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(56) Related Art

Joseph L et al, J. of Med. Chem., 1977, 20(6), 762-766

Hiroshi H et al, Chem. Lett., 1984, 9, 1591-1594

Ernst A et al, Synthesis, 1978, 12, 899

Black ML et al, J. of Med. Chem., 1967, 10(4), 565-575

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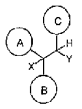
(54) Title: POTASSIUM CHANNEL INHIBITORS



(I)

(57) Abstract: The present invention relates to compounds having the structure useful as potassium channel inhibitors to treat cardiac arrhythmias, and the like.

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POTASSIUM CHANNEL INHIBITORS

BACKGROUND OF THE INVENTION

The present invention relates broadly to compounds that are useful as potassium channel inhibitors. Compounds in this class may be useful as Kv1.5 antagonists for treating and preventing cardiac arrhythmias, and the like.

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in clinical practice and is likely to increase in prevalence with the aging of the population. While AF is rarely fatal, it can impair cardiac function and lead to complications such as the development of congestive heart failure, thromboembolism, or ventricular fibrillation.

Currently available antiarrhythmic agents have been developed for the treatment of ventricular and atrial/supraventricular arrhythmias. Malignant ventricular arrhythmias are immediately life-threatening and require emergency care. Drug therapy for ventricular arrhythmia includes Class Ia (eg. procainamide, quinidine), Class Ic (eg. flecainide, propafenone), and Class III (amiodarone) agents, which pose significant risks of proarrhythmia. These Class I and III drugs have been shown to convert AF to sinus rhythm and to prevent recurrence of AF (Mounsey, JP, DiMarco, JP, *Circulation, 102*:2665-2670), but pose an unacceptable risk of potentially lethal ventricular proarrhythmia and thus may increase mortality (Pratt, CM, Moye, LA, *Am J. Cardiol., 65*:20B-29B, 1990; Waldo et al, *Lancet, 348*:7-12, 1996; Torp-Pedersen et al, *Expert Opin. Invest. Drugs, 9*:2695-2704, 2000). These observations demonstrate a clear unmet medical need to develop safer and more efficacious drugs for the treatment of atrial arrhythmias. Class III antiarrhythmic agents cause a selective prolongation of the APD without significant depression of cardiac conduction or contractile function. The only selective Class III drug approved for clinical use in atrial fibrillation is dofetilide, which mediates its anti-arrhythmic effects by blocking I_{Kr}, the rapidly activating component of I_K found in both atrium and ventricle in humans (Mounsey, JP, DiMarco, JP, *Circulation, 102*:2665-2670). Since I_{Kr} blockers increase APD and refractoriness both in atria and ventricle without affecting conduction per se, theoretically they represent potentially useful agents for the treatment of arrhythmias like AF (Torp-Pedersen, et al, *Expert Opin. Invest. Drugs, 9*:2695-2704, 2000). However, these agents have the major liability of an enhanced risk of proarrhythmia at slow heart rates.

The ultrarapid delayed rectifier K^+ current, I_{Kur}, has been observed specifically in human atrium and not in ventricle. The molecular correlate of I_{Kur} in the human atrium is the potassium channel designated Kv1.5. I_{Kur} is believed to contribute significantly to repolarization in human atrium. Consequently, a specific blocker of I_{Kur}, that is a compound which blocks Kv1.5, would overcome the shortcoming of other compounds by prolonging refractoriness through retardation of the repolarization in the human atrium without causing the delays in ventricular repolarization that underlie arrhythmogenic afterdepolarizations and acquired long QT syndrome observed during treatment with current Class III drugs. Kv1.5 blockers exhibiting these properties have been described (Peukert et al, *J. Med. Chem.,*

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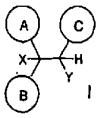
46:486-498, 2003; Knobloch *et al*, *Naunyn-Schmedieberg's* Arch. Pharmacol. 366:482-287, 2002; Merck & Co., Inc. W00224655, 2002).

The compounds described in this invention represent a novel structural class of Kv1.5 antagonist.

SUMMARY OF THE INVENTION

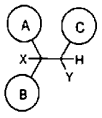
The invention concerns compounds of formula I which antagonize the Kv1.5 potassium channel:



I

The compounds of this invention are useful in the treatment and prevention of cardiac arrhythmias, and the like. Also within the scope of this invention are pharmaceutical formulations comprising a compound of Formula I and a pharmaceutical carrier.

A first aspect of the invention provides for a compound of the formula



I,

or a pharmaceutically acceptable salt thereof, wherein

A is a pyridyl ring, wherein the point of attachment to the pyridyl ring is a carbon atom,

wherein the pyridyl ring is unsubstituted, mono-substituted with R^4, disubstituted with groups independently selected from R^4, trisubstituted with groups independently selected from R^4, or tetrasubstituted with groups independently selected from R^4, and wherein the N pyridyl ring atom is unsubstituted or substituted with oxo;

C is selected from the group consisting of

1) an aryl ring, wherein any stable aryl ring atom is independently unsubstituted or substituted with a group selected from R^4,

2) a heteroaryl ring, wherein the point of attachment to the heteroaryl ring is a carbon atom, and the heteroaryl ring is selected from the group consisting of:

a) a 5-membered unsaturated monocyclic ring with 1, 2, or 3 heteroatom ring atoms selected from the group consisting of N, O or S,

b) a 6-membered unsaturated monocyclic ring with 1 or 2 N atoms, and

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c) an 8-, 9- or 10-membered unsaturated bicyclic ring with 1 or 2 heteroatom ring atoms selected from the group consisting of N, O or S,

wherein any stable atom is independently unsubstituted or substituted with a group selected from R^4;

3) a cyclopropyl ring, wherein any stable ring atom is independently unsubstituted or substituted with a group selected from R^4,

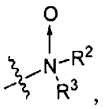
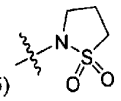
4) a 4-6 membered saturated heterocyclic ring with 1 or 2 heteroatom ring atoms selected from the group consisting of N and O, wherein any stable ring atom is independently unsubstituted or substituted with a group selected from R^4, and

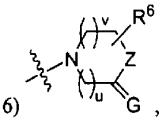
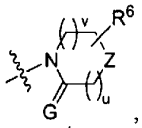
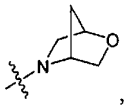
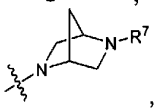
5) C_1-C_6 alkyl, wherein any stable atom is independently unsubstituted or substituted with a group selected from R^4;

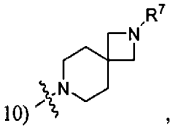
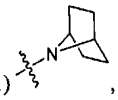
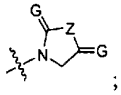
B is a pyridyl ring, wherein the point of attachment to the pyridyl ring is a carbon atom wherein the pyridyl ring is unsubstituted, mono-substituted with R^4, disubstituted with groups independently selected from R^4, trisubstituted with groups independently selected from R^4, or tetrasubstituted with groups independently selected from R^4, and wherein the N pyridyl ring atom is unsubstituted or substituted with oxo;

X is selected from the group consisting of hydrogen, OH, OCH_3 and F;

Y is selected from the group consisting of

1) NR^2R^3, 2)  , 3) OR^5, 4) $S(O)_{0-2}R^5$, 5) 

6)  , 7)  , 8)  , 9)  ,

10)  , 11)  , and 12)  ;

G, each time it occurs, is independently selected from the group consisting of H_2 and O;

Z is selected from the group consisting of $C(R^6)_2$, NR^5, $NC(O)R^5$, $NC(O)OR^5$, $NC(O)N(R^5)_2$, $NS(O)_{1-2}R^5$, $S(O)_{0-2}$, $-N(R^5)C(O)-$, $-C(R^5)=C(R^6)-$ and O;

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R^a, in each instance in which it appears, is independently selected from the group consisting of

1) hydrogen,
2) C_1-C_6 alkyl,
3) halogen,
4) aryl,
5) heterocycle,
6) C_3-C_{10} cycloalkyl, and
7) OR^5,

said alkyl, aryl, heterocycle and cycloalkyl is unsubstituted or substituted with at least one substituent selected from R^6;

R^2 and R^3 are independently selected from the group consisting of

1) hydrogen,
2) $(CR^a_2)_nOR^5$,
3) $(CR^a_2)_nN(R^5)_2$,
4) $(CR^a_2)_n C(O)R^5$,
5) $(CR^a_2)_n C(O)OR^5$,
6) $(CR^a_2)_nR^5$,
7) $(CR^a_2)_n S(O)_mR^5$,
8) $(CR^a_2)_n S(O)_mN(R^5)_2$,
9) $C(O)R^5$,
10) $C(O)OR^5$,
11) $C(O)N(R^5)_2$,
12) $S(O)_mR^5$,
13) $S(O)_mN(R^5)_2$,
14) $(CR^a_2)_nN(R^5)(CR^a_2)_nC(O)N(R^5)_2$,
15) $(CR^a_2)_nC(O)N(R^5)_2$,
16) $(CR^a_2)_nN(R^5)(CR^a_2)_nC(O)OR^5$, and
17) $(CR^a_2)_nN(R^5)S(O)_mR^5$;

R^4, in each instance in which it appears, is independently selected from the group consisting of

1) hydrogen,
2) halogen,
3) NO_2,
4) CN,
5) $CR^4{=}C(R^5)_2$,
6) $C{\equiv}CR^5$,
7) $(CR^a_2)_nOR^5$,
8) $(CR^a_2)_nN(R^5)_2$,

9) $(CR^a_2)_n C(O)R^5$,
10) $(CR^a_2)_n C(O)OR^5$,
11) $(CR^a_2)_nR^5$,
12) $(CR^a_2)_n S(O)_mR^5$,
13) $(CR^a_2)_n S(O)_mN(R^5)_2$,
14) $OS(O)_mR^5$,
15) $N(R^5)C(O)R^5$,
16) $N(R^5)S(O)_mR^5$,
17) $(CR^a_2)_nN(R^6)R^5$,
18) $(CR^a_2)_nN(R^5)(CR^a_2)_nC(O)N(R^5)_2$,
19) $(CR^a_2)_nN(R^5)(CR^a_2)_nC(O)OR^5$,
20) $N(R^5)(CR^a_2)_nR^5$,
21) $N(R^5)(CR^a_2)_nN(R^5)_2$, and
22) $(CR^a_2)_nC(O)N(R^5)_2$;

R^5, in each instance in which it appears, is independently selected from the group consisting of

1) hydrogen,
2) unsubstituted or substituted C_1-C_6 alkyl,
3) unsubstituted or substituted C_3-C_{10} cycloalkyl,
4) unsubstituted or substituted aryl,
5) unsubstituted or substituted heterocycle,
6) CF_3,
7) unsubstituted or substituted C_2-C_6 alkenyl, and
8) unsubstituted or substituted C_2-C_6 alkynyl,

or in the case where R^5 is attached to a nitrogen atom that is disubstituted with R^5, each R^5 is independently selected from C_1-C_6 alkyl, and the nitrogen atom together with each R^5 form a ring;

R^6, in each instance in which it appears, is independently selected from the group consisting of

1) hydrogen,
2) unsubstituted or substituted C_1-C_6 alkyl,
3) halogen,
4) OR^5,
5) CF_3,
6) unsubstituted or substituted aryl,
7) unsubstituted or substituted C_3-C_{10} cycloalkyl,
8) unsubstituted or substituted heterocycle,
9) $S(O)_mN(R^5)_2$,
10) $C(O)OR^5$,

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11) $C(O)R^5$,
12) CN,
13) $C(O)N(R^5)_2$,
14) $N(R^5)C(O)R^5$,
15) $N(R^5)C(O)OR^5$,
16) $N(R^5)C(O)N(R^5)_2$,
17) $OC(O)N(R^5)_2$,
18) $S(O)_mR^5$,
19) $OS(O)_mR^5$,
20) NO_2,
21) $N(R^5)_2$;
22) $SC(O)R^5$,
23) $N(R^5)S(O)_mR^5$,

R^7 is independently selected from the group consisting of
1) $S(O)_mN(R^5)_2$,
2) $C(O)OR^5$,
3) $C(O)R^5$,
4) $C(O)N(R^5)_2$, and
5) $S(O)_mR^5$;

m is independently 0, 1 or 2;
n is independently 0, 1, 2, 3, 4, 5 or 6;
u is 0, 1 or 2; and
v is 0, 1 or 2.

A second aspect of the invention provides for a method of treating a condition in a mammal, the treatment of which is effected or facilitated by Kv1.5 inhibition, which comprises administering a compound of the first aspect of the invention, or a pharmaceutically acceptable salt thereof, in an amount that is effective at inhibiting Kv1.5.

A third aspect of the invention provides for a pharmaceutical formulation comprising a pharmaceutically acceptable carrier and the compound of the first aspect of the invention or a pharmaceutically acceptable crystal form or hydrate thereof.

A fourth aspect of the invention provides for a pharmaceutical composition made by combining the compound the first aspect of the invention, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

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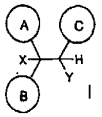
DETAILED DESCRIPTION OF THE DISCLOSURE

The invention includes compounds of formula I:



I

or a pharmaceutically acceptable salt, wherein:

A is selected from the group consisting of

1) an aryl ring,

2) a heteroaryl ring, wherein the point of attachment to the heteroaryl ring is a carbon atom, and the heteroaryl ring is selected from the group consisting of:

a) a 5-membered unsaturated monocyclic ring with 1, 2, 3, or 4 heteroatom ring atoms selected from the group consisting of N, 0 or S,

b) a 6-membered unsaturated monocyclic ring with 1, 2, 3, or 4 heteroatom ring atoms selected from the group consisting of N, 0 or S, and

c) an 8-, 9- or 10-membered unsaturated bicyclic ring with 1, 2, 3, or 4 heteroatom ring atoms selected from the group consisting of N, 0 or S;

3) C1-C10 alkyl, wherein any stable atom is independently unsubstituted or substituted with a group selected from R4,

4) a C3-C cycloalkyl ring, wherein any stable ring atom is independently unsubstituted or substituted with a group selected from R4, and

5) a 4-6 membered saturated heterocyclic ring with 1, 2 or 3 heteroatom ring atoms selected from the group consisting of N, 0 and S,

said aryl, heteroaryl, cycloalkyl, and saturated heterocyclic ring is unsubstituted, mono-substituted with R^4, disubstituted with groups independently selected from R^4, trisubstituted with groups independently selected from R^4, or tetrasubstituted with groups independently selected from R^4, and wherein any stable S or N heteroaryl or heterocyclic ring atom is unsubstituted or substituted with oxo;

B is a heteroaryl ring, wherein the point of attachment to the heteroaryl ring is a carbon atom, and wherein the heteroaryl ring is selected from the group consisting of

a) a 5-membered unsaturated monocyclic ring with 1, 2, 3, or 4 heteroatom ring atoms selected from the group consisting of N, O or S,

b) a 6-membered unsaturated monocyclic ring with 1, 2, 3, or 4 heteroatom ring atoms selected from the group consisting of N, O or S, and

c) an 8-, 9- or 10-membered unsaturated bicyclic ring with 1, 2, 3, or 4 heteroatom ring atoms selected from the group consisting of N, O or S;

said heteroaryl ring is unsubstituted, mono-substituted with R^4, disubstituted with groups independently selected from R^4, trisubstituted with groups independently selected from R^4, or tetrasubstituted with groups independently selected from R^4, and wherein any stable S or N heteroaryl ring atom is unsubstituted or substituted with oxo;

C is selected from the group consisting of

1) an aryl ring, wherein any stable aryl ring atom is independently unsubstituted or substituted with a group selected from R^4,

2) a heteroaryl ring, wherein the point of attachment to the heteroaryl ring is a carbon atom, and the heteroaryl ring is selected from the group consisting of:

a) a 5-membered unsaturated monocyclic ring with 1,2,3,or 4 heteroatom ring atoms selected from the group consisting of N, O or S,

b) a 6-membered unsaturated monocyclic ring with 1,2,3,or 4 heteroatom ring atoms selected from the group consisting of N, O or S, and

c) an 8-, 9- or 10-membered unsaturated bicyclic ring with 1,2,3,or 4 heteroatom ring atoms selected from the group consisting of N, O or S;

3) a C_3-C_{10} cycloalkyl ring, wherein any stable ring atom is independently unsubstituted or substituted with a group selected from R^4,

4) a 4-6 membered saturated heterocyclic ring with 1, 2 or 3 heteroatom ring atoms selected from the group consisting of N, O and S, wherein any stable ring atom is independently unsubstituted or substituted with a group selected from R^4,

5) C_1-C_{10} alkyl, wherein any stable atom is independently unsubstituted or substituted with a group selected from R^4,

6) $C(O)R^5$,

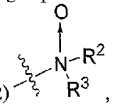
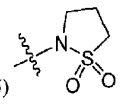
7) $C(O)OR^5$, and

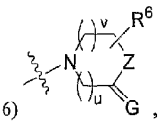
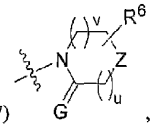
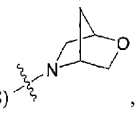
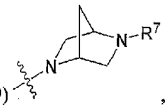
8) $C(O)N(R^5)_2$, wherein two R^5 groups can be linked to form a ring,

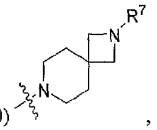
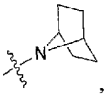
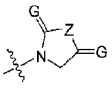
said aryl, heteroaryl, cycloalkyl, and saturated heterocyclic ring is unsubstituted, mono-substituted with R^4, disubstituted with groups independently selected from R^4, trisubstituted with groups independently selected from R^4, or tetrasubstituted with groups independently selected from R^4, and wherein any stable S or N heteroaryl or heterocyclic ring atom is unsubstituted or substituted with oxo;

X is selected from the group consisting of H, OR^5, NR^5R^5, F, CN, $S(O)_{0-2}R^5$, $C(O)OR^5$, and $C(O)N(R^5)_2$;

Y is selected from the group consisting of

1) NR^2R^3, 2)  , 3) OR^5, 4) $S(O)_{0-2}R^5$, 5) 

6)  , 7)  , 8)  , 9)  ,

10)  , 11)  , 12)  and

13) a nitrogen-containing heteroaryl ring, wherein the point of attachment to the heteroaryl ring is a nitrogen atom, and wherein the heteroaryl ring is selected from the group consisting of :

a) a 5-membered unsaturated monocyclic ring with 1, 2, 3, or 4 heteroatom ring atoms selected from the group consisting of N, O or S,

b) a 6-membered unsaturated monocyclic ring with 1, 2, 3, or 4 heteroatom ring atoms selected from the group consisting of N, O or S, and

c) an 8-, 9- or 10-membered unsaturated bicyclic ring with 1, 2, 3, or 4 heteroatom ring atoms selected from the group consisting of N, O or S;

said nitrogen-containing heteroaryl ring is unsubstituted, mono-substituted with R^4, disubstituted with groups independently selected from R^4, trisubstituted with groups independently selected from R^4, or tetrasubstituted with groups independently selected from R^4, and wherein any stable S or N heteroaryl or heterocyclic ring atom is unsubstituted or substituted with oxo;

G, each time it occurs, is independently selected from the group consisting of H_2 and O;

Z is selected from the group consisting of $C(R^6)_2$, NR^5, $NC(O)R^5$, $NC(O)OR^5$, $NC(O)N(R^5)_2$, $NS(O)_{1-2}R^5$, $S(O)_{0-2}$, $-N(R^5)C(O)-$, $-C(R^5)=C(R^6)-$ and O;

R^a, in each instance in which it appears, is independently selected from the group consisting of

1) hydrogen,
2) C_1-C_6 alkyl,
3) halogen,
4) aryl,
5) heterocycle,
6) C_3-C_{10} cycloalkyl, and
7) OR^5,

said alkyl, aryl, heterocycle and cycloalkyl is unsubstituted or substituted with at least one substituent selected from R^6;

R^2 and R^3 are independently selected from the group consisting of

1) hydrogen,
2) $(CR^a_2)_nOR^5$,
3) $(CR^a_2)_nN(R^5)_2$,
4) $(CR^a_2)_n C(O)R^5$,
5) $(CR^a_2)_n C(O)OR^5$,
6) $(CR^a_2)_nR^5$,
7) $(CR^a_2)_n S(O)_mR^5$,
8) $(CR^a_2)_n S(O)_mN(R^5)_2$,
9) $C(O)R^5$,
10) $C(O)OR^5$,
11) $C(O)N(R^5)_2$,
12) $S(O)_mR^5$,
13) $S(O)_mN(R^5)_2$,
14) $(CR^a_2)_nN(R^5)(CR^a_2)_nC(O)N(R^5)_2$,
15) $(CR^a_2)_nC(O)N(R^5)_2$,
16) $(CR^a_2)_nN(R^5)(CR^a_2)_nC(O)OR^5$, and
17) $(CR^a_2)_nN(R^5)S(O)_mR^5$;

R^4, in each instance in which it appears, is independently selected from the group consisting of

1) hydrogen,
2) halogen,
3) NO_2,
4) CN,
5) $CR^4{=}C(R^5)_2$,
6) $C{\equiv}CR^5$,
7) $(CR^a_2)_nOR^5$,
8) $(CR^a_2)_nN(R^5)_2$,
9) $(CR^a_2)_n C(O)R^5$,
10) $(CR^a_2)_n C(O)OR^5$,

11) $(CR^a_2)_nR^5$,
12) $(CR^a_2)_n S(O)_mR^5$,
13) $(CR^a_2)_n S(O)_mN(R^5)_2$,
14) $OS(O)_mR^5$,
15) $N(R^5)C(O)R^5$,
16) $N(R^5)S(O)_mR^5$,
17) $(CR^a_2)_nN(R^6)R^5$,
18) $(CR^a_2)_nN(R^5)(CR^a_2)_nC(O)N(R^5)_2$,
19) $(CR^a_2)_nN(R^5)(CR^a_2)_nC(O)OR^5$,
20) $N(R^5)(CR^a_2)_nR^5$,
21) $N(R^5)(CR^a_2)_nN(R^5)_2$, and
22) $(CR^a_2)_nC(O)N(R^5)_2$;

R^5, in each instance in which it appears, is independently selected from the group consisting of
1) hydrogen,
2) unsubstituted or substituted C_1-C_6 alkyl,
3) unsubstituted or substituted C_3-C_{10} cycloalkyl,
4) unsubstituted or substituted aryl,
5) unsubstituted or substituted heterocycle,
6) CF_3,
7) unsubstituted or substituted C_2-C_6 alkenyl, and
8) unsubstituted or substituted C_2-C_6 alkynyl,

or in the case where R^5 is attached to a nitrogen atom that is disubstituted with R^5, each R^5 is independently selected from C_1-C_6 alkyl, and the nitrogen atom together with each R^5 form a ring;

R^6, in each instance in which it appears, is independently selected from the group consisting of
1) hydrogen,
2) unsubstituted or substituted C_1-C_6 alkyl,
3) halogen,
4) OR^5,
5) CF_3,
6) unsubstituted or substituted aryl,
7) unsubstituted or substituted C_3-C_{10} cycloalkyl,
8) unsubstituted or substituted heterocycle,
9) $S(O)_mN(R^5)_2$,
10) $C(O)OR^5$,
11) $C(O)R^5$,
12) CN,
13) $C(O)N(R^5)_2$,
14) $N(R^5)C(O)R^5$,

15) $N(R^5)C(O)OR^5$,
16) $N(R^5)C(O)N(R^5)_2$,
17) $OC(O)N(R^5)_2$,
18) $S(O)_mR^5$,
19) $OS(O)_mR^5$,
20) NO_2,
21) $N(R^5)_2$;
22) $SC(O)R^5$,
23) $N(R^5)S(O)_mR^5$,

R^7 is independently selected from the group consisting of
1) $S(O)_mN(R^5)_2$,
2) $C(O)OR^5$,
3) $C(O)R^5$,
4) $C(O)N(R^5)_2$, and
5) $S(O)_mR^5$;

m is independently 0, 1 or 2;
n is independently 0, 1, 2, 3, 4, 5 or 6;
u is 0, 1 or 2; and
v is 0, 1 or 2.

An embodiment of the invention is a compound or a pharmaccutically acceptable salt there of wherein

B is a heteroaryl ring, wherein the point of attachment to the heteroaryl ring is a carbon atom, and wherein the heteroaryl ring is selected from the group consisting of pyridine and pyrimidine, wherein the heteroaryl ring is unsubstituted, mono-substituted with R^4, disubstituted with groups independently selected from R^4, trisubstituted with groups independently selected from R^4, or tetrasubstituted with groups independently selected from R^4, and wherein the N heteroaryl ring atom is unsubstituted or substituted with oxo; and

X is selected from the group consisting of hydrogen, OH, OCH_3 and F.

A preferred embodiment of the invention is a compound or a pharmaceutically acceptable salt thereof wherein

A is selected from the group consisting of
1) a phenyl ring,
2) a pyridyl ring, wherein the point of attachment to the pyridyl ring is a carbon atom, and
3) C_1-C_{10} alkyl, wherein any stable atom is independently unsubstituted or substituted with a group selected from R^4,

wherein the phenyl ring and pyridyl ring are unsubstituted, mono-substituted with R^4, disubstituted with groups independently selected from R^4, trisubstituted with groups independently selected from

R^4, or tetrasubstituted with groups independently selected from R^4, and wherein the N pyridyl ring atom is unsubstituted or substituted with oxo; and

C is selected from the group consisting of

1) an aryl ring, wherein any stable aryl ring atom is independently unsubstituted or substituted with a group selected from R^4,

2) a heteroaryl ring, wherein the point of attachment to the heteroaryl ring is a carbon atom, and the heteroaryl ring is selected from the group consisting of:

a) a 5-membered unsaturated monocyclic ring with 1, 2, or 3 heteroatom ring atoms selected from the group consisting of N, O or S,

b) a 6-membered unsaturated monocyclic ring with 1 or 2 N atoms, and

c) an 8-, 9- or 10-membered unsaturated bicyclic ring with 1 or 2 heteroatom ring atoms selected from the group consisting of N, O or S,

wherein any stable atom is independently unsubstituted or substituted with a group selected from R^4;

3) a cyclopropyl ring, wherein any stable ring atom is independently unsubstituted or substituted with a group selected from R^4,

4) a 4-6 membered saturated heterocyclic ring with 1 or 2 heteroatom ring atoms selected from the group consisting of N and O, wherein any stable ring atom is independently unsubstituted or substituted with a group selected from R^4, and

5) C_1-C_6 alkyl, wherein any stable atom is independently unsubstituted or substituted with a group selected from R^4.

A more preferred embodiment of the invention is a compound or a pharmaceutically acceptable salt thereof wherein

B is a pyridyl ring, wherein the point of attachment to the pyridyl ring is a carbon atom, and wherein the pyridyl ring is unsubstituted, mono-substituted with R^4, disubstituted with groups independently selected from R^4, trisubstituted with groups independently selected from R^4, or tetrasubstituted with groups independently selected from R^4, and wherein the N atom is unsubstituted or substituted with oxo;

X is selected from the group consisting of hydrogen, OH, OCH_3 and F;

A is selected from the group consisting of

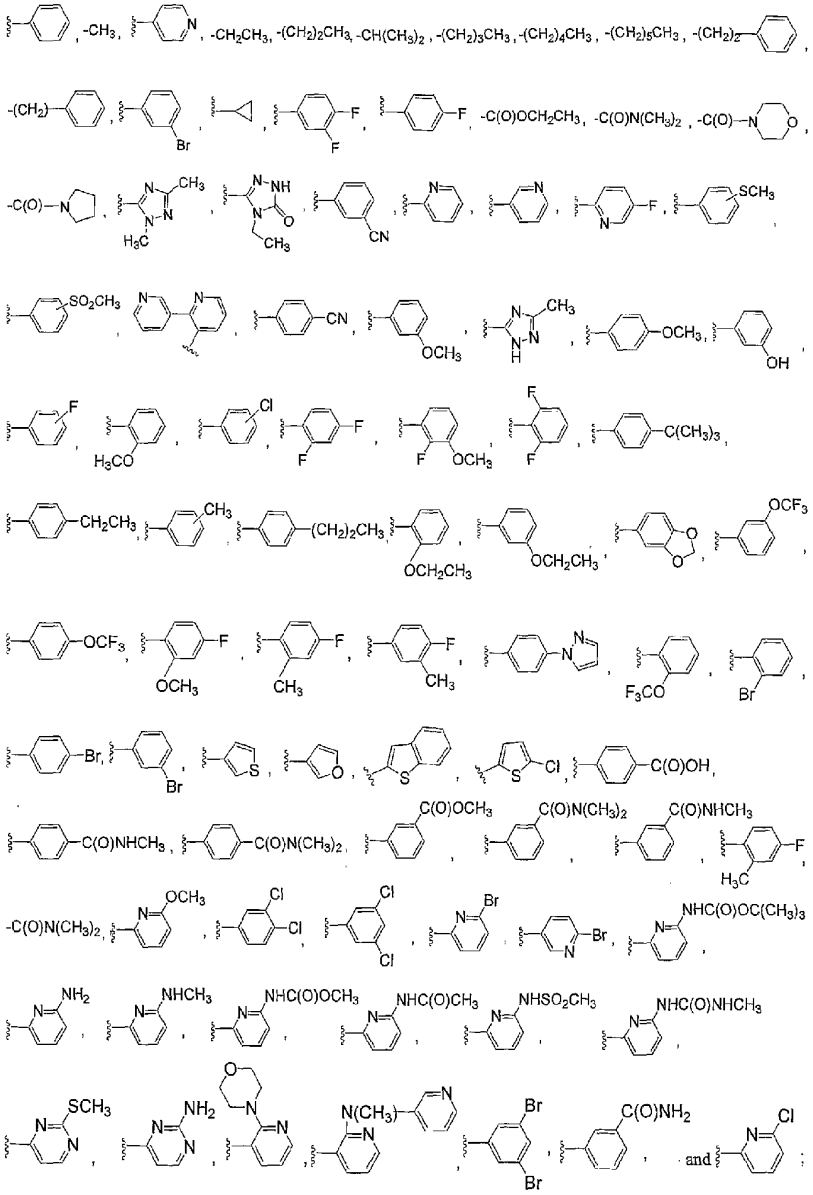
1) a phenyl ring,

2) a pyridyl ring, wherein the point of attachment to the pyridyl ring is a carbon atom, and

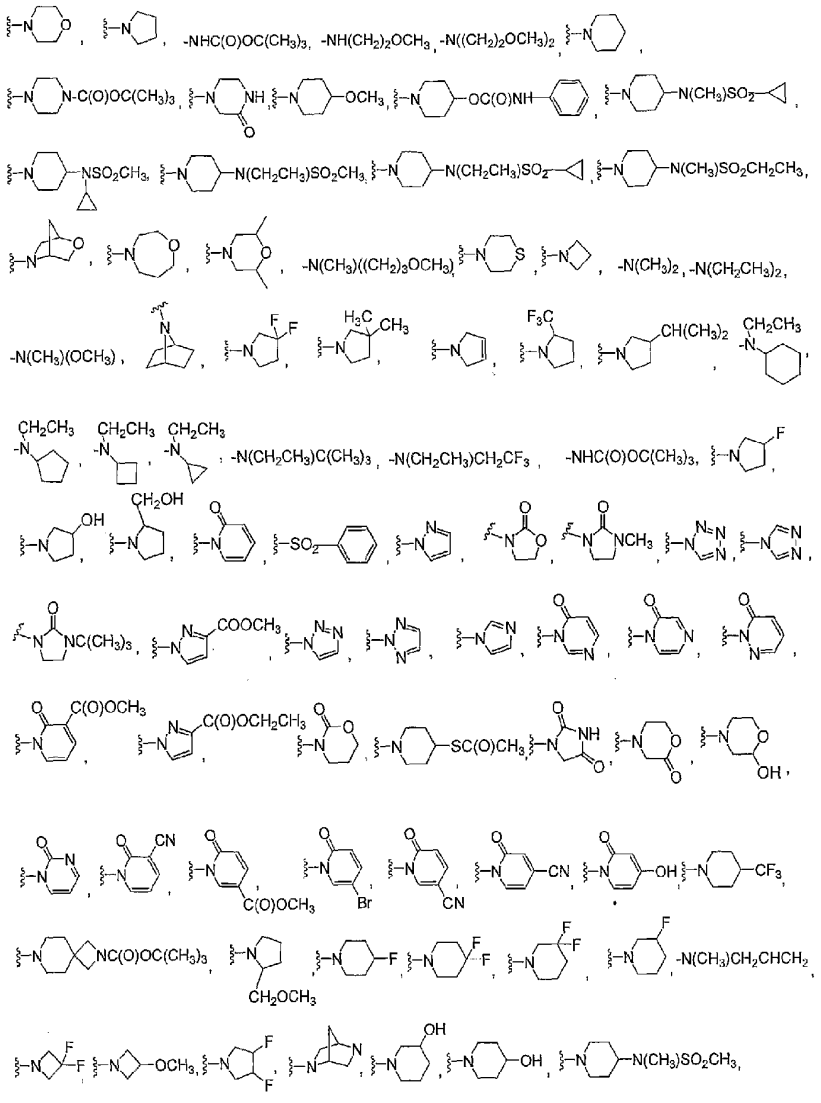
3) $-C(CH_3)_3$,

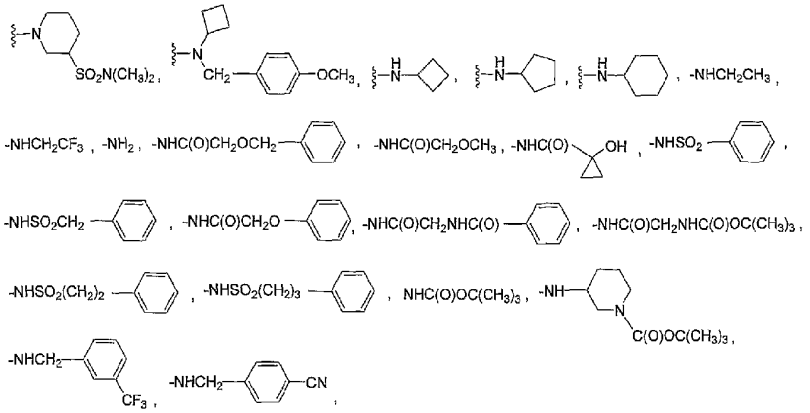
wherein the phenyl ring and pyridyl ring are unsubstituted, mono-substituted with R^4, disubstituted with groups independently selected from R^4, trisubstituted with groups independently selected from R^4, or tetrasubstituted with groups independently selected from R^4, and wherein the N pyridyl ring atom is unsubstituted or substituted with oxo;

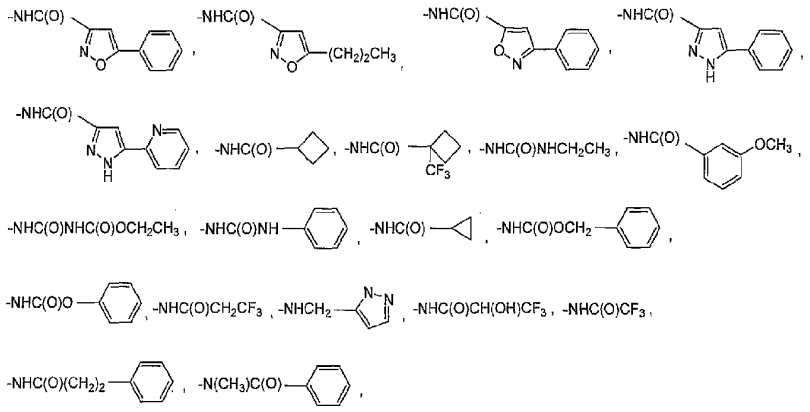
C is selected from the group consisting of



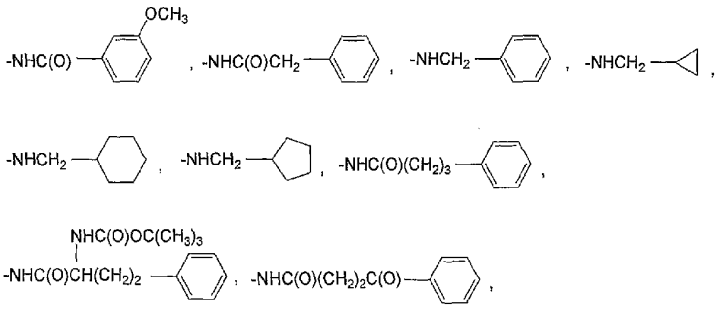
Y is selected from the group consisting of

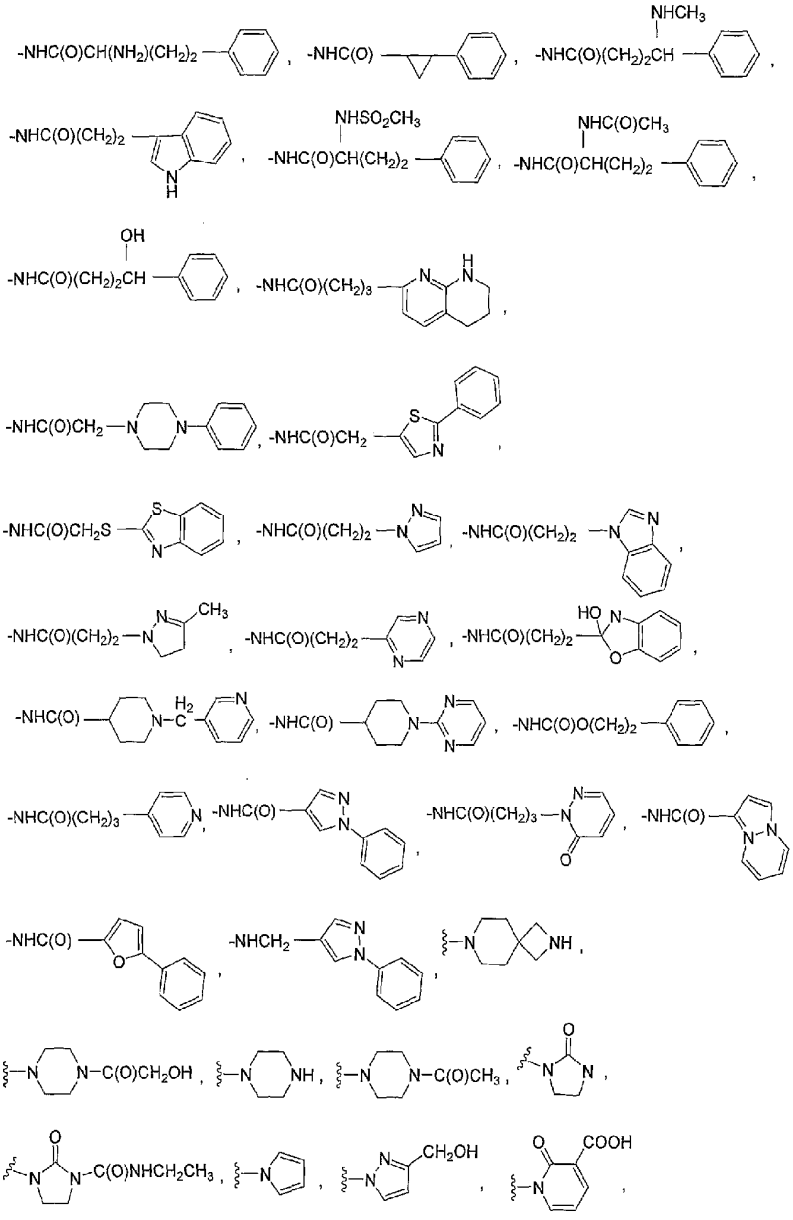


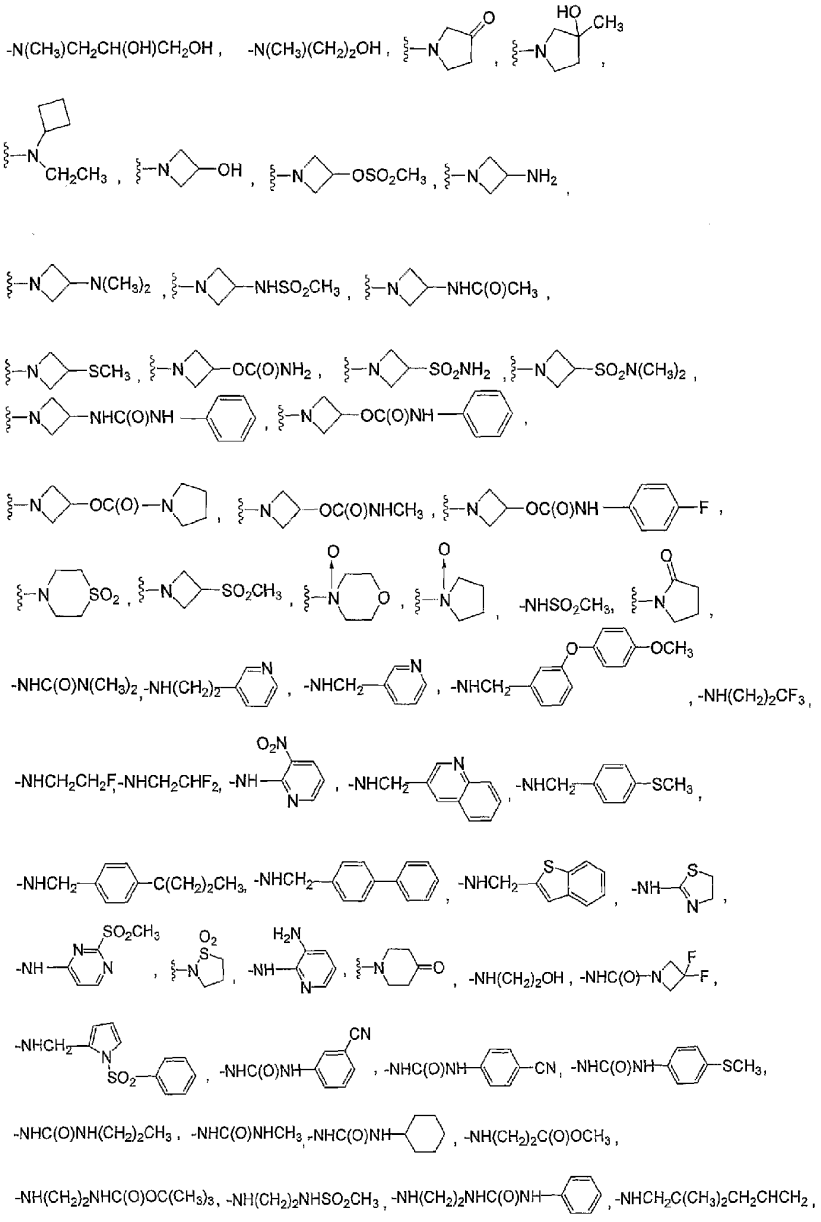

SO2N(CH3)2
CH2
OCH3
-NHCH2CH3
-NHCH2CF3
-NH2
-NHC(O)CH2OCH2
-NHC(O)CH2OCH3
-NHC(O)
OH
-NHSO2
-NHSO2CH2
-NHC(O)CH2O
-NHC(O)CH2NHC(O)
-NHC(O)CH2NHC(O)OC(CH3)3
-NHSO2(CH2)2
-NHSO2(CH2)3
NHC(O)OC(CH3)3
-NH
C(O)OC(CH3)3
-NHCH2
CF3
-NHCH2
CN

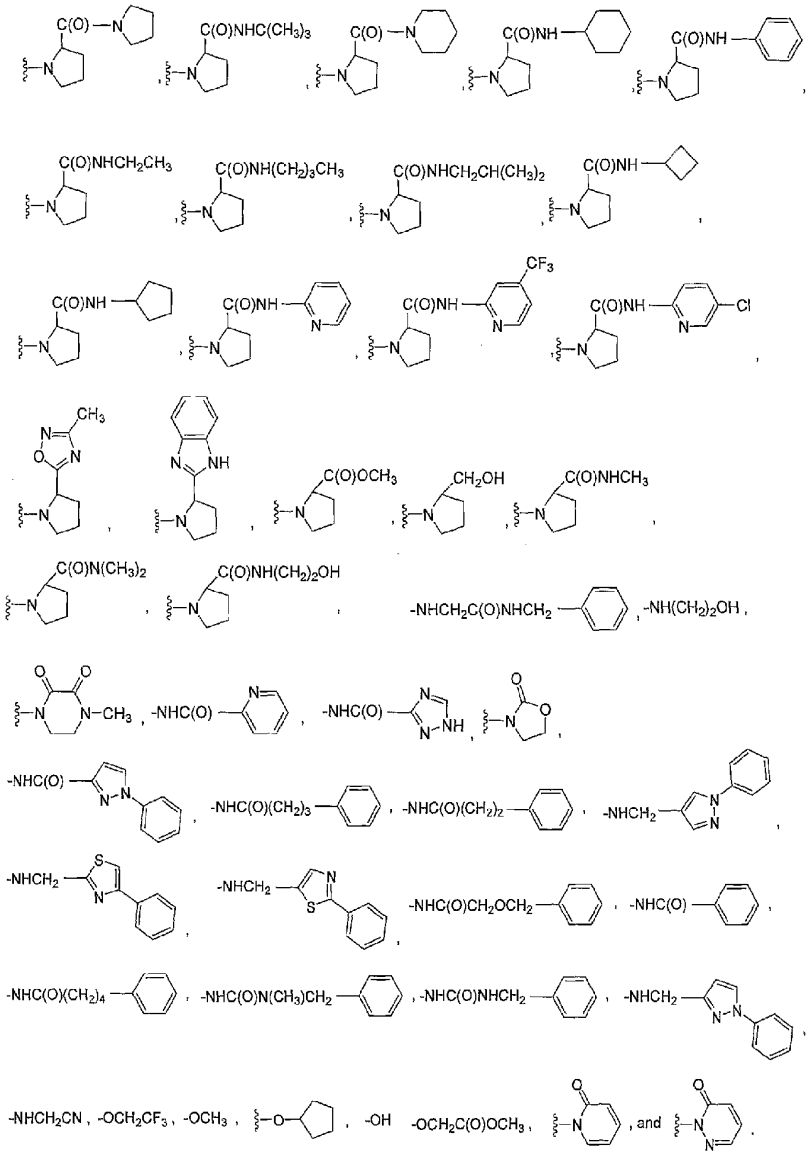

-NHC(O)
(CH2)2CH3
-NHC(O)
-NHC(O)NHCH2CH3
-NHC(O)
OCH3
-NHC(O)NHC(O)OCH2CH3
-NHC(O)NH
-NHC(O)
-NHC(O)OCH2
-NHC(O)O
-NHC(O)CH2CF3
-NHCH2
-NHC(O)CH(OH)CF3
-NHC(O)CF3
-NHC(O)(CH2)2
-N(CH3)C(O)

5

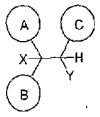

OCH3
-NHC(O)
-NHC(O)CH2
-NHCH2
-NHCH2
-NHCH2
-NHC(O)(CH2)3
NHC(O)OC(CH3)3
-NHC(O)CH(CH2)2
-NHC(O)(CH2)2C(O)







Another embodiment of the invention includes compounds of formula 1:



I

wherein:

A is selected from the group consisting of

1) an aryl ring,

2) a heteroaryl ring, wherein the point of attachment to the heteroaryl ring is a carbon atom, and the heteroaryl ring is selected from the group consisting of:

a) a 5-membered unsaturated monocyclic ring with 1, 2, 3, or 4 heteroatom ring atoms selected from the group consisting of N, O or S,

b) a 6-membered unsaturated monocyclic ring with 1, 2, 3, or 4 heteroatom ring atoms selected from the group consisting of N, O or S, and

c) an 8-, 9- or 10-membered unsaturated bicyclic ring with 1, 2, 3, or 4 heteroatom ring atoms selected from the group consisting of N, O or S;

3) C_1-C_{10} alkyl, wherein any stable atom is independently unsubstituted or substituted with a group selected from R^4,

4) a C_3-C_{10} cycloalkyl ring, wherein any stable ring atom is independently unsubstituted or substituted with a group selected from R^4, and

5) a 4-6 membered saturated heterocyclic ring with 1, 2 or 3 heteroatom ring atoms selected from the group consisting of N, O and S,

said aryl, heteroaryl, cycloalkyl, and saturated heterocyclic ring is unsubstituted, mono-substituted with R^4, disubstituted with groups independently selected from R^4, trisubstituted with groups independently selected from R^4, or tetrasubstituted with groups independently selected from R^4, and wherein any stable S or N heteroaryl or heterocyclic ring atom is unsubstituted or substituted with oxo;

B is a heteroaryl ring, wherein the point of attachment to the heteroaryl ring is a carbon atom, and wherein the heteroaryl ring is selected from the group consisting of

a) a 5-membered unsaturated monocyclic ring with 1, 2, 3, or 4 heteroatom ring atoms selected from the group consisting of N, O or S,

b) a 6-membered unsaturated monocyclic ring with 1, 2, 3, or 4 heteroatom ring atoms selected from the group consisting of N, O or S, and

c) an 8-, 9- or 10-membered unsaturated bicyclic ring with 1, 2, 3, or 4 heteroatom ring atoms selected from the group consisting of N, O or S;

said heteroaryl ring is unsubstituted, mono-substituted with R^4, disubstituted with groups independently selected from R^4, trisubstituted with groups independently selected from R^4, or

tetrasubstituted with groups independently selected from R^4, and wherein any stable S or N heteroaryl ring atom is unsubstituted or substituted with oxo;

C is selected from the group consisting of

1) an aryl ring, wherein any stable aryl ring atom is independently unsubstituted or substituted with a group selected from R^4,

2) a heteroaryl ring, wherein the point of attachment to the heteroaryl ring is a carbon atom, and the heteroaryl ring is selected from the group consisting of:

a) a 5-membered unsaturated monocyclic ring with 1,2,3,or 4 heteroatom ring atoms selected from the group consisting of N, O or S,

b) a 6-membered unsaturated monocyclic ring with 1,2,3,or 4 heteroatom ring atoms selected from the group consisting of N, O or S, and

c) an 8-, 9- or 10-membered unsaturated bicyclic ring with 1,2,3,or 4 heteroatom ring atoms selected from the group consisting of N, O or S;

3) a C_3-C_{10} cycloalkyl ring, wherein any stable ring atom is independently unsubstituted or substituted with a group selected from R^4,

4) a 4-6 membered saturated heterocyclic ring with 1, 2 or 3 heteroatom ring atoms selected from the group consisting of N, O and S, wherein any stable ring atom is independently unsubstituted or substituted with a group selected from R^4,

5) C_1-C_{10} alkyl, wherein any stable atom is independently unsubstituted or substituted with a group selected from R^4,

6) $C(O)R^5$,

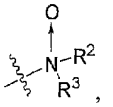
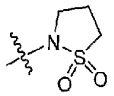
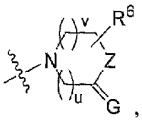
7) $C(O)OR^5$, and

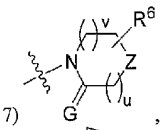
8) $C(O)N(R^5)_2$, wherein two R^5 groups can be linked to form a ring,

said aryl, heteroaryl, cycloalkyl, and saturated heterocyclic ring is unsubstituted, mono-substituted with R^4, disubstituted with groups independently selected from R^4, trisubstituted with groups independently selected from R^4, or tetrasubstituted with groups independently selected from R^4, and wherein any stable S or N heteroaryl or heterocyclic ring atom is unsubstituted or substituted with oxo;

X is selected from the group consisting of H, OR^5, NR^5R^5, F, CN, $S(O)_{0-2}R^5$, $C(O)OR^5$, and $C(O)N(R^5)_2$;

Y is selected from the group consisting of

1) NR^2R^3, 2)  , 3) OR^5, 4) $S(O)_{0-2}R^5$, 5)  , 6)  ,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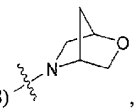
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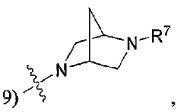
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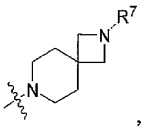
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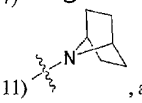

11), and

12) a nitrogen-containing heteroaryl ring, wherein the point of attachment to the heteroaryl ring is a nitrogen atom, and wherein the heteroaryl ring is selected from the group consisting of :

a) a 5-membered unsaturated monocyclic ring with 1, 2, 3, or 4 heteroatom ring atoms selected from the group consisting of N, O or S,

b) a 6-membered unsaturated monocyclic ring with 1, 2, 3, or 4 heteroatom ring atoms selected from the group consisting of N, O or S, and

c) an 8-, 9- or 10-membered unsaturated bicyclic ring with 1, 2, 3, or 4 heteroatom ring atoms selected from the group consisting of N, O or S;

said nitrogen-containing heteroaryl ring is unsubstituted, mono-substituted with R^4, disubstituted with groups independently selected from R^4, trisubstituted with groups independently selected from R^4, or tetrasubstituted with groups independently selected from R^4, and wherein any stable S or N heteroaryl or heterocyclic ring atom is unsubstituted or substituted with oxo;

G is selected from the group consisting of H_2 and O;

Z is selected from the group consisting of $C(R^6)_2$, NR^5, $NC(O)R^5$, $NC(O)OR^5$, $NC(O)N(R^5)_2$, $NS(O)_{1\text{-}2}R^5$, $S(O)_{0\text{-}2}$, $-N(R^5)C(O)-$, $-C(R^5)=C(R^6)-$ and O;

R^a, in each instance in which it appears, is independently selected from the group consisting of

1) hydrogen,

2) C_1-C_6 alkyl,

3) halogen,

4) aryl,

5) heterocycle,

6) C_3-C_{10} cycloalkyl, and

7) OR^5,

said alkyl, aryl, heterocycle and cycloalkyl is unsubstituted or substituted with at least one substituent selected from R^6;

R^2 and R^3 are independently selected from the group consisting of

1) hydrogen,

2) $(CR^a_2)_nOR^5$,

3) $(CR^a_2)_nN(R^5)_2$,

4) $(CR^a_2)_n C(O)R^5$,

5) $(CR^a_2)_n C(O)OR^5$,
6) $(CR^a_2)_nR^5$,
7) $(CR^a_2)_n S(O)_mR^5$,
8) $(CR^a_2)_n S(O)_mN(R^5)_2$,
9) $C(O)R^5$,
10) $C(O)OR^5$,
11) $C(O)N(R^5)_2$,
12) $S(O)_mR^5$,
13) $S(O)_mN(R^5)_2$,
14) $(CR^a_2)_nN(R^5)(CR^a_2)_nC(O)N(R^5)_2$, and
15) $(CR^a_2)_nC(O)N(R^5)_2$;

R^4, in each instance in which it appears, is independently selected from the group consisting of
1) hydrogen,
2) halogen,
3) NO_2,
4) CN,
5) $CR^4=C(R^5)_2$,
6) $C\equiv CR^5$,
7) $(CR^a_2)_nOR^5$,
8) $(CR^a_2)_nN(R^5)_2$,
9) $(CR^a_2)_n C(O)R^5$,
10) $(CR^a_2)_n C(O)OR^5$,
11) $(CR^a_2)_nR^5$,
12) $(CR^a_2)_n S(O)_mR^5$,
13) $(CR^a_2)_n S(O)_mN(R^5)_2$,
14) $OS(O)_mR^5$,
15) $N(R^5)C(O)R^5$,
16) $N(R^5)S(O)_mR^5$,
17) $(CR^a_2)_nN(R^6)R^5$,
18) $(CR^a_2)_nN(R^5)(CR^a_2)_nC(O)N(R^5)_2$,
19) $(CR^a_2)_nN(R^5)(CR^a_2)_nC(O)OR^5$,
20) $N(R^5)(CR^a_2)_nR^5$,
21) $N(R^5)(CR^a_2)_nN(R^5)_2$, and
22) $(CR^a_2)_nC(O)N(R^5)_2$;

R^5, in each instance in which it appears, is independently selected from the group consisting of
1) hydrogen,
2) unsubstituted or substituted C_1-C_6 alkyl,
3) unsubstituted or substituted C_3-C_{10} cycloalkyl,

4) unsubstituted or substituted aryl,

5) unsubstituted or substituted heterocycle,

6) CF_3,

7) unsubstituted or substituted C_2-C_6 alkenyl, and

8) unsubstituted or substituted C_2-C_6 alkynyl,

or in the case where R^5 is attached to a nitrogen atom that is disubstituted with R^5, each R^5 is independently selected from C_1-C_6 alkyl, and the nitrogen atom together with each R^5 form a ring;

R^6, in each instance in which it appears, is independently selected from the group consisting of

1) hydrogen,

2) unsubstituted or substituted C_1-C_6 alkyl,

3) halogen,

4) OR^5,

5) CF_3,

6) unsubstituted or substituted aryl,

7) unsubstituted or substituted C_3-C_{10} cycloalkyl,

8) unsubstituted or substituted heterocycle,

9) $S(O)_mN(R^5)_2$,

10) $C(O)OR^5$,

11) $C(O)R^5$,

12) CN,

13) $C(O)N(R^5)_2$,

14) $N(R^5)C(O)R^5$,

15) $N(R^5)C(O)OR^5$,

16) $N(R^5)C(O)N(R^5)_2$,

17) $OC(O)N(R^5)_2$,

18) $S(O)_mR^5$,

19) $OS(O)_mR^5$,

20) NO_2, and

21) $N(R^5)_2$;

R^7 is independently selected from the group consisting of

1) $S(O)_mN(R^5)_2$,

2) $C(O)OR^5$,

3) $C(O)R^5$,

4) $C(O)N(R^5)_2$, and

5) $S(O)_mR^5$;

m is independently 0, 1 or 2;

n is independently 0, 1, 2, 3, 4, 5 or 6;

u is 0, 1 or 2; and

v is 0, 1 or 2.

An embodiment of the invention is a compound wherein

B is a heteroaryl ring, wherein the point of attachment to the heteroaryl ring is a carbon atom, and wherein the heteroaryl ring is selected from the group consisting of pyridine and pyrimidine, wherein the heteroaryl ring is unsubstituted, mono-substituted with R^4, disubstituted with groups independently selected from R^4, trisubstituted with groups independently selected from R^4, or tetrasubstituted with groups independently selected from R^4, and wherein the N heteroaryl ring atom is unsubstituted or substituted with oxo; and

X is selected from the group consisting of hydrogen, OH, OCH_3 and F.

A preferred embodiment of the invention is a compound wherein

A is selected from the group consisting of

1) a phenyl ring,

2) a pyridyl ring, wherein the point of attachment to the pyridyl ring is a carbon atom, and

3) C_1-C_{10} alkyl, wherein any stable atom is independently unsubstituted or substituted with a group selected from R^4,

wherein the phenyl ring and pyridyl ring are unsubstituted, mono-substituted with R^4, disubstituted with groups independently selected from R^4, trisubstituted with groups independently selected from R^4, or tetrasubstituted with groups independently selected from R^4, and wherein the N pyridyl ring atom is unsubstituted or substituted with oxo; and

C is selected from the group consisting of

1) an aryl ring, wherein any stable aryl ring atom is independently unsubstituted or substituted with a group selected from R^4,

2) a heteroaryl ring, wherein the point of attachment to the heteroaryl ring is a carbon atom, and the heteroaryl ring is selected from the group consisting of:

a) a 5-membered unsaturated monocyclic ring with 1, 2, or 3 heteroatom ring atoms selected from the group consisting of N, O or S,

b) pyridine, and

c) an 8-, 9- or 10-membered unsaturated bicyclic ring with 1 or 2 heteroatom ring atoms selected from the group consisting of N, O or S;

3) a cyclopropyl ring, wherein any stable ring atom is independently unsubstituted or substituted with a group selected from R^4,

4) a 4-6 membered saturated heterocyclic ring with 1 or 2 heteroatom ring atoms selected from the group consisting of N and O, wherein any stable ring atom is independently unsubstituted or substituted with a group selected from R^4, and

5) C_1-C_6 alkyl, wherein any stable atom is independently unsubstituted or substituted with a group selected from R^4.

A more preferred embodiment of the invention is a compound wherein

B is a pyridyl ring, wherein the point of attachment to the pyridyl ring is a carbon atom, and wherein the pyridyl ring is unsubstituted, mono-substituted with R^4, disubstituted with groups independently selected from R^4, trisubstituted with groups independently selected from R^4, or tetrasubstituted with groups independently selected from R^4, and wherein the N atom is unsubstituted or substituted with oxo;

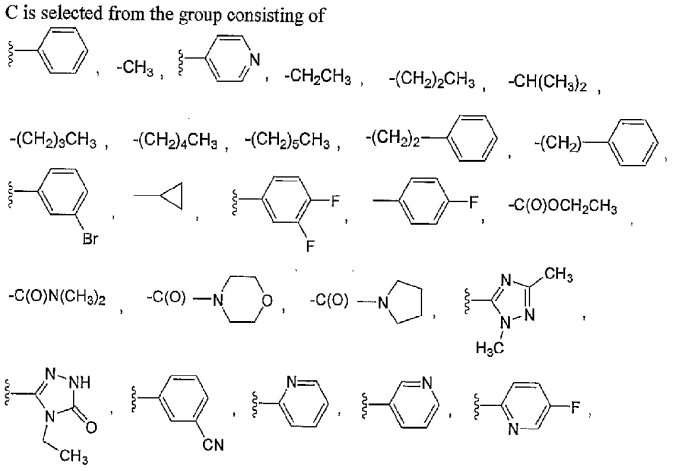
X is selected from the group consisting of hydrogen, OH, OCH_3 and F;

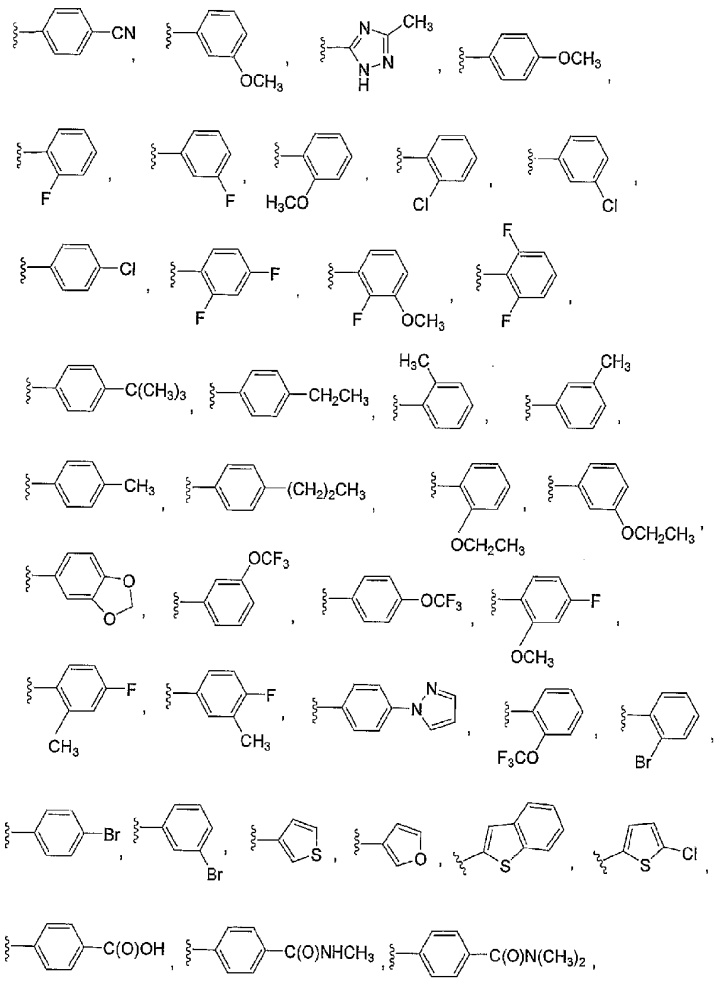
A is selected from the group consisting of

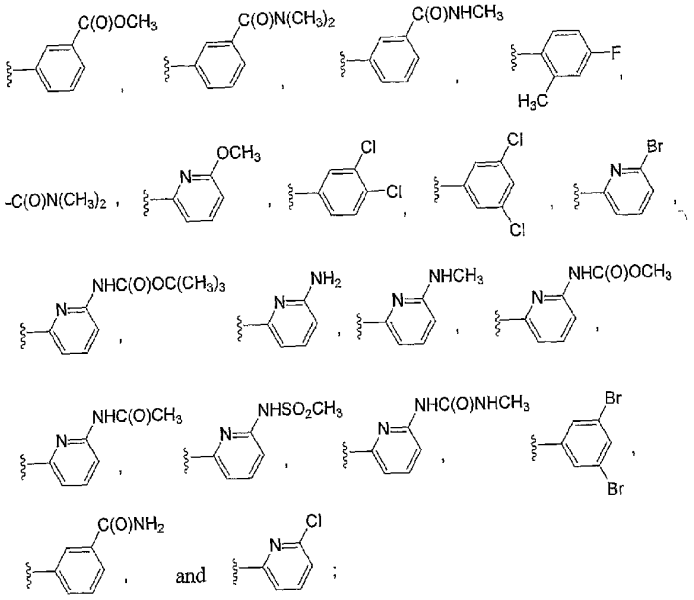
1) a phenyl ring,
2) a pyridyl ring, wherein the point of attachment to the pyridyl ring is a carbon atom, and
3) $-C(CH_3)_3$,

wherein the phenyl ring and pyridyl ring are unsubstituted, mono-substituted with R^4, disubstituted with groups independently selected from R^4, trisubstituted with groups independently selected from R^4, or tetrasubstituted with groups independently selected from R^4, and wherein the N pyridyl ring atom is unsubstituted or substituted with oxo;

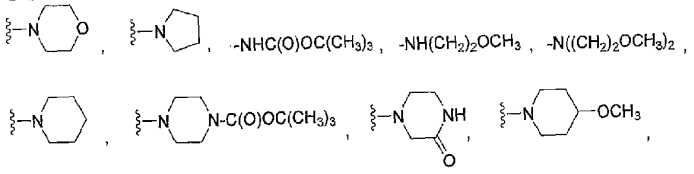
C is selected from the group consisting of

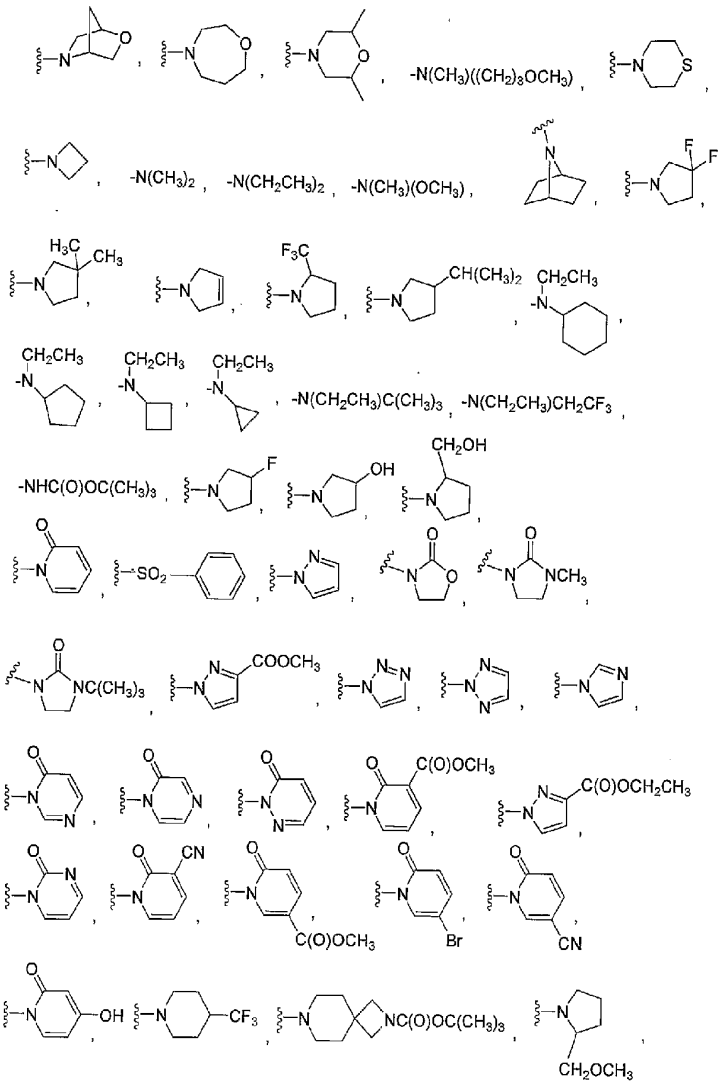


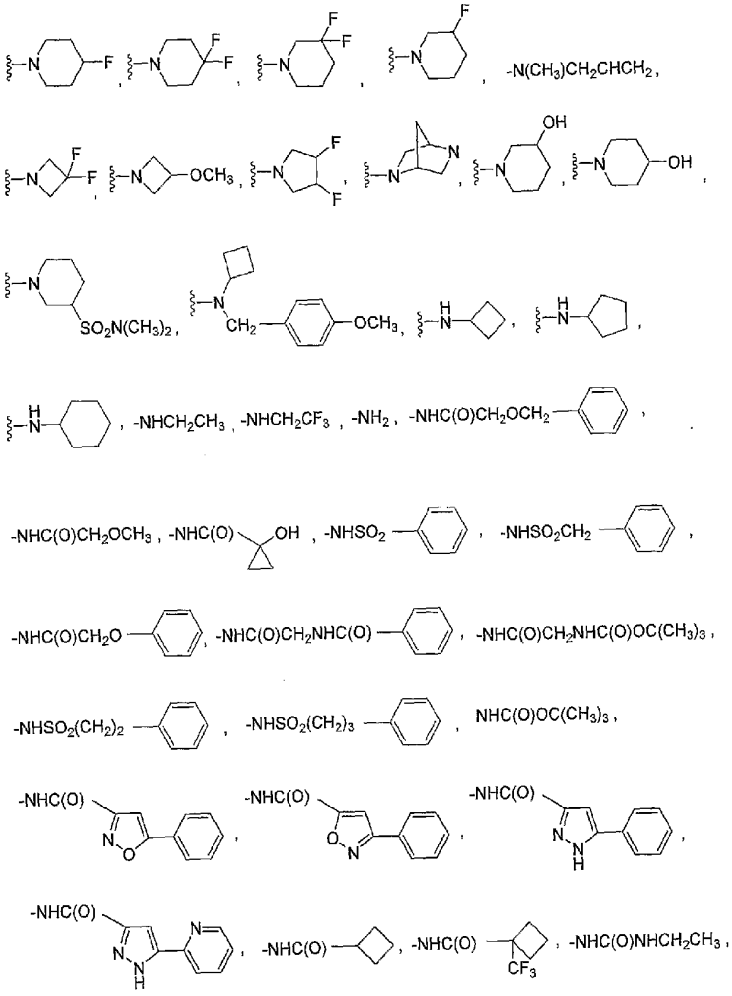




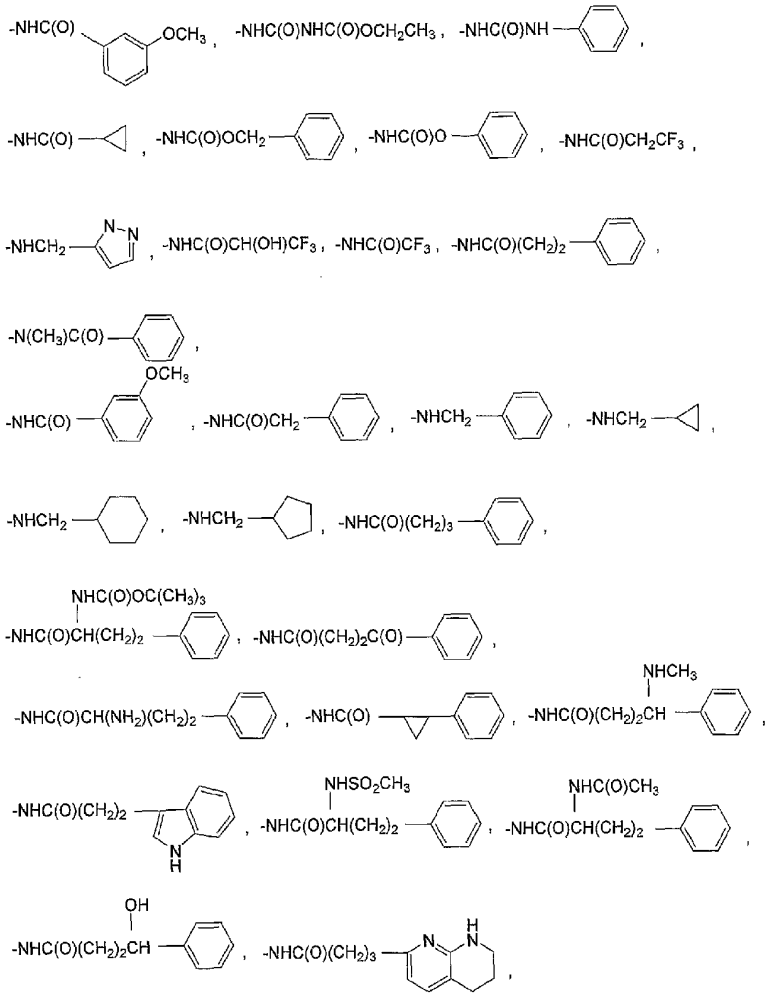
Y is selected from the group consisting of

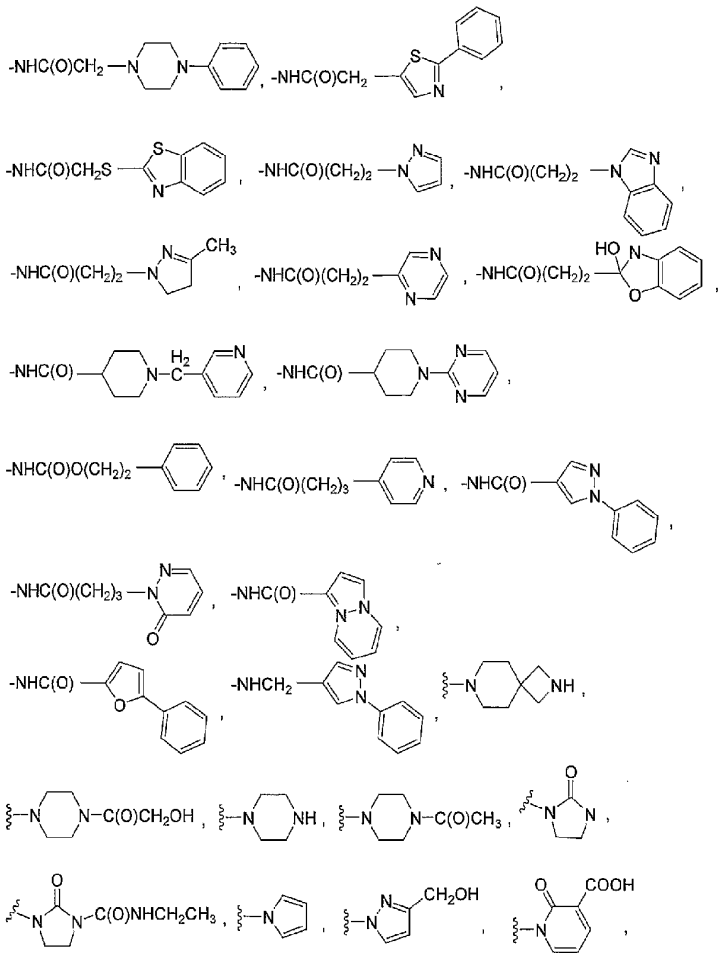


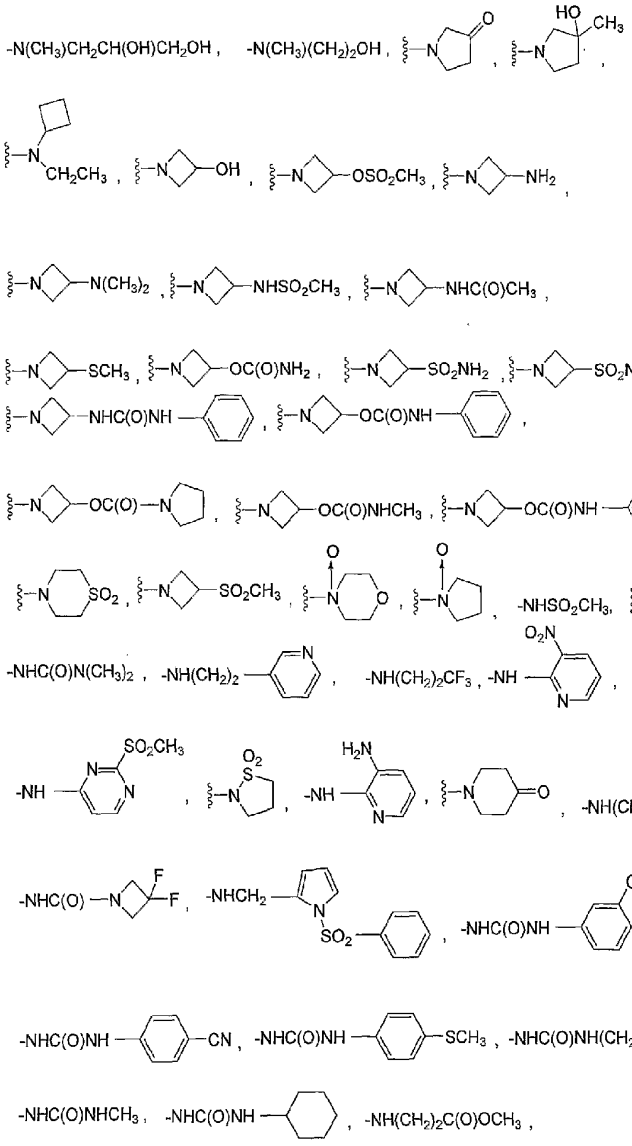

-N(CH3)((CH2)8OCH3)
-N(CH3)2
-N(CH2CH3)2
-N(CH3)(OCH3)
-N(CH2CH3)C(CH3)3
-N(CH2CH3)CH2CF3
-NHC(O)OC(CH3)3
C(O)OCH3
C(O)OCH2CH3
CN
Br
OH
CF3
NC(O)OC(CH3)3
CH2OCH3


-N(CH3)CH2CHCH2,
OCH3,
OH
SO2N(CH3)2,
CH2
OCH3,
-NHCH2CH3,
-NHCH2CF3,
-NH2,
-NHC(O)CH2OCH2
-NHC(O)CH2OCH3,
-NHC(O)
OH
-NHSO2
-NHSO2CH2
-NHC(O)CH2O
-NHC(O)CH2NHC(O)
-NHC(O)CH2NHC(O)OC(CH3)3,
-NHSO2(CH2)2
-NHSO2(CH2)3
NHC(O)OC(CH3)3,
-NHC(O)
-NHC(O)
-NHC(O)
-NHC(O)
-NHC(O)
-NHC(O)
CF3
-NHC(O)NHCH2CH3,

5


-NHC(O)
OCH3
-NHC(O)NHC(O)OCH2CH3
-NHC(O)NH
-NHC(O)
-NHC(O)OCH2
-NHC(O)O
-NHC(O)CH2CF3
-NHCH2
N
N
-NHC(O)CH(OH)CF3
-NHC(O)CF3
-NHC(O)(CH2)2
-N(CH3)C(O)
OCH3
-NHC(O)
-NHC(O)CH2
-NHCH2
-NHCH2
-NHCH2
-NHC(O)(CH2)3
NHC(O)OC(CH3)3
-NHC(O)CH(CH2)2
-NHC(O)(CH2)2C(O)
-NHC(O)CH(NH2)(CH2)2
-NHC(O)
NHCH3
-NHC(O)(CH2)2CH
-NHC(O)(CH2)2
N
H
NHSO2CH3
-NHC(O)CH(CH2)2
NHC(O)CH3
-NHC(O)CH(CH2)2
OH
-NHC(O)(CH2)2CH
-NHC(O)(CH2)3
N
H





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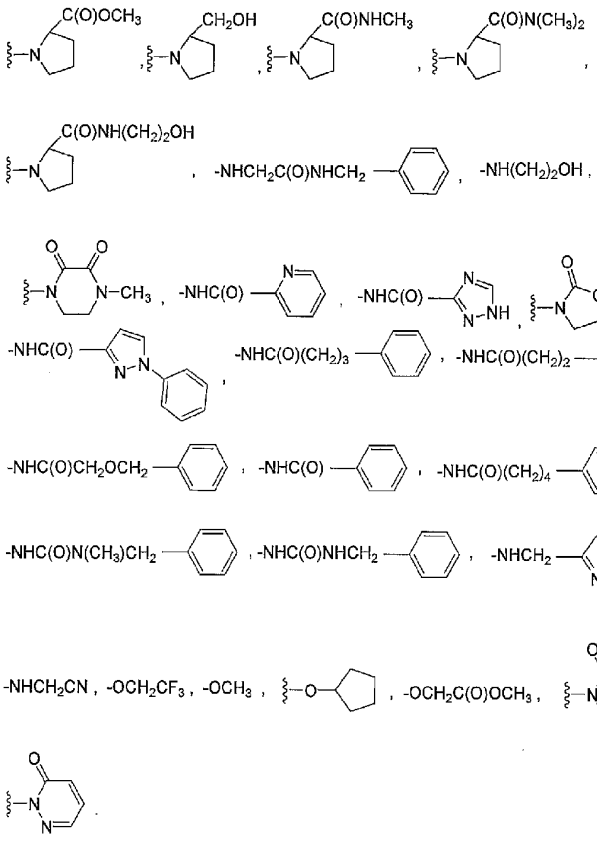


An example of a compound of the invention is a compound selected from the group consisting of

(±)-2-Morpholin-4-*yl*-2-phenyl-1,1-dipyridin-3-*yl*-ethanol,
(±)-3-methyl-2-morpholin-4-yl-1,1-dipyridin-3-ylbutan-1-ol,
(±)-2-[(2-methoxyethyl)(methyl)amino]-2-phenyl-1,1-dipyridin-3-ylethanol,
(±)-2-phenyl-2-piperidin-1-yl-1,1-dipyridin-3-ylethanol,
(±)-2-phenyl-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol,
(±)-*tert*-butyl 4-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)piperazine-1-carboxylate,
2-[(1*S*,4*S*)-2-oxa-5-azabicyclo[2.2.1]hept-5-yl]-2-phenyl-1,1-dipyridin-3-ylethanol,
(±)-2-(1,4-oxazepan-4-yl)-2-phenyl-1,1-dipyridin-3-ylethanol,
(±)-2-phenyl-1,1-dipyridin-3-yl-2-thiomorpholin-4-ylethanol,
(±)-2-(diethylamino)-2-phenyl-1,1-dipyridin-3-ylethanol,
(±)-2-(7-azabicyclo[2.2.1]hept-7-yl)-2-phenyl-1,1-dipyridin-3-ylethanol,

(±)-2-(3,3-difluoropyrrolidin-1-yl)-2-phenyl-1,1-dipyridin-3-ylethanol,
(±)-2-phenyl-1,1-dipyridin-3-yl-2-[2-(trifluoromethyl)pyrrolidin-1-yl]ethanol,
(±)-2-(2-isopropylpyrrolidin-1-yl)-2-phenyl-1,1-dipyridin-3-ylethanol,
(2*R*)-2-cyclopropyl-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol,
(±)-2-[cyclobutyl(ethyl)amino]-2-phenyl-1,1-dipyridin-3-ylethanol,
(±)-2-[ethyl(2,2,2-trifluoroethyl)amino]-2-phenyl-1,1-dipyridin-3-ylethanol,
(±)-2-(3-fluoropyrrolidin-1-yl)-2-phenyl-1,1-dipyridin-3-ylethanol,
(±)-2-morpholin-4-*yl*-1,2-diphenyl-1-pyridin-2-*yl*-ethanol,
2-morpholin-4-yl-2-phenyl-1-pyridin-2-yl-1-pyridin-3-ylethanol,
(±)-2-phenyl-2-(phenylsulfonyl)-1,1-dipyridin-3-ylethanol,
(±)-2-(1,3-dimethyl-1*H*-1,2,4-triazol-5-yl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol,
(±)-1,2-diphenyl-2-(1*H*-pyrazol-1-yl)-1-pyridin-4-ylethanol,
(±)-3-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)-1,3-oxazolidin-2-one,
(±)-3-[2-hydroxy-1-(2-oxo-1,3-oxazolidin-3-yl)-2,2-dipyridin-3-ylethyl]benzonitrile,
(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-3-methylimidazolidin-2-one,
(±)-1-*tert*-butyl-3-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]imidazolidin-2-one,
(±)-3-(2-hydroxy-1-pyridin-2-yl-2,2-dipyridin-3-ylethyl)-1,3-oxazolidin-2-one,
(±)-2-(1*H*-pyrazol-1-yl)-2-pyridin-2-yl-1,1-dipyridin-3-ylethanol,
(±)-2-(1*H*-pyrazol-1-yl)-1,1,2-tripyridin-3-ylethanol,
(±)-1,1,2-tripyridin-3-yl-2-(1H-1,2,3-triazol-1-yl)ethanol,
(±)-4-[2-hydroxy-2,2-dipyridin-3-yl-1-(2H-1,2,3-triazol-2-yl)ethyl]benzonitrile,
(±)-3-[2-hydroxy-2,2-dipyridin-3-yl-1-(1H-1,2,3-triazol-1-yl)ethyl]benzonitrile,
(±)-(1-benzyl-1H-pyrazol-5-yl)(dipyridin-3-yl)methanol,
(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]pyridin-2(1H)-one,
(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]pyrazin-2(1H)-one,
(±)-2-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]pyridazin-3(2H)-one,
(*R*)-1-(2-hydroxy-1-pyridin-2-yl-2,2-dipyridin-3-ylethyl)pyridin-2(1H)-one,
(*S*)-1-(2-hydroxy-1-pyridin-2-yl-2,2-dipyridin-3-ylethyl)pyridin-2(1H)-one,
(±)-3-(2-hydroxy-2,2-dipyridin-3-yl-1-pyrrolidin-1-ylethyl)benzonitrile,
(±)-2-(4-fluorophenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol,
(±)-2-(3-methoxyphenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol,
2-[(2r)-2-(methoxymethyl)pyrrolidin-1-yl]-2-phenyl-1,1-dipyridin-3-ylethanol,
(±)-2-(3-bromophenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol,
(±)-2-(3,3-difluoroazetidin-1-yl)-2-(4-fluorophenyl)-1,1-dipyridin-3-ylethanol,
(±)-2-(5-chloro-2-thienyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol,
2-[(3*R*,4*R*)-3,4-difluoropyrrolidin-1-yl]-2-phenyl-1,1-dipyridin-3-ylethanol,
(±)-1-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)piperidin-3-ol,
2-(4-fluorophenyl)-2-[(2*S*)-2-(hydroxymethyl)pyrrolidin-1-yl]-1,1-dipyridin-3-ylethanol,

(±)-2-(cyclobutylamino)-2-(4-fluorophenyl)-1,1-dipyridin-3-ylethanol,
(±)-2-phenyl-1,1-dipyridin-3-yl-2-[(2,2,2-trifluoroethyl)-amino]ethanol,
2-(benzyloxy)-N-[(1*R*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]acetamide,
N-[(1*R*)-1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-3-pyridin-2-yl-1H-pyrazole-5-carboxamide,
N-[(1*R*)-1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-4-phenylbutanamide,
benzyl [(1*R*)-1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]carbamate,
N-[(1*R*)-1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-1-phenyl-1H-pyrazole-4-carboxamide,
(±)-2-phenyl-1,1-dipyridin-3-yl-2-(1*H*-pyrrol-1-yl)ethanol,
(±)-3-(2-hydroxy-1-morpholin-4-yl-2,2-dipyridin-3-ylethyl)benzonitrile,
(±)-3,3'-(1-fluoro-2-phenyl-2-pyrrolidin-1-ylethane-1,1-diyl)dipyridine,
(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]azetidin-3-ol,
(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]azetidin-3-yl phenylcarbamate,
(±)-2-(3,3-difluoroazetidin-1-yl)-2-(4-fluorophenyl)-1-(1-oxidopyridin-3-yl)-1-pyridin-3-ylethanol,
(±)-4-[1-(6-methoxypyridin-2-yl)-2,2-dipyridin-3-ylethyl]morpholine,
(±)-*N*-[1-(4-fluorophenyl)-2-phenyl-2-pyridin-3-ylethyl]-2-methoxyacetamide,
(±)-4-[1-(4-fluorophenyl)-2-phenyl-2-pyridin-3-ylethyl]morpholine,
(±)-1-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl]pyrrolidin-2-one,
(±)-4-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl]morpholine,
(±)-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl](2,2,2-trifluoroethyl)amine,
(±)-4-[1-(3,4-dichlorophenyl)-2,2-dipyridin-3-ylethyl]morpholine,
(±)-4-(1-pyridin-2-yl-2,2-dipyridin-3-ylethyl)morpholine,
(±)-3,3'-[2-(4-fluorophenyl)-2-pyrrolidin-1-ylethane-1,1-diyl]dipyridine,
(±)-4-[1-(4-fluorophenyl)-2-pyridin-2-yl-2-pyridin-3-ylethyl]morpholine,
(±)-4-[1-(3-chlorophenyl)-2,2-dipyridin-3-ylethyl]morpholine,
(±)-4-[1-(3,5-dichlorophenyl)-2,2-dipyridin-3-ylethyl]morpholine,
(±)-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl](3,3,3-trifluoropropyl)amine,
(±)-[1-(3-chlorophenyl)-2,2-dipyridin-3-ylethyl](2,2,2-trifluoroethyl)amine,
(±)-[1-(3,5-dichlorophenyl)-2,2-dipyridin-3-ylethyl](2,2,2-trifluoroethyl)amine,
(±)-[1-(3,4-dichlorophenyl)-2,2-dipyridin-3-ylethyl](2,2,2-trifluoroethyl)amine,
(±)-3,3'-[2-(1,1-dioxidoisothiazolidin-2-yl)-2-(4-fluorophenyl)ethane-1,1-diyl]dipyridine,
(±)-4-[1-(6-methoxypyridin-2-yl)-2-phenyl-2-pyridin-2-ylethyl]morpholine,
(±)-4-[1-(6-bromopyridin-2-yl)-2,2-dipyridin-3-ylethyl]morpholine,
(±)-6-(1-morpholin-4-yl-2,2-dipyridin-3-ylethyl)pyridin-2-amine,
(±)-N-methyl-6-(1-morpholin-4-yl-2,2-dipyridin-3-ylethyl)pyridin-2-amine,
(±)-methyl [6-(1-morpholin-4-yl-2,2-dipyridin-3-ylethyl)pyridin-2-yl]carbamate,
(±)-[1-(3-bromophenyl)-2,2-dipyridin-3-ylethyl]{[1-(phenylsulfonyl)-1H-pyrrol-2-yl]methyl}amine,

(±)-methyl 1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]prolinate,
(±)-3-{1-[2-(hydroxymethyl)pyrrolidin-1-yl]-2,2-dipyridin-3-ylethyl}benzonitrile,
(±)-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-*N,N*-dimethylprolinamide,
(±)-1-[1-(3-bromophenyl)-2,2-dipyridin-3-ylethyl]-4-methylpiperazine-2,3-dione,
(±)-3-[1-(6-bromopyridin-2-yl)-2,2-dipyridin-3-ylethyl]-1,3-oxazolidin-2-one,
(±)-3-[1-(2-oxo-1,3-oxazolidin-3-yl)-2,2-dipyridin-3-ylethyl]benzonitrile,
(±)-benzyl (1,2,2-tripyridin-3-ylethyl)carbamate,
(±)-n-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-2-phenylcyclopropanecarboxamide,
(±)-3-(1-{[(1-phenyl-1h-pyrazol-4-yl)methyl]amino}-2,2-dipyridin-3-ylethyl)benzonitrile,
(*R*)-3-(1-morpholin-4-yl-2,2-dipyridin-3-ylethyl)benzonitrile,
(*S*)-3-(1-morpholin-4-yl-2,2-dipyridin-3-ylethyl)benzonitrile,
(±)-3-[2-(4-fluorophenyl)-1-pyridin-3-yl-2-(2,2,2-trifluoroethoxy)ethyl]pyridine,
(±)-3-[2-(4-fluorophenyl)-2-methoxy-1-pyridin-3-ylethyl]pyridine,
(±)-3-[2-(cyclopentyloxy)-2-(4-fluorophenyl)-1-pyridin-3-ylethyl]pyridine,
(±)-1-[1-(6-chloropyridin-2-yl)-2,2-dipyridin-3-ylethyl]pyridin-2(1*H*)-one,
(±)-1-(1-pyridin-2-yl-2,2-dipyridin-3-ylethyl)pyridin-2(1*H*)-one,
(*R*)-1-(1-pyridin-2-yl-2,2-dipyridin-3-ylethyl)pyridin-2(1*H*)-one,
(*S*)-1-(1-pyridin-2-yl-2,2-dipyridin-3-ylethyl)pyridin-2(1*H*)-one,
(±)-2-[1-(1H-pyrazol-1-yl)-2,2-dipyridin-3-ylethyl]pyridine,
(±)-2-[2-(4-fluorophenyl)-1-(1*H*-pyrazol-1-yl)-2-pyridin-3-ylethyl]pyridine,
(±)-2-[2-(4-fluorophenyl)-1-(1*H*-pyrazol-1-yl)-2-pyridin-3-ylethyl]pyridine,
(±)-2-[1-(4-fluorophenyl)-2-(1*H*-imidazol-1-yl)-2-pyridin-3-ylethyl]pyridine,
(±)-1-(1,2,2-tripyridin-3-ylethyl)pyridin-2(1*H*)-one,
(±)-2-[2,2-dipyridin-3-yl-1-(1H-1,2,3-triazol-1-yl)ethyl]pyridine,
(±)-3-[2,2-dipyridin-3-yl-1-(1H-1,2,3-triazol-1-yl)ethyl]benzonitrile, and
(±)-1-[1(2*H*)-yl)-2,2-dipyridin-3-ylethyl]pyridin-2(1*H*)-one.

The above-listed compounds are active in one or more of the assays for Kv1.5 described below.

Another embodiment of the invention is a method of treating or preventing a condition in a mammal, the treatment or prevention of which is effected or facilitated by $K_v1.5$ inhibition, which comprises administering an amount of a compound of Formula I that is effective at inhibiting $K_v1.5$.

A preferred embodiment is a method of treating or preventing cardiac arrhythmias, e.g. atrial fibrillation, atrial flutter, atrial arrhythmia, and supraventricular tachycardia, in a mammal, which comprises administering a therapeutically effective amount of a compound of Formula I.

Another preferred embodiment is a method of preventing thromboembolic events, such as stroke.

Another preferred embodiment is a method of preventing congestive heart failure.

Another preferred embodiment is a method of treating or preventing immunodepression or a disorder involving immunodepression, such as AIDS, cancer, senile dementia, trauma (including wound healing, surgery and shock) chronic bacterial infection, certain central nervous system disorders, and conditions including resistance by transplantation of organs or tissue, graft-versus-host diseases brought about by medulla ossium transplantation. Within this embodiment is a method for treating or preventing immunodepression by administering a compound of the invention with an immunosuppresant compound.

Another preferred embodiment is a method of treating or preventing gliomas including those of lower and higher malignancy, preferably those of higher malignancy.

Another preferred embodiment is a method for inducing in a patient having atrial fibrillation, a condition of normal sinus rhythm, in which the induced rhythm corresponds to the rhythm that would be considered normal for an individual sharing with the patient similar size and age characteristics, which comprises treating the patient with a compound of the invention.

Another preferred embodiment is a method for treating tachycardia, (i.e., rapid heart rate e.g. 100 beats per minute) in a patient which comprises treating the patient with an antitachycardia device (e.g. a defibrillator or a pacemaker) in combination with a compound of Claim 1.

The present invention also encompasses a pharmaceutical formulation comprising a pharmaceutically acceptable carrier and the compound of Formula I or a pharmaceutically acceptable crystal form or hydrate thereof. A preferred embodiment is a pharmaceutical composition of the compound of Formula I, comprising, in addition, a second agent.

The compounds of the present invention may have asymmetric centers or asymmetric axes, and this invention includes all of the optical isomers and mixtures thereof. Unless specifically mentioned otherwise, reference to one isomer applies to any of the possible isomers. Whenerevr the isomeric composition is unspecified, all possible isomers are included.

In addition compounds with carbon-carbon double bonds may occur in Z- and E- forms with all isomeric forms of the compounds being included in the present invention.

List of abbreviations:

AAS	atomic absorption spectroscopy
AIDS	acquired immunodeficiency syndrome
AF	atrial fibrillation
ACE	angiotensin converting enzyme
ACN	acetonitrile
APD	action potential duration
CHO	Chinese hamster ovary
DAST	(diethylamino)sulfur trifluoride
DCM	dichloromethane
dba	dibenzylidineacetone

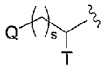
DMA	dimethylacetamide
DMF	dimethylformamide
DMSO	dimethylsulfoxide
dppf	1,1'-(diphenylphosphino)ferrocene
EDTA	ethylenediaminetetraacetic acid
EGTA	ethylenebis(oxyethylenenitrilo)tetraacetic acid
ESI	electrospray ionization
EtOAc	ethyl acetate
Et_2O	diethyl ether
FAAS	flame atomic absorption spetroscopy
FBS	fetal bovine serum
HBSS	Hank's balanced salt solution
HEPES	N-2-hydroxyethylpiperazine-N'-2-ethanesulphonic acid
HPLC	high pressure liquid chromatography
HRMS	high resolution mass spectrum
i-BuOH	isobutanol
i-Pr2Net	*N,N*-diisopropylethylamine
INH	inhibition
LDA	lithium diisopropylamide
LiHMDS	lithium hexamethyldisilazide
LRMS	low resolution mass spectrum
LYS	lysate
MCPBA	*m*-chloroperbenzoic acid
MeOH	methanol
MS	mass spectrum
MsCl	methanesulfonyl chloride
n-BuLi	*n*-butyllithium
NMO	*N*-methylmorpholine-*N*-oxide
NMR	nuclear magnetic resonance
NSAID	non-steroidal antiinflammatory drug
PBS	phosphate-buffered saline
RT	room temperature
SUP	supernatant
TAFI	thrombin-activatable fibrinolysis inhibitor
TFA	trifluoroacetic acid
THF	tetrahydrofuran
$TMSCHN_2$	trimethylsilyldiazomethane
TPAP	tetrapropylammonium perruthenate

As used herein except where noted, "alkyl" is intended to include both branched- and straight-chain saturated aliphatic hydrocarbon groups, including all isomers, having the specified number of carbon atoms. Commonly used abbreviations for alkyl groups are used throughout the specification, e.g. methyl may be represented by "Me" or CH_3, ethyl may be represented by "Et" or CH_2CH_3, propyl may be represented by "Pr" or $CH_2CH_2CH_3$, butyl may be represented by "Bu" or $CH_2CH_2CH_2CH_3$, etc. "C_{1-6} alkyl" (or "C_1-C_6 alkyl") for example, means linear or branched chain alkyl groups, including all isomers, having the specified number of carbon atoms. C_{1-6} alkyl includes all of the hexyl alkyl and pentyl alkyl isomers as well as n-, iso-, sec- and t-butyl, n- and isopropyl, ethyl and methyl. "C_{1-4} alkyl" means n-, iso-, sec- and t-butyl, n- and isopropyl, ethyl and methyl. The term "alkoxy" represents a linear or branched alkyl group of indicated number of carbon atoms attached through an oxygen bridge.

The term "alkenyl" includes both branched and straight chain unsaturated hydrocarbon groups containing at least two carbon atoms joined by a double bond. The alkene ethylene is represented, for example, by "CH_2CH_2" or alternatively, by "$H_2C{=}CH_2$". "C_{2-5} alkenyl" (or "C_2-C_5 alkenyl") for example, means linear or branched chain alkenyl groups having from 2 to 5 carbon atoms and includes all of the pentenyl isomers as well as 1-butenyl, 2-butenyl, 3-butenyl, 1-propenyl, 2-propenyl, and ethenyl (or ethylenyl). Similar terms such as "C_{2-3} alkenyl" have an analogous meaning.

The term "alkynyl" includes both branched and straight chain unsaturated hydrocarbon groups containing at least two carbon atoms joined by a triple bond. The alkyne acetlycne is represented, for example, by "CHCH" or alternatively, by "HC≡CH". "C_{2-5} alkynyl" (or "C_2-C_5 alkynyl") for example, means linear or branched chain alkynyl groups having from 2 to 5 carbon atoms and includes all of the pentynyl isomers as well as 1-butynyl, 2-butynyl, 3-butynyl, 1-propynyl, 2-propynyl, and ethynyl (or acetylenyl). Similar terms such as "C_{2-3} alkynyl" have an analogous meaning.

Unless otherwise specifically noted as only "unsubstituted" or only "substituted", alkyl, alkenyl and alkynyl groups are unsubstituted or substituted with 1 to 3 substituents on each carbon atom, with halo, C_1-C_{20} alkyl, CF_3, NH_2, $N(C_1$-C_6 alkyl$)_2$, NO_2, oxo, CN, N_3, -OH, -O(C_1-C_6 alkyl), C_3-C_{10} cycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, (C_0-C_6 alkyl) S(O)$_{0-2}$-, (C_0-C_6 alkyl)S(O)$_{0-2}$(C_0-C_6 alkyl)-, (C_0-C_6 alkyl)C(O)NH-, H_2N-C(NH)-, -O(C_1-C_6 alkyl)CF_3, (C_0-C_6 alkyl)C(O)-, (C_0-C_6 alkyl)OC(O)-, (C_0-C_6 alkyl)O(C_1-C_6 alkyl)-, (C_0-C_6 alkyl)C(O)$_{1-2}$(C_0-C_6 alkyl)-, (C_0-C_6 alkyl)OC(O)NH-, aryl, aralkyl, heterocycle, heterocyclylalkyl, halo-aryl, halo-aralkyl, halo-heterocycle, halo-heterocyclylalkyl, cyano-aryl, cyano-aralkyl, cyano-heterocycle and cyano-heterocyclylalkyl.

The term "C_0" as employed in expressions such as "C_{0-6} alkyl" means a direct covalent bond. Similarly, when an integer defining the presence of a certain number of atoms in a group is equal to zero, it means that the atoms adjacent thereto are connected directly by a bond. For example, in the structure  , wherein s is an integer equal to zero, 1 or 2, the structure is  when s is zero.

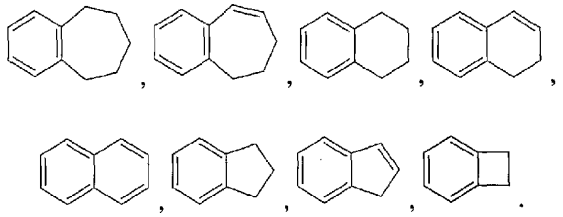
The term "C_{3-8} cycloalkyl" (or "C_3-C_8 cycloalkyl") means a cyclic ring of an alkane having three to eight total carbon atoms (i.e., cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl,

cycloheptyl, or cyclooctyl). The terms "C3-7 cycloalkyl", "C3-6 cycloalkyl", "C5-7 cycloalkyl" and the like have analogous meanings.

The term "halogen" (or "halo") refers to fluorine, chlorine, bromine and iodine (alternatively referred to as fluoro (F), chloro (Cl), bromo (Br), and iodo (I)).

The term "C_{1-6} haloalkyl" (which may alternatively be referred to as "C_1-C_6 haloalkyl" or "halogenated C_1-C_6 alkyl") means a C_1 to C_6 linear or branched alkyl group as defined above with one or more halogen substituents. The term "C_{1-4} haloalkyl" has an analogous meaning. The term "C_{1-6} fluoroalkyl" has an analogous meaning except that the halogen substituents are restricted to fluoro. Suitable fluoroalkyls include the series $(CH_2)_{0-4}CF_3$ (i.e., trifluoromethyl, 2,2,2-trifluoroethyl, 3,3,3-trifluoro-n-propyl, etc.).

The term "carbocycle" (and variations thereof such as "carbocyclic" or "carbocyclyl") as used herein, unless otherwise indicated, refers to (i) a C_3 to C_8 monocyclic, saturated or unsaturated ring or (ii) a C_7 to C_{12} bicyclic saturated or unsaturated ring system. Each ring in (ii) is either independent of, or fused to, the other ring, and each ring is saturated or unsaturated. The carbocycle may be attached to the rest of the molecule at any carbon atom which results in a stable compound. The fused bicyclic carbocycles are a subset of the carbocycles; i.e., the term "fused bicyclic carbocycle" generally refers to a C_7 to C_{10} bicyclic ring system in which each ring is saturated or unsaturated and two adjacent carbon atoms are shared by each of the rings in the ring system. A fused bicyclic carbocycle in which one ring is saturated and the other is saturated is a saturated bicyclic ring system. A fused bicyclic carbocycle in which one ring is benzene and the other is saturated is an unsaturated bicyclic ring system. A fused bicyclic carbocycle in which one ring is benzene and the other is unsaturated is an unsaturated ring system. Saturated carbocyclic rings are also referred to as cycloalkyl rings, e.g., cyclopropyl, cyclobutyl, etc. Unless otherwise noted, carbocycle is unsubstituted or substituted with C_{1-6} alkyl, C_{1-6} alkenyl, C_{1-6} alkynyl, aryl, halogen, NH_2 or OH. A subset of the fused bicyclic unsaturated carbocycles are those bicyclic carbocycles in which one ring is a benzene ring and the other ring is saturated or unsaturated, with attachment via any carbon atom that results in a stable compound. Representative examples of this subset include the following:



The term "aryl" refers to aromatic mono- and poly-carbocyclic ring systems, wherein the individual carbocyclic rings in the polyring systems are fused or attached to each other via a single bond. Suitable aryl groups include phenyl, naphthyl, and biphenylenyl.

The term "heterocycle" (and variations thereof such as "heterocyclic" or "heterocyclyl") broadly refers to (i) a stable 4- to 8-membered, saturated or unsaturated monocyclic ring, or (ii) a stable 7- to 12-membered bicyclic ring system, wherein each ring in (ii) is independent of, or fused to, the other ring or rings and each ring is saturated or unsaturated, and the monocyclic ring or bicyclic ring system contains one or more heteroatoms (e.g., from 1 to 6 heteroatoms, or from 1 to 4 heteroatoms) selected from N, O and S and a balance of carbon atoms (the monocyclic ring typically contains at least one carbon atom and the ring systems typically contain at least two carbon atoms); and wherein any one or more of the nitrogen and sulfur heteroatoms is optionally oxidized, and any one or more of the nitrogen heteroatoms is optionally quaternized. The heterocyclic ring may be attached at any heteroatom or carbon atom, provided that attachment results in the creation of a stable structure. When the heterocyclic ring has substituents, it is understood that the substituents may be attached to any atom in the ring, whether a heteroatom or a carbon atom, provided that a stable chemical structure results.

Unless otherwise specifically noted as only "unsubstituted" or only "substituted", cycloalkyl, aryl and heterocycle groups are unsubstituted or substituted. As used herein, the terms "substituted C_3-C_{10} cycloalkyl", "substituted aryl" and "substituted heterocycle" are intended to include the cyclic group containing from 1 to 3 substituents in addition to the point of attachment to the rest of the compound. Preferably, the substituents are selected from the group which includes, but is not limited to, halo, C_1-C_{20} alkyl, CF_3, NH_2, $N(C_1$-C_6 alkyl$)_2$, NO_2, oxo, CN, N_3, -OH, -O(C_1-C_6 alkyl), C_3-C_{10} cycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, (C_0-C_6 alkyl) S(O)$_{0\text{-}2}$-, aryl-S(O)$_{0\text{-}2}$-, (C_0-C_6 alkyl)S(O)$_{0\text{-}2}$(C_0-C_6 alkyl)-, (C_0-C_6 alkyl)C(O)NH-, H_2N-C(NH)-, -O(C_1-C_6 alkyl)CF_3, (C_0-C_6 alkyl)C(O)-, (C_0-C_6 alkyl)OC(O)-, (C_0-C_6alkyl)O(C_1-C_6 alkyl)-, (C_0-C_6 alkyl)C(O)$_{1\text{-}2}$(C_0-C_6 alkyl)-, (C_0-C_6 alkyl)OC(O)NH-, aryl, aralkyl, heteroaryl, heterocyclylalkyl, halo-aryl, halo-aralkyl, halo-heterocycle, halo-heterocyclylalkyl, cyano-aryl, cyano-aralkyl, cyano-heterocycle and cyano-heterocyclylalkyl.

Saturated heterocyclics form a subset of the heterocycles; i.e., the term "saturated heterocyclic" generally refers to a heterocycle as defined above in which the entire ring system (whether mono- or poly-cyclic) is saturated. The term "saturated heterocyclic ring" refers to a 4- to 8-membered saturated monocyclic ring or a stable 7- to 12-membered bicyclic ring system which consists of carbon atoms and one or more heteroatoms selected from N, O and S. Representative examples include piperidinyl, piperazinyl, azepanyl, pyrrolidinyl, pyrazolidinyl, imidazolidinyl, oxazolidinyl, isoxazolidinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, and tetrahydrofuryl (or tetrahydrofuranyl).

Heteroaromatics form another subset of the heterocycles; i.e., the term "heteroaromatic" (alternatively "heteroaryl") generally refers to a heterocycle as defined above in which the entire ring system (whether mono- or poly-cyclic) is an aromatic ring system. The term "heteroaromatic ring" refers a 5- or 6-membered monocyclic aromatic ring or a 7- to 12-membered bicyclic which consists of carbon atoms and one or more heteroatoms selected from N, O and S. In the case of substituted heteroaryl rings containing at least one nitrogen atom (e.g., pyridine), such substitutions can be those resulting in N-oxide formation. Representative examples of heteroaromatic rings include pyridyl, pyrrolyl, pyrazinyl,

pyrimidinyl, pyridazinyl, thienyl (or thiophenyl), thiazolyl, furanyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, oxazolyl, isooxazolyl, oxadiazolyl, thiazolyl, isothiazolyl, and thiadiazolyl.

Representative examples of bicyclic heterocycles include benzotriazolyl, indolyl, isoindolyl, indazolyl, indolinyl, isoindolinyl, quinoxalinyl, quinazolinyl, cinnolinyl, chromanyl, isochromanyl, tetrahydroquinolinyl, quinolinyl, tetrahydroisoquinolinyl, isoquinolinyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzo-1,4-dioxinyl (i.e., ), imidazo(2,1-b)(1,3)thiazole, (i.e., ), and benzo-1,3-dioxolyl (i.e., ). In certain contexts herein,  is alternatively referred to as phenyl having as a substituent methylenedioxy attached to two adjacent carbon atoms.

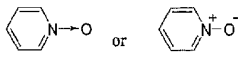
Unless expressly stated to the contrary, an "unsaturated" ring is a partially or fully unsaturated ring. For example, an "unsaturated monocyclic C_6 carbocycle" refers to cyclohexene, cyclohexadiene, and benzene.

Unless expressly stated to the contrary, all ranges cited herein are inclusive. For example, a heterocycle described as containing from "1 to 4 heteroatoms" means the heterocycle can contain 1, 2, 3 or 4 heteroatoms.

When any variable occurs more than one time in any constituent or in any formula depicting and describing compounds of the invention, its definition on each occurrence is independent of its definition at every other occurrence. Also, combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

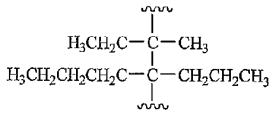
The term "substituted" (e.g., as in "aryl which is optionally substituted with one or more substituents ...") includes mono- and poly-substitution by a named substituent to the extent such single and multiple substitution (including multiple substitution at the same site) is chemically allowed.

In compounds of the invention having N-oxide moieties, e.g., pyridyl N-oxide moieties, the N-oxide moiety is structurally depicted using using conventional representations. For example, a pyridyl-N-oxide portion is structurally depicted as



which have equivalent meanings.

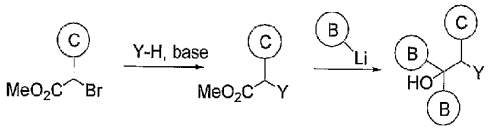
For variable definitions containing terms having repeated terms, e.g., $(CR^iR^j)_r$, where r is the integer 2, R^i is a defined variable, and R^j is a defined variable, the value of R^i may differ in each instance in which it occurs, and the value of R^j may differ in each instance in which it occurs. For example, if R^i and R^j are independently selected from the group consisting of methyl, ethyl, propyl and butyl, then $(CR^iR^j)_2$ can be



Pharmaceutically acceptable salts include both the metallic (inorganic) salts and organic salts; a list of which is given in *Remington's Pharmaceutical Sciences*, 17th Edition, pg. 1418 (1985). It is well known to one skilled in the art that an appropriate salt form is chosen based on physical and chemical stability, flowability, hydro-scopicity and solubility. As will be understood by those skilled in the art, pharmaceutically acceptable salts include, but are not limited to salts of inorganic acids such as hydrochloride, sulfate, phosphate, diphosphate, hydrobromide, and nitrate or salts of an organic acid such as malate, maleate, fumarate, tartrate, succinate, citrate, acetate, lactate, methanesulfonate, p-toluenesulfonate or palmoate, salicylate and stearate. Similarly pharmaceutically acceptable cations include, but are not limited to sodium, potassium, calcium, aluminum, lithium and ammonium (especially ammonium salts with secondary amines). Preferred salts of this invention for the reasons cited above include potassium, sodium, calcium and ammonium salts. Also included within the scope of this invention are crystal forms, hydrates and solvates of the compounds of Formula I.

Methods for preparing the compounds of this invention are illustrated in the following schemes. Other synthetic protocols will be readily apparent to those skilled in the art. The examples illustrate the preparation of the compounds of Formula I and as such are not to be considered as limiting the invention set forth in the claims appended hereto. Example described hereinafter comprises a further embodiment of the present invention.

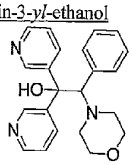
SCHEME 1



The variables C, B, and Y in the scheme are as defined in "Formula I".

EXAMPLE 1

(±)-2-Morpholin-4-*yl*-2-phenyl-1,1-dipyridin-3-*yl*-ethanol



Step A:

Methyl α-bromophenylacetate (3.79 g, 16.5 mmol) was dissolved in 50 mL of dry ACN, to which triethylamine (3.46 mL, 24.8 mmol) and morpholine (1.73 mL, 19.8 mmol) were added and the mixture was stirred for 18 hours. The mixture was poured into water, extracted twice with EtOAc. The

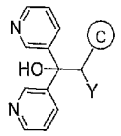
combined organic extracts were dried with Na_2SO_4, filtered and concentrated *in vacuo*, providing methyl morpholin-4-yl(phenyl)acetate. ESI+ MS: 236.2 $[M+H]^+$.

Step B:

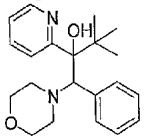
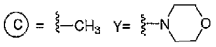
3-Bromopyridine (8.37 mL, 13.9 mmol) was dissolved in 350 mL of dry Et_2O and was cooled to -78 °C. *n*-Butyl lithium (35.1 mL, 2.5M solution in hexanes, 87.8 mmol) was added dropwise via an addition funnel over 30 minutes. After stirring for 15 minutes, a 50 mL (4:1; Et_2O/THF) solution of methyl morpholin-4-*yl*-(phenyl)acetate (6.88 g, 29.3 mmol) was added dropwise over 30 minutes. The reaction was stirred for 1 hour at -78 °C and was warmed to 0 °C and stirred for 30 minutes. The reaction was quenched with $NaHCO_3$(aq sat) and poured into $NaHCO_3$(aq sat), extracted 3X with EtOAc, dried Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by silica gel chromatography (100/0/0 to 92/8/0.8 CH_2Cl_2/MeOH/NH_4OH) to provide the titled compound.

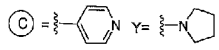
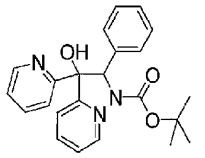
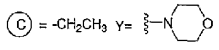
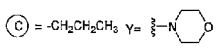
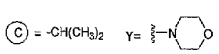
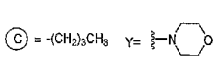
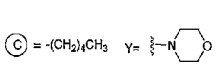
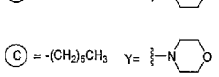
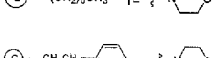
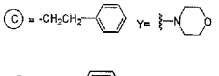
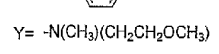
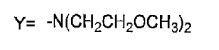
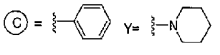
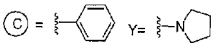
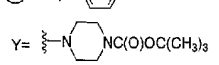
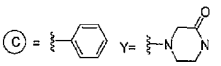
^1H NMR (500 MHz, $CDCl_3$): δ 9.01 (d, *J* = 1.9 Hz, 1H), 6.53 (dd, *J* = 2.4, 0.7 Hz, 1H), 8.48 (dd, *J* = 4.6, 1.5 Hz, 1H), 8.16 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.02 (dt, *J* = 8.0, 2.3 Hz, 1H), 7.58 (d, *J* = 8.3 Hz, 1H), 7.30-7.22 (m, 3H), 7.16-7.08 (m, 3H), 6.95 (dd, *J* = 8.1, 4.9 Hz, 1H), 5.63 (br s, 1H), 4.55 (s, 1H), 3.59-3.51 (m, 4H), 2.41 (br dt, *J* = 12.0, 4.7 Hz, 2H), 2.18 (br dt, *J* = 11.7, 4.8 Hz, 2H). HRMS $[M+H]$ $C_{22}H_{24}N_3O_2$ calcd 362.1863 , found 362.1851.

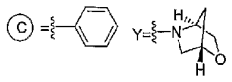
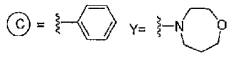
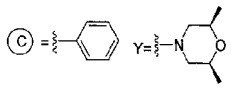
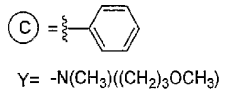
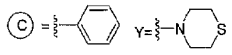
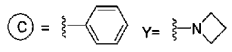
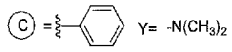
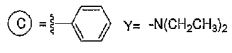
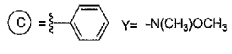
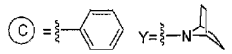
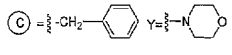
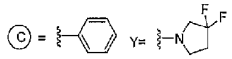
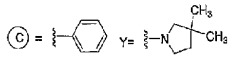
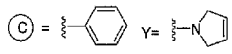
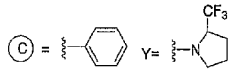
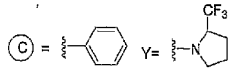
The following compounds were made according to Scheme 1, where intermediates in the scheme were modified according to literature methods. Example 2 was isolated from a reaction of 2-pyridyllithium (prepared from 2-bromopyridine and t-butyl lithium) with methyl 3-morpholin-4-yl-3-phenylpropanoate. Example 51 was prepared from the corresponding secondary alcohol *tert*-butyldimethylsilyl ether by standard deprotection. Unless otherwise shown, structures of compounds in Examples 2-51, 58-121, 4-1 to 4-21, 123-201, 202-302, and 5-1 listed in the tables are represented by defining variables "C" and "Y" of the structure

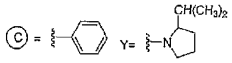
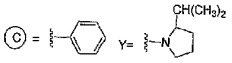
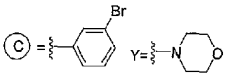
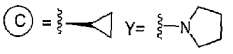
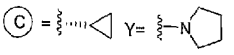
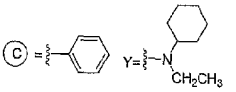
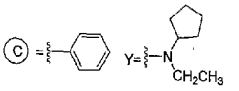
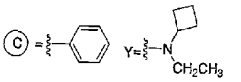
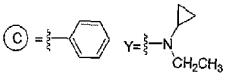
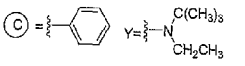
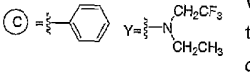
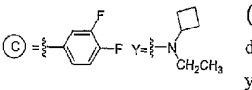


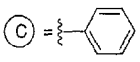
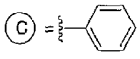
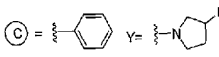
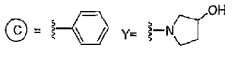
EXAMPLES 2-51

Example	Compound	Name	MS (M+1)
2		(±)-3,3-dimethyl-1-morpholin-4-yl-1-phenyl-2-pyridin-2-ylbutan-2-ol (diastereomer A)	363.2069 ($M+Na^+$)
3		(±)-2-morpholin-4-yl-1,1-dipyridin-3-ylpropan-1-ol	300.1701

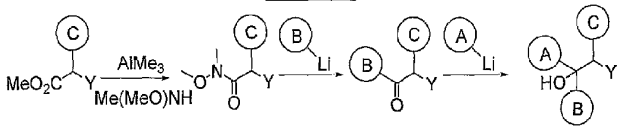
4		(±)-1,1-dipyridin-3-yl-2-pyridin-4-yl-2-pyrrolidin-1-ylethanol	347.1867
5		(±)-*tert*-butyl (2-hydroxy-1-phenyl-2,2-dipyridin-2-ylethyl)carbamate	392.1966
6		(±)-2-morpholin-4-yl-1,1-dipyridin-3-ylbutan-1-ol	314.1864
7		(±)-2-morpholin-4-yl-1,1-dipyridin-3-ylpentan-1-ol	328.2019
8		(±)-3-methyl-2-morpholin-4-yl-1,1-dipyridin-3-ylbutan-1-ol	328.2019
9		(±)-2-morpholin-4-yl-1,1-dipyridin-3-ylhexan-1-ol	342.2173
10		(±)-2-morpholin-4-yl-1,1-dipyridin-3-ylheptan-1-ol	356.2330
11		(±)-2-morpholin-4-yl-1,1-dipyridin-3-yloctan-1-ol	370.2487
12		(±)-2-morpholin-4-yl-4-phenyl-1,1-dipyridin-3-ylbutan-1-ol	390.2176
13		(±)-2-[(2-methoxyethyl)(methyl)amino]-2-phenyl-1,1-dipyridin-3-ylethanol	364.2027
14		(±)-2-[bis(2-methoxyethyl)amino]-2-phenyl-1,1-dipyridin-3-ylethanol	408.2279
15		(±)-2-phenyl-2-piperidin-1-yl-1,1-dipyridin-3-ylethanol	360.2072
16		(±)-2-phenyl-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	346.1910
17		(±)-*tert*-butyl 4-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)piperazine-1-carboxylate	461.2537
18		(±)-4-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)piperazin-2-one	375.1803
19		(±)-2-(4-methoxypiperidin-1-yl)-2-phenyl-1,1-dipyridin-3-ylethanol	390.2167

20		2-[(1*S*,4*S*)-2-oxa-5-azabicyclo[2.2.1]hept-5-yl]-2-phenyl-1,1-dipyridin-3-ylethanol (1:1 mixture diastereomers)	374.1846
21		(±)-2-(1,4-oxazepan-4-yl)-2-phenyl-1,1-dipyridin-3-ylethanol	376.2001
22		(±)-2-[(2*R*,6*S*)-2,6-dimethylmorpholin-4-yl]-2-phenyl-1,1-dipyridin-3-ylethanol	390.2168
23		(±)-2-[(3-methoxypropyl)(methyl)amino]-2-phenyl-1,1-dipyridin-3-ylethanol	378.2167
24		(±)-2-phenyl-1,1-dipyridin-3-yl-2-thiomorpholin-4-ylethanol	378.1617
25		(±)-2-azetidin-1-yl-2-phenyl-1,1-dipyridin-3-ylethanol	332.1760
26		(±)-2-(dimethylamino)-2-phenyl-1,1-dipyridin-3-ylethanol	320.1752
27		(±)-2-(diethylamino)-2-phenyl-1,1-dipyridin-3-ylethanol	348.2064
28		(±)-2-[methoxy(methyl)amino]-2-phenyl-1,1-dipyridin-3-ylethanol	336.1698
29		(±)-2-(7-azabicyclo[2.2.1]hept-7-yl)-2-phenyl-1,1-dipyridin-3-ylethanol	372.2061
30		(±)-2-morpholin-4-yl-3-phenyl-1,1-dipyridin-3-ylpropan-1-ol	376.2035
31		(±)-2-(3,3-difluoropyrrolidin-1-yl)-2-phenyl-1,1-dipyridin-3-ylethanol	382.1717
32		(±)-2-(3,3-dimethylpyrrolidin-1-yl)-2-phenyl-1,1-dipyridin-3-ylethanol	374.2210
33		(±)-2-(2,5-dihydro-1*H*-pyrrol-1-yl)-2-phenyl-1,1-dipyridin-3-ylethanol	344.1762
34		(±)-2-phenyl-1,1-dipyridin-3-yl-2-[2-(trifluoromethyl)pyrrolidin-1-yl]ethanol (diastereomer A)	414.1798
35		(±)-2-phenyl-1,1-dipyridin-3-yl-2-[2-(trifluoromethyl)pyrrolidin-1-yl]ethanol (diastereomer B)	414.1810

36		(±)-2-(2-isopropylpyrrolidin-1-yl)-2-phenyl-1,1-dipyridin-3-ylethanol (diastereomer A)	388.3
37		(±)-2-(2-isopropylpyrrolidin-1-yl)-2-phenyl-1,1-dipyridin-3-ylethanol (diastereomer B)	388.3
38		(±)-2-(3-bromophenyl)-2-morpholin-4-yl-1,1-dipyridin-3-ylethanol	440.0978
39		(2*R*)-2-cyclopropyl-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	310.1915
40		(2*S*)-2-cyclopropyl-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	310.1913
41		(±)-2-[cyclohexyl(ethyl)amino]-2-phenyl-1,1-dipyridin-3-ylethanol	402.2542
42		(±)-2-[cyclopentyl(ethyl)amino]-2-phenyl-1,1-dipyridin-3-ylethanol	388.2376
43		(±)-2-[cyclobutyl(ethyl)amino]-2-phenyl-1,1-dipyridin-3-ylethanol	374.2234
44		(±)-2-[cyclopropyl(ethyl)amino]-2-phenyl-1,1-dipyridin-3-ylethanol	360.2067
45		(±)-2-[*tert*-butyl(ethyl)amino]-2-phenyl-1,1-dipyridin-3-ylethanol	376.2378
46		(±)-2-[ethyl(2,2,2-trifluoroethyl)amino]-2-phenyl-1,1-dipyridin-3-ylethanol	402.1807
47		(±)-2-[cyclobutyl(ethyl)amino]-2-(3,4-difluorophenyl)-1,1-dipyridin-3-ylethanol	410.2053

48	 Y= ····NHC(O)OC(CH$_3$)$_3$	tert-butyl (1*S*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethylcarbamate	392.1986
49	 Y= ━NHC(O)OC(CH$_3$)$_3$	tert-butyl (1*R*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethylcarbamate	392.1985
50		(±)-2-(3-fluoropyrrolidin-1-yl)-2-phenyl-1,1-dipyridin-3-ylethanol (1:1 mixture diastereomers)	364.1813
51		(±)-1-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)pyrrolidin-3-ol (1:1 mixture diastereomers)	362.1879

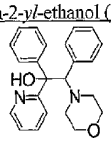
SCHEME 2



The variables C, B, A, and Y in the scheme are as defined in "Formula I".

EXAMPLE 52

(±)-2-Morpholin-4-*yl*-1.2-diphenyl-1-pyridin-2-*yl*-ethanol (diastereomer A)



Step A:

N,O-Dimethylhydroxylamine hydrochloride (1.66 g, 17.0 mmol) was suspended in 20 mL of dry THF and cooled to 0 °C. Trimethylaluminum (8.50 mL, 2.0M solution in toluene, 17.0 mmol) was added slowly and stirred for 30 minutes. Methyl morpholin-4-*yl*-(phenyl)acetate (1.00g, 4.25 mmol) was added to the cooled mixture in an 8 mL THF solution. The reaction was allowed to warm to ambient temperature while for 18 hours. The mixture was poured into 1N HCl(aq) and stirred for 1 hour. The mixture was then poured into NaHCO3(sat) and extracted 3X with EtOAc. The combined organic layers were washed 1X with brine, dried with Na_2SO_4, filtered and concentrated *in vacuo* to provide *N*-methoxy-*N*-methyl-2-morpholin-4-yl-2-phenylacetamide. HRMS [M+H] $C_{14}H_{21}N_2O_3$ calc'd 265.1547, found 265.1553.

Step B:

N-Methoxy-*N*-methyl-2-morpholin-4-*yl*-2-phenylacetamide (215 mg, 0.813 mmol) was dissolved in 10 mL of dry THF and cooled to -78 °C. In a separate flask, 2-bromopyridine (97 µL, 1.0

mmol) was dissolved in 5 mL of dry THF and cooled to -78 °C, to which was added *tert*-Butyl lithium (1.20 mL, 1.7M solution in pentane, 2.0 mmol) dropwise. After stirring for 30 minutes, the mixture transferred to the amide flask dropwise and stirred for approximately one hour. The mixture was quenched with $NaHCO_3$(sat), warmed to ambient temperature and poured into water. The aqueous layer was extracted 3X with EtOAc and the combined organic extracts were dried with Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by silica gel chromatography (100/0/0 to 9/1/0.1 CH_2Cl_2/MeOH/NH_4OH), providing partially purified titled product. The residue was further purified by preparative reverse phase HPLC. The appropriate fractions were poured into $NaHCO_3$(aq sat) and extracted twice with EtOAc. The combined organic extracts were dried with Na_2SO_4, filtered and concentrated *in vacuo* to provide 2-morpholin-4-yl-2-phenyl-1-pyridin-2-ylethanone. ESI+ MS: 283.1 $[M+H]^+$.

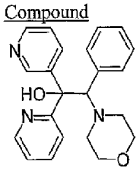
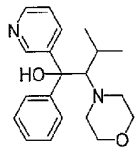
Step C:

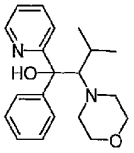
2-Morpholin-4-*yl*-2-phenyl-1-pyridin-2-*yl*-ethanone (15 mg, 0.053 mmol) was dissolved in 3 mL of dry THF and cooled to -78 °C. Phenylmagnesium bromide (159 µL, 1.0 M solution in THF, 0.159 mmol) was added dropwise and the mixture was allowed to stir for 15 minutes. The reaction was quenched with 1 mL of aqueous $NaHCO_3$(sat) and warmed to ambient temperature. The mixture was poured into $NaHCO_3$(sat) and extracted 2X with EtOAc. The combined organic extracts were dried with Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by preparative HPLC. The appropriate fractions were poured into $NaHCO_3$(sat) and extracted 2X with EtOAc. The combined organic extracts were dried with Na_2SO_4, filtered and concentrated *in vacuo* to provide the titled compound.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.19 (d, *J* = 4.6 Hz, 1H), 7.86 (d, *J* = 7.6 Hz, 2H), 7.47-7.41 (m, 2H), 7.36-7.28 (m, 4H), 7.22 (t, *J* = 7.2 Hz, 1H), 7.13-7.05 (m, 2H), 6.86 (ddd, *J* = 6.5, 4.9, 1.4 Hz, 1H), 6.28 br s, 1H), 4.62 (br s, 1H), 3.56-3.39 (br m, 4H), 2.65-2.60 (br m, 2H), 2.42-2.20 (br m, 2H). HRMS [M+H] $C_{23}H_{25}N_2O_2$ calc'd 361.1911, found 361.1914.

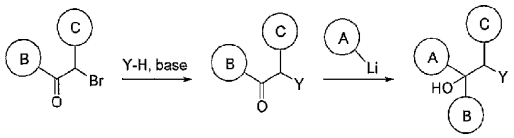
The following compounds were made according to Scheme 2, where intermediates in the scheme were modified according to literature methods.

EXAMPLES 53-55

Example	Compound	Name	MS (M+1)
53		2-morpholin-4-yl-2-phenyl-1-pyridin-2-yl-1-pyridin-3-ylethanol (diastereomer A)	362.1857
54		(±)-3-methyl-2-morpholin-4-yl-1-phenyl-1-pyridin-3-ylbutan-1-ol (diastereomer A)	327.2079

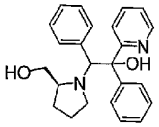
55		(±)-3-methyl-2-morpholin-4-yl-1-phenyl-1-pyridin-2-ylbutan-1-ol (diastereomer A)	327.2079

SCHEME 3

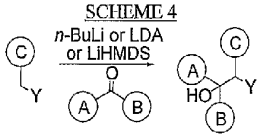


The variables C, B, A, and Y in the scheme are as defined in "Formula I".

The following compound was made according to Scheme 3.

56		2-[(2*S*)-2-(hydroxymethyl)pyrrolidin-1-yl]-1,2-diphenyl-1-pyridin-2-ylethanol (Diastereomer A)	375.2063

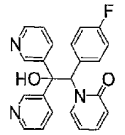
SCHEME 4



The variables C, B, A, and Y in the scheme are as defined in "Formula I".

EXAMPLE 57

(±)-1-[1-(4-Fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]pyridin-2(1*H*)-one



Step A

n-BuLi (42 mL, 1.6M, 67 mmol) was added to a solution of 3-bromopyridine (5.9 mL, 9.74 g, 62 mmol) in ether (200 mL) at -78 C. The resulting yellow suspension was stirred for 1 h. A solution of nicotinaldehyde (5.3 mL, 6 g, 56 mmol) in ether (25 mL) was then added. After stirring for 0.5 h, the reaction mixture was allowed to warm gradually to 0 C. The reaction mixture was then quenched by addition of half saturated brine (100 mL). The resulting mixture was extracted once with ethyl acetate and once with chloroform. Drying (1:1 Na_2SO_4 / K_2CO_3) and concentration gave dipyridin-3-ylmethanol as a very viscous orange oil which was used without further purification.

^{1}HNMR (CD_3OD, 400MHz) δ 8.58 (d, 2H, J = 1.74 Hz); 8.42 (dd, 2H, J = 1.28, 4.85 Hz); 7.82 (m, 2H); 7.39 (m, 2H); 5.93 (s, 1H).

Step B:

To a solution of dipyridin-3-ylmethanol (9 g, 48 mmol) in 9:1 methylene chloride / acetonitrile (100 mL) was added powdered 4A molecular sieves (24 g) and NMO (8.5g, 72 mmol). The resulting mixture was cooled in an ice bath and TPAP (0.85 g, 2.4 mmol) added carefully in 3 portions at 5 min intervals. After stirring for 15 min the ice bath was removed and stirring was continued at RT. After stirring for 3 days, the reaction mixture was filtered through Celite and the cake washed well with methylene chloride and then chloroform. The filtrate was concentrated to approximately 1/3 the original volume then silica gel was added. The remaining solvent was removed leaving the crude material adsorbed onto the silica gel as a dark green powder. This powder was layered on top of an equal volume of silica gel in a Buchner funnel and flushed with ether. These washings were discarded. The silica pad was then flushed repeatedly first with methylene chloride then with chloroform until no further product eluted. The dark red filtrate was concentrated to give a red brown solid. Trituration with ether gave dipyridin-3-ylmethanone as a white powder. The mother liquors were stripped and the residue chromatographed (eluting with 24:1 methylene chloride / methanol). The fractions enriched in product were combined, stripped, and the residue triturated with ether to give a second crop of pure ketone.
^{1}HNMR (CD_3OD, 400MHz) δ 8.92 (m, 2H); 8.79 (m, 2H); 8.22 (m, 2H); 7.61 (m, 2H).

Step C:

NaH (0.61 g, 25 mmol) was added to a solution of 2-hydroxypyridine (2 g, 21 mmol) in DMF (20 mL) at 0 C. After stirring for 15 min, p-fluorobenzyl bromide (4.4 g, 2.9 mmol, 23 mmol) was added and the reaction mixture allowed to warm gradually to RT. The reaction mixture was quenched by addition of ice then poured into ether and extracted several times with ice water. The organic phase was then dried over Na_2SO_4, concentrated and the resulting yellow oil purified by normal phase Gilson chromatography eluting with 10% DCM, 70% Hexane, 20% EtOAc. 1-(4-Fluorobenzyl)pyridin-2(1H)-one was isolated as a white solid.
^{1}HNMR (CD_3OD, 400MHz) δ 7.67 (m, 1H); 7.50 (m, 1H); 7.34 (m, 2H); 7.05 (m, 2H); 6.54 (m, 1H); 6.37 (m, 1H); 5.15 (s, 2H).

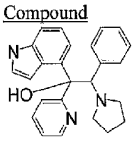
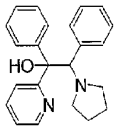
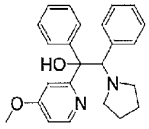
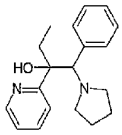
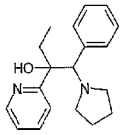
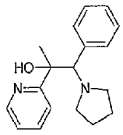
Step D:

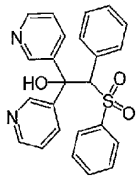
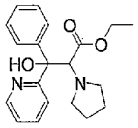
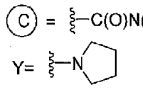
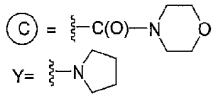
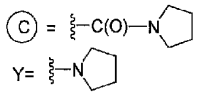
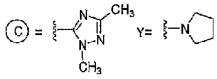
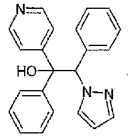
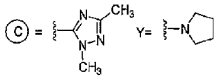
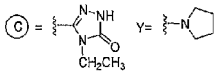
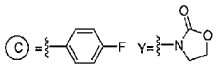
A solution of dipyridin-3-ylmethanone (1 g, 5.9 mmol) and 1-(4-fluorobenzyl)pyridin-2(1H)-one (1 g, 4.9 mmol) in THF (50 mL) was cooled to -78 C. To the resulting white suspension was added in a dropwise manner, LiHMDS (1M in THF, 6 mL). The resulting cream suspension was stirred for 30 min then allowed to warm up gradually to -30 C over 1 h. The reaction mixture was quenched with saturated $NaHCO_3$ and then it was extracted once with ether and once with ethyl acetate. The combined extracts were dried over Na2SO4 and concentrated. The resulting yellow oil was purified by normal phase Gilson chromatography eluting with 98% DCM, 2% methanol. The product was isolated as a white solid.

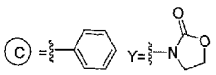
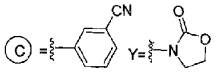
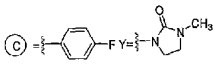
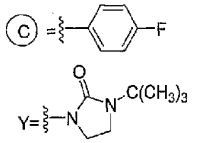
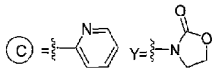
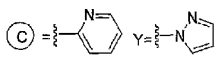
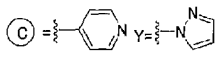
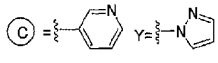
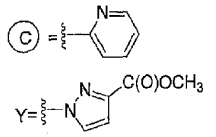
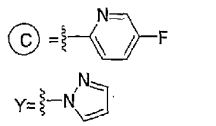
^{1}HNMR (CD_3OD, 400MHz) δ 8.63 (s, 1H); 8.49 (br s, 1H); 8.36 (m, 3H); 7.93 (m, 1H); 7.75 (br s, 1H); 7.54 (br s, 2H); 7.34 (m, 3H); 7.15 (br s, 1H); 6.96 (m, 2H); 6.29 (m, 2H).

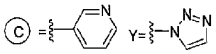
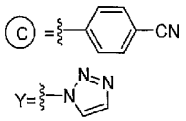
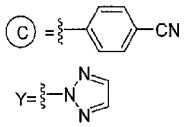
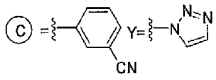
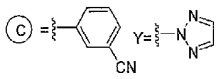
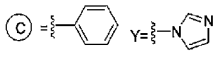
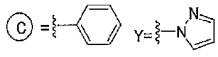
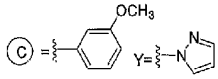
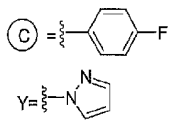
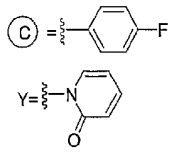
The following compounds were made according to Scheme 4, where intermediates in the scheme were modified according to literature methods. Examples 58-64 were prepared from 1-benzylpyrrolidine and the requisite ketone using the method of Kessar (*Chem Rev.* **1997**, *97*, 721). Example 120 was prepared by trifluoroacetic acid deprotection of the corresponding 1-(2,4-dimethoxybenzyl)-3-methyl-1*H*-pyrazol-1-yl derivative. Example 121 was prepared by hydrogenation of the corresponding pyridinone ring benzyl ether.

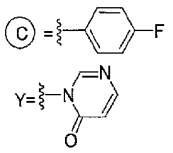
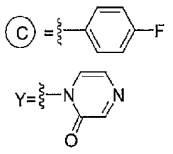
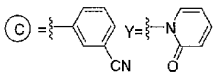
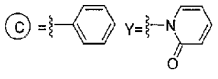
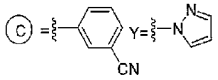
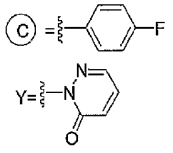
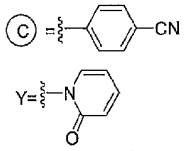
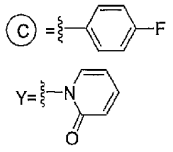
EXAMPLES 58-121 and 4-1 to 4-21

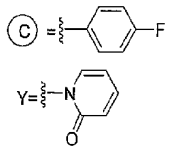
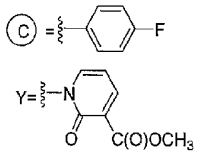
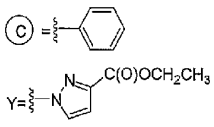
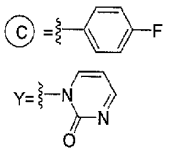
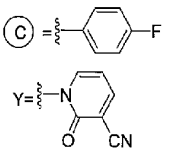
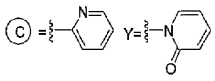
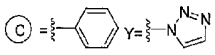
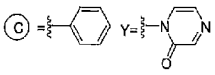
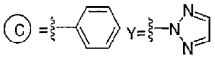
Example	Compound	Name	MS (M+1)
58		(±)-1-(1H-indol-4-yl)-2-phenyl-1-pyridin-2-yl-2-pyrrolidin-1-ylethanol (1:1 mixture of diastereomers)	384.2059
59		(±)-1,2-diphenyl-1-pyridin-2-yl-2-pyrrolidin-1-ylethanol (diastereomer a)	345.1966
60		(±)-1-(4-methoxypyridin-2-yl)-1,2-diphenyl-2-pyrrolidin-1-ylethanol (diastereomer a)	375.2063
61		(±)-1-phenyl-2-pyridin-2-yl-1-pyrrolidin-1-ylbutan-2-ol (diastereomer A)	297.1962
62		(±)-1-phenyl-2-pyridin-2-yl-1-pyrrolidin-1-ylbutan-2-ol (diastereomer B)	297.1959
63		(±)-1-phenyl-2-pyridin-2-yl-1-pyrrolidin-1-ylpropan-2-ol	283.1808

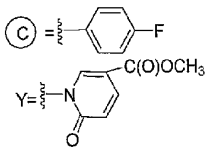
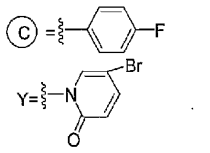
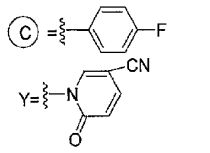
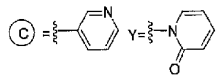
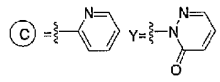
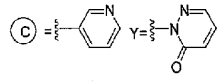
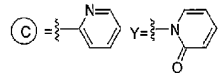
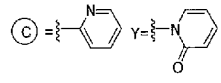
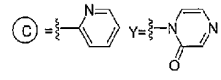
64		(±)-2-phenyl-2-(phenylsulfonyl)-1,1-dipyridin-3-ylethanol	417.1257
65		(±)-ethyl 3-hydroxy-3-phenyl-3-pyridin-2-yl-2-pyrrolidin-1-ylpropanoate (diastereomer A)	341.1855
66		(±)-3-hydroxy-*N*,*N*-dimethyl-3,3-dipyridin-3-yl-2-pyrrolidin-1-ylpropanamide	341.2
67		(±)-3-morpholin-4-yl-3-oxo-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylpropan-1-ol	383.2070
68		(±)-3-oxo-1,1-dipyridin-3-yl-2,3-dipyrrolidin-1-ylpropan-1-ol	367.2124
69		(±)-2-(1,3-dimethyl-1*H*-1,2,4-triazol-5-yl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	365.2090
70		(±)-1,2-diphenyl-2-(1*H*-pyrazol-1-yl)-1-pyridin-4-ylethanol (diastereomer A)	342.1598
71		(±)-2-(1,3-dimethyl-1*H*-1,2,4-triazol-5-yl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	365.2090
72		(±)-4-ethyl-5-(2-hydroxy-2,2-dipyridin-3-yl-1-pyrrolidin-1-ylethyl)-2,4-dihydro-3*H*-1,2,4-triazol-3-one	381.2025
73		(±)-3-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-1,3-oxazolidin-2-one	380.1444

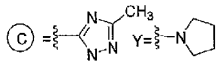
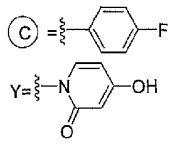
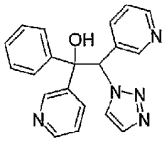
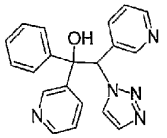
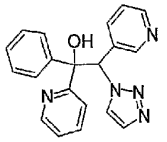
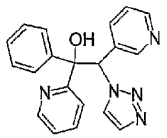
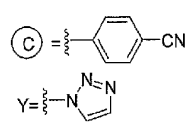
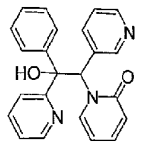
74		(±)-3-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)-1,3-oxazolidin-2-one	362.1542
75		(±)-3-[2-hydroxy-1-(2-oxo-1,3-oxazolidin-3-yl)-2,2-dipyridin-3-ylethyl]benzonitrile	387.1464
76		(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-3-methylimidazolidin-2-one	393.1767
77		(±)-1-*tert*-butyl-3-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]imidazolidin-2-one	435.2203
78		(±)-3-(2-hydroxy-1-pyridin-2-yl-2,2-dipyridin-3-ylethyl)-1,3-oxazolidin-2-one	363.1
79		(±)-2-(1H-pyrazol-1-yl)-2-pyridin-2-yl-1,1-dipyridin-3-ylethanol	344.1502
80		(±)-2-(1H-pyrazol-1-yl)-1,1-dipyridin-3-yl-2-pyridin-4-ylethanol	344.1507
81		(±)-2-(1H-pyrazol-1-yl)-1,1,2-tripyridin-3-ylethanol	344.1504
82		(±)-methyl 1-(2-hydroxy-1-pyridin-2-yl-2,2-dipyridin-3-ylethyl)-1H-pyrazole-3-carboxylate	402.1558
83		(±)-2-(5-fluoropyridin-2-yl)-2-(1H-pyrazol-1-yl)-1,1-dipyridin-3-ylethanol	362.1413

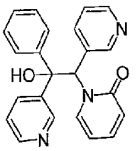
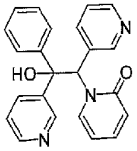
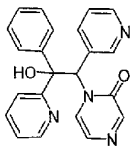
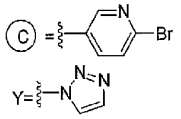
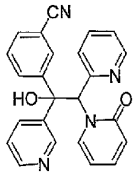
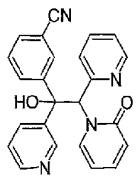
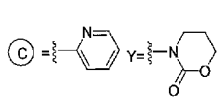
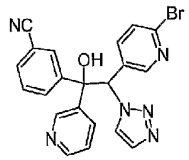
84		(±)-1,1,2-tripyridin-3-yl-2-(1H-1,2,3-triazol-1-yl)ethanol	345.1463
85		(±)-4-[2-hydroxy-2,2-dipyridin-3-yl-1-(2H-1,2,3-triazol-2-yl)ethyl]benzonitrile	369.1456
86		(±)-4-[2-hydroxy-2,2-dipyridin-3-yl-1-(1H-1,2,3-triazol-1-yl)ethyl]benzonitrile	369.1457
87		(±)-3-[2-hydroxy-2,2-dipyridin-3-yl-1-(1H-1,2,3-triazol-1-yl)ethyl]benzonitrile	369.1459
88		(±)-3-[2-hydroxy-2,2-dipyridin-3-yl-1-(2H-1,2,3-triazol-2-yl)ethyl]benzonitrile	369.1454
89		(±)-2-(1H-imidazol-1-yl)-2-phenyl-1,1-dipyridin-3-ylethanol	343.1553
90		(±)-(1-benzyl-1H-pyrazol-5-yl)(dipyridin-3-yl)methanol	343.1554
91		(±)-2-(3-methoxyphenyl)-2-(1H-pyrazol-1-yl)-1,1-dipyridin-3-ylethanol	373.1673
92		(±)-2-(4-fluorophenyl)-2-(1H-pyrazol-1-yl)-1,1-dipyridin-3-ylethanol	361.1466
93		(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]pyridin-2(1H)-one	388.1461

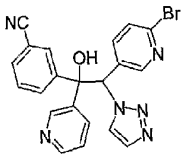
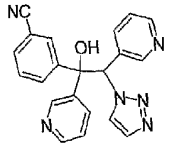
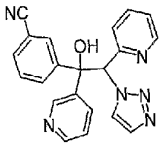
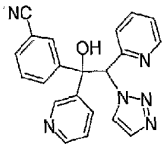
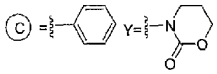
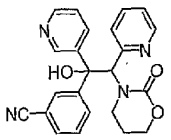
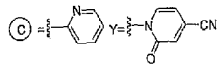
94		(±)-3-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]pyrimidin-4(3H)-one	389.1417
95		(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]pyrazin-2(1H)-one	389.1413
96		(±)-3-[2-hydroxy-1-(2-oxopyridin-1(2H)-yl)-2,2-dipyridin-3-ylethyl]benzonitrile	395.2
97		(±)-1-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)pyridin-2(1H)-one	370.2
98		(±)-3-[2-hydroxy-1-(1H-pyrazol-1-yl)-2,2-dipyridin-3-ylethyl]benzonitrile	368.1506
99		(±)-2-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]pyridazin-3(2H)-one	389.1416
100		(±)-4-[2-hydroxy-1-(2-oxopyridin-1(2H)-yl)-2,2-dipyridin-3-ylethyl]benzonitrile	395.1520
101		1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]pyridin-2(1H)-one (enantiomer A)	388.1

102		1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]pyridin-2(1H)-one (enantiomer B)	388.1
103		(±)-methyl 1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-2-oxo-1,2-dihydropyridine-3-carboxylate	446.1512
104		(±)-ethyl 1-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)-1H-pyrazole-4-carboxylate	415.1786
105		(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]pyrimidin-2(1H)-one	389.2
106		(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-2-oxo-1,2-dihydropyridine-3-carbonitrile	413.1
107		(±)-1-(2-hydroxy-1-pyridin-2-yl-2,2-dipyridin-3-ylethyl)pyridin-2(1H)-one	371.1520
108		(±)-2-phenyl-1,1-dipyridin-3-yl-2-(1H-1,2,3-triazol-1-yl)ethanol	344.1505
109		(±)-1-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)pyrazin-2(1H)-one	371.1516
110		(±)-2-phenyl-1,1-dipyridin-3-yl-2-(2H-1,2,3-triazol-2-yl)ethanol	344.1516

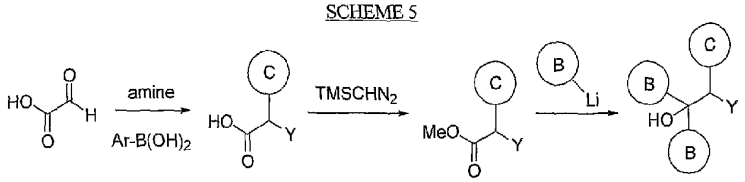
111		(±)-methyl 1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-6-oxo-1,6-dihydropyridine-3-carboxylate	446.5
112		(±)-5-bromo-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]pyridin-2(1H)-one	468.2 (M+2)
113		(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-6-oxo-1,6-dihydropyridine-3-carbonitrile	413.5
114		(±)-1-(2-hydroxy-1,2,2-tripyridin-3-ylethyl)pyridin-2(1H)-one	371.4
115		(±)-2-(2-hydroxy-1-pyridin-2-yl-2,2-dipyridin-3-ylethyl)pyridazin-3(2H)-one	372.5
116		(±)-2-(2-hydroxy-1,2,2-tripyridin-3-ylethyl)pyridazin-3(2H)-one	372.2
117		1-(2-hydroxy-1-pyridin-2-yl-2,2-dipyridin-3-ylethyl)pyridin-2(1H)-one (enantiomer A)	371.2
118		1-(2-hydroxy-1-pyridin-2-yl-2,2-dipyridin-3-ylethyl)pyridin-2(1H)-one (enantiomer B)	371.2
119		(±)-1-(2-hydroxy-1-pyridin-2-yl-2,2-dipyridin-3-ylethyl)pyrazin-2(1H)-one	372.3

120		(±)-2-(3-methyl-1*H*-1,2,4-triazol-5-yl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	351.1
121		(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-4-hydroxypyridin-2(1H)-one	404.5
4-1		(±)-1-phenyl-1,2-dipyridin-3-yl-2-(1H-1,2,3-triazol-1-yl)ethanol (Diastereomer A)	344.1511
4-2		(±)-1-phenyl-1,2-dipyridin-3-yl-2-(1H-1,2,3-triazol-1-yl)ethanol (Diastereomer B)	344.1512
4-3		(±)-1-phenyl-1-pyridin-2-yl-2-pyridin-3-yl-2-(1H-1,2,3-triazol-1-yl)ethanol (Diastereomer A)	344.1504
4-4		(±)-1-phenyl-1-pyridin-2-yl-2-pyridin-3-yl-2-(1H-1,2,3-triazol-1-yl)ethanol (Diastereomer B)	344.1513
4-5		(±)-4-[2-hydroxy-2,2-dipyridin-3-yl-1-(1H-1,2,3-triazol-1-yl)ethyl]benzonitrile	369.1477
4-6		(±)-1-(2-hydroxy-2-phenyl-2-pyridin-2-yl-1-pyridin-3-ylethyl)pyridin-2(1H)-one	370.3

4-7		(±)-1-(2-hydroxy-2-phenyl-1,2-dipyridin-3-ylethyl)pyridin-2(1H)-one (Diastereomer C)	370.3
4-8		(±)-1-(2-hydroxy-2-phenyl-1,2-dipyridin-3-ylethyl)pyridin-2(1H)-one (Diastereomer D)	370.3
4-9		(±)-1-(2-hydroxy-2-phenyl-2-pyridin-2-yl-1-pyridin-3-ylethyl)pyrazin-2(1H)-one	371.3
4-10		(±)-2-(6-bromopyridin-3-yl)-1,1-dipyridin-3-yl-2-(1H-1,2,3-triazol-1-yl)ethanol	423.0582
4-11		(±)-3-[1-hydroxy-2-(2-oxopyridin-1(2H)-yl)-2-pyridin-2-yl-1-pyridin-3-ylethyl]benzonitrile (Diastereomer X)	395.2
4-12		(±)-3-[1-hydroxy-2-(2-oxopyridin-1(2H)-yl)-2-pyridin-2-yl-1-pyridin-3-ylethyl]benzonitrile (Diastereomer Y)	395.2
4-13		(±)-3-(2-hydroxy-1-pyridin-2-yl-2,2-dipyridin-3-ylethyl)-1,3-oxazinan-2-one	377.1607
4-14		(±)-3-[2-(6-bromopyridin-3-yl)-1-hydroxy-1-pyridin-3-yl-2-(1*H*-1,2,3-triazol-1-yl)ethyl]benzonitrile (Diastereomer A)	447.0558

4-15		(±)-3-[2-(6-bromopyridin-3-yl)-1-hydroxy-1-pyridin-3-yl-2-(1*H*-1,2,3-triazol-1-yl)ethyl]benzonitrile (Diastereomer B)	447.0559
4-16		(±)-3-[1-hydroxy-1,2-dipyridin-3-yl-2-(1H-1,2,3-triazol-1-yl)ethyl]benzonitrile	369.1457
4-17		(±)-3-[1-hydroxy-2-pyridin-2-yl-1-pyridin-3-yl-2-(1H-1,2,3-triazol-1-yl)ethyl]benzonitrile (Diastereomer A)	369.1464
4-18		(±)-3-[1-hydroxy-2-pyridin-2-yl-1-pyridin-3-yl-2-(1H-1,2,3-triazol-1-yl)ethyl]benzonitrile (Diastereomer B)	369.1464
4-19		(±)-3-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)-1,3-oxazinan-2-one	376.1646
4-20		(±)-3-[1-hydroxy-2-(2-oxo-1,3-oxazinan-3-yl)-2-pyridin-2-yl-1-pyridin-3-ylethyl]benzonitrile	401.1
4-21		(±)-1-(2-hydroxy-1-pyridin-2-yl-2,2-dipyridin-3-ylethyl 2-oxo-1,2-dihydropyridine-carbonitrile	396.4

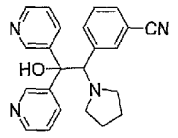
SCHEME 5



The variables C, B, and Y in the scheme are as defined in "Formula I".

EXAMPLE 122

(±)-3-(2-hydroxy-2,2-dipyridin-3-yl-1-pyrrolidin-1-ylethyl)benzonitrile



Step A:

To a mixture of glyoxylic acid monohydrate (1.54 g), pyrrolidine (1.19 g), and 220 mL acetonitrile was added 3-bromophenyl boronic acid (3.35 g). The reaction was heated at 80 C for 93 h. After cooling to room temperature, volatiles were removed in vacuo, and the residue was dissolved in 75 mL of benzene and 38 mL of methanol. Trimethylsilyldiazomethane (2M in hexanes, 16.7 mL) was added via syringe, and the reaction was stirred at room temperature for 2.5 h. The volatiles were removed in vacuo, and the residue was purified by flash chromatography to provide 1.53 g of methyl (3-bromophenyl)(pyrrolidin-1-yl)acetate. MS 298, 300 (Br).

Step B:

A solution of 3-bromopyridine (1.62 g) in 40 mL of diethyl ether was cooled to -78 C. n-BuLi (2.87 M in hexanes, 3.6 mL) was added via syringe, and the resulting mixture was stirred for 15 min. A solution of methyl (3-bromophenyl)-(pyrrolidin-1-yl)acetate (1.53 g) in 10 mL of THF was added via cannula. The reaction was stirred for 5 min at -78 C then for 2.5 h at 0 C. After quenching with saturated aqueous NH_4Cl, the mixture was partitioned between ethyl acetate and saturated aqueous $NaHCO_3$. The aqueous solution was extracted once with ethyl acetate, and the combined organic solutions were dried (Na_2SO_4) and concentrated in vacuo. Flash chromatography provided a solid that was triturated with diethyl ether to give 893 mg of 2-(3-bromophenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol. HRMS calcd for $C_{22}H_{23}BrN_3O$ $(M+H)^+$: 424.1019; found: 424.1025. ^1H NMR ($CDCl_3$, 500 MHz) δ 9.11 (d, J = 2.4 Hz, 1H); 8.51-8.48 (m, 2H); 8.14-8.11 (m, 1H); 7.60 (ddd, J = 1.6, 2.3, 8.2 Hz, 1H); 7.46 (t, J = 3.5 Hz, 1H); 7.29 (dd, J = 4.8, 8.1 Hz, 1H); 7.20 (t, J = 8.7 Hz, 2H); 6.97-6.92 (m, 2H); 5.94 (s, 1H); 4.44 (s, 1H); 2.26 (m, 4H); 1.63 (m, 4H).

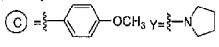
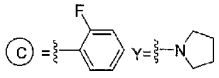
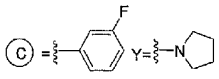
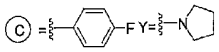
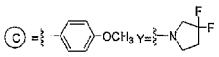
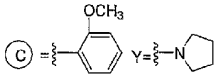
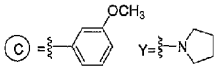
Step C:

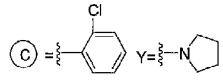
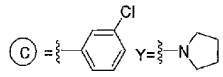
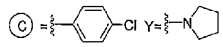
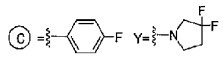
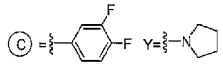
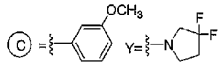
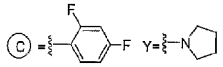
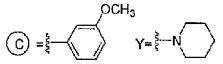
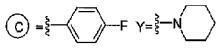
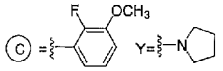
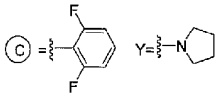
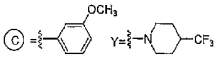
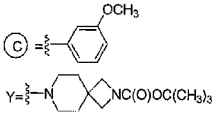
2-(3-bromophenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol (40 mg, 0.094 mmol), $Pd_2(dba)_3$ (3 mg, 0.003 mmol), dppf (4 mg, 0.008 mmol), $Zn(CN)_2$ (22 mg, 0.189 mmol) and zinc powder (1 mg,

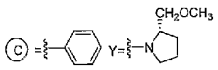
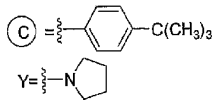
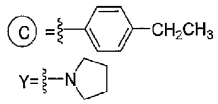
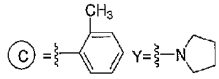
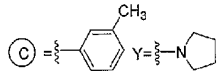
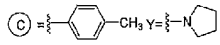
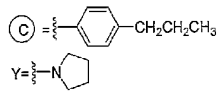
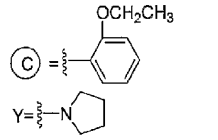
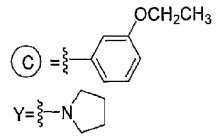
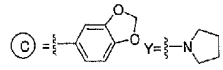
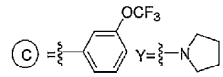
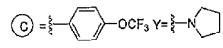
0.011 mmol) were combined in a flask, purged with argon, and then 1.5 mL DMA was added. This mixture was heated at 120 °C for 3.5 h then cooled to room temperature. The reaction mixture was then diluted with EtOAc and washed with 2N aqueous NH_4OH (1x). The organic layer was dried over Na_2SO_4 and concentrated. The resulting viscous liquid was purified by reverse phase HPLC. Pure fractions were combined and extracted from saturated aqueous $NaHCO_3$ with CH_2Cl_2 (3x). The combined organic extracts were dried over Na_2SO_4 and concentrated to yield the titled compound as a white solid (22 mg, 63%). HRMS calcd for $C_{23}H_{22}N_4O$ $(M+H)^+$: 371.1853; found: 371.1867. ^1H NMR ($CDCl_3$, 500 MHz) δ 9.11 (d, J = 2.2 Hz, 1H); 8.51 (dd, J = 1.2, 4.6 Hz, 1H); 8.47 (d, J = 1.9 Hz, 1H); 8.13 (m, 2H); 7.64 (s, 1H); 7.59 (m, 1H); 7.53 (br d, J = 6.6 Hz, 1H); 7.37 (d, J = 7.8 Hz, 1H); 7.31 (dd, J = 4.6, 7.8 Hz, 1H); 7.21 (t, J = 7.8 Hz, 1H); 6.94 (dd, J = 4.6, 8.1 Hz, 1H); 5.71 (br, 1H); 5.30 (s, 1H); 2.25 (br d, J = 26.9 Hz, 4H); 1.65 (s, 4H).

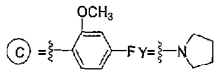
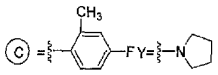
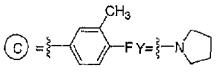
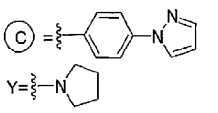
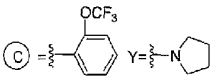
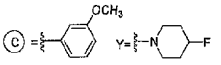
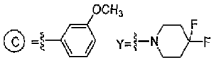
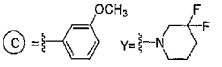
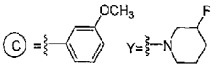
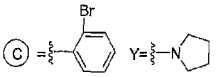
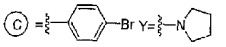
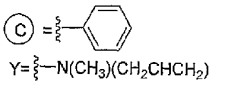
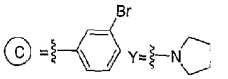
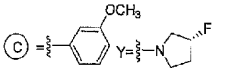
The following compounds were made according to Scheme 5, where intermediates in the scheme were modified according to literature methods. Example 181 was prepared by acid deprotection of the corresponding *tert*-butyl carbamate derivative. Examples 182-189 were prepared by fluoride-mediated deprotection of the corresponding primary or secondary *tert*-butyldimethylsilyl ethers. Example 192 was prepared by trifluoroacetic acid deprotection of Example 191, and Examples 193-201 were prepared in likewise fashion from the corresponding 4-methoxybenzyl amines.

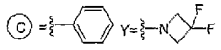
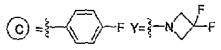
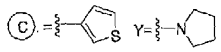
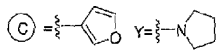
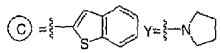
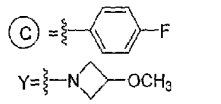
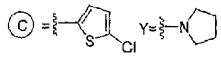
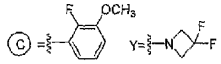
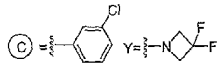
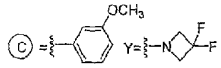
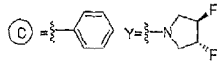
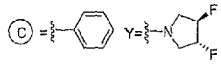
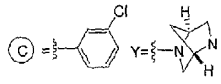
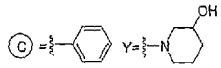
EXAMPLES 123-201

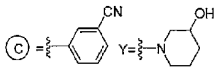
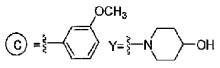
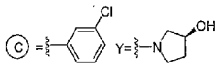
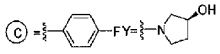
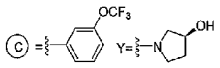
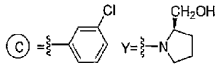
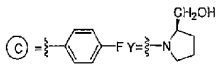
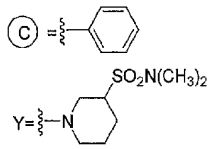
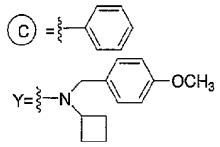
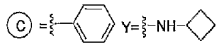
Example	Compound	Name	MS (M+1)
123		(±)-2-(4-methoxyphenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	376.2047
124		(±)-2-(2-fluorophenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	364.1817
125		(±)-2-(3-fluorophenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	364.1816
126		(±)-2-(4-fluorophenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	364.1817
127		(±)-2-(3,3-difluoropyrrolidin-1-yl)-2-(4-methoxyphenyl)-1,1-dipyridin-3-ylethanol	412.1849
128		(±)-2-(2-methoxyphenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	376.2039
129		(±)-2-(3-methoxyphenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	376.2042

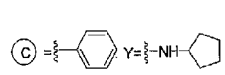
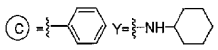
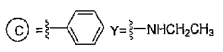
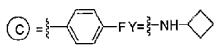
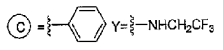
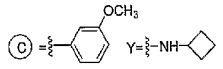
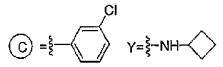
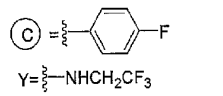
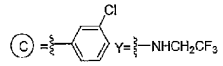
130		(±)-2-(2-chlorophenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	380.1536
131		(±)-2-(3-chlorophenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	380.1525
132		(±)-2-(4-chlorophenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	380.1546
133		(±)-2-(3,3-difluoropyrrolidin-1-yl)-2-(4-fluorophenyl)-1,1-dipyridin-3-ylethanol	400.1646
134		(±)-2-(3,4-difluorophenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	382.1722
135		(±)-2-(3,3-difluoropyrrolidin-1-yl)-2-(3-methoxyphenyl)-1,1-dipyridin-3-ylethanol	412.1837
136		(±)-2-(2,4-difluorophenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	382.1722
137		(±)-2-(3-methoxyphenyl)-2-piperidin-1-yl-1,1-dipyridin-3-ylethanol	390.2173
138		(±)-2-(4-fluorophenyl)-2-piperidin-1-yl-1,1-dipyridin-3-ylethanol	378.1973
139		(±)-2-(2-fluoro-3-methoxyphenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	394.1929
140		(±)-2-(2,6-difluorophenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	382.1719
141		(±)-2-(3-methoxyphenyl)-1,1-dipyridin-3-yl-2-[4-(trifluoromethyl)piperidin-1-yl]ethanol	458.2077
142		(±)-tert-butyl 7-[2-hydroxy-1-(3-methoxyphenyl)-2,2-dipyridin-3-ylethyl]-2,7-diazaspiro[3.5]nonane-2-carboxylate	531.2993

143		2-[(2r)-2-(methoxymethyl)pyrrolidin-1-yl]-2-phenyl-1,1-dipyridin-3-ylethanol (1:1 mixture diastereomers)	390.2175
144		(±)-2-(4-tert-butylphenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	402.2554
145		(±)-2-(4-ethylphenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	374.2264
146		(±)-2-(2-methylphenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	360.2093
147		(±)-2-(3-methylphenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	360.2079
148		(±)-2-(4-methylphenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	360.2078
149		(±)-2-(4-propylphenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	388.2379
150		(±)-2-(2-ethoxyphenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	390.2184
151		(±)-2-(3-ethoxyphenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	390.2188
152		(±)-2-(1,3-benzodioxol-5-yl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	390.1819
153		(±)-1,1-dipyridin-3-yl-2-pyrrolidin-1-yl-2-[3-(trifluoromethoxy)phenyl]ethanol	430.1738
154		(±)-1,1-dipyridin-3-yl-2-pyrrolidin-1-yl-2-[4-(trifluoromethoxy)phenyl]ethanol	430.1736

155		(±)-2-(4-fluoro-2-methoxyphenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	394.1921
156		(±)-2-(4-fluoro-2-methylphenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	378.1975
157		(±)-2-(4-fluoro-3-methylphenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	378.1970
158		(±)-2-[4-(1h-pyrazol-1-yl)phenyl]-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	412.2120
159		(±)-1,1-dipyridin-3-yl-2-pyrrolidin-1-yl-2-[2-(trifluoromethoxy)phenyl]ethanol	430.1743
160		(±)-2-(4-fluoropiperidin-1-yl)-2-(3-methoxyphenyl)-1,1-dipyridin-3-ylethanol	408.2091
161		(±)-2-(4,4-difluoropiperidin-1-yl)-2-(3-methoxyphenyl)-1,1-dipyridin-3-ylethanol	426.1988
162		(±)-2-(3,3-difluoropiperidin-1-yl)-2-(3-methoxyphenyl)-1,1-dipyridin-3-ylethanol	426.1995
163		(±)-2-(3-fluoropiperidin-1-yl)-2-(3-methoxyphenyl)-1,1-dipyridin-3-ylethanol (1:1 mixture diastereomers)	408.2097
164		(±)-2-(2-bromophenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	424.1021
165		(±)-2-(4-bromophenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	424.1021
166		(±)-2-[allyl(methyl)amino]-2-phenyl-1,1-dipyridin-3-ylethanol	346.1923
167		(±)-2-(3-bromophenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	424.1025
168		2-[(3*S*)-3-fluoropyrrolidin-1-yl]-2-(3-methoxyphenyl)-1,1-dipyridin-3-ylethanol	394.1931

		(diastereomer A)	
169		(±)-2-(3,3-difluoroazetidin-1-yl)-2-phenyl-1,1-dipyridin-3-ylethanol	368.1568
170		(±)-2-(3,3-difluoroazetidin-1-yl)-2-(4-fluorophenyl)-1,1-dipyridin-3-ylethanol	386.1466
171		(±)-1,1-dipyridin-3-yl-2-pyrrolidin-1-yl-2-(3-thienyl)ethanol	352.1485
172		(±)-2-(3-furyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	336.1704
173		(±)-2-(1-benzothien-2-yl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	402.1649
174		(±)-2-(4-fluorophenyl)-2-(3-methoxyazetidin-1-yl)-1,1-dipyridin-3-ylethanol	380.1765
175		(±)-2-(5-chloro-2-thienyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol	386.1110
176		(±)-2-(3,3-difluoroazetidin-1-yl)-2-(2-fluoro-3-methoxyphenyl)-1,1-dipyridin-3-ylethanol	416.1573
177		(±)-2-(3-chlorophenyl)-2-(3,3-difluoroazetidin-1-yl)-1,1-dipyridin-3-ylethanol	402.1183
178		(±)-2-(3,3-difluoroazetidin-1-yl)-2-(3-methoxyphenyl)-1,1-dipyridin-3-ylethanol	398.1674
179		2-[(3*R*,4*R*)-3,4-difluoropyrrolidin-1-yl]-2-phenyl-1,1-dipyridin-3-ylethanol (diastereomer A)	382.1744
180		2-[(3*R*,4*R*)-3,4-difluoropyrrolidin-1-yl]-2-phenyl-1,1-dipyridin-3-ylethanol (diastereomer B)	382.1740
181		2-(3-chlorophenyl)-2-[(1*S*,4*S*)-2,5-diazabicyclo[2.2.1]hept-2-yl]-1,1-dipyridin-3-ylethanol (2:1 mixture diastereomers)	407.1617
182		(±)-1-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)piperidin-3-ol (1:1	376.2010

		mixture diastereomers)	
183		(±)-3-[2-hydroxy-1-(3-hydroxypiperidin-1-yl)-2,2-dipyridin-3-ylethyl]benzonitrile (2:1 mixture diastereomers)	401.1947
184		(±)-1-[2-hydroxy-1-(3-methoxyphenyl)-2,2-dipyridin-3-ylethyl]piperidin-4-ol	406.2132
185		(3R)-1-[1-(3-chlorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]pyrrolidin-3-ol (1:1 mixture diastereomers)	396.1490
186		(3R)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]pyrrolidin-3-ol (1:1 mixture diastereomers)	380.1770
187		(3R)-1-{2-hydroxy-2,2-dipyridin-3-yl-1-[3-(trifluoromethoxy)phenyl]ethyl}pyrrolidin-3-ol (1:1 mixture diastereomers)	446.1694
188		2-(3-chlorophenyl)-2-[(2S)-2-(hydroxymethyl)pyrrolidin-1-yl]-1,1-dipyridin-3-ylethanol (diastereomer A)	410.1642
189		2-(4-fluorophenyl)-2-[(2S)-2-(hydroxymethyl)pyrrolidin-1-yl]-1,1-dipyridin-3-ylethanol (diastereomer A)	394.1943
190		(±)-1-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)-n,n-dimethylpiperidine-3-sulfonamide (diastereomer A)	467.2109
191		(±)-2-[cyclobutyl(4-methoxybenzyl)amino]-2-(4-fluorophenyl)-1,1-dipyridin-3-ylethanol	484.2425
192		(±)-2-(cyclobutylamino)-2-phenyl-1,1-dipyridin-3-ylethanol	346.1918

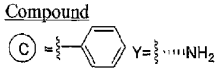
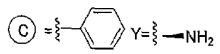
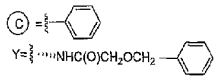
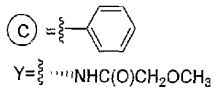
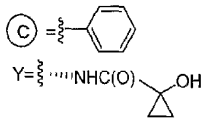
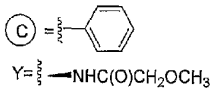
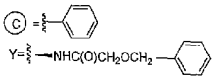
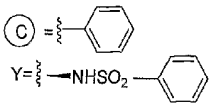
193		(±)-2-(cyclopentylamino)-2-phenyl-1,1-dipyridin-3-ylethanol	360.2075
194		(±)-2-(cyclohexylamino)-2-phenyl-1,1-dipyridin-3-ylethanol	374.2230
195		(±)-2-(ethylamino)-2-phenyl-1,1-dipyridin-3-ylethanol	320.1769
196		(±)-2-(cyclobutylamino)-2-(4-fluorophenyl)-1,1-dipyridin-3-ylethanol	364.1818
197		(±)-2-phenyl-1,1-dipyridin-3-yl-2-[(2,2,2-trifluoroethyl)amino]ethanol	374.1471
198		(±)-2-phenyl-1,1-dipyridin-3-yl-2-[(2,2,2-trifluoroethyl)amino]ethanol	376.2016
199		(±)-2-(3-chlorophenyl)-2-(cyclobutylamino)-1,1-dipyridin-3-ylethanol	380.1521
200		(±)-2-(4-fluorophenyl)-1,1-dipyridin-3-yl-2-[(2,2,2-trifluoroethyl)amino]ethanol	392.1378
201		(±)-2-(3-chlorophenyl)-1,1-dipyridin-3-yl-2-[(2,2,2-trifluoroethyl)amino]ethanol	408.1100

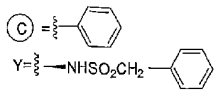
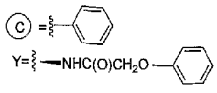
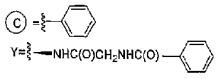
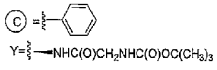
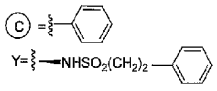
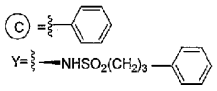
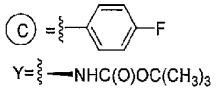
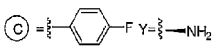
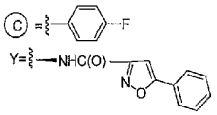
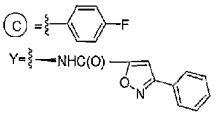
The following compounds were made from compounds in Examples 1-201, using methods known to those skilled in the art. Examples 202, 203, 281 and 284 were prepared by acid deprotection of Examples 48, 49, 142 and 17, respectively. Example 217 was prepared by acid deprotection of the corresponding *tert*-butyl carbamate. Examples 204-280, 282 and 285, were prepared from Examples 202, 203, 217 or 284 by acylations or reductive aminations or combinations of both. Example 283 was prepared by *O*-alkylation of Example 1. Example 286 was prepared by trifluoroacetic acid treatment of Example 77, and Example 287 was prepared from Example 286. Example 288 was prepared by MnO_2 oxidation for Example 33. Examples 289 and 290 were prepared by reduction of Examples 82 and 104, respectively. The acid 291 was prepared from bromide 165 by palladium mediated carbonylation, and was converted to amides 292 and 293 by standard amide coupling. Amides 295 and 296 were prepared in likewise fashion from the carboxylic acid derived from carbonylation of bromide 167, and ester 294 was prepared from the same acid using trimethylsilyldiazomethane. Example 297 was prepared by hydrolysis of Example 103. Example 298 was prepared by palladium mediated cyanation of bromide 38.

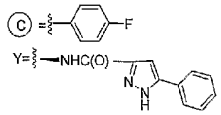
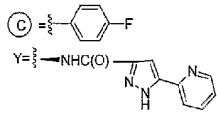
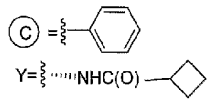
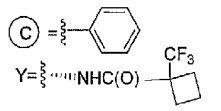
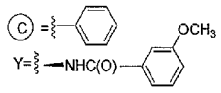
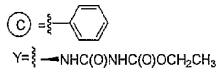
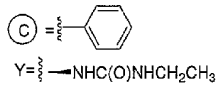
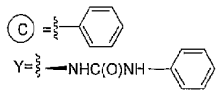
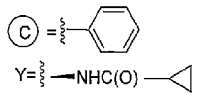
Example 299 was prepared from example 166 by olefin dihydroxylation, and Example 300 was prepared from example 299 by $NaIO_4$ oxidative cleavage followed by sodium borohydride reduction. Example 301 was prepared by oxidation of example 51, and 301 was converted to 302 using excess methyl Grignard.

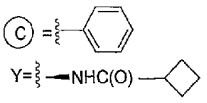
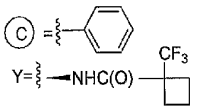
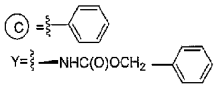
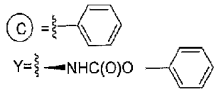
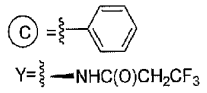
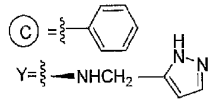
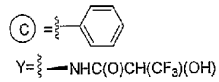
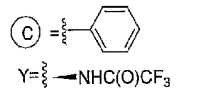
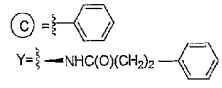
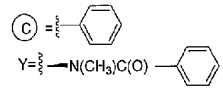
5

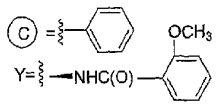
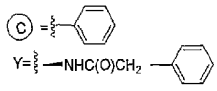
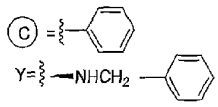
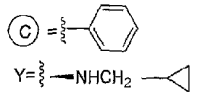
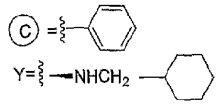
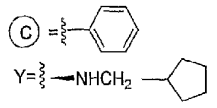
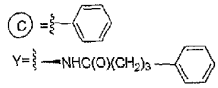
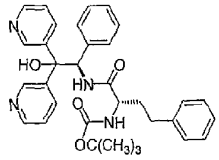
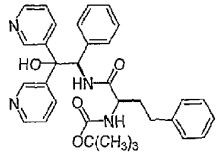
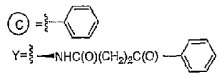
EXAMPLES 202-302 and 5-1

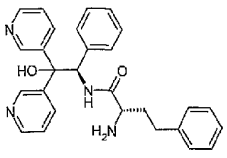
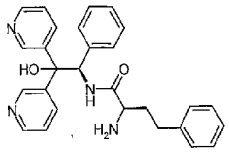
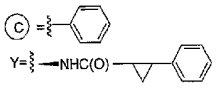
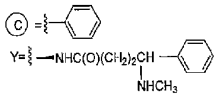
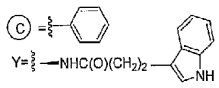
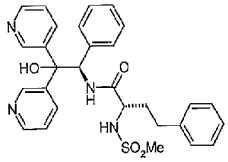
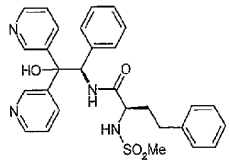
Example	Compound	Name	MS (M+1)
202		(2*S*)-2-amino-2-phenyl-1,1-dipyridin-3-ylethanol	292.1454
203		(2*R*)-2-amino-2-phenyl-1,1-dipyridin-3-ylethanol	292.1455
204		2-(benzyloxy)-N-[(1*S*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]acetamide	440.1970
205		N-[(1*S*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-2-methoxyacetamide	364.1657
206		1-hydroxy-N-[(1*S*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]cyclopropanecarboxamide	376.1664
207		N-[(1*R*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-2-methoxyacetamide	364.2
208		2-(benzyloxy)-N-[(1*R*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-acetamide	440.1974
209		N-[(1*R*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]benzenesulfonamide	432.2

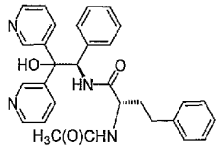
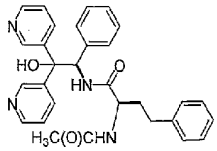
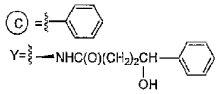
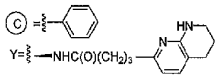
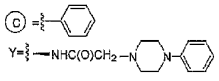
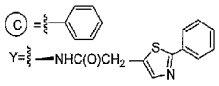
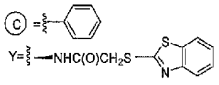
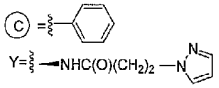
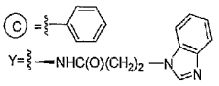
210		N-[(1*R*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-1-phenylmethanesulfonamide	446.3
211		N-[(1*R*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-2-phenoxyacetamide	426.4
212		(1*R*)-N^2-benzoyl-N^1-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)glycinamide	453.2
213		(1*R*)-N^2-Boc-N^1-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)glycinamide	449.5
214		N-[(1*R*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-2-phenylethanesulfonamide	460.0
215		N-[(1*R*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-3-phenylpropane-1-sulfonamide	474.2
216		tert-butyl (1*R*)-1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethylcarbamate	410.1879
217		(2*R*)-2-amino-2-(4-fluorophenyl)-1,1-dipyridin-3-ylethanol	310.2
218		N-[(1*R*)-1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-5-phenylisoxazole-3-carboxamide	481.3
219		N-[(1*R*)-1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-3-phenylisoxazole-5-carboxamide	481.3

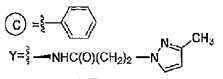
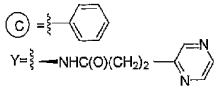
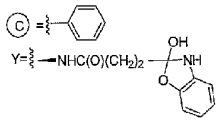
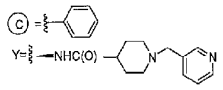
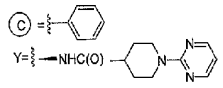
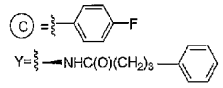
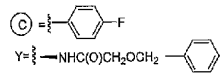
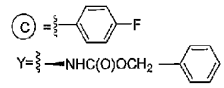
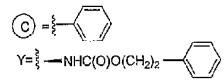
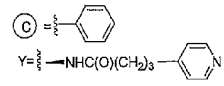
220		N-[(1*R*)-1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-3-phenyl-1H-pyrazole-5-carboxamide	480.6
221		N-[(1*R*)-1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-3-pyridin-2-yl-1H-pyrazole-5-carboxamide	481.3
222		N-[(1*S*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]cyclobutanecarboxamide	374.1886
223		N-[(1*S*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-1-(trifluoromethyl)cyclobutane carboxamide	442.1736
224		N-ethyl-N'-[(1*S*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]urea	363.1816
225		N-[(1*R*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-3-methoxybenzamide	426.1801
226		(1*R*)-ethyl {[(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)amino]carbonyl}carbamate	407.1717
227		(1*R*)-N-ethyl-N'-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)urea	363.1815
228		(1*R*)-N-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)-N-phenylurea	411.1816
229		*N*-[(1*R*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]cyclopropanecarboxamide	360.1

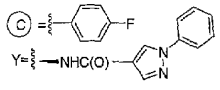
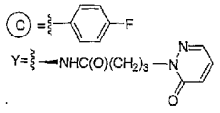
230		(1*R*)-N-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)cyclobutanecarboxamide	374.1855
231		(1*R*)-N-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)-1-(trifluoromethyl)cyclobutanecarboxamide	442.1714
232		benzyl [(1*R*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]carbamate	426.1799
233		phenyl [(1*R*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]carbamate	412.1655
234		(1*R*)-3,3,3-trifluoro-n-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)propanamide	402.1405
235		(2*R*)-2-phenyl-2-[(1*H*-pyrazol-5-ylmethyl)amino]-1,1-dipyridin-3-ylethanol	372.1825
236		(1*R*)-3,3,3-trifluoro-2-hydroxy-N--(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)propanamide	418.1369
237		(1*R*)-2,2,2-trifluoro-N-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)acetamide	388.1283
238		(1*R*)-N-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)-3-phenylpropanamide	424.2017
239		(1*R*)-N-[(1R)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-N-methylbenzamide	410.1860

240		(1*R*)-N-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)-2-methoxybenzamide	426.4
241		(1*R*)-N-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)-2-phenylacetamide	410.1860
242		(1*R*)-2-(benzylamino)-2-phenyl-1,1-dipyridin-3-ylethanol	382.1912
243		(1*R*)-2-[(cyclopropylmethyl)amino]-2-phenyl-1,1-dipyridin-3-ylethanol	346.1913
244		(1*R*)-2-[(cyclohexylmethyl)amino]-2-phenyl-1,1-dipyridin-3-ylethanol	388.2381
245		(2*R*)-2-[(cyclopentylmethyl)amino]-2-phenyl-1,1-dipyridin-3-ylethanol	374.2218
246		(1*R*)-N--(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)-4-phenylbutanamide	438.2174
247		tert-butyl [(1*S*)-1-({[(1*R*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]amino}carbonyl)-3-phenylpropyl]carbamate	553.2786
248		tert-butyl [(1*R*)-1-({[(1*R*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]amino}carbonyl)-3-phenylpropyl]carbamate	553.2787
249		N-[(1*R*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-4-oxo-4-phenylbutanamide	452.1950

250		(2*S*)-2-amino-*N*-[(1*R*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-4-phenylbutanamide	453.2269
251		(2*R*)-2-amino-*N*-[(1*R*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-4-phenylbutanamide	453.2268
252		*trans*-*N*-[(1*R*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-2-phenylcyclopropanecarboxamide	436.2015
253		N-[(1R)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-4-(methylamino)-4-phenylbutanamide	467.2435
254		N-[(1R)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-3-(1H-indol-3-yl)propanamide	463.2127
255		(2S)--[(1R)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-2-[(methylsulfonyl)amino]-4-phenylbutanamide	531.2051
256		(2S)-[(1R)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-2-[(methylsulfonyl)amino]-4-phenylbutanamide	531.2054

257		(2S)-2-(acetylamino)-N-[(1R)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-4-phenylbutanamide	495.2394
258		(2R)-2-(acetylamino)-N-[(1R)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-4-phenylbutanamide	495.2395
259		4-hydroxy-N-[(1R)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-4-phenylbutanamide	454.2137
260		*N*-[(1*R*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butanamide	494.2547
261		N-[(1R)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-2-(4-phenylpiperazin-1-yl)acetamide	494.2552
262		N-[(1R)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-2-(2-phenyl-1,3-thiazol-5-yl)acetamide	493.1699
263		2-(1,3-benzothiazol-2-ylthio)--N-[(1R)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]acetamide	499.1249
264		3-(1-H-benzimidazol-1-yl)-N-[(1R)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]propanamide	464.2077
265		N-[(1R)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-3-(1-H-pyrazol-1-yl)propanamide	414.1927

266		N-[(1-R)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-3-(3-methyl-1-h-pyrazol-1-yl)propanamide	428.2076
267		N-[(1R)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-3-pyrazin-2-ylpropanamide	426.1920
268		3-(2-hydroxy-2,3-dihydro-1,3-benzoxazol-2-yl)-N-[(1R)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]propanamide	483.2040
269		*N*-[(1*R*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-1-(pyridin-3-ylmethyl)piperidine-4-carboxamide	494.2562
270		*N*-[(1*R*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-1-pyrimidin-2-ylpiperidine-4-carboxamide	481.2350
271		N-[(1R)-1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-4-phenylbutanamide	456.2089
272		2-(benzyloxy)-N-[(1R)-1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]acetamide	458.1885
273		benzyl [(1*R*)-1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]carbamate	444.1725
274		2-phenylethyl [(1R)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]carbamate	440.1907
275		N-[(1R)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-4-pyridin-4-ylbutanamide	439.2129

276		N-[(1R)-1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-1-phenyl-1H-pyrazole-4-carboxamide	480.1830
277		N-[(1R)-1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-4-(6-oxopyridazin-1(6H)-yl)butanamide	474.1928
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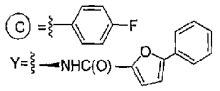
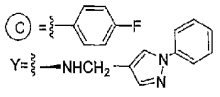
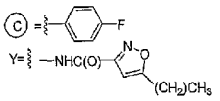
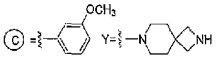
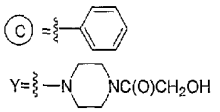
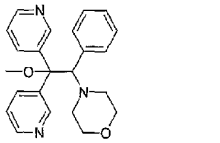
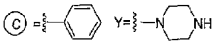
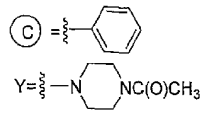
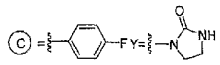
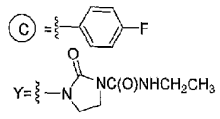
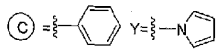
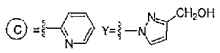
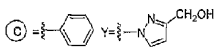
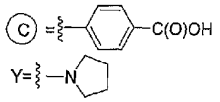
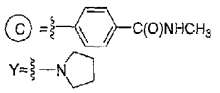
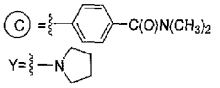
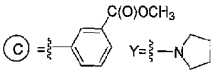
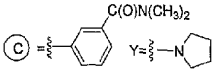
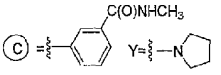
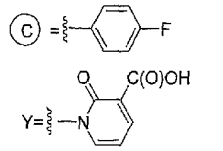
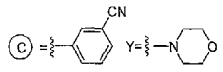
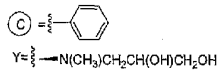
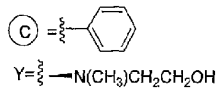
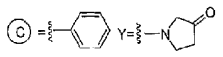
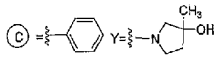
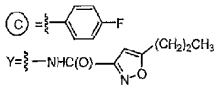
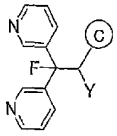
279		N-[(1R)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]-5-phenyl-2-furamide	462.1818
280		(2R)-2-phenyl-2-{[(1-phenyl-1h-pyrazol-4-yl)methyl]amino}-1,1-dipyridin-3-ylethanol	448.2136
280a		(±)-*N*-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-5-propylisoxazole-3-carboxamide	447.1849
281		(±)-2-(2,7-diazaspiro[3.5]non-7-yl)-2-(3-methoxyphenyl)-1,1-dipyridin-3-ylethanol	461.2435
282		(±)-2-phenyl-2-(N-hydroxyacetyl)-piperazin-1-yl-1,1-dipyridin-3-ylethanol	419.2097
283		(±)-4-(2-methoxy-1-phenyl-2,2-dipyridin-3-ylethyl)morpholine	376.2023
284		(±)-2-phenyl-2-piperazin-1-yl-1,1-dipyridin-3-ylethanol	361.2020

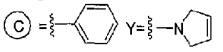
285		(±)-2-(4-acetylpiperazin-1-yl)-2-phenyl-1,1-dipyridin-3-ylethanol	403.2126
286		(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]imidazolidin-2-one	379.1575
287		(±)-*N*-ethyl-3-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-2-oxoimidazolidine-1-carboxamide	450.1
288		(±)-2-phenyl-1,1-dipyridin-3-yl-2-(1*H*-pyrrol-1-yl)ethanol	342.1607
289		(±)-2-[3-(hydroxymethyl)-1H-pyrazol-1-yl]-2-pyridin-2-yl-1,1-dipyridin-3-ylethanol	374.1624
290		(±)-2-[4-(hydroxymethyl)-1H-pyrazol-1-yl]-2-phenyl-1,1-dipyridin-3-ylethanol	373.2
291		(±)-4-(2-hydroxy-2,2-dipyridin-3-yl-1-pyrrolidin-1-ylethyl)benzoic acid	390.1795
292		(±)-4-(2-hydroxy-2,2-dipyridin-3-yl-1-pyrrolidin-1-ylethyl)-N-methylbenzamide	403.2108
293		(±)-4-(2-hydroxy-2,2-dipyridin-3-yl-1-pyrrolidin-1-ylethyl)-N,N-dimethylbenzamide	417.2287
294		(±)-methyl 3-(2-hydroxy-2,2-dipyridin-3-yl-1-pyrrolidin-1-ylethyl)benzoate	404.1956
295		(±)-3-(2-hydroxy-2,2-dipyridin-3-yl-1-pyrrolidin-1-ylethyl)-N,N-dimethylbenzamide	417.2301
296		(±)-3-(2-hydroxy-2,2-dipyridin-3-yl-1-pyrrolidin-1-ylethyl)-N-methylbenzamide	403.2147

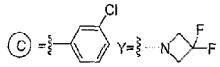
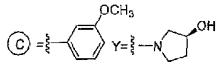
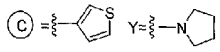
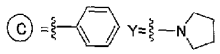
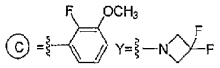
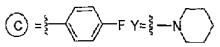
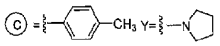
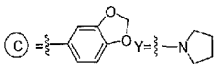
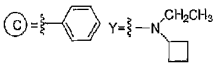
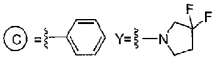
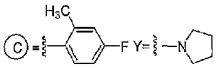
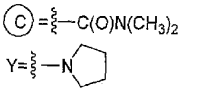
297		(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-2-oxo-1,2-dihydropyridine-3-carboxylic acid	432.1354
298		(±)-3-(2-hydroxy-1-morpholin-4-yl-2,2-dipyridin-3-ylethyl)benzonitrile	387.1817
299		(±)-3-[(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)(methyl)amino]propane-1,2-diol (1:1 mixture diastereomers)	380.1959
300		(±)-2-[hydroxyethyl(methyl)amino]-2-phenyl-1,1-dipyridin-3-ylethanol	350.1851
301		(±)-1-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)pyrrolidin-3-one	360.1709
302		(±)-1-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)-3-methylpyrrolidin-3-ol (5:1 mixture diastereomers)	376.2009
5-1		(±)-*N*-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-5-propylisoxazole-3-carboxamide	447.1849

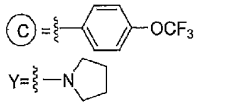
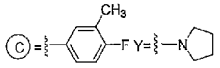
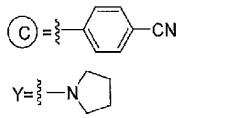
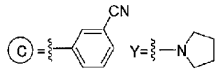
The following fluorinated compounds were made by treatment of Examples 1-201 compounds with DAST, in accordance with literature methods. Structures of compounds 303-319 are represented by defining variables "C" and "Y" of the structure



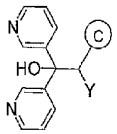
EXAMPLES 303-319

Example	Compound	Name	MS (M+1)
303		(±)-3,3'-[2-(2,5-dihydro-1*H*-pyrrol-1-yl)-1-fluoro-2-phenylethane-1,1-	346.1719

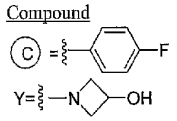
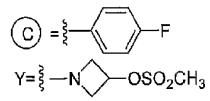
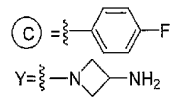
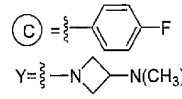
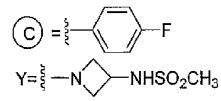
		diyl]dipyridine	
304		(±)-3,3'-[2-(3-chlorophenyl)-2-(3,3-difluoroazetidin-1-yl)-1-fluoroethane-1,1-diyl]dipyridine	404.2
305		(3*R*)-1-[2-fluoro-1-(3-methoxyphenyl)-2,2-dipyridin-3-ylethyl]pyrrolidin-3-ol	394.1921
306		(±)-3,3'-[1-fluoro-2-pyrrolidin-1-yl-2-(3-thienyl)ethane-1,1-diyl]dipyridine	354.1448
307		(±)-3,3'-(1-fluoro-2-phenyl-2-pyrrolidin-1-ylethane-1,1-diyl)dipyridine	348.1871
308		(±)-3,3-difluoro-1-[2-fluoro-1-(2-fluoro-3-methoxyphenyl)-2,2-dipyridin-3-ylethyl]azetidine	418.3
309		(±)-3,3'-[1-fluoro-2-(4-fluorophenyl)-2-piperidin-1-ylethane-1,1-diyl]dipyridine	380.1938
310		(±)-3,3'-[1-fluoro-2-(4-methylphenyl)-2-pyrrolidin-1-ylethane-1,1-diyl]dipyridine	362.2031
311		(±)-3,3'-[2-(1,3-benzodioxol-5-yl)-1-fluoro-2-pyrrolidin-1-ylethane-1,1-diyl]dipyridine	392.1822
312		(±)-*N*-ethyl-*N*-(2-fluoro-1-phenyl-2,2-dipyridin-3-ylethyl)cyclobutanamine	376.2190
313		(±)-3,3'-[2-(3,3-difluoropyrrolidin-1-yl)-1-fluoro-2-phenylethane-1,1-diyl]dipyridine	384.1681
314		(±)-3,3'-[1-fluoro-2-(4-fluoro-2-methylphenyl)-2-pyrrolidin-1-ylethane-1,1-diyl]dipyridine	380.1943
315		(±)-3-fluoro-*N*,*N*-dimethyl-3,3-dipyridin-3-yl-2-pyrrolidin-1-ylpropanamide	343.1932

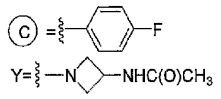
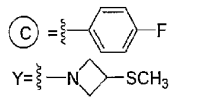
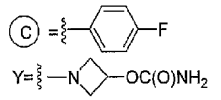
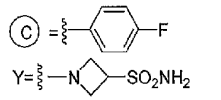
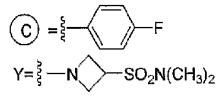
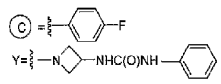
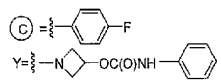
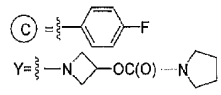
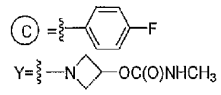
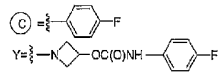
316		(±)-3,3'-{1-fluoro-2-pyrrolidin-1-yl-2-[4-(trifluoromethoxy)phenyl]ethane-1,1-diyl}dipyridine	432.1736
317		(±)-3,3'-[1-fluoro-2-(4-fluoro-3-methylphenyl)-2-pyrrolidin-1-ylethane-1,1-diyl]dipyridine	380.1957
318		(±)-4-(2-fluoro-2,2-dipyridin-3-yl-1-pyrrolidin-1-ylethyl)benzonitrile	373.1834
319		(±)-3-(2-fluoro-2,2-dipyridin-3-yl-1-pyrrolidin-1-ylethyl)benzonitrile	373.1828

The following compounds were made from 2-(3-{[*tert*-butyl(dimethyl)silyl]oxy}azetidin-1-yl)-2-(4-fluorophenyl)-1,1-dipyridin-3-ylethanol, which was prepared in accordance with scheme 5, using methods known to those skilled in the art. Unless otherwise shown, structures of compounds 320-334 and 335-342 are represented by defining variables "C" and "Y" of the structure



EXAMPLES 320-334

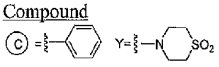
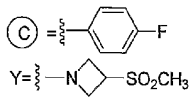
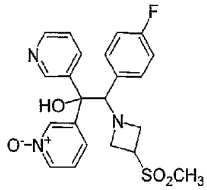
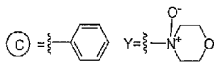
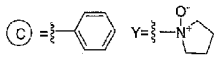
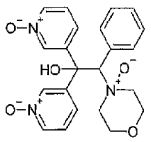
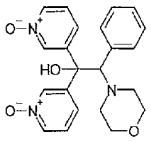
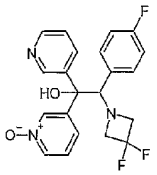
Example	Compound	Name	MS (M+1)
320		(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]azetidin-3-ol	366.1595
321		(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]azetidin-3-yl methanesulfonate	444.1374
322		(±)-2-(3-aminoazetidin-1-yl)-2-(4-fluorophenyl)-1,1-dipyridin-3-ylethanol	365.1763
323		(±)-2-[3-(dimethylamino)azetidin-1-yl]-2-(4-fluorophenyl)-1,1-dipyridin-3-ylethanol	393.2064
324		(±)-*N*-{1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]azetidin-3-	443.1534

		yl}methanesulfonamide	
325		(±)-*N*-{1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]azetidin-3-yl}acetamide	407.1857
326		(±)-2-(4-fluorophenyl)-2-[3-(methylthio)azetidin-1-yl]-1,1-dipyridin-3-ylethanol	396.1554
327		(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]azetidin-3-yl carbamate	409.1667
328		(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]azetidine-3-sulfonamide	429.1357
329		(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-*N*,*N*-dimethylazetidine-3-sulfonamide	457.1700
330		(±)-*N*-{1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]azetidin-3-yl}-*N*'-phenylurea	484.2135
331		(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]azetidin-3-yl phenylcarbamate	485.1966
332		(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]azetidin-3-yl pyrrolidine-1-carboxylate	463.2154
333		(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]azetidin-3-yl methylcarbamate	423.1845
334		(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]azetidin-3-yl (4-fluorophenyl)carbamate	503.1897

The following compounds were made from compounds in Examples 1-201, using oxidation methods known to those skilled in the art. MCPBA oxidation was used to convert example 24 to 335,

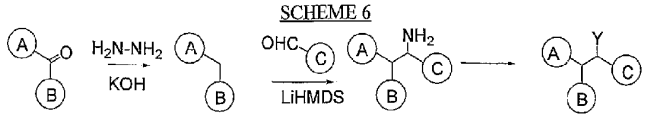
example 316 to 336 and 337, example 1 to 338, and example 16 to 339. Methyltrioxorhenium was used to convert example 1 to 340 and 341, and example 170 to 342

EXAMPLES 335-342

Example	Compound	Name	MS (M+1)
335		(±)-2-(1,1-dioxidothiomorpholin-4-yl)-2-phenyl-1,1-dipyridin-3-ylethanol	410.1513
336		(±)-2-(4-fluorophenyl)-2-[3-(methylsulfonyl)azetidin-1-yl]-1,1-dipyridin-3-ylethanol	428.1457
337		(±)-2-(4-fluorophenyl)-2-[3-(methylsulfonyl)azetidin-1-yl]-1-(1-oxidopyridin-3-yl)-1-pyridin-3-ylethanol (1:1 mixture diastereomers)	444.1391
338		(±)-2-(4-oxidomorpholin-4-yl)-2-phenyl-1,1-dipyridin-3-ylethanol	378.1799
339		(±)-2-(1-oxidopyrrolidin-1-yl)-2-phenyl-1,1-dipyridin-3-ylethanol	362.1859
340		(±)-2-(4-oxidomorpholin-4-yl)-1,1-bis(1-oxidopyridin-3-yl)-2-phenylethanol	410.1711
341		(±)-2-morpholin-4-yl-1,1-bis(1-oxidopyridin-3-yl)-2-phenylethanol	394.1762
342		(±)-2-(3,3-difluoroazetidin-1-yl)-2-(4-fluorophenyl)-1-(1-oxidopyridin-3-yl)-1-pyridin-3-ylethanol (1:1 mixture diastereomers)	402.1447

5

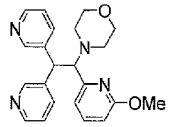
SCHEME 6



The variables C, B, A, and Y in the scheme are as defined in "Formula I".

EXAMPLE 343

(±)-4-[1-(6-methoxypyridin-2-yl)-2,2-dipyridin-3-ylethyl]morpholine



Step A

Dipyridin-3-ylmethanone (1-1, 2.630 g, 14.28 mmol) was suspended in ethylene glycol (28 mL). KOH (1.682 g, 29.98 mmol) was added and the reaction was stirred at RT for 1 hr until most of the solids were dissolved. Hydrazine monohydrate (1.596 mL, 32.84 mmol) was added and the mixture was heated to 185°C. After 1 hr 45 min, the reaction was cooled to RT, diluted with H_2O (150 mL), and extracted with CH_2Cl_2 (4 x 100 mL). The combined organics were washed with water, washed with brine (2x), dried over Na_2SO_4, filtered, and concentrated *in vacuo* to afford 3-(pyridin-3-ylmethyl)pyridine as a light yellow solid. ^{1}H NMR ($CDCl_3$) δ 8.52-8.49 (m, 4H), 7.47-7.45 (m, 2H), 7.25-7.22 (m, 2H), 3.99 (s, 2H). [M+H]+ = 171.2.

Step B

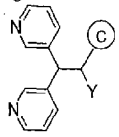
LiHMDS (2.45 mL, 1.2 M in THF, 2.94 mmole) was added to a flame-dried round bottom flask. The mixture was cooled to 0°C then 6-methoxypyridine-2-carbaldehyde (Comins, Daniel L.; Killpack, Michael O. *J.Org.Chem.* **1990**, *55*, 69-73, 161 mg, 1.18 mmole) was added. After 30 minutes di-3-pyridylmethane (200 mg, 1.18 mmole) in dry THF (2.0 mL) was added. After 2 hr the mixture was warmed to RT, quenched with saturated NH_4Cl, and extracted with CH_2Cl_2(3x) and iBuOH (2x). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated. The residue was taken up in MeOH (5 mL) and H_2NOH (0.4 mL, 50% in H_2O) was added. After 18 hr the mixture was concentrated. Flash column (gradient, 0-10% MeOH/CH_2Cl_2) gave 1-(6-methoxypyridin-2-yl)-2,2-dipyridin-3-ylethanamine as a pale yellow oil (168 mg, 47%): ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.64 (d, J = 1.95 Hz, 1 H), 8.51 (dd, J = 1.46 and 3.17 Hz, 1 H), 8.36 (d, J = 1.95 Hz, 1 H), 8.32 (dd, J = 1.46 and 3.18 Hz, 1 H), 7.76 (d, J = 7.82 Hz, 1 H), 7.49 (d, J = 8.06 Hz, 1 H), 7.37-7.27 (m, 2 H), 7.09 (m, 1 H), 6.56 (d, J = 7.08 Hz, 1 H), 6.52 (d, J = 7.81 Hz, 1 H), 4.59 (d, J = 9.28 Hz, 1 H), 4.42 (d, J = 9.28 Hz, 1 H), 3.91 (s, 3 H).

Step C

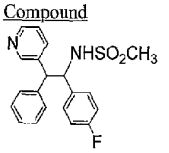
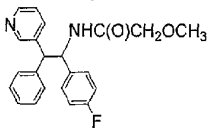
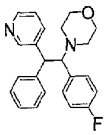
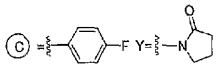
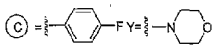
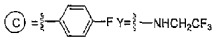
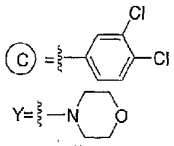
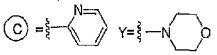
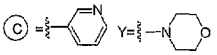
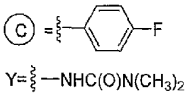
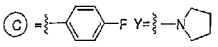
To a solution of 1-(6-methoxypyridin-2-yl)-2,2-dipyridin-3-ylethanamine (75 mg, 0.25 mmole) in CH_3CN (1 mL) was added a solution of 2,2'-oxydiacetaldehyde in H_2O (1.47 mL, 0.5 M, 0.73 mmole). After 10 minutes $NaBH_3CN$ (92 mg, 1.47 mmole) was added. After 2 hr 1N HCl (2 mL) was added.

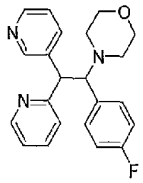
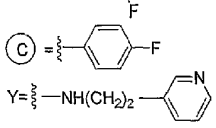
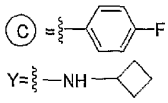
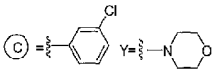
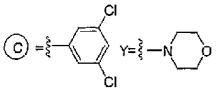
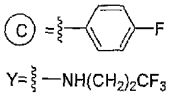
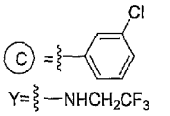
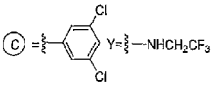
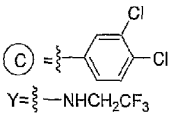
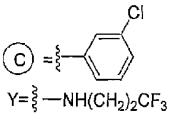
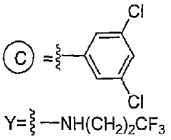
After 1 hr the pH was adjusted to 8 and the mixture extracted with CH_2Cl_2 (3x) and iBuOH (1x). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated. Flash column (gradient, 0-10% MeOH/CH_2Cl_2) gave mixed fractions. Fractions containing the product were pooled and concentrated. The mixture was purified by reverse phase HPLC (5-100% CH_3CN/H_2O + 0.1% TFA). Fractions containing the product were pooled, made basic with saturated $NaHCO_3$, and extracted with CH_2Cl_2 (3x). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated to give the title compound (15 mg, 16%) as a white solid: ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.70 (bs, 1 H), 8.48 (bs, 1 H), 8.39 (bs, 1 H), 8.26 (bd, J = 3.9 Hz, 1 H), 7.71 (d, J = 7.82 Hz, 1 H), 7.44-7.36 (m, 2 H), 7.28 (m, 1 H), 7.03 (m, 1 H), 6.52 (m, 2 H), 5.01 (d, J = 11.72 Hz, 1 H), 4.27 (d, J = 11.72 Hz, 1 H), 3.96 (s, 3 H), 3.49 (m, 2 H), 3.35 (m, 2 H), 2.63 (m, 2 H), 2.42 (m, 2 H); HRMS, calc'd for $C_{22}H_{25}N_4O_2$ (M+1), 377.1972; found 377.1944.

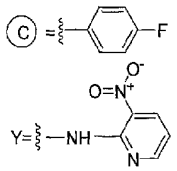
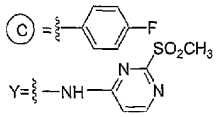
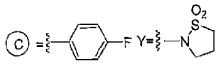
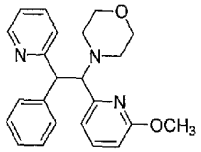
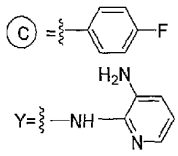
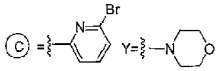
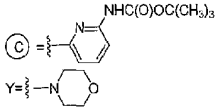
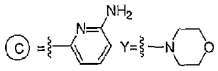
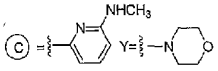
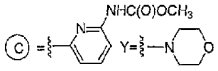
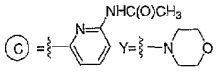
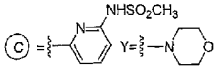
The following compounds were made according to Scheme 6, where intermediates in the Scheme were modified according to literature methods. Example 347 was prepared by reaction of the corresponding (1-aryl-2,2-dipyridin-3-ylethyl)amine with 4-chlorobutyryl chloride followed by ring closure under basic conditions. Example 368 was prepared by reaction of the amine with 3-chloropropanesulfonyl chloride followed by ring closure under basic conditions. Examples 372, 375-378 were prepared by palladium catalyzed amination of 371 with the corresponding carbamate, amide, sulfonamide or urea. Example 373 was prepared by deprotection of 372. Example 379 was prepared by methylation of 372 and deprotection. Examples 380 and 381 were prepared from the corresponding (1-aryl-2,2-dipyridin-3-ylethyl)amine using the method of Tschaen et al. (*J. Org. Chem.* **1995**, *60*, 4324). Example 394 was prepared by treatment of the corresponding primary amine with methyl-4-bromo-2-oxopentanoate under reductive amination conditions. Ester reduction of the compound in example 394 provided example 395. Ester hydrolysis of the compound in example 394 provided the corresponding carboxylic acid, which was subjected to standard peptide coupling conditions to provide the amides in examples 396, 397, and 398. Example 401 was prepared by reductive amination of [1-(3-bromophenyl)-2,2-dipyridin-3-ylethyl]amine with methyl [methyl(2-oxoethyl)amino](oxo)acetate, according to a published procedure (*Tetrahedron Lett.* **2000**, *41*, 8735). Examples 405 and 406 were prepared by reaction of the corresponding (1-aryl-2,2-dipyridin-3-ylethyl)amine with 2-chloroethyl chloroformate followed by ring closure under basic conditions. Unless otherwise shown, structures of compounds 344-420 and 6-1 to 6-87 are represented by defining variables "C" and "Y" of the structure

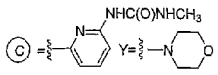
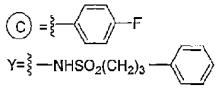
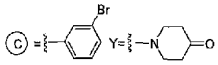
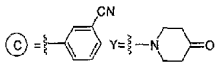
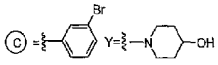
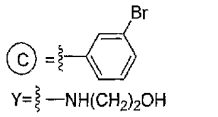
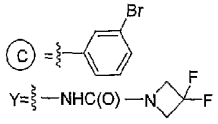
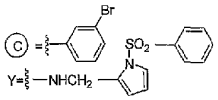
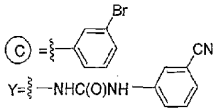
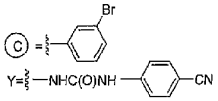
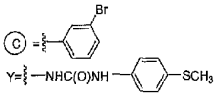
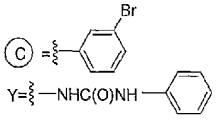


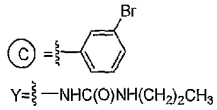
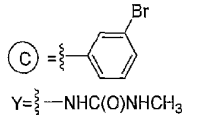
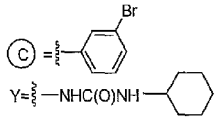
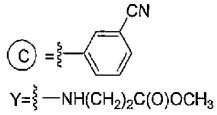
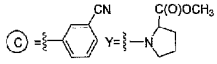
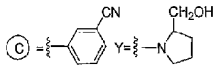
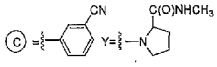
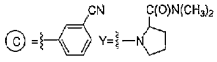
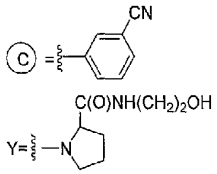
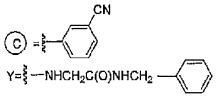
EXAMPLES 344-420 and 6-1 to 6-87

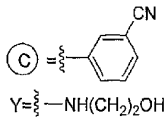
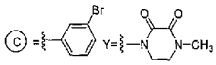
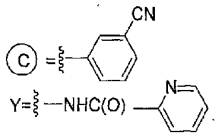
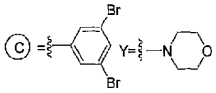
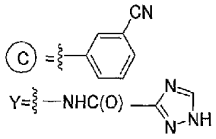
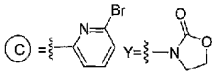
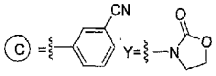
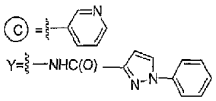
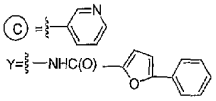
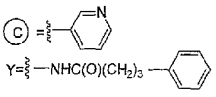
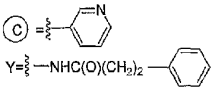
Example	Compound	Name	MS (M+1)
344		(±)-N-[1-(4-fluorophenyl)-2-phenyl-2-pyridin-3-ylethyl]methanesulfonamide	371.3
345		(±)-N-[1-(4-fluorophenyl)-2-phenyl-2-pyridin-3-ylethyl]-2-methoxyacetamide	365.1642
346		(±)-4-[1-(4-fluorophenyl)-2-phenyl-2-pyridin-3-ylethyl]morpholine	363.1862
347		(±)-1-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl]pyrrolidin-2-one	362.1663
348		(±)-4-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl]morpholine	364.1
349		(±)- [1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl](2,2,2-trifluoroethyl)amine	376.2
350		(±)-4-[1-(3,4-dichlorophenyl)-2,2-dipyridin-3-ylethyl]morpholine	414.1111
351		(±)-4-(1-pyridin-2-yl-2,2-dipyridin-3-ylethyl)morpholine	347.1893
352		(±)-4-(1,2,2-tripyridin-3-ylethyl)morpholine	347.1896
353		(±)-*N*'-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl]-*N*,*N*-dimethylurea	365.1763
354		(±)-3,3'-[2-(4-fluorophenyl)-2-pyrrolidin-1-ylethane-1,1-diyl]dipyridine	348.1879

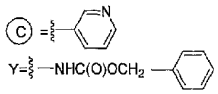
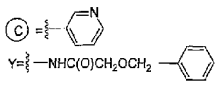
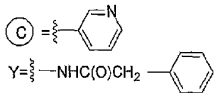
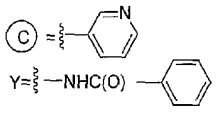
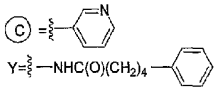
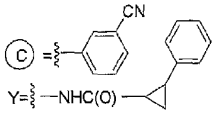
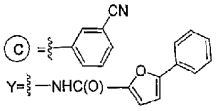
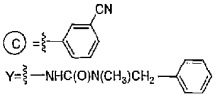
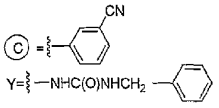
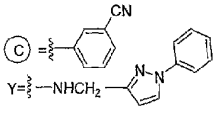
355		(±)-4-[1-(4-fluorophenyl)-2-pyridin-2-yl-2-pyridin-3-ylethyl]morpholine	364.1834
356		(±)- [1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl](2-pyridin-3-ylethyl)amine	399.2
357		(±)-N-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl]cyclobutanamine	347.9
358		(±)-4-[1-(3-chlorophenyl)-2,2-dipyridin-3-ylethyl]morpholine	380.1504
359		(±)-4-[1-(3,5-dichlorophenyl)-2,2-dipyridin-3-ylethyl]morpholine	414.1114
360		(±)-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl](3,3,3-trifluoropropyl)amine	390.1
361		(±)-[1-(3-chlorophenyl)-2,2-dipyridin-3-ylethyl](2,2,2-trifluoroethyl)amine	392.1
362		(±)-[1-(3,5-dichlorophenyl)-2,2-dipyridin-3-ylethyl](2,2,2-trifluoroethyl)amine	426.0
363		(±)-[1-(3,4-dichlorophenyl)-2,2-dipyridin-3-ylethyl](2,2,2-trifluoroethyl)amine	427.8
364		(±)-N-[1-(3-chlorophenyl)-2,2-dipyridin-3-ylethyl]-3,3,3-trifluoropropan-1-amine	406.0
365		(±)-*N*-[1-(3,5-dichlorophenyl)-2,2-dipyridin-3-ylethyl]-3,3,3-trifluoropropan-1-amine	441.8

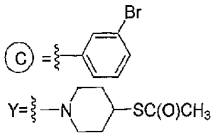
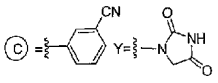
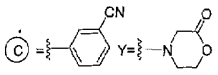
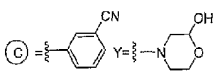
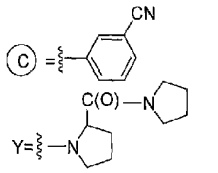
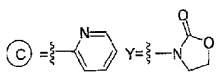
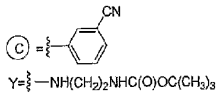
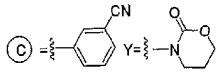
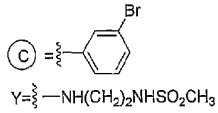
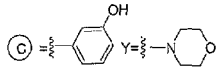
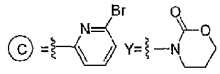
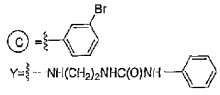
366		(±)-N-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl]-3-nitropyridin-2-amine	416.1
367		(±)-N-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl]-2-(methylsulfonyl)pyrimidin-4-amine	450.1
368		(±)-3,3'-[2-(1,1-dioxidoisothiazolidin-2-yl)-2-(4-fluorophenyl)ethane-1,1-diyl]dipyridine	398.1
369		(±)-4-[1-(6-methoxypyridin-2-yl)-2-phenyl-2-pyridin-2-ylethyl]morpholine	398.1830 (M+Na+)
370		(±)-N~2~-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl]pyridine-2,3-diamine	386.1
371		(±)-4-[1-(6-bromopyridin-2-yl)-2,2-dipyridin-3-ylethyl]morpholine	425.1005
372		(±)-tert-butyl [6-(1-morpholin-4-yl-2,2-dipyridin-3-ylethyl)pyridin-2-yl]carbamate	462.2547
373		(±)-6-(1-morpholin-4-yl-2,2-dipyridin-3-ylethyl)pyridin-2-amine	362.1957
374		(±)-N-methyl-6-(1-morpholin-4-yl-2,2-dipyridin-3-ylethyl)pyridin-2-amine	376.2126
375		(±)-methyl [6-(1-morpholin-4-yl-2,2-dipyridin-3-ylethyl)pyridin-2-yl]carbamate	420.2017
376		(±)-N-[6-(1-morpholin-4-yl-2,2-dipyridin-3-ylethyl)pyridin-2-yl]acetamide	404.2068
377		(±)-N-[6-(1-morpholin-4-yl-2,2-dipyridin-3-ylethyl)pyridin-2-	440.1734

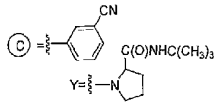
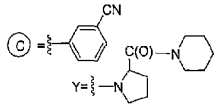
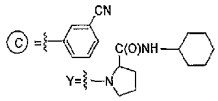
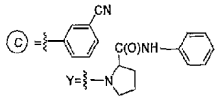
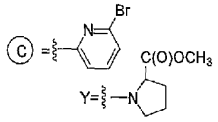
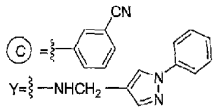
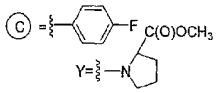
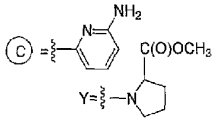
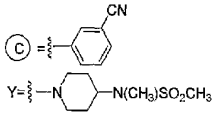
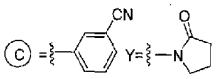
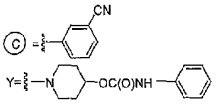
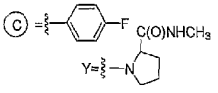
		yl]methanesulfonamide	
378		(±)-N-methyl-N'-[6-(1-morpholin-4-yl-2,2-dipyridin-3-ylethyl)pyridin-2-yl]urea	419.2182
379		(±)-N-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl]-3-phenylpropane-1-sulfonamide	476.1794
380		(±)-1-[1-(3-bromophenyl)-2,2-dipyridin-3-ylethyl]piperidin-4-one	436.1023
381		(±)-3-[1-(4-oxopiperidin-1-yl)-2,2-dipyridin-3-ylethyl]benzonitrile	383.1859
382		(±)-1-[1-(3-bromophenyl)-2,2-dipyridin-3-ylethyl]piperidin-4-ol	438.1181
383		(±)-2-{[1-(3-bromophenyl)-2,2-dipyridin-3-ylethyl]amino}ethanol	398.0875
384		(±)-N-[1-(3-bromophenyl)-2,2-dipyridin-3-ylethyl]-3,3-difluoroazetidine-1-carboxamide	473.0779
385		(±)-[1-(3-bromophenyl)-2,2-dipyridin-3-ylethyl]{[1-(phenylsulfonyl)-1H-pyrrol-2-yl]methyl}amine	573.0959
386		(±)-N-[1-(3-bromophenyl)-2,2-dipyridin-3-ylethyl]-N'-(3-cyanophenyl)urea	498.0930
387		(±)-N-[1-(3-bromophenyl)-2,2-dipyridin-3-ylethyl]-N'-(4-cyanophenyl)urea	498.0930
388		(±)-N-[1-(3-bromophenyl)-2,2-dipyridin-3-ylethyl]-N'-[4-(methylthio)phenyl]urea	519.0850
389		(±)-N-[1-(3-bromophenyl)-2,2-dipyridin-3-ylethyl]-N'-phenylurea	473.0966

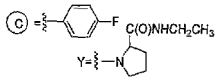
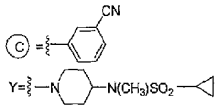
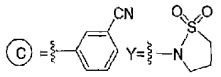
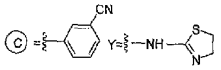
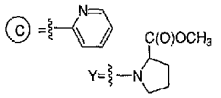
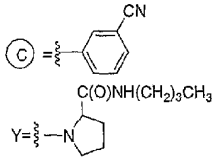
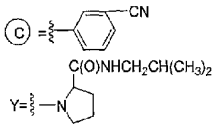
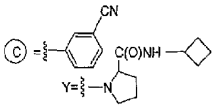
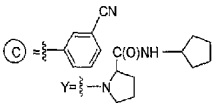
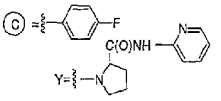
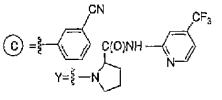
390		(±)-N-[1-(3-bromophenyl)-2,2-dipyridin-3-ylethyl]-N'-propylurea	439.1134
391		(±)-N-[1-(3-bromophenyl)-2,2-dipyridin-3-ylethyl]-N'-methylurea	411.0821
392		(±)-N-[1-(3-bromophenyl)-2,2-dipyridin-3-ylethyl]-N'-cyclohexylurea	479.1448
393		(±)-methyl N-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-beta-alaninate	387.1815
394		(±)-methyl 1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]prolinate (diastereomer A)	413.1978
395		(±)-3-{1-[2-(hydroxymethyl)pyrrolidin-1-yl]-2,2-dipyridin-3-ylethyl}benzonitrile (diastereomer A)	385.2020
396		(±)-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-N-methylprolinamide (diastereomer A)	412.2137
397		(±)-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-N,N-dimethylprolinamide (diastereomer A)	446.2291
398		(±)-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-N-(2-hydroxyethyl)prolinamide (diastereomer A)	442.2235
399		(±)-N1-benzyl-N2-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]glycinamide	448.2143

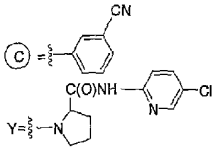
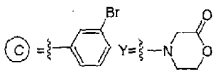
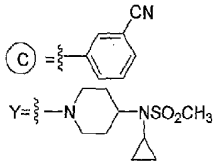
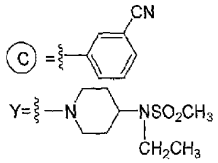
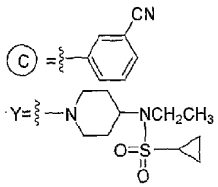
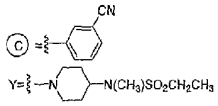
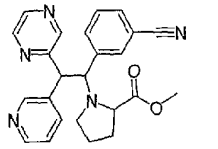
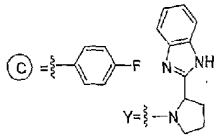
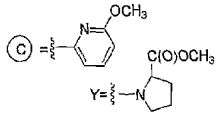
400		(±)-3-{1-[(2-hydroxyethyl)amino]-2,2-dipyridin-3-ylethyl}benzonitrile	345.1
401		(±)-1-[1-(3-bromophenyl)-2,2-dipyridin-3-ylethyl]-4-methylpiperazine-2,3-dione	465.0928
402		(±)-N-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]pyridine-2-carboxamide	406.1652
403		(±)-4-[1-(3,5-dibromophenyl)-2,2-dipyridin-3-ylethyl]morpholine	502.0123
404		(±)-N-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-1H-1,2,4-triazole-3-carboxamide	396.1578
405		(±)-3-[1-(6-bromopyridin-2-yl)-2,2-dipyridin-3-ylethyl]-1,3-oxazolidin-2-one	425.0603
406		(±)-3-[1-(2-oxo-1,3-oxazolidin-3-yl)-2,2-dipyridin-3-ylethyl]benzonitrile	371.1473
407		(±)-1-phenyl-N-(1,2,2-tripyridin-3-ylethyl)-1H-pyrazole-4-carboxamide	447.1928
408		(±)-5-phenyl-N-(1,2,2-tripyridin-3-ylethyl)-2-furamide	447.1814
409		(±)-4-phenyl-N-(1,2,2-tripyridin-3-ylethyl)butanamide	423.2181
410		(±)-3-phenyl-N-(1,2,2-tripyridin-3-ylethyl)propanamide	409.2021

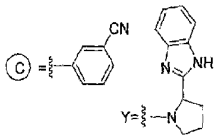
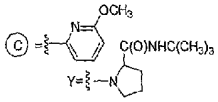
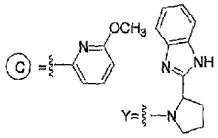
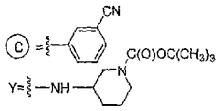
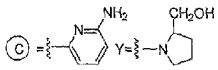
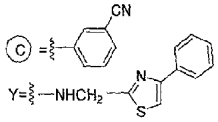
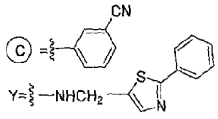
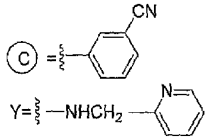
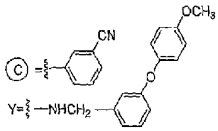
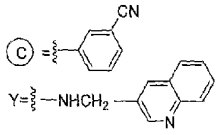
411		(±)-benzyl (1,2,2-tripyridin-3-ylethyl)carbamate	411.1805
412		(±)-2-(benzyloxy)-N-(1,2,2-tripyridin-3-ylethyl)acetamide	425.1955
413		(±)-2-phenyl-N-(1,2,2-tripyridin-3-ylethyl)acetamide	395.1867
414		(±)-N-(1,2,2-tripyridin-3-ylethyl)benzamide	381.1671
415		(±)-5-phenyl-N-(1,2,2-tripyridin-3-ylethyl)pentanamide	437.6
416		(±)-N-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-2-phenylcyclopropanecarboxamide	445.1980
417		(±)-N-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-5-phenyl-2-furamide	471.1780
418		(±)-N-benzyl-N'-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-N-methylurea	448.2105
419		(±)-N-benzyl-N'-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]urea	434.1936
420		(±)-3-(1-{[(1-phenyl-1H-pyrazol-4-yl)methyl]amino}-2,2-dipyridin-3-ylethyl)benzonitrile	457.7

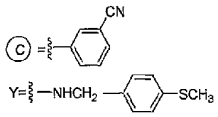
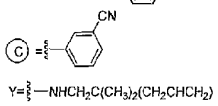
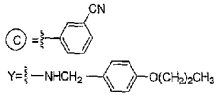
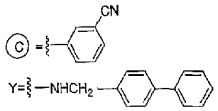
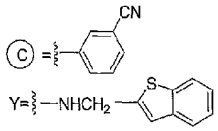
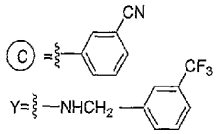
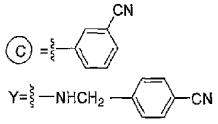
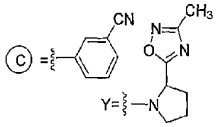
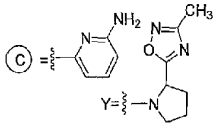
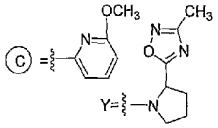
6-1		(S)-{1-[1-(3-bromophenyl)-2,2-dipyridin-3-ylethyl]piperidin-4-yl} ethanethioate	496.1062
6-2		(±)-3-[1-(2,4-dioxoimidazolidin-1-yl)-2,2-dipyridin-3-ylethyl]benzonitrile	384.1
6-3		(±)-3-[1-(2-oxomorpholin-4-yl)-2,2-dipyridin-3-ylethyl]benzonitrile	385.1655
6-4		(±)-3-[1-(2-hydroxymorpholin-4-yl)-2,2-dipyridin-3-ylethyl]benzonitrile	387.1815
6-5		(±)-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-*N*,*N*-bis(1-{1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]prolyl}-pyrrolidin-2-yl)prolinamide	452.2435
6-6		(±)-3-(1-pyridin-2-yl-2,2-dipyridin-3-ylethyl)-1,3-oxazolidin-2-one	347.1487
6-7		(±)-*tert*-butyl 2-{[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]amino}ethylcarbamate	444.2414
6-8		(±)-3-[1-(2-oxo-1,3-oxazinan-3-yl)-2,2-dipyridin-3-ylethyl]benzonitrile	384.1655
6-9		(±)-*N*-(2-{[1-(3-bromophenyl)-2,2-dipyridin-3-ylethyl]amino}ethyl)-methanesulfonamide	475.08
6-10		(±)-3-(1-morpholin-4-yl-2,2-dipyridin-3-ylethyl)phenol	362.1864
6-11		(±)-3-[1-(6-bromopyridin-2-yl)-2,2-dipyridin-3-ylethyl]-1,3-oxazinan-2-one	439.0767
6-12		(±)-*N*-(2-{[1-(3-bromophenyl)-2,2-dipyridin-3-ylethyl]amino}-ethyl)-*n*'-phenylurea	516.1428

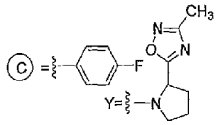
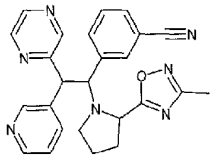
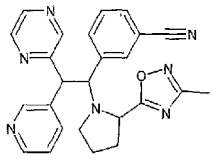
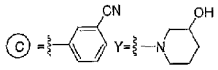
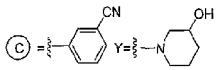
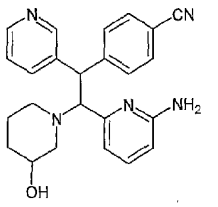
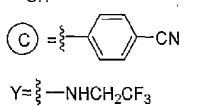
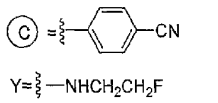
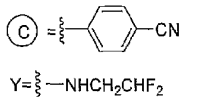
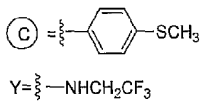
6-13		(±)-*N*-(*tert*-butyl)-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]prolinamide	454.261
6-14		(±)-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-piperidinylprolinamide	466.2577
6-15		(±)-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-*N*-cyclohexylprolinamide	480.1538
6-16		(±)-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-*N*-phenylprolinamide	474.2268
6-17		(±)-methyl 1-[1-(6-bromopyridin-2-yl)-2,2-dipyridin-3-ylethyl]prolinate	467.1065
6-18		(±)-3-(1-{[(1-phenyl-1H-pyrazol-4-yl)methyl]amino}-2,2-dipyridin-3-ylethyl)benzonitrile	404.2073
6-19		(±)-methyl 1-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl]prolinate	406.192
6-20		(±)-methyl 1-[1-(6-aminopyridin-2-yl)-2,2-dipyridin-3-ylethyl]prolinate	404.2073
6-21		(±)-*N*-{1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]piperidin-4-yl}-*N*-methylmethanesulfonamide	476.2107
6-22		(±)-3-[1-(2-oxopyrrolidin-1-yl)-2,2-dipyridin-3-ylethyl]benzonitrile	369.172
6-23		(±)-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]piperidin-4-yl phenylcarbamate	504.2386
6-24		(±)-1-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl]-*N*-methylprolinamide	405.2085

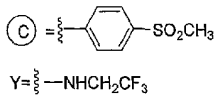
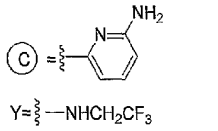
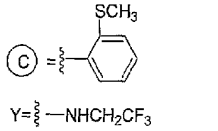
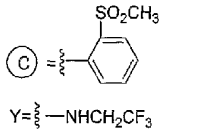
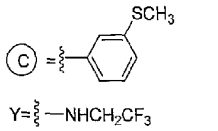
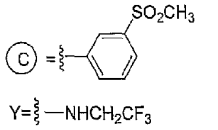
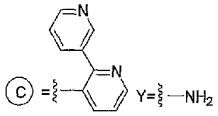
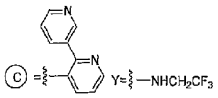
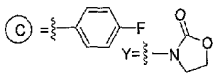
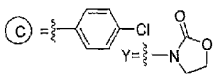
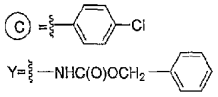
6-25		(±)-*N*-ethyl-1-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl]prolinamide	419.2228
6-26		(±)-*N*-{1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]piperidin-4-yl}-*N*-methylcyclopropanesulfonamide	502.2268
6-27		(±)-3-[1-(1,1-dioxidoisothiazolidin-2-yl)-2,2-dipyridin-3-ylethyl]benzonitrile	405.1381
6-28		(±)-3-[1-(4,5-dihydro-1,3-thiazol-2-ylamino)-2,2-dipyridin-3-ylethyl]benzonitrile	471.1398
6-29		(±)-methyl 1-(1-pyridin-2-yl-2,2-dipyridin-3-ylethyl)prolinate	389.1964
6-30		(±)-*N*-butyl-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]prolinamide	454.2573
6-31		(±)-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-*N*-isobutylprolinamide	454.2603
6-32		(±)-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-*N*-cyclobutylprolinamide	452.2435
6-33		(±)-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-*N*-cyclopentylprolinamide	466.2597
6-34		(±)-1-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl]-*N*-pyridin-2-ylprolinamide	468.2193
6-35		(±)-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-*N*-[4-(trifluoromethyl)pyridin-2-yl]prolinamide	543.2113

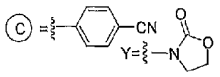
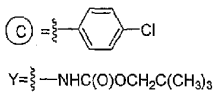
6-36		(±)-*N*-(5-chloropyridin-2-yl)-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]prolinamide	509.1885
6-37		(±)-4-[1-(3-bromophenyl)-2,2-dipyridin-3-ylethyl]morpholin-2-one	438.0836
6-38		(±)-*N*-{1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]piperidin-4-yl}-*N*-cyclopropylmethanesulfonamide	502.2274
6-39		(±)-*N*-{1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]piperidin-4-yl}-*N*-ethylmethanesulfonamide	490.2277
6-40		(±)-*N*-{1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]piperidin-4-yl}-*N*-ethylcyclopropanesulfonamide	516.4
6-41		(±)-*N*-{1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]piperidin-4-yl}-*N*-methylethanesulfonamide	490.2301
6-42		(±)-methyl 1-[1-(3-cyanophenyl)-2-pyrazin-2-yl-2-pyridin-3-ylethyl]prolinate	414.1946
6-43		(±)-2-{1-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl]pyrrolidin-2-yl}-1H-benzimidazole	464.2278
6-44		(±)-methyl 1-[1-(6-methoxypyridin-2-yl)-2,2-dipyridin-3-ylethyl]prolinate	419.2099

6-45		(±)-3-{1-[2-(1H-benzimidazol-2-yl)pyrrolidin-1-yl]-2,2-dipyridin-3-ylethyl}benzonitrile	471.2305
6-46		(±)-*N*-(*tert*-butyl)-1-[1-(6-methoxypyridin-2-yl)-2,2-dipyridin-3-ylethyl]prolinamide	460.2725
6-47		(±)-2-{1-[1-(6-methoxypyridin-2-yl)-2,2-dipyridin-3-ylethyl]pyrrolidin-2-yl}-1H-benzimidazole	477.2426
6-48		(±)-*tert*-butyl 3-{[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]amino}piperidine-1-carboxylate	484.5
6-49		(±)-{1-[2-(6-aminopyridin-2-yl)-1,2-dipyridin-3-ylethyl]-pyrrolidin-2-yl}methanol	376.2137
6-50		(±)-3-(1-{[(4-phenyl-1,3-thiazol-2-yl)methyl]amino}-2,2-dipyridin-3-ylethyl)benzonitrile	474.1764
6-51		(±)-3-(1-{[(2-phenyl-1,3-thiazol-5-yl)methyl]amino}-2,2-dipyridin-3-ylethyl)benzonitrile	474.1772
6-52		(±)-3-{2,2-dipyridin-3-yl-1-[(pyridin-2-ylmethyl)amino]ethyl}benzonitrile	392.1875
6-53		(±)-3-(1-{[3-(4-methoxy-phenoxy)benzyl]amino}-2,2-dipyridin-3-ylethyl)benzonitrile	513.2304
6-54		(±)-3-{2,2-dipyridin-3-yl-1-[(quinolin-3-ylmethyl)amino]-ethyl}benzonitrile	442.2035

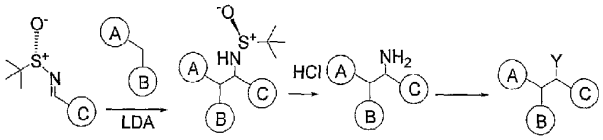
6-55		(±)-3-(1-{[4-(methylthio)benzyl]amino}-2,2-dipyridin-3-ylethyl)benzonitrile	437.1817
6-56		(±)-3-{1-[(2,2-dimethylpent-4-en-1-yl)amino]-2,2-dipyridin-3-ylethyl}benzonitrile	397.2395
6-57		(±)-3-{1-[(4-propoxybenzyl)amino]-2,2-dipyridin-3-ylethyl}benzonitrile	449.2351
6-58		(±)-3-{1-[(biphenyl-4-ylmethyl)amino]-2,2-dipyridin-3-ylethyl}benzonitrile	467.2251
6-59		(±)-3-{1-[(1-benzothien-2-ylmethyl)amino]-2,2-dipyridin-3-ylethyl}benzonitrile	447.1645
6-60		(±)-3-(2,2-dipyridin-3-yl-1-{[3-(trifluoromethyl)benzyl]amino}ethyl)benzonitrile	459.1804
6-61		(±)-3-{1-[(4-cyanobenzyl)amino]-2,2-dipyridin-3-ylethyl}benzonitrile	416.1876
6-62		(±)-3-{1-[2-(3-methyl-1,2,4-oxadiazol-5-yl)pyrrolidin-1-yl]-2,2-dipyridin-3-ylethyl}benzonitrile	437.2085
6-63		(±)-6-{1-[2-(3-methyl-1,2,4-oxadiazol-5-yl)pyrrolidin-1-yl]-2,2-dipyridin-3-ylethyl}pyridin-2-amine	428.2174
6-64		(±)-2-methoxy-6-{1-[2-(3-methyl-1,2,4-oxadiazol-5-yl)pyrrolidin-1-yl]-2,2-dipyridin-3-ylethyl}pyridine	443.2168

6-65		(±)-3-{2-(4-fluorophenyl)-2-[2-(3-methyl-1,2,4-oxadiazol-5-yl)pyrrolidin-1-yl]-1-pyridin-3-ylethyl}pyridine	430.2014
6-66		(±)-3-{1-[2-(3-methyl-1,2,4-oxadiazol-5-yl)pyrrolidin-1-yl]-2-pyrazin-2-yl-2-pyridin-3-ylethyl}benzonitrile	438.2012
6-67		(±)-3-{1-[2-(3-methyl-1,2,4-oxadiazol-5-yl)pyrrolidin-1-yl]-2-pyrazin-2-yl-2-pyridin-3-ylethyl}benzonitrile	438.2013
6-68		(±)-3-[1-(3-hydroxypiperidin-1-yl)-2,2-dipyridin-3-ylethyl]-benzonitrile (Diastereomer A)	385.2012
6-69		(±)-3-[1-(3-hydroxypiperidin-1-yl)-2,2-dipyridin-3-ylethyl]-benzonitrile (Diastereomer B)	385.2012
6-70		(±)-4-[2-(6-aminopyridin-2-yl)-2-(3-hydroxypiperidin-1-yl)-1-pyridin-3-ylethyl]benzonitrile	400.2129
6-71		(±)-4-{2,2-dipyridin-3-yl-1-[(2,2,2-trifluoroethyl)amino]-ethyl}benzonitrile	383.145
6-72		(±)-4-{1-[(2-fluoroethyl)amino]-2,2-dipyridin-3-ylethyl}benzonitrile	347.167
6-73		(±)-4-{1-[(2,2-difluoroethyl)amino]-2,2-dipyridin-3-ylethyl}benzonitrile	365.1576
6-74		(±)-*N*-{1-[4-(methylthio)-phenyl]-2,2-dipyridin-3-ylethyl}-*N*-(2,2,2-trifluoroethyl)amine	404.1407

6-75		(±)-*N*-{1-[4-(methylsulfonyl)-phenyl]-2,2-dipyridin-3-ylethyl}-*N*-(2,2,2-trifluoroethyl)amine	436.1305
6-76		(±)-6-{2,2-dipyridin-3-yl-1-[(2,2,2-trifluoroethyl)amino]ethyl}pyridin-2-amine	374.1596
6-77		(±)-*N*-{1-[2-(methylthio)phenyl]-2,2-dipyridin-3-ylethyl}-*N*-(2,2,2-trifluoroethyl)amine	404.1411
6-78		(±)-*N*-{1-[2-(methylsulfonyl)phenyl]-2,2-dipyridin-3-ylethyl}-*N*-(2,2,2-trifluoroethyl)amine	436.1301
6-79		(±)-*N*-{1-[3-(methylthio)phenyl]-2,2-dipyridin-3-ylethyl}-*N*-(2,2,2-trifluoroethyl)amine	404.1404
6-80		(±)-*N*-{1-[3-(methylsulfonyl)phenyl]-2,2-dipyridin-3-ylethyl}-*N*-(2,2,2-trifluoroethyl)amine	436.1305
6-81		(±)-1-(2,3'-bipyridin-3-yl)-2,2-dipyridin-3-ylethanamine	354
6-82		(±)-1-(2,3'-bipyridin-3-yl)-2,2-dipyridin-3-yl-*N*-(2,2,2-trifluoroethyl)ethanamine	436.1
6-83		(±)-3-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl]-1,3-oxazolidin-2-one	364.0
6-84		(±)-3-[1-(4-chlorophenyl)-2,2-dipyridin-3-ylethyl]-1,3-oxazolidin-2-one	371.1
6-85		benzyl (±)-1-(4-chlorophenyl)-2,2-dipyridin-3-ylethylcarbamate	444.0

6-86		(±)-4-[1-(2-oxo-1,3-oxazolidin-3-yl)-2,2-dipyridin-3-ylethyl]benzonitrile	317.15
6-87		(±)-neopentyl 1-(4-chlorophenyl)-2,2-dipyridin-3-ylethylcarbamate	424

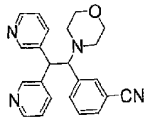
SCHEME 7



The variables C, B, A, and Y in the scheme are as defined in "Formula I".

EXAMPLE 421

3-(1-morpholin-4-yl-2,2-dipyridin-3-ylethyl)benzonitrile (enantiomer B)



Step A

In a flame dried flask under N_2, 3-cyanobenzaldehyde (7.050 g, 53.76 mmol) was dissolved in anhydrous dioxane (100 mL). Ti(IV) ethoxide (28.183 mL, 134.40 mmol) was added followed by (S)-(-)-2-methyl-2-propanesulfinamide (7.167 g, 59.14 mmol). The rxn was heated to 110°C. After 2.5 hr the reaction was cooled to RT and brine (150 mL) was added. A precipitate formed and the reaction was rapidly stirred for 1hr. The suspension was filtered through celite and the filter cake was washed with brine and ethyl acetate. The layers of the filtrate were separated. The aqueous layer was extracted with ethyl acetate (1x). The combined organics were dried over Na_2SO_4, filtered, and concentrated *in vacuo* to afford (S)-N-[(3-cyanophenyl)methylidene]-2-methylpropane-2-sulfinamide as a light orange solid. ^1H NMR (CD_3OD) δ 8.61 (s, 1H), 8.26 (s, 1H), 8.22-8.20 (m, 1H), 7.94-7.92 (m, 1H), 7.72 (t, 1H, J = 7.81 Hz), 1.28 (s, 9H).

Step B

In a flame dried flask under N_2, diisopropylamine (1.647 mL, 11.75 mmol) was dissolved in anhydrous THF (5 mL) and the solution was cooled to 0°C. nBuLi (2.5 M solution in hexanes, 4.406 mL, 11.02 mmol) was added and the reaction was stirred at 0°C for 15 min. A solution of 3-(pyridin-3-ylmethyl)pyridine (1.250 g, 7.34 mmol) in anhydrous THF (15 mL) was slowly added and the reaction became dark red. After 15 min, a solution of (S)-N-[(3-cyanophenyl)methylidene]-2-methylpropane-2-sulfinamide (1.893 g, 8.08 mmol) in anhydrous THF (10 mL) was added. The reaction was stirred at 0°C for 2.5 h and was quenched with saturated aqueous NH_4Cl (150 mL). The product was extracted with

ethyl acetate (4 x 100 mL). The combined organics were dried over Na_2SO_4, filtered, concentrated *in vacuo* and purified by reverse phase HPLC (DeltaPak C18, 47 mm x 300 mm, 15 □, 0% CH_3OH / 100% H_2O to 100% CH_3OH / 0% H_2O). The fractions containing each diastereomer were separately combined and concentrated *in vacuo* to afford N-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-2-methylpropane-2-sulfinamide as two diastereomers;

diastereomer A as a foamy white solid and diastereomer B as a white solid.

Diastereomer A: ^{1}H NMR ($CDCl_3$) δ 8.67 (s, 1H), 8.62 (d, 1H, J = 4.64 Hz), 8.37 (d, 1H, J = 4.64 Hz), 8.17 (d, 1H, J = 1.95 Hz), 7.94-7.93 (m, 1H), 7.57 (s, 1H), 7.53-7.51 (m, 1H), 7.43 (dd, 1H, J = 4.88 Hz), 7.39-7.37 (m, 2H), 7.32 (t, 1H, J = 7.57 Hz), 7.13 (dd, 1H, J = 4.64 Hz), 5.15 (d, 1H, J = 10.75 Hz), 4.22 (d, 1H, J = 10.98 Hz), 1.06 (s, 9H). [M+H]+ = 405.1.

Diastereomer B: ^{1}H NMR ($CDCl_3$) δ 8.66 (s, 1H), 8.54 (d, 1H, J = 3.91 Hz), 8.37 (s, 2H), 7.73-7.71 (m, 1H), 7.55-7.50 (m, 3H), 7.47-7.45 (m, 1H), 7.39 (t, 1H, J = 7.57 Hz), 7.43 (dd, 1H, J = 4.88 Hz), 7.14 (dd, 1H, J = 4.88 Hz), 5.16 (dd, 1H, J = 7.57 Hz), 4.44 (d, 1H, J = 10.74 Hz), 3.52 (d, 1H, J = 7.81 Hz), 0.96 (s, 9H). [M+H]+ = 404.9.

Step C

N-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-2-methylpropane-2-sulfinamide (Diastereomer B, 1.567 g, 3.87 mmol) was dissolved in CH_3OH (15 mL) and the solution was cooled to 0°C. HCl (4 M solution in dioxane, 2.905 mL, 11.62 mmol) was added drop-wise. The reaction was allowed to warm to RT and was stirred for 7 hr. The reaction was diluted with H_2O and the pH was adjusted to pH=7 using saturated aqueous $NaHCO_3$. The product was extracted with ethyl acetate (3 x 75 mL) followed by isobutanol (6 x 50 mL). The combined organics were dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford 3-(1-amino-2,2-dipyridin-3-ylethyl)benzonitrile as a foamy light yellow solid.

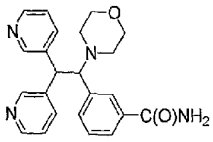
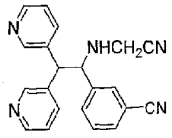
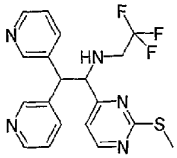
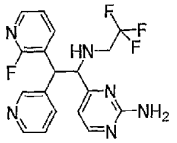
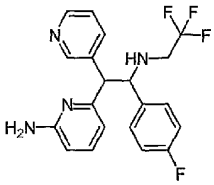
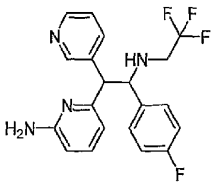
Enantiomer B: ^{1}H NMR (CD_3OD) δ 8.78 (d, 1H, J = 1.53 Hz), 8.51 (d, 1H, J = 3.66 Hz), 8.35 (d, 1H, J = 1.53 Hz), 8.25-8.24 (m, 1H), 8.18-8.14 (m, 1H), 7.84-7.79 (m, 2H), 7.72-7.70 (m, 1H), 7.60-7.43 (m, 3H), 7.26 (dd, 1H, J = 4.88 Hz), 5.13 (d, 1H, J = 10.99 Hz), 4.53 (d, 1H, J = 11.29 Hz). [M+H]+ = 301.1.

Step D

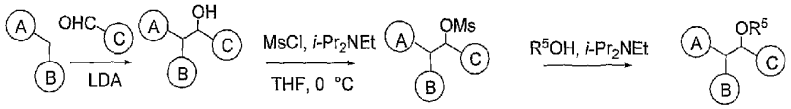
According to the procedure in Example 343, Step C, 3-(1-Amino-2,2-dipyridin-3-ylethyl)benzonitrile (Enantiomer B, 0.503 g, 1.68 mmol) was converted to the title compound. The product was purified by reverse phase HPLC (5-95% CH_3CN / H_2O + 0.05% NH_4OH) followed by flash column chromatography (0-9% CH_3OH / CH_2Cl_2). The fractions were combined and concentrated *in vacuo* to afford the title compound as a foamy white solid. Enantiomer B: ^{1}H NMR ($CDCl_3$) δ 8.67 (d, 1H, J = 1.95 Hz), 8.51 (dd, 1H, J = 1.22 Hz), 8.37 (d, 1H, J = 2.20 Hz), 8.30 (dd, 1H, J = 1.22 Hz), 7.69-7.67 (m, 1H), 7.52-7.50 (m, 1H), 7.43-7.37 (m, 4H), 7.29 (dd, 1H, J = 4.88 Hz), 7.07 (dd, 1H, J = 4.88 Hz), 4.62 (d, 1H, J = 11.96 Hz), 4.37 (d, 1H, J = 12.21 Hz), 3.53-3.50 (m, 2H), 3.49-3.37 (m, 2H), 2.50-2.47 (m, 2H), 2.29-2.26 (m, 2H). [M+H]+ = 371.1870.

The following compounds were made according to Scheme 7, where intermediates in the scheme were modified according to literature methods. Examples 7-3 and 7-4 were synthesized using the *tert*-butyl sulfonimine rather than the *tert*-butyl sulfinimine using literature procedures.

EXAMPLES 422-423 and 7-1 to 7-4

422		(±)-3-(1-morpholin-4-yl-2,2-dipyridin-3-ylethyl)benzamide	389.1989
423		(±)-3-{1-[(cyanomethyl)amino]-2,2-dipyridin-3-ylethyl}benzonitrile	340.1561
7-1		(±)-*N*-{1-[2-(methylthio)pyrimidin-4-yl]-2,2-dipyridin-3-ylethyl}-n-(2,2,2-trifluoroethyl)amine	406.1318
7-2		(±)-4-{2-(2-fluoropyridin-3-yl)-2-pyridin-3-yl-1-[(2,2,2-trifluoroethyl)amino]ethyl}pyrimidin-2-amine (mixture of diastereomers)	393.1443
7-3		(±)-6-{2-(4-fluorophenyl)-1-pyridin-3-yl-2-[(2,2,2-trifluoroethyl)amino]ethyl}pyridin-2-amine (diastereomer 1)	391
7-4		(±)-6-{2-(4-fluorophenyl)-1-pyridin-3-yl-2-[(2,2,2-trifluoroethyl)amino]ethyl}pyridin-2-amine (diastereomer 2)	391

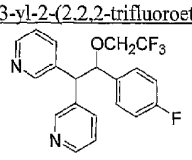
SCHEME 8



The variables C, B, A, and R^5 in the scheme are as defined in "Formula I".

EXAMPLE 424

(±)-3-[2-(4-fluorophenyl)-1-pyridin-3-yl-2-(2,2,2-trifluoroethoxy)ethyl]pyridine



Step A

To the solution of 3-(pyridin-3-ylmethyl)pyridine (0.195 g, 1.15 mmol) in THF (5 mL) at -78 °C was added LDA (0.7 mL, 1.8 M) and stirred for 1 h. 4-Fluorobenzaldehyde (0.171 g, 1.37 mmol) in THF (1 mL) was added. The mixture was stirred at -78 °C for 10 min and at -45 °C for 0.5 h. The reaction was quenched with ice and extracted with CH_2Cl_2. The combined organic layer was dried, filtered, and concentrated to give a solid. The solid was triturated with CH_2Cl_2 to give 1-(4-fluorophenyl)-2,2-dipyridin-3-ylethanol. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.60 (d, 1H, J = 1.7), 8.45 (d, 1H, J = 1.9), 8.38 (dd, 1H, J = 4.7, 1.2), 8.27 (dd, 1H, J = 4.6, 1.2), 7.91 (d, 1H, J = 7.8), 7.76 (d, 1H, J = 8.0), 7.34-7.29 (m, 3H), 7.19 (dd, 1H, J = 7.8, 4.9), 7.02 (t, 2H, J = 8.8), 5.68 (d, 1H, J = 4.9), 5.45 (dd, 1H, J = 8.5, 4.8), 4.34 (d, 1H, J = 8.8). LRMS m/z (M+H) Calcd: 295.3, found: 295.1.

Step B

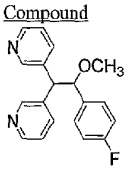
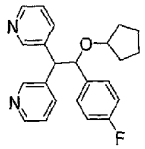
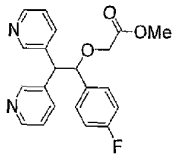
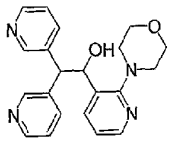
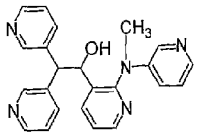
To the solution of 1-(4-fluorophenyl)-2,2-dipyridin-3-ylethanol (0.2 g, 0.68 mmol) in THF (4 mL) was added *i*-Pr_2NEt (0.4 mL, 2.3 mmol) at 0 °C followed by methanesulfonyl chloride (0.1 mL, 1.3 mmol). The reaction mixture was stirred for 10 h. Diluted with saturated $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic layer was dried, filtered, and concentrated to give 1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl methanesulfonate. LRMS m/z (M+H) Calcd: 373.4, found: 373.0.

Step C

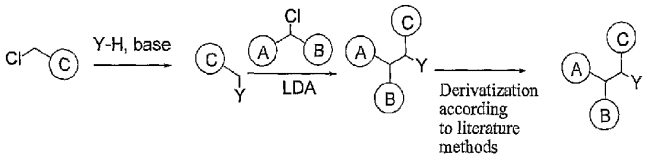
The mixture of 1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl methanesulfonate (0.1 g, 0.27 mmol) and *i*-Pr_2NEt (0.1 mL) in CF_3CH_2OH (1 mL) was heated to reflux for 10 h. Diluted with aqueous Na_2CO_3 (2M) and extracted with CH_2Cl_2. The combined organic layer was dried, filtered, and concentrated. The residue was purified by reverse phase HPLC (5-100% CH_3CN/H_2O + 0.1% TFA) to give the trifluoroacetate salt of (±)-3-[2-(4-fluorophenyl)-1-pyridin-3-yl-2-(2,2,2-trifluoroethoxy)ethyl]pyridine. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 11.38 (broad, 2H), 8.68 (d, 2H, J = 32.7), 8.55 (d, 2H, J = 14.9), 8.0 (d, 1H, J = 8.0), 7.75 (d, 1H, J = 8.0), 7.58-7.60 (m, 1H), 7.40-7.42 (m, 1H), 7.08-7.11 (m, 2H), 6.99-7.02 (t, 2H, J = 8.3), 5.16 (d, 1H, J = 7.3), 4.40 (d, 1H, J = 7.3), 3.63-3.76 (m, 2H). (LRMS m/z (M+H) Calcd: 377.3, found: 377.2.

The following compounds were made according to Scheme 8, where intermediates in the Scheme were modified according to literature methods.

EXAMPLES 425-427 and 8-1 to 8-2

Example	Compound	Name	MS (M+1)
425		(±)-3-[2-(4-fluorophenyl)-2-methoxy-1-pyridin-3-ylethyl]pyridine	309.3
426		(±)-3-[2-(cyclopentyloxy)-2-(4-fluorophenyl)-1-pyridin-3-ylethyl]pyridine	363.2
427		(±)-methyl [1-(4-fluorophenyl)-2,2-dipyridin-3-ylethoxy]acetate	367.1
8-1		(±)-1-(2-morpholin-4-ylpyridin-3-yl)-2,2-dipyridin-3-ylethanol	363.182
8-2		(±)-1-{2-[methyl(pyridin-3-yl)amino]pyridin-3-yl}-2,2-dipyridin-3-ylethanol	384.1798

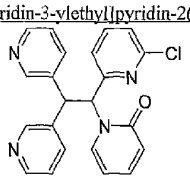
SCHEME 9



The variables C, B, A, and Y in the scheme are as defined in "Formula I".

EXAMPLE 428

(±)-1-[1-(6-chloropyridin-2-yl)-2,2-dipyridin-3-ylethyl]pyridin-2(1H)-one



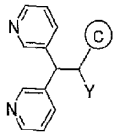
Step A

To the solution of 2-chloro-6-chloromethylpyridine (1.62 g g, 10 mmol) in DMF (10 mL) was added 2-hydroxypyridine (0.95 g, 10 mmol) and Cs_2CO_3 (6.52 g, 20 mmol). The mixture was stirred overnight, then diluted with water and extracted with CH_2Cl_2. The combined organic layer was dried, filtered, and concentrated to give a solid. The solid was purified by silica gel chromatography (2-4% MeOH in CH_2Cl_2) to give 1-[(6-chloropyridin-2-yl)methyl]pyridin-2(1H)-one. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.62 (t, 1H, J = 7.8), 7.51 (dd, 1H, J = 6.8, 2.0), 7.31-7.37 (m, 2H), 7.25 (d, 1H, J = 8.3), 6.59 (d, 1H, J = 9.2), 6.21 (td, 1H, J = 6.6, 1.3), 5.19 (s, 2H). LRMS m/z (M+H) Calcd: 221.7, found: 221.0.

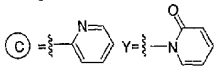
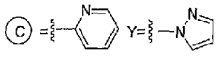
Step B

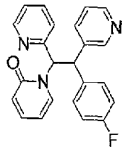
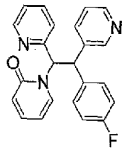
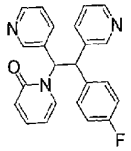
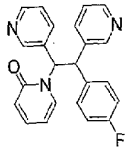
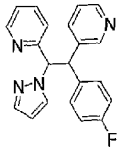
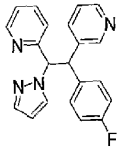
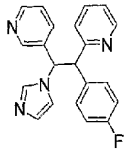
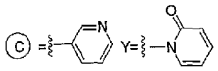
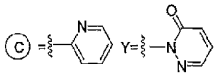
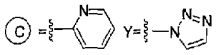
To the solution of 1-[(6-chloropyridin-2-yl)methyl]pyridin-2(1H)-one (0.3 g, 1.36 mmol) in THF (6 mL) at -78 °C was added LDA(0.83 mL, 1.8 M) and stirred at -78 °C for 1 h. The solution of 3-[chloro(pyridin-3-yl)methyl]pyridine (0.278 g, 1.36 mmol) in THF (3 mL) was added and the mixture was warmed to 0 °C and stirred at 0 °C for 1 h. The reaction was quenched with water and extracted with CH_2Cl_2. The combined organic layer was dried, filtered, and concentrated. The residue was purified by silica gel chromatography (3% MeOH in CH_2Cl_2) to give (±)-1-[1-(6-chloropyridin-2-yl)-2,2-dipyridin-3-ylethyl]pyridin-2(1H)-one. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.58 (d, 1H, J = 2.2), 8.53 (d, 1H, J = 2.0), 8.42(dd, 1H, J = 4.6, 1.2), 8.35 (dd, 1H, J = 4.6, 1.2), 7.92 (d, 1H, J = 6.6), 7.84 (d, 1H, J = 8.0), 7.64 (d, 1H, J = 8.0), 7.48 (t, 1H, J = 7.7), 7.25-7.09(m, 6H), 6.41 (d, 1H, J = 9.0), 6.09 (t, 1H, J = 6.7), 5.30 (d, 1H, J = 12.2). LRMS m/z (M+H) Calcd: 389.8, found: 389.0.

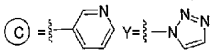
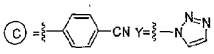
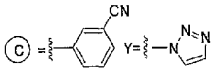
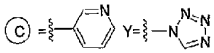
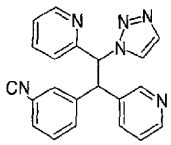
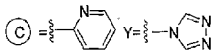
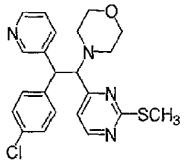
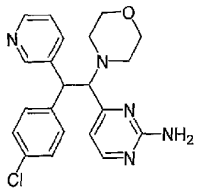
The following compounds were made according to Scheme 9 where intermediates in the Scheme were modified according to literature methods. Unless otherwise shown, structures of compounds 429-437, 9-1 to 9-5 and 444-446 are represented by defining variables "C" and "Y" of the structure



EXAMPLES 429-437 and 9-1 to 9-5

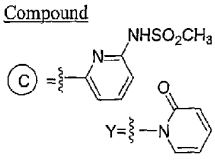
Example	Compound	Name	MS (M+1)
429		(±)-1-(1-pyridin-2-yl-2,2-dipyridin-3-ylethyl)pyridin-2(1H)-one	355.0
430		(±)-2-[1-(1H-pyrazol-1-yl)-2,2-dipyridin-3-ylethyl]pyridine	328.0

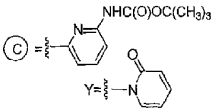
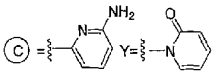
431		(±)-1-[2-(4-fluorophenyl)-1-pyridin-2-yl-2-pyridin-3-ylethyl]pyridin-2(1H)-one (Diastereomer A)	372.1499
432		(±)-1-[2-(4-fluorophenyl)-1-pyridin-2-yl-2-pyridin-3-ylethyl]pyridin-2(1H)-one (Diastereomer B)	372.1499
433		(±)-1-[2-(4-fluorophenyl)-1,2-dipyridin-3-ylethyl]pyridin-2(1H)-one (Diastereomer A)	372.1500
434		(±)-1-[2-(4-fluorophenyl)-1,2-dipyridin-3-ylethyl]pyridin-2(1H)-one (Diastereomer B)	372.1505
435		(±)-2-[2-(4-fluorophenyl)-1-(1H-pyrazol-1-yl)-2-pyridin-3-ylethyl]pyridine (Diastereomer A)	345.1503
436		(±)-2-[2-(4-fluorophenyl)-1-(1H-pyrazol-1-yl)-2-pyridin-3-ylethyl]pyridine (Diastereomer B)	345.1502
437		(±)-2-[1-(4-fluorophenyl)-2-(1H-imidazol-1-yl)-2-pyridin-3-ylethyl]pyridine (mixture of idastereomers)	345.1503
438		(±)-1-(1,2,2-tripyridin-3-ylethyl)pyridin-2(1*H*)-one	355.5
439		(±)-2-(1-pyridin-2-yl-2,2-dipyridin-3-ylethyl)pyridazin-3(2*H*)-one	356.5
440		(±)-2-[2,2-dipyridin-3-yl-1-(1H-1,2,3-triazol-1-	329.3

		yl)ethyl]pyridine	
441		(±)-3,3',3"-[2-(1H-1,2,3-triazol-1-yl)ethane-1,1,2-triyl]tripyridine	329.2
442		(±)-4-[2,2-dipyridin-3-yl-1-(1H-1,2,3-triazol-1-yl)ethyl]benzonitrile	353.3
443		(±)-3-[2,2-dipyridin-3-yl-1-(1H-1,2,3-triazol-1-yl)ethyl]benzonitrile	353.3
9-1		(±)-3,3',3"-[2-(1H-tetrazol-1-yl)ethane-1,1,2-triyl]tripyridine	330.1464
9-2		(±)-3-[2-pyridin-2-yl-1-pyridin-3-yl-2-(1H-1,2,3-triazol-1-yl)ethyl]benzonitrile	353.4
9-3		(±)-2-[2,2-dipyridin-3-yl-1-(4H-1,2,4-triazol-4-yl)ethyl]pyridine	329.1525
9-4		(±)-4-{2-(4-chlorophenyl)-1-[2-(methylthio)pyrimidin-4-yl]-2-pyridin-3-ylethyl}morpholine	427.1
9-5		(±)-4-[2-(4-chlorophenyl)-1-morpholin-4-yl-2-pyridin-3-ylethyl]pyrimidin-2-amine	396

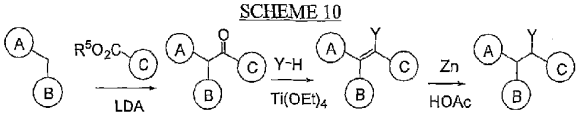
The following compounds were made from Example 428 using methods known to those skilled in the art.

EXAMPLES 444-446

Example	Compound	Name	MS (M+1)
444		(±)-1-(1-{6-[(2-hydroxyethyl)amino]pyridin-2-yl}-2,2-dipyridin-3-ylethyl)pyridin-2(1H)-one	448.1

445		(±)-N-{6-[1-(2-oxopyridin-1(2H)-yl)-2,2-dipyridin-3-ylethyl]pyridin-2-ylcarbamate	470.0
446		(±)-1-[1(2H)-yl)-2,2-dipyridin-3-ylethyl]pyridin-2(1H)-one	370.1

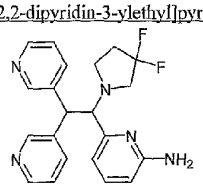
SCHEME 10



The variables A, B, C, Y, and R^5 in the scheme are as defined in "Formula I".

EXAMPLE 447

(±)-6-[1-(3,3-difluoropyrrolidin-1-yl)-2,2-dipyridin-3-ylethyl]pyridin-2-amine



Step A

To a solution of di-3-pyridylmethane (250 mg, 1.47 mmol) in dry THF (5 mL) was added LDA (2.1 mL, 3.16 mmol) slowly at -78°C. After 30 min a solution of methyl 2-bromopyridine-6-carboxylate (349 mg, 1.62 mmol) in dry THF (3 mL) was added slowly. After 30 min the cooling bath was removed and the mixture allowed to warm to RT. After 4 hr the mixture was diluted with saturated NH_4Cl and extracted with EtOAc (3x). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated. Flash column (100% EtOAc) gave 1-(6-bromopyridin-2-yl)-2,2-dipyridin-3-ylethanone as a yellow oil. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.66 (m, 2 H), 8.53 (m, 2 H), 8.06 (dd, J = 0.98 and 6.35 Hz, 1 H), 7.80 (m, 4 H), 7.28 (m, 2 H), 6.79 (s, 1 H).

Step B

To a solution of 1-(6-bromopyridin-2-yl)-2,2-dipyridin-3-ylethanone (154 mg, 0.44 mmol) in dry 1,4-dioxane (2 mL) was added 3,3-difluoropyrrolidine hydrochloride (75 mg, 0.52 mmol), TEA (0.079 mL, 0.57 mmol), and $Ti(OEt)_4$ (0.18 mL, 0.87 mmol). The mixture was heated to reflux. After 2 hr the mixture was cooled to RT, diluted with brine, and filtered through a pad of Celite. The pad was washed with EtOAc. The filtrate layers were separated and the aqueous layer extracted with EtOAc (3x). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated to a brown foam which was used in the next step without purification.

Step C

To a solution of crude imine (134 mg, 0.3 mmol) in HOAc (3 mL) was added Zn dust (198 mg, 3.02 mmol) at RT. After 16 hr the mixture was filtered through a pad of Celite and concentrated. The residue was taken up in 1M NaOH and extracted with CH_2Cl_2 (3x). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated. Flash column (gradient, 0-10% MeOH/CH_2Cl_2) gave 2-bromo-6-[1-(3,3-difluoropyrrolidin-1-yl)-2,2-dipyridin-3-ylethyl]pyridine as a yellow solid. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.72 (s, 1 H), 8.49 (d, J = 4.89 Hz, 1 H), 8.37 (s, 1 H), 8.27 (d, J = 4.88 Hz, 1 H), 7.75 (d, J = 7.57 Hz, 1 H), 7.43 (d, J = 7.57 Hz, 1 H), 7.37 (t, J = 7.32 Hz, 1 H), 7.30 (m, 2 H), 7.04 (dd, J = 4.89 and 2.93 Hz, 1 H), 6.88 (d, J = 7.33 Hz, 1 H), 4.88 (d, J = 11.71 Hz, 1 H), 4.53 (d, J = 11.48 Hz, 1 H), 3.10 (m, 1 H), 2.88 (m, 2 H), 2.70 (m, 1 H), 2.0 (m, 2 H).

Step D

The 2-bromo-6-[1-(3,3-difluoropyrrolidin-1-yl)-2,2-dipyridin-3-ylethyl]pyridine (73 mg, 0.16 mmol), *tert*-butyl carbamate (23 mg, 0.2 mmol), Cs_2CO_3 (75 mg, 0.23 mmol), $Pd_2(dba)_3$ (3 mg, 0.003 mmol), and xantphos (6 mg, 0.01 mmol) were combined in dry 1,4-dioxane (1.5 mL). The mixture was degassed (3 x pump/N_2) then heated to 100°C. After 5 hr the mixture was cooled to RT, diluted with EtOAc, filtered through a pad of Celite, and concentrated. The residue was taken up in 1 mL CH_2Cl_2 to which was added 1 mL TFA at RT. After 90 min the mixture was concentrated. The residue was taken up in saturated $NaHCO_3$ and extracted with CH_2Cl_2 (3x). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated. Flash column (gradient, 0-10% MeOH/CH_2Cl_2) gave the title compound as a yellow foam. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.68 (d, J = 2.20 Hz, 1 H), 8.47 (d, J = 4.15 Hz, 1 H), 8.37 (d, J = 2.19 Hz, 1 H), 8.25 (d, J = 3.90 Hz, 1 H), 7.74 (d, J = 8.06 Hz, 1 H), 7.41 (d, J = 7.81 Hz, 1 H), 7.25 (m, 2 H), 7.02 (m 1 H), 6.27 (m, 2 H), 4.85 (d, J = 11.47 Hz, 1 H), 4.39 (s, 2 H), 4.35 (d, J = 11.72 Hz, 1 H), 3.10 (m, 1 H), 2.86 (m, 2 H), 2.67 (m, 1 H), 2.0 (m, 2 H); MS $(M+H)^+$ 382.0.

Using the methodologies described below, representative compounds of the invention were evaluated and found to exhibit activity in the Kv1.5 assays, thereby demonstrating and confirming the utility of the compounds of this invention as Kv1.5 inhibitors and antiarrhythmics. Compounds of this type may exhibit forward rate-dependence, blocking the outward K^+ currents to a greater extent or preferentially at faster rates of depolarization or heart rates. Such a compound could be identified in electrophysiological studies as described below. For example, during a train of depolarizations delivered at frequencies of 1 Hz and 3 Hz, the block is "rate-dependent" if the amount of block observed during a 10 second train at 3 Hz is greater than that at 1 Hz. A Kv1.5 blocker may also display use-dependence, during which the block of the outward K^+ currents increases with use, or during repetitive depolarization of a cardiac cell. Use dependence of block occurs to a greater extent with each successive depolarization in a train or sequence of pulses or depolarizations at a given rate or frequency. For example, during a train of 10 depolarizations at a frequency of 1 Hz, the block is "use-dependent" if the amount of block is greater for the 10th pulse than for the 1st pulse of the train. A Kv1.5 blocker may exhibit both use-dependence and rate-dependence.

A Kv1.5 blocker may also be identified through electrophysiological studies of native I_{Kur} using cardiac myocytes or other tissue from various species including, but not limited to, human, rat, mouse, dog, monkey, ferret, rabbit, guinea pig, or goat. In native tissues Kv1.5 may exist as a homo-oligomer, or as a hetero-oligomer with other Kv family members, or may exist in a complex with a β-subunit. Compounds of this invention may block Kv1.5 homo- or hetero-oligomers or Kv1.5 in complexes with β-subunits.

Kv1.5 assays

The high throughput Kv1.5 planar patch clamp assay is a systematic primary screen. It confirms activity and provides a functional measure of the potency of agents that specifically affect Kv1.5 potassium channels. Kiss et al. (Assay and Drug Dev. Tech., 1(1-2):127-135,2003) and Schroeder et al. (J. of Biomol. Screen., 8(1);50-64, 2003) describe the use of this instrument for Kv1.5 as well as other voltage gated ion channels.

Chinese hamster ovary cells (CHO) stably expressing the human Kv1.5 potassium channel alpha subunit, cloned from human heart, are grown to 90-100% confluence in Ham's F12 medium supplemented with 10% FBS, 100 U/ml penicillin, 100 μg/ml streptomycin, 1000 μg/ml G-418 sulfate. Cells are subcultured by treatment with Versene, then suspended in phosphate-buffered saline (PBS) and centrifuged The cell pellet is resuspended in PBS and the resulting suspension placed in the cell reservoir of the IonWorks™ HT instrument.

Electrophysiological recordings are performed with intracellular solution containing (mM): K-gluconate 100, KCl 40, $MgCl_2$ 3.2, EGTA 3, *N*-2-hydroxylethylpiperazine-*N*'-2-ethanesulphonic acid (HEPES) 5, adjusted to pH 7.3. Amphotericin (Sigma) is prepared as 30 mg/ml stock solution and diluted to a final working concentration of 0.1 mg/ml in internal buffer solution. The external solution is Dulbecco's PBS (Invitrogen) and contains (mM): $CaCl_2$ 0.90, KCl 2.67, K_3PO_4 1.47, $MgCl_2$ 0.50, NaCl 138, Na_3PO_4 8.10 and has a pH of 7.4. All compounds are prepared as 10 mM stock solutions in DMSO. Compounds are diluted into external buffer, then transferred from the drug plate to the Patchplate during the experiment (final DMSO concentration <0.66% vol.).

Kv1.5 ionic currents are recorded at room temperature. Membrane currents are amplified (RMS ~10pA) and sampled at 10 kHz. Leak subtraction was performed in all experiments by applying a 160 ms hyperpolarizing (10 mV) pre-pulses 200 ms before the test pulses to measure leak conductance. The patch clamp stimulus protocol is as follows:

1. Patchplate wells are loaded with 3.5 μL of external buffer.
2. Planar micropipette hole resistances (Rp) is determined by applying a 10 mV, 160 ms potential difference across each hole (Hole test).
3. Cells are pipetted into the Patchplate and form high resistance seals with the 1-2 μm holes at the bottom of each Patchplate well. A seal test scan is performed to determine how many of the Patchplate wells have cells that have formed seals.
4. In order to gain electrical access to the cells, intracellular solution containing amphotericin is circulated for 4 minutes on the bottom side of the Patchplate.

5. Pre-compound addition test pulse is applied to each well on the Patchplate. Protocol: Cells are voltage clamped at a membrane holding potential of –80 mV for 15 seconds. This is followed by application of a 5 Hz stimulus train (27 x 150 ms depolarizations to +40 mV). The membrane potential steps to +40 mV evoke outward (positive) ionic currents.
6. Compound is added to each well of the Patchplate. Compounds are allowed to incubate for 5 minutes.
7. Post-compound addition test pulse protocol is applied. Protocol: Cells are voltage clamped at a membrane holding potential of –80 mV for 15 seconds. This is followed by application of a 5 Hz stimulus train (27 x 150 ms depolarizations to +40 mV).

Data analysis is conducted off-line. Paired comparisons between pre-drug and post-drug additions are used to determine the inhibitory effect of each compound. % inhibition of the peak control current during the 27th depolarization to +40 mV (in the 5 Hz train) is plotted as a function of antagonist concentration. The concentrations of drug required to inhibit current by 50 % (IC_{50}) are determined by fitting of the Hill equation to the concentration response data: % of Control = 100 X $(1 + ([Drug]/IC_{50})^{p})^{-1}$

For each cell four arithmetic metrics are obtained:

1) seal resistance
2) baseline metric (the mean current at –70 mV from 5 to 45 ms before the first depolarization to +40 mV)
3) current run up metric (pre-compound mean current amplitude during the 1st depolarization to +40 mV minus the pre-compound mean current amplitude during the 27th depolarization to +40 mV)
4) peak current (maximum current amplitude during the 27th depolarization to +40 mV during the 5 Hz train).

All metrics are obtained during both the pre- and post-compound addition traces. Cells are eliminated from further analysis if:

1) seal resistance is <50 MΩ
2) baseline metric is >±100 pA during the pre-compound
3) current run up metric is >-0.2 nA
4) pre-read peak metric is <400 pA.

The above-listed compounds provide ≥ 20% inhibition at a concentration of 33 μM or less in the high throughput Kv1.5 planar patch clamp assay described above.

Atomic Absorption Spectroscopy Protocol:

This assay identifies agents that specifically block the human Kv1.5 K+ channel heterologously expressed in CHO cells as measured by Rb^{+} efflux using Flame Atomic Absorption Spectroscopy (FAAS). The application of FAAS for measuring ion channel activity was adapted from Terstappen *et al*, *Anal. Biochem.*, 272:149-155, 1999.

CHO cells expressing human Kv1.5 are cultured as described above, then harvested with trypsin-EDTA and washed with medium.

1. 40,000 cells per well are seeded in a 96-well cell culture plate (assay plate) and the cells are allowed to grow for 48 hours at 37°C.
2. The medium is removed and 200 µl of Rb Load Buffer (Aurora Biomed, Vancouver, BC) is added for 3 hours at 37°C under 5% CO_2.
3. The cells are washed 5 times with 200 µl Hank's Balanced Salt Solution (HBSS) followed by the addition of 100 µl HBSS containing test compound or 0.5 % DMSO.
4. After 10 min, 100 µl of HEPES-buffered saline containing 140 mM KCl is added and plate is incubated at RT for 5 min. with gentle shaking.
5. Immediately thereafter, 150 µl of supernatant is transferred to a fresh 96 well plate and the remaining supernatant aspirated.
6. 120 µl of Cell Lysis Buffer (Aurora Biomed, Vancouver, BC) is added to the assay plate and shaken for 10 min. prior to analysis.
7. Rb content is measured in samples of supernatant (SUP) and lysate (LYS) using an ICR-8000 automated AAS instrument (Aurora Biomed, Vancouver, BC).

% FLUX=100%*(SUP/(LYS+SUP)). % INH=100%*(1-(A-B)/(C-B)), where A is % FLUX in the presence of tested compound, B is % FLUX in the presence of 10 mM (6-methoxy-2-methyl-1-oxo-4-phenyl-1,2-dihydroisoquinolin-3-yl)-*N,N*-dimethylmethanaminium chloride, C is % FLUX in the presence of 0.25% DMSO.

The above-listed compounds provide $\geq$ 25% inhibition at a concentration of 25 µM or less in the AAS assay described above.

The compounds of this invention can be administered for the treatment or prevention of afflictions, diseases and illnesses according to the invention by any means that effects contact of the active ingredient compound with the site of action in the body of a warm-blooded animal. For example, administration, can be oral, topical, including transdermal, ocular, buccal, intranasal, inhalation, intravaginal, rectal, intracisternal and parenteral. The term "parenteral" as used herein refers to modes of administration which include subcutaneous, intravenous, intramuscular, intraarticular injection or infusion, intrasternal and intraperitoneal.

The compounds can be administered by any conventional means available for use in conjunction with pharmaceuticals, either as individual therapeutic agents or in a combination of therapeutic agents. They can be administered alone, but are generally administered with a pharmaceutical carrier selected on the basis of the chosen route of administration and standard pharmaceutical practice.

For the purpose of this disclosure, a warm-blooded animal is a member of the animal kingdom possessed of a homeostatic mechanism and includes mammals and birds.

The dosage administered will be dependent on the age, health and weight of the recipient, the extent of disease, kind of concurrent treatment, if any, frequency of treatment and the nature of the effect desired. Usually, a daily dosage of active ingredient compound will be from about 1-500 milligrams per day. Ordinarily, from 10 to 100 milligrams per day in one or more applications is

effective to obtain desired results. These dosages are the effective amounts for the treatment and prevention of afflictions, diseases and illnesses described above, e.g., cardiac arrhythmias such as atrial fibrillation, atrial flutter, atrial arrhythmia, and supraventricular tachycardia, thromboembolic events such as stroke and congestive heart failure, and immunodepression.

The active ingredient can be administered orally in solid dosage forms, such as capsules, tablets, troches, dragées, granules and powders, or in liquid dosage forms, such as elixirs, syrups, emulsions, dispersions, and suspensions. The active ingredient can also be administered parenterally, in sterile liquid dosage forms, such as dispersions, suspensions or solutions. Other dosages forms that can also be used to administer the active ingredient as an ointment, cream, drops, transdermal patch or powder for topical administration, as an ophthalmic solution or suspension formation, i.e., eye drops, for ocular administration, as an aerosol spray or powder composition for inhalation or intranasal administration, or as a cream, ointment, spray or suppository for rectal or vaginal administration.

Gelatin capsules contain the active ingredient and powdered carriers, such as lactose, starch, cellulose derivatives, magnesium stearate, stearic acid, and the like. Similar diluents can be used to make compressed tablets. Both tablets and capsules can be manufactured as sustained release products to provide for continuous release of medication over a period of hours. Compressed tablets can be sugar coated or film coated to mask any unpleasant taste and protect the tablet from the atmosphere, or enteric coated for selective disintegration in the gastrointestinal tract.

Liquid dosage forms for oral administration can contain coloring and flavoring to increase patient acceptance.

In general, water, a suitable oil, saline, aqueous dextrose (glucose), and related sugar solutions and glycols such as propylene glycol or polyethylene gycols are suitable carriers for parenteral solutions. Solutions for parenteral administration preferably contain a water soluble salt of the active ingredient, suitable stabilizing agents, and if necessary, buffer substances. Antioxidizing agents such as sodium bisulfite, sodium sulfite, or ascorbic acid, either alone or combined, are suitable stabilizing agents. Also used are citric acid and its salts and sodium EDTA. In addition, parenteral solutions can contain preservatives, such as benzalkonium chloride, methyl- or propylparaben, and chlorobutanol.

Suitable pharmaceutical carriers are described in *Remington's Pharmaceutical Sciences*, A. Osol, a standard reference text in this field.

For administration by inhalation, the compounds of the present invention may be conveniently delivered in the form of an aerosol spray presentation from pressurized packs or nebulisers. The compounds may also be delivered as powders which may be formulated and the powder composition may be inhaled with the aid of an insufflation powder inhaler device. The preferred delivery system for inhalation is a metered dose inhalation (MDI) aerosol, which may be formulated as a suspension or solution of a compound of Formula I in suitable propellants, such as fluorocarbons or hydrocarbons.

For ocular administration, an ophthalmic preparation may be formulated with an appropriate weight percent solution or suspension of the compounds of Formula I in an appropriate

ophthalmic vehicle, such that the compound is maintained in contact with the ocular surface for a sufficient time period to allow the compound to penetrate the corneal and internal regions of the eye.

Useful pharmaceutical dosage-forms for administration of the compounds of this invention include, but are not limited to, hard and soft gelatin capsules, tablets, parenteral injectables, and oral suspensions.

A large number of unit capsules are prepared by filling standard two-piece hard gelatin capsules each with 100 milligrams of powdered active ingredient, 150 milligrams of lactose, 50 milligrams of cellulose, and 6 milligrams magnesium stearate.

A mixture of active ingredient in a digestible oil such as soybean oil, cottonseed oil or olive oil is prepared and injected by means of a positive displacement pump into gelatin to form soft gelatin capsules containing 100 milligrams of the active ingredient. The capsules are washed and dried.

A large number of tablets are prepared by conventional procedures so that the dosage unit is 100 milligrams of active ingredient, 0.2 milligrams of colloidal silicon dioxide, 5 milligrams of magnesium stearate, 275 milligrams of microcrystalline cellulose, 11 milligrams of starch and 98.8 milligrams of lactose. Appropriate coatings may be applied to increase palatability or delay absorption.

A parenteral composition suitable for administration by injection is prepared by stirring 1.5% by weight of active ingredient in 10% by volume propylene glycol. The solution is made to volume with water for injection and sterilized.

An aqueous suspension is prepared for oral administration so that each 5 milliliters contain 100 milligrams of finely divided active ingredient, 100 milligrams of sodium carboxymethyl cellulose, 5 milligrams of sodium benzoate, 1.0 grams of sorbitol solution, U.S.P., and 0.025 milliliters of vanillin.

The same dosage forms can generally be used when the compounds of this invention are administered stepwise or in conjunction with another therapeutic agent. When drugs are administered in physical combination, the dosage form and administration route should be selected depending on the compatibility of the combined drugs. Thus the term coadministration is understood to include the administration of the two agents concomitantly or sequentially, or alternatively as a fixed dose combination of the two active components.

Compounds of the invention can be administered as the sole active ingredient or in combination with a second active ingredient, including other antiarrhythmic agents having Kv1.5 blocking activities such as quinidine, propafenone, ambasilide, amiodarone, flecainide, sotalol, bretylium, dofetilide, almokalant, bepridil, clofilium, other compounds having Kv1.5 blocking activities such as clotrimazole, ketoconazole, bupivacaine, erythromycin, verapamil, nifedipine, zatebradine, bisindolylmaleimide, or other cardiovascular agents such as, but not limited to, ACE inhibitors such as benazepril, captopril, enalapril, fosinopril, lisinopril, moexipril, perindopril erbumine, quinapril, ramipril, and trandolapril, angiotensin II antagonists such as candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, and valsartan, cardiac glycosides such as digoxin, L-type calcium channel blockers, T-type calcium channel blockers, selective and nonselective beta blockers, an

immunosuppresant compound, endothelin antagonists, thrombin inhibitors, aspirin, nonselective NSAIDs other than aspirin such as naproxen, warfarin, factor Xa inhibitors, low molecular weight heparin, unfractionated heparin, clopidogrel, ticlopidine, IIb/IIIa receptor antagonists such as tirofiban, 5HT receptor antagonists, integrin receptor antagonists, thromboxane receptor antagonists, TAFI inhibitors and P2T receptor antagonists. Compounds of the invention can also be administered as the sole active ingredient or in combination with a pacemaker or defibrillator device.

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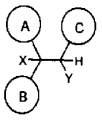
The claims defining the invention are as follows:

1. A compound of the formula



I,

or a pharmaceutically acceptable salt thereof, wherein

A is a pyridyl ring, wherein the point of attachment to the pyridyl ring is a carbon atom,

wherein the pyridyl ring is unsubstituted, mono-substituted with R^4, disubstituted with groups independently selected from R^4, trisubstituted with groups independently selected from R^4, or tetrasubstituted with groups independently selected from R^4, and wherein the N pyridyl ring atom is unsubstituted or substituted with oxo;

C is selected from the group consisting of

1) an aryl ring, wherein any stable aryl ring atom is independently unsubstituted or substituted with a group selected from R^4,

2) a heteroaryl ring, wherein the point of attachment to the heteroaryl ring is a carbon atom, and the heteroaryl ring is selected from the group consisting of:

a) a 5-membered unsaturated monocyclic ring with 1, 2, or 3 heteroatom ring atoms selected from the group consisting of N, O or S,

b) a 6-membered unsaturated monocyclic ring with 1 or 2 N atoms, and

c) an 8-, 9- or 10-membered unsaturated bicyclic ring with 1 or 2 heteroatom ring atoms selected from the group consisting of N, O or S,

wherein any stable atom is independently unsubstituted or substituted with a group selected from R^4;

3) a cyclopropyl ring, wherein any stable ring atom is independently unsubstituted or substituted with a group selected from R^4,

4) a 4-6 membered saturated heterocyclic ring with 1 or 2 heteroatom ring atoms selected from the group consisting of N and O, wherein any stable ring atom is independently unsubstituted or substituted with a group selected from R^4, and

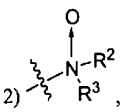
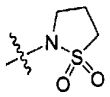
5) C_1-C_6 alkyl, wherein any stable atom is independently unsubstituted or substituted with a group selected from R^4;

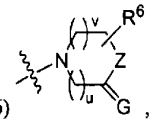
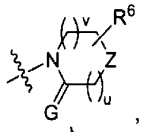
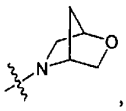
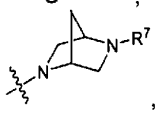
B is a pyridyl ring, wherein the point of attachment to the pyridyl ring is a carbon atom wherein the pyridyl ring is unsubstituted, mono-substituted with R^4, disubstituted with groups independently selected from R^4, trisubstituted with groups independently

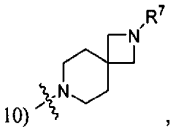
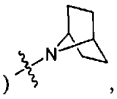
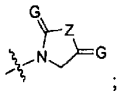
selected from R^4, or tetrasubstituted with groups independently selected from R^4, and wherein the N pyridyl ring atom is unsubstituted or substituted with oxo;

X is selected from the group consisting of hydrogen, OH, OCH_3 and F;

Y is selected from the group consisting of

1) NR^2R^3, 2)  , 3) OR^5, 4) $S(O)_{0-2}R^5$, 5) 

6)  , 7)  , 8)  , 9)  ,

10)  , 11)  , and 12)  ;

G, each time it occurs, is independently selected from the group consisting of H_2 and O;

Z is selected from the group consisting of $C(R^6)_2$, NR^5, $NC(O)R^5$, $NC(O)OR^5$, $NC(O)N(R^5)_2$, $NS(O)_{1-2}R^5$, $S(O)_{0-2}$, $-N(R^5)C(O)-$, $-C(R^5)=C(R^6)-$ and O;

R^a, in each instance in which it appears, is independently selected from the group consisting of

1) hydrogen,
2) C_1-C_6 alkyl,
3) halogen,
4) aryl,
5) heterocycle,
6) C_3-C_{10} cycloalkyl, and
7) OR^5,

said alkyl, aryl, heterocycle and cycloalkyl is unsubstituted or substituted with at least one substituent selected from R^6;

R^2 and R^3 are independently selected from the group consisting of

1) hydrogen,
2) $(CR^a_2)_nOR^5$,
3) $(CR^a_2)_nN(R^5)_2$,
4) $(CR^a_2)_n C(O)R^5$,
5) $(CR^a_2)_n C(O)OR^5$,
6) $(CR^a_2)_nR^5$,
7) $(CR^a_2)_n S(O)_mR^5$,
8) $(CR^a_2)_n S(O)_mN(R^5)_2$,
9) $C(O)R^5$,
10) $C(O)OR^5$,
11) $C(O)N(R^5)_2$,
12) $S(O)_mR^5$,
13) $S(O)_mN(R^5)_2$,
14) $(CR^a_2)_nN(R^5)(CR^a_2)_nC(O)N(R^5)_2$,
15) $(CR^a_2)_nC(O)N(R^5)_2$,
16) $(CR^a_2)_nN(R^5)(CR^a_2)_nC(O)OR^5$, and
17) $(CR^a_2)_nN(R^5)S(O)_mR^5$;

R^4, in each instance in which it appears, is independently selected from the group consisting of

1) hydrogen,
2) halogen,
3) NO_2,

4) CN,
5) $CR^4=C(R^5)_2$,
6) $C\equiv CR^5$,
7) $(CR^a_2)_nOR^5$,
8) $(CR^a_2)_nN(R^5)_2$,
9) $(CR^a_2)_n C(O)R^5$,
10) $(CR^a_2)_n C(O)OR^5$,
11) $(CR^a_2)_nR^5$,
12) $(CR^a_2)_n S(O)_mR^5$,
13) $(CR^a_2)_n S(O)_mN(R^5)_2$,
14) $OS(O)_mR^5$,
15) $N(R^5)C(O)R^5$,
16) $N(R^5)S(O)_mR^5$,
17) $(CR^a_2)_nN(R^6)R^5$,
18) $(CR^a_2)_nN(R^5)(CR^a_2)_nC(O)N(R^5)_2$,
19) $(CR^a_2)_nN(R^5)(CR^a_2)_nC(O)OR^5$,
20) $N(R^5)(CR^a_2)_nR^5$,
21) $N(R^5)(CR^a_2)_nN(R^5)_2$, and
22) $(CR^a_2)_nC(O)N(R^5)_2$;

R^5, in each instance in which it appears, is independently selected from the group consisting of

1) hydrogen,
2) unsubstituted or substituted C_1-C_6 alkyl,
3) unsubstituted or substituted C_3-C_{10} cycloalkyl,
4) unsubstituted or substituted aryl,
5) unsubstituted or substituted heterocycle,
6) CF_3,
7) unsubstituted or substituted C_2-C_6 alkenyl, and
8) unsubstituted or substituted C_2-C_6 alkynyl,

or in the case where R^5 is attached to a nitrogen atom that is disubstituted with R^5, each R^5 is independently selected from C_1-C_6 alkyl, and the nitrogen atom together with each R^5 form a ring;

R^6, in each instance in which it appears, is independently selected from the group consisting of

1) hydrogen,
2) unsubstituted or substituted C_1-C_6 alkyl,
3) halogen,
4) OR^5,

5) CF_3,

6) unsubstituted or substituted aryl,

7) unsubstituted or substituted C_3-C_{10} cycloalkyl,

8) unsubstituted or substituted heterocycle,

9) $S(O)_mN(R^5)_2$,

10) $C(O)OR^5$,

11) $C(O)R^5$,

12) CN,

13) $C(O)N(R^5)_2$,

14) $N(R^5)C(O)R^5$,

15) $N(R^5)C(O)OR^5$,

16) $N(R^5)C(O)N(R^5)_2$,

17) $OC(O)N(R^5)_2$,

18) $S(O)_mR^5$,

19) $OS(O)_mR^5$,

20) NO_2,

21) $N(R^5)_2$;

22) $SC(O)R^5$,

23) $N(R^5)S(O)_mR^5$,

R^7 is independently selected from the group consisting of

1) $S(O)_mN(R^5)_2$,

2) $C(O)OR^5$,

3) $C(O)R^5$,

4) $C(O)N(R^5)_2$, and

5) $S(O)_mR^5$;

m is independently 0, 1 or 2;

n is independently 0, 1, 2, 3, 4, 5 or 6;

u is 0, 1 or 2; and

v is 0, 1 or 2.

2. A compound of Claim 1, or a pharmaceutically acceptable salt thereof, wherein

B is a pyridyl ring, wherein the point of attachment to the pyridyl ring is a carbon atom, and wherein the pyridyl ring is unsubstituted, mono-substituted with R^4, disubstituted with groups independently selected from R^4, trisubstituted with groups independently selected from R^4, or tetrasubstituted with groups independently selected from R^4, and wherein the N atom is unsubstituted or substituted with oxo;

X is selected from the group consisting of hydrogen, OH, OCH_3 and F;

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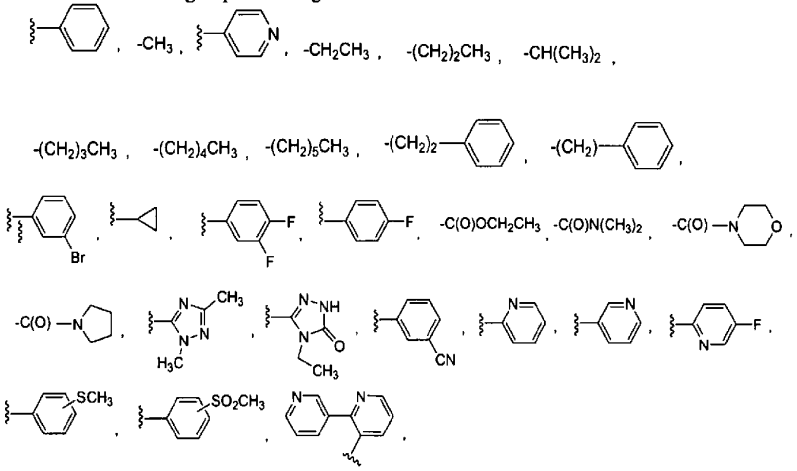
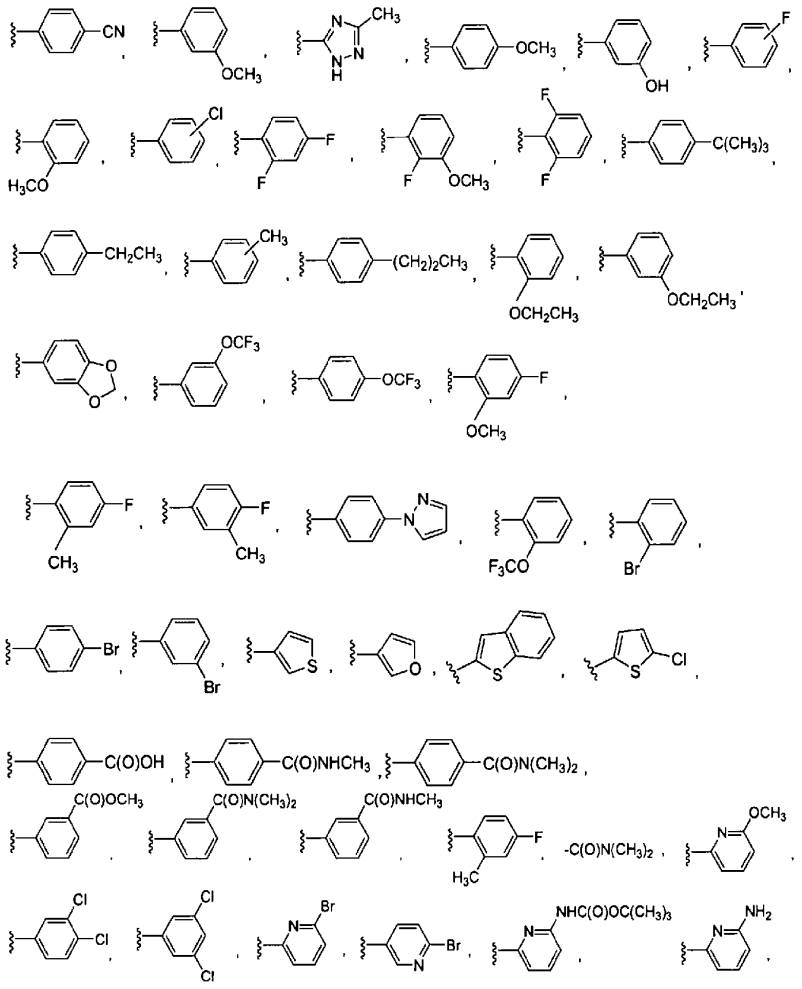
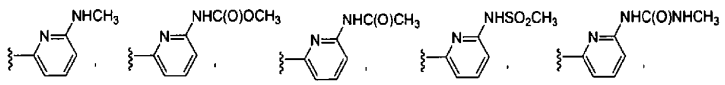
a pyridyl ring, wherein the point of attachment to the pyridyl ring is a carbon atom,

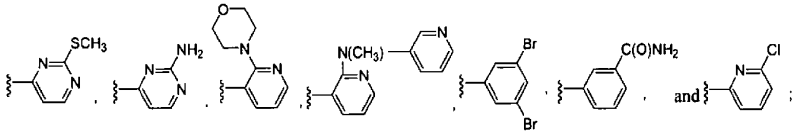
wherein the pyridyl ring is unsubstituted, mono-substituted with R^4, disubstituted with groups independently selected from R^4, trisubstituted with groups independently selected from R^4, or tetrasubstituted with groups independently selected from R^4, and wherein the N pyridyl ring atom is unsubstituted or substituted with oxo;

C is selected from the group consisting of

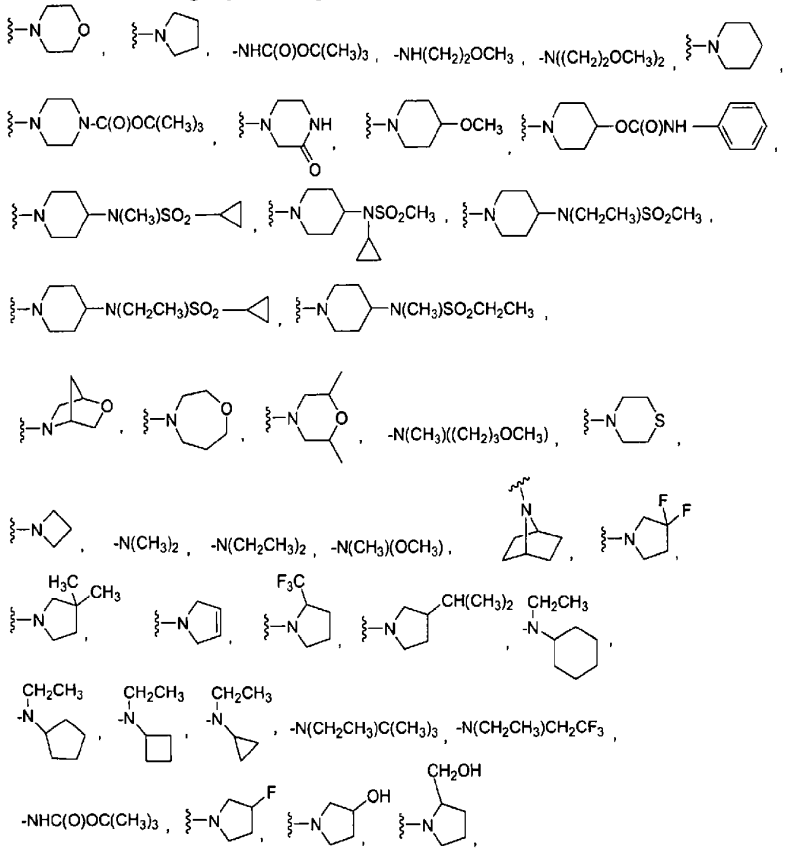








Y is selected from the group consisting of



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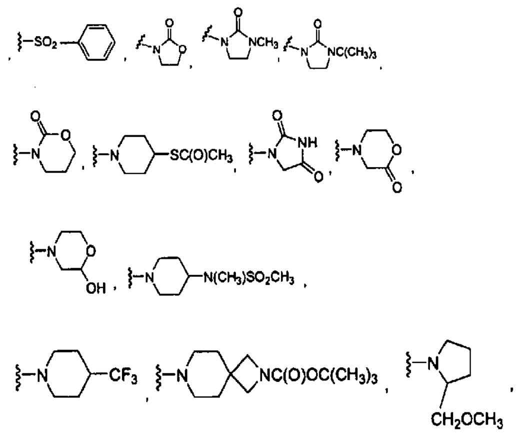
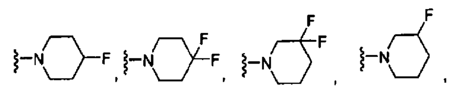
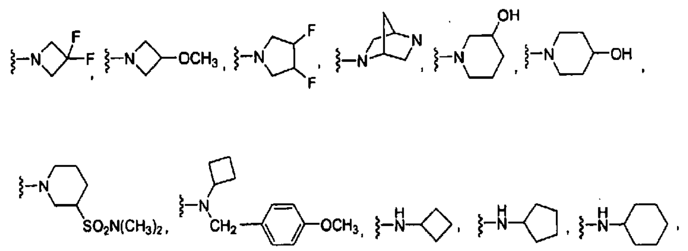
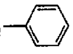
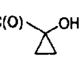
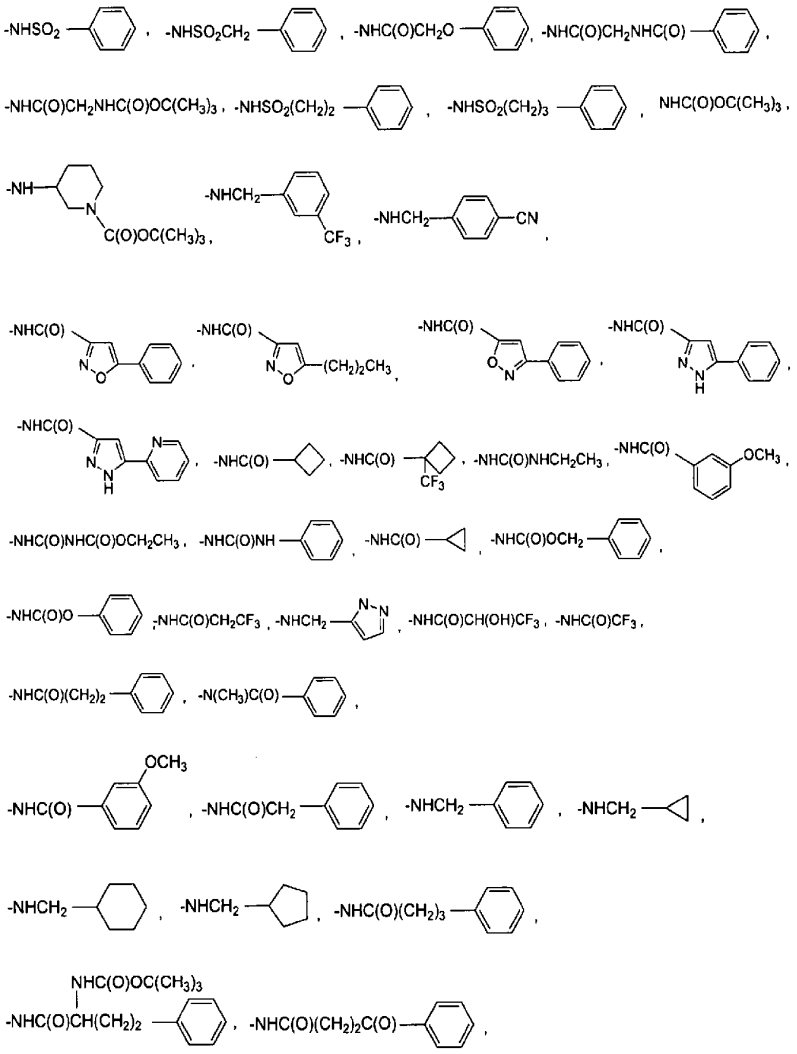


 , $-N(CH_3)CH_2CHCH_2$,



$-NHCH_2CH_3$, $-NHCH_2CF_3$, $-NH_2$, $-NHC(O)CH_2OCH_2-$  , $-NHC(O)CH_2OCH_3$, $-NHC(O)$  ,


-NHSO2
-NHSO2CH2
-NHC(O)CH2O
-NHC(O)CH2NHC(O)
-NHC(O)CH2NHC(O)OC(CH3)3
-NHSO2(CH2)2
-NHSO2(CH2)3
NHC(O)OC(CH3)3
-NH
C(O)OC(CH3)3
-NHCH2
CF3
-NHCH2
CN
-NHC(O)
-NHC(O)
(CH2)2CH3
-NHC(O)
-NHC(O)
-NHC(O)
-NHC(O)
-NHC(O)
-NHC(O)NHCH2CH3
-NHC(O)
OCH3
-NHC(O)NHC(O)OCH2CH3
-NHC(O)NH
-NHC(O)
-NHC(O)OCH2
-NHC(O)O
-NHC(O)CH2CF3
-NHCH2
-NHC(O)CH(OH)CF3
-NHC(O)CF3
-NHC(O)(CH2)2
-N(CH3)C(O)
OCH3
-NHC(O)
-NHC(O)CH2
-NHCH2
-NHCH2
-NHCH2
-NHC(O)(CH2)3
NHC(O)OC(CH3)3
-NHC(O)CH(CH2)2
-NHC(O)(CH2)2C(O)

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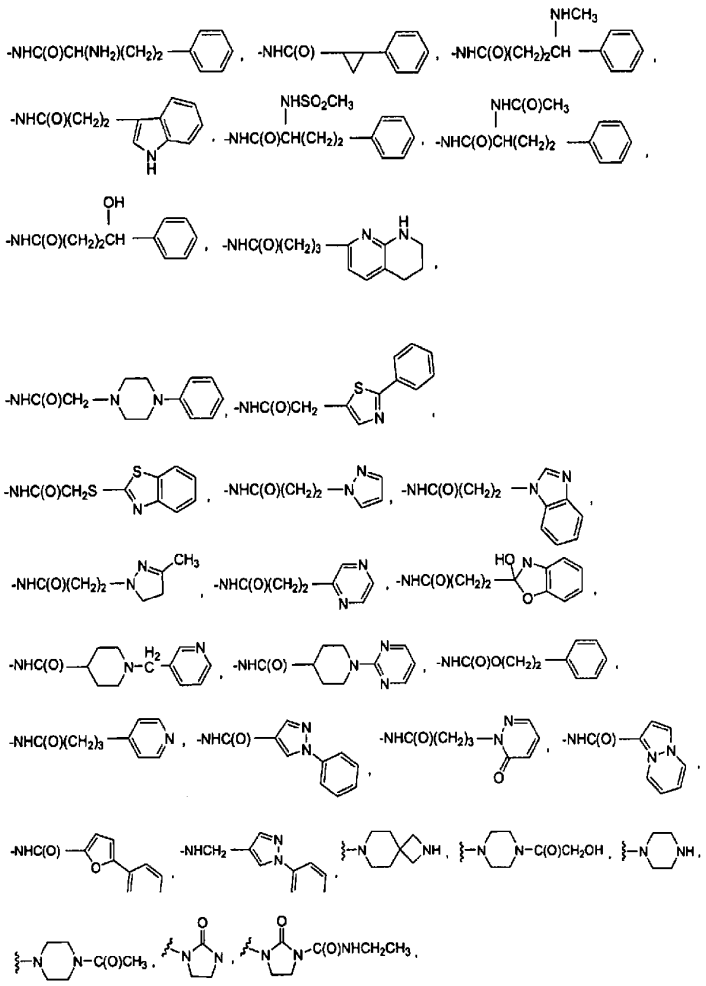

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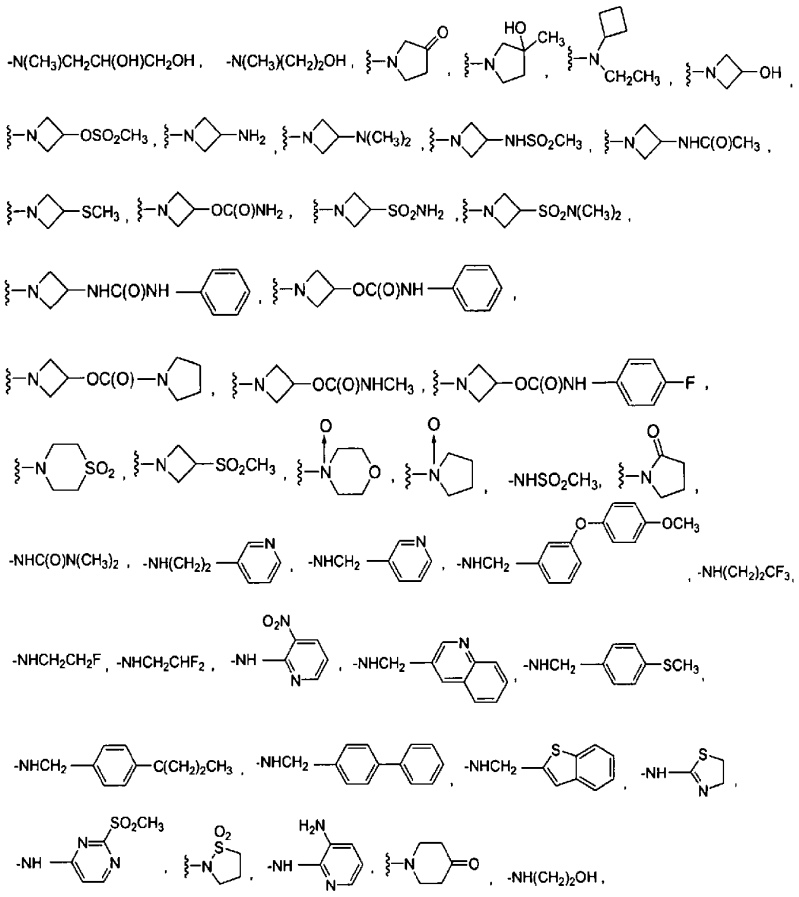

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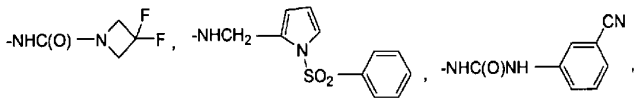

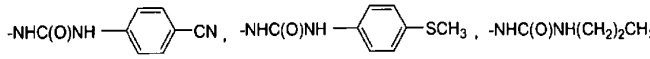

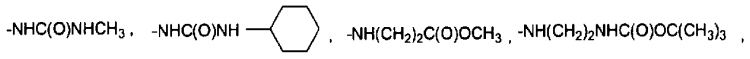

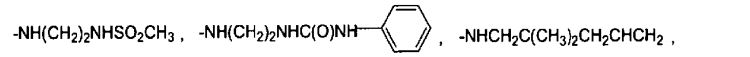

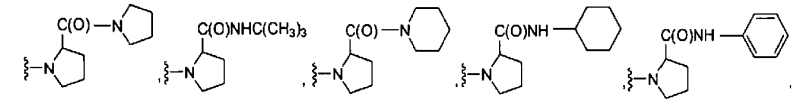

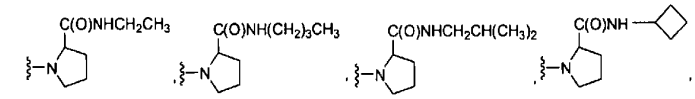

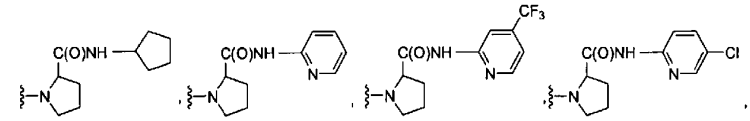

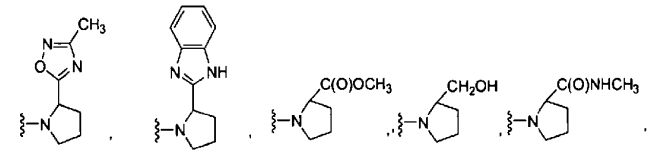

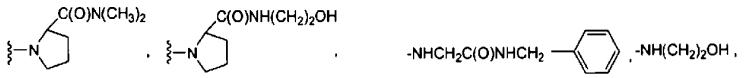

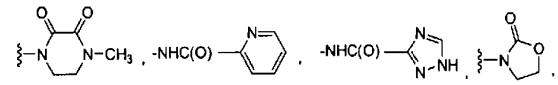

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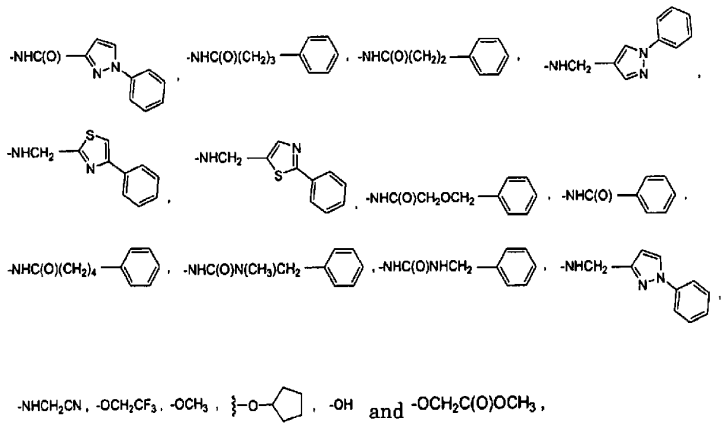

3. A compound of Claim 2, or a pharmaceutically acceptable salt thereof, selected from the group consisting of:

(±)-2-Morpholin-4-*yl*-2-phenyl-1,1-dipyridin-3-*yl*-ethanol,

(±)-3-methyl-2-morpholin-4-yl-1,1,-dipyridin-3-ylbutan-1-ol,

(±)-2-[(2-methoxyethyl)(methyl)amino]-2-phenyl-1,1-dipyridin-3-ylethanol,

(±)-2-phenyl-2-piperidin-1-yl-1,1-dipyridin-3-ylethanol,

(±)-2-phenyl-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol,

(±)-*tert*-butyl 4-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)piperazine-1-carboxylate,

2-[(1*S*,4*S*)-2-oxa-5-azabicyclo[2.21]hept-5-yl]-2-phenyl-1,1-dipyridin-3-ylethanol,

(±)-2(1,4-oxazepan-4-yl)-2-phenyl-1,1-dipyridin-3-ylethanol,

(±)-2-phenyl-1,1-dipyridin-3-yl-2-thiomorpholin-4-ylethanol,

(±)-2-(diethylamino)-2-phenyl-1,1-dipyridin-3-ylethanol,

(±)-2-(7-azabicyclo[2.2.1]hept-7-yl)-2-phenyl-1,1-dipyridin-3-ylethanol,

(±)-2-(3,3-difluoropyrrolidin-1-yl)-2-phenyl-1,1-dipyridin-3-ylethanol,

(±)-2-phenyl-1,1-dipyridin-3-yl-2-[2-(trifluoromethyl)pyrrolidin-1-yl]ethanol,

(±)-2-(2-isopropylpyrrolidin-1-yl)-2-phenyl-1,1-dipyridin-3-ylethanol,

(2*R*)-2-cyclopropyl-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol,

(±)-2-[cyclobutyl(ethyl)amino]-2-phenyl-1,1-dipyridin-3-ylethanol,

(±)-2-[ethyl(2,2,2-trifluoroethyl)amino]-2-phenyl-1,1-dipyridin-3-ylethanol,

(±)-2-(3-fluoropyrrolidin-1-yl)-2-phenyl-1,1-dipyridin-3-ylethanol,

(±)-2-phenyl-2-(phenylsulfonyl)-1,1-dipyridin-3-ylethanol,

(±)-2-(1,3-dimethyl-1*H*-1,2,4-triazol-5-yl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol,

(±)-3-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)-1,3-oxazolidin-2-one,
(±)-3-[2-hydroxy-1-(2-oxo-1,3-oxazolidin-3-yl)-2,2-dipyridin-3-ylethyl]benzonitrile,
(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-3-methylimidazolidin-2-one,
(±)-1-*tert*-butyl-3[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]imidazolidin-2-one,
(±)-3-(2-hydroxy-2,2-dipyridin-3-yl-1-pyrrolidin-1-ylethyl)benzonitrile,
(±)-2-(4-fluorophenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol,
(±)-2-(3-methoxyphenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol,
2-[(2r)-2-(methoxymethyl)pyrrolidin-1-yl]-2-phenyl-1,1-dipyridin-3-ylethanol,
(±)-2-(3-bromophenyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol,
(±)-2-(3,3-difluoroazetidin-1-yl)-2-(4-fluorophenyl)-1,1-dipyridin-3-ylethanol,
(±)-2-(5-chloro-2-thienyl)-1,1-dipyridin-3-yl-2-pyrrolidin-1-ylethanol,
2-[(3*R*,4*R*)-3,4-difluoropyrrolidin-1-yl]-2-phenyl-1,1-dipyridin-3-ylethanol,
(±)-1-(2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl)piperidin-3-ol,
2-(4-fluorophenyl)-2-[(2,5)-2-(hydroxymethyl)pyrrolidin-1-yl]-1,1-dipyridin-3-ylethanol,
(±)-2-(cyclobutylamino)-2-(4-fluorophenyl)-1,1-dipyridin-3-ylethanol,
(±)-2-phenyl-1,1-dipyridin-3-yl-2-[(2,2,2-trifluoroethyl)-amino]ethanol,
2-(benzyloxy)-N-[(1*R*)-2-hydroxy-1-phenyl-2,2-dipyridin-3-ylethyl]acetamide,
N[(1*R*)-1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]-4-phenylbutanamide,
benzyl[(1*R*)-1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]carbamate,
(±)-2-phenyl-1,1-dipyridin-3-yl-2-(1*H*-pyrrol-1-yl)ethanol,
(±)-3-(2-hydroxy-1-morpholin-4-yl-2,2-dipyridin-3-ylethyl)benzonitrile,
(±)-3,3'-(1-fluoro-2-phenyl-2-pyrrolidin-1-ylethane-1,1-diyl)dipyridine,
(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ethyl]azetidin-3-ol,
(±)-1-[1-(4-fluorophenyl)-2-hydroxy-2,2-dipyridin-3-ylethyl]azetidin-3-yl phenylcarbamate,
(±)-1-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl]pyrrolidin-2-one,
(±)-4-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl]morpholine,
(±)-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl](2,2,2-trifluoroethyl)amine,
(±)-4-[1-(3,4-dichlorophenyl)-2,2-dipyridin-3-ylethyl]morpholine,
(±)-3,3'-[2-(4-fluorophenyl)-2-pyrrolidin-1-ylethane-1,1-diyl]dipyridine,
(±)-4-[1-(4-fluorophenyl)-2-pyridin-2-yl-2-pyridin-3-ylethyl]morpholine,
(±)-4-[1-(3-chlorophenyl)-2,2-dipyridin-3-ylethyl]morpholine,
(±)-4-[1-(3,5-dichlorophenyl)-2,2-dipyridin-3-ylethyl]morpholine,
(±)-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl](3,3,3-trifluoropropyl)amine,

(±)-[1-(3-chlorophenyl)-2,2-dipyridin-3-ylethyl(2,2,2-trifluoroethyl)amine,
(±)-[1-(3,5-dichlorophenyl)-2,2-dipyridin-3-ylethyl](2,2,2-trifluoroethyl)amine,
(±)-[1-(3,4-dichlorophenyl)-2,2-dipyridin-3-ylethyl(2,2,2-trifluoroethyl)amine,
(±)-3,3'???42-(1,1-dioxidoisothiazolidin-2-y1)-2-(4-fluorophenyl)ethane-1,1-diyl]pyridine,
(±)-methyl 1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]prolinate,
(±)-3-1[2-(hydroxymethyl)pyrrolidin-1-yl]-2,2-dipyridin-3-ylethyl]benzonitrile,
(±)-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-*N,N*-dimethylprolinamide,
(±)-3-(2-oxo-1,3-oxazolidin-3-yl)-2,2-dipyridin-3-ylethyl]benzonitrile,
(±)-3-(1-{[(1-phenyl-1h-pyrazol-4-yl)methyl]amino-2,2-dipyridin-3-ylethyl)benzonitrile,
(*R*)3-(1-morpholin-4-yl-2,2-dipyridin-3-ylethyl)benzonitri1e,
(*S*)-3-(1-morpholin-4-yl-2,2-dipyridin-3-ylethyl)benzonitrile,
(*S*)-{1-[1-(3-bromophenyl)-2,2-dipyridin-3-ylethyl]piperidin-4-yl}ethanethioate,
(±)-3-[1-(2,4-dioxoimidazolidin-1-yl)-2,2-dipyridin-3-ylethyl]benzonitrile,
(±)-3-[1-(2-oxomorpholin-4-yl)-2,2-dipyridin-3-ylethyl]benzonitrile,
(±)-3[1-(2-hydroxymorpholin-4-yl)-2,2-dipyridin-3-ylethyl]benzonitrile,
(±)-*tert*-butyl-2-{[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]amino}ethylcarbamate,
(±)-*N*-(2-{[1-(3-bromophenyl)-2,2-dipyridin-3-ylethyl]amino}ethyl)methanesulfonamide,
(±)-3-(1-morpholin-4-yl-2,2-dipyridin-3-ylethyl)phenol,
(±)-N-(*tert*-butyl)-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]prolinamide,
(±)-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-piperidinylprolinamide,
(±)-1 [1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-*N*-cyclohexylprolinamide,
(±)-methyl 1-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl]prolinate,
(±)-*N*-{1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]piperidin-4-yl)-*N*-methylmethanesulfonamide,
(±)-3-[1-(2-oxopyrrolidin-l-yl)-2,2-dipyridin-3-ylethyl]benzonitrile,
(±)-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]piperidin-4-yl phenylcarbamate,
(±)-1-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl]-*N*-methylprolinamide,
(±)-*N*-ethyl-1-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl]prolinamide,
(±)-(*N*)-{1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]piperidin-4-y1}-*N*-methylcyclopropanesulfonamide,
(±)-3-[1-(1,1-dioxidolsothiazolidin-2-y1)-2,2-dipyridin-3-ylethyl]benzonitrile,
(±)-*N*-butyl-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]prolinamide,
(±)-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-*N*-isobutylprolinamid,
(±)-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-*N*-cyclobutylprolinamide,
(±)-1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]-*N*-cyclopentylprolinamide,

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(±)-4-[1-(3-bromophenyl)-2,2-dipyridin-3-ylethyl]morpholin-2-one,

(±)-N-{1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]piperidin-4-yl}-*N*-cyclopropylmethanesulfonamide,

(±)-N-{1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]piperidin-4-yl}-*N*-ethylmethanesulfonamide,

(±)-N-{1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]piperidin-4-yl}-*N*-ethylcyclopropanesulfonamide,

(±)-N-{1-[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethylipiperidin-4-yl-*N*-methylethanesulfonamide,

(±)-2-{1-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl]pyrrolidin-2-yl}-1H-benzimidazole,

(±)-3-{1-[2-(1H-benzimidazol-2-yl)pyrrolidin-1-yl]-2,2-dipyridin-3-ylethyl)benzonitrile,

(±)-*tert*-butyl 3-{[1-(3-cyanophenyl)-2,2-dipyridin-3-ylethyl]amino}piperidine-1-carboxylate,

(±)-3-{1-[2-(3-methyl-1,2,4-oxadiazol-5-yl)pyrrolidin-1-yl]-2,2-dipyridin-3-ylethyl}benzonitrile,

(±)-6-{1-[2-(3-methyl-1,2,4-oxadiazo1-5-yl)pyrrolidin-1-yl]-2,2-dipyridin-3-ylethyl}pyridin-2-amine,

(±)-3-[1-(3-hydroxypiperidin-1-yl)-2,2-dipyridin-3-ylethyl]benzonitrile,

(±)-4-{2,2-dipyridin-3-yl-1-[(2,2,2-trifluoroethyl)amino]ethyl}benzonitrile,

(±)-4-{1-{(2-fluoroethyl)amino-2,2-dipyridin-3-ylethyl}benzonitrile,

(±)-4-{1-[(2,2-difluoroethyl)amino]-2,2-dipyridin-3-ylethyl}benzonitrile,

(±)-*N*-{1-[4-(methylthio)phenyl]-2,2-dipyridin-3-ylethyl}-*N*-(2,2,2-trifluoroethyl)amino,

(±)-*N*-{1-[4-(methylsulfonyl)phenyl]-2,2-dipyridin-3-ylethyl}--(2,2,2-trifluoroethyl)amine,

(±)-6-{2,2-dipyridin-3-yl-1-[(2,2,2-trifluoroethyl)amino]ethyl}pyridin-2-amine,

(±)-*N*-{1-[2-(methylthio)phenyl]-2,2-dipyridin-3-ylethyl}-*N*-(2,2,2-trifluoroethyl)amine,

(±)-N-{1-[2-(methylsulfonyl)phenyl]-2,2-dipyridin-3-ylethyl)-*N*-(2,2,2-trifluoroethyl)amine,

(±)-*N*-[1-[3-(methylthio)phenyl]-2,2-dipyridin-3-ylethyl}-*N*-(2,2,2-trifluoroethyl)amine,

(±)-*N*-{1-[3-(methylsulfonyl)phenyl]-2,2-dipyridin-3-ylethyl)-*N*-(2,2,2-trifluoroethyl)amine,

(±)-3-[1-(4-fluorophenyl)-2,2-dipyridin-3-ylethyl]-1,3-oxazolidin-2-one,

(±)-3-[1-(4-chlorophenyl)-2,2-dipyridin-3-ylethyl]-1,3-oxazolidin-2-one,

benzyl (±)-1-(4-chlorophenyl)-2,2-dipyridin-3-ylethylcarbamate,

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(±)-4-[1-(2-oxo-1,3-oxazolidin-3-yl)-2,2-dipyridin-3-ylethyl]benzonitrile,

(±)-neopentyl 1-(4-chlorophenyl)-2,2-dipyridin-3-ylethylcarbamate,

(±)-*N*-{1-[2-(methylthio)pyrimidin-4-yl]-2,2-dipyridin-3-ylethyl}-n-(2,2,2-trifluoroethyl)amine.

4. A method of treating a condition in a mammal, the treatment of which is effected or facilitated by $K_V1.5$ inhibition, which comprises administering a compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, in an amount that is effective at inhibiting $K_V1.5$.

5. A method of Claim 4, wherein the condition is arrhythmia.

6. A method of Claim 5, wherein the cardiac arrhythmia is atrial fibrillation.

7. A method of Claim 5, wherein the cardiac arrhythmia is selected from the group consisting of atrial flutter, atrial arrhythmia and supraventricular tachycardia.

8. A method of preventing a condition in a mammal, the prevention of which is effected or facilitated by $K_V1.5$ inhibition, which comprises administering a compound of any one of claims 1-3 in an amount that is effective at inhibiting $K_V1.5$.

9. A method of Claim 8, wherein the condition is cardiac arrhythmia.

10. A method of Claim 9, wherein the cardiac arrhythmia is atrial fibrillation.

11. A method of Claim 9, wherein the cardiac arrhythmia is selected from the group consisting of atrial flutter, atrial arrhythmia and supraventricular tachycardia.

12. A method of Claim 8, wherein the condition is a thromboembolic event.

13. A method of Claim 12, wherein the thromboembolic event is a stroke.

14. A method of Claim 8, wherein the condition is congestive heart failure.

15. A pharmaceutical formulation comprising a pharmaceutically acceptable carrier and the compound of any one of claims 1-3 or a pharmaceutically acceptable crystal form or hydrate thereof.

16. A pharmaceutical composition made by combining the compound of claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

17. A method of treating cardiac arrhythmia comprising administering a compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, with a

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compound selected from one of the classes of compounds consisting of antiarrhythmic agents having Kv1.5 blocking activities, ACE inhibitors, angiotensin II antagonists, cardiac glycosides, L-type calcium channel blockers, T-type calcium channel blockers, selective and nonselective beta blockers, endothelin antagonists, thrombin inhibitors, aspirin, nonselective NSAIDs, warfarin, factor Xa inhibitors, low molecular weight heparin, unfractionated heparin, clopidogrel, ticlopidine, IIb/IIIa receptor antagonists, 5HT receptor antagonists, integrin receptor antagonists, thromboxane receptor antagonists, TAFI inhibitors and P2T receptor antagonists.

18. A method for inducing a condition of normal sinus rhythm in a patient having atrial fibrillation, which comprises treating the patient with a compound of any one of claims 1-3 or a pharmaceutically acceptable salt thereof.

19. A method for treating tachycardia in a patient which comprises treating the patient with an antitachycardia device in combination with a compound of any one of claims 1-3 or a pharmaceutically acceptable salt thereof.

20. Use of a compound of any one of Claims 1 to 3, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for (1) treating a condition in a mammal, which is effected or facilitated by KV1.5 inhibition; or (2) treating cardiac arrythmia; or (3)treating atrial fibrillation; or (4) treating cardiac arrythmia selected from the group consisting of atrial flutter, atrial arrhythmia and supraventricular tachycardia; (5) preventing a condition in a mammal, the prevention of which is effected or facilitated by KV1.5 inhibition; (6) preventing cardiac arrythmia; (7) preventing atrial fibrillation; (8) preventing atrial flutter, atrial arrhythmia and supraventricular tachycardia; or (9) preventing a thromboembolic event; or (10) preventing a stroke; or (11) preventing congestive heart failure; or (12) inducing a condition of normal sinus rhythm in a patient having atrial fibrillation; or (13) treating tachycardia.

Dated 31 March, 2011
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