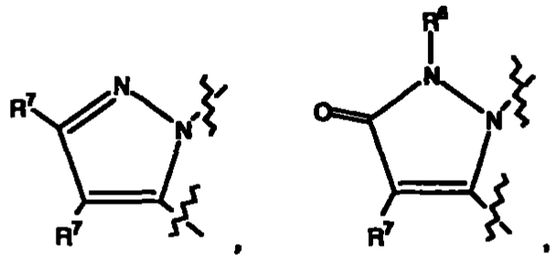
R^2 is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo, carbocyclo or substituted carbocyclo

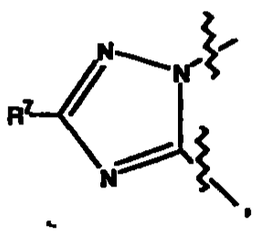
R^3 is $-(CH_2)_n-Z^2$, $-(CH_2)_n-C(O)Z^3-(CH_2)_r-Z^2$, or $-(CH_2)_n-C(O)NZ^4-(CH_2)_p-Z^2$;

R^4 is alkyl or substituted alkyl,

R^5 is hydrogen, or $-(CH_2)_n-Z^2$; and

X^1, X^2 and X^3, together with the atoms to which they are bonded, form a ring selected from.





or

wherein the ring substituents are the same or different.

The method of claim 14 where in formula I

R^3 is $-(CH_2)_n-Z^2$, $-(CH_2)_n-C(O)Z^3-(CH_2)_p-Z^2$, or $-(CH_2)_n-C(O)NZ^4-(CH_2)_p-Z^2$ wherein

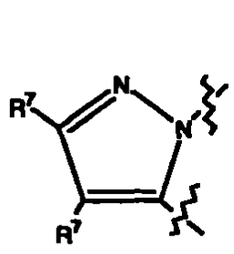
Z^2 is selected from $-C(O)NZ^5Z^6$, $-CO_2Z^5$, $-SO_2Z^5$, $-NZ^5Z^6$, $-NZ^5CO_2Z^6$, $-NZ^5C(O)Z^6$, $-OZ^5$, aryl, substituted aryl, heterocyclo, substituted heterocyclo, alkyl or substituted alkyl,

Z^3 is heterocyclo or substituted heterocyclo; and

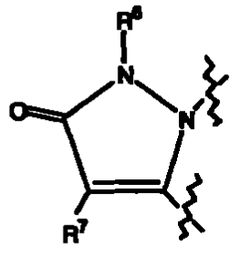
n and p are independently selected from integers 0 to 3,

R^5 is hydrogen, or $-(CH_2)_n-Z^2$ wherein Z^2 is selected from $-C(O)NZ^5Z^6$, CO_2Z^5, $-NZ^5Z^6$, aryl, substituted aryl, alkyl, or substituted alkyl, and

X^1, X^2 and X^3, together with the atoms to which they are bonded, form a ring selected from.



, or



16 The method of claim 15 where in formula I

R^3 is heterocyclo or substituted heterocyclo, $-C(O)NZ^5Z^6$, $-C(O)Z^3$-$CONZ^5Z^6$, $-C(O)Z^3$-Z^2, or $-C(O)Z^3$-CO_2Z^5, wherein Z^3 is heterocyclo or substituted heterocyclo, and Z^2 is aryl or substituted aryl,

17 The method of claim 1 wherein the compound of formula I is selected from

7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid methyl ester;

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid methyl ester

7-(4-Chlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid methyl ester;

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1,1-dimethylethyl ester;

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-2-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1,1-dimethylethyl ester;

7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-2-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1,1-dimethylethyl ester;

7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1,1-dimethylethyl ester;

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1,1-dimethylethylester, enantiomer A,

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1,1-dimethylethylester, enantiomer B,

7-(3,4-Dichlorophenyl)-4,7-dihydro-2,5-dimethylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1,1-dimethylethyl ester;

3-Chloro-7-(3-chlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1,1-dimethylethyl ester;

7-(2,3-Dichlorophenyl)-4,7-dihydro-4,5-dimethylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1,1-dimethylethyl ester;

7-(3,4-Dichlorophenyl)-4,7-dihydro-4,5-dimethylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1,1-dimethylethyl ester;

4,7-Dihydro-5-methyl-7-(1-methylethyl)pyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1,1-dimethylethyl ester;

7-Cyclopropyl-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1,1-dimethylethyl ester;

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid,

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-2-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidine-6-carboxylic acid,

1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine,

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-propylpyrazolo[1,5-a]pyrimidine-6-carboxamide;

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-phenyl-pyrazolo[1,5-a]pyrimidine-6-carboxamide;

4-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]morpholine;

7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-N-propylpyrazolo[1,5-a]pyrimidine-6-carboxamide;

7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-N-phenylpyrazolo[1,5-a]pyrimidine-6-carboxamide,

7-(2,3-Dichlorophenyl)-4 7-dihydro-5-methyl-N-(2-phenylethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide;

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7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-(2-phenylethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide;

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-3-pyridinylpyrazolo[1,5-a]pyrimidine-6-carboxamide,

1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenyl-piperazine, enantiomer A,

1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenyl-piperazine, enantiomer B,

1-[[7-(4-Chlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-(phenyl-methyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide,

4-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]morpholine,

1-[[7-(3 4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-methyl-piperazine,

7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-N-(phenylmethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide;

7-(4-Chlorophenyl)-4,7-dihydro-5-methyl-N-(phenylmethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide,

4-[[7-(4-Chlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]morpholine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperidine,

1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperidine;

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-(3-phenyl-propyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide;

1-[[5-(3,4-Dichlorophenyl)-5,8-dihydro-7-methyl-imidazo[1,2-a]pyrimidin-6-yl]carbonyl]-4-phenyl-piperazine;

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(phenyl-methyl)piperidine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(phenyl-methyl)piperazine,

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N,N-dipropylpyrazolo[1,5-a]pyrimidine-6-carboxamide,

1-[[7-(3-Chlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(3,4-Difluorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidm-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl[1,2,4]triazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine,

1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine;

1-(4-Fluorophenyl)-4-[(4,7-dihydro-5-methyl-7-phenylpyrazolo[1,5-a]pyrimidin-6-yl)carbonyl]piperazine;

1-(4-Fluorophenyl)-4-[(4,7-dihydro-5-methyl-7-phenylpyrazolo[1,5-a]pyrimidin-6-yl)carbonyl]piperazine,

1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine, enantiomer A

1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine, enantiomer A,

1-[[5-(2,3-Dichlorophenyl)-5,8-dihydro-7-methyl-imidazo[1,2-a]pyrimidin-6-yl]carbonyl]-4-phenyl-piperazine,

1-(4-Fluorophenyl)-4-[[7-(3-fluorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-piperazine,

1-[[7-(3,5-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine;

1-[(7-Cyclohexyl-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl)carbonyl]-4-phenylpiperazine,

1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)carbonyl]-4-phenyl-piperazine,

1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenyl-piperazine,

7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-6-[(4-phenyl-1-piperazinyl)-carbonyl]pyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester;

1-[[4-(2,3-Dichlorophenyl)-4,6,7,8-tetrahydro-2-methyl-1H-pyrimido[1,2-a]pyrimidin-3-yl]carbonyl]-4-phenyl-piperazine,

4-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1-piperazinecarboxylic acid 1,1-dimethylethyl ester;

4-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1-pipera-zinecarboxylic acid 1,1-dimethylethyl ester;

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-2-phenylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine,

7-(3,4-Dichlorophenyl)-4,7-dihydro-2,5-dimethyl-N-(3-phenyl-propyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide,

1-[[7-(2,3-Dichlorophenyl)-2-(1,1-dimethylethyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenyl-piperidine,

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-6-[[(3-phenyl-propyl)amino]carbonyl]pyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester;

7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-6-[(4-phenyl-1-piperazinyl)-carbonyl]pyrazolo[1,5-a]pyrimidine-2-carboxylic acid ethyl ester;

1-[[3-Cyano-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-2-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-2-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(2,3-Dichlorophenyl)-4,7dihydro-5-methyl-2-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine, enantiomer B,

1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine, enantiomer B,

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-(3-phenylpropyl)-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide,

7-(3,4-Dichlorophenyl)-6-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-2-carboxylic acid methyl ester;

(2S)-1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxymethyl)pyrrolidine,

1-[[7-(2,3-Dichlorophenyl)-2-fluoro-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

(2S)-1-[[2-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxymethyl)pyrrolidine;

(2S)-1-[[2-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxymethyl)pyrrolidine,

(2S)-1-[[7-(2,3-Dichloro-phenyl)-2-fluoro-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxy-methyl)pyrrolidine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-2,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine;

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-2,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine, enantiomer A,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine, enantiomer B,

7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-N,N-dipropylpyrazolo[1,5-a]pyrimidine-6-carboxamide;

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(2,3-Difluorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

4-[6-[[4-(4-Fluorophenyl)-1-piperazinyl]carbonyl]-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-7-yl]benzoic acid methyl ester;

1-(4-Fluorophenyl)-4-[[7-(2-fluorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-piperazine,

1-[[7-(2-Chlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(2,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine,

1-[[4,7-Dihydro-7-(2-methoxyphenyl)-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(2,3-Dimethoxyphenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine,

1-[[7-(2,4-Dimethoxyphenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine,

1-[[7-(2,5-Dimethoxyphenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine;

1-[[4,7-Dihydro-5-methyl-7-[2-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-5-methyl-7-(2-methylphenyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-5-methyl-7-(3-phenoxyphenyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(3,4-Dimethoxyphenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine,

1-[[7-(3,5-Dimethoxyphenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine;

1-[[4,7-Dihydro-5-methyl-7-[3-(phenylmethoxy)phenyl]pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine,

1-[[4,7-Dihydro-7-(3-hydroxyphenyl)-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine;

1-[[4,7-Dihydro-5-methyl-7-[3-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine,

1-[[4,7-Dihydro-5-methyl-7-(3-methylphenyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(4-Cyanophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-(4-Fluorophenyl)-4-[[7-(4-fluorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-piperazine;

N-[4-[6-[[4-(4-Fluorophenyl)-1-piperazinyl]carbonyl]-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-7-yl]phenyl]acetamide,

1-[[7-[4-(Dimethyl-amino)phenyl]-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-7-(4-methoxyphenyl)-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-5-methyl-7-[4-(phenylmethoxy)phenyl]pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine,

1-[[7-(4-Butoxyphenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine;

1-[[4,7-Dihydro-5-methyl-7-(2-thienyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-5-methyl-7-(3-thienyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine;

1-[[4,7-Dihydro-5-methyl-7-[4-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine,

1-[[4,7-Dihydro-5-methyl-7-(4-methylphenyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-5-methyl-7-(2-nitrophenyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine;

1-[[4,7-Dihydro-5-methyl-7-(4-nitrophenyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(2,6-Difluorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(2,4-Difluorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(2,5-Difluorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine;

1-[[7-(3,5-Difluorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-5-methyl-7-[2-(phenylmethoxy)phenyl]pyra-zolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine,

1-[[7-(3,4-Dimethylphenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine,

1-[[4,7-Dihydro-5-methyl-7-[4-(trifluoromethoxy)phenyl]py-razolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine,

1-[[4,7-Dihydro-5-methyl-7-[3-(trifluoromethoxy)phenyl]py-razolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine,

1-[[7-(3-Cyanophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-7-(3-methoxyphenyl)-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine,

1-[[7-(4-Chlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-5-methyl-7-(4-phenoxyphenyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-5-methyl-7-(3-nitrophenyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-5-methyl-7-(5-methyl-2-furanyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-7-(1H-imidazol-2-yl)-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-5-methyl-7-(1H-pyrrol-2-yl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-5-methyl-7-(2-pyridinyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(3-Chloro-4-methoxy-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-7-(4-methoxy-1,3-benzodioxol-6-yl)-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-7-[5-(hydroxymethyl)-2-furanyl]-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-7-(1H-indol-3-yl)-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-5-methyl-7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine;

1-[[4,7-Dihydro-5-methyl-7-(3-quinolinyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-5-methyl-7-(4-quinolinyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine;

1-[[7-(2,3-Dihydro-1,4-benzodioxin-6-yl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-5-methyl-7-(2,3,5-trichloro-phenyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(2,5-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-(4-Fluorophenyl)-4-[[7-(3-furanyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-piperazine,

1-[[7-(2-Benzofuranyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-5-methyl-7-(3-methylbenzo[b]thiophen-2-yl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-5-methyl-7-(2-quinolinyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-5-methyl-7-(2-thiazolyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-(4-Fluorophenyl)-4-[[7-(2-furanyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-piperazine,

1-[[4,7-Dihydro-7-[3-methoxy-4-(phenylmethoxy)phenyl]-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-7-[4-methoxy-3-(phenylmethoxy)phenyl]-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4,7-Dihydro-5-methyl-7-(2-naphthalenyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-[3,4-Bis(phenyl-methoxy)phenyl]-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

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1-[[7-(1,3-Benzodioxol-5-yl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine;

1-[[7-[3,5-Bis(trifluoro-methyl)phenyl]-4,7-dihydro-5-methylpyrazolo[1,5-a]pyri-midin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine;

1-[[4,7-Dihydro-5-methyl-7-[5-[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]-2-thienyl]pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(5-Ethyl-2-furanyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine;

1-[[7-(2,3-Dihydro-5-benzofuranyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(3-Bromophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine;

1-[[4,7-Dihydro-5-methyl-7-[4-(1-pyrrolidinyl)-phenyl]pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine;

1-[[4,7-Dihydro-5-methyl-7-(3-methyl-2-thienyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine;

1-[[4,7-Dihydro-5-methyl-7-(5-methyl-2-thienyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(1,3-Benzodioxol-4-yl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(5-Chloro-2-thienyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(3,5-Dimethylphenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine,

1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-2,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine, enantiomer A,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine, enantiomer B,

1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine, enantiomer B,

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1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine, enantiomer A,

8-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,4-dioxa-8-azaspiro[4 5]decane,

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-(2-methoxy-phenyl)piperazine,

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]-pyrimidin-6-yl]carbonyl]-4-[3-(trifluoromethyl)-phenyl]piperazine,

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-nitrophenyl)piperazine;

1-(4-Acetylphenyl)-4-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidm-6-yl]carbonyl]piperazine,

1-(2-Chlorophenyl)-4-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperazine,

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]-carbonyl]-4-(4-methoxy-phenyl)piperazine,

1-(3,4-Dichlorophenyl)-4-[[7-(3,4-dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]-carbonyl]piperazine,

1-(3,5-Dichlorophenyl)-4-[[7-(3,4-dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]-carbonyl]piperazine,

1-(4-Chlorophenyl)-4-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperazine

1-(3-Chlorophenyl)-4-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperazine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-(3-methoxyphenyl)piperazine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-(4-methylphenyl)piperazine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5a]-pyrimidm-6-yl]car-bonyl]-4-[4-(trifluoromethyl)-phenyl]piperazine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(2-fluorophenyl)piperazine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-(3,4-dimethylphenyl)piperazine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(2-pyrimidinyl)piperazine,

7-(3,4-Dichlorophenyl)-N-[2-[(4-fluorophenyl)amino]ethyl]-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidine-6-carboxamide,

4-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1-piperazinecarboxylic acid phenylmethyl ester;

7-(3,4-Dichlorophenyl)-N-ethyl-N-[(2-fluorophenyl)methyl]-4,7-dihydro-5-methylpyrazolo[1,5-a]pyri-midine-6-carboxamide;

N-[(3-Chloro-4-methoxyphenyl)methyl]-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyri-midine-6-carboxamide,

1-(1,3-Benzodioxol-5-ylmethyl)-4-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperazine;

4-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1-piperazinecarboxylic acid ethyl ester;

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(2-pyridinyl)piperazine,

(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxymethyl)pyrrolidine;

1-[Bis(4-fluorophenyl)-methyl]-4-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperazine,

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-(2-furanyl-carbonyl)piperazine,

1-Cyclohexyl-4-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperazine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(2-methoxyethyl)piperazine,

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(9H-fluoren-9-yl)piperazine,

(2R)-1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-2-(methoxy-methyl)pyrrolidine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-(2,3-dimethylphenyl)piperazine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-2-piperidinecarboxylic acid ethyl ester;

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-N,N-diethyl-3-piperidinecarboxamide;

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-3-piperidine-carboxylic acid ethyl ester;

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-3-methyl-piperidine,

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-3,5-dimethyl-piperidine,

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-hydroxy-piperidine,

4-(4-Chlorophenyl)-1-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyri-midin-6-yl]carbonyl]-4-hydroxypiperidine,

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-piperidine-carboxylic acid ethyl ester;

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-methylpiperidine,

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,4-tetrahydroquinoline,

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]-pyrimidin-6-yl]carbonyl]-decahydroquinoline,

2-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidm-6-yl]carbonyl]-1,2,3,4-tetrahydroisoquinoline,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-propylpiperidine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidm-6-yl]carbonyl]-4-(hydroxydiphenylmethyl)piperidine;

7-(3,4-Dichlorophenyl)-N-[(2-fluorophenyl)methyl]-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidine-6-carboxamide,

2-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole;

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-[2-(phenylamino)-ethyl]pyrazolo[1,5-a]pyrimidine-6-carboxamide;

(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-[(phenylamino)methyl]pyrrolidine,

N-Cyclohexyl-7-(3,4-dichlorophenyl)-4,7-dihydro-N,5-dimethylpyrazolo[1,5-a]pyrimidine-6-carboxamide,

3-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]thiazole,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]pyrrolidine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-3,4-dihydro-1H-indole,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]azetidine;

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]hexahydro-1H-azepine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]octahydroazocine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,6-tetrahydropyridine,

7-(3,4-Dichlorophenyl)-4,7dihydro-N,5-dimethyl-N-[2-(2-pyridinyl)-ethyl]pyrazolo[1,5-a]pyrimidine-6-carboxamide,

N-[[7-(3,4-Dichlorophenyl)-4,7dihydro-5-methylpyrazolo[1,5-a]pyrimidm-6-yl]carbonyl]-N-(phenylmethyl)glycine ethyl ester;

trans-7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-(2-phenylcyclopropyl)pyrazolo[1,5-a]pyrimidine-6-carboxamde,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-methylpyrrolidine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-methylaziridine;

(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-[[(2,6-dimethylphenyl)amino]methyl]pyrrolidine,

7-(3,4-Dichlorophenyl)-N-ethyl-4,7-dihydro-5-methyl-N-(4-pyridinylmethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide;

7-(3,4-Dichlorophenyl)-4,7-dihydro-N,5-dimethyl-N-[(1R)-1-phenylethyl]pyrazolo[1,5-a]pyrimidine-6-carboxamide,

7-(3,4-Dichlorophenyl)-4,7-dihydro-N,5-dimethyl-N-[(1S)-1-phenylethyl]pyrazolo[1,5-a]pyrimidine-6-carboxamide,

6-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,3,3-trimethyl-6-azabicyclo[3 2 1]octane,

7-(3,4-Dichlorophenyl)-N-(hexahydro-1H-azepin-1-yl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxamide,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]azaridine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]octahydro-1H-azonine,

(2R-trans)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2,5-bis(methoxymethyl)-pyrrolidine,

(2S-trans)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2,5-bis-(methoxymethyl)pyrrolidine;

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-L-prolinamide,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-D-prolinamide,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2,3-dihydro-2-methyl-1H-indole,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2,3-dihydro-5-nitro-1H-indole,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2,3-dihydro-6-nitro-1H-indole,

4-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-thiomorpholine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-L-proline methyl ester;

(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxymethyl)pyrro-lidine, enantiomer A,

(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxymethyl)pyrrolidine, enantiomer B,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-L-proline 1,1-dimethylethyl ester;

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-N-(2-naphthalenyl)-L-prolinamide,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,4-tetrahydro-2-methylquinoline,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-6-fluoro-1,2,3,4-tetrahydro-2-methylquinoline,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-L-proline phenylmethyl ester;

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-D-proline phenylmethyl ester;

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-hydroxy-L-proline phenylmethyl ester;

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)-2-methylpiperazine;

3-Chloro-N-cyclohexyl-7-(3,4-dichlorophenyl)-4,7-dihydro-N,5-dimethyl-pyrazolo[1,5-a]pyri-midine-6-carboxamide;

4-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-thiomorpholine,

1-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2,3-dihydro-1H-indole,

1-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]hexahydro-1H-azepine,

1-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-octahydroazocine,

1-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,6-tetrahydropyridine,

3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-N,5-dimethyl-N-[(1S)-1-phenylethyl]-pyrazolo[1,5-a]pyrimidine-6-carboxamide;

3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-N,5-dimethyl-N-[(1R)-1-phenylethyl]-pyrazolo[1,5-a]pyrimidine-6-carboxamide,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]-carbonyl]-2-(methoxy-methyl)piperidine;

[(3R)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-3-pyrrolidinyl]carbamic acid 1,1-dimethylethyl ester;

[(3S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-3-pyrrolidinyl]carbamic acid 1,1-dimethylethyl ester;

(3R)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-3-(dimethylamino)pyrrolidine;

N-[1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-3-pyrrolidinyl]acetamide,

N-[1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-3-pyrrolidinyl]-N-methylacetamide,

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N,N-dipentylpyrazolo[1,5-a]pyri-midine-6-carboxamide,

7-(3,4-Dichlorophenyl)-N,N-dihexyl-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxamide;

1-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperidine;

3-Chloro-7-(3-chlorophenyl)-N-cyclohexyl-4,7-dihydro-N,5-dimethyl-pyrazolo[1,5-a]pyrimidine-6-carboxamide,

(2S)-1-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxy-methyl)pyrrolidine;

1-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-decahydroquinoline,

2-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,4-tetrahydroisoquinoline,

4-[[3-Chloro-7-(3-chlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-thiomorpholine,

N-Cyclohexyl-7-(3,4-dichlorophenyl)-4,7-dihydro-N,5-dimethyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide;

7-(3,4-Dichlorophenyl)-N,N-diethyl-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxamide,

N,N-Dibutyl-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxamide,

7-(3,4-Dichlorophenyl)-N,N-diheptyl-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxamide,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-azacyclotridecane,

9-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-dodecahydro-1H-fluorene;

(2S)-1-[[7-(3,4-Di-chlorophenyl)-4,7-dihydro-5-methyl-2-(tri-fluoromethyl)pyrazolo-[1,5-a]pyrimidin-6-yl]car-bonyl]-2-(methoxy-methyl)pyrrolidine,

1-[[3-Chloro-7-(3-chlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]piperidine,

1-[[3-Chloro-7-(3-chloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]hexahydro-1H-azepine;

1-[[3-Chloro-7-(3-chlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-octahydroazocine;

1-[[3-Chloro-7-(3-chlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,6-tetrahydropyridine;

3-Chloro-7-(3-chlorophenyl)-4,7-dihydro-N,5-dimethyl-N-[(1S)-1-phenyl-ethyl]pyrazolo[1,5-a]pyrimidine-6-carboxamide,

(2S)-1-[[3-Chloro-7-(3-chlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxymethyl)pyrrolidine,

1-[[3-Chloro-7-(3-chlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-decahydroquinoline,

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2-[[3-Chloro-7-(3-chlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,4-tetrahydroisoquinoline,

1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]hexahydro-1H-azepine,

1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,6-tetrahydropyridine;

(2S)-1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimi-din-6-yl]carbonyl]-2-(methoxymethyl)pyrrolidine,

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methyl-2-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2,3-dihydro-1H-indole,

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methyl-2-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]hexahydro-1H-azepine,

7-(3,4-Dichlorophenyl)-4,7-dihydro-N,5-di-methyl-N-[(1S)-1-phenylethyl]-2-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide,

7-(3,4-Dichlorophenyl)-4,7-dihydro-N,5-dimethyl-N-[(1R)-1-phenylethyl]-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide;

7-(3,4-Dichlorophenyl)-4,7-dihydro-N,N-bis(2-methoxyethyl)-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxamide;

7-(3,4-Dichlorophenyl)-N,N-bis(2-ethoxyethyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxamide,

7-(3,4-Dichlorophenyl)-4,7-dihydro-N-(2-methoxyethyl)-N,5-dimethylpyrazolo[1,5-a]pyrimidine-6-carboxamide;

7-(3,4-Dichlorophenyl)-4,7-dihydro-N-(2-methoxyethyl)-5-methyl-N-propylpyrazolo[1,5-a]pyrimidine-6-carboxamide,

1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-*methyl*pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperidine;

2-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,4-tetrahydroisoquinoline,

1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-octahydroazocine,

3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-N,5-dimethyl-N-[(1S)-1-phenylethyl]-pyrazolo[1,5-a]pyrimi-dine-6-carboxamide,

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3-Chloro-N-cyclohexyl-7-(2,3-dichlorophenyl)-4,7-dihydro-N,5-dimethyl-pyrazolo[1,5-a]pyrimidine-6-carboxamide,

3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methyl-N-(phenylmethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide,

7-(3,4-Dichlorophenyl)-N-ethyl-4,7-dihydro-N-(2-methoxyethyl)-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxamide;

N-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-N-methylglycine ethyl ester;

N-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-N-methylglycine 1,1-dimethylethyl ester;

N-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-N-(2-ethoxy-2-oxoethyl)glycine ethyl ester;

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(3-pyridinyl)piperidine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,4-tetrahydro-6-methylquinoline,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-propylpiperidine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-[(diethylamino)methyl]piperidine;

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-(2-phenoxyethyl)-pyrazolo[1,5-a]pyrimidine-6-carboxamide,

1-[(7-Cyclopropyl-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl)carbonyl]-4-(4-fluorophenyl)piperazine;

1-[[4,7-Dihydro-5-methyl-7-(1-methylethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine;

(2S)-1-[[4,7-Dihydro-5-methyl-7-(1-methyl-ethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxymethyl)pyrrolidine,

1-[[4,7-Dihydro-5-methyl-7-(1-methyl-ethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2,3-dihydro-1H-indole,

1-[[4,7-Dihydro-5-methyl-7-(1-methylethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1,2,3,6-tetrahydropyridine,

3-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]thiazolidine, enantiomer A,

3-[[7-(3,4-Dichlorophenyl)-4 7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]thiazolidine, enantiomer B,

7-(3,4-Dichlorophenyl)-4,7-dihydro-N,5-dimethyl-N-(phenylmethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide,

7-(3,4-Dichlorophenyl)-4,7-dihydro-N,5-dimethyl-N-(2-phenylethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide,

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-(2-phenylethyl)-N-(phenylmethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide,

(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(phenoxymethyl)pyrrolidine,

(2R)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(phenoxymethyl)pyrrolidine,

(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-[(4-fluorophenoxy)methyl]pyrrolidine,

(2R)-1-[[7-(3,4-Dichlorophenyl)-4 7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-[(4-fluorophenoxy)methyl]-pyrrolidine;

7-(3,4-Dichlorophenyl)-N-ethyl-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxamide;

N-Butyl-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxamide,

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-pentylpyrazolo[1,5-a]pyrimidine-6-carboxamide,

7-(3,4-Dichlorophenyl)-4,7-dihydro-N-(2-methoxyethyl)-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxamide,

(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(hydroxydiphenylmethyl)pyrrolidine,

(2R)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(hydroxydiphenylmethyl)pyrrolidine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(3-pyridinyl)pyrrolidine,

(2S)-1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxymethyl)pyrrolidine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-phenylpyrrolidine,

3-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-phenylthiazolidine,

3-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-thiazolidinecarboxylic acid methyl ester;

7-(3,4-Dichlorophenyl)-4,7-dihydro-N,5-dimethyl-N-(3-phenylpropyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide,

7-(3,4-Dichlorophenyl)-N-ethyl-4,7-dihydro-5-methyl-N-(3-phenylpropyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide,

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-(3-phenylpropyl)-N-propylpyrazolo[1,5-a]pyrimidine-6-carboxamide,

N-Butyl-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-N-(3-phenylpropyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide,

2-(4-Chlorophenyl)-3-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]thiazolidine,

N-(Cyclopropylmethyl)-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-N-propylpyrazolo[1,5-a]pyrimidine-6-carboxamide

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(2,3-dihydro-2-oxo-1H-benzimidazol-1-yl)piperidine,

8-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-1-phenyl-1,3,8-triazaspiro[4 5]decan-4-one,

4-(4-Chlorophenyl)-1-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-1,2,3,6-tetrahydropyridine;

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(2-phenylethyl)pyrrolidine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(4-methoxyphenyl)pyrrolidine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(2-methoxyphenyl)pyrrolidine,

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(4-fluoro-phenyl)pyrrolidine;

(3R)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-3-phenoxypyrrolidine,

(2S)-2-[(Cyclohexyloxy)methyl]-1-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]pyrrolidine;

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(phenylmethyl)pyrrolidine;

(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(phenoxymethyl)pyrrolidine, diastereomer A,

(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(phenoxymethyl)pyrrolidine, diastereomer B,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(3-methoxyphenyl)pyrrolidine;

(2S)-2-(Butoxymethyl)-1-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]pyrrolidine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(2-thienyl)pyrrolidine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(4-pyridinyl)pyrrolidine,

(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-[(methoxymethoxy)-methyl]pyrrolidine;

(2S)-2-(1H-Benzimidazol-1-ylmethyl)-1-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]pyrrolidine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(3-furanyl)pyrrolidine;

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(2-pyridinyl)pyrrolidine,

(3S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-3-phenoxypyrrolidine,

(3S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-3-phenoxypyrrolidine,

(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(methoxymethyl)pyrrolidine, enantiomer A,

(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]-pyrimidm-6-yl]carbonyl]-2-(methoxymethyl)pyrrolidine, enantiomer B,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-L-proline,

7-(3,4-Dichlorophenyl)-4,7-dihydro-N-[(1R)-2,3-dihydro-1H-inden-1-yl]-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide;

7-(3,4-Dichlorophenyl)-N-(2,3-dihydro-1H-inden-2-yl)-4,7-dihydro-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide,

N-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-D-phenylalanine methyl ester;

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-(1,2,3,4-tetrahydro-1-naphthalenyl)-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide;

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-[3-(2-oxo-1-pyrrolidinyl)propyl]-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide;

7-(3,4-Dichlorophenyl)-N-(2-furanylmethyl)-4,7-dihydro-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide,

7-(3,4-Dichlorophenyl)-N-[(3,4-dichlorophenyl)methyl]-4,7-dihydro-5-methyl-2-(trifluoromethyl)pyra-zolo[1,5-a]pyrimidine-6-carboxamide,

7-(3,4-Dichlorophenyl)-4,7-dihydro-N-[(2R)-2-(methoxymethyl)-1-pyrrolidinyl]-5-methyl-2-(trifluoromethyl)pyra-zolo[1,5-a]pyrimidine-6-carboxamide,

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-N-[(tetrahydro-2-furanyl)-methyl]-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide,

7-(3,4-Dichlorophenyl)-4,7-dihydro-N-[(1S)-2,3-dihydro-1H-inden-1-yl]-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide;

7-(3,4-Dichlorophenyl)-N-[2-(3,4-dichloro-phenyl)ethyl]-4,7-dihydro-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-6-carboxamide,

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-2-(trifluoromethyl)-N-[[4-[(trifluoromethyl)thio]-phenyl]methyl]pyrazolo-[1,5-a]pyrimidine-6-carboxamide,

(2S)-1-[[7-(3,4-Dichlorophenyl)-4,7di-hydro-5-methyl-2-(trifluoro-methyl)pyra-zolo[1,5-a]pyrimidin-6-yl]carbonyl]-2-(1-pyrrolidinylmethyl)-pyrrolidine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(1-naphthalenylsulfonyl)piperazine,

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-[(4-ethylphenyl)sulfonyl]-piperazine;

1-[(4-Bromo-5-chloro-2-thienyl)sulfonyl]-4-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimi-din-6-yl]carbonyl]-piperazine,

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-[[2-(trifluoro-methoxy)phenyl]sulfonyl]piperazine,

1-[(5-Chloro-3-methyl-benzo[b]thiophen-2-yl)sulfonyl]-4-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyra-zolo[1,5-a]pyrimidin-6-yl]carbonyl]piperazine,

1-[[7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-[(3-methoxyphenyl)carbonyl]piperazine,

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(1-oxo-3-phenyl-2-propenyl)-piperazine;

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-pyridinylcarbonyl)piperazine,

1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-4,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine,

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-4,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]piperidine,

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-4,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine;

1-[[7-(2,3-Dichloro-phenyl)-4,7-dihydro-4,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine;

1-[[7-(2,3-Dichloro-phenyl)-4,7-dihydro-4,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine, enantiomer B,

1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-4,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine, enantiomer A,

1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-2,4,5-trimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine;

1-[[7-(2,3-Dichlorophenyl)-4-[(4-fluorophenyl)methyl]-4,7dihydro-2,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

7-(2,3-Dichlorophenyl)-6-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-N,N,2,5-tetramethylpyrazolo[1,5-a]pyrimidine-4(7H)-acetamide,

7-(2,3-Dichlorophenyl)-6-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-N,N,2,5-tetramethylpyrazolo[1,5-a]pyrimidine-4(7H)-acetamide;

1-[[7-(2,3-Dichlorophenyl)-4-[2-(dimethylamino)ethyl]-4,7-dihydro-2,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[4-(Cyclopropylmethyl)-7-(2,3-dichlorophenyl)-4,7-dihydro-2,5-dimethylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine;

7-(2,3-Dichlorophenyl)-6-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-N,N,2,5-tetramethylpyrazolo[1,5-a]pyrimidine-4(7H)-carboxamide;

1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-4-methyl-5-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(2,3-Dichlorophenyl)-4,7-dihydro-5-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine,

1-[[7-(2,3-Dichloro-phenyl)-4,7-dihydro-2-methyl-5-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-(4-fluoro-phenyl)piperazine,

1-[[7-(2,3-Dichloro-phenyl)-4,7-dihydro-2,4-dimethyl-5-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidm-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(2,3-Dichloro-phenyl)-4,7-dihydro-2,4-dimethyl-5-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidm-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine, enantiomer B,

1-[[7-(3,4-Dichlo-rophenyl)-4,7-dihydro-5-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-(4-fluorophenyl)piperazine;

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-2-methyl-5-(trifluoro-methyl)pyrazolo[1,5-a]pyrimidm-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine;

1-[[1-Benzoyl-7-(2,3-dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine,

1-[[1-Benzoyl-7-(3,4-dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-phenylpiperazine,

1-[[1-Acetyl-7-(3,4-dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-phenylpiperazine;

1-[[7-(3,4-Dichloro-phenyl)-1,2,4,7-tetrahydro-5-methyl-2-oxo-1-(1-oxobutyl)-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine,

1-[[1-(Cyclopropyl-carbonyl)-7-(3,4-dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-phenylpiperazine;

1-[[1-(Cyclopropyl-carbonyl)-7-(2,3-dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(2,3-Dichloro-phenyl)-1,2,4,7-tetra-hydro-5-methyl-1-(3-methyl-1-oxobutyl)-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)-piperazine,

1-[[7-(2,3-Dichloro-phenyl)-(2,2-dimethyl-1-oxopropyl)-1,2,4,7-tetrahydro-5-methyl-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenyl-piperazine,

1-[[1-(Cyclopropyl-carbonyl)-7-(3,4-dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine,

1-[[1-(Cyclobutyl-carbonyl)-7-(3,4-dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluoro-phenyl)piperazine,

1-[[7-(3,4-Dichloro-phenyl)-1,2,4,7-tetrahydro-5-methyl-1-(2-methyl-1-oxopropyl)-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]car-bonyl]-4-(4-fluoro-phenyl)piperazine;

1-[[7-(2,3-Dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-1-[(1-methylethyl)sulfonyl]-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine,

1-[[7-(3,4-Dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-1-[(1-methylethyl)sulfonyl]-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine;

7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-N-(1-methylethyl)-2-oxo-6-[(4-phenyl-1-piperazinyl)carbonyl]pyrazolo[1,5-a]pyrimidine-1(2H)-carboxamide,

7-(2,3-Dichlorophenyl)-4,7-dihydro-N,5-dimethyl-2-oxo-6-[(4-phenyl-1-piperazinyl)-carbonyl]pyrazolo[1,5-a]pyrimidine-1(2H)-carboxamide,

7-(2,3-Dichlorophenyl)-4,7-dihydro-5-methyl-2-oxo-6-[(4-phenyl-1-piperazinyl)carbonyl]-pyrazolo[1,5-a]pyri-midine-1(2H)-carboxamide,

7-(3,4-Dichlorophenyl)-6-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-4,7-dihydro-N,N,5-trimethyl-2-oxopyrazolo[1,5-a]pyrimidine-1(2H)-carboxamide;

1-[[1-(3-Butenyl)-7-(3,4-dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-2-oxopyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(3,4-Dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-2-oxo-1-(2,2,2-trifluoroethyl)pyrazolo-[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[7-(3,4-Dichlorophenyl)-1,2,4,7-tetrahydro-5-methyl-2-oxo-1,4-bis(2,2,2-trifluoroethyl)pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

7-(3,4-Dichlorophenyl)-6-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-4,7-dihydro-5-methyl-2-oxopyrazolo[1,5-a]pyrimidine-1(2H)-carboxylic acid 1-methylethyl ester;

1-[(4,7-Dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl)carbonyl]-4-phenylpiperazine,

7-(3,4-Dichlorophenyl)-6-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-2-carboxylic acid,

7-(3,4-Dichlorophenyl)-N,N-diethyl-6-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-2-carboxamide;

7-(3,4-Dichlorophenyl)-6-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-4,7-dihydro-N-(4-hydroxyphenyl)-5-methylpyrazolo[1,5-a]pyrimidine-2-carboxamide;

1-[[7-(3,4-Dichloro-phenyl)-4,7dihydro-5-methyl-2-[[(2S)-2-(1-pyrrolidinylmethyl)-1-pyrrolidinyl]carbonyl]-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

7-(3,4-Dichlorophenyl)-6-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-2-carboxamide;

7-(3,4-Dichlorophenyl)-6-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-4,7-dihydro-5-methyl-N-(phenylmethyl)pyrazolo-[1,5-a]pyrimidine-2-carboxamide;

7-(3,4-Dichlorophenyl)-6-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-4,7-dihydro-5-methyl-N-(2-phenylethyl)-pyrazolo[1,5-a]pyri-midine-2-carboxamide,

1-[[2-Cyano-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

3-Bromo-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1,1-dimethylethyl ester;

1-[[3-Bromo-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine,

1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine,

1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine;

1-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine,

1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenylpiperazine, enantiomer B,

1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-phenyl-piperazine, enantiomer A,

1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine, enantiomer A,

1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine, enantiomer B,

1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine, enantiomer A,

1-[[3-Chloro-7-(2,3-dichlorophenyl)-4,7-dihydro-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine, enantiomer B,

1-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine, enantiomer A,

1-[[3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(4-fluorophenyl)piperazine, enantiomer B,

3-Chloro-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylic acid 1,1-dimethylethyl ester;

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-6-(5-phenyl-2-oxazolyl)pyrazolo[1,5-a]pyrimidine,

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-6-(5-phenyl-1,3,4-oxa-diazol-2-yl)pyrazolo[1,5-a]pyrimidine,

6-(1H-Benzimidazol-2-yl)-7-(3,4-dichloro-phenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidine,

6-(2-Benzothiazolyl)-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidine,

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-6-(1-methyl-1H-benzimi-dazol-2-yl)pyrazolo[1,5-a]pyrimidine,

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-6-[5-(trifluoromethyl)-1-propyl-1H-benzimidazol-2-yl]pyrazolo[1,5-a]pyrimidine,

6-(5-Butyl-1,3,4-oxadiazol-2-yl)-7-(3,4-dichlorophenyl)-4,7dihydro-5-methylpyrazolo[1,5-a]pyrimidine,

1-[[7-(3,4-Dichloro-phenyl)-4,7-dihydro-5-methyl-6-(4-methyl-1H-benzimidazol-2-yl)pyra-zolo[1,5-a]pyrimidine,

1-[[7-(2,3-Dichloro-phenyl)-4,7-dihydro-5-methyl-6-(1-methyl-1H-benzimidazol-2-yl)pyra-zolo[1,5-a]pyrimidine;

7-(3,4-Dichlorophenyl)-4,7-dihydro-6-(imida-zo[1,5-a]pyridin-3-yl)-5-methylpyrazolo[1,5-a]pyrimidine,

7-(3,4-Dichlorophenyl)-6-(1-ethyl-5-nitro-1H-benzimidazol-2-yl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidine;

6-[5-Chloro-1-(1-methylethyl)-1H-benzimidazol-2-yl]-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidine,

6-(5-Chloro-1-ethyl-1H-benzimidazol-2-yl)-7-(3,4-dichlorophenyl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidine,

7-(3,4-Dichlorophenyl)-6-(5-fluoro-1-propyl-1H-benzimidazol-2-yl)-4,7-dihydro-5-methylpyra-zolo[1,5-a]pyrimidine,

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-6-[1-(1-methylethyl)-5-(trifluoromethyl)-1H-benzimidazol-2-yl]pyrazolo[1,5-a]pyrimidine,

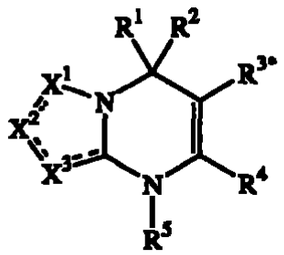
7-(3,4-Dichlorophenyl)-6-(5-fluoro-1-methyl-1H-benzimidazol-2-yl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyrimidine;

7-(3,4-Dichlorophenyl)-6-(5-fluoro-1-methyl-1H-benzimidazol-2-yl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyri-midine, enantiomer A,

7-(3,4-Dichlorophenyl)-6-(5-fluoro-1-methyl-1H-benzimidazol-2-yl)-4,7-dihydro-5-methyl-pyrazolo[1,5-a]pyri-midine, enantiomer B

7-(3,4-Dichlorophenyl)-4,7-dihydro-5-methyl-6-[1-(phenylmethyl)-1H-benzimidazol-2-yl]pyrazolo[1,5-a]pyrimidine

18 A compound of the formula I*



(I*)

enantiomers, diastereomers and pharmaceutically acceptable salts thereof, wherein

X^1, X^2 and X^3 are independently selected from N, NR^6, $(CR^7)_q$, $(CHR^7)_q$, or C=O, wherein the bonds connecting X^1, X^2 and X^3 to adjacent atoms may be single or double bonds forming a 5 to 7-membered saturated, partially unsaturated or aromatic ring,

R^1, R^2, R^4, R^5, R^6 and R^7 are independently selected from groups of the formula $-(CH_2)_n-(Z^1)_m-(CH_2)_p-Z^2$, or

R^1, R^2, R^4 and R^5 may, in one or more pairs of two, together with the atoms to which they are bonded, form a carbocyclic, substituted carbocyclic heterocyclic or substituted heterocyclic group, or

R^6 and R^7 may, in one or more pairs of two, together with the atoms to which they are bonded, form a carbocyclic, substituted carbocyclic, heterocyclic or substituted heterocyclic group,

Z^1 is $-CZ^3Z^4-$, -O-, $-NZ^3-$ -S-, -SO-, $-SO_2-$, -C(O)-, $-C(O)Z^3-$, $-C(O)NZ^4$, -C(S)-, $-C(=NOZ^3)-$, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, carbocyclo, substituted carbocyclo, aryl, substituted aryl, heterocyclo, or substituted heterocyclo,

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Z^2 is hydrogen, $-OZ^5$, $-OC(O)Z^5$, $-NZ^5-C(O)-Z^6$, $-NZ^5-CO_2-Z^6$, $-NZ^5(C=O)-NZ^6Z^7$, $-NZ^5Z^6$, $-NO_2$, halo, $-CN$, $-C(O)Z^5$, $-CO_2Z^5$, $-C(S)Z^5$, $-(C=NOZ^5)Z^6$, $-C(O)NZ^5Z^6$, $-C(S)NZ^5Z^6$, $-SZ^5$, $-SOZ^5$, $-SO_2Z^5$, $-SO_2NZ^5Z^6$, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, carbocyclo, substituted carbocyclo, aryl, substituted aryl, heterocyclo, or substituted heterocyclo,

Z^3, Z^4, Z^5, Z^6 and Z^7 are independently hydrogen, halo, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, carbocyclo; substituted carbocyclo, aryl, substituted aryl, heterocyclo; or substituted heterocyclo, or

Z^3, Z^4, Z^5, Z^6 and Z^7 may, in one or more pairs of two, together with the atoms to which they are bonded, form a carbocyclic, substituted carbocyclic, heterocyclic or substituted heterocyclic group,

R^{3*} is $-OZ^5$, $-OC(O)-Z^5$, $-NZ^5-C(O)_2-Z^6$, $-NZ^5(C=O)-NZ^6Z^7$, $-NZ^5Z^6$ $-(C=NOZ^5)Z^6$, $-C(O)NZ^{5*}Z^{6*}$, $-C(S)NZ^{5*}Z^{6*}$, $-SZ^5$, $-SOZ^5$, $-SO^2Z^5$, $-SO_2NZ^5Z^6$, $-C(O)Z^{3*}-Z^{2*}$, halo, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, carbocyclo; substituted carbocyclo, aryl, substituted aryl, heterocyclo or substituted heterocylco;

Z^{2*} is other than hydrogen when Z^{3*} is heterocyclo,

Z^{3*} is heterocyclo or substituted heterocyclo;

Z^{5*} is substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, carbocyclo, substituted carbocyclo, aryl, substituted aryl, heterocyclo, or substituted heterocyclo, and

Z^{6*} is hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, carbocyclo, substituted carbocyclo; aryl, substituted aryl, heterocyclo; or substituted heterocyclo, provided that Z^{6*} is not hydrogen when Z^{5*} is unsubstituted cycloalkyl, unsubstituted aryl, or unsubstituted benzyl,

or Z^{5*} and Z^{6*} may together with the nitrogen atom to which they are bonded form a heterocyclic group or substituted heterocyclic group, provided

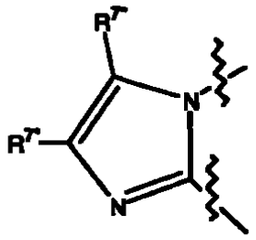
that Z^{5*} and Z^{6*} do not together form unsubstituted piperidinyl, unsubstituted pyrrolidinyl, or unsubstituted morpholinyl, and further provided that when

(i) R^1 and R^5 are each hydrogen, and

(ii) R^2 is aryl or substituted aryl, and

(iii) R^4 is heterocyclo-substituted aryl, and

(iv) X^1, X^2 and X^3 form the ring



where R^{7*} is H or alkyl,

Z^{5*} and Z^{6*} do not together form unsubstituted piperazinyl or N-alkyl-substituted piperazinyl,

n and p are independently selected from integers from 0 to 10 wherein, when m is 0, p is also 0,

m is an integer selected from 0 or 1, and

q is an integer selected from 1 to 3

19 A compound of claim 18 wherein

R^{3*} is heterocyclo, substituted heterocyclo; $-C(O)NZ^{5*}Z^{6*}$, $-C(O)Z^{3*}$-$C(O)NZ^5Z^6$, $-C(O)Z^{3*}$-CO_2Z^5, $-C(O)Z^{3*}$-(aryl), $-C(O)Z^{3*}$-(substituted aryl), $-C(O)Z^{3*}$-(heterocyclo), or $-C(O)Z^{3*}$-(substituted heterocyclo)

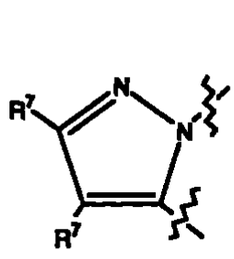
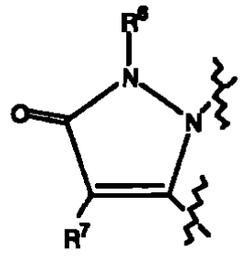
20 A compound of claim 19 wherein

R^1 is H,

R^2 is aryl, substituted aryl, heterocyclo, substituted heterocyclo, carbocyclo or substituted carbocyclo,

R^4 is alkyl or substituted alkyl, and

X^1, X^2 and X^3, together with the atoms to which they are bonded, form a ring selected from

where the ring substituents are the same or different.

21 A compound of claim 18 wherein R^{3a} is heterocyclo or substituted heterocyclo.

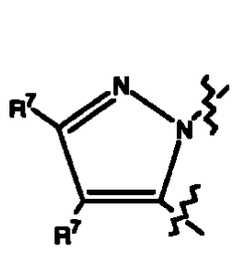
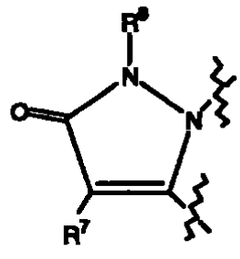
22 A compound of claim 21 wherein

R^1 is H,

R^2 is aryl, substituted aryl, heterocyclo, substituted heterocyclo, carbocyclo or substituted carbocyclo,

R^4 is alkyl or substituted alkyl, and

X^1, X^2 and X^3, together with the atoms to which they are bonded, form a ring selected from.

where the ring substituents are the same or different.

23 A compound of claim 18 selected from the title compounds of examples 18, 19, 25-30, 33, 39-42, 44-82, 84-221, 223-273, 277-282, 286-288, 290-307, 309-312, 314-336, 340-400, 402-450, 452-463, and 465-483

24 A pharmaceutical composition comprising a therapeutically effective amount of at least one compound of claim 18 and a pharmaceutically acceptable vehicle or carrier thereof.

25 A pharmaceutical composition comprising a therapeutically effective amount of at least one compound of claim 19 and a pharmaceutically acceptable vehicle or carrier thereof

26 A pharmaceutical composition comprising a therapeutically effective amount of at least one compound of claim 20 and a pharmaceutically acceptable vehicle or carrier thereof

27 A pharmaceutical composition comprising a therapeutically effective amount of at least one compound of claim 21 and a pharmaceutically acceptable vehicle or carrier thereof

28 A pharmaceutical composition comprising a therapeutically effective amount of at least one compound of claim 22 and a pharmaceutically acceptable vehicle or carrier thereof

29 A pharmaceutical composition comprising a therapeutically effective amount of at least one compound of claim 23 and a pharmaceutically acceptable vehicle or carrier thereof

30 A method of treating arrhythmias comprising administering to a patient in need thereof an effective amount of at least one compound of claim 18

31 A method of treating arrhythmias comprising administering to a patient in need thereof an effective amount of at least one compound of claim 19

32 A method of treating arrhythmias comprising administering to a patient in need thereof an effective amount of at least one compound of claim 20

33 A method of treating arrhythmias comprising administering to a patient in need thereof an effective amount of at least one compound of claim 21

34 A method of treating arrhythmias comprising administering to a patient in need thereof an effective amount of at least one compound of claim 22

35 A method of treating arrhythmias comprising administering to a patient in need thereof an effective amount of at least one compound of claim 23

2B

HETEROCYCLIC DIHYDROPYRIMIDINE COMPOUNDS

Abstract of the Disclosure

Novel heterocyclic dihydropyrimidine compounds, methods of using such compounds in the prevention and treatment of arrhythmia and I_{Kur}-associated conditions, and pharmaceutical compositions containing such compounds

83663

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ESTADOS UNID S DE AMERICA

A QUIENES PUEDA LLEGAR LA PRESENTE

DEPARTAMENTO DE COMERCIO DE LOS ESTADOS UNIDOS

Oficina de Patentes y Marcas de los Estados Unidos

Septiembre 25, 2000

LA PRESENTE ES PARA CERTIFICAR QUE ANEXA A LA MISMA SE ENCUENTRA UNA COPIA AUTENTICA DE LOS REGISTROS DE LA OFICINA DE PATENTES Y MARCAS DE LOS ESTADOS UNIDOS, DE LOS DOCUMENTOS DE LA SOLICITUD DE PATENTE ABAJO IDENTIFICADA, QUE CUMPLE CON LOS REQUISITOS PARA QUE SE LE CONCEDA UNA FECHA DE PRESENTACION CONFORME A LA 35 USC 111

NUMERO DE SOLICITUD *60/169,091*

FECHA DE PRESENTACION *Diciembre 06 1999*

(SELLO)

Por Autoridad del
COMISIONADO DE PATENTES Y MARCAS

(Rubrica)
T LAWRENCE
Oficial de Certificaciones

Documento del Abogado No. HA726*

220

HOJA DE CUBIERTA DE LA SOLICITUD PROVISIONAL

Esta es una petición para llenar una SOLICITUD PROVISIONAL bajo la CFR 37 1 53 (c)

Número de Documento HA726*		Tipo un signo de más (+) dentro de este cuadro	+

INVENTOR(ES)/SOLICITANTE(S)

ULTIMO NOMBRE	PRIMER NOMBRE	INICIAL INTERMEDIA	RESIDENCIA (CIUDAD Y CUALQUIER ESTADO O PAIS ANTERIOR)
Atwal	Karnail	S	Newtown. Pennsylvania
Vaccaro	Wayne		Yardley Pennsylvania
Lloyd	John		Yardley Pennsylvania
Finlay	Heather		Lawrenceville. New Jersey
Yan	Lin		Princeton. New Jersey

TITULO DE LA INVENCION (280 caracteres max)

COMPUESTOS DE DIHIDROPIRIMIDINA HETEROCICLICOS

DIRECCION PARA CORRESPONDENCIA

BURTON RODNEY
PATENT DEPARTMENT
BRISTOL-MYERS QUIBB COMPANY
PO BOX 4000
PRINCETON NJ 08543-4000

PARTES DE LA SOLICITUD ADJUNTAS (*Checar todas las que se aplican*)

☒ Especificación 208 Número de páginas	☐ Pequeña declaración total
☐ Dibujo(s) ☐Número de Hojas	☐Otro (especificar)

CORREO EXPRESS No. EM260263971US

METODO DE PAGO

☒ El comisionado está con ello autorizado a cargar el cálculo de presentación y el Numero de Cuenta de Depósito 19-3880 La cantidad del Calculo de Tasas Provisional es ($) 150.00 El comisionado está con ello autorizado a cargar cualquier tasa adicional la cual puede ser requerida excepto por la Tasa Publicada, o cualquier crédito de sobre pago a la Cuenta de Depósito 19-3880

Se elabora la invención por una agencia del Gobierno de los Estados Unidos o bajo un contrato con una agencia del Gobierno de los Estados Unidos

☒ NO

221

☐ SI el Nombre de la Agencia del Gobierno de U S y el número de contrato Gubernamental son ____

_____

Respetuosamente,

FIRMA _____ Fecha 9/22/1999

SIGNO O NOMBRE IMPRESO Ronald S. Hermenau
REGISTRO No 34,620
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☐ Los inventores adicionales son mencionados en hojas numeradas de manera separada adjuntas a esta.

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EN LA OFICINA DE PATENTES Y MARCAS COMERCIALES DE LOS ESTADOS UNIDOS

Solicitante	Karnail Atwal, Wayne Vaccaro, John Lloyd, Heather Finlay & Lin Yan
Serie No	No asignada
Presentada	Concurrentemente con esta
Para	Compuestos de Dihidropirimidina Heterociclicos

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Comisionado Asistente para Patentes
Washington, D C 20231
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Fecha del Depósito 6 Diciembre 1999

La presente es para certificar que la solicitud provisional captada anteriormente, adjunta a esta, incluye una especificación de 208 páginas, incluyendo reivindicaciones y resumen, y la hoja de cubierta con los nombres de los inventores de esta, está siendo depositada en el Sevicio Postal de los Estados Unidos "Express Mail Post Office to Addresse" bajo el 37 CFR 1 10 en la fecha indicada anteriormente y dirigida al Comisionado Asistente para Patentes, Washington, D C 20231

Atentamente,

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C MPUESTOS DE DIHIDROPIRIMIDINA HETER CICLIC S

Campo de la Invención

La presente ınvención se refıere a compuestos de dıhıdropırımıdına heterocíclıcos, a métodos para usar tales compuestos en el tratamıento de arrıtmıa y alteracıones asocıadas con I_{Kur}, y a composıcıones farmacéutıcas que contıenen tales compuestos

Antecedentes de la Invención

La fıbrılación del atrıo y el palpıtar son las arrıtmıas más comunes encontradas en la práctıca clınıca Aunque algunos fármacos antıarrıtmıcos actualmente dısponıbles pueden convertır la fıbrılación sostenıda a rıtmo del seno, son solamente efectıvos en la fıbrılación aguda del atrıo y aún así su eficacıa es baja Además, estos fármacos son de uso lımıtado debıdo a una varıedad de efectos potencıalmente adversos, ıncluyendo proarrıtmıa ventrıcular Así, exıste actualmente una necesıdad médıca no satısfecha para un tratamıento seguro y eficaz de la fıbrılación del atrıo y otras arrıtmıas

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supraventriculares

La corriente de potasio rectificadora de liberación ultra rápida (I_{Kur}), es una corriente sostenida de activación rápida que ha sido identificada en los miocitos del atrio humano, pero está aparentemente ausente de los miocitos ventriculares humanos (Konarzewska et al , *Circulation J Physiol , 491,* 13 (1996)) Los datos farmacológicos y biofísicos, biológicos moleculares considerables, indican que el I_{Kur} es codificado por el gen del canal de potasio Kv1 5 El I_{Kur} juega un papel significante en la repolarización de la inhibición potencial y selectiva de la acción del atrio de esta corriente, en los miocitos del atrio humano prolonga la duración de la acción potencial por más del 50% (Wang et al , *Circ Res 73,* 1061 (1993)) La prolongación de la acción potencial, consecuentemente prolonga el periodo refractorio efectivo del atrio, esto es, la inhibición del I_{Kur} produce un efecto antiarrítmico de clase III De manera importante, un inhibidor de I_{Ku-} puede tener utilidad contra la fibrilación atrial sin tener el riesgo proarrítmico ventricular concomitante asociado con otros agentes de clase III que tienen canales de calcio objetivo expresados en ambos, atrio y

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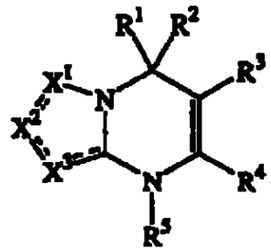
ventrículo

Breve Descripción de la Invencion

La presente invención proporciona compuestos de dihidropirimidina heterocíclicos de la siguiente fórmula I, incluyendo enantiómeros, diastereómeros, y sales de los mismos, para el tratamiento de la arritmia y alteraciones asociadas con I_{Kur}



(I)

donde

X^1, X^2 y X^3 son independientemente seleccionados de N, NR^6, $(CR^7)_q$, $(CHR^7)_q$, o C=O, en donde los enlaces que conectan X^1, X^2 y X^3 a los átomos adyacentes, pueden ser enlaces únicos o dobles que forman un anillo aromático de 5 a 7 elementos saturados o parcialmente insaturados,

R^1, R^2, R^3, R^4, R^5, R^6 y R^7 son los mismos o diferentes y son seleccionados de manera independiente de

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los grupos de la fórmula $-(CH_2)_q-(Z)_n-(CH_2)_p-Z^-$, o

R^1, R^2, R^3, R^4 y R^5 pueden, en uno o más pares de dos (tal como R^1 y R^2, R^1 y R^3, R^2 y R^3, R^3 y R^4 o R^4 y R^5), junto con los átomos a los cuales estan enlazados, formar un grupo carbocíclico, carbocíclico substituido, heterocíclico o heterocíclico substituido, o

R^6 y R^7 pueden, en uno o más pares de dos (tal como R^6 y R^7, R^6 y R^6, o R^7 y R^7), junto con los átomos a los cuales están unidos, formar un grupo carbocíclico, carbocíclico substituido, heterocíclico o heterocíclico substituido,

Z^1 es $-CZ^3Z^4-$, $-O-$, $-NZ^3-$, $-S-$, $-SO-$, $-SO_2-$, $-C(O)-$, $-C(O)Z^3-$, $-C(O)NZ^4$, $-C(S)-$, $-C(=NOZ^3)-$, alquilo, alquilo substituido, alquenilo, alquenilo substituido, alquinilo, alquinilo substituido, carbociclo, carbociclo substituido, arilo, arilo substituido, heterociclo, o heterociclo substituido,

Z^2 es hidrógeno, $-OZ^5$, $-OC(O)Z^5$, $-NZ^5-C(O)-Z^6$, $-NZ^5-CO_2-Z^6$, $-NZ^5(C=O)-NZ^6Z^7$, $-NZ^5Z^6$, $-NO_2$, halo, $-CN$, $-C(O)Z^5$, $-CO_2Z^5$, $-C(S)Z^5$, $-(C=NOZ^5)Z^6$, $-C(O)NZ^5Z^6$, $-C(S)NZ^5Z^6$, $-SZ^5$, $-SOZ^5$, $-SO_2Z^5$, $-SO_2NZ^5Z^6$, alquilo, alquilo substituido,

alquenilo, alquenilo substituido, alquinilo, alquinilo substituido, carbociclo, carbociclo substituido, arilo, arilo substituido, heterociclo (tal como heteroarilo), o heterociclo substituido

Z^3, Z^4, Z^5, Z^6 y Z^7 son independientemente hidrógeno, halo, alquilo, alquilo substituido, alquenilo, alquenilo substituido, alquinilo, alquinilo substituido, carbociclo, carbociclo substituido, arilo, arilo substituido, heterociclo, o heterociclo substituido, o

Z^3, Z^4, Z^5, Z^6 y Z^7 puede, en uno o más pares de dos (tal como Z^3 y Z^4, Z^5 y Z^6 o Z^6 y Z^7), junto con los átomos de carbono a los cuales están unidos, formar un grupo carbocíclico carbocíclico substituido, heterocíclico o heterocíclico substituido,

n y p son independientemente seleccionados de los enteros a partir de 0 a 10 en donde m es 0, p es también 0,

m es un entero seleccionado de 0 o 1, y

q es un entero seleccionado de 1 a 3

La presente invención proporciona nuevos métodos para la prevención y tratamiento de la arritmia y alteraciones asociadas con I_{Kur}, empleando

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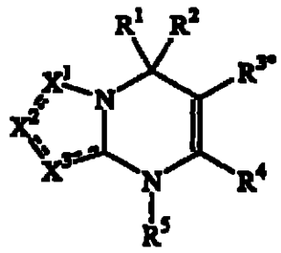
uno o más compuestos de la fórmula I, enantiómeros, diastereómeros o sales del mismo farmacéuticamente aceptables En particular, la presente invención proporciona un nuevo método para la prevención selectiva y tratamiento de arritmias supraventriculares

Además, los compuestos dentro de la fórmula I, así como también enantiómeros, diastereómeros y sales de los mismos son compuestos nuevos, incluyendo compuestos de la fórmula I* y sales de los mismos



(I*)

en donde

X^1, X^2, X^3, R^1, R^2, R^4 y R^5 son como se definen anteriormente,

R^{3*} es $-OZ^5$, $-OC(O)Z^5$, $-NZ^5-C(O)_2-Z^6$, $-NZ^5(C=O)-NZ^6Z^7$, $-NZ^5Z^6$, $-(C=NOZ^5)Z^6$, $-C(O)NZ^{5*}Z^{6*}$, $-C(S)NZ^{5*}Z^{6*}$, $-SZ^5$, $-SOZ^5$, $-SO^2Z^5$, $-SO_2NZ^5Z^6$, $-C(O)Z^{3*}Z^{2*}$, halo, alquilo, alquilo substituido,

alquenilo, alquenilo substituido, alquinilo, alquinilo substituido, carbociclo, carbociclo substituido, arilo, arilo substituido, heterociclo o heterociclo substituido,

Z^{2*} es preferentemente hidrógeno cuando Z^{1*} es heterociclo,

Z^{3*} es heterociclo o heterociclo substituido,

Z^{5*} es alquilo substituido, alquenilo, alquenilo substituido, alquinilo, alquinilo substituido, carbociclo, carbociclo substituido, arilo, arilo substituido, heterociclo, o heterociclo substituido, y

Z^{6*} es hidrógeno, alquilo, alquilo substituido, alquenilo, alquenilo substituido, alquinilo, alquinilo substituido, carbociclo, carbociclo subsituido, arilo, arilo substituido, heterociclo, o heterociclo substituido, con la condición de que Z^{6*} no sea hidrógeno cuando Z^{5*} es cicloalquilo insubstituido, arilo insubstituido, o bencilo insubstituido,

o Z^{5*} y Z^{6*} pueden, junto con el átomo de nitrógeno al cual están unidos, formar un grupo heterocíclico o un grupo heterociclico substituido, con la condición de que Z5* y Z6* no formen juntos piperidinilo insubstituido,

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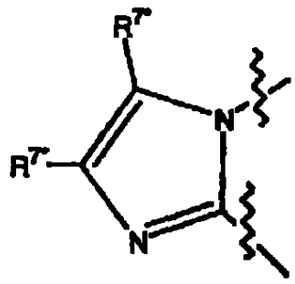
pirrolidinilo insubstituido, o morfolinilo insubstituido, y demás, con la condición de que

(i) R^1 y R^5 sean cada uno hidrogeno, y

(ii) R^2 es arilo o arilo substituido, y

(iii) R^3 es heterocíclico-arilo substituido, y

(iv) X^1, X^2 y X^3 forman el anillo



donde R^{7*} es H o alquilo

Z^{5*} y Z^{6*} no forman juntos el piperazinilo insubstituido o piperazinilo N-alquil-substituido,

Compuestos Preferidos

Los compuestos de la fórmula I y la sales del mismo, en donde uno o más, y especialmente todos,

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de X^1, X^2, X^3, R^1, R^2, R^3, R^4 y R^5 se seleccionan a partir de las siguientes definiciones, son compuestos preferidos de la presente invención

R^1 es hidrógeno,

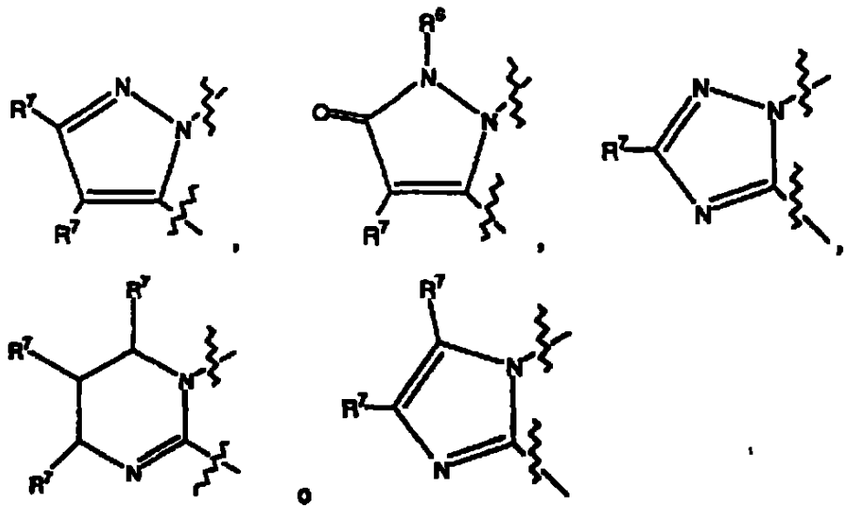
R^2 es hidrógeno, alquilo, alquilo substituido, arilo, arilo substituido, heterociclo, heterociclo substituido, carbociclo o carbociclo substituido,

R^3 es $-(CH_2)_n-Z^2$, $-(CH_2)_n-C(O)Z^3-(CH_2)_p-Z^2$, o $-(CH_2)_n-C(O)NZ^4-(CH_2)_p-Z^2$,

R^4 es alquilo o alquilo substituido, y

R^5 es hidrógeno, o $-(CH_2)_n-Z^2$, y

X^1, X^2 y X^3, junto con los átomos a los cuales están unidos, forman un anillo, seleccionado de



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en donde R^6 y/o R^7 son los mismos o diferentes, como se definen anteriormente

Los compuestos de la fórmula I y las sales de los mismos, en donde uno o más, y especialmente, todos de X^1, X^2, X^3, R^1, R^2, R^3, R^4 y R^5 se seleccionan a partir de las siguientes definiciones, son más preferidos los compuestos de la presente invención

R^1 es hidrógeno,

R^2 es arilo (especialmente cuando arilo es fenilo), arilo substituido, heterociclo, heterociclo substituido, carbociclo o carbociclo substituido,

R^3 es $-(CH_2)_n-Z^2$, $-(CH_2)_n-C(O)Z^3-(CH_2)_p-Z_2$, o $-(CH_2)_n-C(O)NZ^4-(CH_2)_p-Z^2$, en donde Z^2 se selecciona a partir de $-C(O)NZ^5Z^6$, $-CO_2Z^5$, $-SO_2Z^5$, $-NZ^5Z^6$, $-NZ^5CO_2Z^6$, $-NZ^5C(O)Z^6$, $-OZ^5$, arilo, arilo substituido, heterociclo, heterociclo substituido, alquilo o alquilo substituido,

Z^3 es heterociclo o heterociclo substituido, y

n y p son independientemente, seleccionados a partir de los enteros 0 a 3,

R^4 es alquilo, o alquilo substituido,

R^5 es hidrógeno, o $-(CH_2)_n-Z^2$, en donde Z^2 se selecciona a partir de $-C(O)NZ^5Z^6$, $-CO_2Z^5$, -

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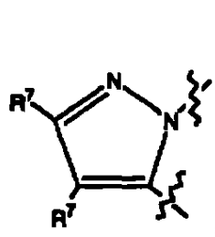
NZ^5Z^6, arilo, arilo substituido, alquilo o alquilo substituido, y

X^1, X^2 y X^3, junto con los átomos a los cuales están unidos, forman un anillo seleccionado de



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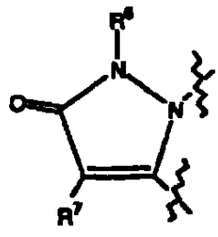

Los compuestos de la fórmula I y las sales de los mismos, en donde uno o más, y especialmente, todos de X^1, X^2, X^3, R^1, R^2, R^3, R^4 y R^5 se seleccionan a partir de las siguientes definiciones, son más preferidos, los compuestos de la presente invención

R^1 es hidrógeno,

R^2 es arilo (especialmente cuando arilo es fenilo), arilo substituido, heterociclo, heterociclo substituido, carbociclo o carbociclo substituido,

R^3 es heterociclo o heterociclo substituido, $-C(O)NZ^5Z^6$, $-CO_2Z^3-CONZ^5Z^6$, $-C(O)Z^3Z^2$, o $-C(O)Z^3-CO_2Z^5$,

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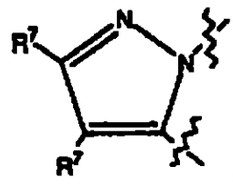
en donde Z^1 es heterociclo o heterociclo substituido, y Z^2 es arilo o arilo substituido,

R^4 es alquilo (especialmente alquilo inferior) o alquilo substituido (especialmente alquilo halo substituido),

R^5 es hidrógeno, alquilo o alquilo substituido, y

X^-, X^2 y X^3, junto con los átomos a los cuales están unidos, forman un anillo seleccionado a partir de



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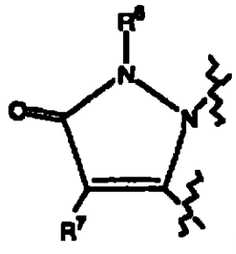

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en donde

R^6 es H o $C(O)Z^5$, en donde Z^5 es alquilo o carbociclo, y

R^7 es independientemente seleccionado a partir de H, alquilo, alquilo substituido (especialmente halo alquilo), halo, o CN

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Descripción Detallada de la Invencion

Las siguientes son definiciones de los términos usados en esta especificación La definición inicial proporcionada para un grupo o término aquí aplica a tal grupo o término a través de toda la especificación, individualmente o como parte de otro grupo, a menos que se indique de otro modo

Los término "alq" o "alquilo" se refieren a grupos hidrocarburos de cadena lineal o recta o ramificada, que tienen de 1 a 12 átomos de carbono, preferiblemente, 1 a 8 átomos de carbono, tal como metilo, etilo, n-propilo, i-propilo, n-butilo, i-butilo, t-butilo, pentilo, hexilo, heptilo, octilo, etc Los grupos alquilo inferior, esto es, los grupos alquilo de 1 a 6 átomos de carbono, son generalmente más preferidos El término "alquilo substituido" se refiere a grupos alquilo substituidos con uno o más grupos (tal como por grupos descritos anteriormente en la definición de R^1), preferiblemente se seleccionan de arilo, arilo substituido, heterociclo, heterociclo substituido, carbociclo, carbociclo substituido, halo, hidroxi, alcoxi (opcionalmente substituido), ariloxi (opcionalmente substituido), alquiléster (opcionalmente substituido), arilester

(opcionalmente substituido), alcanoilo (opcionalmente substituido), ariol (opcionalmente substituido), ciano, nitro, amino, amino substituido, amido, lactama, urea, uretano, sulfonilo, etc

El término "alquenilo" se refiere a grupos hidrocarburos de cadena lineal o recta o ramificada, que tienen de 2 a 12 átomos de carbono, preferiblemente 2 a 4 átomos de carbono, y al menos, un doble carbono para el enlace de carbono (ya sea cis o trans), tal como etenilo El término "alquenilo substituido" se refiere a grupos alquenilos substituidos con uno o más grupos (tal como por los grupos descritos anteriormente en las definiciones de R^1), preferiblemente, seleccionados de arilo, arilo substituido, heterociclo, heterociclo substituido, carbociclo, carbociclo substituido, halo, hidroxi, alcoxi (opcionalmente substituido), ariloxi (opcionalmente substituido), alquiléster (opcionalmente substituido), arilester (opcionalmente substituido), alcanoilo (opcionalmente substituido), ariol (opcionalmente substituido), ciano, nitro, amino, amino substituido, amido, lactama, urea, uretano, sulfonilo, etc

El término "alquinilo" se refiere a grupos hidrocarburos de cadena lineal o recta o rafimicada,

que tienen de 2 a 12 átomos de carbono, preferiblemente 2 a 4 átomos de carbono y al menos, un triple carbono para el enlace de carbono, tal como etinilo El término "alquinilo substituido" se refiere a grupos alquinilo substituidos con uno o más grupos (tal como por grupos descritos anteriormente en la definicion de R^1), preferiblemente seleccionados de arilo, arilo substituido, heterociclo, heterociclo substituido, carbociclo, carbociclo substituido, halo, hidroxi, alcoxi (opcionalmente substituido), ariloxi (opcionalmente substituido), alquiléster (opcionalmente substituido), ariléster (opcionalmente substituido), alcanoilo (opcionalmente substituido), ariol (opcionalmente substituido), ciano, nitro, amino, amino substituido, amido, lactama, urea, uretano, sulfonilo, etc

Los términos "ar" o "arilo" se refieren a grupos que contienen anillos homocíclicos aromáticos (por ejemplo, hidrocarburos), mono, bi o tricíclicos, preferiblemente tienen 6 a 12 elementos, tal como fenilo, naftilo y bifenilo Fenilo es un grupo arilo preferido El término "arilo substituido" se refiere a grupos arilo substituidos con uno o más grupos (tal como por grupos descritos anteriormente en la

definicion de R^1), preferiblemente seleccionados de alquilo, alquilo substituido, alquenilo (opcionalmente substituido), arilo (opcionalmente substituido), heterociclo (opcionalmente substituido), halo, hidroxi, alcoxi (opcionalmente substituido), ariloxi (opcionalmente substituido), alcanoilo (opcionalmente substituido), aroilo (opcionalmente substituido), alquiléster (opcionalmente substituido), ariléster (opcionalmente substituido), ciano, nitro, amino, amino substituido, amido, lactama, urea, uretano, sulfonilo, etc , en donde opcionalmente, uno o más pares de substituyentes junto con los átomos a los cuales estan enlazados, forman un anillo de 3 a 7 elementos,

Los términos "cicloalquilo" y "cicloalquenilo" se refieren a grupos de anillos mono, bi o tri- homocíclicos de 3 a 15 átomos de carbono, los cuales son, respectivamente, completamente saturados y parcialmente saturados El término "cicloalquenilo" incluye sistemas de anillos bi y tricíclicos que no son aromáticos como un total, pero contienen porciones aromáticas (por ejemplo, fluoreno, tetrahidronaftaleno, dihidroindeno y similares) Los términos "cicloalquilo substituido" y "cicloalquenilo substituido" se refieren,

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respectivamente, a grupos cicloalquilo y cicloalquenilo, substituidos con uno o más grupos (tal como por grupos descritos anteriormente en la definición de R^1), preferiblemente seleccionados de arilo, arilo substituido, heterociclo, heterociclo substituido, carbociclo, carbociclo substituido, halo, hidroxi, alcoxi (opcionalmente substituido), ariloxi (opcionalmente substituido), alquiléster (opcionalmente substituido), ariléster (opcionalmente substituido), alcanoilo (opcionalmente substituido), ariol (opcionalmente substituido), ciano, nitro, amino, amino substituido, amido, lactama, urea, uretano, sulfonilo, etc

Los términos "carbociclo", "carbocíclico" o "grupo carbocíclico" se refiere a ambos grupos cicloalquilo y cicloalquenilo Los términos "carbociclo substituido", "carbocíclico substituido" o "grupo carbocíclico substituido", se refieren a los grupos carbociclo o carbocíclico, substituidos con uno o más grupos como se describen en la definición de cicloalquilo o cicloalquenilo

Los términos "halógeno" y "halo" se refieren a flúor, cloro, bromo y yodo

Los términos "heterociclo", "heterocíclico", "grupo heterocíclico" o "heterociclo", se refieren a

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grupos cíclicos completamente o parcialmente saturados o completamente insaturado, incluyendo aromáticos ("heteroarilo"), o no aromáticos (por ejemplo, sistemas de anillos 3 a 13 elementos monocíclicos, 7 a 17 elementos bicíclicos, o 10 a 20 elementos tricíclicos, preferiblemente que contienen un total de 3 a 10 átomos de anillos), los cuales tienen al menos un heteroátomo, en al menos un anillo que contiene un átomo de carbono Cada uno de los anillos del grupo heterocíclico que contiene un heteroátomo, puede tener 1, 2, 3 o 4 heteroátomos seleccionados a partir de átomos de nitrógeno, átomos de oxígeno y/o átomos de azufre, en donde los heteroátomos de ' nitrógeno y azufre pueden opcionalmente ser oxidados y los heteroátomos de nitrógeno pueden ser opcionalmente cuaternizados El grupo heterocíclico puede estar unido a cualquier heteroátomo o átomo de carbono del anillo o sistema de anillo Los anillos de los heterocíclos de anillos múltiples, pueden estar ya sea fusionados, en puentes y/o unidos a través de una o más uniones espiro

Los grupos heterocíclicos monocíclicos ejemplares incluyen, azetidinilo, pirrolidinilo, pirrolilo, pirazolilo, oxetanilo, pirazolinilo, imidazolilo, imidazolinilo, imidazolidinilo,

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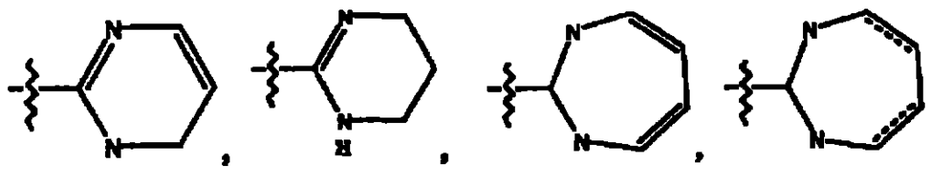
oxazolilo, oxazolidinilo, isoxazolinilo, isoxazolilo, tiazolilo, tiadiazolilo, tiazolidinilo, isotiazolilo, isotiazolidinilo, furilo, tetrahidrofurilo, tienilo, oxadiazolilo, piperidinilo, piperazinilo, 2-oxopiperazinilo, 2-oxopiperidinilo, 2-oxopirrolidinilo, 2-oxoazepinilo, azepinilo, 4-piperidonilo, piridilo, pirazinilo, pirimidinilo, piridazinilo, triazinilo, tetrahidropiranilo, tetrazolilo, triazolilo, morfolinilo, tiamorfolinilo, sulfóxido de tiamorfolinilo, sulfona de tiamorfolinilo, 1,3-dioxolano y tetrahidro-1,1-dioxotienilo,



y similares

Los grupos heterocíclicos bicíclicos ejemplares incluyen indolilo, benzotiazolilo, benzoxazolilo, benzotienilo, quinuclidinilo, quinolinilo, tetra-hidroisoquinolinilo, isoquinolinilo, bencimidazolilo, benzopiranilo, indolizinilo, benzofurilo, benzofuranilo, dihidrobenzofuranilo, cromonilo, cumarinilo,

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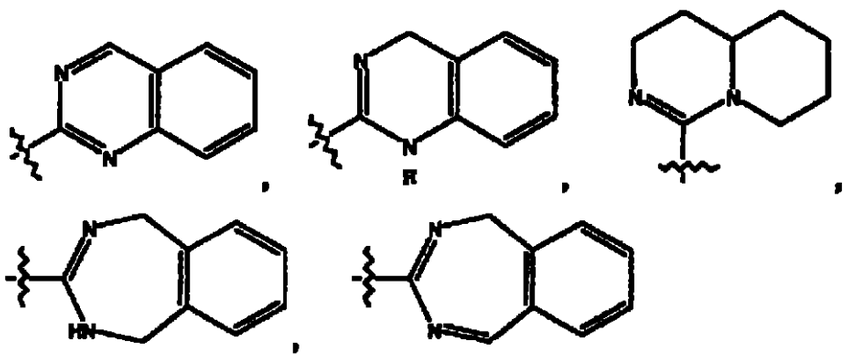
benzodioxolilo, dihidrobenzodioxolilo, benzodioxinilo, cinolinilo, quinoxalinilo, indazolilo, pirrolopiridilo, furopiridinilo (tal como furo[2,3-c]piridinilo, furo[3,2-b]piridinilo] o furo[2,3-b]piridinilo), dihidroisoindolilo, dihidroquinazolinilo (tal como 3,4-dihidro-4-oxo-quinazolinilo), tetrahidroquinolinilo, azabiciclоalquilos (tal como 6-azabiciclo[3 2 1]octano), azaspiroalquilos (tal como 1,4-dioxa-8-azaespiro[4 5]decano), imidazopiridinilo (tal como imidazo[1,5-a]piridin-3-il), triazolopiridinilo (tal como 1,2,4-triazolo[4,3-a]piridin-3-il), y hexahidroimidazopiridinilo (tal como 1,5,6,7,8,8a-hexahidroimidazo[1,5-a]piridin-3-ilo),



y similares

Los grupos heterocíclicos tricíclicos ejemplares incluyen carbazolilo, bencidolilo, fenantrolinilo, acridinilo, fenantridinilo, xantenilo y similares

Los términos "heterociclo substituido", heterocíclico substituido", "grupo heterocíclico substituido" y "heterociclo substituido" se refieren a grupos heterociclo, heterocíclico y heterociclo substituidos con uno o más grupos (tal como por los grupos descritos anteriormente en la definición de R^1), preferiblemente seleccionado de alquilo, alquilo substituido, alquenilo, oxo, arilo, arilo substituido, heterociclo, heterociclo substituido, carbociclo (opcionalmente substituido), halo, hidroxi, alcoxi (opcionalmente substituido) ariloxi (opcionalmente substituido), alcanoilo (opcionalmente substituido), aroilo (opcionalmente substituido), alquiléster (opcionalmente substituido), ariléster (opcionalmente substituido), ciano, nitro, amido, amino, amino substituido, lactama, urea, uretano, sulfonilo, etc , en donde uno o más pares de substituyentes junto con los átomos a los cuales están unidos, forman un anillo de 3 a 7 elementos

El término "alcanoilo" se refiere al grupo alquilo (el cual puede ser opcionalmente substituido

como se describe anteriormente) ligado a un grupo carbonilo (es decir, -C(O)-alquilo) De manera similar, el término "aroilo" se refiere a un grupo arilo (el cual puede ser opcionalmente substituido como se define anteriormente) ligado a un grupo carbonilo (es decir, -C(O)-arilo)

A través de la especificación, los grupos y substituyentes de los mismos, pueden ser seleccionados para proporcionar porciones y compuestos estables

Los compuestos de fórmula I forman sales, las cuales estan también dentro del ámbito de esta invención La referencia a un compuesto de la fórmula I aquí se entiende incluye la referencia a las sales de los mismos, a menos que se indique de otro modo El término "sal(es)", como se emplea aquí, denota sales acídicas y/o básicas formadas con ácidos y bases inorgánicas y/o orgánicas Además, cuando un compuesto de formula I contiene ambas, una porción básica y una porción acidica, zwitteriones ("sales inertes") pueden ser formada y están incluidas dentro del término "sal(es)" como se usó aquí Se prefieren las sales farmacéuticamente aceptables (es decir, no tóxicas, fisiológicamente aceptables), aunque otras sales son también empleados, por ejemplo, en etapas

de aislamiento o purificación, las cuales pueden ser empleadas durante la preparación Las sales de los compuestos de formula I pueden ser formadas, por ejemplo, al hacer reaccionar un compuesto I con una cantidad de ácido o base, tal como una cantidad equivalente, en un medio tal como uno en el cual, la sal precipita en un medio acuoso seguido por liofilización

Los compuestos de fórmula I los cuales contienen una porción básica pueden formar sales con una variedad de sales orgánicas e inorgánicas Las sales de adición ejemplares incluyen acetatos (tal como aquellos formados con ácido acético o ácido trihaloacético, por ejemplo, ácido trifluoroacético), adipatos, alginatos, ascorbatos, aspartatos, benzoatos, bencensulfonatos, bisulfatos, boratos, butiratos, citratos, canforatos, canforsulfonatos, ciclopentanopropionatos, digluconatos, dodecilsulfatos, etanosulfonatos, fumaratos, glucoheptanoatos, glicerofosfatos, hemisulfatos, heptanoatos, hexanoatos, clorhidratos (formados con ácido clorhídrico), bromhidratos (formados con bromuro de hidrógeno), yodohidratos, 2-hidroxietanosulfonatos, lactatos, maleatos (formados con acido maleico), metanosulfonatos (formados con

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ácido metanosulfónico), 2-naftalenosulfonatos, nicotinatos, nitratos, oxalatos, pectinatos, persulfatos, 3-fenilpropionatos, fosfatos, picratos, pivalatos, propionatos, salicilatos, succinatos, sulfatos (tal como aquellos formados con ácido sulfúrico), sulfonatos (tal como aquellos mencionados aquí), tatratos, tiocianatos, toluensulfonatos tal como tosilatos, undecanoatos y similares

Los compuestos de fórmula I los cuales contienen una porción acídica pueden formar sales con una variedad de bases orgánicas e inorganicas Las sales básicas ejemplares incluyen sales de amonio, sales de metal álcali tal como sales de sodio, litio y potasio, sales de metales alcalino térreos tal como sales de calcio y magnesio, sales con bases orgánicas (por ejemplo, aminas orgánicas) tal como benzatinas, diciclohexilaminas, hidrabaminas (formadas con N,N-bis(deshidroabietil)etilendiamina), N-metil-D-glucaminas, N-metil-D-glucamidas, t-butil-aminas y sales con aminoácidos tal como arginina, lisina y similares

Los grupos que contienen nitrógeno básico pueden ser cuaternizados con agentes tal como haluros de alquilo inferior (por ejemplo, metilo, etilo, propilo y cloruros, bromuros y yoduros de butilo),

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sulfatos dialquilo (por ejemplo dimetilo, dietilo, dibutilo, y sulfatos de diamino), haluros de cadena larga (por ejemplo, cloruros, bromuros y yoduros de decilo, laurilo, miristilo y estearilo), haluros de aralquilo (por ejemplo bromuros de bencilo y fenetilo), y otros

Los profármacos y solvatos de los compuestos de la invención están también contemplados aquí El término "profármaco" como se empleó aquí, denota un compuesto el cual, después de la administración a un sujeto, se somete a conversión química mediante el proceso metabólico o químico para proporcionar un compuesto de la fórmula I, o una sal y/o solvato del mismo Los solvatos de los compuestos de fórmula I son preferiblemente hidratos

Hasta cierto punto tales compuestos de fórmula I, y sales del mismo, pueden existir en su forma tautomérica, todas las tales formas tautoméricas estan contempladas aquí como parte de la presente invención

Todos los estereoisómeros de los presentes compuestos, tales como aquellos los cuales pueden existir debido a los carbonos asimétricos en los varios substituyentes R y Z, incluyendo formas enantioméricas (las cuales pueden existir aún en la

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ausencia de carbonos asimétricos) y formas diastereoméricas, están contempladas dentro del ámbito de esta invención Los estereoisomeros individuales de los compuestos de la invención pueden, por ejemplo, estar substancialmente libres de otros isómeros, o pueden ser mezclados, por ejemplo, como racematos o con todos los otros, u otros estereoisómeros seleccionados Los centros quirales de la presente invención pueden tener la configuración S o R como se define por las recomendaciones IUPAC 1974

Los términos "incluyendo", "tal como", "por ejemplo" y similares, están propuestos para referirse a las modalidades ejemplares y no limitan el ámbito de la presente invención

Esquemas

Los compuestos de fórmula I pueden ser preparados usando la secuencia de las etapas resumidas abajo

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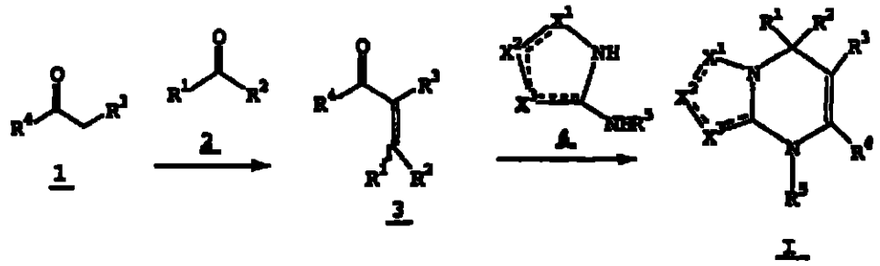
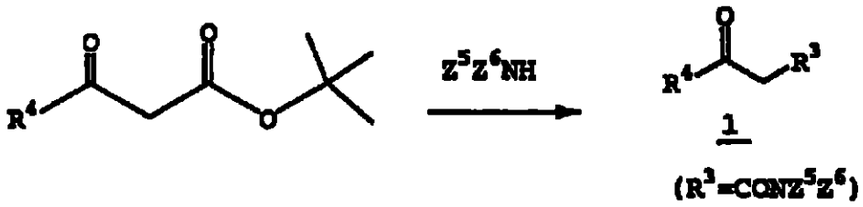


Los compuestos 1, 2 y 4 usados en esta preparación, están comercialmente disponibles o son fácilmente preparados por métodos bien conocidos por aquellos expertos en la técnica Por ejemplo, los compuestos de fórmula 1, donde R^3 = $CONZ^5Z^6$ pueden ser preparados por el método de Witzeman (JOC 1991, 56(5), 1713), el cual involucra el calentamiento de una amina y un t-butoxi-β-cetoéster puro o en un solvente adecuado (xilenos, toluenos, etc)



1

$(R^3=CONZ^5Z^6)$

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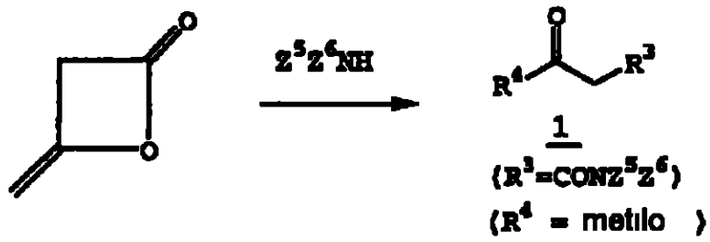
Alternativamente, los compuestos de fórmula 1, donde R' = metilo y R^3 =$CONZ^5Z^6$ pueden ser preparados mediante la reacción de una amina con diceteno en un solvente adecuado tal como diclorometano a temperaturas entre -100-22 °C

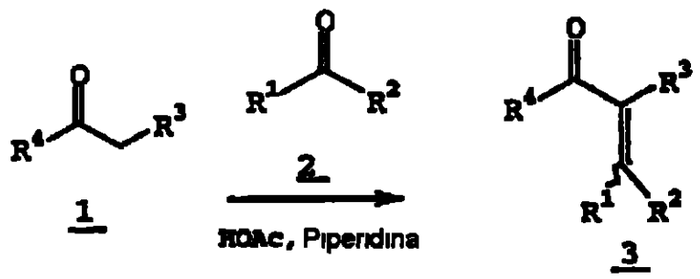


1

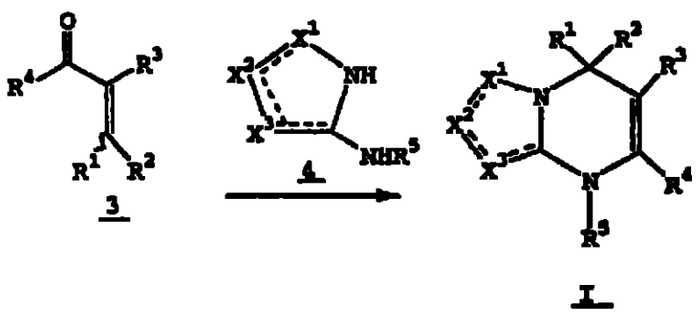
(R^3=$CONZ^5Z^6$)

(R^4 = metilo)

Los compuestos de fórmula 3, pueden ser preparados mediante la modificación de la condensación Knovenagel Por ejemplo, la condensación de un compuesto de fórmula 1, y un compuesto de formula 2 a temperaturas entre 22-170°C en solventes tal como tolueno o dimetilformamida en la presencia de un ácido tal como acido acético y una base tal como piperidina con remocion de agua generada durante la reacción por el uso de tamices moleculares secos de 4Å o una trampa Dean-Starl proporcionando compuestos de fórmula 3 como una mezcla de estereoisómeros cis y trans



Los compuestos de fórmula I pueden también, ser preparados mediante la condensación de compuestos de fórmula 3 con compuestos de fórmula 4 por el calentamiento a temperaturas entre 30-150 °C en solventes alcohólicos tal como etanol o propanol o mediante el calentamiento entre 30-150°C en un solvente tal como dimetilformamida y en la presencia de una base tal como acetato de sodio



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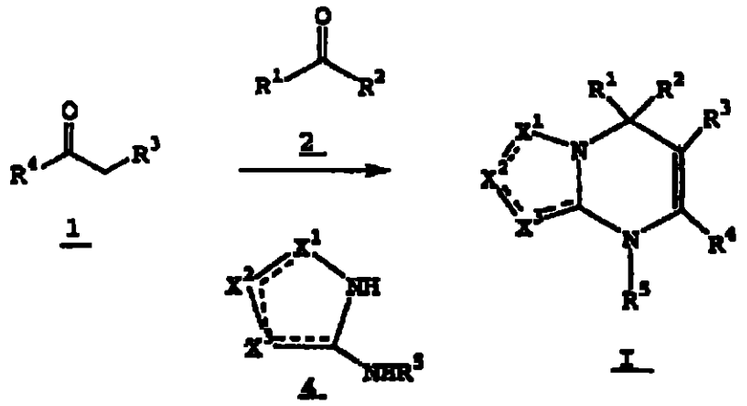
Los compuestos de fórmula I en donde R^3 = éster, pueden ser preparados por la condensación de compuestos de fórmula 1, fórmula 2 y heterociclos de fórmula 4 mediante el calentamiento entre temperaturas de 30-150°C en la presencia de una base tal como carbonato de sodio o bicarbonato de sodio en un solvente adecuado tal como dimetilformamida



Los compuestos de fórmula I donde R^3 = amida, pueden ser preparados por el tratamiento de los compuestos de fórmula I donde R^3 = éster con una amina adecuada y trietilaluminio en un solvente tal como tolueno a temperaturas entre 0-150°C

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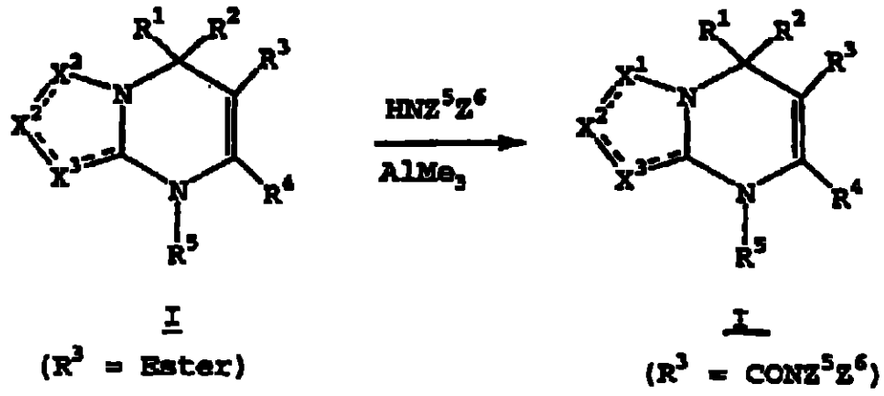

I
(R^3 = Ester)

I
(R^3 = $CONZ^5Z^6$)

Los compuestos de fórmula I donde R^3 = amida, pueden ser preparados mediante la condensación de los compuestos de formula I donde R^3 = COOH con una amina adecuada mediante los métodos de amidación, bien conocidos por aquellos expertos en la técnica Para el tratamiento ejemplo de un compuesto de fórmula I donde R^3 = COOH, con clorhidrato de 1-[3-(dimetilamino)propil]-3-etilcarbodiimida (EDCI) y dimetilaminopiridina (DMAP) en un solvente tal como diclorometano proporciona compuestos de fórmula I donde R^3 = amida

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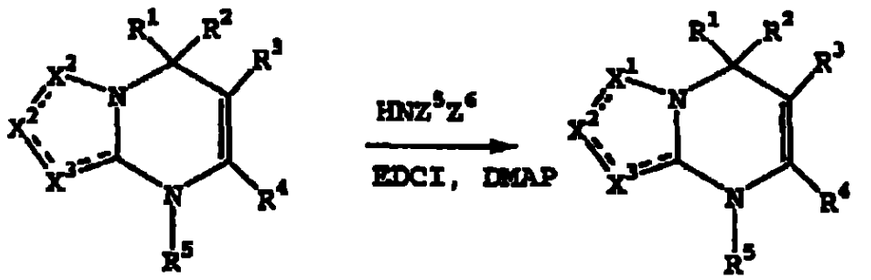
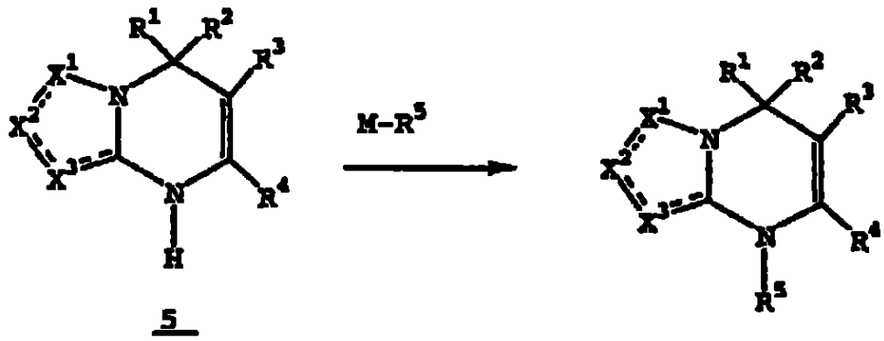


I
(R^3 = COOH)

I
(R^3 = $CONZ^5Z^6$)

Los compuestos de fórmula I donde R^5 es un substituyente preferentemente hidrógeno, pueden ser formados al hacer reaccionar un compuesto de fórmula 5 con una especie reactiva M-R^5, de manera tal que se obtiene un compuesto de fórmula Ia, donde M es Cl, Br, OR, etc , y R^5 es como se define anteriormente (preferentemente hidrógeno)



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Ia

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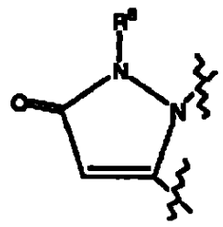
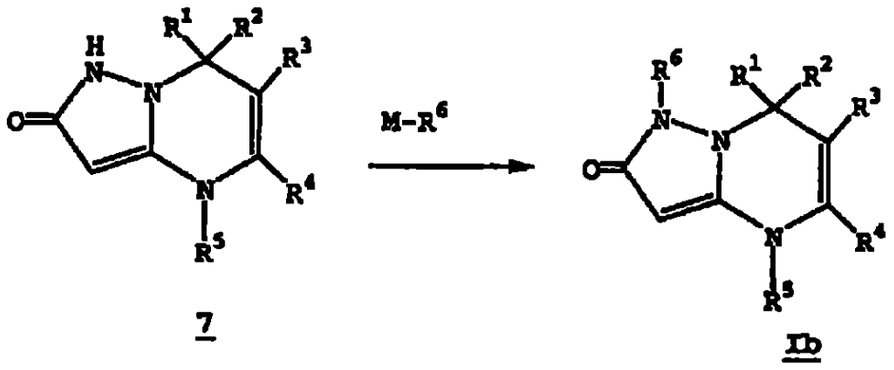
Los compuestos de fórmula I, donde X , X^2 y X^3 forman un anillo de la estructura



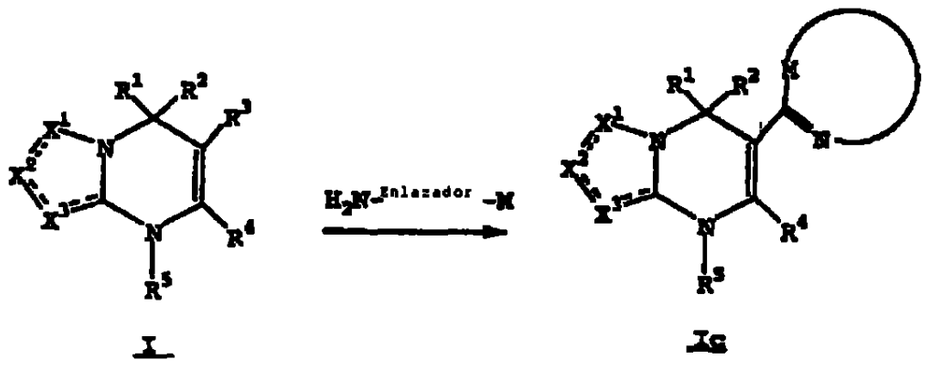
en donde R^6 es un substituyente preferentemente hidrógeno, puede ser formado al hacer reaccionar un compuesto de fórmula 7 con una especie reactiva $M-R^6$ de manera tal que se obtiene un compuesto de fórmula Ib, donde M es Cl, Br, OR, etc y R^6 es como se define anteriormente



7 Ib

Los compuestos de fórmula Ic donde R^3 es un amino, que contienen un heterociclo, pueden ser

formados mediante la condensacion de compuestos de fórmula I donde R^3 es un ácido o éster con una amina la cual está unida a través de un enlazador a M M puede ser NH_2, NHR, SH o OH La unidad enlazadora puede ser seleccionada de manera tal que se forman los heterociclos insubstituidos, substituidos o fusionados



I Ic

R^3= Ester o ácido

Los compuestos adicionales dentro del ámbito de la presente invencion, pueden ser preparados a partir de los compuestos obtenidos por los métodos descritos anteriormente a través de la conversión de los grupos substituyentes a otra funcionalidad mediante los métodos usuales de síntesis quimica, como se ilustra en los siguientes ejemplo

Los compuestos de fórmula I que contienen centros quirales pueden ser obtenidos en formas no

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racémicas mediante la síntesis o resolución no racemica por métodos bien conocidos por aquellos expertos en la técnica Los compuestos que no son racémicos, son designados como "quirales" en los ejemplos

En los ejemplos descritos abajo, puede ser necesario proteger la funcionalidad reactiva tal como grupos hidroxi, amino, tio o carboxi, cuando estos se desean en el producto final, para evitar su participación indeseada en las reacciones La introducción y remoción de los grupos protectores son bien conocidas por aquellos expertos en la técnica, véase por ejemplo (Gree, T W en "Protective Groups in Organic Synthesis", John Wiley and Sons, 1991)

Utilidad

Los compuestos de la presente invención son agentes antirrítmicos los cuales son empleados en la prevención y tratamiento (incluyendo alivіación parcial o cura) de arritmias Los presentes compuestos son particularmente empleados en la prevención selectiva y tratamiento de arritmias supraventriculares tal como fibrilación atrial, y palpitación atrial Mediante "prevención selectiva y

tratamiento de arritmias supreventriculares", se sugiere la prevención o tratamiento de arritmias supreventriculares, en donde la relación de la prolongación del periodo retractorio efectivo atrial hasta la prolongación del periodo refractorio efectivo ventricular es mayor que 1 1 Esta relacion es preferiblemente mayor que 4 1, más preferiblemente mayor que 10 1, y más preferiblemente de manera tal que la prolongación del periodo de respuesta refractorio efectivo atrial se alcanza sin prolongación significantemente detectable del periodo refractorio efectivo ventricular

Además, los presentes compuestos pueden bloquear el I_{Kur}, y así, pueden ser empleados en la prevención y tratamiento de todas las condiciones asociadas con I_{Kur} "Una condición asociada con I_{Kur}" es una alteración la cual se puede prevenir, parcialmente aliviar o curar mediante la administracion de un bloqueador I_{Kur} El gen KV1 5 se conoce por estar expresado en el tejido estomacal, tejido intestinal/colón, la arteria pulmonar, y las células beta pancreáticas Así, la administración de un bloqueador I_{Kur} podrá proporcionar tratamiento útil para la alteraciones tales como esofagitis con reflujo, dispepsia funcional, constipación, asma y

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diabetes Adicionalmente, el Kv1 5 se conoce por estar expresado en la pituitaria anterior Además, la administración de un bloqueador I_{Kur} podrá estimular la secreción de la hormona de crecimiento Los inhibidores de I_{Ku-} pueden adicionalmente, ser empleados en las alteraciones proliferativas celulares tales como leucemia, y padecimientos autoinmunes tales como artritis rehumatoide y rechazo al transplante

La presente invención además, proporciona métodos para la prevención o tratamiento de una o más alteraciones mencionadas anteriormente, que comprenden la etapa de administrar a un sujeto en necesidad del mismo, de una cantidad efectiva de al menos, un compuesto de la formula I Otros agentes terapéuticos tal como aquellos descritos abajo, pueden ser empleados con los compuestos inventivos en los presentes métodos En los métodos de la presente invención, tales otros agente(s) terapéuticos pueden ser administrados antes de, simultáneamente con o despues de la administración de los compuesto(s) de la presente invención

La presente invención también proporciona composiciones farmacéuticas que comprenden al menos, uno de los compuestos de la fórmula I o sales de los

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mismos, capaces de prevenir o tratar una o más de las alteraciones mencionadas anteriormente en una cantidad efectiva del mismo, y un vehículo o diluyente farmacéuticamente aceptable Las composiciones de la presente invención pueden contener otros agentes terapéuticos tal como se describe abajo, y pueden ser formuladas por ejemplo, mediante el empleo de vehículos o diluyentes sólidos o líquidos convencionales, así como también aditivos farmacéuticos de un tipo apropiado al modo de administración deseado (por ejemplo, excipientes, atadores, preservativos, estabilizadores, saborizantes, etc) de conformidad con las técnicas así como también aquellas conocidas en la técnica de formulación farmaceutica

Los compuestos de la fórmula I pueden ser administrados por cualquier medio adecuado, por ejemplo, oralmente, tal como en la forma de tabletas, cápsulas, gránulos o polvos, sublingualmente, bucalmente, parenteralmente, tal como por técnicas de infusión o inyección subcutánea, intravenosa, intramuscular o inyección intrasternal (por ejemplo, como soluciones o suspensiones acuosas o no acuosas estériles inyectables), nasalmente tal como por atomización para inhalación, tópicamente, tal como en

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la forma de crema o ungüento, o rectalmente tal como en la forma de supositorios, en formulaciones de dosificaciones unitarias que contienen vehículos o diluyentes farmacéuticamente aceptables no tóxicos Los presentes compuestos pueden, por ejemplo, ser administrados en una forma adecuada para liberación inmediata o liberación prolonada La liberacion inmediata o liberación prolongada puede ser alcanzada por el uso de composiciones farmacéuticas adecuadas que comprenden los presentes compuestos, o, particularmente en el caso de liberación prolongada, por el uso de dispositivos tal como implantes subcutáneos o bombas osmóticas En el caso en donde los compuestos de la fórmula I están siendo administrados para prevenir o tratar arritmias, los compuestos pueden ser administrados para alcanzar la conversión química a ritmo del seno normal, o pueden ser opcionalmente usados en conjunto con cardioconversión eléctrica

Las composiciones ejemplares para la administración oral incluyen suspensiones, las cuales pueden contener, por ejemplo, celulosa microcristalina para impartir volumen, ácido algínico o alginato de sodio como un agente de suspension, metilcelulosa como un incrementador de la viscosidad,

y agentes endulzadores o saborizantes tal como aquellos conocidos en la tecnica, y tabletas de liberación inmediata las cuales pueden contener, por ejemplo, celulosa microcristalina, fosfato dicálcico, almidón, estearato de magnesio y/o lactosa y/o otros excipientes, atadores, extendedores, desintegradores, diluyentes y lubricantes tal como aquellos conocidos en la técnica Los compuestos de fórmula I pueden también ser liberados a través de la cavidad oral mediante la administración sublingual y/o bucal Las tabletas moldeadas, tabletas comprimidas o tabletas secadas por congelamiento, son formas ejemplares las cuales pueden ser usadas Las composiciones ejemplares incluyen aquellas que formulan el presente compuesto(s) con diluyentes de disolución rápida, tal como manitol, lactosa, sucrosa y/o ciclodextrinas También incluidas en tales formulaciones pueden ser excipientes de peso molecular alto, tal como celulosas (avicel) o glicoles de polietileno (PEG) Tales formulaciones pueden también incluir un excipiente para ayudar a la adhesión de la mucosa tal como hidroxipropilcelulosa (HPC), hidroxipropilmetilcelulosa (HPMC), carboximetilcelulosa de sodio (SCMC), copolímero de anhídrido maleico (por ejemplo, Gantrez), y agentes

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para el control de la liberación tal como un polímero poliacrílico (por ejemplo, Carbopol 934) Lubricantes, deslizantes, saborizantes, agentes colorantes y estabilizadores pueden también ser agregados para facilidad de fabricación y uso

Las composiciones ejemplares para la administración por inhalación o aerosol nasal, incluyen soluciones en salina, la cual puede contener por ejemplo, alcohol bencílico u otros preservativos adecuados, promotores de la absorción para incrementar la biodisponibilidad, y/o otros agentes de solubilización o dispersion tal como aquellos conocidos en la técnica

Las composiciones ejemplares para la administración parenteral incluyen soluciones o suspensiones inyectables las cuales pueden contener, por ejemplo, diluyentes o solventes parenteralmente aceptables, no tóxicos adecuados, tal como manitol, 1,3-butandiol, agua, solución Ringer, una solución de cloruro de sodio isotónico, u otros agentes de suspensión y humectacion o dispersión adecuados, incluyendo mono o diglicéridos sintéticos, y ácidos grasos, incluyendo ácido oléico

Las composiciones ejemplares para la administración rectal incluyen supositorios, los

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cuales pueden contener, por ejemplo, un excipiente no irritante adecuado, tal como manteca de cacao, ésteres glicéridos sintéticos o polietilenglicoles, los cuales son sólidos a temperaturas ordinarias, pero se licúan y/ disuelven en la cavidad rectal para liberar el fármaco

Las composiciones ejemplares para la administración tópica incluyen un portador tópico tal como Plastibase (aceite mineral gelificado con polietileno)

La cantidad efectiva de un compuesto de la presente invención puede ser determinada por un experto ordinario en la técnica, e incluye cantidades de dosificaciones ejemplares para un humano adulto desde aproximadamente 0 001 hasta 100 mg/kg de peso corporal de un compuesto activo por día, el cual puede ser administrado en una dosis única o en la forma de dosis divididas, tal como de 1 a 4 veces por día Se entenderá que el nivel de dosis específica y la frecuencia de dosificacion para cualquier sujeto particular puede variarse y dependerá de una variedad de factores que incluyen la actividad del compuesto específico empleado, la estabilidad metabólica y la longitud de acción de tal compuesto, las especies, edad, peso corporal, salud general, sexo y dieta de

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sujeto, el modo y tiempo de administración, relacion de excreción, combinación del fármaco y severidad de la condición particular Los sujetos preferidos para el tratamiento incluyen animales, más preferiblemente especies de mamíferos tal como humanos, y animales domésticos tal como perros, gatos y similares, sometidos a las alteraciones mencionadas anteriormente

Los compuestos de la presente invención pueden ser empleados solos o en combinación con cada uno de los otros y/o otros agentes terapéuticos adecuados empleados en el tratamiento de las alteraciones mencionadas anteriormente, tales como otros agentes antirrítmicos, bloqueadores del canal de calcio, inhibidores de la ciclooxigenasa, inhibidores de la agregación de plaquetas, antagonistas del fibrinógeno, diuréticos, inhibidores de la enzima que convierten la angiotensina, antagonistas de la angiotensina II, agentes trombolíticos, antagonistas del receptor tromboxano, meméticos de la prostaciclina, o inhibidores de la fosfodiesterasa Otros agentes ejemplares antirrítmicos incluyen gentes Clase I (tal como propafenona y quinidina), agentes Clase II (tal como sotalol), y agentes Clase III (tal como dofetilido y

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amiodarona) Los bloqueadores del canal de calcio ejemplares, incluyen diltiazem, verapamil, nifedipina, y amlodipina Los inhibidores de la ciclooxigenasa ejemplares incluyen aspirina o indometacina Los inhibidores de la agregación de plaquetas ejemplares incluyen clopidogrel, ticlopideno o aspirina Los diuréticos ejemplares incluyen clorotiazida, clorhidrotiazida, flumetiazida, hidroflumetiazida, bendroflumetiazida, metilcorotiazida, triclorometiazida, politiazida, benztiazida, tricrinafeno de ácido etacrínico, clortalidona, furosemida, musolimina, bumetanida, triametrereno, amilorido o espironolactona Los inhibiodres de enzima que convierten la angiotensina ejemplares incluyen captopril, zofenopril, fosinopril, enalapril, ceranopril, cilazopril, delapril, pentopril, quinapril, ramipirilo, lisinopirilo o sales de tales compuestos Los antagonistas de la angiotensina II ejemplares incluyen, losartan, irbesartan o valsartan Los agentes trombilíticos ejemplares incluyen al activador del plasminogeno del tejido (tPA), tPA recombinante, estreptocinasa, urocinasa, prourocinasa, complejo activador de la estreptocinasa del plasminógeno anisoilado (APSAC, Eminase, Beecham

Laboratories) o activadores del plasminógeno de la glándula salival animal Los antagonistas del receptor tromboxano ejemplares incluyen ifetrobano

Los otros agentes terapéuticos anteriores, cuando se emplean en combinación con los compuestos de la presente invención, pueden ser usados, por ejemplo, en tales cantidades indicadas en la Physician's Desk Reference (PDR) o como de otro modo se determina por uno de los expertos ordinarios en la técnica

Todos los documentos citados en la presente especificación están incorporados aquí por referencia en su totalidad

Los siguientes ejemplos y preparaciones describen la manera y proceso de elaboración y uso de la invención, y son ilustrativos en lugar de limitativos Se entenderá que pueden ser otras modalidades las cuales caen dentro del espíritu y ámbito de la invención como se define por las reivindicaciones adjuntas a estos Las abreviaciones empleadas aquí están definidas abajo

DCM= diclorometano

DMPA= dimetilaminopiridina

DMF= dimetilformamida

DMPU= 1,3-dimetil-3,4,5,6-tetrahidro-2(1*H*)-

pirimidinona

EDCI (o EDC) = clorhidrato de 1-(3-dimetilaminopropil)-3-etilcarbodiimida

M + H = masa monoisotópica más un proton

Et = etilo

h = horas

HPLC = cromatografía líquida de alta resolución

HOBT = hidroxibenzotriazol

LC/MS = cromatografía líquida/espectrometría de masas

Me = metilo

min = minutos

MS = espectrometría de masas

NaOAc = acetato de sodio

Ph = fenilo

PPA = ácido fosfórico

Pr = propilo

Py = piridina

PyBrOP= hexafluorofosfato de bromo-tris-pirrolidino-fosfonio

TA = temperatura ambiente

Rt = tiempo de retención

TEA = trietilamina

TFA = ácido trifluoroacético

TLC = cromatografía de capa delgada

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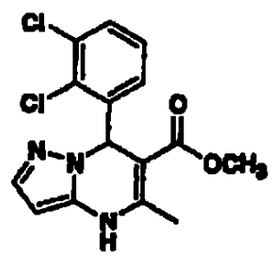
THF = tetrahidrofurano

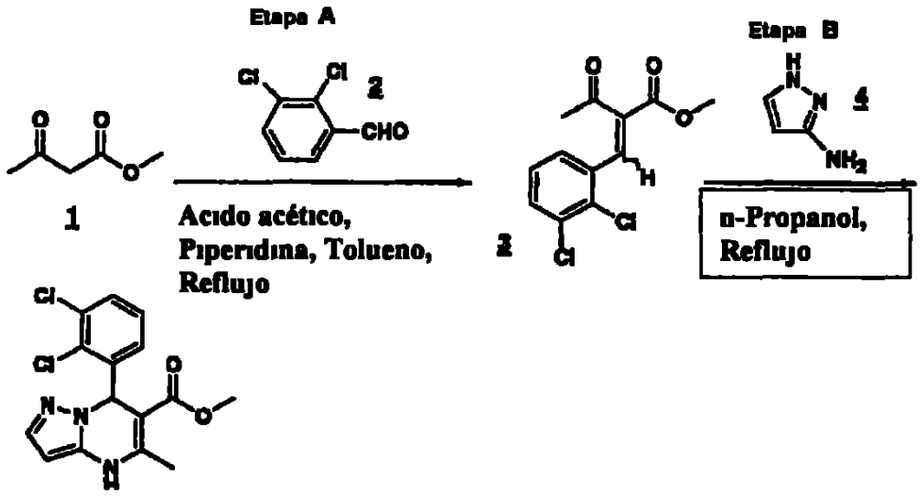
TMSOTf = trifluorometanosulfonato de trimetilsililo

Ejemplo 1

Ester metílico del ácido 7-(2,3-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxílico



Método



Etapa A Una mezcla de acetoacetato de metilo 1 (5 mL, 46 mmol), 2,3-diclorobenzaldehido 2 (8 1 g, 46 mmol), piperidina (1 1 ml, 12 mmol), y ácido acético (0 6 mL, 11 mmol) en tolueno (200 mL) se sometió a reflujo durante la noche con remoción azeotrópica del agua vía una Trampa Dean-Stark La mezcla se enfrió a temperatura ambiente, se enfrió rápidamente con agua, se transfirió a un embudo separador, se diluyó con acetato de etilo, se lavó con NaOH (1M), acuoso, HCl(1M) acuoso, agua y salmuera y se concentró in vacuo El residuo se purificó por cromatografía instantanea (gel de sílice, acetato de etilo/hexanos al 33%) para proporcionar 10 8 g (85% de rendimiento) del compuesto 3 como una mezcla de diasterómeros Columna Balística LC/MS de Fase Inversa YMC S5 ODS 4 6 x 50 mm, detección UV a 220λ, gradiente 4 minutos (MeOH/H_2O al 10% con TFA al 0 1% - MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Diastereomero A, Rt= 3 51 min, (53%) Diastereómero B, Rt= 3 70 min (45%) MS (M+H 273)

Etapa B Una mezcla del compuesto 3 (5g, 18 3 mmol), 3-aminopirazol 4 (1 5 g, 18 3 mol) en 1-propanol (60 mL) se sometió a reflujo por 6 horas La mezcla se enfrió a temperatura ambiente se concentró y

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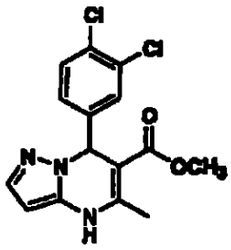
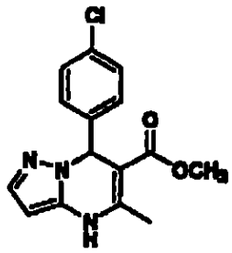
recristalizó de acetato de etilo/hexanos para dar 1 25 g (20%) del compuesto del titulo como un sólido amarillo El licor madre se concentró y purificó por cromatografía instantánea (gel de sílice, metanol/diclorometano al 5%) para dar una adicional de 1 62 g (26%) del compuesto del titulo Rendimiento combinado 2 87 g (46%) Columna Balística LC/MS de Fase Inversa YMC S5 ODS 4 6 x 50 mm, detección UV a 220λ, gradiente 4 minutos (MeOH/H_2O al 10% con TFA al 0 1% - MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt= 3 38 min, (96% puro) MS (M+H 338) HMR ($CDCl_3$, 400 MHz), 7 9 (1H, app S), 7 15 (3H, m), 6 91 (1H, s), 5 52 (1H, app s), 3 61 (3H, s), 2 39 (3H, s)

Ejemplos 2 y 3

Los compuestos de los Ejemplos 2 y 3, mostrados en la tabla proporcionada abajo, se prepararon de una manera similar a aquella descrita en el Ejemplo 1

Ejemplo	Estructura	Nombre	(M+H)
2		Éster metílico del ácido 7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxílico	338
3		Éster metílico del ácido 7-(4-clorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxílico	303

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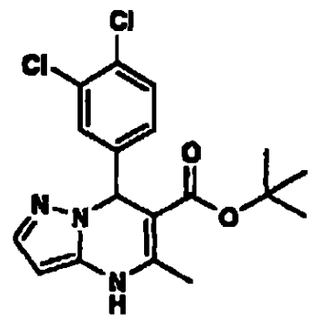
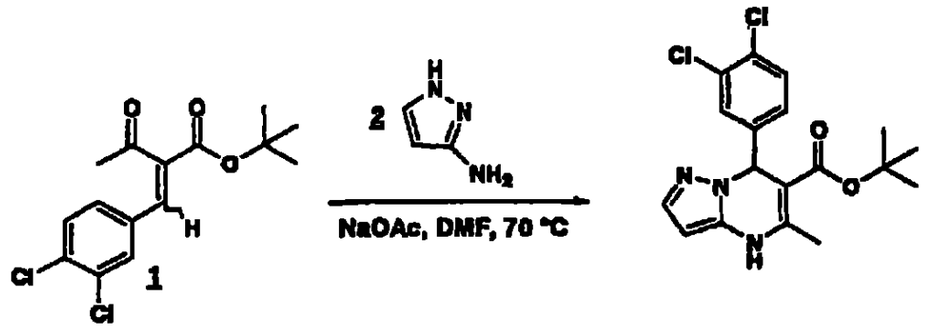
Ejemplo 4

Ester 1,1-dimetiletílico del ácido 7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxílico



Método 1

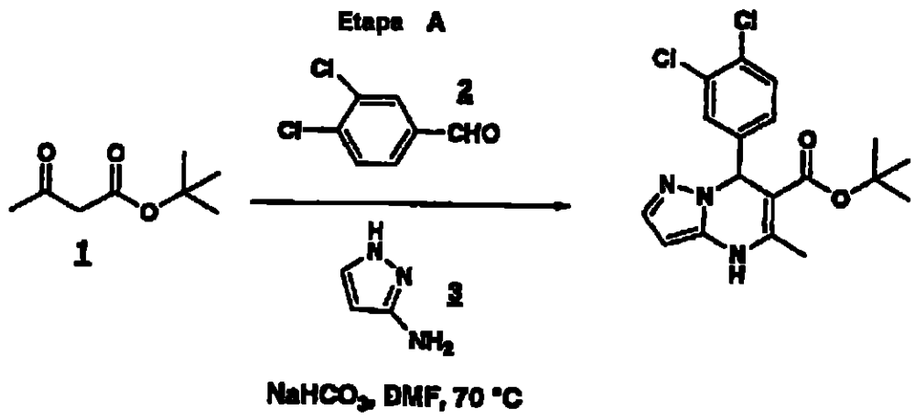


Compuesto 1 El compuesto 1 se preparó por la condensación de t-butoxiacetoacetato y 2,4-diclorobenzaldehido como se describe en el Ejemplo 1 etapa A

Compuest del Titul Una mezcla del compuesto 1 (44 4 g, 141 mg, 141 mmol), 3-aminopirazol 2 (17 6 g 212 mmol) y acetato de sodio (46 3 g, 564 mmol) en dimetilformamida (300 mL) se agitó a 70°C durante la noche (17 h) La mezcla se enfrió a temperatura ambiente, se transfirió a un embudo separador, se diluyó con agua y acetato de etilo, se lavó con agua (una pequeña cantidad de metanol se agregó para la dispersión de las emulsiones que se formaron) y salmuera, se secó sobre sulfato de sodio anhidro y se concentró Se formó un precipitado Lo precipitado se colectó y se lavó con acetato de etilo, éter etílico y hexanos y se secaron para dar 8 93 g El licor madre se concentró para dar una segunda cosecha del precipitado 9 32 g El análisis LC/MS indicó que los precipitados no fueron puros Lo precipitado se combinó, se disolvió en diclorometano y se concentró en suficiente gel de sílice, de manera que se obtuvo un polvo de fluencia suave El polvo resultante se cargó en una columna de cromatografía empacada con gel de silice y diclorometano La elución con diclorometano al 100% seguida por metanol/dicloromento al 3% dio 15 1 g (29% rendimiento) del compuesto del titulo La Columna Balística LC/MS de Fase Inversa YMC S5 ODS 4 6 x 50

mm, detección UV a 220λ, gradiente 4 minutos ($MeOH/H_2O$ al 10% con TFA al 0 1% - $MeOH/H_2O$ al 90% con TFA al 0 1%), 4 mL/min Rt= 4 63 min, (97% puro) MS (M+H 380 HNM ($CDCl_3$, 400 MHz), 7 41 (2H, m), 7 33 (1H, d, J=2 Hz), 7 08 (1H, m), 6 21 (1H, s), 5 68 (1H, d, J=2 Hz), 2 43 (3H, s), 1 37 (9H, s)

Metodo 2



Una mezcla de t-butoxiacetoacetato 1 (22 6 g, 143 mmol), 3,4-diclorobenzaldehido 2 (25 0 g, 143 mmol), 3-aminopirazol 3 (15 4 g, 185 mmol) y bicarbonato de sodio (36 g, 428 mmol) en dimetilformamida (250 mL) se agitó a 70°C durante la noche (18 h) La mezcla se enfrió a temperatura ambiente, se enfrió rápidamente con acetato de etilo

y agua, se transfirió a un embudo separador, se lavó con agua y salmuera, se secó sobre sulfato de sodio, se filtró y se concentró El residuo se recristalizó de acetato de etilo/hexanos para dar 16 8 g (31% rendimiento) del compuesto del titulo como un sólido blanco

Los datos para el compuesto del titulo se dan en el método 1

Ejemplos 5 y 6

Los compuestos de los Ejemplos 5 y 6 mostrados en la tabla proporcionada a bajo, se prepararon de una manera similar a aquella descrita en el Ejemplo 4, Método 1

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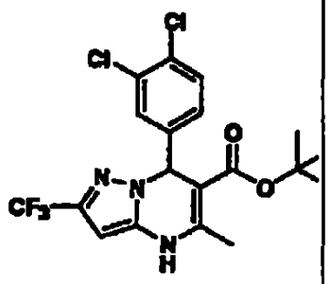
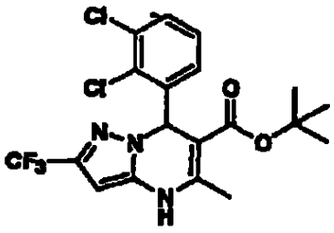
Ejemplo	Estructura	Nombre	(M+H)
5		Éster 1,1-dimetiletílico del ácido 7-(3,4-diclorofenil)-4,7-dihidro-5-metil-2-(trifluorometil) pirazolo[1,5-a]pirimidin-6-carboxílico	448
6		Ester 1,1-dimetiletílico del ácido 7-(2,3-diclorofenil)-4,7-dihidro-5-metil-2-(trifluorometil) pirazolo[1,5-a]pirimidin-6-carboxílico	448

Ejemplos 7-11

Los compuestos de los Ejemplos 7-11, mostrados en la tabla proporcionada a bajo, se prepararon en una manera similar a aquella descrita en el Ejemplo 4, Método 2 El compuesto del Ejemplo 4, Método 2 podría resolverse en los correspondiente enantiómeros **A** (Ejemplo 8) y **B** (Ejemplo 9) por HPLC quiral preparativo (Columna Chiracel OD (50 x 500 mm), elutendo con 7% de isopropanol/hexanos que contienen 0 1% de trietilamina amina a 50 mL/min), detección UV a 254 λ, HPLC analitico (Columna Chiracel OD (4 6 x 250 mm), eluyendo con 10% de isopropanol/hexanos que contienen 0 1% de trietilamina amina a 1 mL/min), detección UV a 254 λ, enantiómero **A** (Rt= 6 98 min, 98% ee), enantiómero **B** (Rt= 9 22 min, 98% ee)

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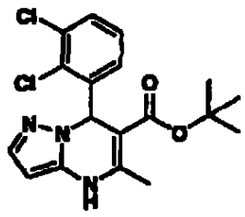
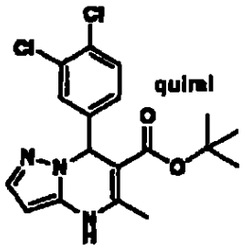
Ejemplo	Estructura	Nombre	(M+H)
7		Ester 1,1-dimetiletílico del ácido 7-(2,3-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxílico	380
8		Enantiómero A del Ester 1,1-dimetiletílico del ácido 7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxílico	380

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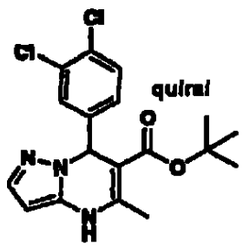
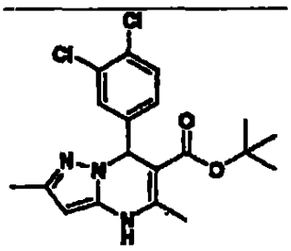
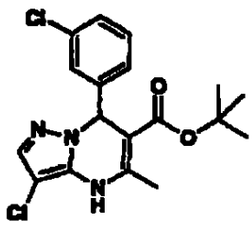
9		Enantiómeor B del Ester 1,1-dimetiletílico del ácido 7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxílico	380
10		Ester 1,1-dimetiletílico del ácido 7-(3,4-diclorofenil)-4,7-dihidro-2,5-dimetilpirazolo[1,5-a]pirimidin-6-carboxílico	394
11		Ester 1,1-dimetiletílico del ácido 3-cloro-7-(3-clorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxílico	380

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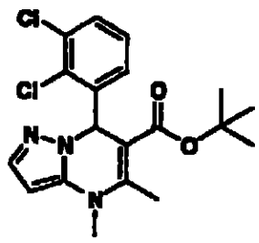
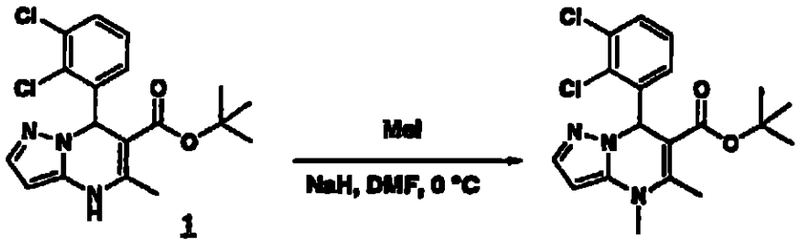
Ejemplo 12

Ester 1,1-dimetiletílico del ácido 7-(2,3-diclorofenil)-4,7-dihidro-4,5-dimetilpirazolo[1,5-a]pirimidin-6-carboxílico



Método



1

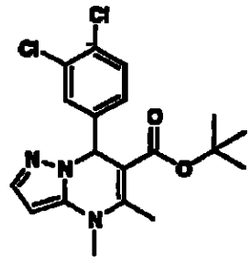
Compuesto 1 El compuesto 1 se preparó como se describe en el Ejemplo 4, método 1

Compuesto del título Se agrego hidruro de sodio (0 186 g, 7 76 mmol) a una solución a 0°C de 1 (2 27 g, 5 97 mmol) en dimetilformamida (30 mL) Después de 10 minutos, se agregó yoduro de metilo (0 41 mL, 6 57

mmol) Después de un adicional de 85 minutos, la mezcla se enfrió rápidamente con una solución de cloruro de amonio saturado, se diluyó con acetato de metilo, se transfirió a un embudo separador, se lavo con cloruro de amonio saturado, agua y salmuera, se secó sobre sulfato de sodio anhidro y se concentró con suficiente gel de sílice de manera que se obtuvo un polvo de fluencia suave El polvo resultante se cargó en una columna de cromatografía empacada con diclorometano al 100% La elución con acetato de etilo/diclorometano 0-10% dio 1 16 g (49%) del compuesto del titulo como un sólido ligeramente amarillo Columna Balística LC/MS de Fase Inversa YMC S5 ODS 4 6 x 50 mm, detección UV a 220λ, gradiente 4 minutos, Solvente B/A gradiente 40-100% (Solvente A MeOH/H_2O al 10% con TFA, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt= 3 46 min, (96% puro) MS (M+H 394) HMR (CD_3Cl, 400 MHz) 7 39 (1H, d, J=2 Hz), 7 35 (1H, m), 7 11 (1H, m), 6 91 (1H, s), 5 58 (1H, d, J=2 Hz), 2 38 (3H, s), 2 62 (3H, s), 1 27 (9H, s)

Ejemplo 13

Ester 1,1-dimetiletílico del ácido 7-(3,4-diclorofenil)-4,7-dihidro-4,5-dimetilpirazolo[1,5-a]pirimidin-6-carboxílico



El compuesto del titulo se preparó de una manera similar a aquella proporcionada en el Ejemplo 12, proporcionando un compuesto con (M+H) 394

Ejemplo 14

Ester 1,1-dimetiletílico del ácido 4,7-dihidro-5-metil-7-(1-metiletil)pirazolo[1,5-a]pirimidin-6-carboxílico

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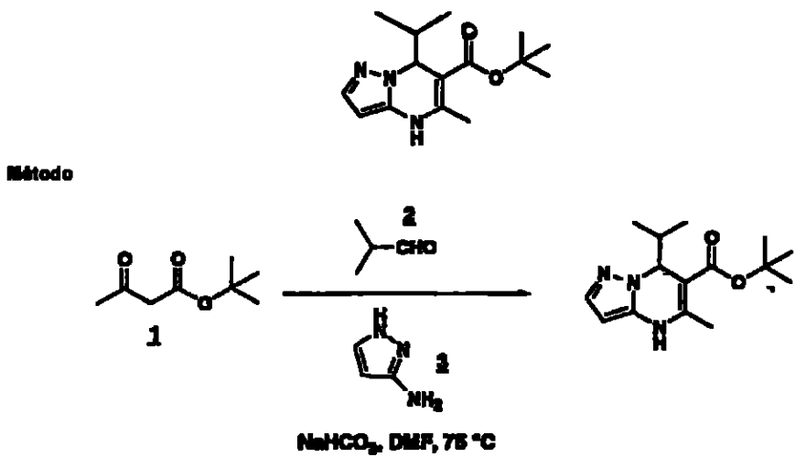


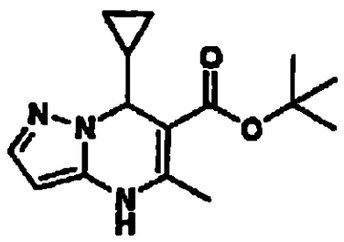
Tubo sellado

Un tubo de presión se secó con un disparo de calor bajo nitrógeno El tubo de presión se cargó en el siguiente orden con isobutiraldehido 2 (0 262 g, 3 63 mmol), dimetilformamida (3 mL), t-butoacetoacetato 1 (0 574 g, 3 63 mmol), 3-aminopirazol 3 (0 362 g, 4 36 mmol) y acetato de sodio (1 22 g, 14 5 mmol) La mezcla se chorreó con nitrógeno El tubo se selló y calentó a 75°C y se agitó durante la noche La mezcla se enfrió a temperatura ambiente, se diluyó con acetato de etilo a un volumen de 20 mL, se lavó con cloruro de litio (2 4 M, 10 mL) y salmuera, se secó sobre sulfato de sodio anhidro, se filtró y concentró para dar 1 02 de un aceite amarillo El aceite se purificó por cromatografía instantánea (sílice, acetato de

etilo/heptano al 45%) para dar 0 42 g (41% rendimiento) del compuesto del titulo Columna Balística LC/MS de Fase Inversa YMC S5 ODS 4 6 x 50 mm, detección UV a 220λ, gradiente 4 minutos Solvente B/A 0-100% (Solvente A MeOH/H_2O al 10% con PPA al 0 2%, Solvente B MeOH/H_2O al 90% con PPA al 0 2%), 4 mL/min Rt= 3 83 min, (100% puro) Columna Balística LC/MS de Fase Inversa YMC S5 ODS 4 6 x 50 mm, deteccion UV a 220λ, gradiente 4 minutos, Solvente B/A 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt= 3 06 MS (EM, M+1 278) HMR ($CDCl_3$, 400 MHz) 7 37 (1H, d, J=2 2 Hz), 6 35 (1H, s), 5 55 (1H, d, J=1 8Hz), 5 29 (1H, d, J=2 2 Hz), 2 41 (3H, s), 1 50 (9H, s), 1 28-1 19 (1H, m), 1 07 (3H, d, J=7 0Hz), 0 60 (3H, d, J=7 0 Hz)

Ejemplo 15

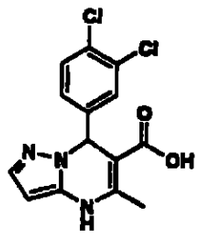
Ester 1,1-dimetiletílico del ácido 7-ciclopropil-4,7-dihidro-5-metilpirazolo-[1,5-a]pirimidin-6-carboxílico



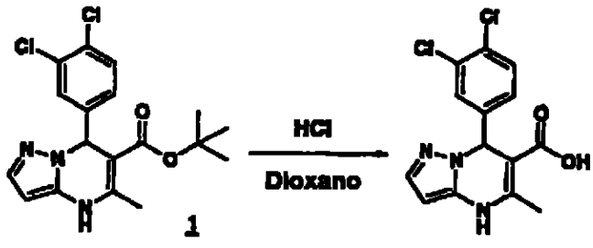
El compuesto del título se preparó de una manera similar como aquella proporcionada en el Ejemplo 14, proporcionando un compuesto con (M+H) 275

Ejemplo 16

Acido 7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxílico



Método



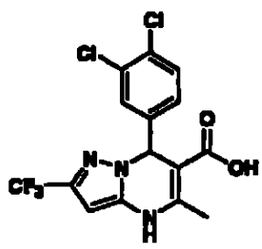
1

Compuesto 1 El compuesto 1 se preparo como se describe en el Ejemplo 4

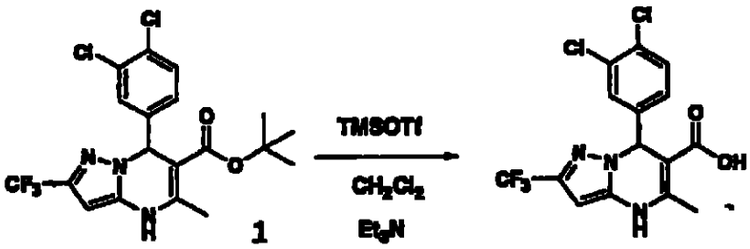
Compuesto del Titulo Se agregó HCl (4M en dioxano) al compuesto sólido 1 (1 13 g, 2 97 mmol) a temperatura ambiente Se disuelven los sólidos y se forman precipitados La mezcla de reacción espesa resultante se dejó agitar durante la noche y se concentró in vacuo para dar 1 14 g (contiene dioxano al 120%) del compuesto del titulo como un sólido blanco Columna Balística LC/MS de Fase Inversa YMC S5 ODS 4 6 x 50 mm, detección UV a 220λ, gradiente 4 minutos, Solvente B/A (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt= 3 54 min, (93% puro) MS (M+H 324) HMR (CD_3OD, 400 MHz), 7 96 (1H, d, J=3Hz), 7 51 (2H, m), 7 21 (1H, m), 6 49(1H, s), 6 11 (1H, d, J=3Hz), 2 51 (3H, s) El compuesto del titulo se usó en las reacciones subsecuentes sin purificación adicional

Ejemplo 17

Acido 7-(3,4-diclorofenil)-4,7-dihidro-5-metil-2-(trifluorometil)pirazolo[1,5-a]pirimidin-6-carboxílico



Método



1

Compuesto 1 Compuesto 1 (el compuesto del Ejemplo 5) se preparó de una manera similar a aquella que se describe en el Ejemplo 4

Compuesto del Titulo Se agregó trifluorometanosulfonato de trimetilsililo (0 873 mL, 4 82 mmol) a una solución a temperatura ambiente del

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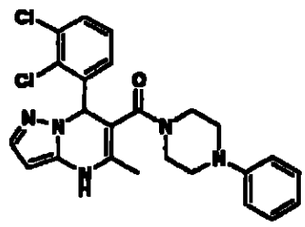
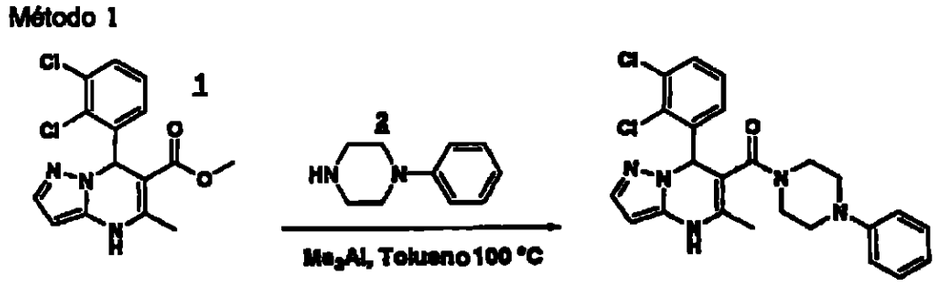
compuesto 1 (1 08 g, 2 41 mmol) en diclorometano (50 mL) Después de 2 horas, se agregó trietilamina (0 672 ml, 4 82 mmol), y la mezcla de reacción se vertió en agua La capa orgánica se separó y se secó sobre Na_2SO_4, se concentró, y purificó por cromatografía instantánea (acetato de etilo/hexano al 10% → acetato de etilo 100%) para dar 0 71 g (75% rendimiento) del compuesto del titulo como un sólido blanco MS (M+H 392)

Ejemplo 18

1-[[7-(2,3-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-fenilpiperazina



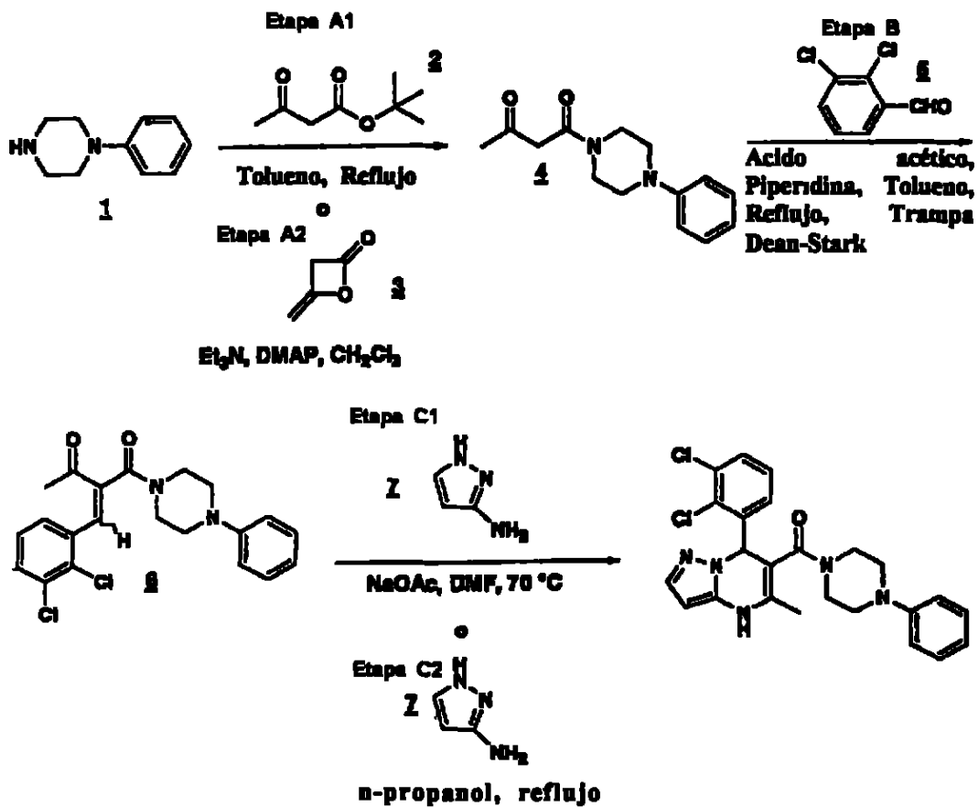


290

Compuesto 1 El compuesto 1 se preparó como se describe en el Ejemplo 1

Compuesto del Título Se agregó trimetilaluminio (1 1 mL, 2 2 mmol, 2M en tolueno) en forma de gotas a una solución a temperatura ambiente de 1-fenilpiperazina 2 (0 4 mL, 2 2 mmol) en tolueno (7 mL) Después de una hora, el compuesto 1 (0 50 g, 1 5 mmol) se agregó y la mezcla resultante se agitó a 100°C por 18 horas La mezcla se enfrió a temperatura ambiente, se enfrió rápidamente con agua, se diluyó con acetato de etilo, se transfirió a un embudo separador, se lavó con HCl acuoso (1M), agua y salmuera, se secó sobre sulfato de sodio anhidro y se concentró in vacuo El residuo se purificó por cromatografía instantánea (gel de sílice, acetato de etilo/hexanos al 50%, seguido por metanol/diclorometano al 5% para proporcionar 0 22 g (32%) de un sólido, el cual se purificó además por recristalización de metanol/éter etílico para dar 0 15 g (22%) del compuesto del titulo Columna Balística LC/MS de Fase Inversa YMC S5 ODS 4 6 x 50 mm, detección UV a 220λ, gradiente 4 minutos, Solvente B/A 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt= 3 58 min, (92% puro) MS

(M+H 468) Los datos adicionales para el compuesto del título se reportan en el Método 2, etapa C, variación 1



Etapa A Variación 1 Una mezcla de N-fenilpiperazina 1 (6 7 mL, 41 mmol) y t-butoxiacetoacetato 2 (6 8 mL, 45 mmol) en tolueno (50 mL) se sometio a reflujo durante la noche La mezcla se enfrió a temperatura ambiente, se transfirió a un embudo separador, se diluyó con acetato de etilo y se extrajo (3X) con HCl (1M) acuoso Los extractos HCl se combinaron y se lavaron con éter etílico (2X), se hicieron basicos (pH 9) con NaOH acuoso (p/v al 50%) y se extrajeron con acetato de etilo Los extractos de acetato de etilo se combinaron, se lavaron con agua y salmuera, se secaron sobre sulfato de sodio anhidro, se filtraron y concentraron para dar 9 76 g (97 6%) del compuesto 4 como un aceite ámbar espeso Columna Balística LC/MS de Fase Inversa YMC S5 ODS 4 6 x 50 mm, detección UV a 220λ, gradiente 4 minutos, Solvente B/A 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt= 1 65 min, (100% puro) MS (M+H 247) HMR ($CDCl_3$, 400 MHz), 7 28 (2H, m), 6 91 (3H, m), 3 80 (2H, m), 3 78 (2H, m), 3 59 (4H, m), 3 19 (4H, m), 2 30 (3H, s)

Etapa A Variación 2 Se agregó lentamente Diceteno 3 (5 50 g, 65 5 mmol) durante 15 minutos, a una solución a 0°C de 4-fenilpiperazina 1 (5 31 , 32 27 mmol) en diclorometano (50 mL) El TLC después de 4 horas, indicó que el compuesto 1 no se consumió completamente Se agrego diceteno adicional (5 50 g, 65 5 mmol) Después de unas 1 5 horas adicionales, la reacción se enfrió rapidamente con NaOH 1N, se transfirio a un embudo separador, lavado con NaOH 1H y salmuera, se secó sobre sulfato de sodio, se concentró en suficiente gel de sílice de manera tal que se obtuvo un polvo de flujo suave El polvo resultante se cargó en una columna de cromatografía preempacada con gel de sílice y acetato de etilo/hexanos al 50% La elución con acetato de etilo/hexanos al 50-100% dió 8 2 g (100%) de un compuesto 4 como un aceite amarillo espeso Los datos para el compuesto 4 se dio anteriormente en la Etapa A variación 1

Etapa B Una mezcla del compuesto 4 (9 76 g, 40 mmol), 2,3-diclorobenzaldehido 6 (7 89 g, 45 mmol), piperidina (1 0 ml, 10 mmol), ácido acético (0 59 mL, 10 mmol) en tolueno (100 mL) se sometió a reflujo

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durante la noche con remoción azeotrópica de agua vía una trampa Dean-Stark La mezcla se enfrió a temperatura ambiente y se concentró in vacuo y se usó típicamente en las reacciones subsecuente sin purificación El compuesto **6** puede ser Purificado por cromatografía en gel de sílice (acetato de etilo/hexanos al 30-40%) Columna Balística LC/MS de Fase Inversa YMC S5 ODS 4 6 x 50 mm, detección UV a 220λ, gradiente 4 minutos, Solvente B/A 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt= 3 83 min, (96% puro) MS (M+H 404) HMR ($CDCl_3$ 400 MHz), 7 82 (1H, s), 7 55 (1H, dd, J=1, 8 Hz), 7 48 (1H, dd, J=1, 8 Hz), 7 23 (3H, m), 6 89 (1H, app T, 7 Hz), 6 81 (2H, d, J=8 Hz), 3 78 (2H, m), 3 34 (1H, m), 3 23 (2H, m), 2 96 (1H, m), 2 85 (1H, m), 2 50 (3H, s), 2 42 (1H, M)

Etapa C Variación 1 Una mezcla del compuesto **6** (16 g, 40 mmol), 3-aminopirazol **7** (5 1 g, 62 mmol) y acetato de sodio (10 1 g, 123 mmol) en dimetilformamida (100 mL) se agitó a 70°C durante la noche (17 h) La mezcla se enfrió a temperatura ambiente, se transfirió a un embudo separador, se

diluyó con agua y acetato de etilo, se lavó con agua (una pequeña cantidad de metanol se agregó para dispersar las emulsiones que se formaron), y salmuera, se secó sobre sulfato de sodio anhidro y se concentró El residuo resultante se purificó por cromatografía en gel de sílice La elución con acetato de etilo/hexanos al 50%, seguida por acetato de etilo al 100%, proporcionó 6 2 g (33% rendimiento del compuesto 1) del compuesto del titulo El compuesto del titulo podrá resolverse en los enantiómeros correspondientes **A** (Ejemplo 28) y **B** (Ejemplo 29) por HPLC quiral preparativo (Columna Chiracel OD (50 X 500 mm), eluyendo con isopropanol/hexanos al 30%, conteniendo 0 1% de trietilamina a 50 mL/min), detección UV a 254 λ, enantiómero **A** Rt= 42 min, enantiómero **B** Rt= 54 min HPLC analítico (Columna Chiracel OD (4 6 x 250 mm), eluyendo con isopropanol/hexanos al 30% contiene 0 1% de trietilamina a 1 mL/ min), detección UV a 254 λ, enantiómero **A** Rt= 11 7 min, enantiómero **B** Rt= 17 6 min Los datos dados para el enantiómero **A** Columna Balística LC/MS de Fase Inversa YMC S5 ODS 4 6 x 50 mm, detección UV a 220λ, gradiente 4 minutos, Solvente B/A 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al

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0 1%), 4 mL/mın Rt= 3 54 mın, (91% puro) MS (M+H 468) HMR (Sal de HCl de 8a, $CDCl_3$ 400 MHz), 7 94 (1H, d, J=3 Hz), 7 56 (8H, m), 7 38 (1H, m), 6 05 (1H, d, J= 3Hz), 4 23 (1H, m), 3 57 (7H, m), 2 01 (3H, s)

Etapa C Varıacıón 2 Una mezcla del compuesto 5 (6 0g, 15 mmol), 3-amınopırazol 7 (1 24 g, 15 mmol) en n-propanol (50 mL), se sometıó a reflujo durante la noche (19 h) La mezcla se enfrıó a temperatura ambıente, se transfırıó a un embudo separador, se dıluyó con acetato de etılo Un ıntenso por lavar la solucıón con cloruro de amonıo saturado, resultó en la formacıón de un precıpıtado Lo precıpıtado se dısolvıó con agua y metanol La mezcla resultante se lavó con agua y salmuera, se secó sobre sulfato de sodıo anhıdro y se concentró El resıduo resultante se purıfıcó por cromatografía en gel de sílice La elucıón con acetato de etılo/hexanos al 70% seguıdo por acetato de etılo al 100%, proporcıonó 2 7 g (39% rendımıento) del compuesto del tıtulo como un sólıdo blanco El compuesto podrá resolverse en los enantıómeros **A** y **B** correspondıentes como se descrıben en la Etapa C varıacıón 1

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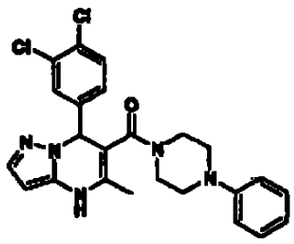
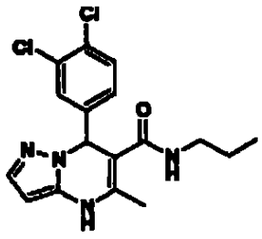
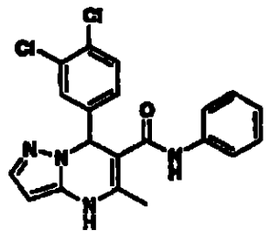
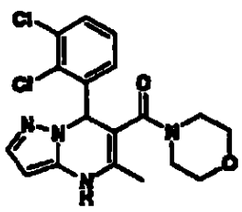
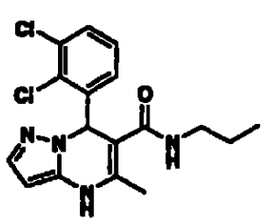
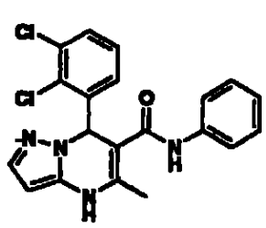
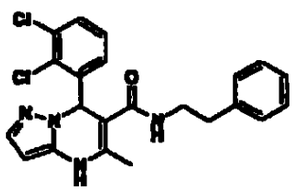
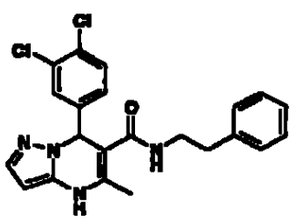
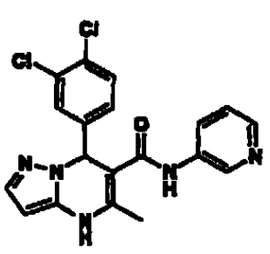
Ejemplos 19-27

Los compuestos de los Ejemplos 19-27, mostrados en la tabla proporcionada abajo, se prepararon de una manera similar a aquella descrita en el Ejemplo 18, Método 1

Ejemplo	Estructura	Nombre	(M+H)
19		1[[7-(3,4-Diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-fenilpiperazina	468
20		7-(3,4-Diclorofenil)-4,7-dihidro-5-metil-N-propilpirazolo[1,5-a]pirimidin-6-carboxamida	365

21		7-(3,4-Diclorofenil)-4,7-dihidro-5-metil-N-fenil-pirazolo[1,5a] piramidin-6-carboxamida	399
22		4-[[7-(2,3-Diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]morfolina	393
23		7-(2,3-Diclorofenil)-4,7-dihidro-5-metil-N-propilpirazolo[1,5a] pirimidin-6-carboxamida	365
24		7-(2,3-Diclorofenil)-4,7-dihidro-5-metil-N-fenilpirazolo[1,5-a]pirimidin-6-carboxamida	399

299

25		7-(2,3-Diclorofenil)-4,7-dihidro-5-metil-N-2-feniletil)pirazolo[1,5-a]pirimidin-6-carboxamida	427
26		7-(3,4-Diclorofenil)-4,7-dihidro-5-metil-N-(2-feniletil) pirazolo[1,5-a]pirimidin-6-carboxamida	427
27		7-(3,4-Diclorofenil)-4,7-dihidro-5-metil-N-3-piridinilpirazolo[1,5-a]pirimidin-6-carboxamida	400

300

Ejemplos 28-82

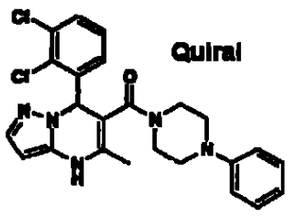
Los compuestos de los Ejemplos 28-81, mostrados en la tabla proporcionada abajo, se prepararon de una manera similar a aquella descrita en el Ejemplo 18, Método 2

La resolución por HPLC del Ejemplo 47, columna Chiracel OD (50 x 500 mm), eluyendo con isopropanol/hexanos al 30% conteniendo trietilamina al 0 1% a 50 mL/min), detección UV a 254λ, proporcionó enantiómeros **A** (Ejemplo 50) y **B** (Ejemplo 51) La columna Chiracel OD (4 6 x 250 mm), eluyendo con isopropanol/hexanos al 30% conteniendo trietilamina al 0 1% a 1 mL/min), detección UV a 254λ, proporcionó enantiómeros **A** Rt= 9 8 min, > 99% ee >99% ee Enantiómero **B** Rt = 14 2 min, >99% ee

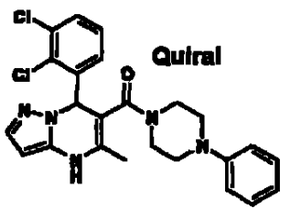
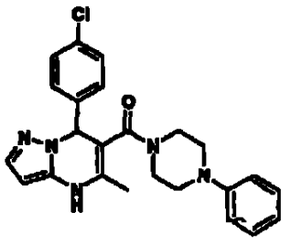
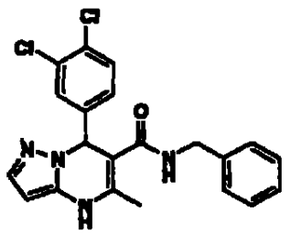
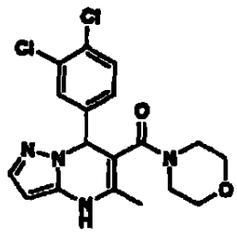
La resolución por HPLC del Ejemplo 70, columna Chiralpak AD (50 x 500 mm), eluyendo con etanol/hexanos al 15% conteniendo trietilamina al 0 1% 50 mL/min), detección UV a 254λ, proporcionó enantiómeros **A** (Ejemplo 72) y **B** (Ejemplo 71) Columna Chiralpak AD (4 6 x 250 mm) eluyendo con etanol/hexanos al 15% conteniendo trietilamina al 0 1% a 1 mL/min), detección UV a 254λ, enantiómero **A** Rt= 6 9 min, >99% ee Enantiómero **B** Rt = 13 4 min,

>99% ee

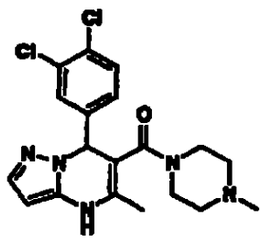
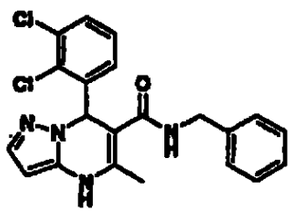
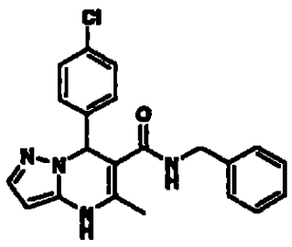
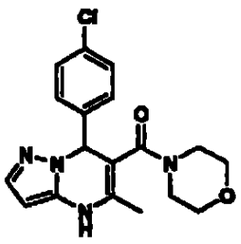
La resolución por HPLC del Ejemplo 80, columna Chiralpak AD (50 x 500 nm), eluyendo con isopropanol/hexanos al 25% conteniendo trietilamina al 0 1% a 50 ml/min), detección UV a 254λ, proporcionó los enantiómeros **A** (Ejemplo 81) y **B** (Ejemplo 82) Columna Chiralpak AD (4 6 x 250 mm) eluyendo con isopropanol/hexanos al 30% conteniendo trietilamina al 0 1% a 1 mL/min), deteccion UV a 254λ, enantiómero **A** Rt= 5 3 min, >99% ee Enantiómero **B** Rt= 7 1 min,>99% ee

Ejemplo	Estructura	Nombre	(M+H)
28		Enantiomero A 1-[[7-(2,3-Diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-fenil-piperazina	468

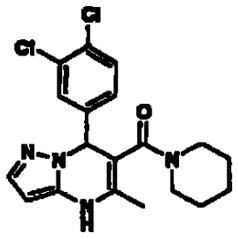
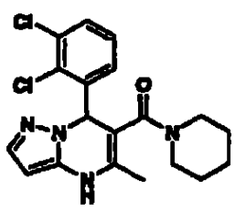
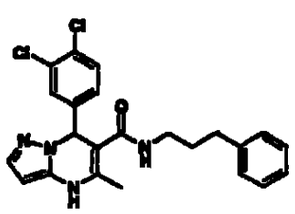
302

29		Enantiomero B 1-[[7-(2,3-Diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-fenil-piperazina	468
30		1-[[7-(4-Clorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-fenilpiperazina	433
31		1-[[7-(3,4-Diclorofenil)-4,7-dihidro-5-metil-N-(fenilmetil)pirazolo[1,5-a]pirimidin-6-carboxamida	413
32		4-[[7-(3,4-Diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]morfolina	393

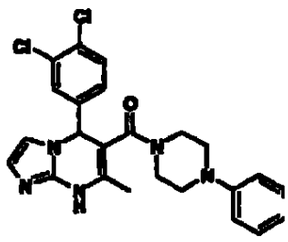
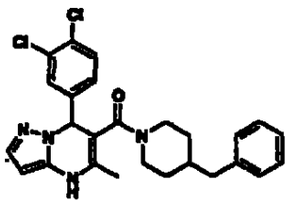
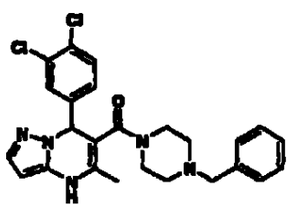
303

33		1-[[7-(3,4-Diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-metil-piperazina	406
34		7-(2,3-Diclorofenil)-4,7-dihidro-5-metil-N-(fenilmetil)pirazolo[1,5-a]pirimidin-6-carboxamida	413
35		7-(4-Clorofenil)-4,7-dihidro-5-metil-N-(fenilmetil) pirazolo[1,5-a] pirimidin-6-carboxamida	378
36		4-[[7-(4-Clorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]morfolina	358

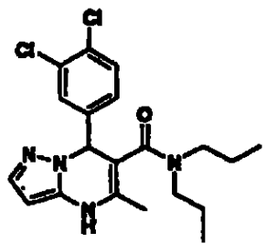
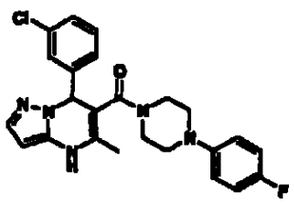
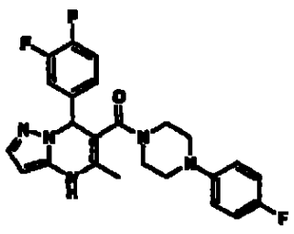
304

37		1-[[7-(3,4-Diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]piramidin-6-il] carbonil]piperidina	391
38		1-[[7-(2,3-Diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il] carbonil]piperidina	391
39		7-(3,4-Diclorofenil)-4,7-dihidro-5-metil-N-(3-fenilpropil) pirazolo[1,5-a]pirimidin-6-carboxamida	441

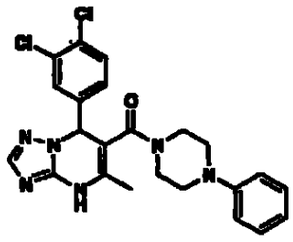
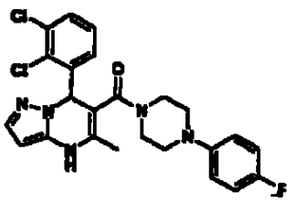
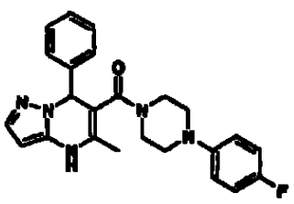
305

40		1-[[5-(3,4-Diclorofenil)-5,8-dihidro-7-metil-imidazol[1,2-a] pirimidin-6-il] carbonil]-4-fenilpiperazina	468
41		1-[[7-(3,4-Diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il] carbonil]-4-(fenil-metil)piperidina	481
42		1-[[7-(3,4-Diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il] carbonil]-4-(fenil-metil)piperazina	482

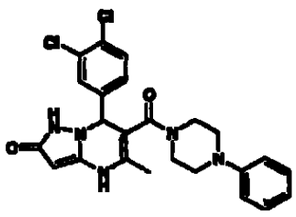
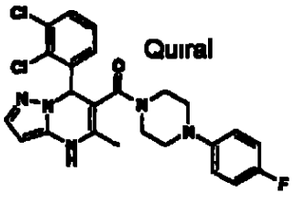
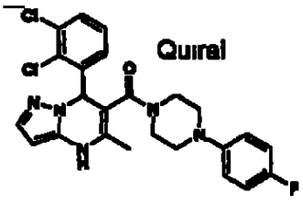
306

43		7-(3,4-Diclorofenil)-4,7-dihidro-5-metil-N,N-dipropilpirazolo[1,5-a]pirimidin-6-carboxamida	407
44		1-[[7-(3-Clorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a] pirimidin-6-il] carbonil]-4-(4-fluorofenil) piperazina	451
45		1-[[7-(3,4-Difluorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a] pirimidin-6-il] carbonil]-4-(4-fluorofenil) piperazina	453

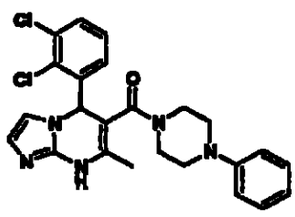
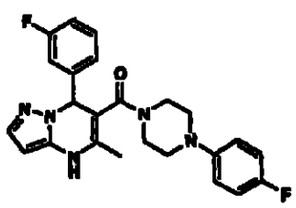
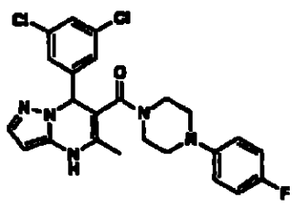
307

46		1-[[7-(3,4-Diclorofenil)-4,7-dihidro-5-metil [1,2,4]triazolo[1,5-a] pirimidin-6-il]carbonil]-4-fenilpiperazina	469
47		1-[[7-(2,3-Diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il]carbonil]-4-(4-fluorofenil) piperazina	486
48		1-(4-Fluorofenil)-4-[(4,7-dihidro-5-metil-7-fenil pirazolo[1,5-a]pirimidin-6-il) carbonil]-piperazina	417

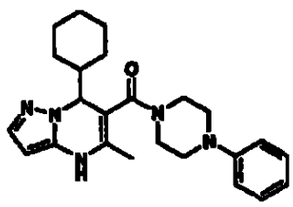
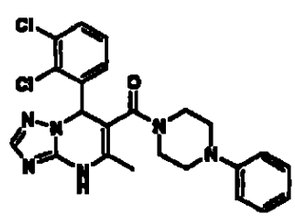
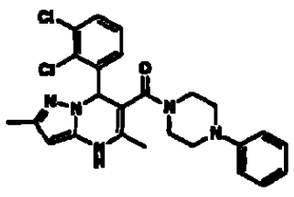
308

49		1-[[7-(3,4-Diclorofenil)-1,2,4,7-tetrahidro-5-metil-2-oxopirazolo[1,5-a] pirimidin-6-il]carbonil]-4-fenilpiperazina	484
50		Enantiomero A 1-[[7-(2,3-Diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il] carbonil]-4-(4-fluorofenil) piperazina	486
51		Enantiomero B 1-[[7-(2,3-Diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il] carbonil]-4-(4-fluoro fenil)piperazina	486

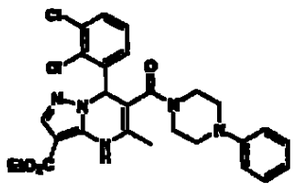
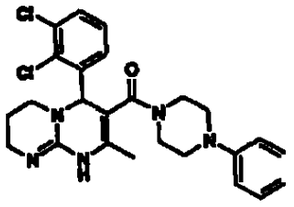
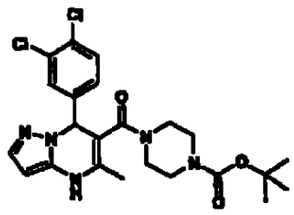
309

52		1-[[5-(2,3-Diclorofenil)-5,8-dihidro-7-metil-imidazo[1,2-a] pirimidin-6-il] carbonil]-4-fenil-piperazina	468
53		1-(4-Fluorofenil)-4-[[7-(3-fluorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a] pirimidin-6-il] carbonil]-piperazina	435
54		1-[[7-(3,5-Diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il] carbonil]-4-(4-fluoro fenil)piperizina	486

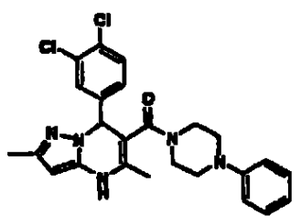
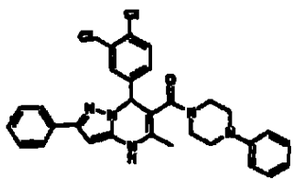
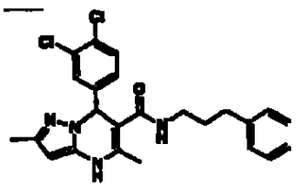
310

55		1-[(7-Cıclohexıl-4,7-dıhıdro-5-metılpırazolo[1,5-a]pırımıdın-6-ıl) carbonıl]-4-fenılpıperazına	405
56		1-[[7-(2,3-Dıclorofenıl)-4,7-dıhıdro-5-metıl-[1,2,4]trıazolo[1,5-a]pırımıdın-6-ıl) carbonıl]-4-fenıl-pıperazına	469
57		1-[[7-(2,3-Dıclorofenıl)-4,7-dıhıdro-2,5-dımetıl-pırazolo[1,5-a] pırımıdın-6-ıl] carbonıl]-4-fenıl-pıperazına	482

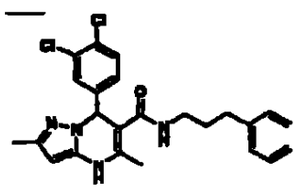
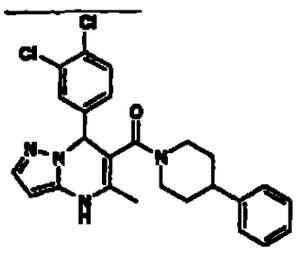
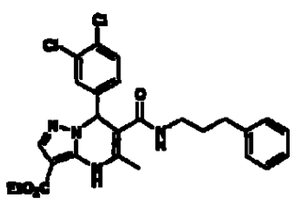
311

58		Ester etílico del ácido 7-(2,3-Diclorofenil)-4,7-dihidro-5-metil-6-[(4-fenil-1-piperazinil)-carbonil]pirazolo [1,5-a]pirimidin-3-carboxílico	540
59		1-[[4-(2,3-Diclorofenil)-4,6,7,8-tetrahidro-2-metil-1H-pirimido[1,2-a] pirimidin-3-il] carbonil]-4-fenil-piperazina	484
60		Ester 1,1-dimetil etílico del ácido 4-[[7-(3,4-Dicloro-fenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il] carbonil]-1-piperazincarboxílico	492

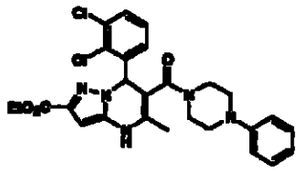
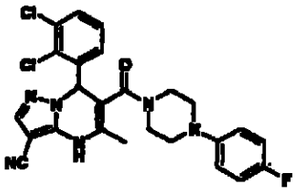
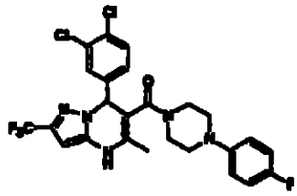
312

61		1-[[7-(3,4-Diclorofenil)-4,7-dihidro-2,5-dimetilpirazolo[1,5-a]pirimidin-6-il] carbonil]-4-fenilpiperazina	482
62		1-[[7-(3,4-Diclorofenil)-4,7-dihidro-5-metil-2-fenilpirazolo[1,5-a] pirimidin-6-il] carbonil]-4-fenilpiperazina	544
63		7-(3,4-Diclorofenil)-4,7-dihidro-2,5-dimetil-N-(3-fenil-propil)pirazolo[1,5-a]pirimidin-6-carboxamida	455

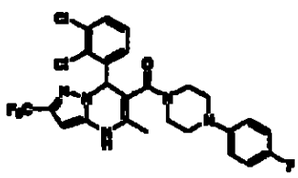
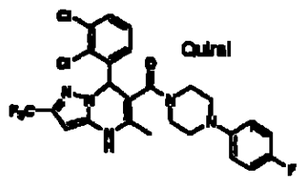
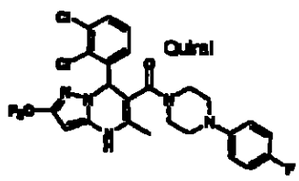
313

64		1-[[7-(2,3-Diclorofenil)-2-(1,1-dimetiletil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-fenilpiperazina	524
65		1-[[7-(3,4-Diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-fenil-piperidina	467
66		Ester etílico del ácido 7-(3,4-Dicloro fenil)-4,7-dihidro-5-metil-6-[[3-fenil propil)amino]carbonil]pirazolo[1,5-a]pirimidin-3-carboxílico	513

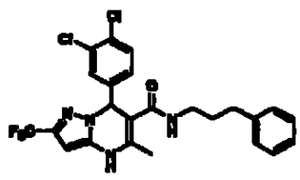
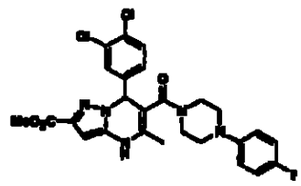
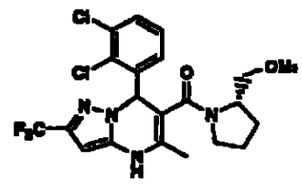
314

67		Ester etílico del ácido 7-(2,3-Dicloro fenil)-4,7-dihidro-5-metil-6-[(4-fenil-1-piperazinil)-carbonil]-pirazolo [1,5-a]pirimidin-2-carboxílico	540
68		1-[[3-Ciano-7-(2,3-diclorofenil)-4,7-dihidro-5-metil pirazolo[1,5-a] pirimidin-6-il] carbonil]-4-(4-fluorofenil) piperazina	511
69		1-[[7-(3,4-Diclorofenil)-4,7-dihidro-5-metil-2-(trifluorometil) pirazolo[1,5-a] pirimidin-6-il] carbonil]-4-(4-fluoro fenil)piperazina	554

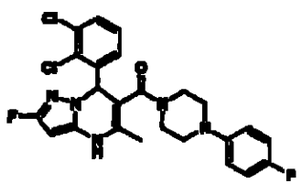
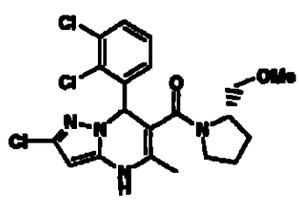
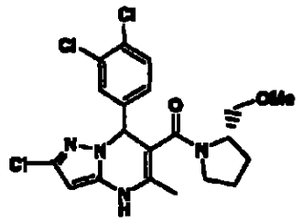
315

70		1-[[7-(2,3-Diclorofenil)-4,7-dihidro-5-metil-2-(trifluorometil) pirazolo[1,5-a] pirimidin-6-il] carbonil]-4-(4-fluoro fenil)piperazina	554
71		Enantiomero B de 1-[[7-(2,3-Dicloro fenil)-4,7-dihidro-5-metil-2-(trifluoro metil)pirazolo[1,5-a] pirimidin-6-il] carbonil]-4-(4-fluoro fenil)piperazina	554
72		Enantiomero B de 1-[[7-(2,3-Dicloro fenil)-4,7-dihidro-2,5-dimetil-pirazolo[1,5-a] pirimidin-6-il] carbonil]-4-(4-fluoro fenil)piperazina	554

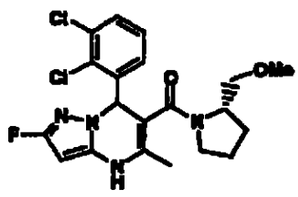
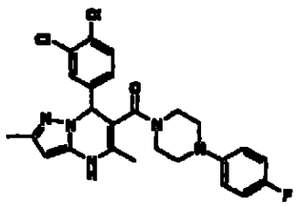
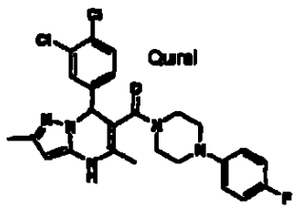
316

73		7-(3,4-Diclorofenil)-4,7-dihidro-5-metil-N-(3-fenilpropil)-2-(trifluorometil) pirazolo[1,5-a] pirimidin-6-carboxamida	509
74		Ester metílico del ácido 7-(3,4-dicloro fenil)-6-[[4-(4-fluorofenil)-1-pipe-razinil]carbonil]-4,7-dihidro-5-metil pirazolo[1,5-a] pirimidin-2-carboxílico	544
75		(2S)-1-[[7-(2,3-diclorofenil)-4,7-dihidro-5-metil-2-(trifluorometil)pira zolo[1,5-a] pirimi-din-6-il]carbonil]-2-(metoximetil) pirrolidina	489

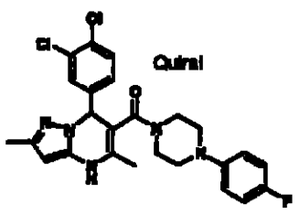
317

76		1-[[7-(2,3-diclorofenil)-2-fluoro-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il] carbonil]-4-(4-fluorofenil) piperazina	504
77		(2S)-1-[[2-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il] carbonil]-2-(metoxi metil)pirrolidina	455
78		(2S)-1-[[2-cloro-7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il] carbonil]-2-(metoxi metil)pirrolidina	455

318

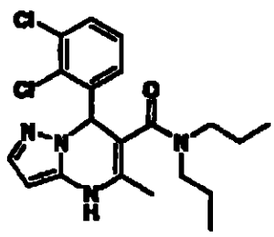
79		(2S)-1-[[7-(2,3-diclorofenil)-2-fluoro-4,7-dihidro-5-metil-pirazolo [1,5-a]pirimidin-6-il]carbonil]-2-(metoximetil)pirrolidina	439
80		1-[[7(-(3,4-diclorofenil)-4,7-dihidro-2,5-dimetil pirazolo[1,5-a] pirimidin-6-il] carbonil]-4-(4-fluorofenil) piperazina	500
81		Enantiómero A de 1-[[7-(3,4-dicloro fenil)-4,7-dihidro-2,5-dimetilpirazolo [1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil) piperazina	500

319

82		Enantiómero de 1-[[7-(3,4-dicloro fenil)-4,7-dihidro-2,5-dimetilpirazolo [1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil) piperazina	500

Ejemplo 83

7-(2,3-diclorofenil)-4,7-dihidro-5-metil-N,N-dipropilpirazolo[1,5-a]pirimidin-6-carboxamida



Metodo

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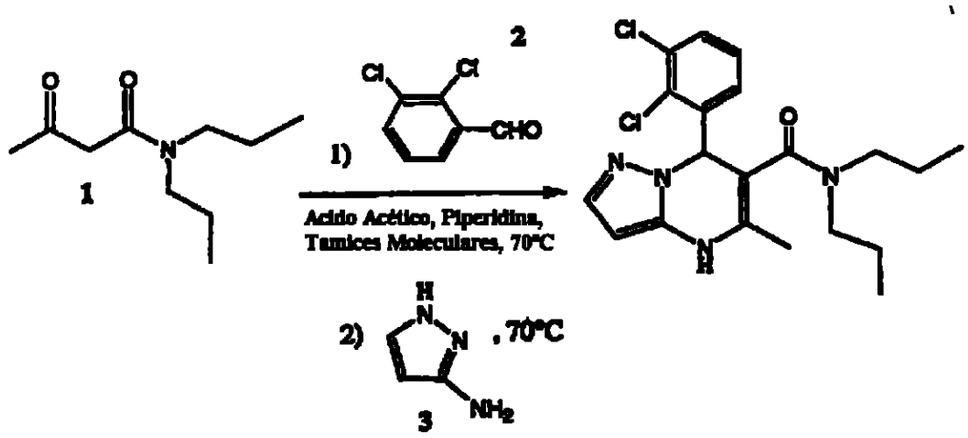

Compuesto 1 El compuesto 1 se preparó como se describe en el Ejemplo 18, Método 2 Etapa A1, a partir de t-butoxiacetoacetato y dipropilamina

Compuesto del Titulo Una mezcla del compuesto 1 (0 2 g, 1 1 mmol), 2,3-diclorobenzaldehido 2 (0 23 g, 1 3 mmol), piperidina (0 015 ml, 0 27 mmol), ácido acético (0 027 mL, 0 27 mmol) y Tamices Moleculares 4A (punta de espátula) en dimetilformamida (1 mL) se agito a 70°C durante la noche La mezcla se enfrio a

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temperatura ambiente Se agregaron 3-aminopirazol 3 (0 13 g, 1 6 mmol) y acetato de sodio (0 28 g, 3 5 mmol), y la mezcla se agitó durante la noche a 70°C La mezcla se enfrió a temperatura ambiente, se transfirió a un embudo separador, se diluyó con agua y acetato de etilo, se lavó con agua (una pequeña cantidad de metanol se agregó para dispersar las emulsiones que se formaron), se secó sobre sulfato de sodio anhidro y se concentró El residuo resultante se purificó por cromatografía en gel de sílice (acetato de etilo/hexanos al 50% seguido por acetato de etilo al 100%) para proporcionar 0 10 g (23% rendimiento del compuesto 1) del compuesto del titulo Columna Balística LC/MS de Fase Inversa YMC S5 ODS 4 6 x 50 mm, detección UV a 220λ, gradiente 4 minutos, Solvente B/A 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt= 2 94 min, (96% puro) MS (M+H 407)

Ejemplos 84-169

Los compuestos de los Ejemplos 84-169, mostrados en la tabla proporcionada abajo, se prepararon de una manera similar a aquella descrita

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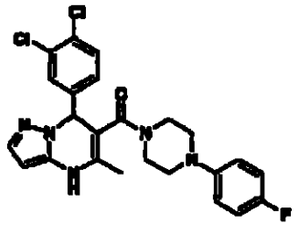
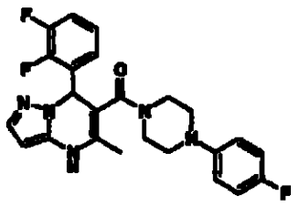
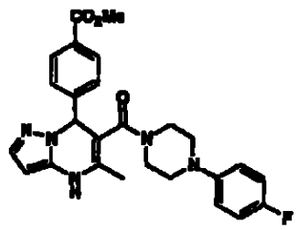
en el Ejemplo 83

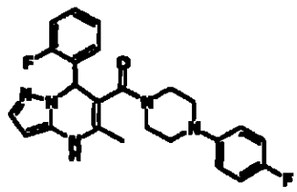
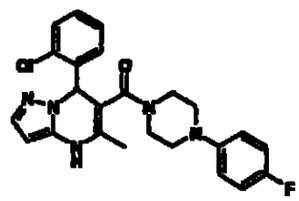
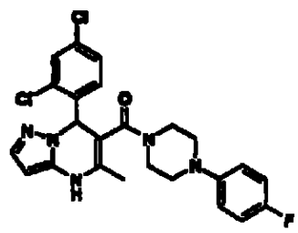
La resolución por HPLC del Ejemplo 84, columna Chiralpak AS (50 x 500 mm), eluyendo con isopropanol/hexanos al 30% conteniendo trietilamina al 0 1% a 50 mL/min), detección UV a 254λ, proporcionó enantiómeros **A** (Ejemplo 166) y **B** (Ejemplo 167) Columna Chiralpak AS (4 6 x 250 mm) eluyendo con isopropanol/hexanos al 40% conteniendo trietilamina al 0 1% a 1 mL/min), detección UV a 254λ, enantiómero **B** Rt= 5 53 min, >99% ee Enantiómero **B** Rt= 12 0 min, 98% ee

Resolución por HPLC del Ejemplo 165, columna Chiralpak AD (50 x 500 mm), eluyendo con isopropanol/hexanos al 20% conteniendo trietilamina al 0 1% a 50 mL/min), detección UV a 254λ proporcionó enantiómeros **A** (Ejemplo 169) y **B** (Ejemplo 168) Columna Chiralpak AD (4 6 X 250 mm) eluyendo con isopropanol/hexanos al 20% conteniendo trietilamina al 0 1% a 1 mL/min), detección UV a 254λ, enantiómero **A** Rt= 8 3 min, >99% ee Enantiómero **B** Rt= 12 8 min, 98% ee

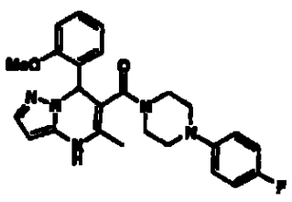
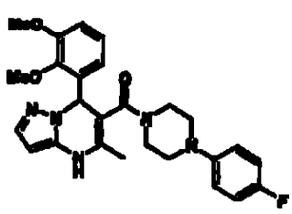
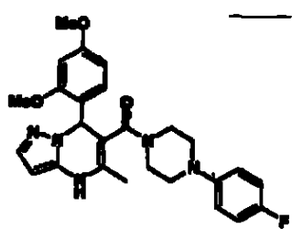
323

Ejemplo	Estructura	Nombre	(M+H)
84		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil) piperazina	486
85		1-[[7-(2,3-diclorofenil)-4,7-dihidro-5-metil pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil) piperazina	453
86		Ester metílico del ácido 4-[6-[[4-(4-fluorofenil)-1-piperazinil]carbonil]-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-7-il] benzoico	475

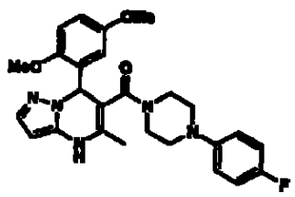
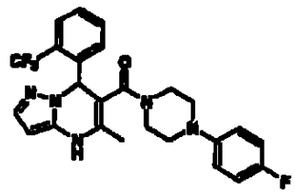
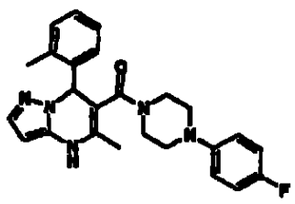
324

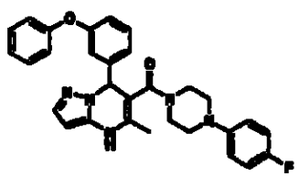
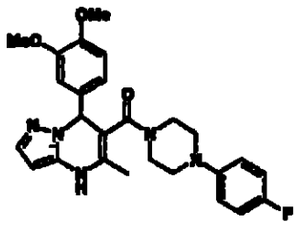
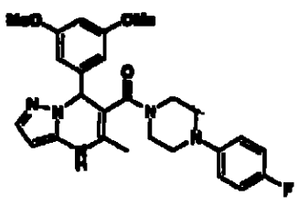
87		1-(4-fluorofenil)-4-[[7-(2-fluorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-piperazina	435
88		1-[[7-(2-cloro fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil) piperazina	451
89		1-[[7-(2,4-dicloro fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil) piperazina	486

325

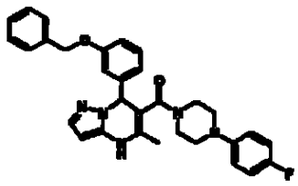
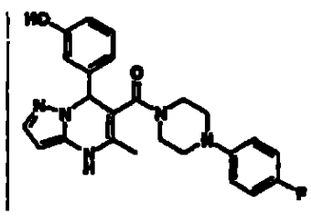
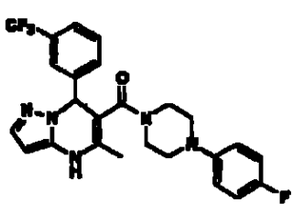
90		1-[[4,7-dihidro-7-(2-metoxifenil)-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil) piperazina	447
91		1-[[7-(2,3-dimetoxi fenil)-4,7-dihidro-5-metil-pirazolo [1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil) piperazina	477
92		1-[[7-(2,4-dimetoxi fenil)-4,7-dihidro-5-metil-pirazolo [1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil) piperazina	477

326

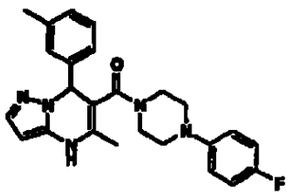
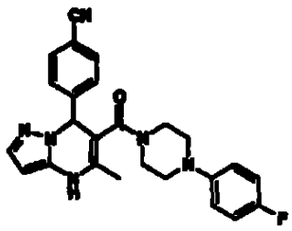
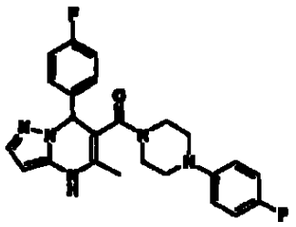
93		1-[[7-(2,5-dimetoxi fenil)-4,7-dihidro-5-metil-pirazolo [1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil) piperazina	477
94		1-[[4,7-dihidro-5-metil-7-[2-(tri fluorometil)fenil] pirazolo[1,5-a] pirimidin-6-il] carbonil]-4-(4-fluorofenil) piperazina	485
95		1-[[4,7-dihidro-5-metil-7-(2-metil fenil)pirazolo[1,5-a]pirimidin-6-il] carbonil]-4-(4-fluorofenil) piperazina	431

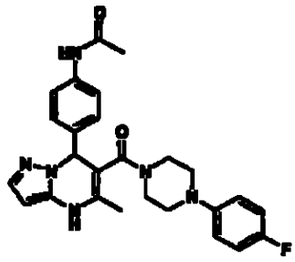
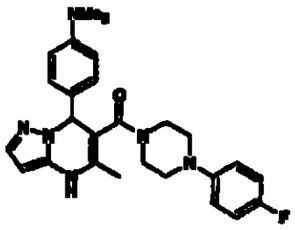
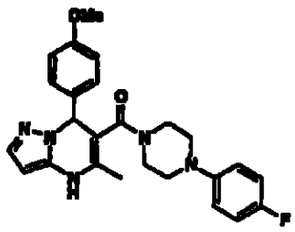
96		1-[[4,7-dihidro-5-metil-7-(3-fenoksi fenil)pirazolo[1,5-a]pirimidin-6-il] karbonil]-4-(4-fluorofenil) piperazina	509
97		1-[[7-(3,4-dimetoksi fenil)-4,7-dihidro-5-metil-pirazolo [1,5-a]pirimidin-6-il]karbonil]-4-(4-fluorofenil) piperazina	477
98		1-[[7-(3,5-dimetoksi fenil)-4,7-dihidro-5-metil-pirazolo [1,5-a]pirimidin-6-il]karbonil]-4-(4-fluorofenil) piperazina	477

328

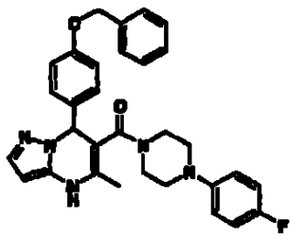
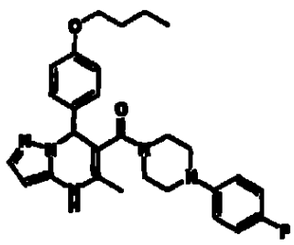
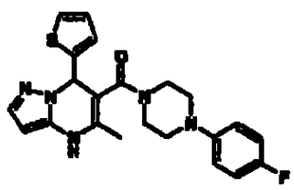
99		1-[[4,7-dihidro-5-metil-7-[3-(fenilmetoxi)fenil]pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil) piperazina	523
100		1-[[4,7-dihidro-7-(3-hidroxifenil)-5-metilpirazolo[1,5-a] pirimidin-6-il] carbonil]-4-(4-fluorofenil) piperazina	433
101		1-[[4,7-dihidro-5-metil-7-[3-(trifluorometil)fenil] pirazolo[1,5-a] pirimidin-6-il] carbonil]-4-(4-fluorofenil) piperazina	485

329

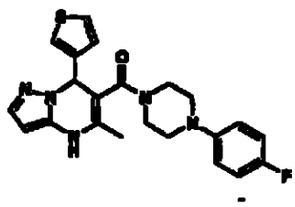
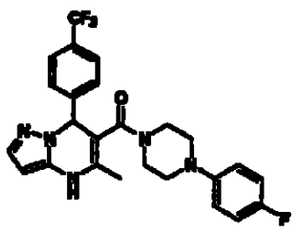
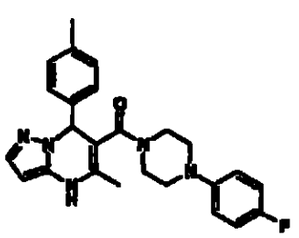
102		1-[[4,7-dihidro-5-metil-7-(3-metil fenil)pirazolo[1,5-a]pirimidin-6-il] carbonil]-4-(4-fluorofenil) piperazina	431
103		1-[[7-(4-ciano fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il] carbonil]-4-(4-fluorofenil) piperazina	442
104		1-(4-fluorofenil)-4-[[7-(4-flubrofenil)-4,7-dihidro-5-metil pirazolo[1,5-a] pirimidin-6-il] carbonil]piperazina	435

105		N-[4-[6-[[4-(4-(fluorofenil)-1-piperazinil]carbonil]-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-7-il]fenil]acetamida	474
106		1-[[7-[4-(dimetil amino)fenil]-4,7-dihidro-5-metil pirazolo [1,5-a] pirimidin-6-il] carbonil]-4-(4-fluorofenil) piperazina	460
107		1-[[4,7-dihidro-7-(4-metoxifenil)-5-metilpirazolo[1,5-a]pirimidin-6-il] carbonil]-4-(4-fluorofenil) piperazina	447

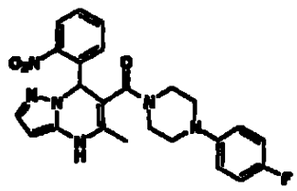
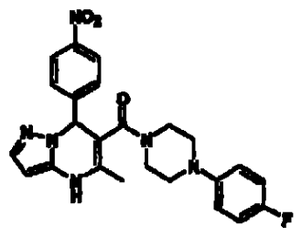
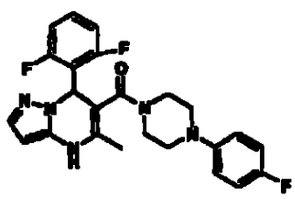
331

108		1-[[4,7-dihidro-5-metil-7-[4-(fenilmetoxi)fenil]pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil) piperazina	523
109		1-[[7-(4-butoxi fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il] carbonil]-4-(4-fluorofenil) piperazina	489
110		1-[[4,7-dihidro-5-metil-7-(2-tienil) pirazolo[1,5-a] pirimidin-6-il] carbonil]-4-(4-fluorofenil) piperazina	423

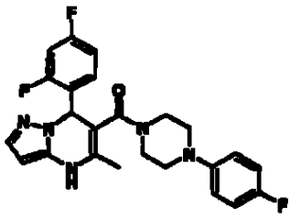
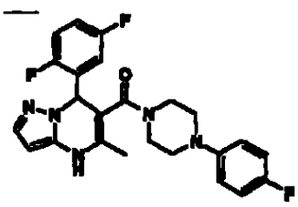
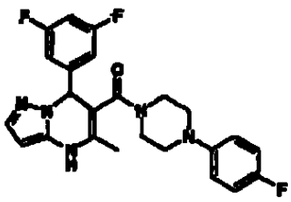
332

111		1-[[4,7-dihidro-5-metil-7-(3-tienil)pirazolo[1,5-a]pirimidin-6-il)carbonil]-4-(4-fluorofenil)piperazina	423
112		1-[[4,7-dihidro-5-metil-7-[4-(trifluorometil)pirazol[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	485
113		1-[[4,7-dihidro-5-metil-7-(4-metilfenil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	431

333

114		1-[[4,7-dihidro-5-metil-7-(2-nitrofenil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	462
115		1-[[4,7-dihidro-5-metil-7-(4-nitrofenil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	462
116		1-[[7-(2,6-difluorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	453

334

117		1-[[7-(2,4-difluorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)pipera-zina	453
118		1-[[7-(2,5-difluoro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)pipera-zina	453
119		1-[[7-(3,5-difluoro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)pipera-zina	453

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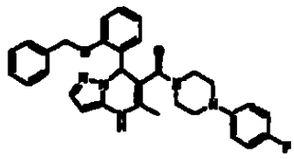
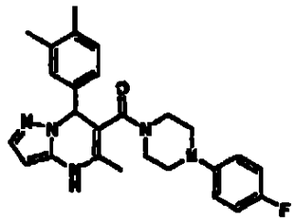
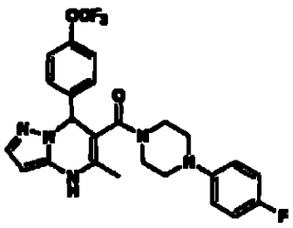
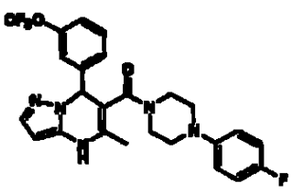
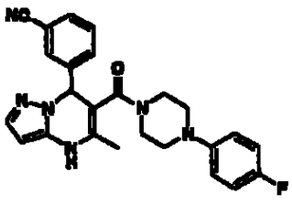
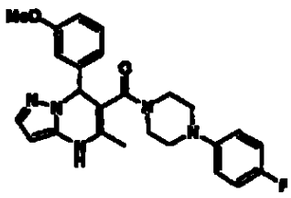
120		1-[[4,7-dihidro-5-metil-7-[2-(fenilmetoxi)fenil]-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)pipera-zina	523
121		1-[[7-(3,4-dimetil-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)pipera-zina	445
122		1-[[4,7-dihidro-5-metil-7-[4-(trifluorometoxi)-fenil]pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)pipera-zina	501

123		1-[[4,7-dihidro-5-metil-7-[3-(trifluorometoxi)-fenil]pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)pipera-zina	501
124		1-[[7-(3-ciano-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)pipera-zina	442
125		1-[[4,7-dihidro-7-(3-metoxifenil)-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)pipera-zina	447

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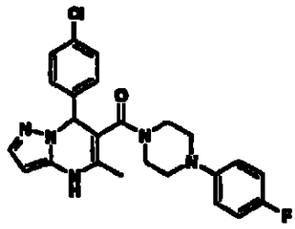
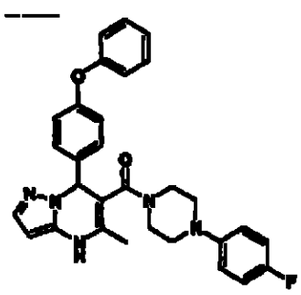
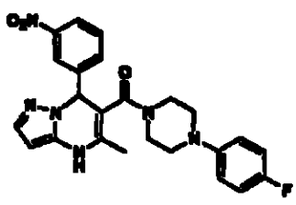
126		1-[[7-(4-cloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)pipera-zina	451
127		1-[[4,7-dihidro-5-metil-7-(4-fenoxifenil) pira-zolo[1,5-a]pirimi-din-6-il]carbonil]-4-(4-fluoro-fenil)piperazina	509
128		1-[[4,7-dihidro-5-metil-7-(3-nitro-fenil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)pipera-zina	462

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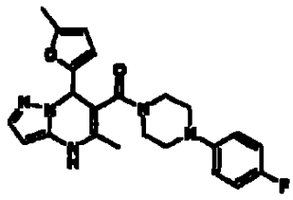
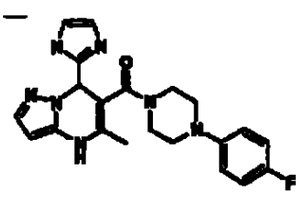
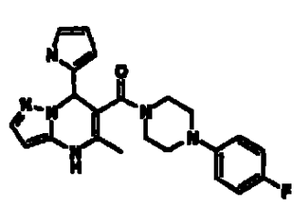
129		1-[[4,7-dıhıdro-5-metıl-7-(5-metıl-2-furanıl)pırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazına	421
130		1-[[4,7-dıhidro-7-(1H-ımıdazol-2-ıl)-5-metılpırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazına	407
131		1-[[4,7-dıhıdro-5-metıl-7-(1H-pırro-2-ıl)pırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazına	406

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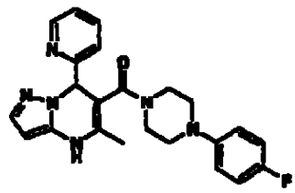
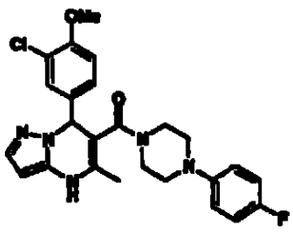
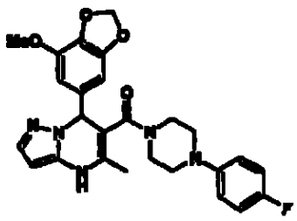
132		1-[[4,7-dihidro-5-metil-7-(2-piridinil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	418
133		1-[[7-(3-cloro-4-metoxifenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	481
134		1-[[4,7-dihidro-7-(4-metoxi-1,3-benzodioxol-6-il)-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	491

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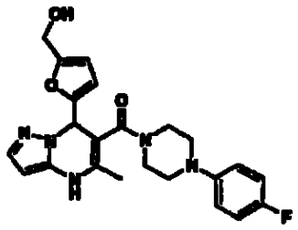
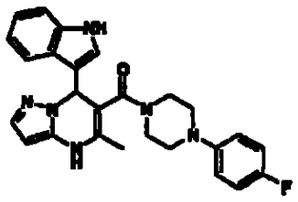
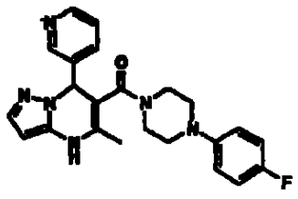
135		1-[[4,7-dihidro-7-[5-(hidroximetil)-2-furanil]-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	437
136		1-[[4,7-dihidro-7-(1H-indol-3-il)-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	456
137		1-[[4,7-dihidro-5-metil-7-(3-piridinil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	418

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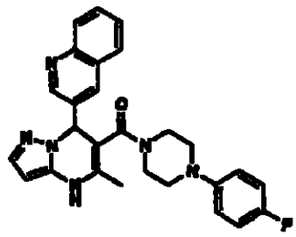
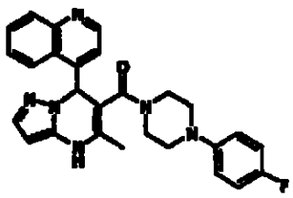
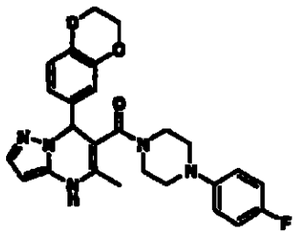
138		1-[[4,7-dihidro-5-metil-7-(3-quinolinil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	468
139		1-[[4,7-dihidro-5-metil-7-(4-quinolinil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	468
140		1-[[7-(2,3-dihidro-1,4-benzodioxol-6-il)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	475

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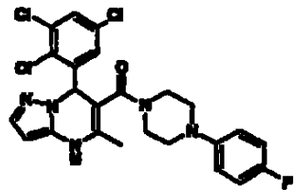
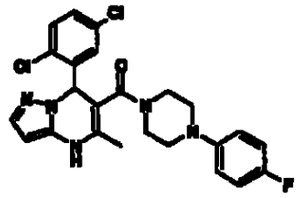
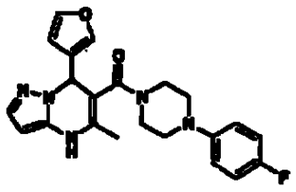
141		1-[[4,7-dihidro-5-metil-7-(2,3,5-triclorofenil)pirazolo-[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	520
142		1-[[7-(2,5-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	486
143		1-(4-fluorofenil)-4-[[7-(3-furanil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-piperazina	407

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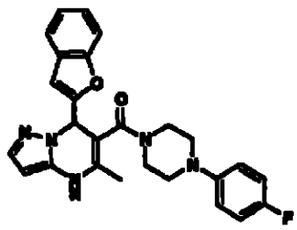
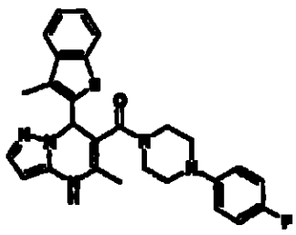
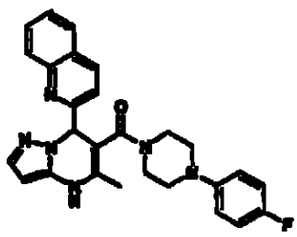
144		1-[[7-(2-benzofuranil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(fluorofenil)piperazina	457
145		1-[[4,7-dihidro-5-metil-7-(3-metilbenzo[b]tiofen-2-il)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	487
146		1-[[4,7-dihidro-5-metil-7-(2-quinolinil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	468

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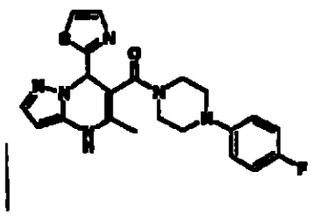
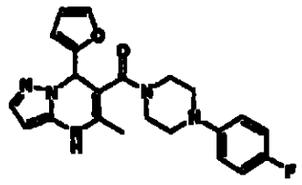
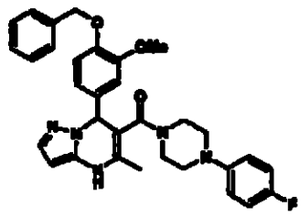
147		1-[[4,7-dihidro-5-metil-7-(2-tiazolil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	424
148		1-(4-fluorofenil)-4-[[7-(2-furanil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]piperazina	407
149		1-[[4,7-dihidro-7-(3-metoxi-4-(fenilmetoxi)fenil]-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	553

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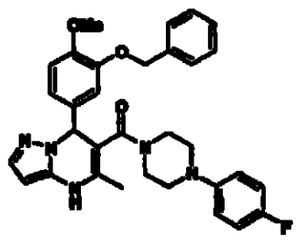
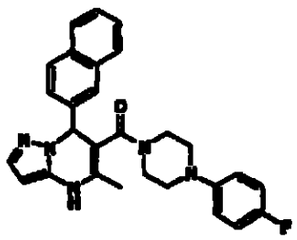
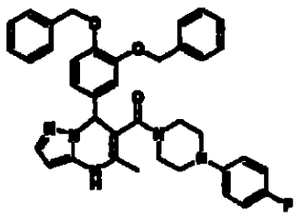
150		1-[[4,7-dihidro-7-[4-metoxi-3-(fenilmetoxi)fenil]-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	553
151		1-[[4,7-dihidro-5-metil-7-(2-naftalenil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	467
152		1-[[7-[3,4-bis-(fenilmetoxi)fenil]-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	629

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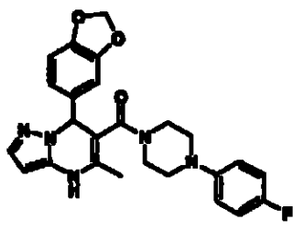
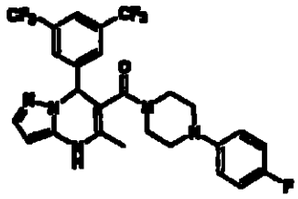
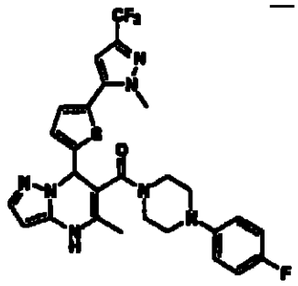
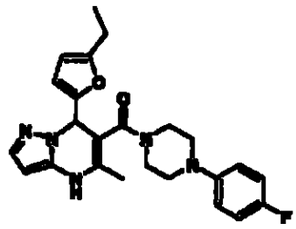
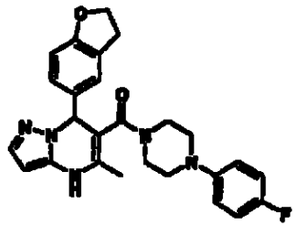
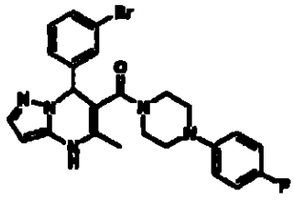
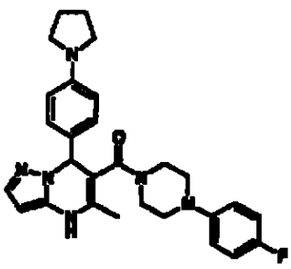
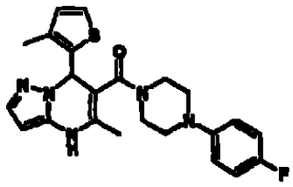
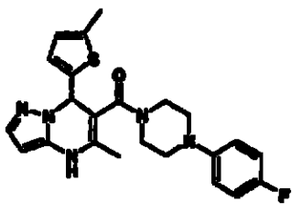
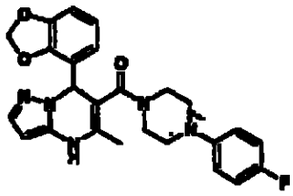
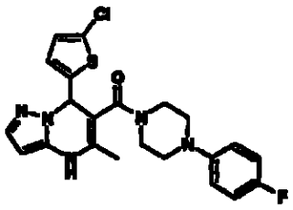
153		1-[[7-(1,3-benzodioxol-5-il)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)pipera-zina	461
154		1-[[7-[3,5-bis-(trifluorome-til)fenil]-4,7-dihidro-5-metil-pirazolo[1,5-a]piri-midin-6-il]carbo-nil]-4-(4-fluoro-fenilpiperazina	553
155		1-[[4,7-dihidro-5-metil-7-[5-[1-metil-3-(trifluorometil)-1H-pirazol-5-il]-2-tienil]pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)pipera-zina	571

347

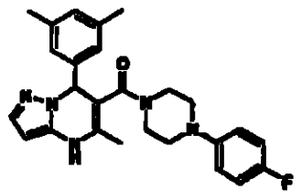
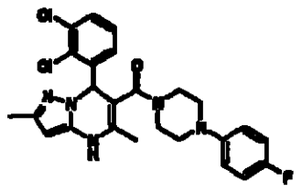
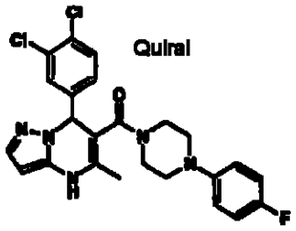
156		1-[[7-(5-etil-2-furanil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il])carbonil]-4-(4-fluorofenil)piperazina	435
157		1-[[7-(2,3-dihidro-5-benzofuranil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	459
158		1-[[7-(3-bromofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	496

348

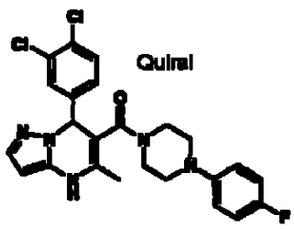
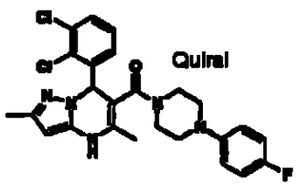
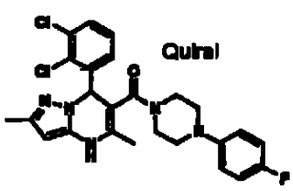
159		1-[[4,7-dihidro-5-metil-7-[4-(1-pirrolidinil)-fenil]pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)pipera-zina	486
160		1-[[4,7-dihidro-5-metil-7-(3-metil-2-tienil)pirazolo[1,5-a]pirimidin-6-il*1-(4-fluorofenil)-4-[[7-(3-furanil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)pipera-zina	437

161		1-[[1-(4,7-dıhıdro-5-metıl-7-(5-metıl-2-tıenıl)pırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-pıperazına	437
162		1-[[7-(1,3-benzodıoxol-4-ıl)-4,7-dohodrp-5-metıl-pırazolo[1,5-a]pırımıdın-6-ıl] carbonıl]-4-(4-fluorofenıl) pıperazına	461
163		1-[[7-(5-cloro-2-tıenıl)-4,7-dıhıdro-5-metılpırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl) pıperazına	457

350

164		1-[[7-3,5-dimetilfenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil) piperazina	445
165		1-[[7-(2,3-diclorofenil)-4,7-dihidro-2,5-dimetilpirazolo[1,5-a]pirimidin-6-il] carbonil]-4-(4-fluorofenil) piperazina	500
166		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il] carbonil]-4-(4-fluorofenil)piperazina, enantiómero A	486

351

167		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina, enantiómero B	486
168		1-[[7-(2,3-diclorofenil)-4,7-dihidro-2,5-dimetil-pirazolo[1,5-a]pirimidin-6-il] carbonil]-4-(4-fluorofenil)piperazina, enantiómero B	500
169		1-[[7-(2,3-diclorofenil)-4,7-dihidro-2,5-dimetil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina, enantiómero A	500

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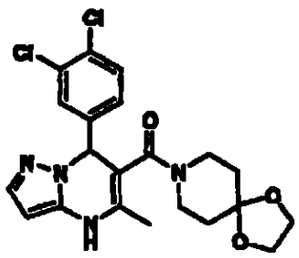
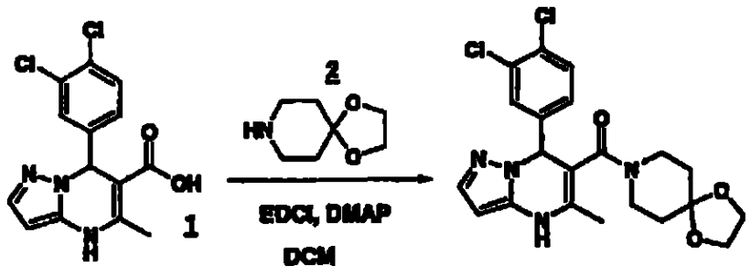
Ejemplo 170

8-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1,4-dioxa-8-azaspiro[4 5]decano



Método



Compuesto 1 El compuesto 1 se preparó como se describe en el Ejemplo 16

Compuesto del Titulo Se agregó el compuesto 2 (0 68 g, 0 47 mmol)a una suspensión del compuesto 1 (0 10 g, 0 32 mmol), EDCI (0 09 g, 0 47 mmol), DMAP (0 004

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g, 0 03 mmol) en dıclormetano (1 mL) Cuando el LC/MS ındıcó que la reacción se completo la mezcla se cargó dırectamente en un CARTUCHO CLEAN-UP Worldwıde Monıtorıng (gel de sílice, CUSIL12M6) el cual ha sıdo equılıbrado con hexano al 100% Elución con hexanos al 100% (40 mL), seguıdo por acetato de etılo/hexanos al 50% (40 mL) y acetato de etılo al 100% (70 mL) Las fracciones puras (análısıs TLC) se combınaron para dar 0 043 g (rendımıento al 30%) del compuesto del tıtulo como un sólıdo blanco LC/MS de fase ınversa columna Ballıstıc YMC S5 ODS 4 6 x 50 mm, detección UV a 220 λ, gradıente 4 mın Solvente B/A (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/mın Rt = 2 12 mın, (97% puro) MS (M+H) 449) HMR (DMSO-d_6, 400 MHz, 100°C) 9 02 (1H, bs), 7 49 (1H, d, J = 8Hz), 7 26 (1H, d, J = 2 Hz), 7 14 (1H, d, J = 2 Hz), 6 95 (1H, d, J = 8 Hz), 6 08 (1H, s), 5 55 (1H, d, J =2 Hz), 3 84 (4H, m), 3 55 (2H, m), 3 20 (2H, m), 1 86 (3H, s), 1 37 (2H, m), 1 26 (2H, m)

Ejemplos 171-377

Los compuestos de las Ejemplos 171-377,

mostrados en la tabla proporcionada abajo, se prepararon en una manera similar a aquella descrita en el Ejemplo 170

La resolución HPLC del Ejemplo 194, columna AD Chiralpak (50 x 500 mm), elucion con isopropanol/hexanos al 30% conteniendo trietilamina al 0 1% a 50 mL/min), detección UV a 254 λ, proporciona enatiómeros A (Ejemplo 250) y B (Ejemplo 251) Columna AD Chiralpak (4 6 x 250 mm) elución con isopropanol/hexanos al 30% conteniendo trietilamina al 0 1% a 1 mL/min), detección UV a 254 λ, enatiómero A Rt = 5 32 min, 99% ee Enantiómero B Rt = 8 59 min, 98% ee

La resolución HPLC del Ejemplo 221, columna AS Chiralpak (50 x 500 mm), elución con isopropanol/hexanos al 50% conteniendo trietilamina al 0 1% a 42 mL/min), detección UV a 254 λ proporcionando anatiómeros A (Ejemplo 328) y B (Ejemplo 329) Columna AS Chiralpak (4 6 x 250 mm), elución con isopropanol/hexanos al 30% conteniendo amina de trietilamina al 0 1% a 1 mL/min), detección UV a 254 λ, enantiómero A Rt = 5 12 min, >99% ee Enantiómero B Rt = 8 70 min, > 99% ee

La resolución HPLC del Ejemplo 288, columna AD Chiralpak (50 x 500 mm), elución con

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isopropanol/hexanos al 30% conteniendo trietilamina al 0 1% a 50 mL/min), detección UV a 254 λ proporcionando enantiómeros A (Ejemplo 376) y B (Ejemplo 377) Columna AD Chiralpak (4 6 x 250 mm), elución con isopropanol/hexanos al 30% conteniendo trietilamina al 0 1% a 1 mL/min), detección UV a 254 λ, enantiómero A Rt = 3 8 min, > 99% ee Enantiómero B Rt = 5 6 min, > 99% ee

La resolución HPLC del Ejemplo 333, columna AD Chiralpak (50 x 500 mm), elución con isopropanol/hexanos al 40% conteniendo trietilamina al 0 1% a 50 mL/min), detección UV a 254 λ, proporcionando enantiómeros A (Ejemplo 364) y B (Ejemplo 365) Columna AD Chiralpak (4 6 x 250 mm), elución con isopropanol/hexanos al 40%, conteniendo trietilamina al 40% a 1 mL/min), detección UV a 254 λ, enantiómero A Rt = 4 92 min, > 99% ee Enantiómero B Rt = 8 0 min, > 97% ee

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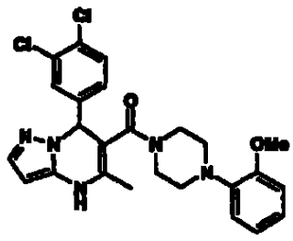
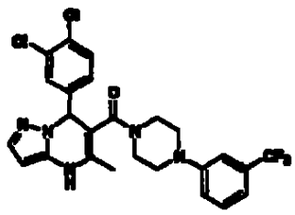
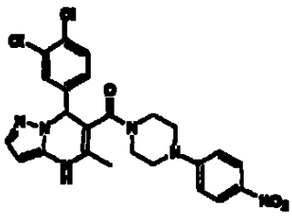
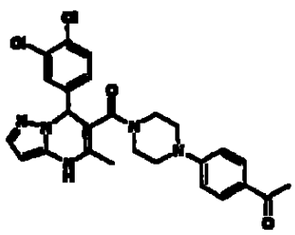
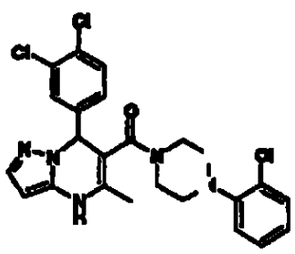
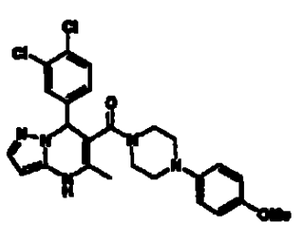
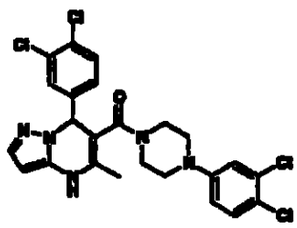
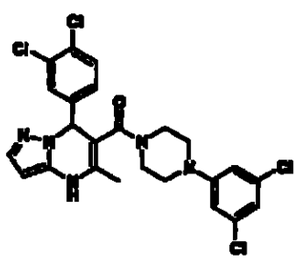
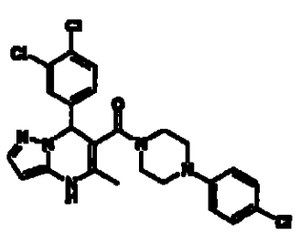
Ejempl	Estructura	Nombre	(M+H)
171		1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(2-metoxifenil)pipera-zina	498
172		1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-[3-(trifluorometil)-fenil]piperazina	536
173		1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-nitrofenil)pipera-zina	513

174		1-(4-acetilfenil)-4-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]pipera-zina	510
175		1-(2-Clorofenil)-4-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]pipera-zina	502
176		1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-metoxifenil)pipera-zina	498

177		1-(3,4-Dıcloro-fenıl)-4-[[7-(3,4-dıclorofenıl)-4,7-dıhıdro-5-metıl-pırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]pıpera-zına	537
178		1-(3,5-Dıcloro-fenıl)-4-[[7-(3,4-dıclorofenıl)-4,7-dıhıdro-5-metıl-pırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]pıpera-zına	537
179		1-(4-Clorofenıl)-4-[[7-(3,4-dıcloro-fenıl)-4,7-dıhıdro-5-metılpırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]pıpera-zına	502

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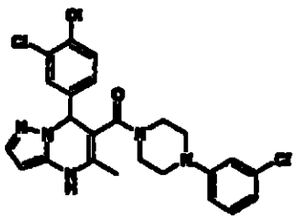
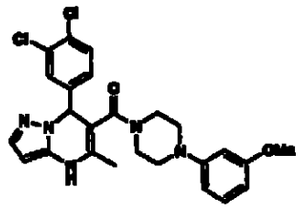
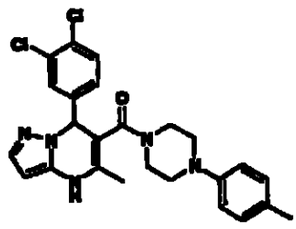
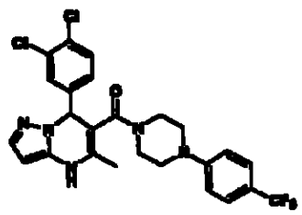
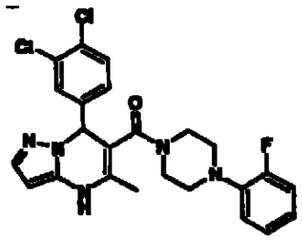
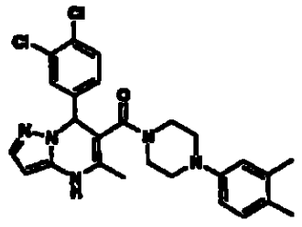
180		1-(3-clorofenil)-4-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]pipera-zina	502
181		1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(3-metoxifenil)pipera-zina	498
182		1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-metilfenil)pipera-zina	482

360

183		1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]car-bonil]-4-[4-(trifluorometil)-fenil]piperazina	536
184		1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(2-fluorofenil)pipera-zina	486
185		1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(3,4-dimetilfenil)pipera-zina	496

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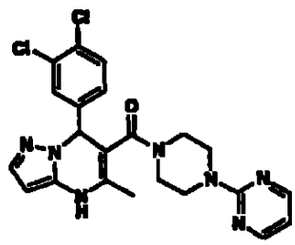
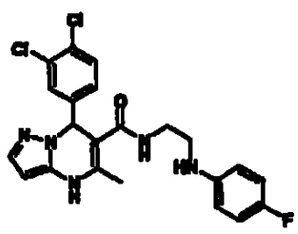
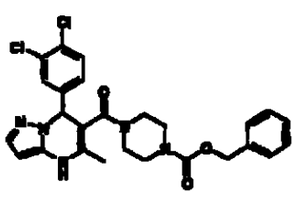
186		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil pirazolo[1,5-a] pirimidin-6-il] carbonil]-4-(2-pirimidin-piperazina	470
187		7-(3,4-diclorofenil)-N-[2-[(4-fluoro-fenil)amino]etil]-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-carboxamida	460
188		Ester fenilmetílico del ácido 4-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1-perazincarboxílico	526

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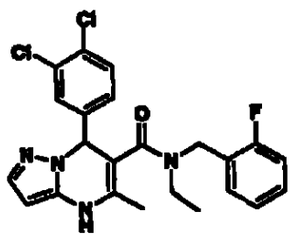
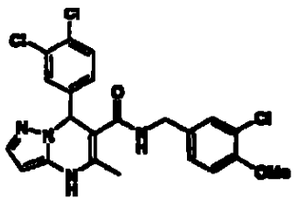
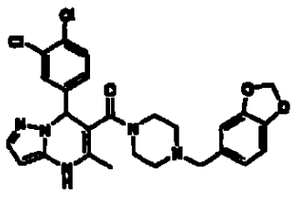
189		7-(3,4-diclorofenil)N-etil-N-[(2-fluorofenil)metil)]-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxamida	459
190		N-[(3-cloro-4-metoxifenil)metil]-7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-carboxamida	477
191		1-(1,3-benzodioxol-5-ilmetil)-4-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil] piperazina	526

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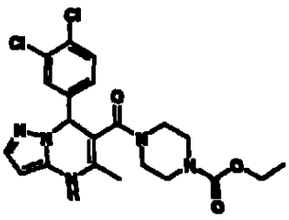
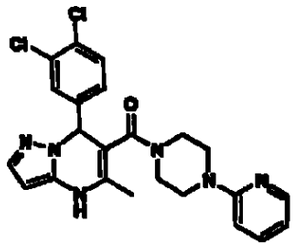
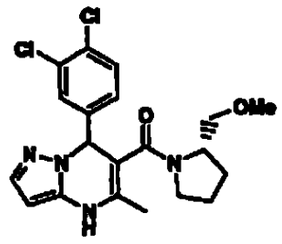
192		Ester etílico del ácido 4-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1-piperazincarboxílico	464
193		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(2-piridinil)piperazina	469
194		(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(metoximetil)pirrolidina	421

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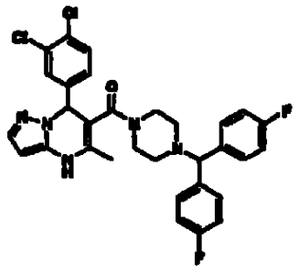
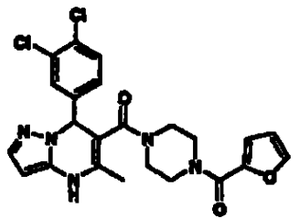
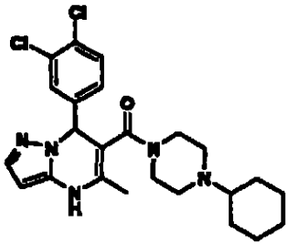
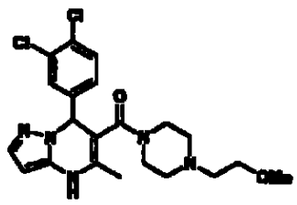
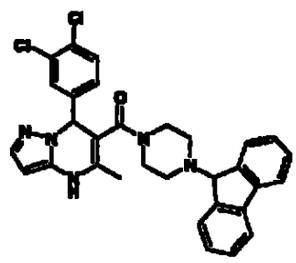
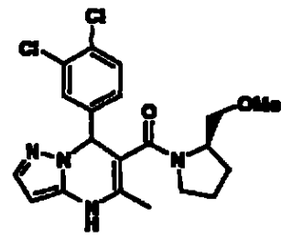
195		1-[bis(4-fluorofenil)-metil]-4-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil pirazolo[1,5-a] pirimidin-6-il] carbonil]piperazina	594
196		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(2-furanil-carbonil)piperazina	486
197		1-ciclohexil-4-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil pirazolo[1,5-a] pirimidin-6-il] carbonil]piperazina	474

365

198		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil pirazolo[1,5-a] pirimidin-6-il] carbonil]-4-(2-metoxietil) piperazina	450
199		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(9H-fluoren-9-il)piperazina	556
200		2(R)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil pirazolo[1,5-a] pirimidin-6-il] carbonil]-2-(metoximetil) pirrolidina	421

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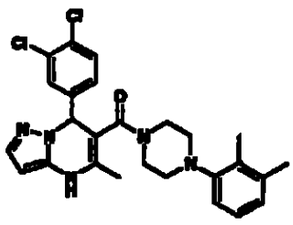
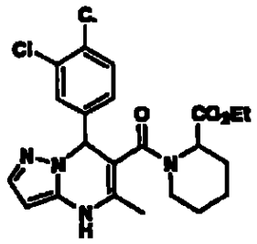
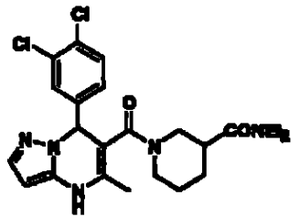
201		1-[[7(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(2,3-dimetilfenil) piperazina	496
202		Ester etílico del ácido 1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil pirazolo[1,5-a] pirimidin-6-il] carbonil]-2-pipe-ridin-carboxílico	463
203		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-N,N-dietil-3-piperidincarboxamida	490

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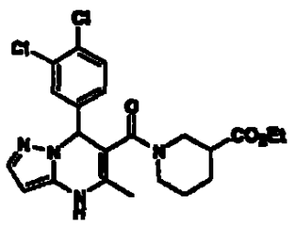
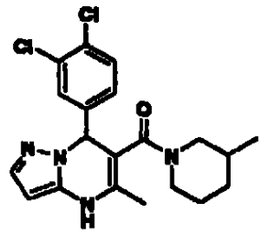
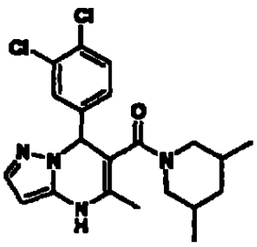
204		Ester etílico del ácido 1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-3-piperidin-carboxílico	463
205		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-3-metil-piperidina	405
206		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-3,5-dimetil-piperidina	419

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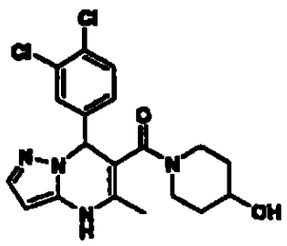
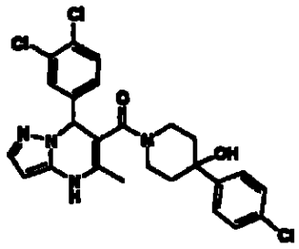
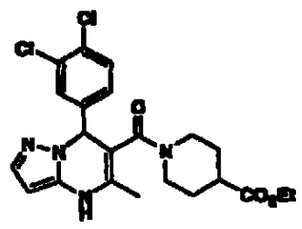
207		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-hidroxi-piperidina	407
208		4-(4-clorofenil)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-hidroxipiperidina	517
209		Ester etílico del ácido 1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-piperidin-carboxílico	463

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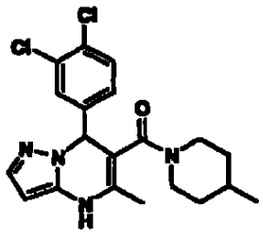
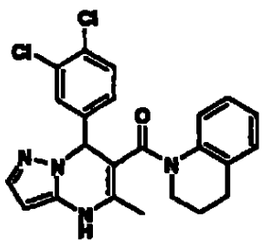
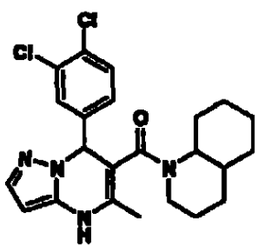
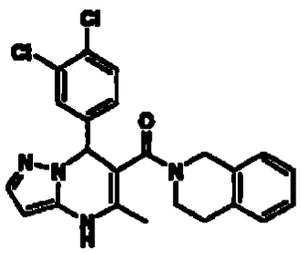
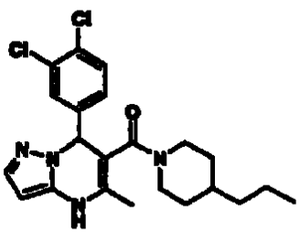
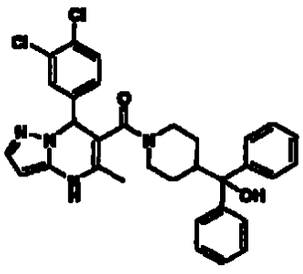
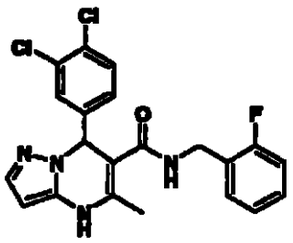
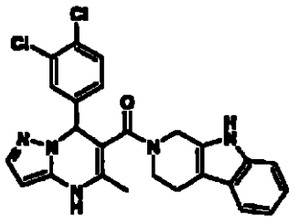
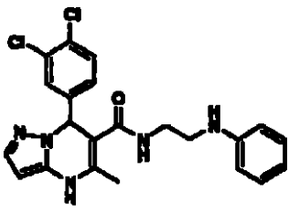
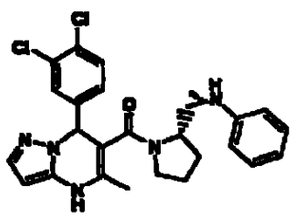
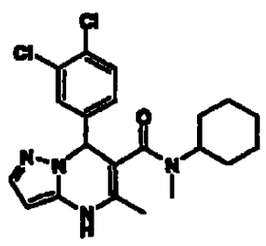
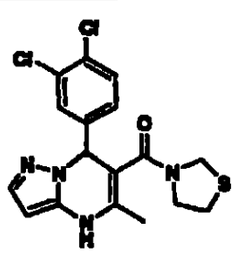
210		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-metilpiperidina	405
211		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1,2,3,4-tetrahidroquinolina	439
212		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-decahidroquinolina	445

213		2-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il] carbonil]-1,2,3,4-tetra-hidrosoquinolina	439
214		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-propilpiperidina	433
215		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(hidroxidifenil-metil)piperidina	573

371

216		7-(3,4-diclorofenil)-N-[(2-fluorofenil)metil]-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxamida	431
217		2-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2,3,4,9-tetrahidro-1H-pirido[3,4-b]indol	478
218		7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N-[2-(fenilamino)-etil]pirazolo[1,5-a]pirimidin-6-carboxamida	442

372

219		(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-[(fenilamino) metil]pirrolidina	482
220		N-ciclohexil-7-(3,4-diclorofenil)-4,7-dihidro-N,5-dimetil-pirazolo[1,5-a]pirimidin-6-carboxamida	419
221		3-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]tiazolo	395

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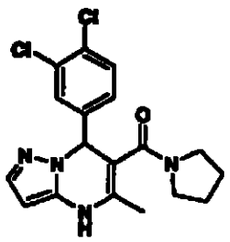
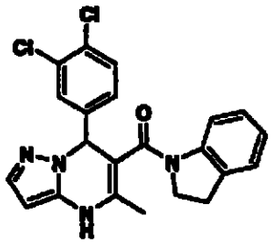
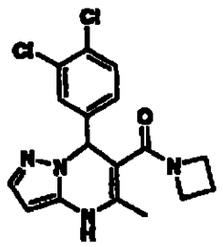
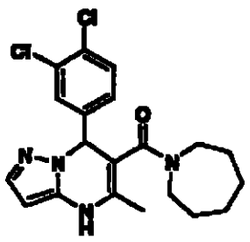
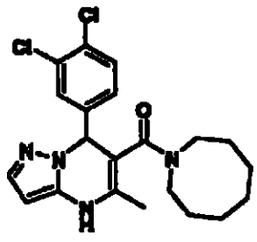
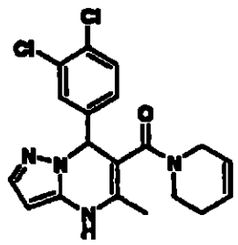
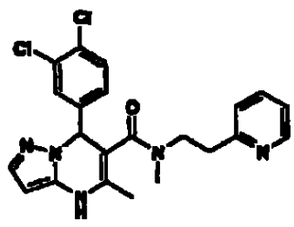
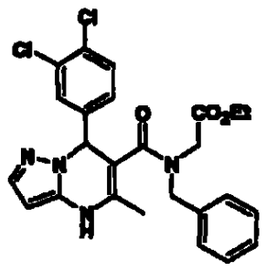
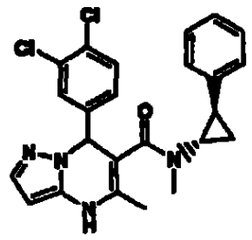
222		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-pirrolidina	377
223		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-3,4-dihidro-1H-indol	425
224		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-azetidina	363

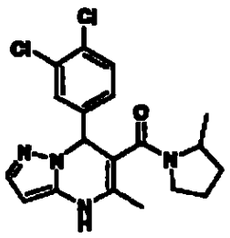
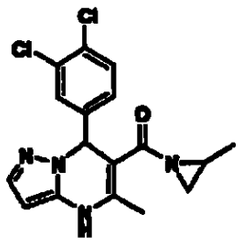
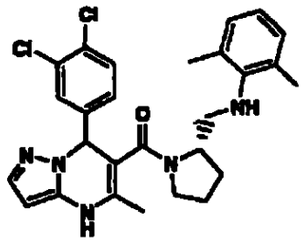
374

225		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-hexahidro-1H-azepina	405
226		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-octahidroazocina	419
227		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1,2,3,6-tetrahidropiridina	389

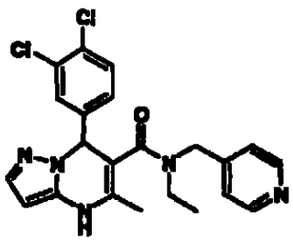
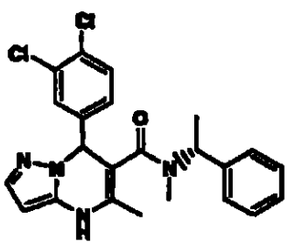
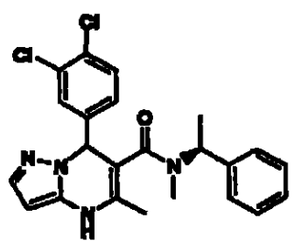
375

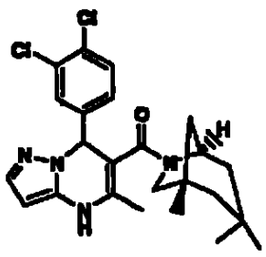
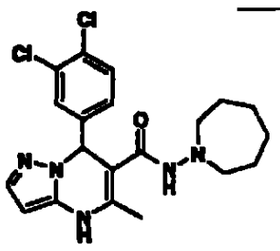
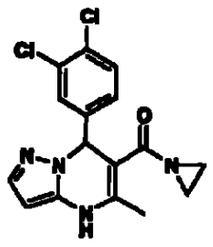
228		7-(3,4-diclorofenil)-4,7-dihidro-N,5-dimetil-N-[2-(2-piridinil)-etil]pirazolo[1,5-a]pirimidin-6-carboxamida	442
229		Ester etílico de N-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-N-(fenilmetil)glicina	499
230		Trans-7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N-(2-fenilciclo propil)pirazolo[1,5-a]pirimidin-6-carboxamida	439

376

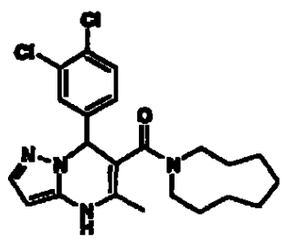
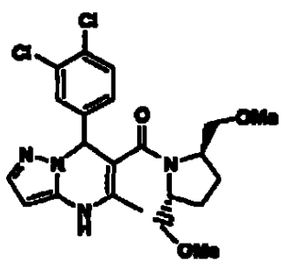
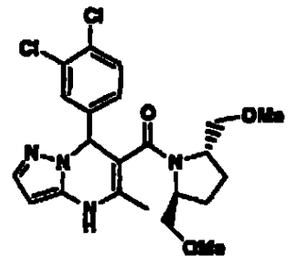
231		1-[[7(3,4-diclorofenil)-4,7-dihidro-5-metil pirazolo[1,5-a] pirimidin-6-il] carbonil]-2-metilpirrolidina	391
232		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a] pirimidin-6-il] carbonil]-2-metilaziridina	363
233		(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-[[(2,6-dimetil fenil)amino]metil] pirrolidina	510

377

234		7-(3,4-dıcloro fenıl)-N-etıl-4,7-dıhıdro-5-metıl-N-(4-pırıdınıl metıl)pırazolo[1,5-a]pırımıdın-6-carboxamıda	442
235		7-(3,4-dıcloro fenıl)-4,7-dıhıdro-N,5-dımetıl-N-[(1R)-1-fenıletıl]pırazolo [1,5-a]pırımıdın-6-carboxamıda	441
236		7-(3,4-dıclorofenıl)-4,7-dıhıdro-N,5-dımetıl-N-[(1S)-1-fenıletıl]pırazolo [1,5-a]pırımıdın-6-carboxamıda	441

237		6-[[7-(3,4-dıcloro fenıl)-4,7-dıhıdro-5-metılpırazolo[1,5-a]pırımıdın-6-ıl] carbonıl]-1,3,3-trımetıl-6-azabıcıclo[3 2 1] octano	459
238		7-(3,4-dıclorofenıl)-N-(hexahıdro-1H-azepın-1-ıl)-4,7-dıhidro-5-metilpirazolo[1,5-a]pirımıdın-6-carboxamıda	420
239		1-[[7-(3,4-dıclorofenıl)-4,7-dıhıdro-5-metılpırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-azırıdına	349

379

240		1-[[7-(3,4-dıcloro fenıl)-4,7-dıhıdro-5-metılpırazolo[1,5-a]pırımıdın-6-ıl] carbonıl]-octahıdro-1H-azonına	433
241		(2R-trans)-1-[[7-(3,4-dıclorofenıl)-4,7-dıhıdro-5-metılpırazolo[1,5-a]pırımıdın-6-ıl] carbonıl]-2,5-bıs(metoxımetıl)-pırrolıdına	465
242		(2S-trans)-1-[[7-(3,4-dıclorofenıl)-4,7-dıhıdro-5-metılpırazolo[1,5-a]pırımıdın-6-ıl] carbonıl]-2,5-bıs-(metoxımetıl) pırrolıdına	465

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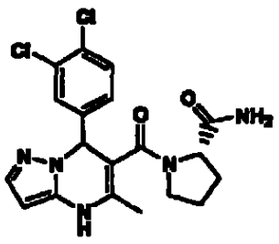
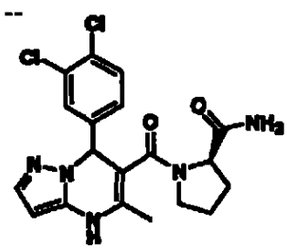
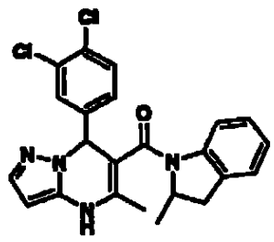
243		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-L-prolinamida	420
244		1-[[7-(3,4-dicloro fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il] carbonil]-D-prolinamida	420
245		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2,3-dihidro-2-metil-1H-indol	439

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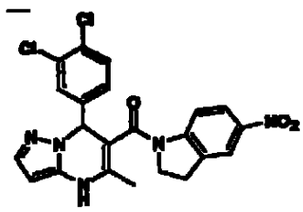
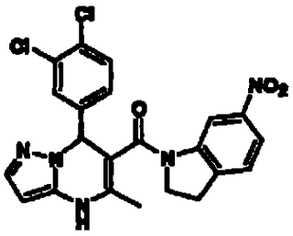
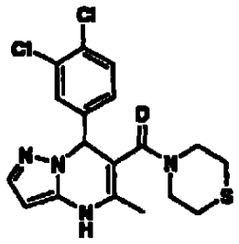
246		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil pirazolo[1,5-a] pirimidin-6-il] carbonil]-2,3-dihidro-5-nitro-1H-indol	470
247		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2,3-dihidro-6-nitro-1H-indol	470
248		4-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-tiomorfolina	409

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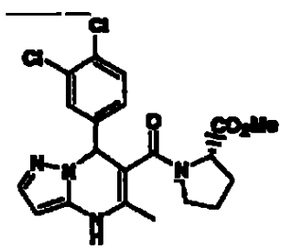
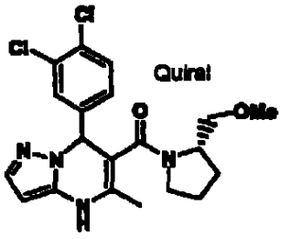
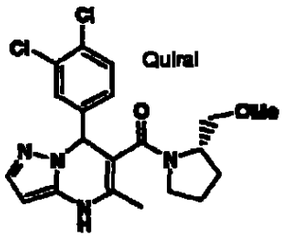
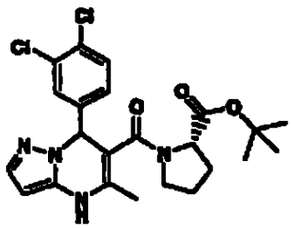
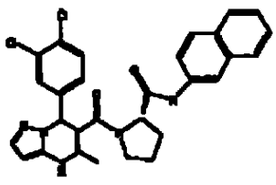
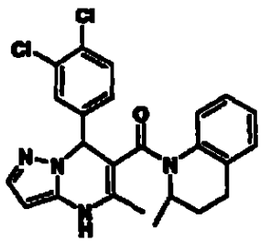
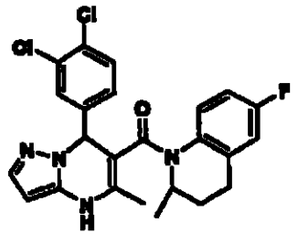
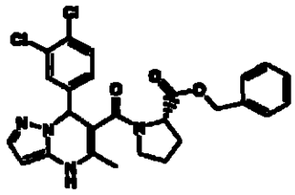
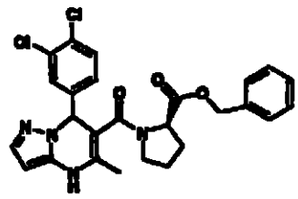
249		Ester metílico de 1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-L-prolina	435
250		Enantiómero A de (2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il] carbonil]-2-(metoxi-metil)pirrolidina	421
251		Enantiómero B de (2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a] pirimidin-6-il] carbonil]-2-(metoxi-metil)pirrolidinina	421

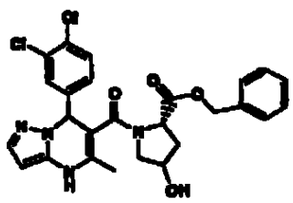
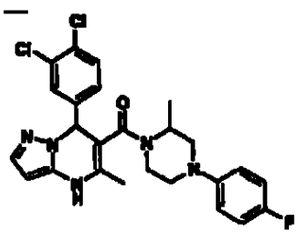
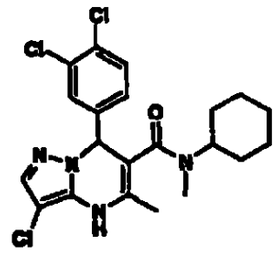
383

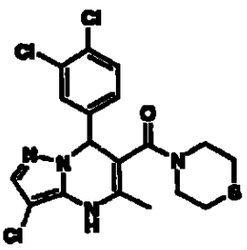
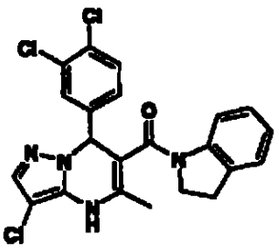
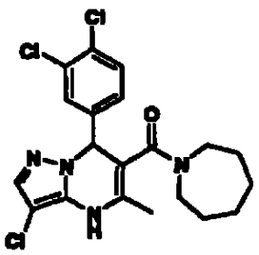
252		Ester 1,1-dimetiletílico de 1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-L-prolina	477
253		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-N-(2-naftalenil)-L-prolinamida	560
254		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1,2,3,4-tetrahidro-2-metilquinolina	453

384

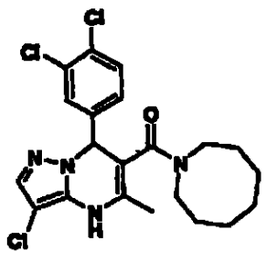
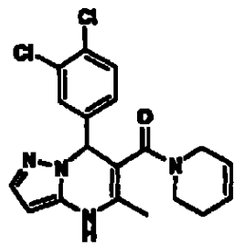
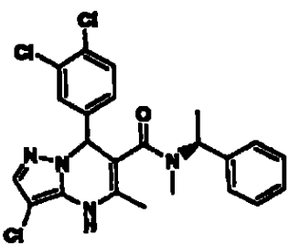
255		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-6-fluoro-1,2,3,4-tetrahidro-2-metilquinolina	471
256		Ester fenilmetílico de 1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-L-prolina	511
257		Ester fenilmetílico 1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-D-prolina	511

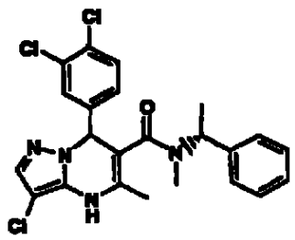
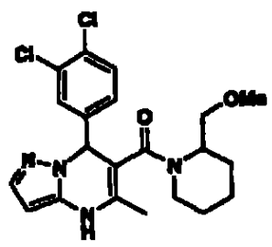
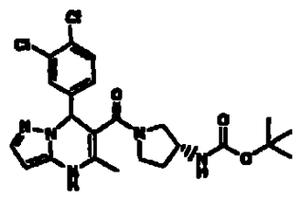
385

258		Ester fenilmetílico de 1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-hidroxi-L-prolina	527
259		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)-2-metilpiperazina	500
260		3-cloro-N-ciclohexil-7-(3,4-diclorofenil)-4,7-dihidro-N,5-dimetil pirazolo[1,5-a] pirimidin-6-carboxamida	453

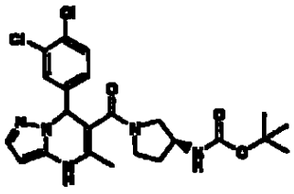
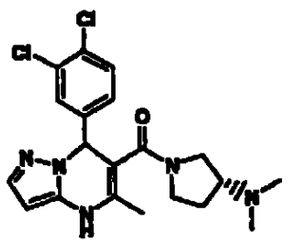
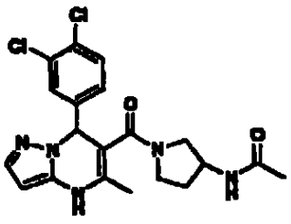
261		4-[[3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-5-metil pirazolo[1,5-a] pirimidin-6-il] carbonil]-tiomorfolina	443
262		1-[[3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2,3-dihidro-1H-indol	459
263		1-[[3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il] carbonil]hexahidro-1H-azepina	439

387

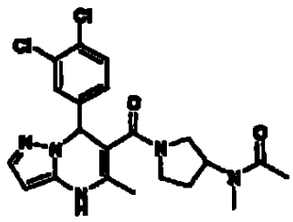
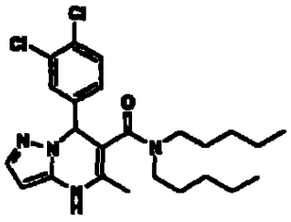
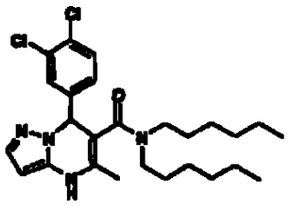
264		1-[[3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-octahidroazocina	453
265		1-[[3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1,2,3,6-tetrahidropiridina	423
266		3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-N,5-dimetil-N-[1(S)-1-feniletil]-pirazolo [1,5-a]pirimidin-6-carboxamida	475

267		3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-N,5-dimetil-N-[(1R)-1-feniletil]-pirazolo[1,5-a]pirimidin-6-carboxamida	475
268		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(metoxi-metil)piperidina	435
269		Ester 1,1-dimetiletílico del ácido [(3R)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-3-pirro-lidinil]carbámico	492

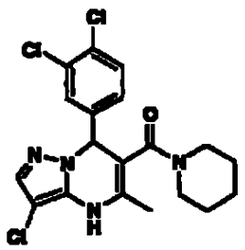
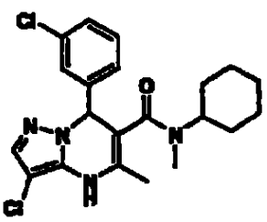
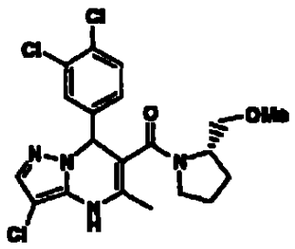
389

270		Ester 1,1-dimetiletílico del ácido [(3S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il] carbonil]-3-pirrolidinil] carbámico	492
271		(3R)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il] carbonil]-3-(dimetilamino) pirrolidina	420
272		N-[1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il] carbonil]-3-pirrolidinil]acetamida	434

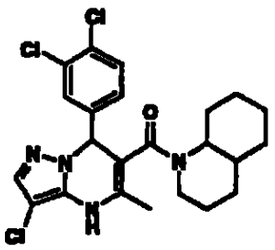
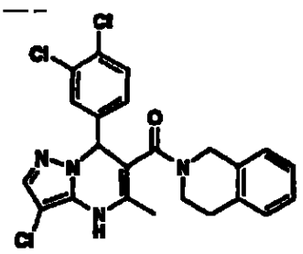
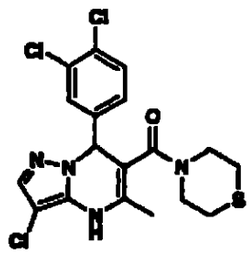
390

273		N-[1-[[(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-3-pirrolidinil]-N-metilacetamida	448
274		7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N,N-dipentil-pirazolo[1,5-a]pirimidin-6-carboxamida	463
275		7-(3,4-diclorofenil)-N,N-dihexil-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxamida	491

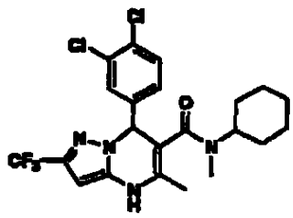
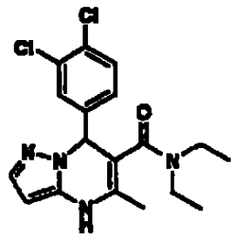
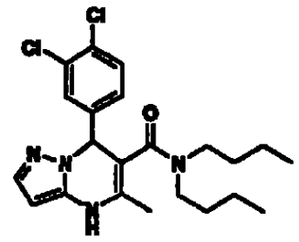
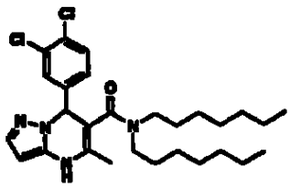
391

276		1-[[3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il] carbonil]piperidina	425
277		3-cloro-7-(3-clorofenil)-N-ciclohexil-4,7-dihidro-N,5-dimetil-pirazolo[1,5-a]pirimidin-6-carboxamida	419
278		(2S)-1-[[3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a] pirimidin-6-il] carbonil]-2-(metoxi-metil)pirrolidina	455

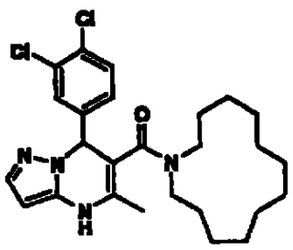
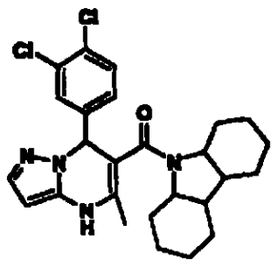
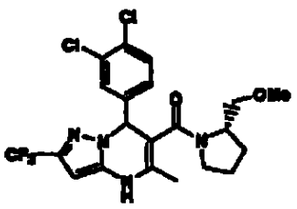
392

279		1-[[3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-decahidroquinolina	479
280		2-[[3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il] carbonil]-1,2,3,4-tetrahidro-isoquinolina	473
281		4-[[3-cloro-7-(3-clorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-tiomorfolina	409

393

282		N-ciclohexil-7-(3,4-diclorofenil)-4,7-dihidro-N,5-metil-2-(trifluorometil) pirazolo[1,5-a] pirimidin-6-carboxamida	487
283		7-(3,4-diclorofenil)-N,N-dietil-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxamida	379
284		N,N-dibutil-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxamida	435
285		7-(3,4-dicloro fenil)-N,N-diheptil-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-carboxamida	519

394

286		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il] carbonil]-azaciclotridecano	489
287		9-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il] carbonil]-dodecahidro-1H-fluoreno	485
288		(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-2-(trifluorometil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(metoximetil) pirrolidina	489

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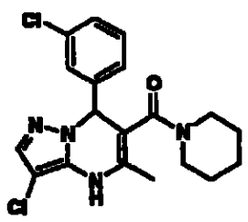
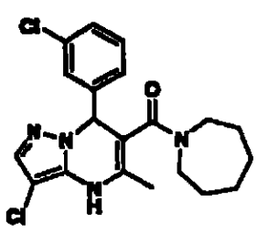
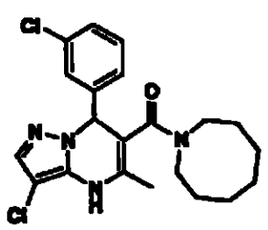
289		1-[[3-cloro-7-(3-clorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il] carbonil]piperidina	391
290		1-[[3-cloro-7-(3-clorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il] carbonil]hexahidro-1H-azepina	405
291		1-[[3-cloro-7-(3-clorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il] carbonil]-octahidroazocina	419

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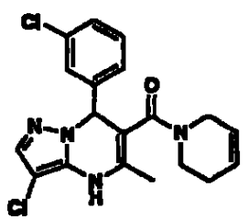
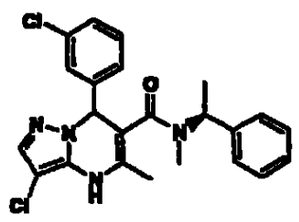
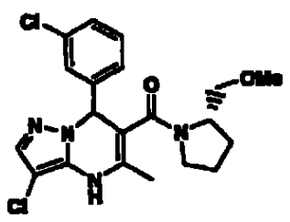
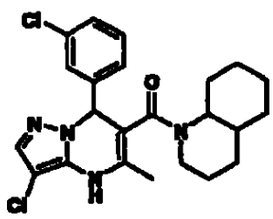
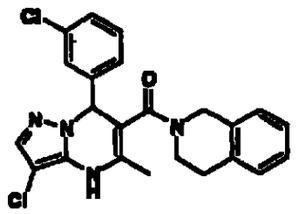
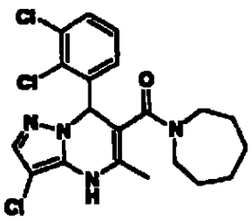
292		1-[[3-cloro-7-(3-clorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-1,2,3,6-tetrahidropiridina	389
293		3-cloro-7-(3-clorofenil)-4,7-dihidro-N,5-dimetil-N-[(1S)-1-fenil-etil]pirazolo[1,5-a]pirimidin-6-carboxamida	441
294		(2S)-1-[[3-cloro-7-(3-clorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(metoxi-metil)pirrolidina	421

397

295		1-[[3-cloro-7-(3-clorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-decahidroquinolina	445
296		2-[[3-cloro-7-(3-clorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-1,2,3,4-tetrahidroisoquinolina	439
297		1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]hexahidro-1H-azepina	439

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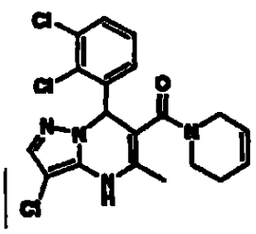
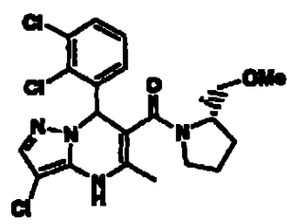
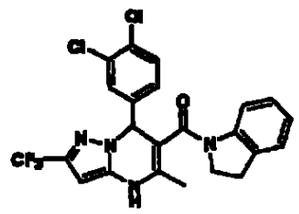
298		1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il] carbonil]-1,2,3,6-tetrahidropiridina	423
299		(2S)-1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il] carbonil]-2-(metoxi-metil)pirrolidina	455
300		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-2-(trifluorometil)pirazolo[1,5-a] pirimidin-6-il] carbonil]-2,3-dihidro-1H-indol	493

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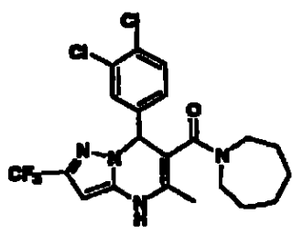
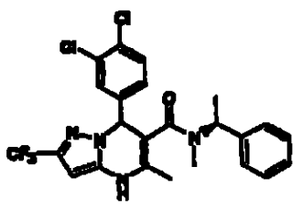
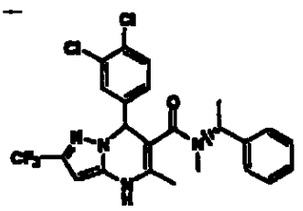
301		1-[[7-(3,4-dıcloro-fenıl)-4,7-dıhıdro-5-metıl-2-(trıfluoro-metıl)pırazolo[1,5-a]pırımıdın-6-ıl] carbonıl]hexahıdro-1H-azepına	473
302		7-(3,4-dıclorofenıl)-4,7-dıhıdro-N,5-metıl-N-[(1S)-1-fenıletıl]-2-(trıfluoro-metıl)pırazolo[1,5-a]pırımıdın-6-carboxamıda	509
303		7-(3,4-dıclorofenıl)-4,7-dıhıdro-N,5-dımetıl-N-[(1R)-1-fenıl-etıl]-2-(trıfluoro-metıl)pırazolo[1,5-a]pırımıdın-6-carboxamıda	509

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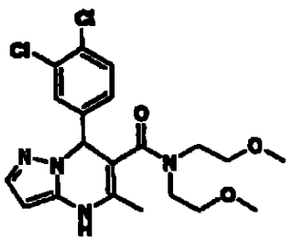
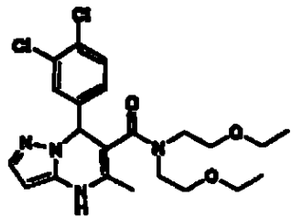
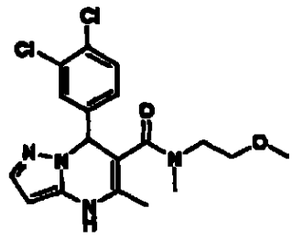
304		7-(3,4-diclorofenil)-4,7-dihidro-N,N-bis(2-metoxietil)-5-metilpirazolo[1,5-a]pirimidin-6-carboxamida	439
305		7-(3,4-diclorofenil)-N,N-bis(2-etoxietil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxamida	467
306		7-(3,4-diclorofenil)-4,7-dihidro-N-(2-metoxietil)-N,5-dimetilpirazolo[1,5-a]pirimidin-6-carboxamida	395

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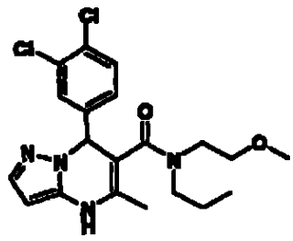
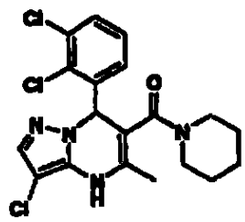
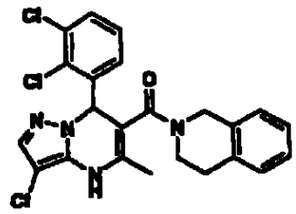
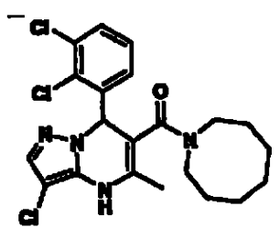
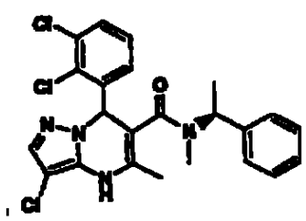
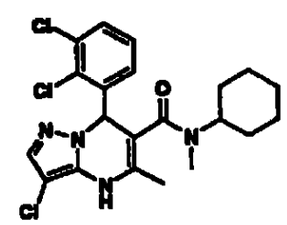
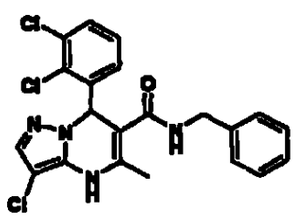
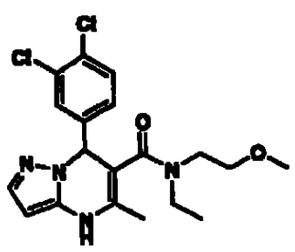
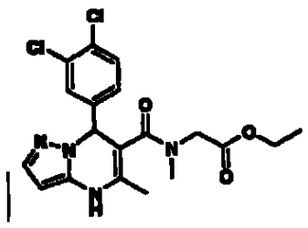
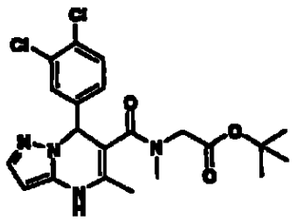
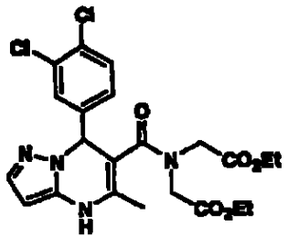
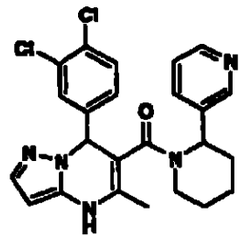
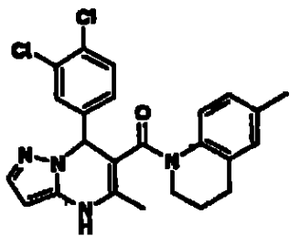
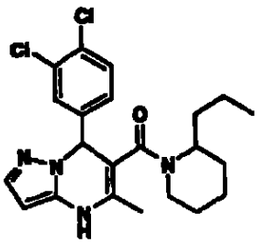
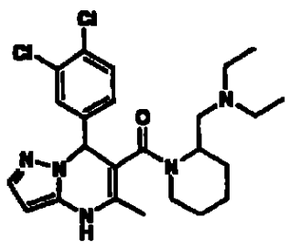
307		7-(3,4-diclorofenil)-4,7-dihidro-N-(2-metoxietil)-5-metil-N-propilpirazolo [1,5-a]pirimidin-6-carboxamida	423
308		1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il] carbonil]piperidina	425
309		2-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a] pirimidin-6-il] carbonil]-1,2,3,4-tetra-hidroisoquinolina	473

310		1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il] carbonil]-octahidroazocina	453
311		3-cloro-7-(2,3-diclofenil)-4,7-dihidro-N,5-dimetil-N-[(1S)-1-feniletil]-pirazolo[1,5-a]pirimidin-6-carboxamida	475
312		3-cloro-N-ciclohexil-7-(2,3-diclorofenil)-4,7-diidro-N,5-dimetil-pirazolo[1,5-a] pirimidin-6-carboxamida	453

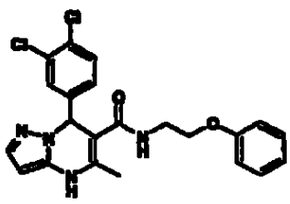
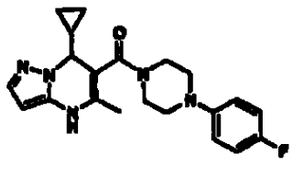
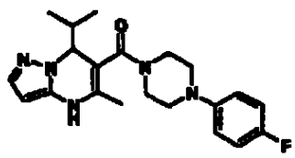
313		3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metil-N-(fenilmetil)pirazolo[1,5-a]pirimidin-6-carboxamida	447
314		7-(3,4-diclorofenil)-N-etil-4,7-dihidro-N-(2-metoxietil)-5-metilpirazolo[1,5-a]pirimidin-6-carboxamida	409
315		Ester etílico de N-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-N-metilglicina	423

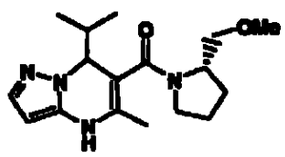
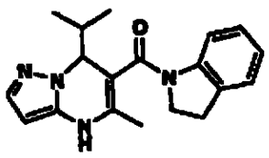
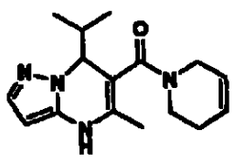
316		Ester 1,1-dimetiletílico de N-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il] carbonil]-N-metilglicina	451
317		Ester etílico de N-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il] carbonil]-N-(2-etoxi-2-oxoetil) glicina	495
318		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(3-piridinil)piperidina	468

405

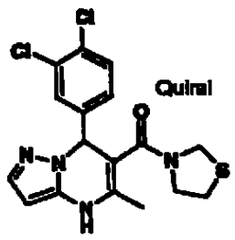
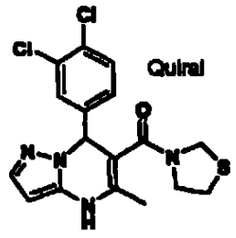
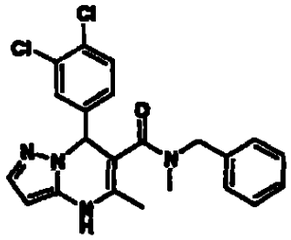
319		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1,2,3,4-tetrahidro-6-metilquinolina	453
320		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-propilpiperidina	433
321		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-[(dietilamino)metil]piperidina	476

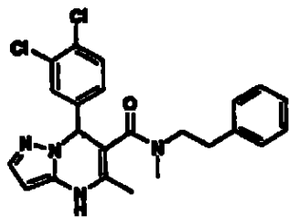
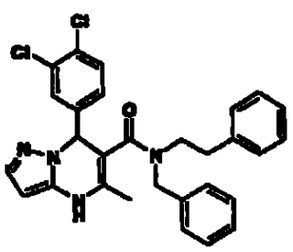
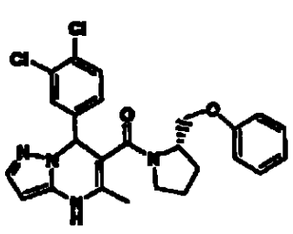
406

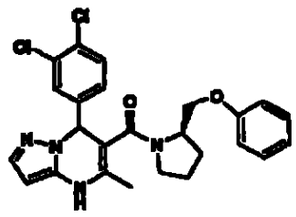
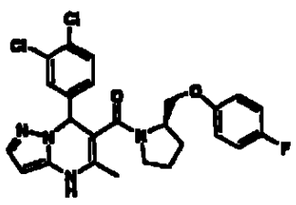
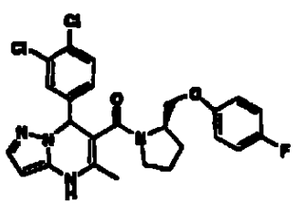
322		7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N-(2-fenoxietil)-pirazolo[1,5-a]pirimidin-6-carboxamida	443
323		1-[(7-ciclopropil-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il) carbonil]-4-(4-fluorofenil) piperazina	381
324		1-[[4,7-dihidro-5-metil-7-(1-metil-etil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil) piperazina	383

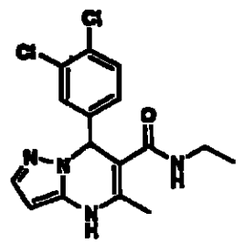
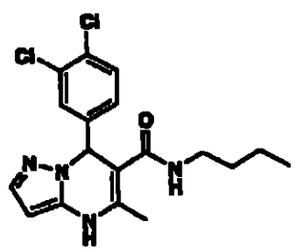
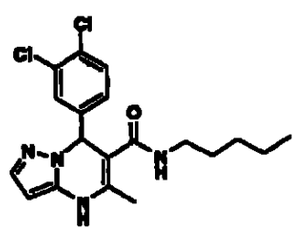
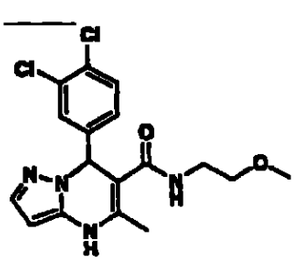
325		(2S)-1-[[4,7-dihidro-5-metil-7-(1-metil-etil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(metoximetil) pirrolidina	318
326		1-[[4,7-dihidro-5-metil-7-(1-metil-etil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-2,3-dihidro-1H-indol	322
327		1-[[4,7-dihidro-5-metil-7-(1-metil-etil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-1,2,3,6-tetrahidropiridina	286

408

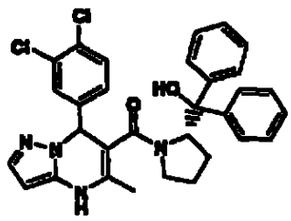
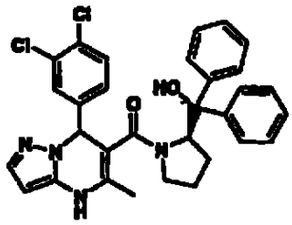
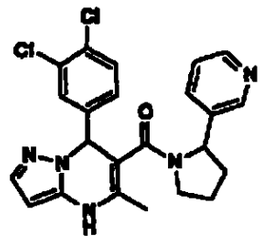
328		Enantiómero A de 3-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-tiazolidina	395
329		Enantiómero B de 3-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-tiazolidina	395
330		7-(3,4-diclorofenil)-4,7-dihidro-N,5-dimetil-N-(fenilmetil) pirazolo[1,5-a] pirimidin-6-carboxamida	427

331		7-(3,4-diclorofenil)-4,7-dihidro-N,5-dimetil-N-(2-feniletil) pirazolo[1,5-a] pirimidin-6-carboxamida	441
332		7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N-(2-feniletil)-N-(fenilmetil)pirazolo [1,5-a]pirimidin-6-carboxamida	517
333		(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il] carbonil]-2-(fenoxi-metil)pirrolidina	483

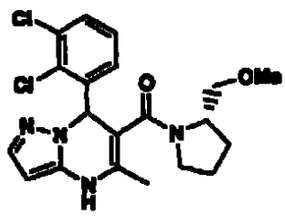
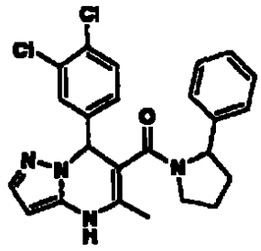
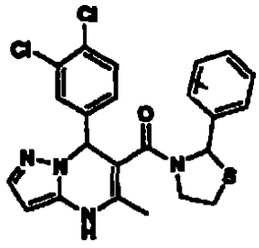
334		(2R)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il] carbonil]-2-(fenoxi-metil)pirrolidina	483
335		(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-[(4-fluorofenoxi)metil]-pirrolidina	501
336		(2R)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-[(4-fluorofenoxi)metil]-pirrolidina	501

337		7-(3,4-diclorofenil)-N-etil-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxamida	351
338		N-butil-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxamida	379
339		7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N-pentilpirazolo[1,5-a]pirimidin-6-carboxamida	393
340		7-(3,4-diclorofenil)-4,7-dihidro-N-(2,-metoxietil)-5-metilpirazolo[1,5-a]pirimidin-6-carboxamida	381

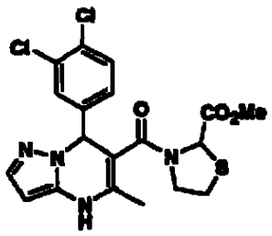
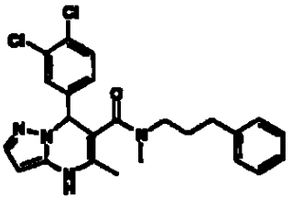
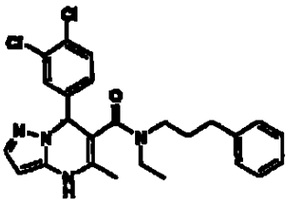
A12

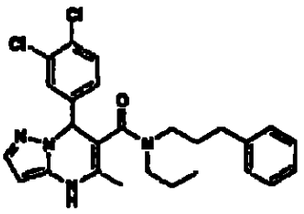
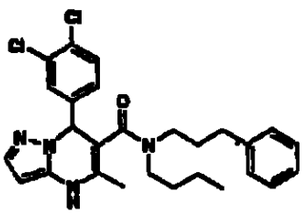
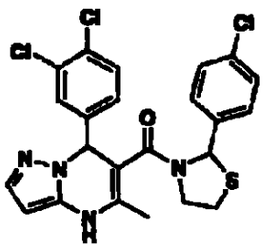
341		(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il] carbonil]-2-(hidroxidifenil-metil)pirrolidina	559
342		(2R)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(hidroxidifenil-metil)pirrolidina	559
343		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il] carbonil]-2-(3-piridinil) pirrolidina	454

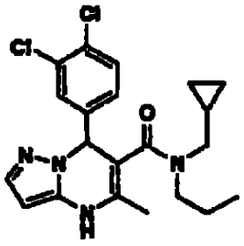
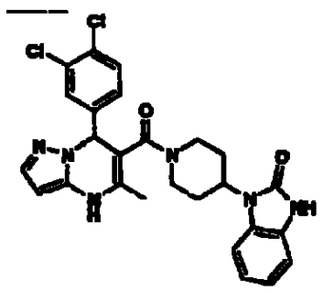
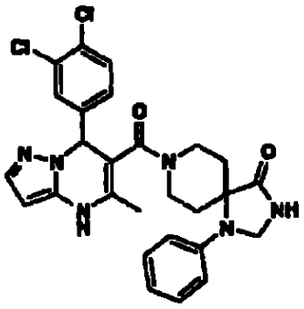
913

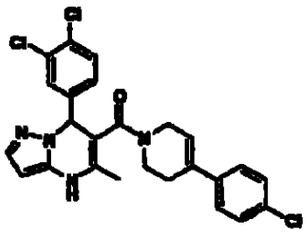
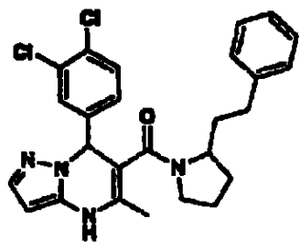
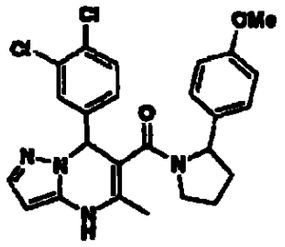
344		(2S)-1-[[7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(metoximetil) pirrolidina	421
345		1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-fenilpirrolidina	453
346		3-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-feniltiazolidina	471

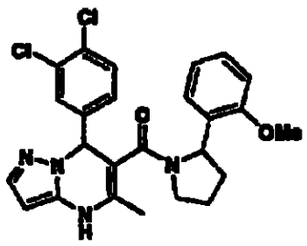
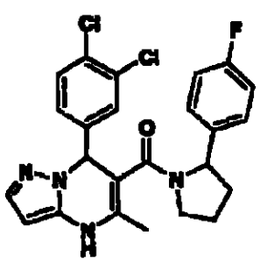
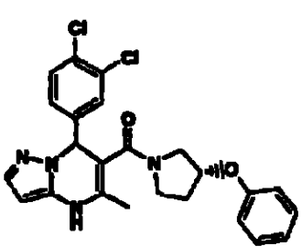
414

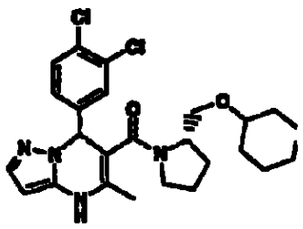
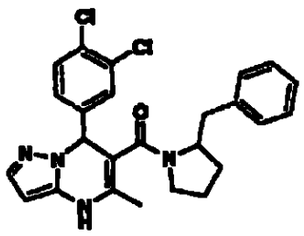
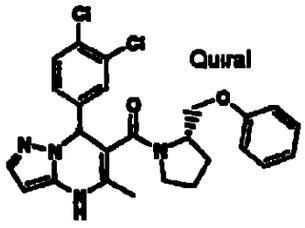
347		Ester metílico del ácido 3-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il] carbonil]-2-tiazo-lidinocarboxílico	453
348		7-(3,4-diclorofenil)-4,7-dihidro-N,5-dimetil-N-(3-fenilpropil) pirazolo[1,5-a]pirimidin-6-carboxamida	455
349		7-(3,4-diclorofenil)-N-etil-4,7-dihidro-5-metil-N-(3-fenil-propil)pirazolo[1,5-a]pirimidin-6-carboxamida	469

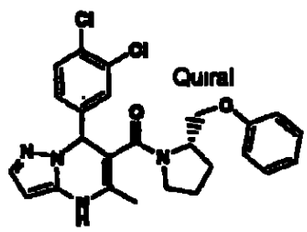
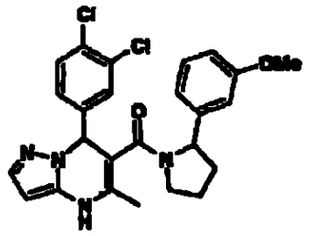
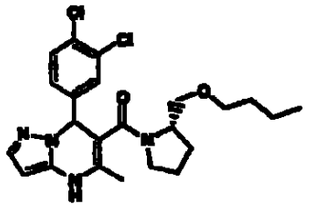
350		7-(3,4-Dicloro-fenil)-4,7-dihidro-5-metil-N-(3-fenilpropil)-N-propilpirazolo[1,5-a]pirimidin-6-carboxamida	483
351		N-Butil-7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N-(3-fenilpropil) pirazolo[1,5-a] carboxamida	497
352		2-(4-clorofenil)-3-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il] carbonil]tiazolidina	505

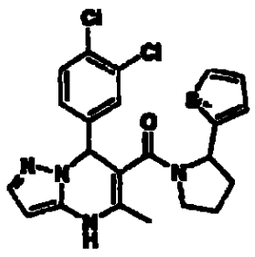
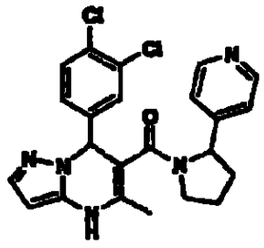
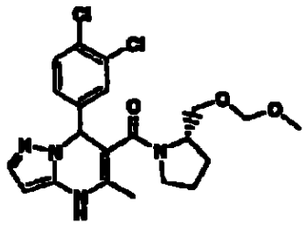
353		N-(ciclopropil-metil)-7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N-propilpirazolo[1,5-a]pirimidin-6-carboxamida	419
354		1-[[-7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il] carbonil]-4-(2,3-dihidro-2-oxo-1H-bencimidazol-1-il)piperidina	523
355		8-[[7-(2,3-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1-fenil-1,3,8-triazaspiro[4,5] decan-4-ona	537

356		4-(4-clorofenil)-1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il] carbonil]-1,2,3,6-tetrahidropiridina	499
357		1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(2-feniletil) pirrolidina	481
358		1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(4-metoxifenil) pirrolidina	483

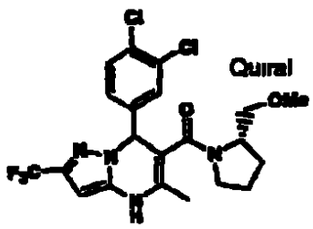
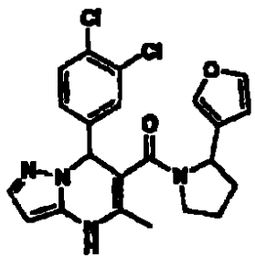
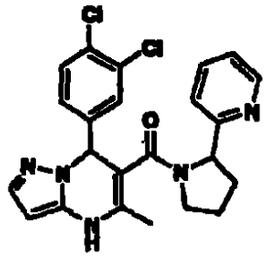
359		1-[[7-(3,4-Dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(2-metoxifenil) pirrolidona	483
360		1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazol[1,5-a]pirimidin-6-il]carbonil]-2-(4-fluorofenil) pirrolidina	471
361		(3R)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-3-fenoxipirrolidina	469

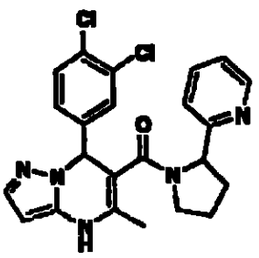
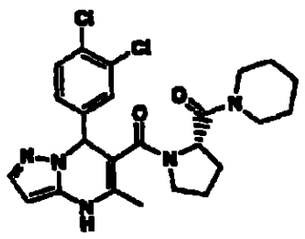
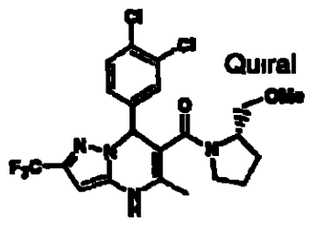
362		(2S)-2-[(ciclo-hexiloxi)metil]-1-[[7-(3,4-Dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il] carbonil]pirrolidina	489
363		1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il] carbonil]-2-(fenil-metil)pirrolidina	467
364		(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il] carbonil]-2-(fenoxi-metil)pirrolidina, diastereómero A	483

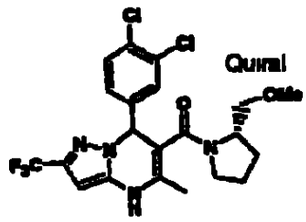
365		(2S)-1-[[7-(3,4-Diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il] carbonil]-2-(fenoxi-metil)pirrolidina, Diastereómero B	483
366		1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(3-metoxifenil) pirrolidina	483
367		(2S)-2-(butoxi-metil-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]pirro-lidina,	463

368		1-[[7-(3,4-Dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(2-tienil)pirrolidina	459
369		1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il] carbonil]-2-4-piridinil) pirrolidina	454
370		(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il] carbonil]-2-[(metoximetoxi)-metil]pirrolidina	451

422

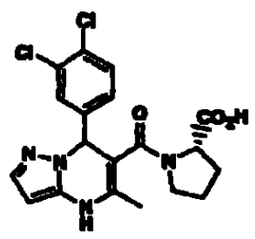
371		(2S)-2-[(1H-Bencimidazol-1-ilmetil)-[[7-(3,4-Diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a] pirimidin-6-il] carbonil]pirrolidina	507
372		1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(3-furanil)pirrolidina	443
373		1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(2-piridinil) pirrolidina	454

374		(3S)-1-[[7-(3,4-Diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-3-fenoxipirrolidina	469
375		(3S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-3-fenoxi-pirrolidina	488
376		(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-2-(trifluorometil) pirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(metoxi-metil)pirrolidina, enantiómero A	489

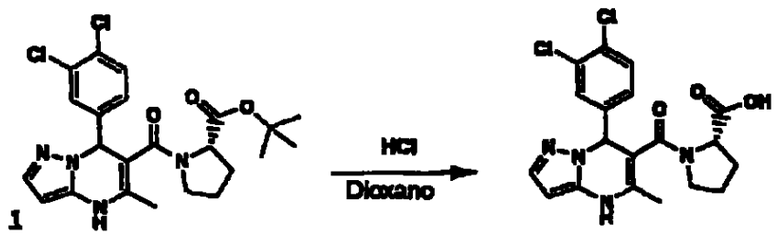
377		(2S)-1-[[7-(3,4-Diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(metoxi-metil)pirrolidina enatiómero B	489

Ejemplo 378

1-[[7-(3,4-Diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-L-prolina



Método



Compuesto 1 El compuesto 1 (el compuesto del ejemplo 252) se preparó en una manera similar a aquella descrita en el ejemplo 170

Compuesto del titulo Se agregó ácido clorhídrico (5 mL, 4M en Dioxano) al compuesto 1 (0 05 g, 0 1 mmol) La mezcla resultante se agitó a temperatura ambiente Después de 3 horas la mezcla se concentro in vacuo El análisis LC/MS del residuo indicó que permaneció el material iniciador Se agregó ácido clorhídrico adicional (5 mL, 4M en dioxano) La mezcla resultante se agitó a temperatura ambiente por 7 horas El análisis TLC indicó que el compuesto 1 se consumió La mezcla se concentró in vacuo El residuo se purifico por HPLC preparativa en fase inversa para dar el compuesto del titulo como una mezcla de diastereómeros El LC/MS indicó que el compuesto es todavía impuro (50% puro) LC/MS de fase inversa YMC S5 ODS 4 6 x 50 mm balistica, detección de UV a 220 λ, gradiente 4 min , Solvente B/A al 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con con TFA al 0 1%), 4 mL/min Diastereómero A Rt - 3 34, Diastereómero B Rt - 3 49 min MS (M+H 421) El producto se trituro con diclorometano para dar 0 014 g (rendimiento al 32%)

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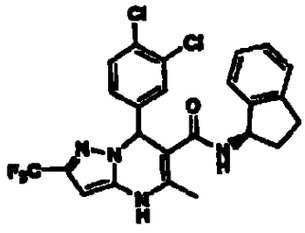
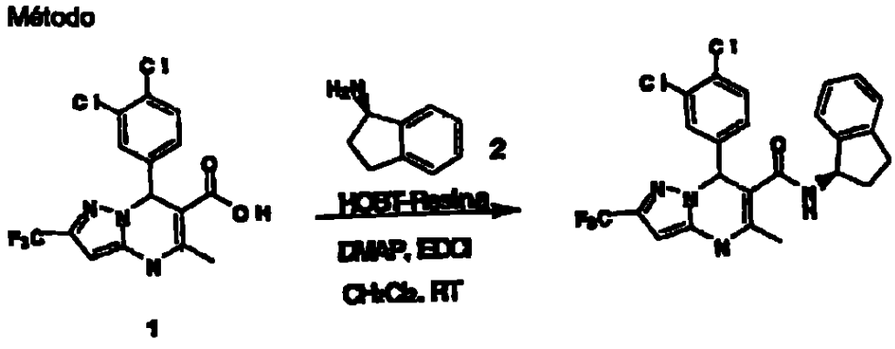
del compuesto del título (85% puro por HPLC) LC/MS de fase inversa YMC S5 4 6 x 50 mm combiscreen, detección de UV a 220 λ, gradiente 4 min, Solvente B/A al 0-100% (Solvente A MeOH/H_2O al 10% con H_3PO_4 al 0 2%, Solvente B MeOH/H_2O al 90% con H_3PO_4 al 0 2%) 4 mL/min Diastereómero A Rt = 2 82, Diastereómero B Rt - 2 97 min

Ejemplo 379

7-(3,4-Diclorofenil)-4,7-dihidro-N-[(1R)-2,3-dihidro-1H-inden-1-il]-5-metil-2-(trifluorometil)pirazolo[1,5-a]pirimidin-6-carboxamida





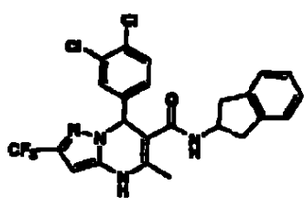
Compuesto 1 El compuesto 1 se preparó como se describe en el Ejemplo 1/

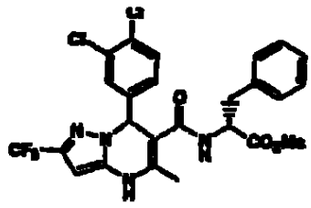
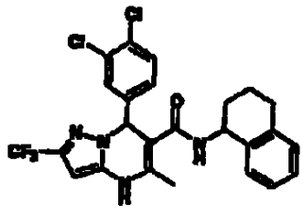
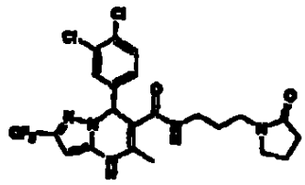
Compuesto del titulo A una suspensión de resina HOBt soportada con poliestireno (NovaBiochem, > 1 2 mmol/g, 50 mg, 1 0 eq) en CH_2Cl_2 anhidro (1 0 mL) se agrego el compuesto 1 (47 mg, 2 0 eq), EDCI (23 mg, 2 0 eq) y DMPA (0 / mg, 0 1 eq) La suspensión se sacudió vigorosamente usando un VORTEX-GENIE2 por 1 hora El solvente entonces se drenó y la resina se lavó secuencialmente con DMF (3x2 mL), THF (3x2 mL) y CH_2Cl_2 (3x2 mL) con agitación vigorosa La resina se resuspendió en CH_2Cl_2 (1 mL) y a la cuál se agregó (R)-(-)-Aminoidano 2 (0 006 mL, 0 8 eq) La mezcla se sacudio por 2 horas El solvente se dreno y la resina se lavó con CH_2Cl_2 (3x1 mL) con agitación vigorosa Todas las soluciones lavadas se combinaron y el solvente se removió bajo presión reducida El residuo se purificó a través de un cartucho del gel de silice eluido con EtOAc al 100% para dar el compuesto del titulo como un sólido blanco Columna LC/MS de fase inversa Ballistica YMC S5 ODS 4 6 x 50 mm, detección de UV a 220 λ, gradiente 4 min , Solvente B/A al 0-100% (Solvente A MeOH/H_2O al 10% con H_3PO_4 al 0 2%, Solvente B MeOH/H_2O al 90% con H_3PO_4 al 0 2%), 4

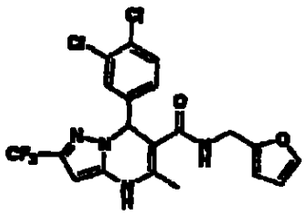
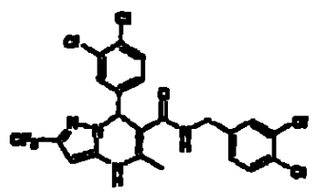
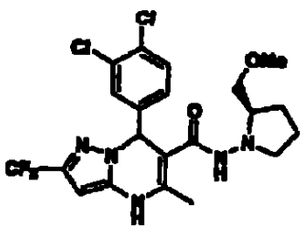
mL/min Rt = 2 96 min, (Diastereómero, puro al 96%) MS (M+H) 507)

Ejemplos 380-391

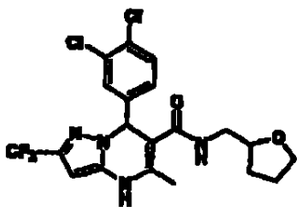
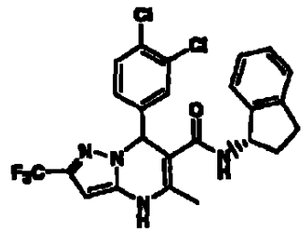
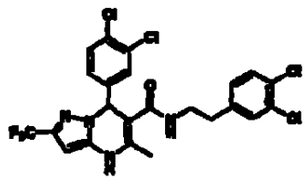
Los compuestos de los ejemplos 380-391, mostrados en la tabla proporcionada abajo, se prepararon de una manera similar a aquella descrita en el ejemplo 379

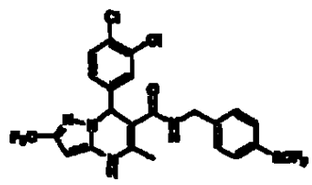
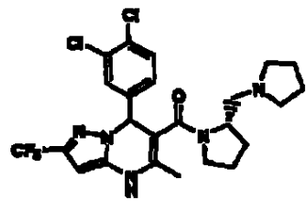
Ejemplo	Estructura	Nombre	(M+H)
380		/-(3,4-Diclorofenil)-N-(2,3-dihidro-1H-inden-2-il)-4,7-dihidro-5-metil-2-(trifluorometil)pirazolo[1,5-a]pirimidin-6-carboxamida	507

381		Ester metílico N-[[7-(3,4-Dicloro-fenil)-4,7-dihidro-5-metil-2-(tri-fluorometil)pirazolo [1,5-a]pirimidin-6-il]carbonil]-D-fenilalanina	553
382		7-(3,4-Dicloro-fenil)-4,7-dihidro-5-metil-N-(1,2,3,4-tetrahidro-1-naftalenil)-2-(tri-fluorometil)pirazolo [1,5-a]pirimidin-6-carboxamida	521
383		7-(3,4-Dicloro-fenil)-4,7-dihidro-5-metil-N-[3-(2-oxo-1-pirrolidinil)-propil]-2-(tri-fluorometil)pirazolo [1,5-a]pirimidin-6-carboxamida	516

384		7-(3,4-Dicloro-fenil)-N-(2-furanilmetil-4,7-dihidro-5-metil-2-(trifluorometil) pirazolo[1,5-a] pirimidin-6-carboxamida	471
385		7-(3,4-Dicloro-fenil)-N-(3,4-diclorofenil)metil]-4,7-dihidro-5-metil-2-(trifluorometil)-pirazolo[1,5-a]pirimidin-6-carboxamida	550
386		7-(3,4-Dicloro-fenil)-4,7-dihidro-N-[(2R)-2-(metoxi-metil)-1-pirrolidin]-5-metil-2-(trifluorometil)-pirazolo[1,5-a] pirimidin-6-carboxamida	504

431

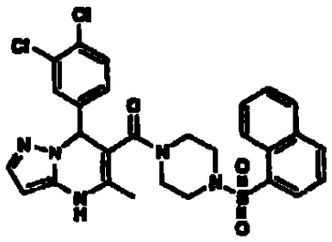
387		7-(3,4-Dicloro-fenil)-4,7-dihidro-5-metil-N-[(tetra-hidro-2-furanil)-metil]-2-(trifluoro-metil)pirazolo[1,5-a]pirimidin-6-carboxamida	475
388		7-(3,4-Dicloro-fenil)-4,7-dihidro-N-[(1S)-2,3-dihidro-1H-inden-1-il]-5-metil-2-(trifluoro-metil)pirazolo[1,5-a]pirimidin-6-carboxamida	507
389		7-(3,4-Dicloro-fenil)-N-[2-(3,4-diclorofenil)etil]-4,7-dihidro-5-metil-2-(trifluorometil) pirazolo[1,5-a] pirimidin-6-carboxamida	564

390		7-(3,4-Dıcloro-fenıl)-4,7-dıhıdro-5-metıl-2-(trıfluoro metıl)-N-[[4-[(trıfluorometıl)-tıo]fenıl]metıl] pırazolo[1,5-a] pırımıdın-6-carboxamıda	581
391		(2S)-1-[[7-(3,4-Dıclorofenıl)-4,7dı-hidro-5-metıl-2-(trifluorometıl) pırazolo[1,5-a] pırımıdın-6-ıl] carbonıl]-2-(1-pırrolıdınılmetıl)-pırrolıdına	666

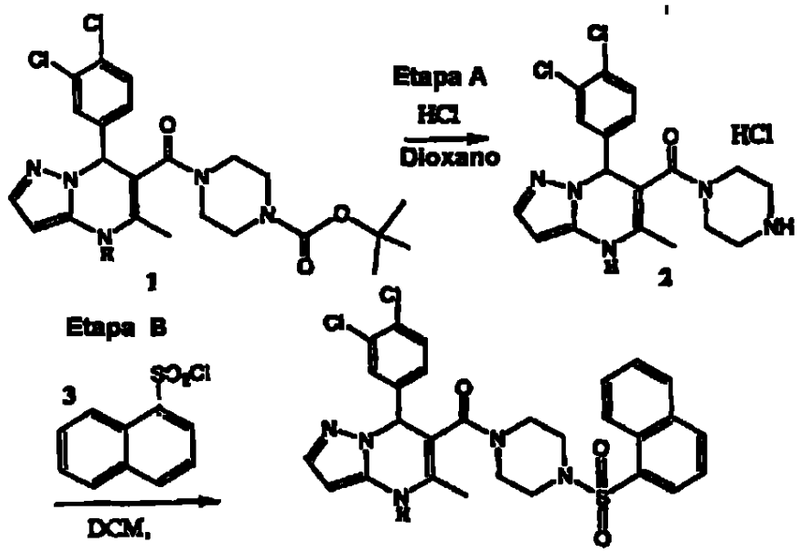
933

Ejemplo 392

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(1-naftalenilsulfonil)piperazina



Método



Compuesto 1 El compuesto 1 (el compuesto del ejemplo 60) se preparó en una manera similar a aquella descrita en el ejemplo 18, del método 2

Etapa A Se agregó HCl (4M en dioxano) a un compuesto sólido 1 (0 53 g, 1 1 mmol) Un precipitado gomoso se forma inmediatamente Se agrega diclorometano, el precipitado gomoso permanece El solvente se decantó y el residuo se trituro con acetato de etilo (3X), se concentró para dar 0 63 g (contenido de dioxano residual al 130%) de la sal de clorhidrato del compuesto 2 como un polvo amarillo ligero LC/MS de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección de UV a 220 λ, gradiente 4 min , Solvente B/A al 40-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt = 0 57, (92% puro) MS (M+H) 392) El compuesto 2 se usó sin purificación

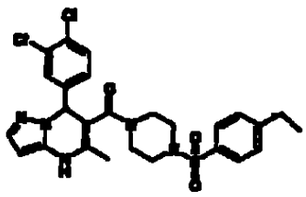
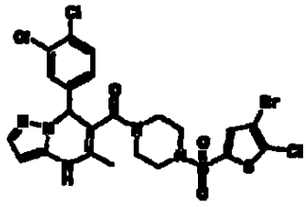
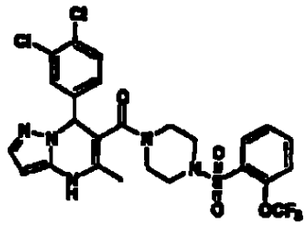
Etapa B El compuesto 2 (0 077 g, 0 18 mmol) y el compuesto 3 (0 049 g, 0 22 mmol) se suspendieron en diclorometano (1 mL) Se agregó trietilamina (0 05 mL, 0 36 mmol) Resultando una solución clara Después de 30 minutos el TLC indicó el consumo del material iniciador La mezcla se cargó directamente

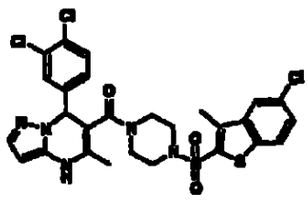
935

en un cartucho Wordlwıde Monıtorıng CLEAN-UP (CUSIL12M6, sılíce) el cual ha sıdo equilıbrado con hexanos al 100% Eluyendose con hexanos al 100% (40 mL), seguıdo por acetato de etılo/hexanos al 50% (40 mL) y acetato de etılo al 100% (40 mL) Las fraccıones más puras (análısıs TLC) se combinaron para dar 0 068 g (rendımıento al 65%) del compuesto del tıtulo como un sólıdo blanco LC/MS de fase ınversa columna Ballistıc YMC S5 ODS 4 6 x 50 mm, detección de UV a 220 λ, gradıente 4 mın , Solvente B/A al 40-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con con TFA al 0 1%), 4 mL/mın Rt = 3 46 min, (90% puro) MS (M+H) 582) HMR ($CDCl_3$, 400 HMz) 8 60 (1H, d, J = 8), 8 05 (2H, m), 7 95 (1H, m), 7 62 (4H, m), 7 35 (1H, d, J = 2 Hz), 7 17 (1H, d, J = 8 Hz), 7 06 (1H, d, J = 2 Hz), 6 81 (1H, d, J = Hz), 6 17 (1H, m), 5 54 (1H, d, J = 2 Hz), 3 23 (8H, m), 1 86 (3H, s)

Ejemplos 393-396

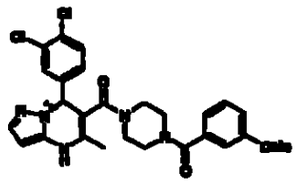
Los compuestos de los Ejemplos 393-396, mostrados en la tabla proporcıonada abajo, se prepararon en una manera sımılar a aquella descrıta en el Ejemplo 392

Ejemplo	Estructura	Nombre	(M+H)
393		1-[[7-(3,4-Dıcloro-fenıl)-4,7-dıhıdro-5-metılpırazolo[1,5-a]pırımidın-6-ıl]carbonıl]-4-[(4-etılfenıl)sulfonıl]-pıperazına	560
394		1-[(4-bromo-5-cloro-2-tıenıl)sulfonıl]-4-[[7-(3,4-Dıcloro-fenıl)-4,7-dıhıdro-5-metılpırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-pıperazına	651
395		1-[[7-(3,4-Dıcloro-fenıl)-4,7-dıhıdro-5-metılpirazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-[[2-(trıfluorometoxı)-fenıl]sulfonıl] pıperazına	616

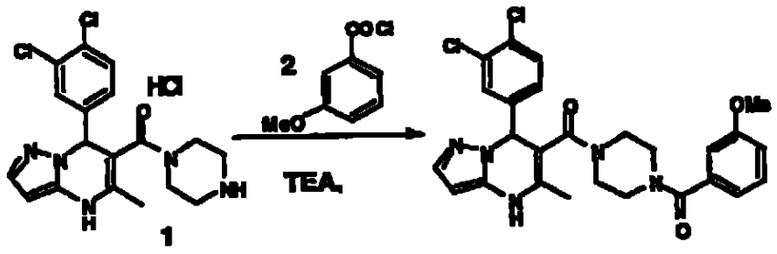
396		1-[(5-cloro-3-metil-benzo[b]tiofen-2-il)sulfonil]-4-[[7-(3,4-Dicloro-fenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil] piperazina	637

Ejemplo 397

1-[[7-(3,4-Diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-[(3-metoxifenil)carbonil]piperazina



Método

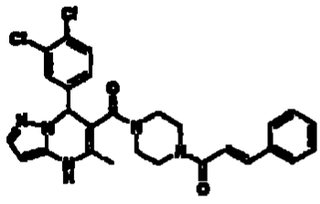
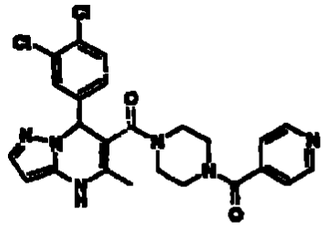


Compuest 1 El compuesto 1 se preparó como se describe en la Etapa A del Ejemplo 392

Compuesto del titulo El compuesto 1 (0 062 g, 0 15 mmol) y el compuesto 2 (0 025 mL, 0 17 mmol) se suspendieron en diclorometano (1 mL) Se agregó trietilamina (0 040, 0 29 mmol) Resulto una solución clara Después de 30 minutos el TLC indicó el consumo del material iniciador La mezcla se cargo directamente en un cartucho Worldwide Monitoring CLEAN-UP (CUSIL12M6) el cuál ha sido equilibrado con hexanos al 100% Eluyéndose con hexanos al 100% (40 mL), seguido por acetato de etilo/hexanos al 50% (100 mL) y acetato de etilo al 100% (100 mL) Las fracciones más puras (análisis TLC) se combinaron para dar 0 022 g (rendimiento al 29%) del compuesto del titulo como un sólido blanco LC/MS de fase inversa columna Ballistic YMC S5 ODS 4.6 x 50 mm, detección de UV a 220 λ, gradiente 4 min , Solvente B/A al 40-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min 2 69 min, (90% puro) MS (M+H) 526)

Ejemplos 398 y 399

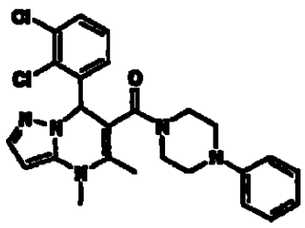
Los compuestos de los ejemplos 398 y 399, mostrados en la tabla proporcionada abajo, se prepararon en una manera similar a aquella descrita en el Ejemplo 397

Ejemplo	Estructura	Nombre	(M+H)
398		1-[[7-(3,4-Dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(1-oxo-3-fenil-2-propenil)-piperazina	522
399		1-[[7-(3,4-Dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-piridinilcarbonil) piperazina	497

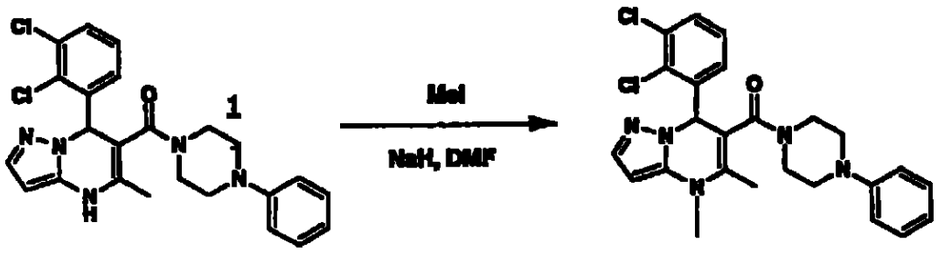
440

Ejemplo 400

1-[[7-(2,3-Diclorofenil)-4,7-dihidro-4,5-dimetilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-fenilpiperazina



Método



Compuesto 1 El compuesto 1 se preparó como se describe en el Ejemplo 18

Compuesto del titulo El compuesto 1 (0 08 g, 0 17 mmol) se disolvió en dimetilformamida (1 0 mL) Se agregó NaH (0 005 g, 0 22 mmol, en aceite al 60%) y

441

la mezcla se agitó por 5 minutos Se agregó yodometano (0 012 mL, 0 18 mmol) Cuando el análisis TLC (metanol/diclorometano al 5%) indicó el consumo del material iniciador, la reacción se enfrió rápidamente con agua, se diluyó con acetato de etilo, se transfirió a un embudo separador, se lavó con agua saturada y salmuera, se secó sobre sulfato de sodio anhidro y se concentró El residuo se purificó por cromatografía de gel de sílice eluido con diclorometano al 100% seguido por metanol/diclorometano al 3% para proporcionar 0 06 g (al 75%) del compuesto del titulo como un aceite ámbar LC/MS de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección de UV a 220 λ, gradiente 4 min , Solvente B/A al 40-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con con TFA al 0 1%), 4 mL/min Rt = 2 99 min, (96% puro) MS (M+H 482)

Ejemplos 401-406

Los compuestos de los Ejemplos 401-406, mostrados en la tabla proporcionada abajo, se preparan en una manera similar a aquella descrita en el Ejemplo 400

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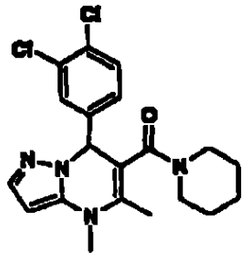
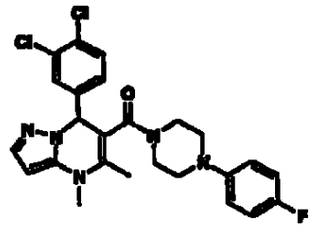
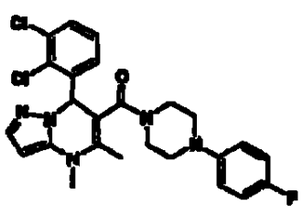
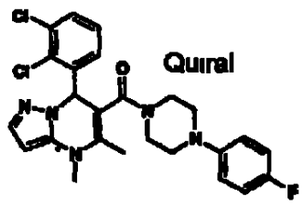
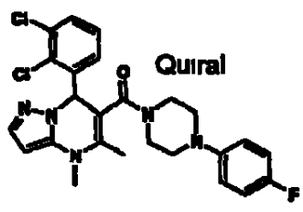
La resolución de HPLC del Ejemplo 403, columna Chiralpak AD (50 x 500 mm), elución con isopropanol/hexanos al 35% conteniendo trietilamina la 0 1% a 50 mL/min), la detección UV a 254 λ proporciona enantiómeros A (Ejemplo 405) y B (Ejemplo 404) Columna Chiralpak AD (4 6 x 250 mm) elución con isopropanol/hexanos al 30% conteniendo trietilamina al 0 1% a 1 mL/min), detección UV a 254 λ, enetiómero A Rt = 14 4 min, > 99% ee Enantiómero B Rt = 28 7 min, > 99% ee

Ejemplo	Estructura	Nombre	(M+H)
401		1-[[7-(3,4-Dicloro-fenil)-4,7-dihidro-4,5-dimetilpirazolo-[1,5-a]pirimidin-6-il]carbonil]piperidina	405
402		1-[[7-(3,4-Dicloro-fenil)-4,7-dihidro-4,5-dimetilpirazolo [1,5-a]pirimidin-6-il]crabonil]-4-(4-fluorofenil) piperazina	500

443

403		1-[[7-(3,4-Dicloro-fenil)-4,7-dihidro-4,5-dimetilpirazolo-[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil) piperazina	500
404		1-[[7-(3,4-Dicloro-fenil)-4,7-dihidro-4,5-dimetilpirazolo-[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil) piperazina, enantiómero B	500
405		1-[[7-(2,3-Dicloro-fenil)-4,7-dihidro-4,5-dimetilpirazol-[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil) piperazina, enantiómero A	500

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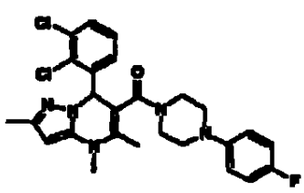
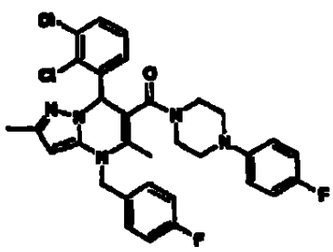
406		1-[[7-(2,3-Dicloro-fenil)-4,7-dihidro-2,4,5-dimetilpira-zolo-[1,5-a]pirimi-din-6-il]carbonil]-4-(4-fluorofenil) piperazina	514

Ejemplo 407

1-[[7-(2,3-Diclorofenil)-4-[(4-fluorofenil)metil]-4,7dihidro-2,5-dimetilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina



Método

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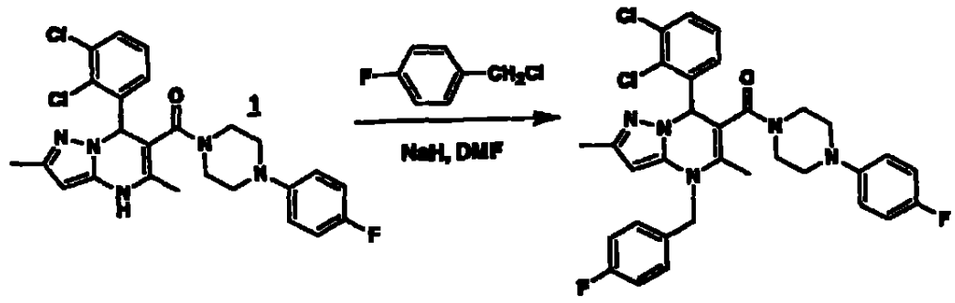

Compuesto 1 El compuesto 1 se preparó en una manera similar a aquella descrita en el Ejemplo 18, del metodo 2

Compuesto del titulo El compuesto 1 (0 10 g, 0 21 mmol) se disolvió en dimetilformamida (1 0 mL), NaH (0 007 g, 0 27 mmol, 60% en aceite) se agregó y la mezcla se agito por 5 minutos Se agregó cloruro de 4-fluorobencilO (0 028 mL, 0 23 mmol) Cuando el análisis TLC (metanol/diclorometano al 5%) indico el consumo del material iniciador, la reacción se enfrió con agua, se diluyó con acetato de etilo, SE transfirió a un embudo separador, se lavó con agua saturada y salmuera, se secó sobre sulfato de sodio anhidro y se concentró El residuo se purificó por cromatografía en gel de sílice, elución con diclorometano al 100% seguido por metanol/diclorometano al 3% para proporcionar 0 09 g

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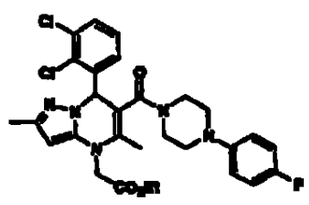
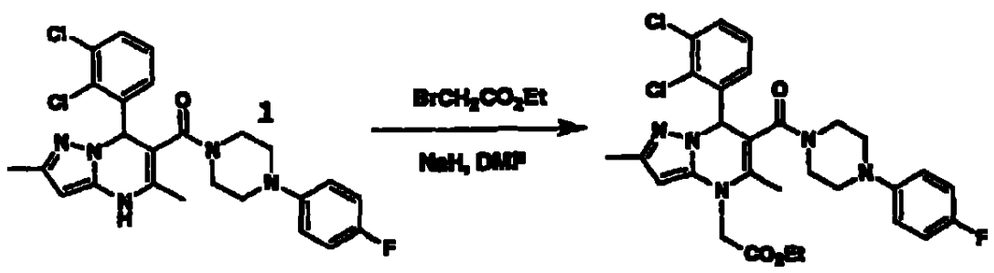
(al 69%) del compuesto del título como un aceite ámbar LC/MS de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección de UV a 220 λ, gradiente 4 min , Solvente B/A al 40-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con con TFA al 0 1%), 4 mL/min Rt = 3 20 min, (93% puro) MS (M+H 608)

Ejemplo 408

Ester etílico del ácido 7-(2,3-diclorofenil)-6-[[4-(4-fluorofenil)-1-piperazinil]carbonil]-2,5-dimetilpirazolo[1,5-a]pirimidina-4-(7H)-acetico



Método



447

C mpuest 1 El compuesto 1 se preparó en una manera similar a aquella descrita en el Ejemplo 18, del método 2

Compuesto del título El compuesto 1 (0 10 g, 0 21 mmol) se disolvió en dimetilformamida (1 0 mL) Se agregó NaH (0 006 g, 0 24 mmol, 60% en aceite) y la mezcla se agitó por 5 minutos Se agregó bromoacetato de etilo (0 029 mL, 0 26 mmol) Cuando el análisis TLC (metanol/diclorometano al 5%) indicó el consumo del material iniciador, la reacción se enfrió rápidamente con agua, se diluyó con acetato de etilo, se transfirió a un embudo separador, se lavó con agua saturada y salmuera, se secó sobre sulfato de sodio anhídro y se concentró El residuo se purificó por cromatografía en gel de sílice elución con diclorometano al 100% seguido por metanol/diclorometano al 3% para proporcionar 0 086 g (al 74%) del compuesto del titulo como un vidrio amarillo LC/MS de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección de UV a 220 λ, gradiente 4 min , Solvente B/A al 40-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con con TFA al 0 1%), 4 mL/min Rt = 3 22 min, (97% puro) MS (M+H 586)

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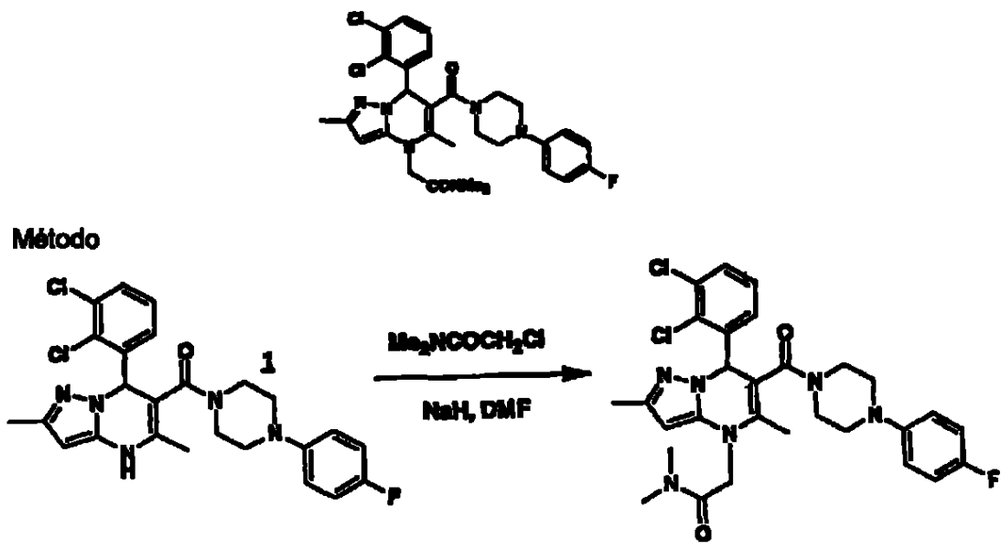
Ejemplo 409

7-(2,3-diclorofenil)-6-[[4-(4-fluorofenil)-1-piperazinil]carbonil]-N,N,2,5-tetrametilpirazolo[1,5-a]pirimidina-4(7H)-acetamida



Compuesto 1 El compuesto 1 se preparó en una manera similar a aquella descrita en el Ejemplo 18, del Método 2

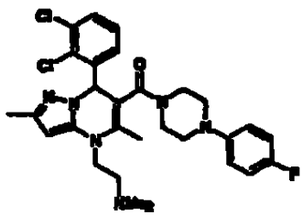
Compuesto del titulo El compuesto 1 (0 08 g, 0 16 mmol) se disolvió en dimetilformamida (0 8 mL) Se agregó NaH (0 005 g, 0 19 mmol, 60% en aceite) y la mezcla se agitó por 5 minutos Se agregó 2-cloro-N,N-dimetilacetamida (0 021 mL, 0 21 mmol) Cuando el

análisis TLC (metanol/diclorometano al 5%) indicó el consumo del material iniciador, la reacción se enfrió rápidamente con agua, se diluyó con acetato de etilo, se transfirió a un embudo separador, se lavó con agua y salmuera saturada, se secó sobre sulfato de sodio anhidro y se concentró El residuo se purificó por cromatografía en gel de sílice elución con diclorometano al 100% seguido por metanol/diclorometano al 3% para proporcionar 0 058 g (al 62%) del compuesto del titulo como un aceite amarillo LC/MS de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección de UV a 220 λ, gradiente 4 min , Solvente B/A al 40-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con con TFA al 0 1%), 4 mL/min Rt = 2 63 min, (93% puro) MS (M+H 585)

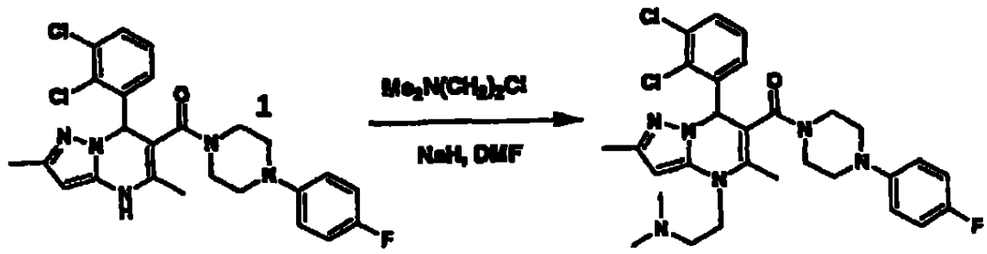
Ejemplo 410

1-[[7-(2,3-Diclorofenil)-4-[2-(dimetilamino)etil]-4,7-dihidro-2,5-dimetilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina

450



Método



Compuesto 1 El compuesto 1 se preparó en una manera similar a aquella descrita en el Ejemplo 18, del método 2

Compuesto del título El compuesto 1 (0 11 g, 0 21 mmol) se disolvió en dimetilformamida (1 0 mL) Se agrego hidruro de sodio (0 054 g, 0 47 mmol, 60% en aceite) y la mezcla se agitó por 5 minutos Se agregó clorhidrato de 1-cloro-2-dimetilaminoetano (0 40 g, 0 27 mmol) Después de 25 minutos la reacción se enfrió rápidamente con agua, se diluyó con acetato de etilo, transferido a un embudo separador, se lavó con

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agua saturada y salmuera, se secó sobre sulfato de sodio anhidro y se concentró El análisis LC/MS del residuo indicó que la mayoría del material iniciador no reaccionó El residuo se disolvió en dimetilformamida (1 0 mL), se agregó hidruro de sodio (0 10 g, 4 2 mmol) y la mezcla se agitó por 5 minutos Se agregó clorhidrato de 1-cloro-2-dimetilaminoetano (0 15 g, 1 05 mmol) Cuando el análisis TLC (metanol/diclorometano al 5%) indicó el consumo del material iniciador, la reacción se enfrió rápidamente con agua, se diluyó con acetato de etilo, transferido a un embudo separador, se lavó con agua saturada y salmuera, se secó sobre sulfato de sodio anhidro y se concentró El residuo se purificó por cromatografía en gel de sílice eluido con diclorometano al 100% seguido por metanol/diclorometano al 3% para proporcionar 0 030 g (al 25%) del compuesto del titulo como un vidrio amarillo LC/MS de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección de UV a 220 λ, gradiente 4 min , Solvente B/A al 40-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt = 1 72 min, (92% puro) MS (M+H 571)

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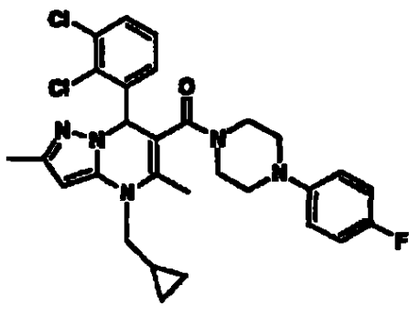
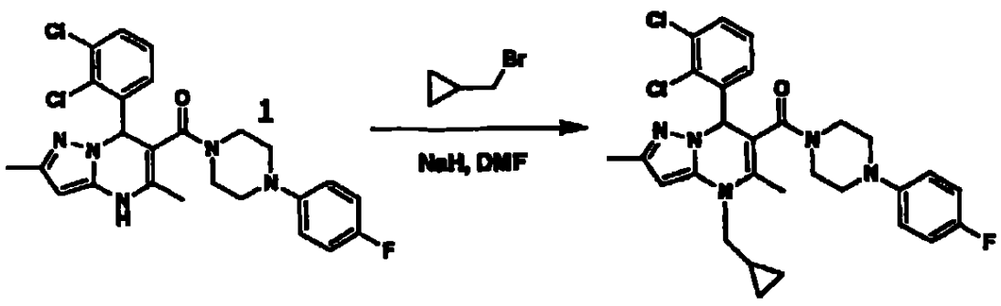
Ejemplo 411

1-[[4-(Ciclopropilmetil)-7-(2,3-diclorofenil)-4,7-dihidro-2,5-dimetilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina



Método

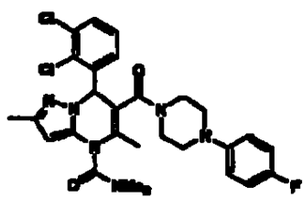


Compuesto 1 El compuesto 1 se preparó en una manera similar a aquella descrita en el Ejemplo 18, del Método 2

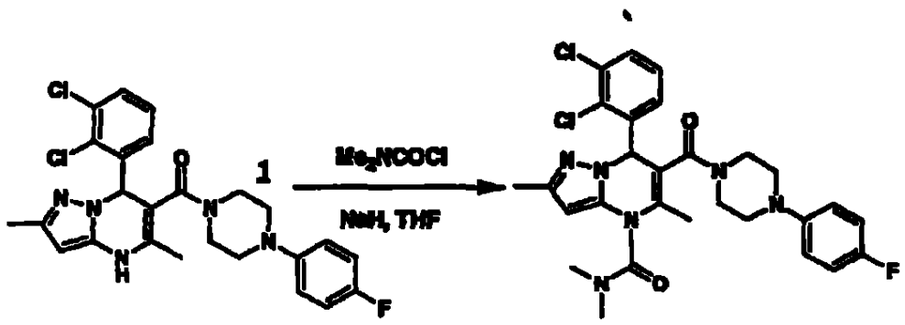
Compuest del titulo El compuesto 1 (0 11 g, 0 21 mmol) se disolvió en dimetilformamida (1 0 mL) Se agregó hidruro de sodio (0 006 g, 0 25 mmol, al 60% en aceite) y la mezcla se agitó por 5 minutos Se agregó (Bromometil)ciclopropano (0 0251 mL, 0 27 mmol) Cuando al análisis TLC (metanol/diclorometano al 5%) indicó el consumo del material iniciador, la reacción se enfrió rápidamente con agua, se diluyó con acetato de etilo, se transfirió a un embudo separador, se lavó con agua saturada y salmuera, se secó sobre sulfato de sodio anhidro y se concentró El residuo se purificó por cromatografía en gel de sílice elución con diclorometano al 100% seguido por metanol/diclorometano al 3% para proporcionar 0 104 g (al 89%) del compuesto del titulo como un vidrio amarillo LC/MS de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección de UV a 220 λ, gradiente 4 min , Solvente B/A al 40-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt = 2 99 min, (95% puro) MS (M+H 554)

Ejemplo 412

7-(2,3-diclorofenil)-6-[[4-(4-fluorofenil)-1-piperazinil]carbonil]-N,N,2,5-tetrametilpirazolo[1,5-a]pirimidina-4(7H)-carboxamida



Método



Compuesto 1 El compuesto 1 se preparó en una manera similar a aquella descrita en el Ejemplo 18, del Método 2

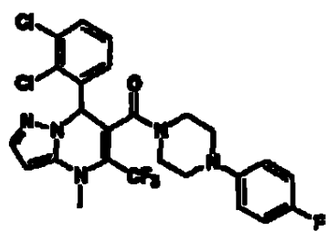
Compuesto del titulo El compuesto 1 (0 22 g, 0 44 mmol) se disolvió en tetrahidrofurano (3 0 mL) Se

agregó hidruro de sodio (0 106 g, 4 44 mmol, al 60% en aceite) y la mezcla se agitó por 5 minutos Se agregó cloruro de N,N-dimetilcarbamoil (0 12 mL, 1 33 mmol) La mezcla se agitó durante la noche El análisis TLC (metanol/diclorometano al 5%) indicó el consumo del material iniciador, la reacción se enfrió rápidamente con agua, se diluyó con acetato de etilo, se transfirió a un embudo separador, se lavó con agua saturada y salmuera, se secó sobre sulfato de sodio anhídro y se concentró El residuo se purificó por cromatografía en gel de sílice elución con diclorometano al 100%, seguido por metanol/diclorometano al 3% para proporcionar 0 22 g (rendimiento del 87%) del compuesto del titulo El LC/MS indicó que el compuesto es impuro El compuesto del titulo se purificó adicionalmente por cromatografía en gel de sílice, elución con acetato de etilo/hexanos al 10%, seguido por acetato de etilo/hexanos al 50% y acetato de etilo al 100% para proporcionar 0 118 g (rendimiento del 47%) del compuesto del titulo como un vidrio blanco LC/MS de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección de UV a 220 λ, gradiente 4 min , Solvente B/A al 40-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA

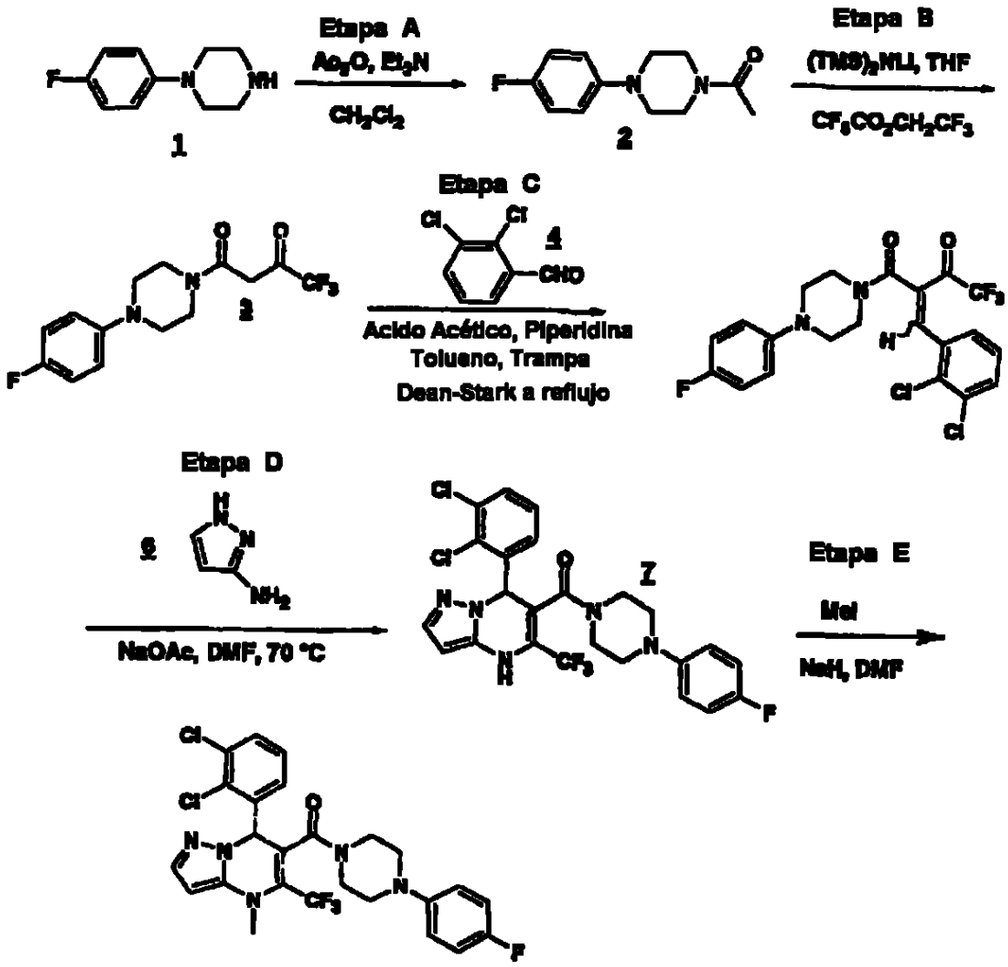
al 0 1%), 4 mL/min Rt = 2 45 min, (95% puro) MS (M+H 571)

Ejemplo 413

1-[[7-(2,3-diclorofenil)-4,7-dihidro-4-metil-5-(trifluorometil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina



Método



Etapa A Se agregó en forma de gotas anhídrido acético (0 77 mL, 8 14 mmol) a una solución de 4-(4-fluorofenil)piperazina 1 (1 17 g, 6 49 mmol) en diclorometano (10 mL) Después de 30 minutos el TLC

indicó que la reacción se completó La mezcla se transfirió a un embudo separador, se lavó con agua y salmuera, se secó sobre sulfato de sodio anhídro y se conentró para dar 1 28 g (rendimiento del 89%) del compuesto 2 como un aceite sólido LC/MS de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección de UV a 220 λ, gradiente 4 min , Solvente B/A al 40-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt = 1 58 min, (92% puro) MS (M+H 223) HMR ($CDCl_3$, 400 MHz) 6 96 (2H, m), 6 89 (2H, m), 3 77 (2H, m), 3 62 (2H, m), 3 07 (4H, m), 2 14 (3H, s) El compuesto 2 se usó sin purificación adicional en la siguiente etapa

Etapa B Se agregó en forma de gotas hexametildisililazida de litio a una solución a -78° del compuesto 2 (1 22 g, 5 5 mmol) en terahidrofurano (25 mL) Después de 40 minutos, se agrego trifluoroacetato de 2,2,2-trifluoroetilo (0 9 mL, 6 6 mmol) a la solución amarilla La reacción se tornó de amarilla a clara Después de 10 minutos adicionales, el baño frió se removió y la mezcla se dejó calentar a temperatura ambiente Después de 30 minutos más, la reacción se enfrió rápidamente con cloruro de amonio

saturado, se diluyó con acetato de etilo, se transfirió a un embudo separador, se lavó con cloruro de amonio saturado, agua y salmuera, se secó sobre sulfato de sodio anhidro y se concentró en suficiente gel de sílice de manera que se obtuvo un polvo de flujo suave El polvo resultante se cargó en una columna de cromatografía preenvasada con gel de sílice y acetato de etilo/hexanos al 30% La elución con acetato de etilo/hexanos al 30% dio 0 998 g (rendimiento al 57%) del compuesto **3** como un sólido amarillo LC/MS de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección de UV a 220 λ, gradiente 4 min , Solvente B/A al 40-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt = 2 87 min, (90% puro) MS (M+H 319) HMR ($CDCl_3$, 400 MHz) (nota el compuesto existe en la forma de enol) 7 00 (2H, m), 5 80 (1H, s), 3 79 (4H, m), 3 13 (4H, m)

Etapa C El compuesto **3** y el compuesto **4** se condensaron como se describe en el Ejemplo 18 del metodo 2, etapa B, para proporcionar el compuesto **5** El compuesto **5** se usó en el siguiente paso sin purificación adicional

Etapa D· El compuesto 5 y el compuesto 6 se condensaron como se describe en el Ejemplo 18 del método 2, etapa C1, para proporcionar el compuesto 7 LC/MS de fase inversa del crudo 6 columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección de UV a 220 λ, gradiente 4 min , Solvente B/A al 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt = 4 12 min, (58% puro) MS (M+H 540) El compuesto 7 se purificó por cromatografía en gel de sílice elución con acetato de etilo/hexanos al 20-50%, seguido por recristalización de acetato de etilo/hexanos para dar 0 084 g (rendimiento al 6%) del compuesto 7 como un sólido blanco LC de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección de UV a 220 λ, gradiente 4 min , Solvente B/A al 0-100% (Solvente A MeOH/H_2O al 10% con H_3PO_4 al 0 2%, Solvente B MeOH/H_2O al 90% con H_3PO_4 al 0 2%), 4 mL/min Rt = 4 15 min, (92% puro)

Etapa E El compuesto 7 (0 08 g, 0 14 mmol) se disolvió en dimetilformamida (1 0 mL) Se agregó NaH (0 005 g, 0 19 mmol, al 60% en aceite) y la mezcla se agitó por 305 minutos Se agregó yodometano (0 010 mL, 0 16 mmol) La mezcla se agitó por 2 horas y

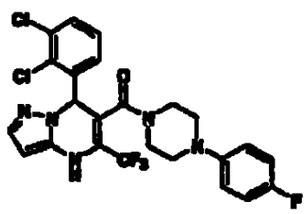
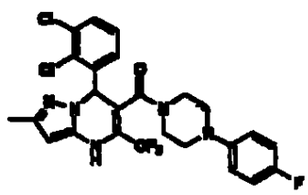
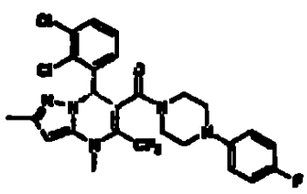
entonces se enfrió rápidamente con cloruro de amonio saturado, se diluyó con acetato de etilo, se transfirió a un embudo separador, se lavó con agua saturada y salmuera, se secó sobre sulfato de sodio anhidro y se concentró El residuo se purificó por preparativa HPLC de fase inversa columna Ballistic YMC S5 ODS 20 x 100 mm, detección de UV a 220 λ, gradiente 10 min , Solvente B/A al 30-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 20 mL/min Rt = 10 6 min , para proporcionar 0 037 g (al 45%) del compuesto del titulo LC/MS de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección de UV a 220 λ, gradiente 4 min , Solvente B/A al 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt = 3 83 min MS (M+H 568) LC de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección de UV a 220 λ, gradiente 4 min , Solvente B/A al 0-100% (Solvente A MeOH/H_2O al 10% con H_3PO_4 al 0 2%, Solvente B MeOH/H_2O al 90% con H_3PO_4 al 0 2%), 4 mL/min Rt = 4 37 min , 89% puro

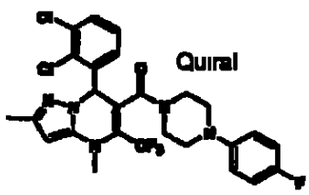
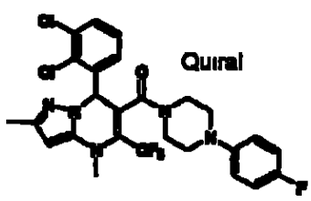
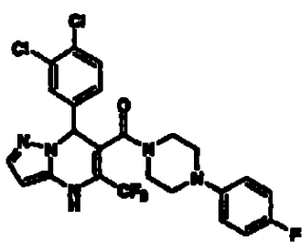
Ejemplos 414-421

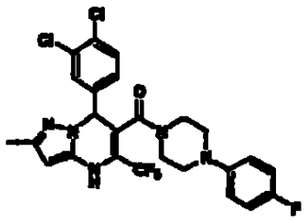
Los compuestos de los Ejemplos 414-421, mostrados en la tabla proporcionada abajo, se prepararon en una manera similar a aquella descrita en el Ejemplo 413

La resolución HPLC del Ejemplo 416, columna AD Chiralpak (50 X 55 mm), elución con isopropanol/hexanos al 50% conteniendo trietilamina al 0 1% a 50 mL/min), detección UV a 254 λ, proporcionó A (Ejemplo 418) y B (Ejemplo 417) Columna AD Chiralpak (4 6 X 250 mm) elución con isopropanol/hexanos al 50%, conteniendo trietilamina al 0 1% a 1 mL(min), detección UV a 254 λ, enantiómero A Rt = 14 4 min, al 89% ee Enantiómero B Rt = 28 7 min, al 87% ee

463

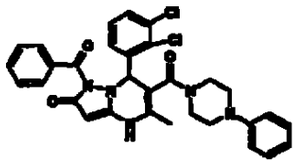
Ejemplo	Estructura	Nombre	(M+H)
414		1-[[7-(2,3-Dicloro-fenil)-4,7-dihidro-5-(trifluorometil) pirazolo-[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil) piperazina	554
415		1-[[7(2,3-Dicloro-fenil)-4,7-dihidro-2-metil-5-dimetil-pirazolo[1,5-a] pirimidin-6-il] carbonil]-4-(4-fluorofenil) piperazina	554
416		1-[[7-(2,3-Dicloro-fenil)-4,7-dihidro-2,4-dimetil-5-(tri-fluorometil)pirazolo -[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil) piperazina	568

417		1-[[7-(2,3-Dicloro-fenil)-4,7-dihidro-2,4-dimetil-5-(tri-fluorometil)pirazolo-[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)pipera-zina, enantiómero B	568
418		1-[[7-(2,3-Dicloro-fenil)-4,7-dihidro-2,4-dimetil-5-(tri-fluorometil)pirazolo-[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)pipera-zina, enantiómero A	568
419		1-[[7-(3,4-Dicloro-fenil)-4,7-dihidro-5-(trifluorometil) pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil) piperazina	540

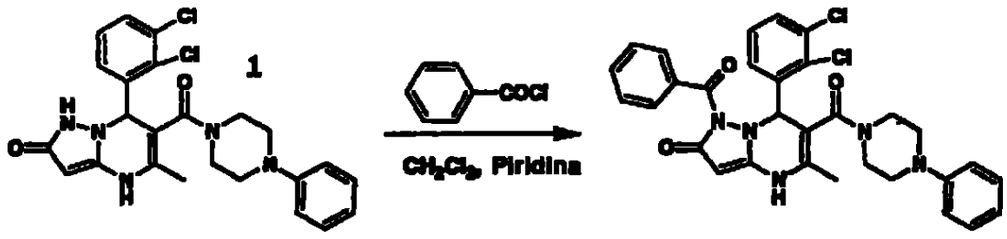
420		1-[[7-(3,4-Dicloro-fenil)-4,7-dihidro-2-metil-5-(trifluorometil)pirazolo-[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil) piperazina	554

Ejemplo 421

1-[[1-Benzoil-7-(2,3-diclorofenil)-1,2,4,7-tetrahidro-5-metil-2-oxopirazolo[1,5-a]pirimidin-6-il]carbonil]-4-fenilpiperazina



Método

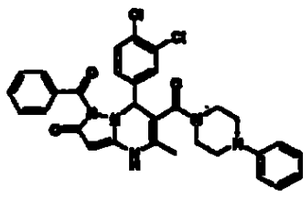
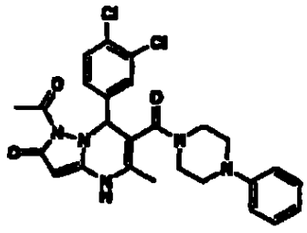


C mpuesto 1 El compuesto 1 se preparó en una manera similar a aquella descrita en el ejemplo 18, del método 2

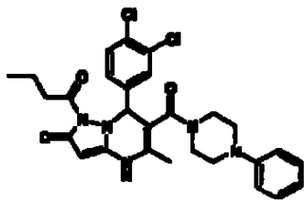
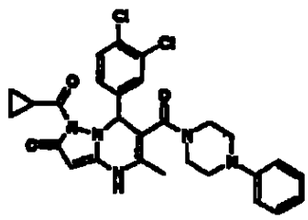
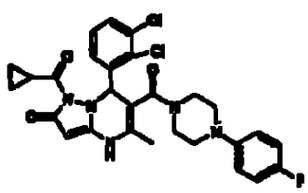
Compuesto del titulo Se agregó cloruro de benzoilo (0 007 mL, 0 06 mmol) y piridina (0 008 mL, 0 10 mmol) a 0°C a una solución del compuesto 1 (0 08 g, 0 17 mmol) en diclorometano (5 mL) Después de 1 hora, el TLC indicó que la reacción se completo La reacción se enfrió rápidamente con metanol y se concentró El residuo se purificó por cromatografía en gel de sílice, elución con acetato de etilo hexanos al 80% para proporcionar 0 024 g del compuesto del titulo (al 81%) como un sólido blanco LC/MS de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección UV a 220 λ, gradiente 4 min Solvente B/A del 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt = 4 05, (86% puro) (M+H 588) HMR ($CDCl_3$, 400 MHz) 8 08 (1H, s), 8 06 (1H,s), 7 51 (1H, m), 7 37 (2H, t, J = 8 Hz), 7 28 (1H, m), 7 18 (2H, m), 7 08 (1H, m), 6 9-6 7 (3H, m), 6 45 (1H, bs), 5 60 (1H, bs), 4 15-2 8 (6H, m), 2 20 (1H, bs), 1 88 (3H, s), 1 45 (1H, bs)

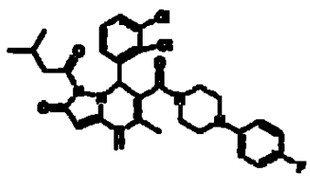
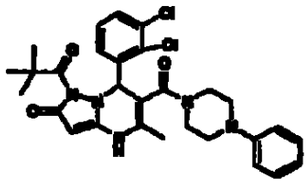
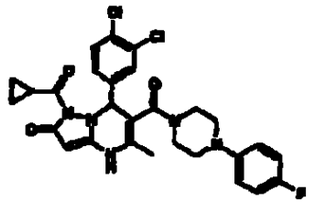
Ejemplos 422-431

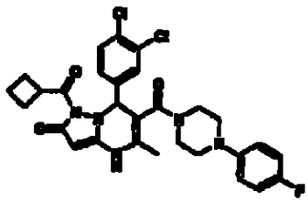
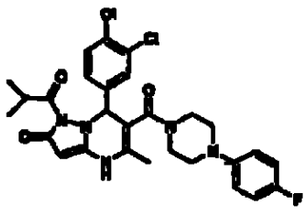
Los compuestos de los Ejemplos 422-431, mostrados en la tabla proporcionada abajo, se prepararon en una manera similar a aquella descrita en el Ejemplo 421

Ejemplo	Estructura	Nombre	(M+H)
422		1-[[1-benzoil-7-(3,4-Diclorofenil)-1,2,4,7-tetrahidro-5-metil-2-oxopirazolo[1,5-a] pirimidin-6-il] carbonil]-4-fenilpiperazina	588
423		1-[[1-Acetil-7-(3,4-Diclorofenil)-1,2,4,7-tetrahidro-5-metil-2-oxopirazolo[1,5-a] pirimidin-6-il] carbonil]-4-fenilpiperazina	526

968

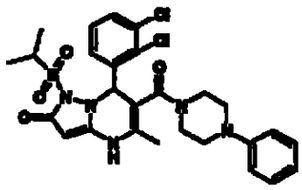
424		1-[[7-(3,4-Dıcloro-fenıl)-1,2,4,7-tetrahıdro-5-metıl-2-oxo-1-(1-oxo-butıl)-pırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-fenılpıperazına	554
425		1-[[1-cıclopropıl-carbonil-7-(3,4-Diclorofenıl)-1,2,4,7-tetrahıdro-5-metıl-2-oxopırazolo[1,5-a] pırımıdın-6-ıl] carbonıl]-4-fenılpıperazına	552
426		1-[[1-cıclopropıl-carbonıl-7-(2,3-dıclorofenıl)-1,2,4,7-tetrahıdro-5-metıl-2-oxopırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazına	570

427		1-[[7-(2,3-Dicloro-fenil)-1,2,4,7-tetrahidro-5-metil-1-(3-metil-1-oxo-butil)-2-oxopirazol[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	586
428		1-[[7-(2,3-Dicloro-fenil)-(2,2-dimetil-1-oxopropil)-1,2,4,7-tetrahidro-5-metil-2-oxopirazol[1,5-a]pirimidin-6-il]carbonil]-4-fenilpiperazina	568
429		1-[[1-ciclopropil-carbonil)-7-(3,4-Diclorofenil)-1,2,4,7-tetrahidro-5-metil-2-oxopirazol[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)-piperazina	570

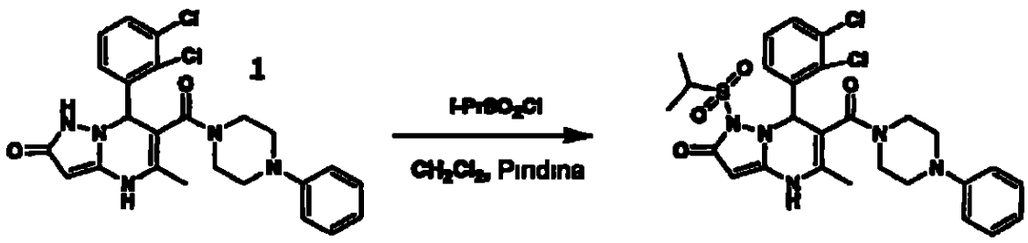
430		1-[[1-Ciclobutil-carbonil-7-(3,4-Diclorofenil)-1,2,4,7-tetrahidro-5-metil-2-oxopirazol[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)-piperazina	584
431		1-[[7-(3,4-Dicloro-fenil)-1,2,4,7-tetrahidro-5-metil-1-(2-metil-1-oxopropil)-2-oxopirazol[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluoro-fenilpiperazina	572

Ejemplo 432

1-[[7-(2,3-diclorofenil)-1,2,4,7-tetrahidro-5-metil-1-[(1-metiletil)sulfonil]-2-oxopirazol[1,5-a]pirimidin-6-il]carbonil]-4-fenilpiperazina



Método



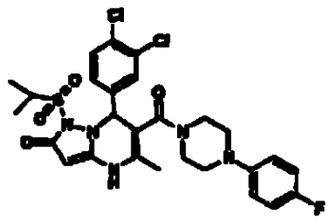
Compuesto 1 El compuesto 1 se preparó en una manera similar a aquella descrita en el Ejemplo 18, del método 12

Compuesto del titulo Se agregó cloruro de isopropilsulfonilo (0 11 mL, 0 97 mmol) y piridina (0 12 mL, 1 46 mmol) a 0°C a una solución del compuesto 1 (0 234 g, 0 487 mmol) en diclorometano (10 mL) La mezcla resultante se dejó calentar a temperatura ambiente Después de 5 horas, el TLC indicó que la reacción se completo La reacción se enfrió rápidamente con metanol y se concentró El residuo se purificó por cromatografía en gel de

sílice, elución con metanol/acetato de etilo al 5% para proporcionar 0 095 g del compuesto del título (al 33%) como un sólido amarillo pálido LC/MS de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección UV a 220 λ, gradiente 4 min Solvente B/A del 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt = 3 57, (92% puro) (M+H 590)

Ejemplo 433

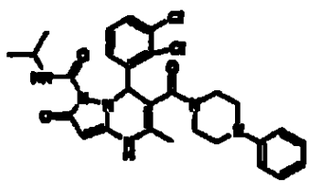
1-[[7-(3,4-diclorofenil)-1,2,4,7-tetrahidro-5-metil-1-[(1-metiletil)sulfonil]-2-oxopirazol[1,5-a]pirimidin-6-il]carbonil]-4-(4-fuorofenil)piperazina



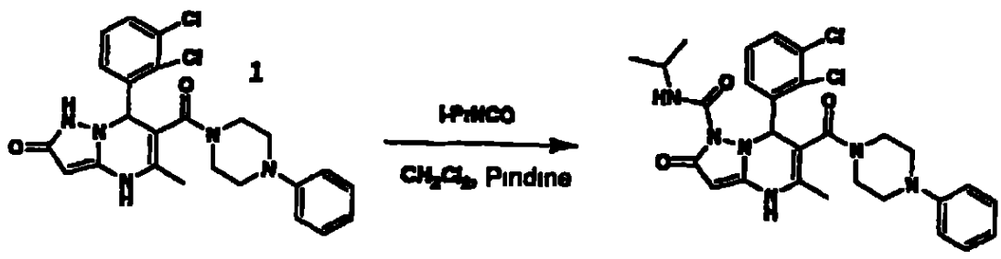
El compuesto del título se preparó en una manera similar a aquella descrita en el Ejemplo 432 (M+H) 608

Ejemplo 434

7-(2,3-diclorofenil)-4,7-dihidro-5-metil-N-(1-metiletil)-2-oxo-6-[(4-fenil-1-piperazinil)carbonil]pirazol[1,5-a]pirimidina-1(2H)-carboxamida



Método



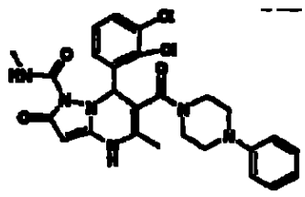
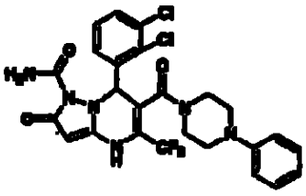
Compuesto 1 El compuesto 1 se preparó en una manera similar a aquella descrita en el Ejemplo 18, del método 2

Compuesto del titulo Se agregó isocianato isopropílico (0 034 mL, 0 35 mmol) y piridina (0 057

mL, 0 706 mmol) a 0°C a una solución del compuesto 1 (0 170 g, 0 350 mmol) en diclorometano (50 mL) La mezcla resultante se dejó calentar a temperatura ambiente Después de 5 horas, la TLC indicó que la reacción se completó La reacción se enfrió rápidamente con metanol y se concentró El residuo se purificó por cromatografía en gel de sílice, elución con acetato de etilo/hexanos al 75% para proporcionar 0 027 g del compuesto del titulo (al 13%) como un sólido blanco LC/MS de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección UV a 220 λ, gradiente 4 min Solvente B/A del 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt = 3 68, (95% puro) (M+H 569)

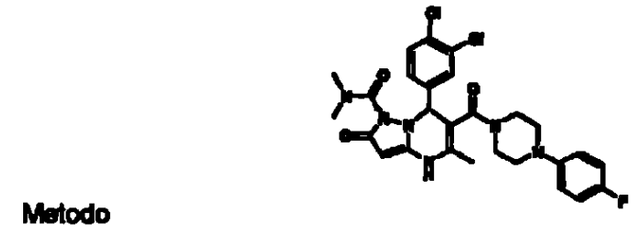
Ejemplos 435 y 436

Los compuestos de los Ejemplos 435 y 436, mostrados en la tabla proporcionada abajo, se prepararon en una manera similar a aquella descrita en el Ejemplo 434

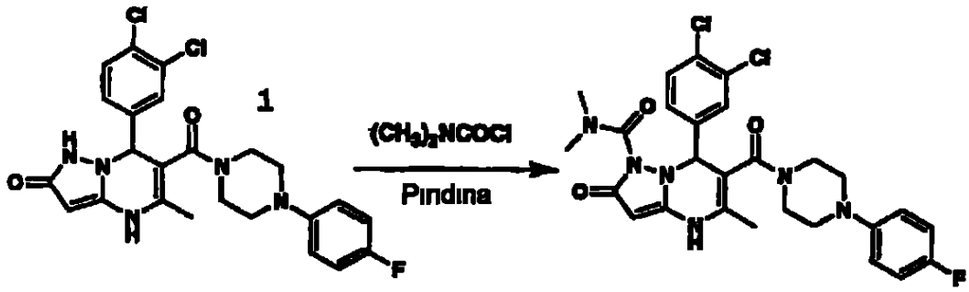
Ejemplo	Estructura	Nombre	(M+H)
435		7-(2,3-Dicloro-fenil)-4,7-dihidro-N,5-dimetil-2-oxo-6-[(4-fenil-1-piperazinil)-carbonil]pirazol[1,5-a]pirimidin-1(2H)-carboxamida	541
436		7-(2,3-Dicloro-fenil)-4,7-dihidro-5-metil-2-oxo-6-[(4-fenil-1-piperazinil)carbonil]pirazol[1,5-a]pirimidin-1(2H)-carboxamida	527

Ejemplo 437

7-(3,4-diclorofenil)-6-[[4-(4-fluorofenil)-1-piperazinil]carbonil]-4,7-dihidro-N,N,5-trimetil-2-oxopirazol[1,5-a]pirimidin-1(2H)-carboxamida



Metodo



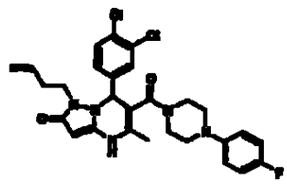
Compuesto 1 El compuesto 1 se preparó en una manera similar a aquella descrita en el Ejemplo 18, del método 2

Compuesto del título Se agregó cloruro de dimetilcarbamoilo (0 10 mL, 1 1 mmol) a 0°C a una solución del compuesto 1 (0 52 g, 1 0 mmol) en pirimidina (5 mL) La mezcla resultante se agitó a 0°C por 30 minutos, el baño enfriante se removió, y la mezcla se concentró El residuo se disolvió en acetato de etilo y se lavó con agua y salmuera, se secó sobre sulfato de sodio anhidro y se concentró

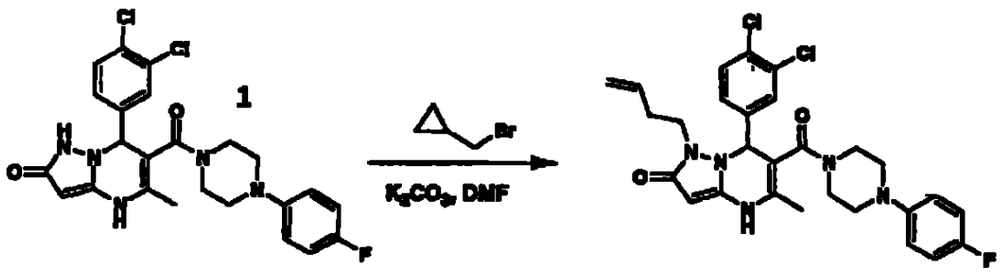
El residuo se purificó por cromatografía en gel de sílice, elución con metano/acetato de etilo al 5% para proporcionar 0 038 g del compuesto del título (al 6%) como un sólido blanco LC/MS de fase inversa columna 4 6 x 33 TurboPack Pro YMC S5, detección UV a 220 λ, gradiente 2 min Solvente B/A del 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt = 1 97, 86% puro) MS (M+H 573)

Ejemplo 438

1-[[1-(3-Butenil)-7-(3,4-diclorofenil)-1,2,4,7-tetrahidro-5-metil-2-oxopirazol[1,5,a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina



Método

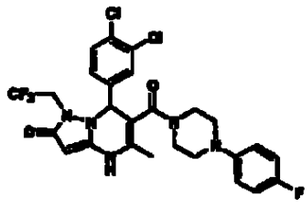
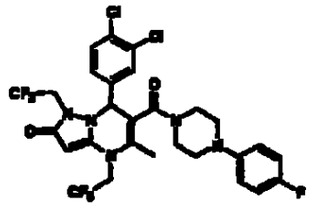


Compuesto 1 El compuesto 1 se preparó en una manera similar a aquella descrita en el Ejemplo 18, del Método 2

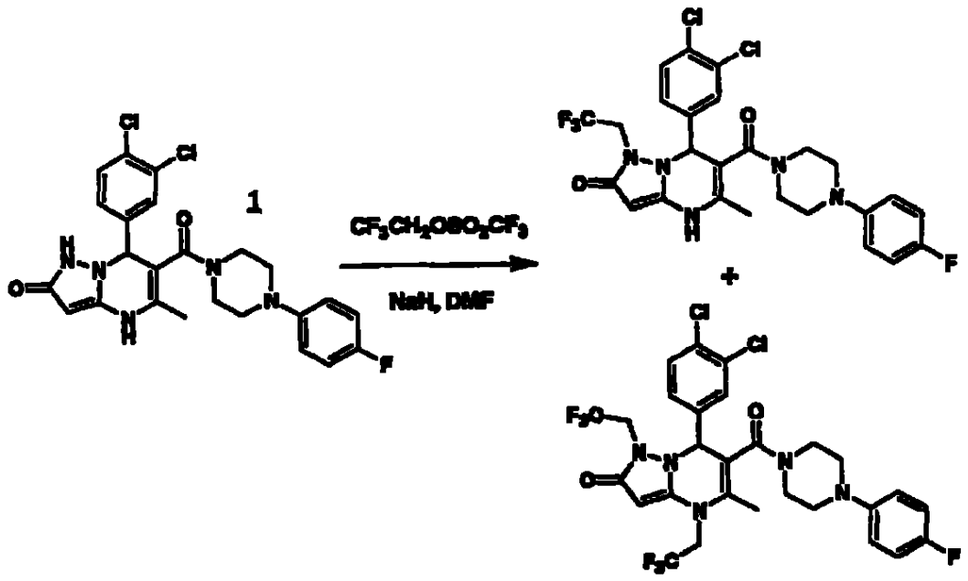
Compuesto del título Se agregó (Bromometil)ciclopropano (0 246 mL, 1 82 mmol) a una mezcla del compuesto 1 (0 831 g, 1 66 mmol) y carbonato de potasio (g, mmol) en dimetilformamida (10 mL) La mezcla resultante se dejó agitar a temperatura ambiente por 4 horas La reacción se diluyó con acetato de etilo, transferido a un embudo separador, se lavo con agua y salmuera, se secó sobre

sulfato de sodio anhidro y se concentró El residuo se purificó por cromatografía en gel de sílice, elución con metanol/acetato de etilo al 5% para proporcionar 0 030 g del compuesto del titulo (al 3%) LC/MS de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección UV a 220 λ, gradiente 4 min Solvente B/A del 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt = 2 99, (87% puro) (M+H 556)

Ejemplos 439 y 440

1-[[7-(3,4-diclorofenil)-1,2,4,7-tetrahidro-5-metil-2-oxo-1-(2,2,2-trifluoroetil)pirazol-[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina	1-[[7-(3,4-diclorofenil)-1,2,4,7-tetrahidro-5-metil-2-oxo-1,4-bis(2,2,2-trifluoroetil)pirazol[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluoroenil)piperazina
	
Ejemplo 439	Ejemplo 440

Método



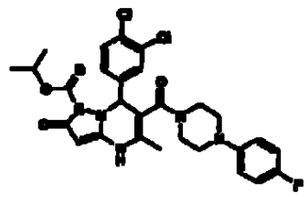
Compuesto 1 El compuesto 1 se preparó en una manera similar a aquella descrita en el Ejemplo 18, del método 2

Compuestos del titulo Se agrego trifluormetansulfonato de 2,2,2-trifluoroetil (0 49 g, 2 1 mmol) a una solución del compuesto 1 (0 967 g, 1 93 mmol) en dimetilformamida (10 mL) Se agregó hidrudro de sodio (0 12 g, 2 89 mmol) La TLC (metanol/acetato de etilo 10%) indicó el consumo del compuesto 1 La mezcla resultante se diluyó con

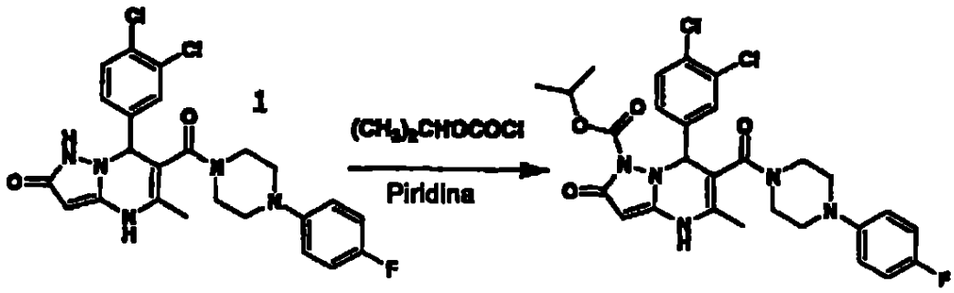
acetato de etilo, se transfirió a un embudo separador, se lavó con agua y salmuera, se secó sobre sulfato de sodio anhidro y se concentró El residuo se purificó por cromatografía en gel de sílice, elución con acetato de etilo seguido por 100% seguido por metanol/acetato de etilo al 10% para dar una mezcla de los compuestos del titulo Los compuestos del titulo se separaron por columna HPLC YMC S5 ODS 20 X 100 mm preparativa de fase inversa, 25 mL/min, gradiente 15 minutos, elución con solvente B/A de 50%-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%) Compuesto del ejemplo 439 Rt = 11 05 min, Compuesto del ejemplo 440 Rt = 11 88 min Compuesto del Ejemplo 439 LC/MS de fase inversa columna Ballistic YMC S5 4 6 x 50, detección UV a 220 λ, gradiente 4 min Solvente B/A del 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt = 2 87 min, 95% puro) MS(M+H 584) Compuesto del Ejemplo 440 LC/MS de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50, detección UV a 220 λ, gradiente 4 min Solvente B/A del 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt = 3 25 min, 85% puro) MS(M+H 666)

Ejemplo 441

Ester 1-metiletílico del ácido 7-(3,4-diclorofenil)-6-[[4-(4-fluorofenil)-1-piperazinil]carbonil]-4,7-dihidro-5-metil-2-oxopirazol[1,5-a]pirimidin-1(2H)-carboxílico



Método



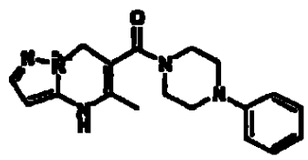
Compuesto 1 El compuesto 1 se prepara en una manera similar a aquella descrita en el Ejemplo 18, del método 2

Compuesto del titulo Se agregó cloroformato de isopropilo (1 0 mL, 1 0 mmol, en 1M de tolueno) a 0°C una solución del compuesto 1 (0 46 g, 0 92 mmol) en

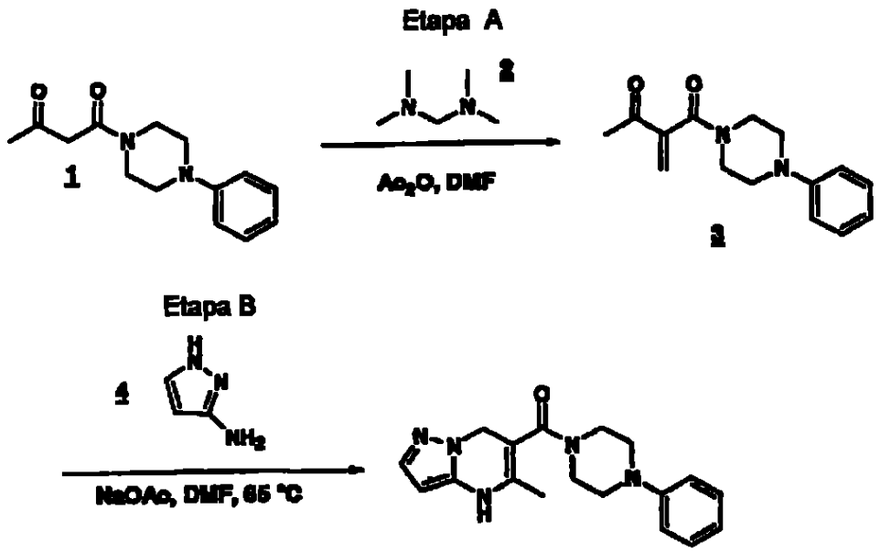
piridina (5 mL) La mezcla resultante se agitó a 0°C por 30 minutos, se removió el baño enfriante Después de 2 horas se agregó metanol la mezcla se enfrió rápidamente y se concentró El residuo se purificó por cromatografía en gel de sílice elución con metanol/acetato de etilo al 5% para proporcionar 0 057 g, del compuesto del titulo (al 11%) como un sólido rosado ligero LC/MS de fase inversa columna YMC S5 ODS 4 6 x 50, detección UV a 220 λ, gradiente 4 min Solvente B/A del 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt = 3 67 min 95% puro) (M+H 573)

Ejemplo 442

1-[(4,7-dihidro-5-metilpirazol[1,5-a]pirimidin-6-il)carbonil]-4-fenilpiperazina



Método



Compuesto 1 El compuesto 1 se preparó en una manera similar a aquella descrita en el Ejemplo 18, del método 2

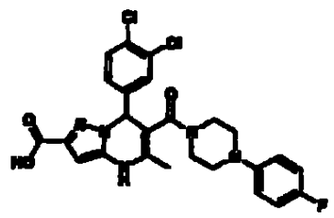
Etapa A Se agregó el compuesto 2 (0 6 mL, 4 4 mmol) y anhidrido acético (0 83 mL, 8 8 mmol) a una solución del compuesto 1 (0 72 g, 2 9 mmol) en dimetilformamida (10 mL) La mezcla se dejó agitar durante la noche, se vertió en agua, se extrajo con

diclorometano Los extractos se combinaron, se secaron sobre sulfato de sodio anhidro y se concentraron El residuo se purificó por cromatografía en gel de sílice, elución con acetato de etilo/hexanos al 50% a acetato de etilo/hexanos al 100% para dar 0 290 g del compuesto 3 (rendimiento de 38%) como un jarabe incoloro (M+H 259)

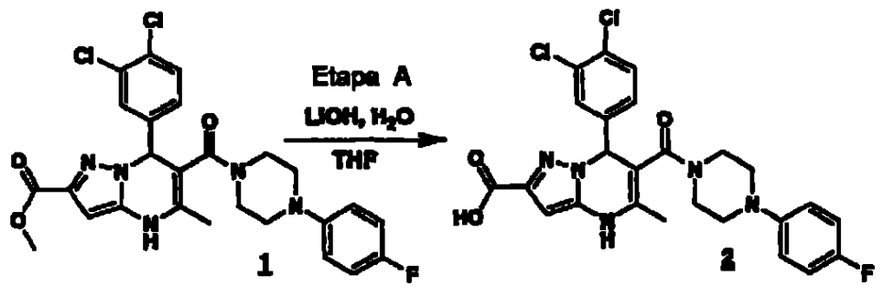
Etapa B La condensación del compuesto 3 y compuesto 4 como se describe en el Ejemplo 18, del Método 2 de la etapa C proporcionó el compuesto del título LC/MS de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección UV a 220 λ, gradiente 4 min Solvente B/A de 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt = 1 96 min, (87% puro) (M+H 323)

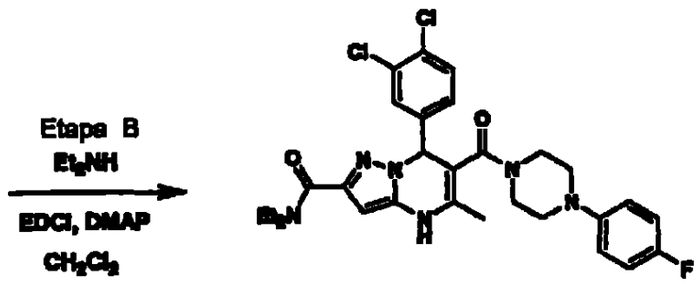
Ejemplo 443

Acido 7-(3,4-diclorofenil)-6-[[4-(4-fluorofenil)-1-piperazinil]carbonil]-4,7-dihidro-5-metilpirazol[1,5-a]pirimidina-2-carboxílico



Método





Compuesto 1 El compuesto 1 se preparó en una manera similar a aquella descrita en el Ejemplo 18 del método 2

Etapa A Se disolvió hidroxido de litio (0 43 g, 1 8 mmol) en agua (3 mL) y se agregó lentamente a temperatura ambiente a una solución del compuesto 1 en tetrahidrofurano (9 mL) La mezcla resultante se agitó agito a temperatura ambiente por 3 horas La TLC indicó que todo el compuesto 1 ha sido consumido La mezcla se enfrió rápidamente por adición de resina Dowex acídica Lo filtrado se diluyó con acetato de etilo, se lavó con agua y salmuera, se secó sobre sulfato de sodio anhidro y se concentró para dar 0 41 g (86% de rendimiento) del compuesto 2 como un sólido amarillo ligero LC/MS de fase inversa columna YMC S5 ODS 4 6 x 50, detección UV a 220 λ, gradiente 4 min Solvente B/A de 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt = 3 37 min, 96% puro) MS(M+H 530)

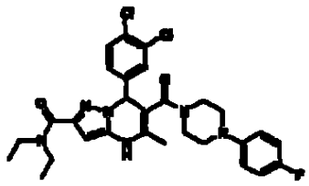
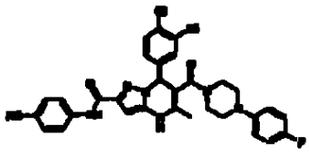
Etapa B Se agregó EDCI (0 025 g, 0 13 mmol), DMPA (0 003 g, 0 02 mmol) a una solución del compuesto 2 (0 0508 g, 0 1 mmol) y dimetilamina (0 014 mL, 0 13 mmol) en diclorometano (3 mL) La mezcla se agitó durante la noche La TLC indicó poco remanente de material iniciador El solvente se removió bajo presión reducida El residuo resultante se purificó

por cromatografía en gel de sílice, elución con metanol/acetato de etilo al 5% para dar el compuesto del título como un sólido blanco LC/MS de fase inversa columna Ballistic YMC S5 4 6 x 50, detección UV a 220 λ, gradiente 4 min Solvente B/A de 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt = 3 74 min, 91% puro) MS(M+H 585)

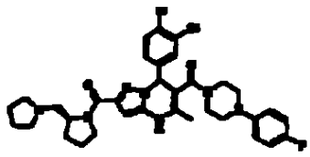
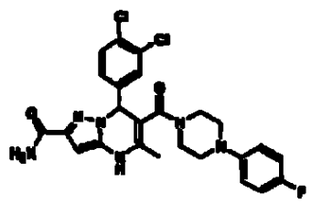
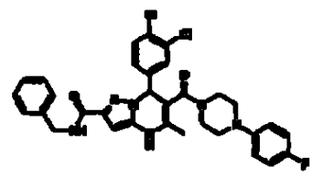
Ejemplos 444-449

Los compuestos de los Ejemplos 445-450, mostrados en la tabla proporcionada abajo, se prepararon en una manera similar a aquella descrita en el Ejemplo 443

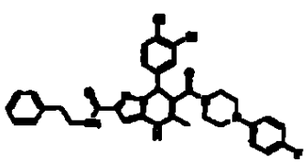
489

Ejemplo	Estructura	Nombre	(M+H)
444		7-(3,4-Dıcloro-fenıl)-N,N-dıetıl-6-[[4-(4-fluorofenıl)-1-pıperazınıl]-carbonil]-4,7-dı-hıdro-5-metıl-pırazol[1,5-a]pırı-mıdın-2-carboxamıda	585
445		7-(3,4-Dıcloro-fenıl)-6-[[4-(4-fluorofenıl)-1-pı-perazınıl]-carbonıl] -4,7-dıhıdro-N-(4-hıdroxıfenıl)-5-metılpırazol[1,5-a]pırımıdın-2-carboxamıda	621

490

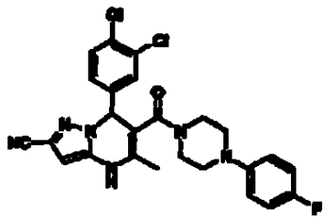
446		1-[[7-(3,4-Dıcloro-fenıl)-4,7-dıhıdro-5-metıl-2-[[(2S)-2-(1-pırrolıdınıl-metıl)-1-pırrolı-dınıl]carbonıl]-pırazol[1,5-a]pırı-mıdın-6-ıl]carbonıl]-4-(4-fluorofenıl) pıperazına	666
447		7-(3,4-Dıcloro-fenıl)-6-[[4-(4-fluorofenil)-1-pıpe-razınil]-carbonıl]-4,7-dihıdro-5-metıl-pirazol[1,5-a]pırı-mıdın-2-carboxamıda	529
448		7-(3,4-Dıcloro-fenıl)-6-[[4-(4-fluorofenıl)-1-pıpe-razınıl]-carbonıl]-4,7-dıhıdro-5-metıl-N-(fenılmetıl)-pırazol-[1,5-a]pırı-mıdın-2-carboxamıda	619

491

449		7-(3,4-Dicloro-fenil)-6-[[4-(4-fluorofenil)-1-piperazinil]-carbonil]-4,7-dihidro-5-metil-N-(2-fenil-etil)-pirazol[1,5-a]piri-midin-2-carboxamida	633

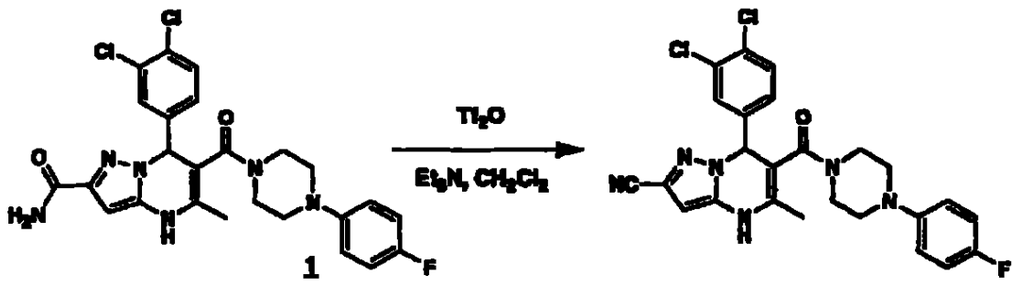
Ejemplo 450

1-[[2-ciano-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazol[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina



492

Método



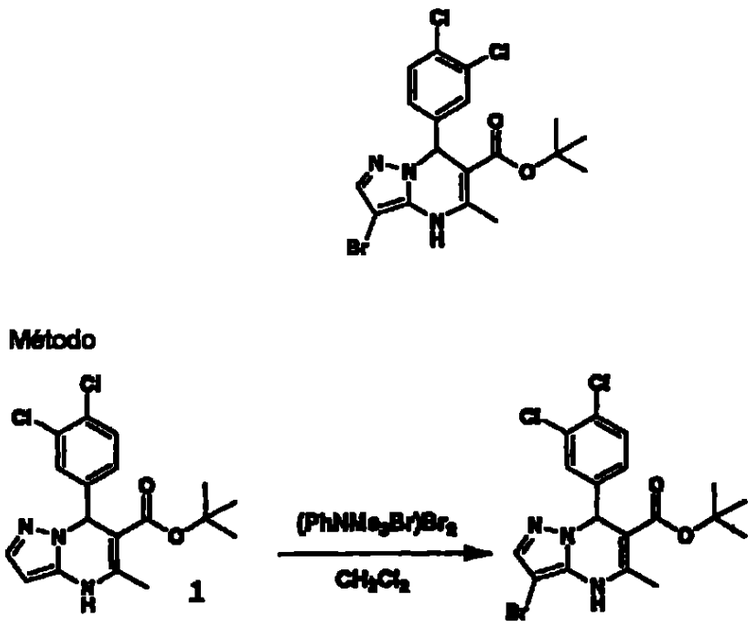
Compuesto 1 El compuesto 1 (el compuesto del Ejemplo 447) se preparó en una manera similar a aquella descrita en el Ejemplo 443

Compuesto del título Se agregó anhidrido tríflico (0 036 mL, 0 21 mmol) a 0°C a una solución del compuesto 1 (0 103 g, 0 19 mmol) y trietilamina (0 054 mL, 0 39 mmol) en diclorometano (5 mL) Después de 10 min, la TLC (metanol/acetato de etilo al 5%) indicó que el compuesto 1 permaneció Adicionalmente se agrega anhidrido tríflico (0 036 mL, 0 21 mmol) y trietilamina (0 054 mL, 0 39 mmol) Después de 10 min, la TLC metanol/acetato de etilo al 5%) indicó que el compuesto 1 permaneció La mezcla se calentó a temperatura ambiente y se agitó por unos 30 minutos adicionales La reacción se vertió en

bicarbonato de sodio saturado, se extrajo con diclorometano Los extractos se combinaron, se secaron sobre sulfato de sodio anhidro y se concentró El residuo resultante se purificó por cromatografía en gel de sílice, elució con metanol/acetato de etilo al 2% para 0 018 g (rendimiento al 19%) del compuesto del titulo como un sólido blanco LC/MS de fase inversa columna YMC S5 4 6 x 33, detección UV a 220 λ, gradiente 2 min Solvente B/A de 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt = 3 60 min, 81% puro) MS(M+H 511)

Ejemplo 451

Ester 1,1-dimetiletilíco del ácido 3-bromo-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazol[1,5-a]pirimidina-6-carboxílico



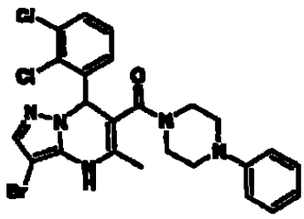
Compuesto 1 El compuesto 1 se preparó como se describe en el Ejemplo 4

Compuesto del titulo Se agregó tribromuro de feniltrimetilamonio (0 057 g, 0 14 mmol) a 0°C a una solución del compuesto 1 (0 05 g, 0 13 mmol) en diclorometano (2 mL) La mezcla se dejó calentar a temperatura ambiente durante 4 horas El solvente se removió bajo presion reducida El residuo resultante se purificó por TLC preparativa (Analtech, gel de silice, 20 x 20 cm, 100 µ) Elución con acetona/hexano al 25% proporciona 0 047 g

(rendimiento del 79%) del compuesto del titulo como un sólido blanco LC/MS de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección UV a 220 λ, gradiente 4 min Solvente B/A del 0-100% (Solvente A MeOH/H_2O al 10% con H_3PO_4 al 0 2%, Solvente B MeOH/H_2O al 90% con H_3PO_4 al 0 2%), 4 mL/min Rt = 4 67 min, (95% puro) LC/MS de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección UV a 220 λ, gradiente 4 min Solvente B/A de 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt = 4 19 min, MS (EM, M+1 458) HMR ($CDCl_3$, 400 MHz) 7 37 (1H, d, J = 2 0 Hz), 7 36 (1H, d, J = 8 0 Hz), 7 33 (1H, s), 7 12 (1H, dd, J = 2 2 y 8 4 Hz), 6 38 (1H, s), 6 27 (1H, s), 2 53 (3H, s), 1 36 (9H, s)

Ejemplo 452

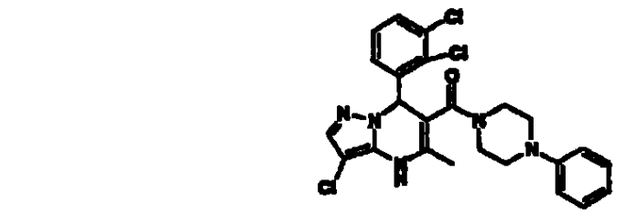
1-[[3-bromo-7-(2,3-diclorofenil)-4,7-dihidro-5-metilpirazol[1,5-a]pirimidin-6-il]carbonil]-4-fenilpiperazina



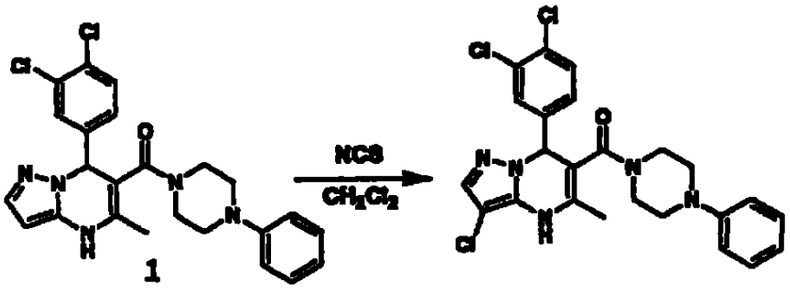
El compuesto del Ejemplo 452 se preparo en una manera similar a aquella descrita en el Ejemplo 451 (M+H) 547

Ejemplo 453

1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metilpirazol[1,5-a]pirimidin-6-il]carbonil]-4-fenilpiperazina



Método



1

Compuesto 1 El compuesto 1 se preparó en una manera similar a aquella descrita en el Ejemplo 18, del método 2

Compuesto del titulo Se agregó N-clorosucinimida (0 0102 g, 0 076 mmol) a 0°C a una solución del compuesto 1 (0 0343 g, 0 073 mmol) en diclorometano (4 mL) La mezcla se dejó calentar a temperatura ambiente durante 2 horas El solvente se removió bajo presión reducida El residuo resultante se purificó

por TLC preparativa (Analtech, gel de sílice, 20 x 20 cm, 100 µ) Elución con acetona/hexano al 50% proporcionando 0 0287 g (rendimiento de 77%) del compuesto del título como un aceite amarillo el cual se solidificó después de reposar HPLC de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección UV a 220 λ, gradiente 4 min Solvente B/A de 0-100% (Solvente A MeOH/H_2O al 10% con PPA al 0 2%, Solvente B MeOH/H_2O al 90% con PPA al 0 2%), 4 mL/min Rt = 4 21 min, (91% puro) LC/MS de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección UV a 220 λ, gradiente 4 min Solvente B/A de 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt = 3 72 MS (EM, M+1 501)

Ejemplos 454-463

Los compuestos de los Ejemplos 454-463, mostrados en la tabla proporcionada abajo, se prepararon en una manera similar a aquella descrita en el Ejemplo 453

El ejemplo 456 se obtuvo a partir del enantiómero B sólo del Ejemplo 30, y el Ejemplo 457 se obtuvo a partir del enantiómero A sólo del Ejemplo 29 Columna AD Chiralpak (4,6 x 250 mm) elución con

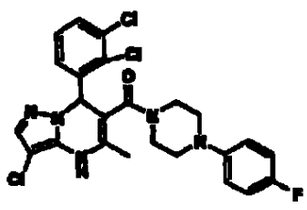
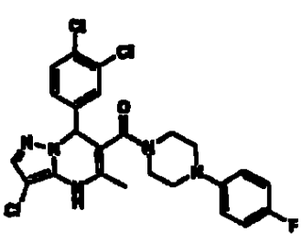
isopropanol/hexanos al 30% conteniendo trietilamina al 1% a 1 mL/min), detección UV a 254 λ, Ejemplo 456 Rt = 5 9 min, >99% ee, Ejemplo 457 Rt = 6 3 min, > 99% ee

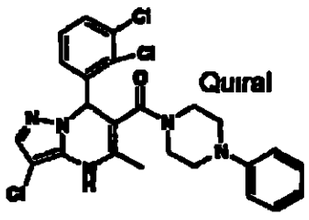
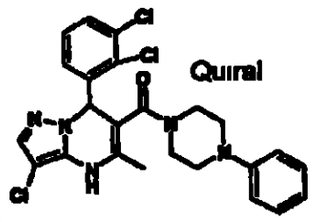
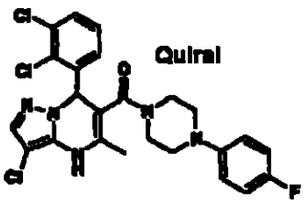
El Ejemplo 458 se obtuvo a partir del enantiómero A sólo del Ejemplo 51, y el Ejemplo 459 se obtuvo a partir del enantiómero B sólo del Ejemplo 52 Columna OD Chirarcel (4 6 x 250 mm), elución con isopropanol/hexanos al 30% conteniendo trietilamina al 0 1% a 1 mL/min), detección UV a 254 λ, Ejemplo 458 Rt = 7 8 min, > 99% ee Ejemplo 459 Rt = 8 4 min, > 99% ee

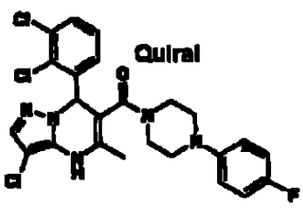
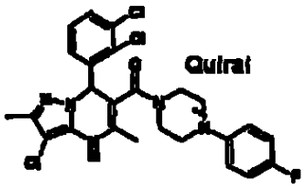
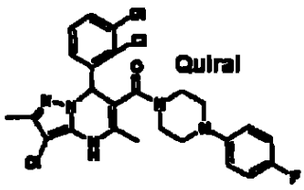
El ejemplo 460 se obtuvo a partir del enentiómero A sólo del Ejemplo 169, y el Ejemplo 461 se obtuvo a partir del enantiómero B sólo del ejemplo 168 Columna AD Chiralpak (4 6 x 250 mm), elución con isopropanol/hexanos al 20% conteniendo trietilamina al 0 1% a 1mL(min), detección UV a 254 λ, Ejemplo 462 Rt = 9 2 min, > 99% ee Ejemplo 460 Rt = 9 4 min, > 99% ee

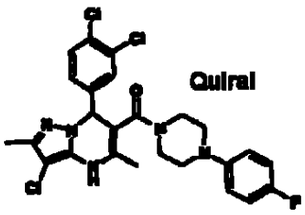
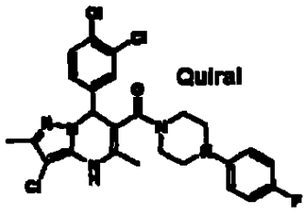
El ejemplo 462 se obtuvo a partir del enantiómero A sólo del Ejemplo 81, y el Ejemplo 463 se obtuvo a partir del enantiómero B sólo del Ejemplo 82 Columna AD Chiralpak (4 6 x 250 mm), elución con isopropanol/hexanos al 20% conteniendo trietilamina

al 0 1% a 1 mL/mın), detección UV a 254 λ, Ejemplo 462 Rt = 8 25 mın, > 99% ee Ejemplo 463 Rt = 8 28 mın, > 99% ee

Ejemplo	Estructura	Nombre	(M+H)
454		1-[[3-cloro-7-(2,3-dıclorofenıl)-4,7-dıhıdro-5-metıl-pırazol[1,5-a]pırı-mıdın-6-ıl]car-bonıl]-4-(4-fluoro-fenıl)pıperazına	520
455		1-[[3-cloro-7-(3,4-dıclorofenıl)-4,7-dıhıdro-5-metıl-pırazol[1,5-a]pırı-mıdın-6-ıl]car-bonıl]-4-(4-fluoro-fenıl)pıperazına	520

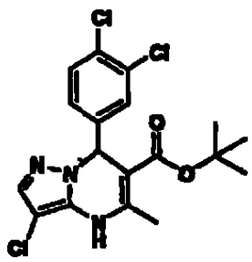
456		1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazol[1,5-a]pirimidin-6-il]carbonil]-4-fenil-piperazina, enantiómero B	502
457		1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazol[1,5-a]pirimidin-6-il]carbonil]-4-fenil-piperazina, enantiómero A	502
458		1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazol[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluoro-fenil)piperazina, enetiómero A	520

459		1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazol[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil) piperazina, enetiómero B	520
460		1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-2,5-dimetil-pirazol[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina, enantiómero A	534
461		1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-2,5-dimetil-pirazol[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina, eantiómero B	534

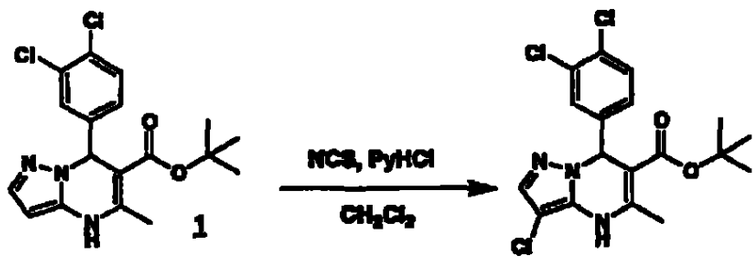
462		1-[[3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-2,5-dimetil-pirazol[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina, enantiómero A	534
463		1-[[3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-2,5-dimetil-pirazol[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina, enantiómero B	534

Ejemplo 464

Ester 1,1-dimetiletílico del ácido 3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazol[1,5-a]pirimidina-6-carboxílico



Método



Compuesto 1 El compuesto 1 se preparo como se describe en el Ejemplo 4

Compuesto del titulo Se agregó clorhidrato de piridina (0 020 g, 0 173 mmol) a 0°C a una solución del compuesto 1 (0 060 g, 0 158 mmol) en diclorometano (4 mL) Después de 2 minutos, se agregó N-clorosucinimida (0 0231 g, 0 174 mmol) La mezcla se dejó calentar a temperatura ambiente y se agito

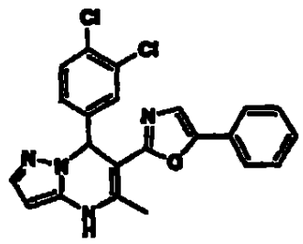
505

por 13 horas El solvente se removió bajo presión reducida El residuo resultante se purificó por TLC preparativa (Analtech, gel de sílce, 20 x 20 cm, 100 µ) Elución con acetona/hexanos al 20% proporcionado 0 0092 g (rendimiento de 14%) del compuesto del título como un aceite amarillo HPLC de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección UV a 220 λ, gradiente 4 min Solvente B/A de 0-100% (Solvente A MeOH/H_2O al 10% con PPA al 0 2%, Solvente B MeOH/H_2O al 90% con PPA al 0 2%), 4 mL/min Rt = 4 61 min, (94% puro). LC/MS de fase inversa columna Ballistic YMC S5 ODS 4 6 x 50 mm, detección UV a 220 λ, gradiente 4 min Solvente B/A de 0-100% (Solvente A MeOH/H_2O al 10% con TFA al 0 1%, Solvente B MeOH/H_2O al 90% con TFA al 0 1%), 4 mL/min Rt = 4 71 min, MS (EM, M+1 414) HMR ($CDCl_3$, 400 MHz) 7 37 (1H, s), 7 36 (1H, d, J = 1 7 Hz), 7 36 (1H, d, J = 8 4 Hz), 7 12 (1H, dd, J = 2 0 y 8 4 Hz), 6 45 (1H, brs), 6 24 (1H, s), 2 52 (3H, s), 1 36 (9H, s)

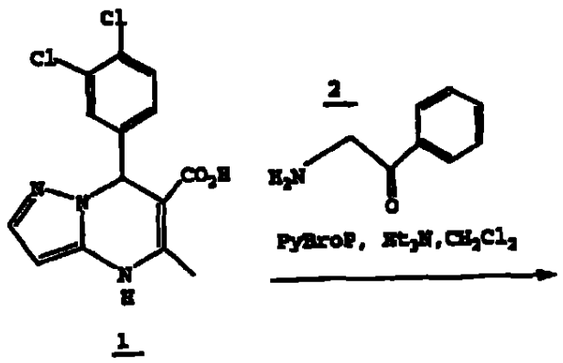
506

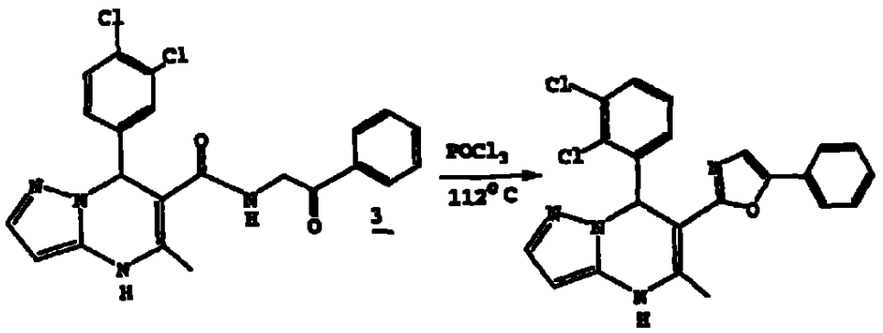
Ejemplo 465

7-(3,4-diclorofenil)-4,7-dihidro-5-metil-6-(5-fenil-2-oxazolilo)pirazol[1,5-a]pirimidina



Método





507

C mpuesto 1 El compuesto 1 se sıntetızó como se describe en el Ejemplo 16

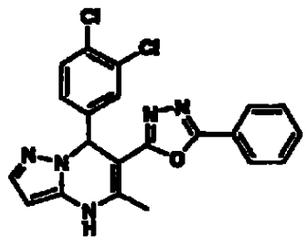
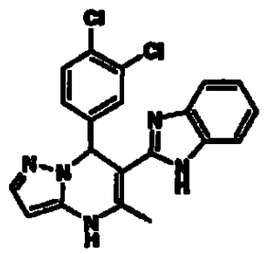
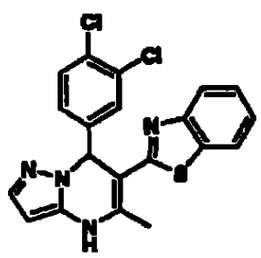
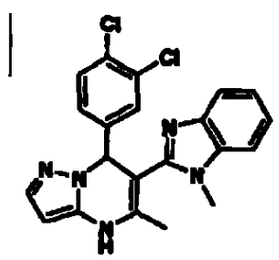
Compuesto 3 El compuesto 1 (200 mg, 0 62 mmol) se suspendió en 2 mL de diclorometano Se agregó trıetılamına (300 µL, 2 2 mmol) y 2-amınoacetofenona 2 (116 mg, 0 68 mmol) seguıdo por hexafluorofosfato de bromo-trıs-pırrolıdıno-fosfonio (PyBrOP) (312 mg, 0 68 mmol) Todos los sólıdos se dısolvıeron después de la adıcıón de PyBrOP y la reacción se agıtó por 4 horas La mezcla se cargó en gel de sılıce y se purıfıcó por cromatografía ınstantánea en gel de sılıce, elucıón con acetona, hexano al 40% para un rendımıento de 106 mg (al 39%) de un sólıdo rosado ^{1}H NMR (400 MHz, CDCl3) 44180-148-16, ^{1}H COSY (400 MHz, CD3OD), ^{13}C NMR (100 MHz, $CDCl_3$), HPLC > 99% a 4 0 mın (columna YMC S5 ODS 4 6 x 50 mm, metanol al 10-90%, agua con ácıdo fosforıco al 0 2% con gradıente de 4 mın , 4 mL/mın , detección UV a 220 nm)

Compuesto del tıtulo La amıda 3 (100 mg, 0 22 mmol) se dısolvıó en 2 mL de oxıcloruro fosforoso y se calentó a 112° por 2 horas La mezcla se enfrıó rápıdamente en hıelo y se extrajo con acetato de

etilo Los extractos se secaron sobre sulfato de magnesio, se filtraron y el solvente se removió para proporcionar 339 mg de un aceite marrón El aceite se purificó por cromatografía instantánea en gel de sílice, elución con acetona, hexano al 20-40% para rendir 50 mg (al 51%) del compuesto del titulo como un polvo blanco p f 229-231°, ^{1}H NMR (400 MHz, CD3OD), MS (ESI) *m/z* 423 (MH+), HPLC > 99% a 4 7 min (columna YMC S5 ODS 4 6 x 50 mm, metanol al 10-90%, agua con ácido fosforico al 0 2% de gradiente 4 min, entonces se conserva a 90% de metanol, agua, 4 mL/min , detección UV a 220 nm)

Ejemplos 466-469

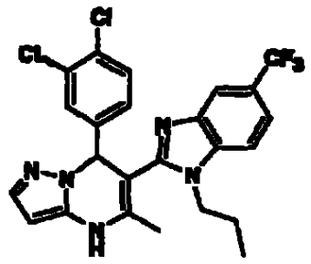
Los compuestos de los Ejemplos 466-473, mostrados en la tabla proporcionada abajo, se preparan en una manera similar a aquella descrita en el Ejemplo 465

Ejemplo	Estructura	Nombre	(M+H)
466		7-(3,4-Dicloro-fenil)-4,7-dihidro-5-metil-6-(5-fenil-1,3,4-oxadiazol-2-il)pirazol[1,5-a]pirimidina	424
467		6-(1H-Bencimidazol-2-il)-7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazol[1,5-a]pirimidina	396
468		6-(2-Benzotiazolil)-7-(3,4-Dicloro-fenil)-4,7-dihidro-5-metilpirazol[1,5-a]pirimidina	413
469		7-(3,4-Dicloro-fenil)-4,7-dihidro-5-metil-6-(5-fenil-1,3,4-oxadiazol-2-il)pirazol[1,5-a]pirimidina	410

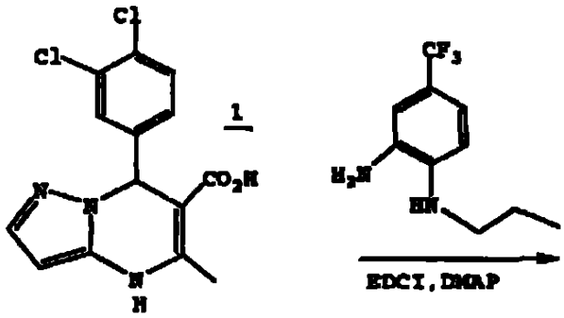
510

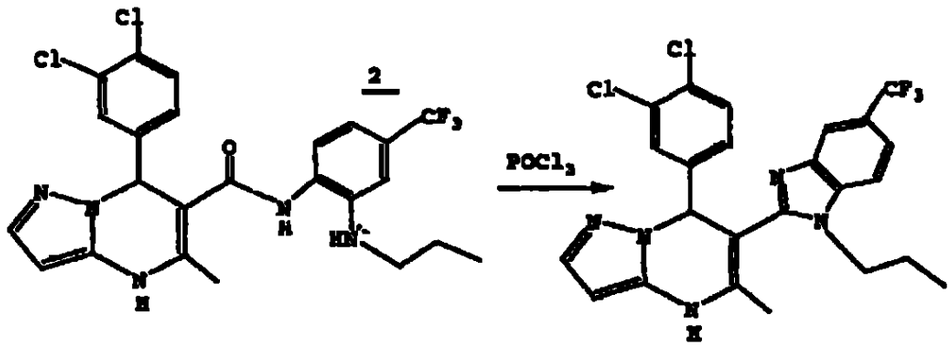
Ejemplo 470

7-(3,4-diclorofenil)-4,7-dihidro-5-metil-6-[5-(trifluorometil)-1-propil-1H-benzimidazol-2-il]pirazol[1,5-a]pirimidina



Método





C mpuest 2 A una solución del ácido 1, preparada como se describe en el Ejemplo 16, (0 15 g, 0 463 mmol), 2-(n-propılamıno)-5-trıfluorometılanılına (0 141 g, 0 648 mmol) y se agregó DMAP (5 mg, cat) EDCI (0 124 g, 0 0648 mmol) y la solución se agıto a temperatura ambıente por 2 horas La reacción se trato con bıcarbonato de sodıo saturado, la solución orgánica se secó con sulfato de magnesıo y el solvente se evaporó El producto crudo 2 se usó sın purıfıcacıón adıcıonal

Compuesto del tıtulo El compuesto 2 se dısolvıo en oxıcloruro fosforoso (4 mL) y se calentó a 80°C por 4 horas La TLC ındıcó que la reacción no se completo Adıcıonalmente se agregó oxıcloruro osforoso (2 mL) y la mezcla se calentó por 2 horas y entonces se dejó a temperatura ambıente durante la noche La mezcla entonces se enfrıó rápıdamente en hıelo, hecho básıcamente con hıdroxıdo de amıno, y se extrajo con acetato de etılo Los extractos se secaron sobre sulfato de magnesıo y se concentraron El producto crudo se purıfıcó por cromatografía de fase ınversa preparativa (columna YMC PACK ODSA S3 20 x 100 mm, metanol 50 -100, agua con TFA al 0 1% gradıente sobre 10 mın , 20 mL/mın , detección uv a

512

220 nm) Las fracciones apropiadas se evaporaron, el residuo se dividió entre bicarbonato de sodio saturado y acetato de etilo, la solución orgánica se secó y el solvente se removió bajo vacío dando el producto (27 mg, al 11 5%) como un cristal bronceado u obscuro $[M+H]^+$ *m/z* 506 HPLC 91 1% A 4 6 min (columna YMC S5 ODS 4 6 x 50 mm, metanol al 10-90%, agus con ácido fosfórico al 0 2% gradiente sobre 4 min , 4 mL/min , detección uv a 220 nm)

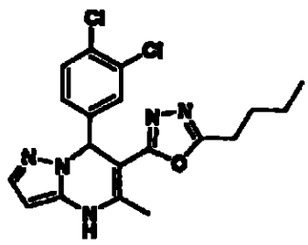
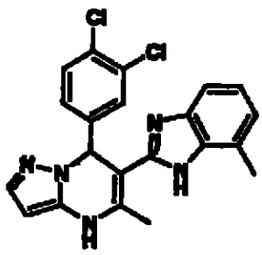
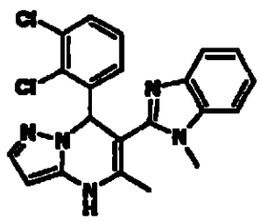
Ejemplos 471-482

Los compuestos de los Ejemplos 471-482, mostrados en la tabla proporcionada abajo, se prepararon de una manera similar a aquella descrita en el Ejemplo 470

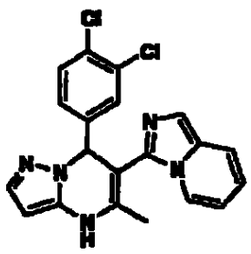
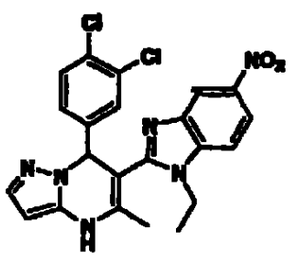
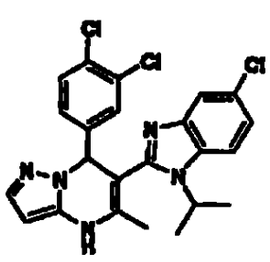
La resolución HPLC del Ejemplo 480, columna Chiralcel OD (50 X 500 mm), elución con isopropanol/hexanos al 25% conteniendo trietilamina al 0 1% a 50 mL/min), detección UV a 254 λ proporcionando enantiómeros A (Ejemplo 481) y B (Ejemplo 482) Columna Analytical Chiralcel OD (4 6 X 250 mm) elución con isopropanol/hexanos al 25%

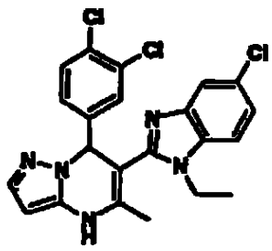
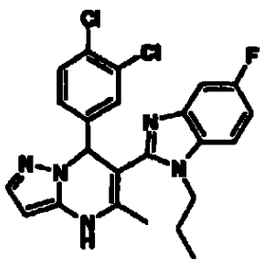
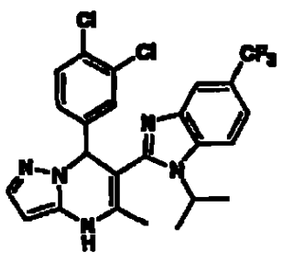
SB

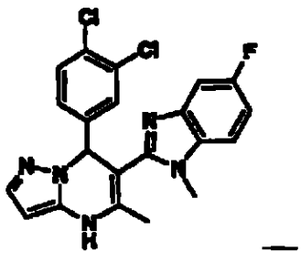
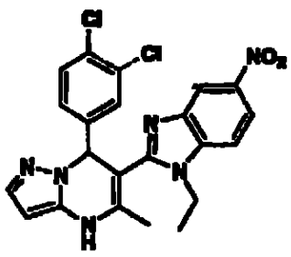
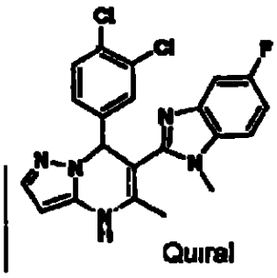
conteniendo trietilamina al 0 1% a 1 mL/min), detección UV a 254 λ, enatiómero A Rt = 7 2 min, > 99% ee Enantiómero B Rt = 10 0 min, > 99% ee

Ejemplo	Estructura	Nombre	(M+H)
471		6-(5-butil-1,3,4-oxadiazol-2-il)-7-(3,4-Diclorofenil)-4,7dihidro-5-metil-pirazol[1,5-a]pirimidina	404
472	 --	1-[[7-(3,4-Dicloro-fenil)-4,7-dihidro-5-metil-6-(4-metil-1H-bencimidazol-2-il)pirazol[1,5-a]pirimidina	410
473		1-[[7-(2,3-Dicloro-fenil)-4,7-dihidro-5-metil-6-(1-metil-1H-bencimidazol-2-il)pirazol[1,5-a]pirimidina	410

514

474		7-(3,4-Dıcloro-fenıl)-4,7-dıhıdro-6-(ımıdazol[1,5-a]pırıdın-3-ıl)-5-metılpirazol[1,5-a]pırımıdına	510
475		7-(3,4-Dıcloro-fenıl)-6-(1-etıl-5-nıtro-1H-bencımıdazol-2-ıl)-4,7-dıhıdro-5-metıl-pırazol[1,5-a]pırımıdına	469
476		6-[5-cloro-1-(1-metıletıl)-1H-bencımıdazol-2-ıl)-7-(3,4-Dıcloro-fenıl)-4,7-dıhıdro-5-metılpırazol[1,5-a]pırımıdına	472

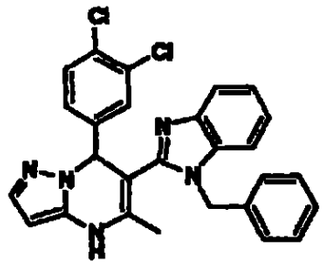
477		6-(5-cloro-1-etil-1H-bencimidazol-2-il)-7-(3,4-Dicloro-fenil)-4,7-dihidro-5-metilpirazol[1,5-a]pirimidina	458
478		7-(3,4-Dicloro-fenil)-6-(5-fluoro-1-propil-1H-benci-midazol-2-il)-4,7-dihidro-5-metil-pirazol[1,5-a]pirimidina	456 35
479		7-(3,4-Dicloro-fenil)-4,7-dihidro-5-metil-6-[1-(1-metiletil)-5-(tri-fluorometil)-1H-bencimidazol-2-il] pirazol[1,5-a]pirimidina	506

480		7-(3,4-Dicloro-fenil)-6-(5-fluoro-1-metil-1H-bencimidazol-2-il)-4,7-dihidro-5-metil-pirazol[1,5-a]pirimidina	428
481		7-(3,4-Dicloro-fenil)-6-(5-fluoro-1-metil-1H-bencimidazol-2-il)-4,7-dihidro-5-metil-pirazol[1,5-a]pirimidina, enantiómero A	428
482	 Quiral	7-(3,4-Dicloro-fenil)-6-(5-fluoro-1-metil-1H-bencimidazol-2-il)-4,7-dihidro-5-metil-pirazol[1,5-a]pirimidina, enantiómero B	428

517

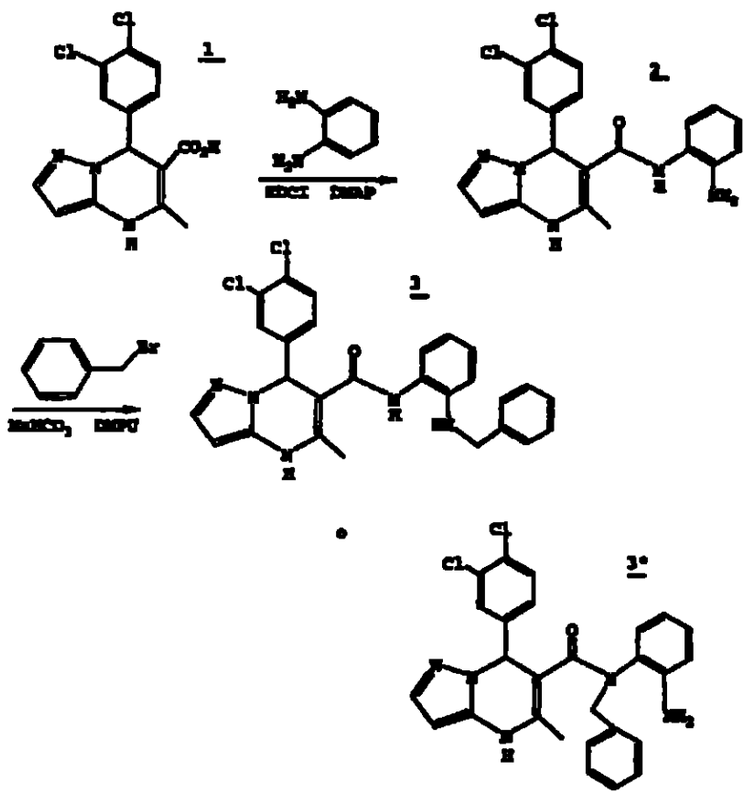
Ejemplo 483

7-(3,4-diclorofenil)-4,7-dihidro-5-metil-6-[1-(fenilmetil)-1H-bencimidazol-2-il]pirazol[1,5-a]pirimidina



518

Método



Compuesto 1 Preparado como se describe en el Ejemplo 16

Compuesto 2 Preparado a partir del compuesto 1 y fenilenediamina en una manera similar a aquella descrita en el Ejemplo 470

Compuesto 3 Una suspensión de 2 (50 mg 0 121 mmol), $NaHCO_3$ (50 mg, 0 6 mmol) y bromuro de bencilo (20 mg, 0 121 mmol) en DMPU (0 5 mL) se agitó a temperatura ambiente durante la noche Otro equivalente de bromuro de bencilo se agregó completando la reacción La suspensión se dividio entre agua y acetato de etilo, la fase orgánica se seco ($MgSO_4$), y el solvente se evaporó El residuo se cromatografio instantáneamente a través de sílice, elución con hexano-acetona 2 1 para proporcionar cualquiera o ambos de los compuestos 3 y 3* (no se determinó exactamente la estructura) (24 8 mg, al 41%) como un sólido blanco P f 135-140, $[M+H]^+$ *m/z* 504, HPLC al 100% a 4 4 min (columna YMC S5 ODS 4 6 x 50 mm, metanol al 10-90%, agua con ácido fosfórico al 0 2% gradiente sobre 4 min , 4 mL/min , detección uv a 220

nm)

Compuesto del titulo Se disolvieron el (los) compuesto(s) 3/3* en oxicloruro de fósforo (1 5 mL) y se calentó a 80°C por 5 horas, El calentamiento se descontinuó y la mezcla se dejó permanecer a temperatura ambiente durante la noche La mezcla se enfrió rápidamente en hielo, hecho básicamente con hidroxido de amonio y se extrajo con acetato de etilo Los extractos se secaron sobre sulfato de magnesio y se concentraron El residuo se purificó por cromatografía instantánea (gel de sílice, acetona/hexanos al 50%) para dar 6 6 mg del compuesto del titulo como un sólido quemado u obscuro P f 225-230, $[M+H]^+$ *m/z* 486, HPLC al 100% a 3 8 min (columna YMC S5 ODS 4 6 x 50 mm, metanol al 10-90%, agua con ácido fosfórico al 0 2% gradiente sobre 4 min , 4 mL/min , detección uv a 220 nm)

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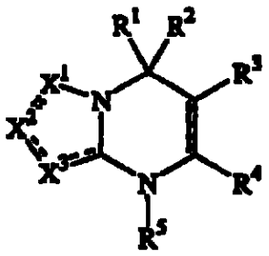
REIVINDICACIONES

1 Un método de tratamiento de la arritmia del atrio que comprende la administración a un paciente en la necesidad del mismo, una cantidad efectiva de al menos un compuesto de la fórmula I



(I)

enántiomeros, diastereomeros y sales farmacéuticamente aceptables del mismo,

en donde

X^1, X^2 y X^3 son independientemente seleccionados de N, NR^6, $(CR^7)_q$, $(CHR^7)_q$, o C=O, en donde los enlaces que conectan X^1, X^2 y X^3 a los átomos adyacentes, pueden ser enlaces únicos o dobles que forman un anillo aromático de 5 a 7 elementos saturados o parcialmente insaturados,

R^1, R^2, R^3, R^4, R^5, R^6 y R^7 son seleccionados de manera independiente de los grupos de la

fórmula $-(CH_2)_n-(Z^1)_m-(CH_2)_p-Z^2$, o

R^1, R^2, R^3, R^4 y R^5 pueden, en uno o más pares de dos, junto con los átomos a los cuales están enlazados, formar un grupo carbocíclico, carbocíclico substituido, heterocíclico o heterocíclico substituido, o

R^6 y R^7 pueden, en uno o más pares de dos, junto con los átomos a los cuales están unidos, formar un grupo carbocíclico, carbocíclico substituido, heterocíclico o heterocíclico substituido,

Z^1 es $-CZ^3Z^4-$, $-O-$, $-NZ^3-$, $-S-$, $-SO-$, $-SO_2-$, $-C(O)-$, $-C(O)Z^3-$, $-C(O)NZ^4$, $-C(S)-$, $-C(=NOZ^3)-$, alquilo, alquilo substituido, alquenilo, alquenilo substituido, alquinilo, alquinilo substituido, carbociclo, carbociclo substituido, arilo, arilo substituido, heterociclo, o heterociclo substituido,

Z^2 es hidrógeno, $-OZ^5$, $-OC(O)Z^5$, $-NZ^5-C(O)-Z^6$, $-NZ^5-CO_2-Z^6$, $-NZ^5(C=O)-NZ^6Z^7$, $-NZ^5Z^6$, $-NO_2$, halo, $-CN$, $-C(O)Z^5$, $-CO_2Z^5$, $-C(S)Z^5$, $-(C=NOZ^5)Z^6$, $-C(O)NZ^5Z^6$, $-C(S)NZ^5Z^6$, $-SZ^5$, $-SOZ^5$, $-SO_2Z^5$, $-SO_2NZ^5Z^6$, alquilo, alquilo substituido, alquenilo, alquenilo substituido, alquinilo, alquinilo

substituido, carbociclo, carbociclo substituido, arilo, arilo substituido, heterociclo, o heterociclo substituido,

Z^3, Z^4, Z^5, Z^6 y Z^7 son independientemente hidrógeno, halo, alquilo, alquilo substituido, alquenilo, alquenilo substituido, alquinilo, alquinilo substituido, carbociclo, carbociclo substituido, arilo, arilo substituido, heterociclo, o heterociclo substituido, o

Z^3, Z^4, Z^5, Z^6 y Z^7 pueden, en uno o más pares de dos, junto con los átomos a los cuales están unidos, formar un grupo carbocíclico carbocíclico substituido, heterocíclico o heterocíclico substituido,

n y p son independientemente seleccionados de los enteros a partir de 0 a 10 en donde m es 0, p es también 0,

m es un entero seleccionado de 0 o 1, y

q es un entero seleccionado de 1 a 3

2 Un método de tratamiento de la fibrilación del atrio, el cual comprende la administración a un paciente en necesidad del mismo en una cantidad efectiva de al menos un compuesto de la reivindicación 1

3 Un método de tratamiento de palpitación del atrio, el cual comprende la administración a un paciente en necesidad del mismo en una cantidad efectiva de al menos un compuesto de la reivindicación 1

4 Un método de tratamiento selectivamente de arritmias supraventricular, el cual comprende la administración a un paciente en necesidad del mismo una cantidad efectiva de al menos uno compuesto de la reivindicación 1

5 Un método de tratamiento de condiciones asociadas a I_{Kur}, el cual comprende la administración a un paciente en necesidad del mismo de una cantidad efectiva de al menos un compuesto de la

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reivindicación 1

6 Un método de tratamiento de esofagitis con reflujo, el cual comprende la administración a un paciente en necesidad del mismo de una cantidad efectiva de al menos un compuesto de la reivindicación 1

7 Un método de tratamiento de dispesia funcional, el cual comprende la administración a un paciente en necesidad del mismo de una cantidad efectiva de al menos un compuesto de la reivindicación 1

8 Un método de tratamiento de constipación, el cual comprende la administración a un paciente en necesidad del mismo de una cantidad efectiva de al menos un compuesto de la reivindicación 1

9 Un método de tratamiento del asma, el cual comprende la administración a un paciente en

necesidad del mismo de una cantidad efectiva de al menos un compuesto de la reivindicación 1

10 Un método de tratamiento de la diabetes, el cual comprende la administración a un paciente en necesidad del mismo una cantidad efectiva de al menos un compuesto de la reivindicación 1

11 Un método estimulante de la secreción de hormonas del crecimiento, el cual comprende la administración a un paciente en necesidad del mismo de una cantidad efectiva de al menos un compuesto de la reivindicación 1

12 Un método de tratamiento de alteraciones proliferativas celulares, el cual comprende la administración a un paciente en necesidad del mismo de una cantidad efectiva de al menos un compuesto de la reivindicación 1

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13 Un método de tratamiento de padecimientos autoimunes, el cual comprende la administración a un paciente en necesidad del mismo de una cantidad efectiva de al menos un compuesto de la reivindicación 1

14 El método de la reivindicación 1, en el cual en la fórmula I

R^1 es hidrógeno,

R^2 es hidrógeno, alquilo, alquilo substituido, arilo, arilo substituido, heterociclo, heterociclo substituido, carbociclo o carbociclo substituido,

R^3 es $-(CH_2)_n-Z^2$, $-(CH_2)_n-C(O)Z^3-(CH_2)_p-Z^2$, o $-(CH_2)_n-C(O)NZ^4-(CH_2)_p-Z^2$,

R^4 es alquilo o alquilo substituido,

R^5 es hidrógeno, o $-(CH_2)_n-Z^2$, y

X^1, X^2 y X^3, junto con los átomos a los cuales están unidos, forman un anillo, seleccionado de

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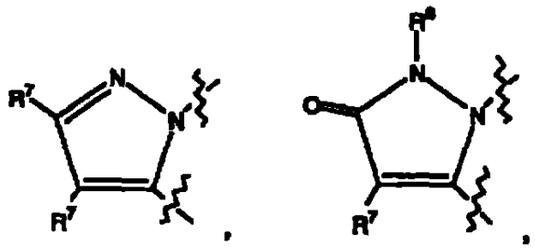
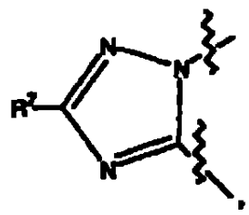
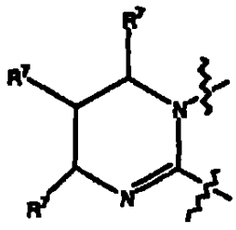
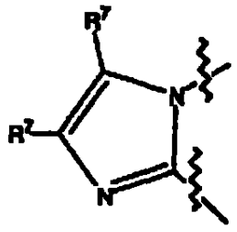






ó



donde los anillos substituyentes son los mismos o diferentes

15 El método de la reivindicación 14, en donde en la fórmula I

R^3 es $-(CH_2)_n-Z^2$, $-(CH_2)_n-C(O)Z^3-(CH_2)_p-Z_2$, o $-(CH_2)_n-C(O)NZ-(CH_2)_p-Z^2$,

en donde

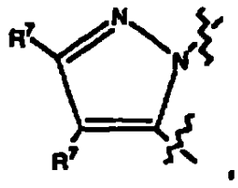
Z^2 se selecciona a partir de $-C(O)NZ^5Z^6$, $-CO_2Z^5$, $-SO_2Z^5$, $-NZ^5Z^6$, $-NZ^5CO_2Z^6$, $-NZ^5C(O)Z^6$, $-OZ^5$, arilo, arilo substituido, heterociclo, heterociclo substituido, alquilo o alquilo substituido,

Z^3 es heterociclo o heterociclo substituido, y

n y p son independientemente, seleccionados a partir de los enteros 0 a 3,

R^5 es hidrógeno, o $-(CH_2)_n-Z^2$, en donde Z^2 se selecciona a partir de $-C(O)NZ^5Z^6$, $-CO_2Z^5$, $-NZ^5Z^6$, arilo, arilo substituido, alquilo o alquilo substituido, y

X^1, X^2 y X^3, junto con los átomos a los cuales están unidos, forman un anillo seleccionado de



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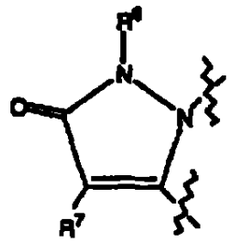

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16 El método de la reivindicación 15, en el cual en la fórmula I

R^3 es heterociclo o heterociclo substituido, $-C(O)NZ^5Z^6$, $-CO_2Z^3$-$CONZ^5Z^6$, $-C(O)Z^3Z^2$, o $-C(O)Z^3$-CO_2Z^5, en donde Z^3 es heterociclo ó heterociclo substituido, y Z^2 es arilo o arilo substituido,

17 El método de la reivindicación 1, en el cual el compuesto de la fórmula I se selecciona de

Ester metílico del ácido 7-(2,3-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxílico,

Ester metílico del ácido 7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxílico,

Ester metílico del ácido 7-(4-clorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxílico,

Ester 1,1-dimetiletílico del ácido 7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxílico,

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Ester 1,1-dimetiletílico del ácido 7-(3,4-diclorofenil)-4,7-dihidro-5-metil-2-(trifluorometil)pirazolo[1,5-a]pirimidin-6-carboxílico,

Ester 1,1-dimetiletílico del ácido 7-(2,3-diclorofenil)-4,7-dihidro-5-metil-2-(trifluorometil)pirazolo[1,5-a]pirimidin-6-carboxílico,

Ester 1,1-dimetiletílico del ácido 7-(2,3-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxílico,

Ester 1,1-dimetiletílico del ácido 7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxílico, enantiómero A,

Ester 1,1-dimetiletílico del ácido 7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxílico, enantiómero B,

Ester 1,1-dimetiletílico del ácido 7-(3,4-diclorofenil)-4,7-dihidro-5-dimetilpirazolo[1,5-a]pirimidin-6-carboxílico,

Ester 1,1-dimetiletílico del ácido 3-cloro-7-(3-clorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxílico,

Ester 1,1-dimetiletílico del ácido 7-(2,3-diclorofenil)-4,7-dihidro-4,5-dimetilpirazolo[1,5-a]pirimidin-6-carboxílico,

Ester 1,1-dimetiletílico del ácido 7-(3,4-diclorofenil)-4,7-dihidro-4,5-metilpirazolo[1,5-a]pirimidin-6-carboxílico,

Ester 1,1-dimetiletílico del ácido 4,7-dihidro-5-metil-7-(1-metiletil)pirazolo[1,5-a]pirimidin-6-carboxílico,

Ester 1,1-dimetiletílico del ácido 7-Ciclopropil-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxílico,

Acido 7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxílico,

Acido 7-(3,4-diclorofenil)-4,7-dihidro-5-metil-2-(trifluorometil)pirazolo[1,5-a]pirimidin-6-carboxílico,

1-[[7-(2,3-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-fenilpiperazina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-fenilpiperazina,

7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N-propilpirazolo[1,5-a]pirimidin-6-carboxamida,

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7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N-fenil-pirazolo[1,5-a]pirimidin-6-carboxamida,

4-[[7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]morfolina,

7-(2,3-diclorofenil)-4,7-dihidro-5-metil-N-propilpirazolo[1,5-a]pirimidin-6-carboxamida,

7-(2,3-diclorofenil)-4,7-dihidro-5-metil-N-fenilpirazolo[1,5-a]pirimidin-6-carboxamida,

7-(2,3-diclorofenil)-4,7-dihidro-5-metil-N-(2-feniletil)pirazolo[1,5-a]pirimidin-6-carboxamida,

7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N-(2-feniletil)pirazolo[1,5-a]pirimidin-6-carboxamida,

7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N-3-piridinilpirazolo[1,5-a]pirimidin-6-carboxamida,

1-[[7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-fenil-piperazina, enantiómero A,

1-[[7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-fenil-piperazina, enatiómero B,

1-[[7-(4-clorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-fenilpiperazina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N-(fenilmetil)pirazolo[1,5-a]pirimidin-6-carboxamida,

4-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]morfolina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-metil-piperazina,

7-(2,3-diclorofenil)-4,7-dihidro-5-metil-N-(fenilmetil)pirazolo[1,5-a]pirimidin-6-carboxamida,

7-(4-clorofenil)-4,7-dihidro-5-metil-N-(fenilmetil)pirazolo[1,5-a]pirimidin-6-carboxamida,

4-[[7-(4-clorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]morfolina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]piperidina,

1-[[7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]pirimidina,

7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N-(3-fenilpropil)pirazolo[1,5-a]pirimidin-6-carboxamida,

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1-[[5-(3,4-diclorofenil)-5,8-dihidro-7-metil-imidazol[1,2-a]pirimidin-6-il]carbonil]-4-piperazina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(fenil-metil)piridina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(fenil-metil)piperazina,

7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N,N-dipropilpirazolo[1,5-a]pirimidin-6-carboxamida,

1-[[7-(3-clorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7-(3,4-difluorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil[1,2,4]triazol[1,5-a]pirimidin-6-il]carbonil]-4-fenilpiperazina,

1-[[7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluoro-fenil)piperazina,

1-(4-fluorofenil)-4-[(4,7-dihidro-5-metil-7-fenilpirazolo[1,5-a]pirimidin-6-il)carbonil]piperazina,

1(4-fluorofenil)-4-[(4,7-dihidro-5-metil-7-fenilpirazolo[1,5-a]pirimidin-6-il)carbonil]piperazina,

1-[[7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluoro-fenil)piperazina, enantiómero A,

1-[[7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluoro-fenil)piperazina, enantiómero A,

1-[[5-(2,3-diclorofenil)-5,8-dihidro-7-metil-imidazol[1,2-a]pirimidin-6-il]carbonil]-4-fenil-piperazina,

1-(4-fluorofenil)-4-[[7-(3-fluorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-piperazina,

1-[[7-(3,5-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-ilo]carbonil]-4-(4-fluoro-fenil)piperazina,

1-[(7-ciclohexil-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il)carbonil]-4-fenilpiperazina,

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1-[[7-(2,3-diclorofenil)-4,7-dihidro-5-metil-[1,2,4]triazol[1,5-a]pirimidin-6-il)carbonil]-4-fenil-piperazina,

1-[[7-(2,3-diclorofenil)-4,7-dihidro-2,5-dimetil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-fenil-piperazina,

Ester etílico del ácido 7-(2,3-diclorofenil)-4,7-dihidro-5-metil-6-[(4-fenil-1-piperazinil)-carbonil]pirazolo[1,5-a]pirimidin-3-carboxílico,

1-[[4-(2,3-diclorofenil)-4,6,7,8-tetrahidro-2-metil-1H-pirimido[1,2-a]pirimidin-3-il]carbonil]-4-fenil-piperazina,

Ester 1,1-dimetiletílico del ácido 4-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-1-piperazinacarboxílico,

Ester 1,1-dimetiletílico del ácido 4-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-1-pipera-zinacarboxílico,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-2-fenilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-fenilpiperazina,

7-(3,4-diclorofenil)-4,7-dihidro-2,5-dimetil-N-(3-fenilpropil)pirazolo[1,5-a]pirimidin-6-carboxamida,

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1-[[7-(2,3-diclorofenil)-2-(1,1-dimetiletil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-fenilpiperazina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-fenil-piperidina,

Ester etílico del ácido 7-(3,4-diclorofenil)-4,7-dihidro-5-metil-6-[[(3-fenilpropil)amino]carbonil]pirazolo[1,5-a]pirimidin-3-carboxílico,

Ester etílico del ácido 7-(2,3-diclorofenil)-4,7-dihidro-5-metil-6-[(4-fenil-1-piperazinil)-carbonil]pirazolo[1,5-a]pirimidin-2-carboxílico,

1-[[3-ciano-7-(2,3-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-2-(trifluorometil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)-piperazina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-2-(trifluorometil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)-piperazina,

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1-[[7-(2,3-diclorofenil)-4,7dihidro-5-metil-2-(trifluorometil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)-piperazina, enantiómero B,

1-[[7-(2,3-diclorofenil)-4,7-dihidro-2,5-dimetil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluoro-fenil)-piperazina, enantiómero B,

7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N-(3-fenilpropil)-2-(trifluorometil)pirazolo[1,5-a]pirimidin-6-carboxamida,

Ester metílico del ácido 7-(3,4-diclorofenil)-6-[[4-(4-fluorofenil)-1-piperazinil]carbonil-4,7-dihidro-5-metilpirazolo[1,5-a]piri-midin-2-carboxílico,

(2S)-1-[[7-(2,3-diclorofenil)-4,7-dihidro-5-metil-2-(trifluorometil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(metoximetil)pirrolidona,

1-[[7-(2,3-diclorofenil)-2-fluoro-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

(2S)-1-[[2-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(metoximetil)pirrolidona,

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(2S)-1-[[2-cloro-7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(metoximetil)pirrolidona,

(2S)-1-[[7-(2,3-dicloro-fenil)-2-fluoro-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(metoxi-metil)pirrolidona,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-2,5-dimetilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-2,5-dimetilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina, enantiómero A,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-2,5-dimetil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluoro-fenil)piperazna, enantiómero B,

7-(2,3-diclorofenil)-4,7-dihidro-5-metil-N,N-dipropilpirazolo[1,5-a]pirimidin-6-carboxamida,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7-(2,3-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

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Ester metílico del ácido 4-[6-[[4-(4-fluorofenil)-1-piperazinil]carbonil]-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-7-il]benzoico,

1-(4-fluorofenil)-4-[[7-(2-fluorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-piperazina,

1-[[7-(2-clorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7-(2,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluoro-fenil)piperazina,

1-[[4,7-dihidro-7-(2-metoxifenil)-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7-(2,3-dimetoxifenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluoro-fenil)piperazina,

1-[[7-(2,4-dimetoxifenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluoro-fenil)piperazina,

1-[[7-(2,5-dimetoxifenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluoro-fenil)piperazina,

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1-{[4,7-dihidro-5-metil-7-[2-trifluorometil)fenil]pirozolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-(2-metilfenil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-(3-fenoxifenil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7-(3,4-dimetoxifenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7-(3,5-dimetoxifenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-[3-(fenilmetoxi)fenil]pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-7-(3-hidroxifenil)-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-[3-(trifluorometil)fenil]pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihıdro-5-metıl-7-(3-metılfenıl)pırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazına,

1-[[7-(4-cıanofenıl)-4,7-dıhıdro-5-metılpirazolo[1,5-a]pırımidın-6-il]carbonıl]-4-(4-fluorofenıl)pıperazına,

1-(4-fluorofenıl)-4-[[7-(4-fluorofenıl)-4,7-dıhıdro-5-metılpırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-pıperazına,

N-[4-[6-[[4-(4-fluorofenıl)-1-pıperazınıl]carbonıl]-4,7-dıhıdro-5-metılpırazolo[1,5-a]pırımıdın-7-ıl]acetamida,

1-[[7-(4-(dımetıl-amıno)fenıl]-4,7-dıhıdro-5-metılpırazolo[ı,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazına,

1-[[4,7-dıhıdro-7-(4-metoxıfenıl)-5-metılpırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazına,

1-[[4,7-dıhidro-5-metıl-7-[4-(fenılmetoxı)fenıl]pırazolo[1,5-a]pırımidın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazına,

1-[[7-(4-butoxıfenıl)-4,7-dıhıdro-5-metılpırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazına,

1-[[4,7-dihidro-5-metil-7-(2-tienil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-(3-tienil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-[4-(trifluorometil)fenil]pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-(4-metilfenil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-(2-nitrofenil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-(4-nitrofenil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7-(2,6-difluorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7-(2,4-difluorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7-(2,5-difluorofenıl)-4,7-dıhıdro-5-metılpırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazına,

1-[[7-(3,5-dıfluorofenıl)-4,7-dıhıdro-5-metilpirazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazına,

1-[[4,7-dıhıdro-5-metıl-7-[2-(fenılmetoxı)fenil]pira-zol[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)piperazına,

1-[[7-(3,4-dımetılfenil)-4,7-dıhıdro-5-metıl-pırazolo[1,5-a]pırimıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazina,

1-[[4,7-dıhıdro-5-metil-7-[4-(trıfluorometoxı)fenil]pı-razol[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazina,

1-[[4,7-dıhıdro-5-metıl-7-[3-(trıfluorometoxı)fenıl]pı-razol[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazına,

1-[[7(3-cıanofenıl)-4,7dihıdro-5-metılpırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazına,

1-[[4,7-dıhıdro-7(3-metoxıfenıl)-5-metıl-pırazolo[1,5-a]pırımıdin-6-ıl]carbonil]-4-(4-fluorofenıl)pıperazına,

1-[[7-(4-clorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-(4-(fenoxifenil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-(3-nitrofenil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-(5-metil-2-furanil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-7-(1H-imidazol-2-il)-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-(1H-pirrol-2-il)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-(2-piridinil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7-(3-cloro-4-metoxi-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-7-(4-metoxi-1,3-benzodioxol-6-il)-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-7-[5-hidroximetil)-2-furanil]-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-7-[1H-indol-3-il)-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)pipeiazina,

1-[[4,7-dihidro-5-metil-7-(3-piridinil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-(3-quinolinil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-(4-quinolinilo)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7-(2,3-dihidro-1,4-benzodioxin-6-il)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-(2,3,5-tricloro-fenil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7(2,5-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-(4-fluorofenil)-4-[[7-(3-furanil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-piperazina,

1-[[7-(2-benzofuranil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-(3-metilbenzo[b]tiofen-2-il)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-(2-quinolinil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-(2-tiazolil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-(4-fluorofenil)-4-[[7-(2-furanil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-piperazina,

1-[[4,7-dihidro-7-[3-metoxi-4-(fenilmetoxi)fenil]-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihıdro-7-[4-metoxı-3-(fenılmetoxi)fenıl]-5-metilpirazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)piperazına,

1-[[4,7-dıhıdro-5-metıl-7-(2-naftalenıl)pırazolo[1,5-a]pırımıdın-6-il]carbonıl]-4-(4-fluorofenıl)pıperazina,

1-[[7-[3,4-Bıs(fenıl-metoxı)fenıl]-4,7-dıhıdro-5-metılpirazolo[1,5-a]pirımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazına,

1-[[7-(1,3-Benzodıoxol-5-ıl)-4,7-dıhıdro-5-metıl-pırazolo[1,5-a]pırımidın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazına,

1-[[7-[3,5-Bis(trıfluoro-metıl)fenıl]-4,7-dıhıdro-5-metılpırazolo[1,5-a]pırı-mıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazına,

1-[[4,7-dıhıdro-5-metıl-7-[5-[1-metıl-3-(trıfluorometıl)-1H-pırazol-5-ıl]-2-tıenıl]pırazolo[1,5-a]pirımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazına,

1-[[7-(5-etıl-2-furanıl)-4,7-dıhıdro-5-metılpırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazına,

1-[[7-(2,3-dıhıdro-5-benzofuranil)-4,7-dıhıdro-5-metılpırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazına,

1-[[7-(3-bromofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-[4-(1-pirrolidinil)-fenil]pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-(3-metil-2-tienil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-(5-metil-2-tienil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7-(1,3-benzodioxol-4-il)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7-(5-cloro-2-tienil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7-(3,5-dimetilfenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7-(2,3-diclorofenil)-4,7-dihidro-2,5-dimetilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

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1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina, enantiómero A,

1-[[7-(3,4-diclrofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina, enantiómero B,

1-[[7-(2,3-diclorofenil)-4,7-dihidro-2,5-dimetil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina, enantiómero B,

1-[[7-(2,3-diclorofenil)-4,7-dihidro-2,5-dimetil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina, enantiómero A,

8-[[7(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1,4-dioxa-8-azaspiro[4,5]decano,

1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]car-bonil]-4-(2-metoxi-fenil)piperazina,

1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-[3-(trifluorometil)-fenil]piperazina,

1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-nitrofenil)piperazina,

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1-(4-acetilfenil)-4-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]piperazina,

1-(2-clorofenil)-4-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]piperazina,

1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-metoxi-fenil)piperazina,

1-(3,4-diclorofenil)-4-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]piperazina,

1-(3,5-diclorofenil)-4-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]piperazina,

1-(4-clorofenil)-4[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]piperazina,

1-(3-clorofenil)-4[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]piperazina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]car-bonil]-4-(3-metoxifenil)piperazina,

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1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]car-bonil]-4-(4-metilfenil)piperazina,

1-[[7(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5a]-pirimidin-6-il]car-bonil]-4-[4-(trifluorometil)-fenil]piperazina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(2-fluorofenil)piperazina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]car-bonil]-4-(3,4-dimetilfenil)piperazina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(2-pirimidinil)piperazina,

7-(3,4-diclorofenil)-N-[2-[(4-fluorofenil)amino]etil]-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-carboxamida,

Ester fenilmetílico del ácido 4-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-1-piperazinacarboxílico,

7-(3,4-diclorofenil)-N-etil-N-[(2-fluorofenil)metil]-4,7-dihidro-5-metilpirazolo[1,5-a]piri-midin-6-carboxamida,

N-[(3-cloro-4-metoxıfenil)metıl]-7-(3,4-dıclorofenıl)-4,7-dihıdro-5-metıl-pırazolo[1,5-a]pirı-mıdına-6-carboxamida,

1-(1,3-Benzodioxol-5-ılmetıl)-4-[[7-(3,4-dıclorofenıl)-4,7-dihıdro-5-metılpirazolo[1,5-a]pırımıdın-6-ıl]carbonıl]pıperazına,

Ester etílico del ácido 4-[[7-3,4-dıclorofenıl)-4,7-dıhıdro-5-metılpirazolo[1,5-a]pırimıdın-6-ıl]carbonil]-1-pıperazıncarboxílico,

1-[[7-(3,4-dıclorofenıl)-4,7-dıhıdro-5-metılpırazolo[1,5-a]pırımidın-6-ıl]carbonıl]-4-(2-pırıdınıl)pıperazına,

(2S)-1-[[7-(3,4-dıclorofenıl)-4,7-dıhıdro-5-metılpirazolo[1,5-a]pırımidın-6-ıl]carbonıl]-2-(metoxımetıl)pırrolıdına,

1-[Bıs(4-fluorofenıl)-metil]-4-[[7-(3,4-dıclorofenıl)-4,7-dıhıdro-5-metıl-pırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]pıperazına,

1-[[7-(3,4-dıcloro-fenıl)-4,7-dıhıdro-5-metıl-pırazolo[1,5-a]pırımıdın-6-ıl]car-bonıl]-4-(2-furanıl-carbonıl)pıperazına,

1-cıclohexıl-4-[[7-(3,4-dıclorofenıl)-4,7-dıhıdro-5-metilpırazolo[1,5-a]pirımıdın-6-ıl]carbonil]pıperazına,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(2-metoxietil)piperazina,

1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(9H-fluoren-9-il]piperazina,

(2R)-1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]car-bonil]-2-(metoxi-metil)pirrolidina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]car-bonil]-4-(2,3-dimetilfenil)piperazina,

Ester etílico del ácido 1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]car-bonil]-2-piperidincarboxílico,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]car-bonil]-N,N-dietil-3-piperidincarboxamida,

Ester etílico del ácido 1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]car-bonil]-3-piperidin-carboxílico,

1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]car-bonil]-3-metil-piperidina,

1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]car-bonil]-3,5-dimetil-piperidina,

1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]car-bonil]-4-hidroxi-piperidina,

4-(4-clorofenil)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]piri-midin-6-il]carbonil]-4-hidroxipiperidina,

Ester etílico del ácido 1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]car-bonil]-4-piperidin-carboxílico,

1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-metilpiperidina,

1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1,2,3,4-tetrahidroquinolina,

1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-decahidroquinolina,

2-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1,2,3,4-tetrahidroquinolina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-propilpiperidina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(hidroxidifenilmetil)piperidina,

7-(3,4-diclorofenil)-N-[(2-fluorofenil)metil]-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxamida,

2-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2,3,4,9-tetrahidro-1H-pirido[3,4-b]indol,

7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N-[2-(fenilamino)-etil]pirazolo[1,5-a]pirimidin-6-carboxamida,

(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-2-[(fenilamino)metil]pirrolidona,

N-ciclohexil-7-(3,4-diclorofenil)-4,7-dihidro-N,5-dimetilpirazolo[1,5-a]pirimidin-6-carboxamida,

3-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]tiazol,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]pirrolidina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-3,4-dihidro-1H-indol,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]azetidina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]hexahidro-1H-azepina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]octahidroazocina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1,2,3,6-tetrahidropiridina,

7-(3,4-diclorofenil)-4,7-dihidro-N,5-dimetil-N-[2-(2-piridinil)-etil]pirazolo[1,5-a]pirimidin-6-carboxamida,

Ester etílico N-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-N-(fenilmetil)glicina,

Trans-7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N-(2-fenilciclopropil)pirazolo[1,5-a]pirimidin-6-carboxamida,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-metilpirrolidina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-metilaziridina,

(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-[[(2,6-dimetilfenil)amino]metil]pirrolidina,

7-(3,4-diclorofenil)-N-etil-4,7-dihidro-5-metil-N-(4-piridinilmetil)pirazolo[1,5-a]pirimidin-6-carboxamida,

7-(3,4-diclorofenil)-4,7-dihidro-N,5-dimetil-N-[(1R)-1-feniletil]pirazolo[1,5-a]pirimidin-6-carboxamida,

7-(3,4-diclorofenil)-4,7-dihidro-N,5-dimetil-N-[(1S)-1-feniletil]pirazolo[1,5-a]pirimidin-6-carboxamida,

6-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1,3,3-trimetil-6-azabiciclo[3,2,1]octano,

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7-(3,4-diclorofenil)-N-(hexahidro-1H-azepin-1-il)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxamida,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]aziridina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]octahidro-1H-azonina,

(2R-trans)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2,5-bis(metoximetil)-pirrolidina,

(2-trans)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2,5-bis-(metoximetil)pirrolidina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-L-prolinamida,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-D-prolinamina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2,3-dihidro-2-metil-1H-indol,

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1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2,3-dihidro-5-nitro-1H-indol,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2,3-dihidro-6-nitro-1H-indol,

4-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-tiomorfolina,

Ester metílico 1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-L-prolina,

(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(metoximetil)pirro-lidina, enantiómero A,

(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(metoximetil)pirrolidina, enantiómero B,

Ester 1,1-dimetiletílico 1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-L-prolina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-N-(2-naftalenil)-L-prolinamida,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1,2,3,4-tetrahidro-2-metilquinolina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-6-fluoro-1,2,3,4-tetrahidro-2-metilquinilina,

Ester fenilmetílico 1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-L-prolina,

Ester fenilmetílico 1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-D-prolina,

Ester fenilmetílico 1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-hidroxi-L-prolina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)-2-metilpiperazina,

3-cloro-N-ciclohexil-7-(3,4-diclorofenil)-4,7-dihidro-N,5-dimetilpirazolo[1,5-a]piri-midin-6-carboxamida,

4-[[3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-tiomorfolina,

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1-[[3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2,3-dihidro-1H-indol,

1-[[3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]hexahidro-1H-azepina,

1-[[3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-octahidroazocina,

1-[[3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1,2,3,6-tetrahidropiridina,

3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-N,5-dimetil-N-[(1S)-1-feniletil]-pirazolo[1,5-a]pirimidin-6-carboxamida,

3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-N,5-dimetil-N-[(1R)-1-feniletil]-pirazolo[1,5-a]pirimidin-6-carboxamida,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(metoxi-metil)piridina,

Ester 1,1-dimetiletílico del ácido [(3R)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-3-pirrolidinil]carbamico,

Ester 1,1-dimetiletílico del ácido [(3S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-3-pirrolidinil]carbamico,

[(3R)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-3-(dimetilamino)pirrolidina,

N-[1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-3-pirrolidinil]acetamida,

N-[1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-3-pirrolidinil]-N-metilacetamida,

7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N,N-dipentilpirazolo[1,5-a]piri-midin-6-carboxamida,

7-(3,4-diclorofenil)-N,N-dihexil-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxamida,

1-[[3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]piperidina,

3-cloro-7-(3-clorofenil)-N-ciclohexil-4,7-dihidro-N,5-dimetilpirazolo[1,5-a]pirimidin-6-carboxamida,

(2S)-1-[[3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(metoxi-metil)pirrolidina,

1-[[3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-decahidroquinolina,

2-[[3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1,2,3,4-tetrahidroisoquinolina,

4-[[3cloro-7-(3-clorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-tiomorfolina,

N-ciclohexil-7-(3,4-diclorofenil)-4,7-dihidro-N,5-metil-2-(trifluorometil)pirazolo[1,5-a]pirimidin-6-carboxamida,

7-(3,4-diclorofenil)-N,N-dietil-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxamida,

N,N-dibutil-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxamida,

7-(3,4-diclorofenil)-N,N-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxamida,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-azaciclotridecano,

9-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-dodecahidro-1H-fluoreno,

(2S)-1-[[7-(3,4-di-clorofenil)-4,7-dihidro-5-metil-2-(trifluorometil)pirazolo[1,5-a]pirimidin-6-il]car-bonil]-2-(metoximetil)pirrolidina,

1-[[3-cloro-7-(3-clorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]car-bonil]-piperidina,

1-[[3-cloro-7-(3-cloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]car-bonil]hexahidro-1H-azepina,

1-[[3-cloro-7-(3-clorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-octahidroazocina,

1-[[3-cloro-7-(3-clorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1,2,3,6-tetrahidropiridina,

3-cloro-7-(3-clorofenil)-4,7-dihidro-N,5-dimetil-N-[(1S)-1-feniletil]pirazolo[1,5-a]pirimidin-6-carboxamida,

(2S)-1-[[3cloro-7-(3-clorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(metoximetil)pirrolidina,

1-[[3cloro-7-(3-clorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-decahidroquinolina,

2-[[3-cloro-7-(3-clorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1,2,3,4-tetrahidroisoquinolina,

1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]hexahidro-1H-azepina,

1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1,2,3,6-tetrahidropiridina,

(2S)-1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimi-din-6-il]carbonil]-2-(metoximetil)pirrolidina,

1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metil-2-(trifluoro-metil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-2,3-dihidro-1H-indol,

1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metil-2-(trifluorometil)pirazolo[1,5-a]pirimidin-6-il]carbonil]hexahidro-1H-azepina,

7-(3,4-diclorofenil)-4,7-dihidro-N,5-dimetil-N-[(1S)-1-feniletil]-2-(trifluoro-metil)pirazolo[1,5-a]pirimidin-6-carboxamida,

7-(3,4-diclorofenil)-4,7-dihidro-N,5-dimetil-N-[(1R)-1-feniletil]-2-(trifluorometil)pirazolo[1,5-a]pirimidin-6-carboxamida,

7-(3,4-diclorofenil)-4,7-dihidro-N,N-bis(2-metoxietil)-5-metilpirazolo[1,5-a]pirimidin-6-carboxamida,

7-(3,4-diclorofenil)-N,N-bis(2-etoxietil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxamida,

7-(3,4-diclorofenil)-4,7-dihidro-N-(2-metoxietil)-N,5-dimetilpirazolo[1,5-a]pirimidin-6-carboxamida,

7-(3,4-diclorofenil)-4,7-dihidro-N-(2-metoxietil)-5-metil-N-propilpirazolo[1,5-a]pirimidin-6-carboxamida,

1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]piperidina,

2-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1,2,3,4-tetrahidroisoquinolina,

1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-octahidrizina,

3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-N,5-dimetil-N-[(1S)-1-feniletil]-pirazolo[1,5-a]pirimi-din-6-carboxamida,

3-cloro-N-ciclohexil-7-(2,3-diclorofenil)-4,7-dihidro-N,5-dimetil-pirazolo[1,5-a]pirimidin-6-carboxamida,

3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metil-N-(fenilmetil)pirazolo[1,5-a]pirimidin-6-carboxamida,

7-(3,4-diclorofenil)-N-etil-4,7-dihidro-N-(2-metoxietil)-5-metilpirazolo[1,5-a]pirimidin-6-carboxamida,

Ester etílico N-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-N-metilglicina,

Ester 1,1-dimetiletílico N-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-N-metilglicina,

Ester etílico N-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-N-(2-etoxi-2-oxoetil)glicina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(3-piridinil)piperidina,

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1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1,2,3,4-tetrahidro-6-metilquinolina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-propilpiperidina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-[(dietilamino)metil]piperidina,

7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N-(2-fenoxietil)-pirazolo[1,5-a]pirimidin-6-carboxamida,

1-[(7-ciclopropil-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4,7-dihidro-5-metil-7-(1-metiletil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

(2S)-1-[[4,7-dihidro-5-metil-7-(1-metil-etil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(metoximetil)pirrolidina,

1-[[4,7-dihidro-5-metil-7-(1-metil-etil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-2,3-dihidro-1H-indol,

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1-[[4,7-dihidro-5-metil-7-(1-metiletil)pirazolo[1,5-a]pirimidin-6-il]çarbonil]-1,2,3,6-tetrahidropiridina,

3-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]tiazolidina, enantiómero A,

3-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]tiazolidina, enantiómero B,

7-(3,4-diclorofenil)-4,7-dihidro-N,5-dimetil-N-(fenil-metil)pirazolo[1,5-a]pirimidin-6-carboxmida,

7-(3,4-diclorofenil)-4,7-dihidro-N,5-dimetil-N-(2-feniletil)pirazolo[1,5-a]pirimidin-6-carboxamida,

7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N-(2-feniletil)-N-(fenilmetil)pirazolo[1,5-a]pirimidin-6-carboxamida,

(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(fenoximetil)pirrolidina,

(2R)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(fenoximetil)pirrolidina,

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(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-[(4-fluorofenoxi)metil]pirrolidina,

(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-[(4-fluorofenoxi)metil]-pirrolidina,

7-(3,4-diclorofenil)-N-etil-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxamida,

N-butil-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxamida,

7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N-pentilpirazolo[1,5-a]pirimidin-6-carboxamida,

7-(3,4-diclorofenil)-4,7-dihidro-N-(2-metoxietil)-5-metilpirazolo[1,5-a]pirimidin-6-carboxamida,

(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(hidroxidifenilmetil)pirrolidina,

(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(hidroxidifenilmetil)pirrolidina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(3-piridinil)pirrolidina,

(2S)-1-[[7-(2,3-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(metoximetil)pirrolidina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-fenilpirrolidina,

3-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-feniltiazolidina,

Ester metílico del ácido 3-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-tiazolidincarboxílico,

7-(3,4-diclorofenil)-4,7-dihidro-N,5-dimetil-N-(3-fenilpropil)pirazolo[1,5-a]pirimidin-6-carboxamida,

7-(3,4-diclorofenil)-N-etil-4,7-dihidro-5-metil-N-(3-fenil-propil)pirazolo[1,5-a]pirimidin-6-carboxamida,

7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N-(3-fenilpropil)-N-propilpirazolo[1,5-a]pirimidin-6-carboxamida,

N-butil-7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N-(3-fenil-propil)pirazolo[1,5-a]pirimidin-6-carboxamida,

2-(4-clorofenil)-3-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]tiazolidina,

N-(ciclopropilmetil)-7-(3,4-diclorofenil)-4,7-dihidro-5-metil-N-propilpirazolo[1,5-a]pirimidin-6-carboxamida,

1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(2,3-dihidro-2-oxo-1H-bencimidazol-1-il)piperidina,

8-[[7-(2,3-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1-fenil-1,3,8-tiazaspiro[4,5]decan-4-ona,

4-(4-clorofenil)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-1,2,3,6-tetrahidropiridina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(2-feniletil)pirrolidina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(4-metoxifenil)pirrolidina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(2-metoxifenil)pirrolidina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(4-fluorofenil)pirrolidina,

(3R)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-3-fenoxipirrolidina,

(2S)-2-[(ciclohexiloxi)metil]-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]pirrolidina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(fenilmetil)pirrolidina,

(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(fenoximetil)pirrolidina, diastereómero A,

(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(fenoximetil)pirrolidina, diastereómero B,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(3-metoxifenil)pirrolidina,

(2S)-2-(butoximetil)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]pirrolidina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(2-tienil)pirrolidina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(4-piridinil)pirrolidina,

(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(metoximetoxi)-metil]pirrolidina,

(2S)-2-(1H-benzimidazol-1-ilmetil)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]pirrolidina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(3-furanil)pirrolidina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(2-piridinil)pirrolidina,

(3S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-3-fenoxipirrolidina,

(3S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-3-fenoxipirrolidina,

(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-2-(trifluorometil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-2-(metoximetil)pirrolidina, enantiómero A,

(2S)-1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-2-(trifluorometil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-2-metoximetil)pirrolidina, enantiómero B,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-L-propina,

7-(3,4-diclorofenil)-4,7-dihidro-N-[(1R)-2,3-dihidro-1H-inden-1-il]-5-metil-2-(trifluoromeil)pirazolo[1,5-a]pirimidin-6-carboxamida,

7-(3,4-diclorofenil)-N-(2,3-dihidro-1H-inden-2-il)-4,7-dihidro-5-metil-2-(trifluorometil)pirazolo[1,5-a]pirimidin-6-carboxamida,

Ester metílico N-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-2-(trifluorometil)pirazolo[1,5-a]pirimidin-6-il]car-bonil]-D-fenilalanina,

7-(3,4-diclorofenil)-4,7-dihıdro-5-metıl-N-(1,2,3,4-tetrahıdro-1-naftalenıl)-2-(trıfluorometıl)pirazolo[1,5-a]pırımıdın-6-carboxamıda,

7-(3,4-dıclorofenıl)-4,7-dihidro-5-metıl-N-[3-(2-oxo-1-pırrolıdınıl)propıl]-2-(trıfluorometil)pirazolo[1,5-a]pırımıdın-6-carboxamıda,

7-(3,4-dıclorofenıl)-N-(2-furanılmetıl)-4,7-dihıdro-5-metıl-2-(trıfluorometil)pırazolo[1,5-a]pırımıdın-6-carboxamıda,

7-(3,4-dıclorofenıl)-N-[(3,4-doclorofenıl)metıl]-4,7-dıhıdro-5-metıl-2-(trıfluorometıl)pıra-zol[1,5-a]pırımıdın-6-carboxamıda,

7-(3,4-dıclorofenıl)-4,7-dıhidro-N-[(2R)-2-(metoxımetıl)-1-pırrolıdınıl]-5-metıl-2-(trıfluorometıl)pıra-zol[1,5-a]pırımıdın-6-carboxamıda,

7-(3,4-dıclorofenıl)-4,7-dıhıdro-5-metil-N-[(tetrahıdro-2-furanıl)-metıl]-2-(trıfluorometıl)pırazolo[1,5-a]pırımıdın-6-carboxamıda,

7-(3,4-diclorofenil)-4,7-dihidro-N-[(1S)-2,3-dihidro-1H-inden-1-il]-5-metil-2-(trifluorometil)pirazolo[1,5-a]pirimidin-6-carboxamida,

7-(3,4-diclorofenil)-N-[2-(3,4-dicloro-fenil)etil]-4,7-dihidro-5-metil-2-(trifluorometil)pirazolo[1,5-a]pirimidin-6-carboxamida,

7-(3,4-diclorofenil)-4,7-dihidro-5-metil-2-(trifluorometil)-N-[[4-[(trifluorometil)tio]-fenil]metil]pirazol-[1,5-a]pirimidin-6-carboxamida,

(2S)-1-[[7-(3,4-diclorofenil)-4,7di-hidro-5-metil-2-(trifluorometil)pira-zol[1,5-a]pirimidin-6-il]carbonil]-2-(1-pirrolidinilmetil)-pirrolidina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(1-naftalenilsulfonilo)piperazina,

1-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-[(4-etilfenil)sulfonil]-piperazina,

1-[(4-bromo-5-cloro-2-tienil)sulfonil]-4-[[7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimi-din-6-il]carbonil]-piperazina,

1-[[7-(3,4-dıcloro-fenıl)-4,7-dıhıdro-5-metılpırazolo[1,5-a]pırımıdın-6-ıl]car-bonıl]-4-[[2-(trıfluoro-metoxı)fenıl]sulfonıl]pıperazına,

1-[(5-cloro-3-metıl-benzo[b]tıofen-2-ıl)sulfonıl]-4-[[7-(3,4-diclorofenıl)-4,7-dıhıdro-5-metıl-pırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]piperazına,

1-[[7-(3,4-dıclorofenıl)-4,7-dıhıdro-5-metılpırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-[(3-metoxıfenıl)carbonıl]pıperazına,

1-[[7-(3,4-dıcloro-fenıl)-4,7-dıhıdro-5-metılpırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(1-oxo-3-fenıl-2-propenıl)-pıperazına,

1-[[7-(3,4-dıcloro-fenıl)-4,7-dıhıdro-5-metılpırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-pırıdınılcarbonıl)pıperazına,

1-[[7-(2,3-dıclorofenıl)-4,7-dıhıdro-4,5-dımetılpırazolo[1,5-a]pırımıdın-6-il]carbonıl]-4-fenılpıperazına,

1-[[7-(3,4-dıcloro-fenıl)-4,7-dıhıdro-4,5-dımetılpırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]piperıdına,

1-[[7-(3,4-dıclorofenıl)-4,7-dıhıdro-4,5-dımetılpırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazına,

1-[[7-(2,3-dicloro-fenil)-4,7-dihidro-4,5-dimetilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7-(2,3-dicloro-fenil)-4,7-dihidro-4,5-dimetilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina, enatiómero B,

1-[[7-(2,3-diclorofenil)-4,7-dihidro-4,5-dimetilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina, enantiómero A,

1-[[7-(2,3-diclorofenil)-4,7-dihidro-2,4,5-trimetilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7-(2,3-diclorofenil)-4-[(4-fluorofenil)metil]-4,7-dihidro-2,5-dimetilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

7-(2,3-diclorofenil)-6-[[4-(4-fluorofenil)-1-piperazinil]carbonil]-N,N,2,5,-tetrametilpirazolo[1,5-a]pirimidin-4(7H)-acetamida,

7-(2,3-diclorofenil)-6-[[4-(4-fluorofenil)-1-piperazinil]carbonil]-N,N,2,5,-tetrametilpirazolo[1,5-a]pirimidin-4(7H)-acetamida,

1-[[7-(2,3-diclorofenil)-4-[2-(dimetilamino)etil]-4,7-dihidro-2,5-dimetilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[4-(ciclopropilmetil)7-(2,3-diclorofenil)-4,7-dihidro-2,5-dimetilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

7-(2,3-diclorofenil)-6-[[4-(4-fluorofenil)-1-piperazinil]carbonil]-N,N,2,5-tetrametilpirazolo[1,5-a]pirimidin-4(7H)-carboxamida,

1-[[7-(2,3-diclorofenil)-4,7-dihidro-4-metil-5-(trifluorometil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7-(2,3-diclorofenil)-4,7-dihidro-5-(trifluoro-metil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7-(2,3-dicloro-fenil)-4,7-dihidro-2-metil-5-(trifluorometil)pirazolo[1,5-a]pirimidin-6-il]car-bonil]-4-(4-fluorofenil)piperazina,

1-[[7-(2,3-dicloro-fenil)-4,7-dihidro-2,4-dimetil-5-(trifluorometil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

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1-[[7-(2,3-dıcloro-fenil)-4,7-dıhidro-2,4-dımetıl-5-(trıfluorometıl)pırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazına, enantiómero B,

1-[[7-(3,4-dıclo-rofenıl)-4,7-dıhıdro-5-(trıfluorometıl)pırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazina,

1-[[7-(3,4-dıcloro-fenıl)-4,7-dıhıdro-2-metıl-5-(trıfluorometil)pırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-fluorofenıl)pıperazına,

1-[[1-benzoıl-7-(2,3-dıclorofenıl)-1,2,4,7-tetrahıdro-5-metıl-2-oxopırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-fenılpiperazına,

1-[[1-benzoıl-7-(3,4-dıclorofenıl)-1,2,4,7-tetrahıdro-5-metıl-2-oxopırazolo[1,5-a]pırımıdın-6-ıl]car-bonıl]-4-fenılpıperazına,

1-[[1-acetıl-7-(3,4-diclorofenıl)-1,2,4,7-tetrahıdro-5-metıl-2-oxopırazolo[1,5-a]pırımıdın-6-ıl]car-bonıl]-4-fenılpıperazına,

1-[[7-(3,4-dıcloro-fenıl)-1,2,4,7-tetrahıdro-5-metıl-2-oxo-1-(1-oxobutıl)-pırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-fenılpıperazına,

1-[[1-(ciclopropil-carbonil)-7-(3,4-diclorofenil)-1,2,4,7-tetrahidro-5-metil-2-oxopirazolo[1,5-a]pirimidin-6-il]car-bonil]-4-fenilpiperazina,

1-[[1-(ciclopropil-carbonil)-7-(2,3-diclorofenil)-1,2,4,7-tetrahidro-5-metil-2-oxopirazolo[1,5-a]pirimidin-6-il]car-bonil]-4-(4-fluorofenil)piperazina,

1-[[7-(2,3-dicloro-fenil)-1,2,4,7-tetra-hidro-5-metil-1-(3-metil-1-oxobutil)-2-oxopirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)-piperazina,

1-[[7-(2,3-dicloro-fenil)-(2,-dimetil-1-oxopropil)-1,2,4,7-tetrahidro-5-metil-2-oxopirazolo[1,5-a]pirimidin-6-il]carbonil]-4-fenil-piperazina,

1-[[1-(ciclopropil-carbonil)-7-(3,4-diclorofenil)-1,2,4,7-tetrahidro-5-metil-2-oxopirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)-piperazina,

1-[[1-(ciclobutil-carbonil)-7-(3,4-diclorofenil)-1,2,4,7-tetrahidro-5-metil-2-oxopirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)-piperazina,

1-[[7-(3,4-dıcloro-fenıl)-1,2,4,7-tetrahıdro-5-metıl-1-(2-metıl-1-oxopropıl)-2-oxopırazolo[1,5-a]pırımidın-6-ıl]car-bonıl]-4-(4-fluorofenıl)pıperazına,

1-[[7-(2,3-dıclorofenıl)-1,2,4,7-tetrahidro-5-metıl-1-[(1-metıletıl)sulfonıl]-2-oxopırazolo[1,5-a]pırımıdın-6-il]carbonıl]-4-fenılpıperazına,

1-[[7-(3,4-diclorofenıl)-1,2,4,7-tetrahıdro-5-metıl-1-[(1-metıletıl)sulfonıl]-2-oxopırazolo[1,5-a]pırımıdın-6-ıl]carbonıl]-4-(4-fluorofenil)-pıperazına,

7-(2,3-dıclorofenıl)-4,7-dıhıdro-5-metıl-N-(1-metıletıl)-2-oxo-6-[(4-fenil-1-pıperazınıl)carbonıl]pırazolo[1,5-a]pırımıdın-1-(2H)-carboxamıda,

7-(2,3-dıclorofenıl)-4,7-dıhıdro-N,5-dımetıl-2-oxo-6-[(4-fenıl-1-pıperazınıl)-carbonıl]pırazolo[1,5-a]pirımıdın-1(2H)carboxamıda,

7-(2,3-dıclorofenıl)-4,7-dihıdro-5-metıl-2-oxo-6-[(4-fenıl-1-pıperazınıl)-carbonıl]-pırazolo[1,5-a]pirı-mıdın-1(2H)carboxamıda,

7-(3,4-dıclorofenıl)-6-[[4-(4-fluorofenıl)-1-pıperazınıl)-carbonıl]-4,7-dıhidro-N,N,5-trımetıl-2-oxopırazolo[1,5-a]pırimıdın-1(2H)carboxamıda,

1-[[1-(3-butenil)-7-(3,4-diclorofenil)-1,2,4,7-tetrahidro-5-metil-2-oxopirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[7-(3,4-diclorofenil)-1,2,4,7-tetrahidro-5-metil-2-oxo-1-(2,2,2-trifluoroetil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-trifluorofenil)piperazina,

1-[[7-(3,4-diclorofenil)-1,2,4,7-tetrahidro-5-metil-2-oxo-1,4-bis(2,2,2-trifluoroetil)pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

Ester 1-metiletílico del ácido 7-(3,4-diclorofenil)-6-[[4-(4-fluorofenil)-1-piperazinil]carbonil]-4,7-dihidro-5-metil-2-oxopirazolo[1,5-a]pirimidin-1(2H)-carboxílico,

1-[4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il)carbonil]-4-(fenilpiperazina,

Acido 7-(3,4-diclorofenil)-6-[[4-(4-fluorofenil)-1-piperazinil]carbonil]-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-2-carboxílico,

7-(3,4-diclorofenil)-N,N-dietil-6-[[4-(4-fluorofenil)-1-piperazinil]carbonil]-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-2-carboxamida,

7-(3,4-diclorofenil)-6-[[4-(4-fluorofenil)-1-piperazinil]carbonil]-4,7-dihidro-N-(4-hidroxifenil)-5-metilpirazolo[1,5-a]pirimidin-2-carboxamida,

1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metil-2-[[(2S)-2-(1-pirrolidinilmetil)-1-pirrolidinil]carbonil]-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

7-(3,4-diclorofenil)-6-[[4-(4-fluorofenil)-1-piperazinil]carbonil]-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-2-carboxamida,

7-(3,4-diclorofenil)-6-[[4-(4-fluorofenil)-1-piperazinil]carbonil]-4,7-dihidro-5-metil-N-(fenilmetil)pirazolo[1,5-a]pirimidin-2-carboxamida,

7-(3,4-diclorofenil)-6-[[4-(4-fluorofenil)-1-piperazinil]carbonil]-4,7-dihidro-5-metil-N-(2-feniletil)-pirazolo[1,5-a]pirimidin-2-carboxamida,

1-[[2-ciano-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

Ester 1,1-dimetiletílico del ácido 3-bromo-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxílico,

1-[[3-bromo-7-(2,3-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-fenilpiperazina,

1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbonil]-4-fenilpiperazina,

1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina,

1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-fenilpiperazina, enatiómero B,

1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]piperazina, enantiómero A,

1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina, enantiómero A,

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1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-il]carbnil]-4-(4-fluorofenil)piperazina, enantiómero B,

1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-2,5-dimetil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina, enantiómero A,

1-[[3-cloro-7-(2,3-diclorofenil)-4,7-dihidro-2,5-dimetil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina, enantiómero B,

1-[[3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-2,5-dimetil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina, enatiómero A,

1-[[3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-2,5-dimetil-pirazolo[1,5-a]pirimidin-6-il]carbonil]-4-(4-fluorofenil)piperazina, enatiómero B,

Ester 1,1-dimetiletílico del ácido 3-cloro-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidin-6-carboxílico,

7-(3,4-diclorofenil)-4,7-dihidro-5-metil-6-(5-fenil-2-oxazolilo)pirazolo[1,5-a]pirimidina,

7-(3,4-diclorofenil)-4,7-dihidro-5-metil-6-(5-fenil-1,3,4-oxa-diol-2-il)pirazolo[1,5-a]pirimidina,

6-(1H-benzimidazol-2-il)-7-(3,4-dicloro-fenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidina,

6-(2-benzotiazolil)-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidina,

7-(3,4-diclorofenil)-4,7-dihidro-5-metil-6-(1-metil-1H-benzimi-dazol-2-il)pirazolo[1,5-a]pirimidina,

7-(3,4-diclorofenil)-4,7-dihidro-5-metil-6-[5-(trifluorometil)-1-propil-1H-benzimidazol-2-il)pirazolo[1,5-a]pirimidina,

6-(5-butil-1,3,4-oxadiazol-2-il)-7-(3,4-diclorofenil)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidina,

1-[[7-(3,4-dicloro-fenil)-4,7-dihidro-5-metil-6-(4-metil-1H-benzimidazol-2-il)pira-zol[1,5-a]pirimidina,

1-[[7-(2,3-dicloro-fenil)-4,7-dihidro-5-metil-6-(1-metil-1H-benzimidazol-2-il)pira-zol[1,5-a]pirimidina,

7-(3,4-diclorofenil)-4,7-dihidro-6-(imida-zol[[1,5-a]pirimidin-3-il)-5-metilpirazolo[1,5-a]pirimidina,

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7-(3,4-diclorofenil)-6-(1-etil-5-nitro-1H-benzimidazol-2-il)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidina,

6-[5-cloro-1-(1-metiletil)-1H-benzimidazol-2-il]-7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidina,

6-[5-cloro-1-etil-1H-bencimidazol-2-il)-7-(3,4-diclorofenil)-4,7-dihidro-5-metil-pirazolo[1,5-a]pirimidina,

7-(3,4-diclorofenil)-6-(5-fluoro-1-propil-1H-benzimidazol-2-il)-4,7-dihidro-5-metilpirazol[1,5-a]pirimidina,

7-(3,4-diclorofenil)-4,7-dihidro-5-metil-6-[1-(1-metietil)-5-(trifluorometil)-1H-bencimidazol-2-il]pirazolo[1,5-a]pirimidina,

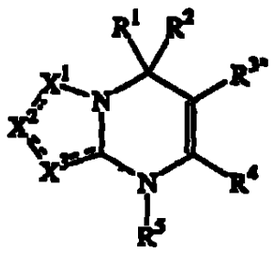
7-(3,4-diclorofenil)-6-(5-fluoro-1-metil-1H-bencimidazol-2-il)-4,7-dihidro-5-metilpirazolo[1,5-a]pirimidina,

7-(3,4-diclorofenil)-6-(5-fluoro-1-metil-1H-benzimidazol-2-il)-4,7-dihidro-5-metil-pirazolo[1,5-a]piri-midina, enantiómero A,

7-(3,4-diclorofenil)-6-(5-fluoro-1-metil-1H-bencimidazol-2-il)-4,7-dihidro-5-metil-pirazolo[1,5-a]piri-midina, enantiómero B,

7-(3,4-diclorofenil)-4,7-dihidro-5-metil-6-[1-(fenilmetil)-1H-bencimidazol-2-il]pirazolo[1,5-a]pirimidina

18 Un compuesto de fórmula I*



(I*)

enatiómeros, diastereómeros y sales del mismo farmacéuticamente aceptables, en donde

X^1, X^2 y X^3 son independientemente seleccionados de N, NR^6, $(CR^7)_q$, $(CHR^7)_q$, o C=O, en donde los enlaces que conectan X^1, X^2 y X^3 a los átomos adyacentes, pueden ser enlaces únicos o dobles que forman un anillo aromático de 5 a 7 elementos saturados o parcialmente insaturados,

R^1, R^2, R^3, R^4, R^5, R^6 y R^7 son los mismos o diferentes y son seleccionados de

manera independiente de los grupos de la fórmula $-(CH_2)_n-(Z^1)_m-(CH_2)_p-Z^c$, o

R^1, R^2, R^3, R^4 y R^5 pueden, en uno o más pares de dos, junto con los átomos a los cuales están enlazados, formar un grupo carbocíclico, carbocíclico substituido, heterocíclico o heterocíclico substituido, o

R^6 y R^7 pueden, en uno o más pares de dos, junto con los átomos a los cuales están unidos, formar un grupo carbocíclico, carbocíclico substituido, heterocíclico o heterocíclico substituido,

Z^1 es $-CZ^3Z^4-$, $-O-$, $-NZ^3-$, $-S-$, $-SO-$, $-SO_2-$, $-C(O)-$, $-C(O)Z^3-$, $-C(O)NZ^4$, $-C(S)-$, $-C(=NOZ^3)-$, alquilo, alquilo substituido, alquenilo, alquenilo substituido, alquinilo, alquinilo substituido, carbociclo, carbociclo substituido, arilo, arilo substituido, heterociclo, o heterociclo substituido,

Z^2 es hidrógeno, $-OZ^5$, $-OC(O)Z^5$, $-NZ^5-C(O)-Z^6$, $-NZ^5-CO_2-Z^6$, $-NZ^5(C=O)-NZ^6Z^7$, $-NZ^5Z^6$, $-NO_2$, halo, $-CN$, $-C(O)Z^5$, $-CO_2Z^5$, $-C(S)Z^5$, $-(C=NOZ^5)Z^6$, $-C(O)NZ^5Z^6$, $-C(S)NZ^5Z^6$, $-SZ^5$, $-SOZ^5$, $-SO_2Z^5$, $-SO_2NZ^5Z^6$, alquilo, alquilo substituido, alquenilo, alquenilo substituido, alquinilo, alquinilo substituido, carbociclo, carbociclo substituido, arilo, arilo substituido, heterociclo o heterociclo substituido

Z^3, Z^4, Z^5, Z^6 y Z^7 son independientemente hidrógeno, halo, alquilo, alquilo substituido, alquenilo, alquenilo substituido, alquinilo, alquinilo substituido, carbociclo, carbociclo substituido, arilo, arilo substituido, heterociclo, o heterociclo substituido, o

Z^3, Z^4, Z^5, Z^6 y Z^7 pueden, en uno o más pares de dos, junto con los átomos de carbono a los cuales están unidos, formar un grupo carbociclico, carbociclico substituido, heterocíclico o

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heterocíclico substituido,

R^{3*} es $-OZ^5$, $-OC(O)Z^5$, $-NZ^5-C(O)_2-Z^6$, $-NZ^5(C=O)-NZ^6Z^7$, $-NZ^5Z^6$, $-(C=NOZ^5)Z^6$, $-C(O)NZ^{5*}Z^{6*}$, $-C(S)NZ^{5*}Z^{6*}$, $-SZ^5$, $-SOZ^5$, $-SO^2Z^5$, $-SO_2NZ^5Z^6$, $-C(O)Z^{3*}-Z^{2*}$, halo, alquilo, alquilo substituido, alquenilo, alquenilo substitudo, alquinilo, alquinilo substituido, carbociclo, carbociclo substituido, arilo, arilo substituido, heterociclo o heterociclo substituido,

Z^{2*} es preferentemente hidrógeno cuando Z^{3*} es heterociclo,

Z^{3*} es heterociclo o heterociclo substituido,

Z^{5*} es alquilo substituido, alquenilo, alquenilo substituido, alquinilo, alquinilo substituido, carbociclo, carbociclo substitudo, arilo, arilo substituido, heterociclo, o heterociclo substituido, y

Z^{6*} es hidrógeno, alquilo, alquilo substituido, alquenilo, alquenilo substituido, alquinilo, alquinilo substituido, carbociclo, carbociclo subsituido,

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arilo, arilo substituido, heterociclo, o heterociclo subtitido, con la condicion de que Z^{6*} no sea hidrógeno cuando Z^{5*} es cicloalquilo insubstituido, arilo insubstituido, o bencilo insubstituido,

o Z^{5*} y Z^{6*} pueden, junto con el atomo de nitrógeno al cual están unidos, formar un grupo heterocíclico o un grupo heterociclico substituido, con la condición de que Z^{5*} y Z^{6*} no formen juntos piperidinilo insubstituido, pirrolidinilo insubstituido, o morfolinilo insubstituido, y demás, con la condición de que

(i) R^1 y R^5 sean cada uno hidrógeno, y

(ii) R^2 sea arilo o arilo substituido, y

(iii) R^4 sea heterocíclico-arilo substituido, y

(iv) X^1, X^2 y X^3 formen el anillo

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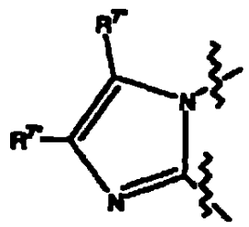

donde R^{7*} es H o alquilo,

Z^{5*} y Z^{6*} no formen juntos el piperazinilo insubstituido o piperazinilo N-alquil-substituido,

n y p son independientemente seleccionados de los enteros a partir de 0 a 10 en donde m es 0, p es también 0,

m es un entero seleccionado de 0 o 1, y

q es un entero seleccionado de 1 a 3

19 Un compuesto de la reivindicación 18, en donde

R^{3*} es heterociclo, heterociclo substituido, $-C(O)NZ^{5*}Z^{6*}$, $-C(O)Z^{3*}-CO_2Z^{5*}$, $C(O)Z^{3*}$-(aril), $-C(O)Z^{3*}$-(arilo substituido), $-C(O)Z^{3*}$-heterociclo), o $-C(O)Z^{3*}$-(heterociclo substituido)

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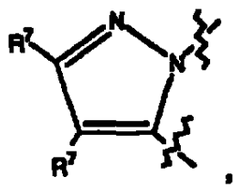
20 Un compuesto de la reivindicación 19, en donde

R^1 es H,

R^2 es arilo, arilo substituido, heterociclo, heterociclo substituido, carbociclo, o carbociclo substituido,

R^4 es alquilo o alquilo substituido, y

X^1, X^2 y X^3, junto con los átomos a los cuales se enlazan, forman un anilo seleccionado de



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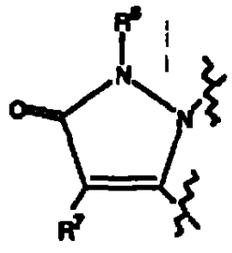

en donde los anillos substituyentes son iguales o diferentes

21 Un compuesto de la reivindicación 18, en donde $R^{3'}$ es heterociclo o heterociclo substituido

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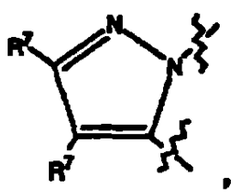
22 Un compuesto de la reivindicación 21, en donde

R^1 es H,

R^2 es arilo, arilo substituido, heterociclo, heterociclo substituido, carbociclo, o carbociclo substituido,

R^4 es alquilo o alquilo substituido, y

X^1, X^2 y X^3, junto con los átomos a los cuales se enlazan, forman un anilo seleccionado de



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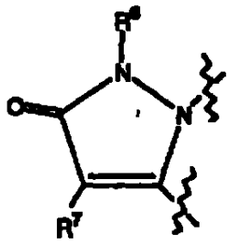

En donde los anillos substitudios son iguales o diferentes

23 Un compuesto de la reivindicación 18, el cual se selecciona de los compuestos del titulo de ejemplos 18, 19, 25-30, 33, 39-42, 44-82, 84-221, 223-273, 277-282, 286-288, 290-307, 309-312, 314-336, 340-400, 402-450, 452-463, y 465-483

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24 Una composición farmacéutica, la cual comprende una catidad terapeúticamente efectiva de al menos un compuesto de la reivindicación 18 y un vehículo o portador del mismo farmacéuticamente aceptable

25 Una composición farmacéutica, la cual comprende una cantidad terapeuticamente efectiva de al menos un compuesto de la reivindicación 19 y un vehículo o portador farmacéuticamente aceptable del mismo

26 Una composición farmacéutica, la cual comprende una cantidad terapeúticamente efectiva de al menos un compuesto de la reivindicación 20 y un vehículo o portador farmacéuticamente aceptable del mismo

27 Una composición farmacéutica, la cual comprende una cantidad terapeúticamente efectiva de al menos un compuesto de la reivindicación 21 y un vehículo o portador farmacéuticamente del mismo

28 Una composición farmacéutica, la cual comprende una cantidad efectiva de al menos un compuesto de la reivindicación 22 y un vehículo o portador farmacéuticamente aceptable del mismo

29 Una composición farmacéutica, la cual comprende una cantidad terapeúticamente efectiva de al menos un compuesto de la reivindicación 23 y un vehículo o portador farmacéuticamente aceptable del mismo

30 Un método para el tratamiento de arritmias, el cual comprende la administración a un paciente en necesidad del mismo de una cantidad efectiva de al menos un compuesto de la reivindicación 18

31 Un método para el tratamiento de arritmias, el cual comprende la administración a un paciente en necesidad del mismo de una cantidad efectiva de al menos un compuesto de la reivindicación 19

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32 Un método para el tratamiento de arritmias, el cual comprende la administración a un paciente en necesidad del mismo de una cantidad efectiva de al menos un compuesto de la reivindicación 20

33 Un método para el tratamiento de arritmias, el cual comprende la administración a un paciente en necesidad del mismo de una cantidad efectiva de al menos un compuesto de la reivindicación 21

34 Un método para el tratamiento de arritmias, el cual comprende la administracion a un paciente en necesidad del mismo de una cantidad efectiva de al menos un compuesto de la reivindicación 22

35 Un método para el tratamiento de arritmias, el cual comprende la administración a un paciente en necesidad del mismo de una cantidad efectiva de al menos un compuesto de la reivindicación 23

RESUMEN DE LA INVENCION

Se describen nuevos compuestos de dihidropirimidina heterociclicos, méotodos para usar tales compuestos en la prevención y tratamientos de arritmias y condiciones asociadas con I_{kur}, y composiciones farmacéuticas que contienen tales compuestos.

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Hacen falta [redacted] radicados en [redacted]

correspondientes a la prioridad [redacted]