(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
3 January 2002 (03.01.2002)

PCT

(10) International Publication Number
WO 02/00647 A1

(51) International Patent Classification^7: C07D 403/10, 417/10, 403/14, 417/14, 401/10, 413/10, 413/14, A61K 31/41, 31/44, A61P 7/02

(21) International Application Number: PCT/US01/20112

(22) International Filing Date: 22 June 2001 (22.06.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/214,033 23 June 2000 (23.06.2000) US

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(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

WO 02/00647 A1

(54) **Title:** HETEROARYL-PHENYL SUBSTITUTED FACTOR XA INHIBITORS

(57) **Abstract:** The present application describes heteroaryl-phenyl substituted compounds and derivatives thereof, or pharmaceutically acceptable salt or prodrug forms thereof, which are useful as inhibitors of factor Xa.

TITLE

Heteroaryl-Phenyl Substituted Factor Xa Inhibitors

FIELD OF THE INVENTION

This invention relates generally to heteroaryl-phenyl substituted compounds and derivatives thereof, which are inhibitors of trypsin-like serine protease enzymes, especially factor Xa, pharmaceutical compositions containing the same, and methods of using the same as anticoagulant agents for treatment and prevention of thromboembolic disorders.

BACKGROUND OF THE INVENTION

Activated factor Xa, whose major practical role is the generation of thrombin by the limited proteolysis of prothrombin, holds a central position that links the intrinsic and extrinsic activation mechanisms in the final common pathway of blood coagulation. The generation of thrombin, the final serine protease in the pathway to generate a fibrin clot, from its precursor is amplified by formation of prothrombinase complex (factor Xa, factor V, Ca^{2+} and phospholipid). Since it is calculated that one molecule of factor Xa can generate 138 molecules of thrombin (Elodi, S., Varadi, K.: Optimization of conditions for the catalytic effect of the factor IXa-factor VIII Complex: Probable role of the complex in the amplification of blood coagulation. *Thromb. Res.* **1979**, *15*, 617-629), inhibition of factor Xa may be more efficient than inactivation of thrombin in interrupting the blood coagulation system.

Therefore, efficacious and specific inhibitors of factor Xa are needed as potentially valuable therapeutic agents for the treatment of thromboembolic disorders. It is thus desirable to discover new factor Xa inhibitors.

SUMMARY OF THE INVENTION

Accordingly, one object of the present invention is to provide novel heteroaryl-phenyl substituted compounds and derivatives thereof that are useful as factor Xa inhibitors or pharmaceutically acceptable salts or prodrugs thereof.

It is another object of the present invention to provide pharmaceutical compositions comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of at least one of the compounds of the present invention or a pharmaceutically acceptable salt or prodrug form thereof.

It is another object of the present invention to provide a method for treating thromboembolic disorders comprising administering to a host in need of such treatment a therapeutically effective amount of at least one of the compounds of the present invention or a pharmaceutically acceptable salt or prodrug form thereof.

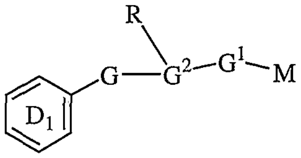
It is another object of the present invention to provide novel heteroaryl-phenyl substituted compounds for use in therapy.

It is another object of the present invention to provide the use of novel heteroaryl-phenyl substituted compounds for the manufacture of a medicament for the treatment of a thromboembolic disorder.

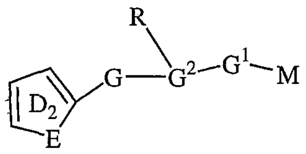
These and other objects, which will become apparent during the following detailed description, have been achieved by the inventors' discovery that the presently claimed heteroaryl-phenyl substituted compounds and derivatives thereof, or pharmaceutically acceptable salt or prodrug forms thereof, are effective factor Xa inhibitors.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

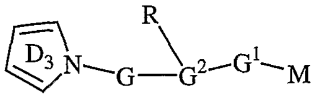
[1] Thus, in a first embodiment, the present invention provides a novel compound of formula Ia, Ib, or Ic:



Ia



Ib



Ic

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

ring D_1 is selected from pyridine, pyrazine, pyridazine, and pyrimidine and is substituted with 1 R^a and 0-1 R^b;

ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-3 N atoms, wherein E is selected from O, S, and N-R^c and ring D_2 is substituted with 1 R^a and 0-1 R^b;

ring D_3 is a 5-membered heteroaromatic ring system comprising carbon atoms and from 0-3 additional N atoms and ring D_3 is substituted with 1 R^a and 0-1 R^b;

R is selected from H, C_{1-4} alkyl, F, Cl, Br, I, OH, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, CN, $C(=NR^8)NR^7R^9$, $NHC(=NR^8)NR^7R^9$, $NR^8CH(=NR^7)$, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, $C(=NH)NH_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl$)_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), $CH_2CH_2N(C_{1-3}$ alkyl$)_2$, $(CR^8R^9)_tNR^7R^8$, $(CR^8R^9)_tC(O)NR^7R^8$, and OCF_3;

R^a is selected from H, C_{1-4} alkyl, F, Cl, Br, I, OH, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, CN, $C(=NR^8)NR^7R^9$, $NHC(=NR^8)NR^7R^9$, $NR^8CH(=NR^7)$, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, $C(=NH)NH_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl$)_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), $CH_2CH_2N(C_{1-3}$ alkyl$)_2$, $(CR^8R^9)_tNR^7R^8$, $(CR^8R^9)_tC(O)NR^7R^8$, and OCF_3;

R^b is selected from H, C_{1-4} alkyl, F, Cl, Br, I, OH, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, CN, $C(=NR^8)NR^7R^9$, $NHC(=NR^8)NR^7R^9$, $NR^8CH(=NR^7)$, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, $C(=NH)NH_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl$)_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), $CH_2CH_2N(C_{1-3}$ alkyl$)_2$, $(CR^8R^9)_tNR^7R^8$, $(CR^8R^9)_tC(O)NR^7R^8$, and OCF_3;

R^c is selected from H, C_{1-4} alkyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, $C(=NH)NH_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl$)_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), $CH_2CH_2N(C_{1-3}$ alkyl$)_2$, $(CR^8R^9)_tNR^7R^8$, $(CR^8R^9)_tC(O)NR^7R^8$, and OCF_3;

G is absent or is selected from CH_2, C(O), O, NR^3, $S(O)_p$, CH_2CH_2, $C(O)CH_2$, $CH_2C(O)$, OCH_2, CH_2O, NR^3CH_2, CH_2NR^3, $S(O)_pCH_2$, $CH_2S(O)_p$, $CH_2CH_2CH_2$, $C(O)CH_2CH_2$, $CH_2C(O)CH_2$, $CH_2CH_2C(O)$, OCH_2CH_2, CH_2OCH_2, CH_2CH_2O, $NR^3CH_2CH_2$, $CH_2NR^3CH_2$, $CH_2CH_2NR^3$, $S(O)_pCH_2CH_2$, $CH_2S(O)_pCH_2$, and $CH_2CH_2S(O)_p$;

G_1 is absent or is selected from $(CR^3R^{3a})_{1-5}$, $(CR^3R^{3a})_{0-2}CR^3{=}CR^3(CR^3R^{3a})_{0-2}$, $(CR^3R^{3a})_{0-2}C{\equiv}C(CR^3R^{3a})_{0-2}$, $(CR^3R^{3a})_uC(O)(CR^3R^{3a})_w$, $(CR^3R^{3a})_uC(O)O(CR^3R^{3a})_w$, $(CR^3R^{3a})_uOC(O)(CR^3R^{3a})_w$, $(CR^3R^{3a})_uO(CR^3R^{3a})_w$, $(CR^3R^{3a})_uNR^3(CR^3R^{3a})_w$, $(CR^3R^{3a})_uC(O)NR^3(CR^3R^{3a})_w$, $(CR^3R^{3a})_uNR^3C(O)(CR^3R^{3a})_w$, $(CR^3R^{3a})_uOC(O)NR^3(CR^3R^{3a})_w$, $(CR^3R^{3a})_uNR^3C(O)O(CR^3R^{3a})_w$, $(CR^3R^{3a})_uNR^3C(O)NR^3(CR^3R^{3a})_w$, $(CR^3R^{3a})_uNR^3C(S)NR^3(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(O)(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(O)_2(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(O)NR^3(CR^3R^{3a})_w$, $(CR^3R^{3a})_uNR^3S(O)_2(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(O)_2NR^3(CR^3R^{3a})_w$, and $(CR^3R^{3a})_uNR^3S(O)_2NR^3(CR^3R^{3a})_w$, wherein u + w total 0, 1, 2, 3, or 4, provided that G_1 does not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached;

G^2 is phenyl, naphthyl, or a 5-10 membered heteroaryl consisting of carbon atoms and from 1-3 heteroatoms selected from N, O, and S;

M is isoxazoline, pyrazoline, isothiazoline, triazoline, tetrazoline, phenyl, or a 5-6 membered aromatic heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from O, N, and S, and is substituted with -Z-A-B;

M is also substituted with 0-2 R^{1a};

Z is selected from a bond, $-(CR^2R^{2a})_{1-4}-$, $(CR^2R^{2a})_qO(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qNR^3(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qC(O)(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qC(O)O(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qOC(O)(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qC(O)NR^3(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qNR^3C(O)(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qOC(O)O(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qOC(O)NR^3(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qNR^3C(O)O(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qNR^3C(O)NR^3(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qS(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qS(O)(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qS(O)_2(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qSO_2NR^3(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qNR^3SO_2(CR^2R^{2a})_{q^1}$, and $(CR^2R^{2a})_qNR^3SO_2NR^3(CR^2R^{2a})_{q^1}$, wherein q + q^1 total 0, 1, or 2, provided that Z does not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached;

R^{1a} is selected from H, $-(CH_2)_r-R^{1b}$, $-CH=CH-R^{1b}$, NCH_2R^{1c}, OCH_2R^{1c}, SCH_2R^{1c}, $NH(CH_2)_2(CH_2)_tR^{1b}$, $O(CH_2)_2(CH_2)_tR^{1b}$, $S(CH_2)_2(CH_2)_tR^{1b}$, $S(O)_p(CH_2)_rR^{1d}$, $O(CH_2)_rR^{1d}$, $NR^3(CH_2)_rR^{1d}$, $OC(O)NR^3(CH_2)_rR^{1d}$, $NR^3C(O)NR^3(CH_2)_rR^{1d}$, $NR^3C(O)O(CH_2)_rR^{1d}$, and $NR^3C(O)(CH_2)_rR^{1d}$, provided that R^{1a} forms other than an N-halo, N-N, N-S, N-O, or N-CN bond;

alternatively, when two R^{1a}'s are attached to adjacent atoms, together with the atoms to which they are attached they form a 5-7 membered ring consisting of: carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and $S(O)_p$, this ring being substituted with 0-2 R^{4b} and comprising: 0-3 double bonds;

R^{1b} is selected from H, C_{1-3} alkyl, F, Cl, Br, I, -CN, -CHO, $(CF_2)_rCF_3$, $(CH_2)_rOR^2$, NR^2R^{2a}, $C(O)R^{2c}$, $OC(O)R^2$, $(CF_2)_rCO_2R^{2a}$, $S(O)_pR^{2b}$, $NR^2(CH_2)_rOR^2$, $C(=NR^{2c})NR^2R^{2a}$, $NR^2C(O)R^{2b}$, $NR^2C(O)NHR^{2b}$, $NR^2C(O)_2R^{2a}$, $OC(O)NR^{2a}R^{2b}$, $C(O)NR^2R^{2a}$, $C(O)NR^2(CH_2)_rOR^2$, $SO_2NR^2R^{2a}$, $NR^2SO_2R^{2b}$, C_{3-6} carbocycle substituted with 0-2 R^{4a}, and 5-10 membered heterocycle consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-2 R^{4a}, provided that R^{1b} forms other than an N-halo, N-N, N-S, N-O, or N-CN bond;

R^{1c} is selected from H, $CH(CH_2OR^2)_2$, $C(O)R^{2c}$, $C(O)NR^2R^{2a}$, $S(O)R^{2b}$, $S(O)_2R^{2b}$, and $SO_2NR^2R^{2a}$;

R^{1d} is selected from C_{3-13} carbocycle substituted with 0-2 R^{4a}, and 5-13 membered heterocycle consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-2 R^{4a}, provided that R^{1d} forms other than an N-N, N-S, or N-O bond;

R^2, at each occurrence, is selected from H, CF_3, C_{1-6} alkyl, benzyl, C_{3-6} carbocyclic residue substituted with 0-2 R^{4b}, and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4b};

R^{2a}, at each occurrence, is selected from H, CF_3, C_{1-6} alkyl, benzyl, phenethyl, C_{3-6} carbocyclic residue substituted with 0-2 R^{4b}, and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4b};

R^{2b}, at each occurrence, is selected from CF_3, C_{1-4} alkoxy, C_{1-6} alkyl, benzyl, C_{3-6} carbocyclic residue substituted with 0-2 R^{4b}, and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4b};

R^{2c}, at each occurrence, is selected from CF_3, OH, C_{1-4} alkoxy, C_{1-6} alkyl, benzyl, C_{3-6} carbocyclic residue substituted with 0-2 R^{4b}, and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4b};

alternatively, R^2 and R^{2a}, together with the atom to which they are attached, combine to form a 5 or 6 membered saturated, partially saturated or unsaturated ring substituted with 0-2 R^{4b} and comprising carbon atoms and from 0-1 additional heteroatoms selected from the group consisting of N, O, and S;

R^3, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

R^{3a}, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

R^{3b}, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

R^{3c}, at each occurrence, is selected from C_{1-4} alkyl, and phenyl;

R^{3d}, at each occurrence, is selected from H, C_{1-4} alkyl, C_{1-4} alkyl-phenyl, and $C(=O)R^{3c}$;

A is selected from:

C_{3-10} carbocyclic residue substituted with 0-2 R^4, and

5-12 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^4;

B is selected from: H, Y, and X-Y, provided that Z and B are attached to different atoms on A;

X is selected from $-(CR^2R^{2a})_{1-4}-$, $-CR^2(CR^2R^{2b})(CH_2)_t-$, $-C(O)-$, $-C(=NR^{1c})-$, $-CR^2(NR^{1c}R^2)-$, $-CR^2(OR^2)-$, $-CR^2(SR^2)-$, $-C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)$, $-S-$, $-S(O)-$, $-S(O)_2-$, $-SCR^2R^{2a}-$, $-S(O)CR^2R^{2a}-$, $-S(O)_2CR^2R^{2a}-$, $-CR^2R^{2a}S-$, $-CR^2R^{2a}S(O)-$, $-CR^2R^{2a}S(O)_2-$, $-S(O)_2NR^2-$, $-NR^2S(O)_2-$, $-NR^2S(O)_2CR^2R^{2a}-$, $-CR^2R^{2a}S(O)_2NR^2-$, $-NR^2S(O)_2NR^2-$, $-C(O)NR^2-$, $-NR^2C(O)-$, $-C(O)NR^2CR^2R^{2a}-$, $-NR^2C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)NR^2-$, $-CR^2R^{2a}NR^2C(O)-$, $-NR^2C(O)O-$, $-OC(O)NR^2-$, $-NR^2C(O)NR^2-$, $-NR^2-$, $-NR^2CR^2R^{2a}-$, $-CR^2R^{2a}NR^2-$, O, $-CR^2R^{2a}O-$, and $-OCR^2R^{2a}-$;

Y is selected from:

C_{3-10} carbocyclic residue substituted with 0-2 R^{4a}; and

5-12 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4a};

R^4, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, $(CH_2)_rF$, $(CH_2)_rCl$, $(CH_2)_rBr$, $(CH_2)_rI$, C_{1-4} alkyl, $(CH_2)_rCN$, $(CH_2)_rNO_2$, $(CH_2)_rNR^2R^{2a}$, $C(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $C(=NS(O)_2R^5)NR^2R^{2a}$, $NHC(=NR^2)NR^2R^{2a}$, $C(O)NHC(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, $NR^2SO_2-C_{1-4}$ alkyl, $NR^2SO_2R^5$, $S(O)_pR^5$, $(CF_2)_rCF_3$, $(CH_2)_r-CF_3$, NCH_2R^{1c}, OCH_2R^{1c}, SCH_2R^{1c}, $N(CH_2)_2(CH_2)_tR^{1b}$, $O(CH_2)_2(CH_2)_tR^{1b}$, $S(CH_2)_2(CH_2)_tR^{1b}$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5;

R^{4a}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, $(CF_2)_rCF_3$, $(CH_2)_r-CF_3$, $(CH_2)_r-F$, $(CH_2)_r-Br$, $(CH_2)_r-Cl$, C_{1-4} alkyl, $(CH_2)_rCN$, $(CH_2)_rNO_2$, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $(CH_2)_rN=CHOR^3$, $C(O)NH(CH_2)_2NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $NHC(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, $NR^2SO_2-C_{1-4}$ alkyl, $NR^2SO_2R^5$, $C(O)NHSO_2-C_{1-4}$ alkyl, $S(O)_pR^5$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5;

R^{4b}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^3$, $(CH_2)_r-F$, $(CH_2)_r-Cl$, $(CH_2)_r-Br$, $(CH_2)_r-I$, C_{1-4} alkyl, $(CH_2)_r-CN$, $(CH_2)_r-NO_2$, $(CH_2)_rNR^3R^{3a}$, $(CH_2)_rC(O)R^3$,

$(CH_2)_rC(O)OR^{3c}$, $NR^3C(O)R^{3a}$, $C(O)NR^3R^{3a}$, $NR^3C(O)NR^3R^{3a}$, $C(=NR^3)NR^3R^{3a}$, $NR^3C(=NR^3)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, $NR^3SO_2NR^3R^{3a}$, NR^3SO_2-C_{1-4} alkyl, $NR^3SO_2CF_3$, NR^3SO_2-phenyl, $S(O)_pCF_3$, $S(O)_p$-C_{1-4} alkyl, $S(O)_p$-phenyl, $(CH_2)_rCF_3$, and $(CF_2)_rCF_3$;

R^5, at each occurrence, is selected from H, C_{1-6} alkyl, =O, $(CH_2)_rOR^3$, F, Cl, Br, I, -CN, NO_2, $(CH_2)_rNR^3R^{3a}$, $(CH_2)_rC(O)R^3$, $(CH_2)_rC(O)OR^{3c}$, $NR^3C(O)R^{3a}$, $C(O)NR^3R^{3a}$, $NR^3C(O)NR^3R^{3a}$, $CH(=NOR^{3d})$, $C(=NR^3)NR^3R^{3a}$, $NR^3C(=NR^3)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, $NR^3SO_2NR^3R^{3a}$, NR^3SO_2-C_{1-4} alkyl, $NR^3SO_2CF_3$, NR^3SO_2-phenyl, $S(O)_pCF_3$, $S(O)_p$-C_{1-4} alkyl, $S(O)_p$-phenyl, $(CF_2)_rCF_3$, phenyl substituted with 0-2 R^6, naphthyl substituted with 0-2 R^6, and benzyl substituted with 0-2 R^6;

R^6, at each occurrence, is selected from H, OH, $(CH_2)_rOR^2$, halo, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2b}$, $NR^2C(O)R^{2b}$, $NR^2C(O)NR^2R^{2a}$, $C(=NH)NH_2$, $NHC(=NH)NH_2$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, and $NR^2SO_2C_{1-4}$ alkyl;

R^7, at each occurrence, is selected from H, OH, C_{1-4} alkoxycarbonyl, C_{6-10} aryloxy, C_{6-10} aryloxycarbonyl, C_{6-10} arylmethylcarbonyl, C_{1-4} alkylcarbonyloxy C_{1-4} alkoxycarbonyl, C_{6-10} arylcarbonyloxy C_{1-4} alkoxycarbonyl, C_{1-6} alkylaminocarbonyl, phenylaminocarbonyl, and phenyl C_{1-4} alkoxycarbonyl;

R^8, at each occurrence, is selected from H, C_{1-6} alkyl, and $(CH_2)_n$-phenyl;

alternatively, R^7 and R^8, when attached to the same nitrogen, combine to form a 5-6 membered heterocyclic ring consisting of carbon atoms and 0-2 additional heteroatoms selected from the group consisting of N, O, and $S(O)_p$;

R^9, at each occurrence, is selected from H, C_{1-6} alkyl, and $(CH_2)_n$-phenyl;

n, at each occurrence, is selected from 0, 1, 2, and 3;

m, at each occurrence, is selected from 0, 1, and 2;

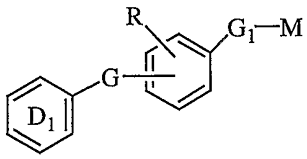
p, at each occurrence, is selected from 0, 1, and 2;

r, at each occurrence, is selected from 0, 1, 2, and 3;

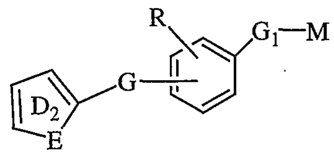
s, at each occurrence, is selected from 0, 1, and 2; and,

t, at each occurrence, is selected from 0, 1, 2, and 3.

[2] In a preferred embodiment, the present invention provides a novel compound, wherein the compound is of formula Ia_1-Ic_1, wherein:



Ia_1



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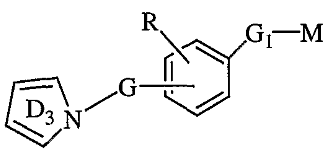


Ic_1

ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N-R^c and ring D_2 is substituted with 1 R^a and 0-1 R^b;

ring D_3 is a 5-membered heteroaromatic ring system comprising carbon atoms and from 0-3 additional N atoms and ring D_3 is substituted with 1 R^a and 0-1 R^b;

R is selected from H, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl$)_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl$)_2$;

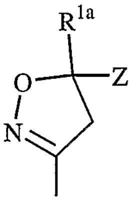
R^a is selected from H, OH, SH, C_{1-3} alkoxy, C_{1-3} thioalkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl$)_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl$)_2$;

R^b is selected from H, C_{1-4} alkyl, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl$)_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl$)_2$;

R^c is selected from H, C_{1-4} alkyl, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl$)_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl$)_2$;

G_1 is absent or is selected from CH_2, C(O), O, NR^3, $S(O)_p$, CH_2CH_2, $C(O)CH_2$, $CH_2C(O)$, OCH_2, CH_2O, NR^3CH_2, CH_2NR^3, $S(O)_pCH_2$, $CH_2S(O)_p$, $CH_2CH_2CH_2$, $C(O)CH_2CH_2$, $CH_2C(O)CH_2$, $CH_2CH_2C(O)$, OCH_2CH_2, CH_2OCH_2, CH_2CH_2O, $NR^3CH_2CH_2$, $CH_2NR^3CH_2$, $CH_2CH_2NR^3$, $S(O)_pCH_2CH_2$, $CH_2S(O)_pCH_2$, and $CH_2CH_2S(O)_p$, and provided that G_1-M form other than a N-N, O-N, or S-N bond;

M is selected from the group: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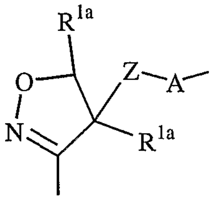
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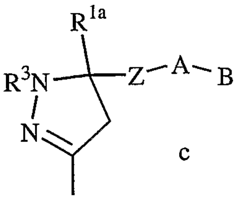
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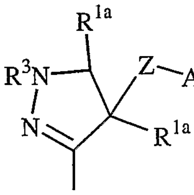
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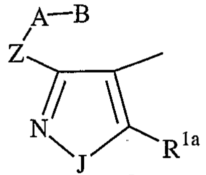
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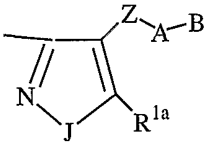
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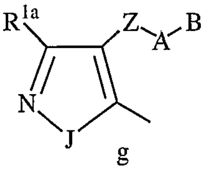
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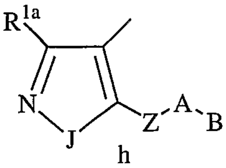
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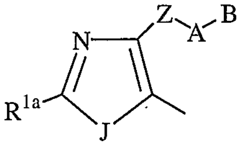
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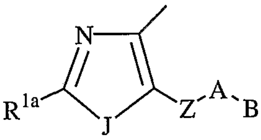
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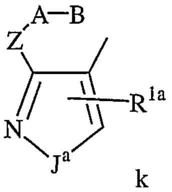
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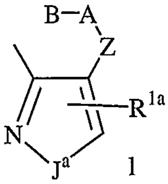
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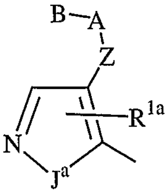
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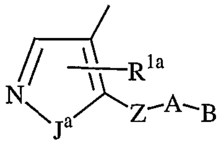
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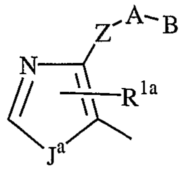
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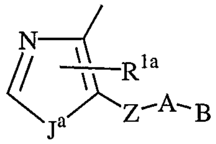
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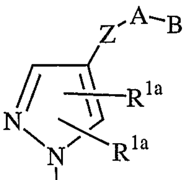
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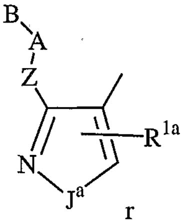
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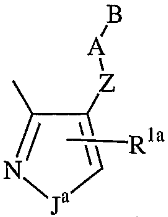
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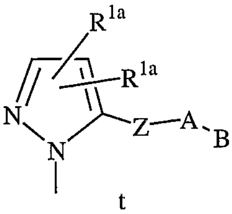
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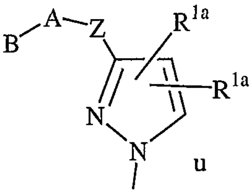
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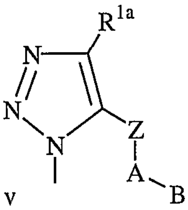
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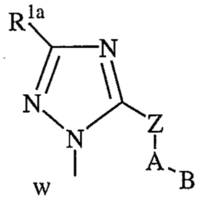
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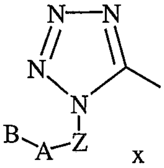
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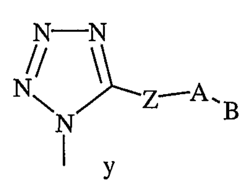
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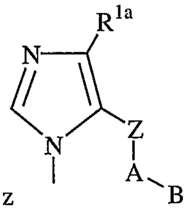
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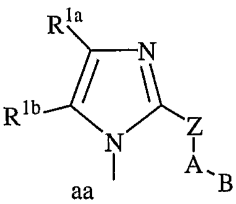
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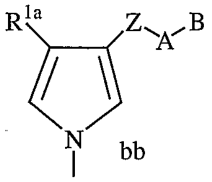
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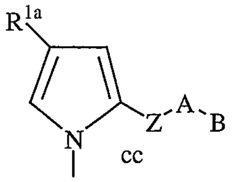
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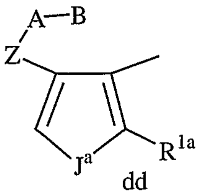
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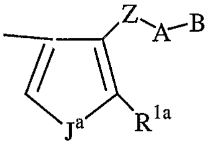
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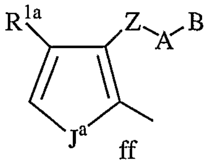
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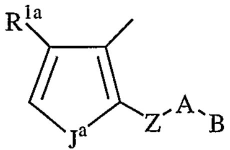
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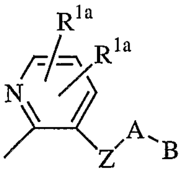
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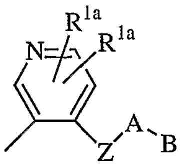
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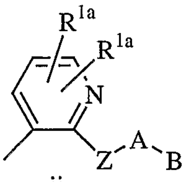
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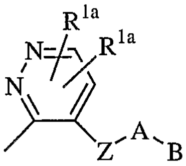
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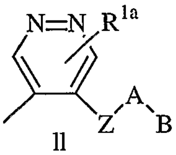
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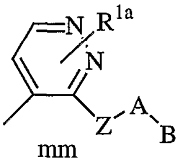
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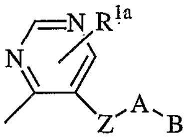
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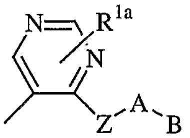
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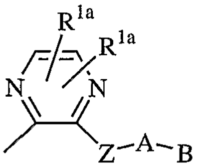
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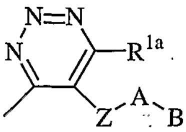
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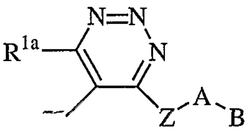
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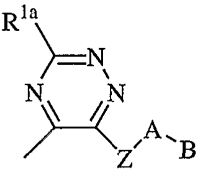
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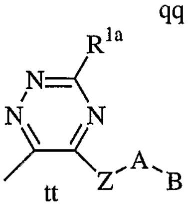
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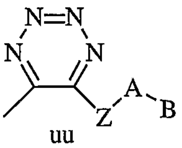
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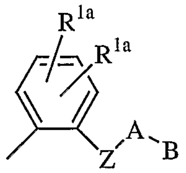
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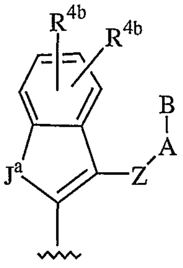
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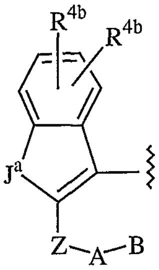
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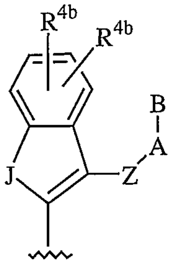
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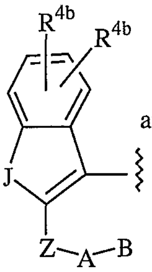
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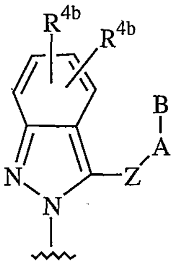
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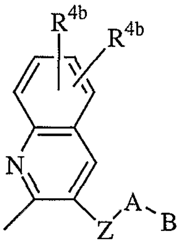
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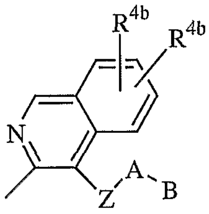
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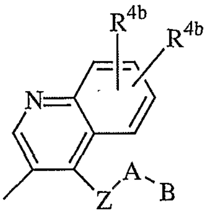
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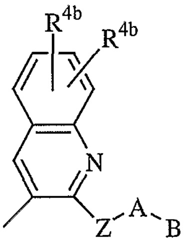
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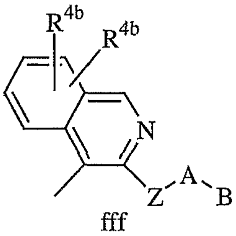
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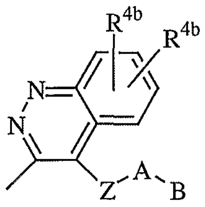
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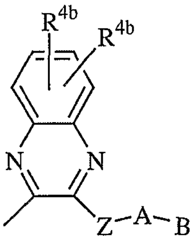
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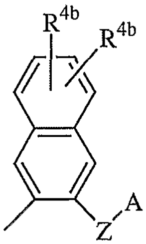
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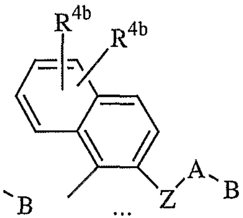
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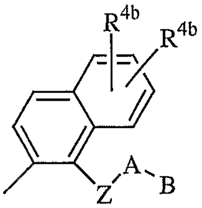

kkk

J is O or S;

J^a is NH or NR^{1a};

G_1 is absent or is selected from $(CR^3R^{3a})_{1-3}$, $(CR^3R^{3a})_uC(O)(CR^3R^{3a})_w$, $(CR^3R^{3a})_uO(CR^3R^{3a})_w$, $(CR^3R^{3a})_uNR^3(CR^3R^{3a})_w$, $(CR^3R^{3a})_uC(O)NR^3(CR^3R^{3a})_w$, $(CR^3R^{3a})_uNR^3C(O)(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(O)(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(O)_2(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(O)NR^3(CR^3R^{3a})_w$, and $(CR^3R^{3a})_uS(O)_2NR^3(CR^3R^{3a})_w$, wherein u + w total 0, 1, or 2, provided that G_1 does not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached;

A is selected from one of the following carbocyclic and heterocyclic systems which are substituted with 0-2 R^4;

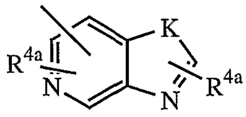
phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, benzoxazolyl, benzthiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, and isoindazolyl;

X is selected from $-(CR^2R^{2a})_{1-4}-$, $-C(O)-$, $-C(=NR^{1c})-$, $-CR^2(NR^{1c}R^2)-$, $-C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)$, $-C(O)NR^2-$, $-NR^2C(O)-$, $-C(O)NR^2CR^2R^{2a}-$, $-NR^2C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)NR^2-$, $-CR^2R^{2a}NR^2C(O)-$, $-NR^2C(O)NR^2-$, $-NR^2-$, $-NR^2CR^2R^{2a}-$, $-CR^2R^{2a}NR^2-$, O, $-CR^2R^{2a}O-$, and $-OCR^2R^{2a}-$;

Y is selected from one of the following carbocyclic and heterocyclic systems that are substituted with 0-2 R^{4a};

cyclopropyl, cyclopentyl, cyclohexyl, phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, isoxazolinyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, benzoxazolyl, benzthiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, and isoindazolyl;

alternatively, Y is selected from the following bicyclic heteroaryl ring systems:



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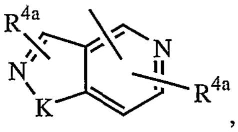

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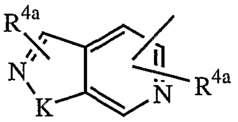

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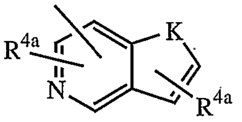

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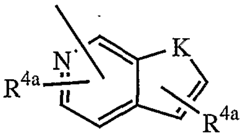

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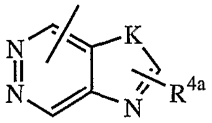

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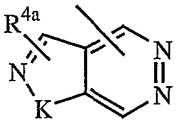

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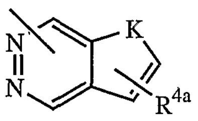


;

K is selected from O, S, NH, and N;

Z is selected from a bond, CH_2O, OCH_2, NH, CH_2NH, $NHCH_2$, $CH_2C(O)$, $C(O)CH_2$, C(O)NH, NHC(O), $CH_2S(O)_2$, $S(O)_2(CH_2)$, SO_2NH, and $NHSO_2$, provided that Z does not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached;

R^4, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, F, Cl, Br, I, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $C(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, NR^2SO_2-C_{1-4} alkyl, $NR^2SO_2R^5$, $S(O)_pR^5$, CF_3, NCH_2R^{1c}, OCH_2R^{1c}, SCH_2R^{1c}, $N(CH_2)_2(CH_2)_tR^{1b}$, $O(CH_2)_2(CH_2)_tR^{1b}$, $S(CH_2)_2(CH_2)_tR^{1b}$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5; and,

R^{4a}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, CF_3, F, Br, Cl, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$,

$(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $NHC(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, NR^2SO_2-C_{1-4} alkyl, $NR^2SO_2R^5$, $C(O)NHSO_2$-C_{1-4} alkyl, $S(O)_pR^5$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5.

[3] In another preferred embodiment, the present invention provides a novel compound, wherein the compound is of formula Ib_1 or Ic_1, wherein;

ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N-R^c and ring D_2 is substituted with 1 R^a and 0-1 R^b;

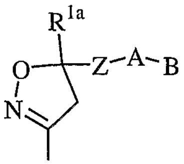
R is selected from H, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl$)_2$;

R^a is selected from H, OH, SH, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl$)_2$;

R^b is selected from H, C_{1-4} alkyl, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl$)_2$;

R^c is selected from H, C_{1-4} alkyl, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl$)_2$;

M is selected from the group: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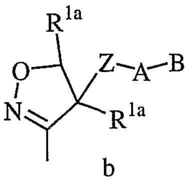
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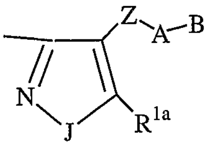
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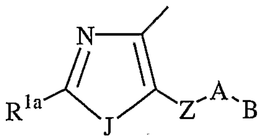
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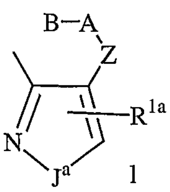
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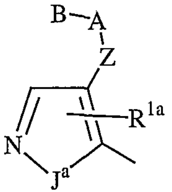
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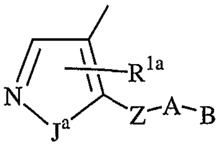
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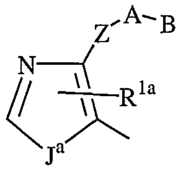
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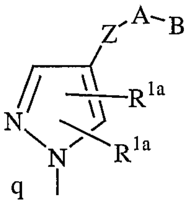
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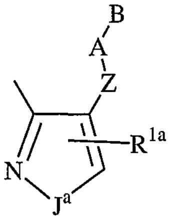
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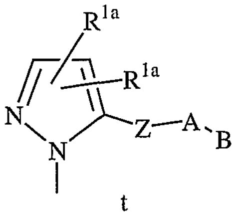
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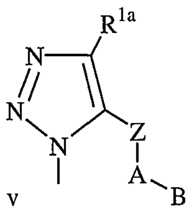
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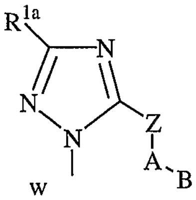
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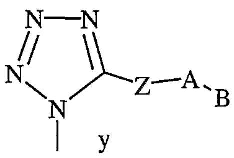
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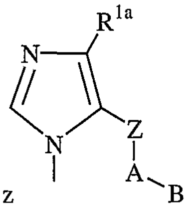
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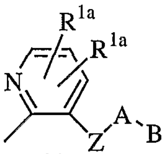
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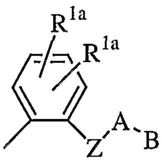

vv

Y is selected from one of the following carbocyclic and heterocyclic systems which are substituted with 0-2 R^{4a};

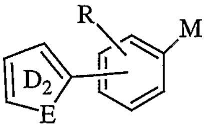
phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazole, thiadiazole, triazole, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole, 1,3,4-thiadiazole, 1,2,3-triazole, 1,2,4-triazole, 1,2,5-triazole, 1,3,4-triazole, benzofuran, benzothiofuran, indole, benzimidazole, benzimidazolone, benzoxazole, benzthiazole, indazole, benzisoxazole, benzisothiazole, and isoindazole;

Z is selected from a bond, CH_2O, OCH_2, NH, CH_2NH, $NHCH_2$, $CH_2C(O)$, $C(O)CH_2$, C(O)NH, NHC(O), $CH_2S(O)_2$, $S(O)_2(CH_2)$, SO_2NH, and $NHSO_2$, provided that Z does not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached;

R^4, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, F, Cl, Br, I, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $C(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, NR^2SO_2-C_{1-4} alkyl, $NR^2SO_2R^5$, $S(O)_pR^5$, CF_3, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5; and,

R^{4a}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, CF_3, F, Br, Cl, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $C(O)NHSO_2$-C_{1-4} alkyl, $S(O)_pR^5$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5.

[4] In another preferred embodiment, the present invention provides a novel compound, wherein the compound is of formula Ib_2:



Ib$_2$

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

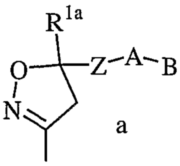
ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N-R^c and ring D_2 is substituted with 1 R^a and 0-1 R^b;

R is selected from H, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, NH(C_{1-3} alkyl), N(C_{1-3} alkyl)$_2$, CH_2NH_2, CH_2NH(C_{1-3} alkyl), and CH_2N(C_{1-3} alkyl)$_2$;

R^a is selected from H, OH, SH, NH_2, NH(C_{1-3} alkyl), and N(C_{1-3} alkyl)$_2$;

R^b is selected from H, C_{1-4} alkyl, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, NH(C_{1-3} alkyl), N(C_{1-3} alkyl)$_2$, CH_2NH_2, CH_2NH(C_{1-3} alkyl), and CH_2N(C_{1-3} alkyl)$_2$;

M is selected from the group: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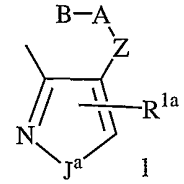
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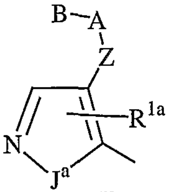
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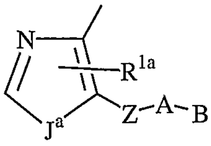
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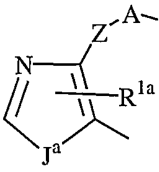
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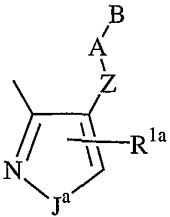
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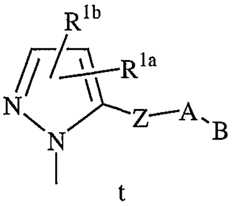
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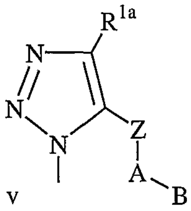
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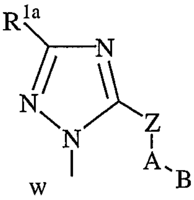
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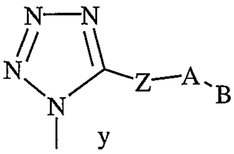
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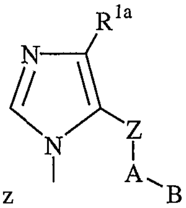
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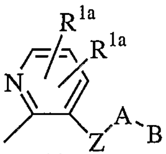
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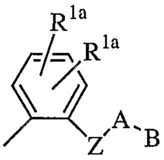
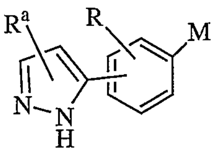
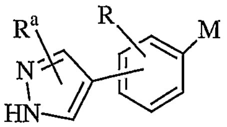
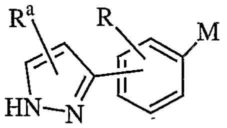
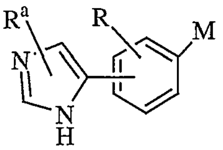
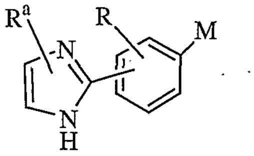
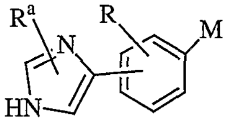
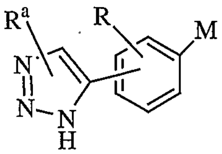
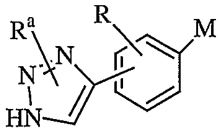
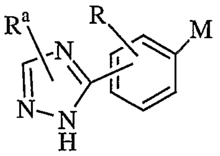
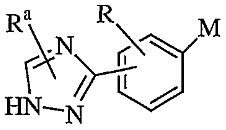
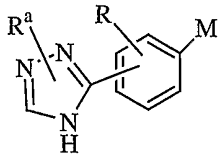
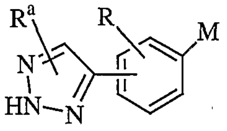
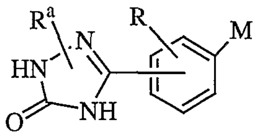
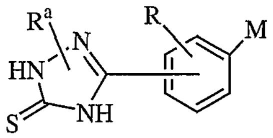

vv

G_1 is absent or is selected from CH_2, CH_2CH_2, CH_2O, OCH_2, NH, CH_2NH, $NHCH_2$, $CH_2C(O)$, $C(O)CH_2$, C(O)NH, NHC(O), $CH_2S(O)_2$, $S(O)_2(CH_2)$, SO_2NH, and $NHSO_2$, provided that G_1 does not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached.

[5] In another preferred embodiment, the present invention provides a novel compound, wherein the compound is selected from one of the formulas:

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

G_1 is absent;

A is selected from phenyl, piperidinyl, pyridyl, and pyrimidyl, and is substituted with 0-2 R^4; and,

B is selected from phenyl, pyrrolidino, N-pyrrolidino-carbonyl, morpholino, N-morpholino-carbonyl, 1,2,3-triazolyl, imidazolyl, and benzimidazolyl, and is substituted with 0-1 R^{4a};

R^2, at each occurrence, is selected from H, CH_3, CH_2CH_3, cyclopropylmethyl, cyclobutyl, and cyclopentyl;

R^{2a}, at each occurrence, is selected from H, CH_3, and CH_2CH_3;

alternatively, R^2 and R^{2a}, together with the atom to which they are attached, combine to form pyrrolidine substituted with 0-2 R^{4b} or piperidine substituted with 0-2 R^{4b};

R^4, at each occurrence, is selected from OH, OR^2, $(CH_2)OR^2$, $(CH_2)_2OR^2$, F, Br, Cl, I, C_{1-4} alkyl, NR^2R^{2a}, $(CH_2)NR^2R^{2a}$, $(CH_2)_2NR^2R^{2a}$, CF_3, and $(CF_2)CF_3$;

R^{4a} is selected from C_{1-4} alkyl, CF_3, OR^2, $(CH_2)OR^2$, $(CH_2)_2OR^2$, NR^2R^{2a}, $(CH_2)NR^2R^{2a}$, $(CH_2)_2NR^2R^{2a}$, SR^5, $S(O)R^5$, $S(O)_2R^5$, $SO_2NR^2R^{2a}$, and 1-CF_3-tetrazol-2-yl;

R^{4b}, at each occurrence, is selected from H, CH_3, and OH;

R^5, at each occurrence, is selected from CF_3, C_{1-6} alkyl, phenyl, and benzyl; and,

r, at each occurrence, is selected from 0, 1, and 2.

[6] In another preferred embodiment, the present invention provides a novel compound, wherein;

A is selected from the group: phenyl, piperidinyl, 2-pyridyl, 3-pyridyl, 2-pyrimidyl, 2-Cl-phenyl, 3-Cl-phenyl, 2-F-phenyl, 3-F-phenyl, 2-methylphenyl, 2-aminophenyl, and 2-methoxyphenyl; and,

B is selected from the group: 2-(aminosulfonyl)phenyl, 2-(methylaminosulfonyl)phenyl, 1-pyrrolidinocarbonyl, 2-(methylsulfonyl)phenyl, 2-(N,N-dimethylaminomethyl)phenyl, 2-(N-methylaminomethyl)phenyl, 2-(N-ethyl-N-methylaminomethyl)phenyl, 2-(N-pyrrolidinylmethyl)phenyl, 1-methyl-2-imidazolyl, 2-methyl-1-imidazolyl, 2-(dimethylaminomethyl)-1-imidazolyl, 2-(methylaminomethyl)-1-imidazolyl, 2-(N-(cyclopropylmethyl)aminomethyl)phenyl, 2-(N-(cyclobutyl)aminomethyl)phenyl, 2-(N-(cyclopentyl)aminomethyl)phenyl, 2-(N-(4-hydroxypiperidinyl)methyl)phenyl, and 2-(N-(3-hydroxypyrrolidinyl)methyl)phenyl.

[7] In another preferred embodiment, the present invention provides a novel compound selected from the group:

1-[3-(1′,3′,4′-Triazol-2′-on-5′-yl)phenyl]-3-trifluoromethyl-5-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(1′,3′,4′-Triazol-2′-on-5′-yl)phenyl]-3-trifluoromethyl-5-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(1′,3′,4′-Triazol-2′-on-5′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(1′,3′,4′-Triazol-2′-on-5′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(1′,3′,4′-Triazol-2′-on-5′-yl)phenyl]-3-trifluoromethyl-5-[(2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(1′,3′,4′-Triazol-2′-on-5′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(2′-Amino-1′,3′,4′-triazol-5′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(2′-Amino-1′,3′,4′-triazol-5′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(2′-Amino-1′,3′,4′-triazol-5′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(2′-Amino-3′,4′-thiadiazol-5′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(2′-Amino-3′,4′-thiadiazol-5′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(2′-Amino-3′,4′-thiadiazol-5′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-5-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]pyrazole;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-5-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]pyrazole;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

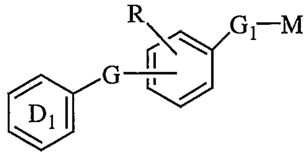
1-[3-(5-Amino-1,3,4-oxadiazol-2-yl)phenyl]-N-{2'-[(dimethylamino)methyl]-3-fluoro-1,1'-biphenyl-4-yl}-3-(trifluoromethyl)-1H-pyrazole-5-carboxamide;

1-[3-(5-Amino-1,3,4-oxadiazol-2-yl)phenyl]-N-(3-fluoro-2'-{[(3S)-3-hydroxy-1-pyrrolidinyl]methyl}-1,1'-biphenyl-4-yl)-3-(trifluoromethyl)-1H-pyrazole-5-carboxamide; and,

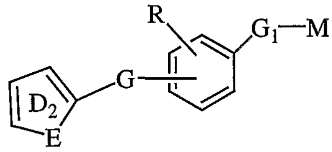
1-[3-(5-Amino-1,3,4-oxadiazol-2-yl)phenyl]-N-(3-fluoro-2'-{[(3S)-3-hydroxy-1-pyrrolidinyl]methyl}-1,1'-biphenyl-4-yl)-5-(trifluoromethyl)-1H-pyrazole-3-carboxamide;

or a pharmaceutically acceptable salt thereof.

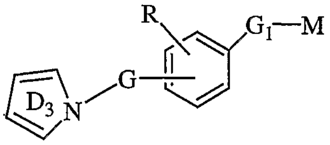
In another embodiment, the present invention provides a novel compound, wherein the compound is of formula Ia_1-Ic_1, wherein:



Ia_1



Ib_1



Ic_1

ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N-R^c and ring D_2 is substituted with 1 R^a and 0-1 R^b;

ring D_3 is a 5-membered heteroaromatic ring system comprising carbon atoms and from 0-3 additional N atoms and ring D_3 is substituted with 1 R^a and 0-1 R^b;

R is selected from H, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl$)_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl$)_2$;

R^a is selected from H, OH, SH, C_{1-3} alkoxy, C_{1-3} thioalkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl$)_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl$)_2$;

R^b is selected from H, C_{1-4} alkyl, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl$)_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl$)_2$;

R^c is selected from H, C_{1-4} alkyl, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl$)_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl$)_2$; and,

G_1 is absent or is selected from CH_2, C(O), O, NR^3, $S(O)_p$, CH_2CH_2, $C(O)CH_2$, $CH_2C(O)$, OCH_2, CH_2O, NR^3CH_2, CH_2NR^3, $S(O)_pCH_2$, $CH_2S(O)_p$, $CH_2CH_2CH_2$, $C(O)CH_2CH_2$, $CH_2C(O)CH_2$, $CH_2CH_2C(O)$, OCH_2CH_2, CH_2OCH_2, CH_2CH_2O, $NR^3CH_2CH_2$, $CH_2NR^3CH_2$, $CH_2CH_2NR^3$, $S(O)_pCH_2CH_2$, $CH_2S(O)_pCH_2$, and $CH_2CH_2S(O)_p$, and provided that G_1-M form other than a N-N, O-N, or S-N bond.

In another embodiment, the present invention provides a novel compound, wherein the compound is of formula Ib_1 or Ic_1, wherein;

ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N-R^c and ring D_2 is substituted with 1 R^a and 0-1 R^b;

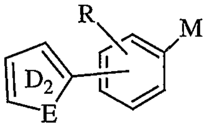
R is selected from H, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl$)_2$;

R^a is selected from H, OH, SH, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl$)_2$;

R^b is selected from H, C_{1-4} alkyl, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl$)_2$; and,

R^c is selected from H, C_{1-4} alkyl, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl$)_2$.

In another embodiment, the present invention provides a novel compound, wherein the compound is of formula Ib_2:



Ib_2

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

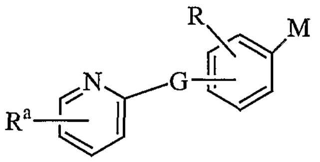
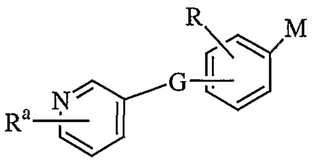
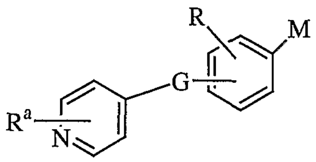
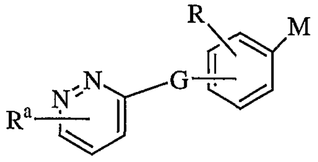
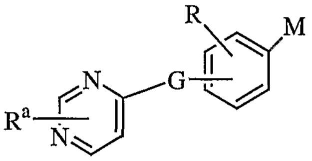
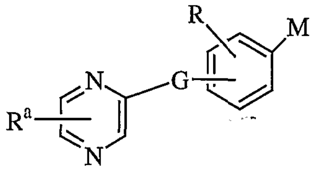
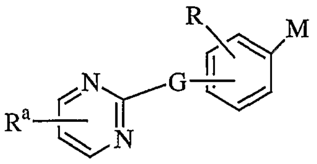
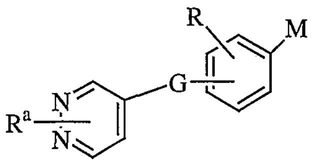
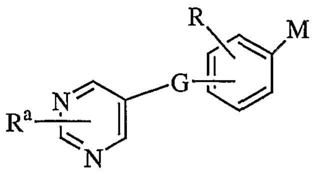
ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N-R^c and ring D_2 is substituted with 1 R^a and 0-1 R^b;

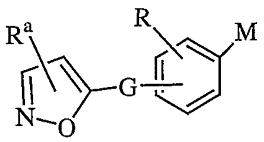
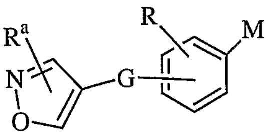
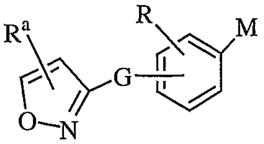
R is selected from H, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, NH(C_{1-3} alkyl), N(C_{1-3} alkyl)$_2$, CH_2NH_2, CH_2NH(C_{1-3} alkyl), and CH_2N(C_{1-3} alkyl)$_2$;

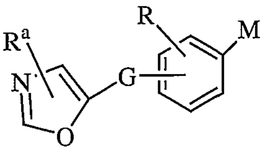
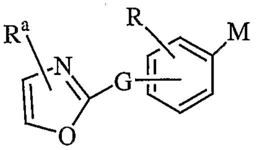
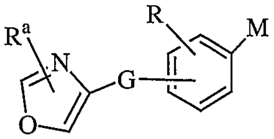
R^a is selected from H, OH, SH, NH_2, NH(C_{1-3} alkyl), and N(C_{1-3} alkyl)$_2$; and,

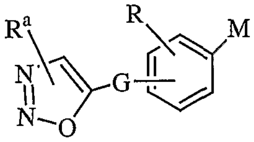
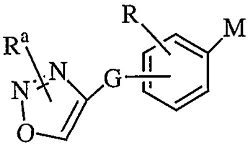
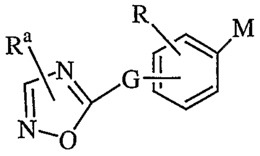
R^b is selected from H, C_{1-4} alkyl, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, NH(C_{1-3} alkyl), N(C_{1-3} alkyl)$_2$, CH_2NH_2, CH_2NH(C_{1-3} alkyl), and CH_2N(C_{1-3} alkyl)$_2$.

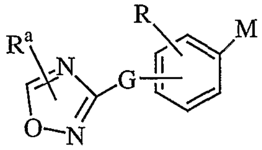
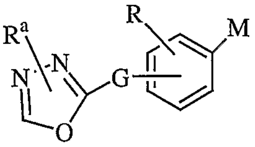
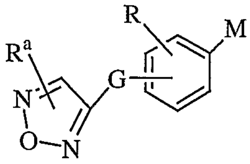
In another embodiment, the present invention provides a novel compound selected from one of the formulas:

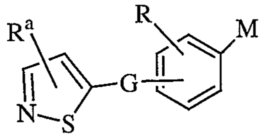
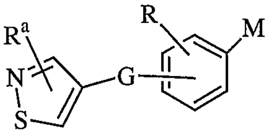
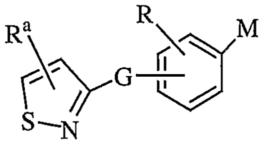










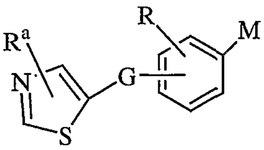
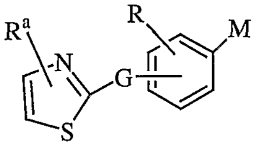
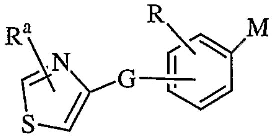




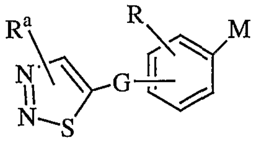
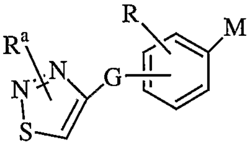
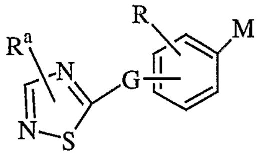




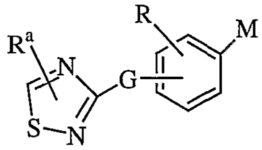
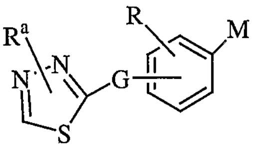
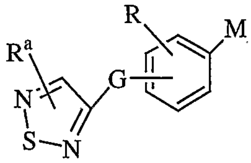




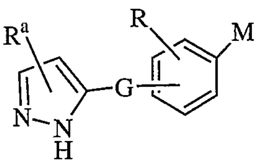
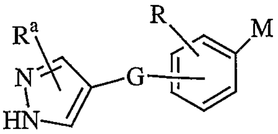
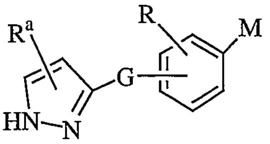
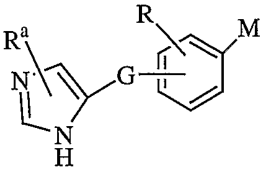
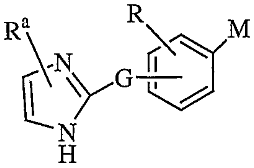
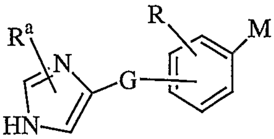
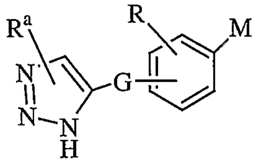
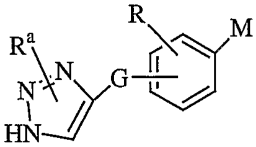
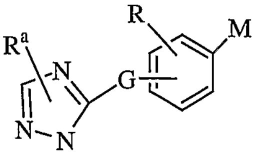
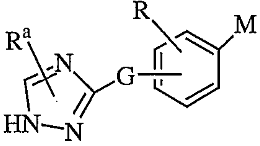
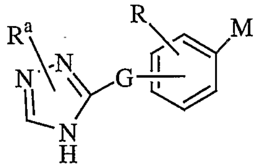
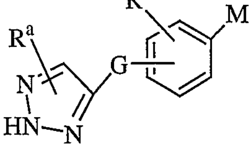
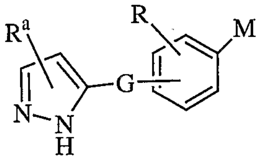
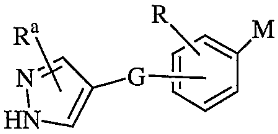
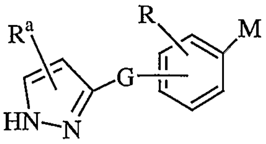
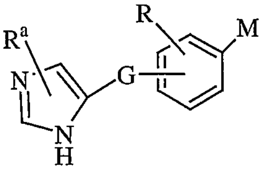
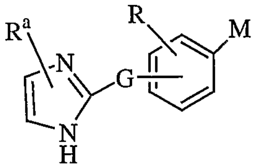
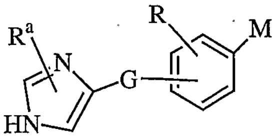
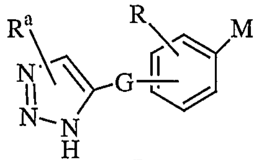
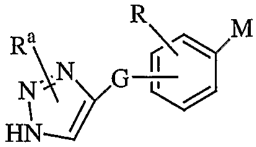
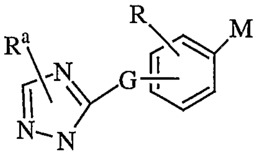
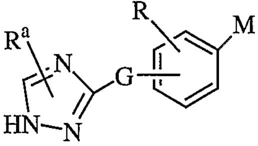
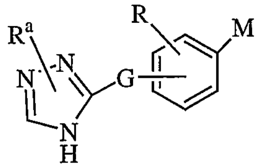
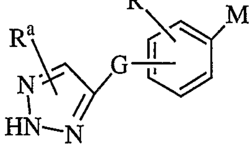
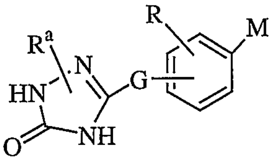
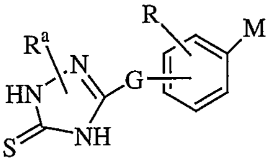




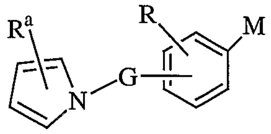
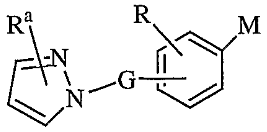
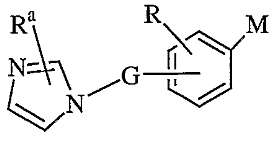
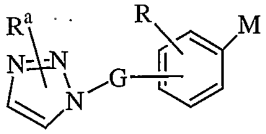
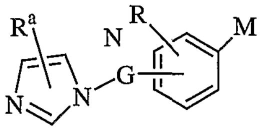
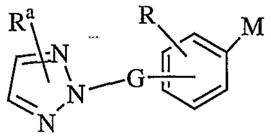
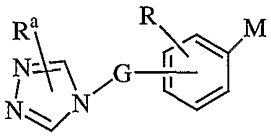




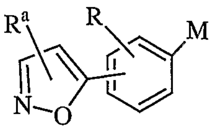
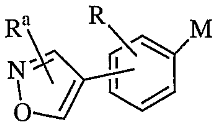
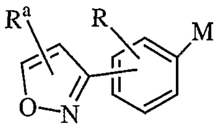
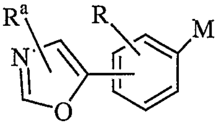
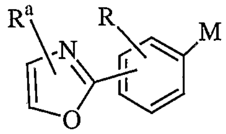
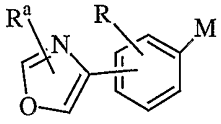
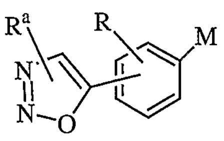
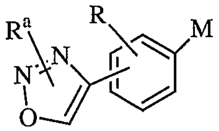
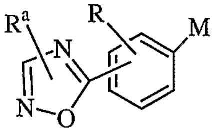
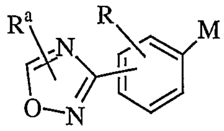
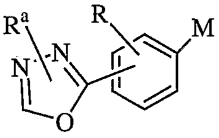
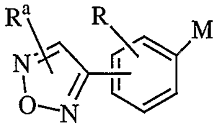




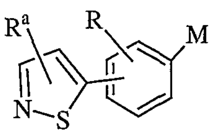
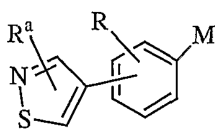
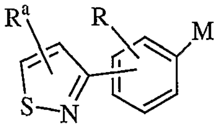
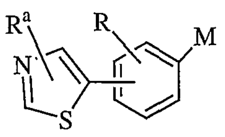
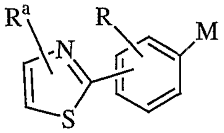
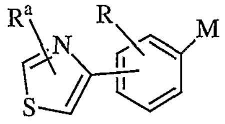
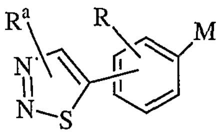
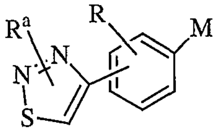
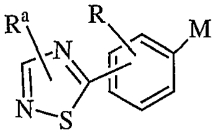
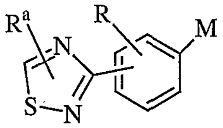
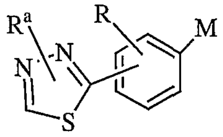
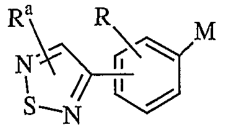
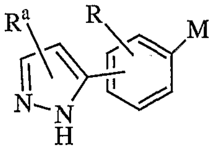
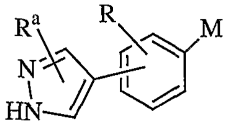
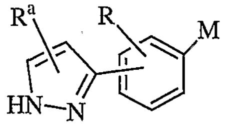
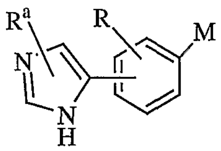
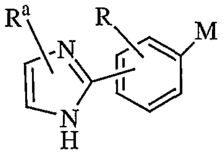
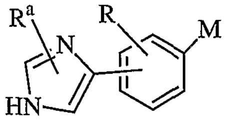
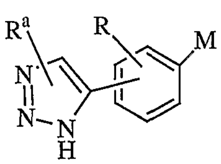
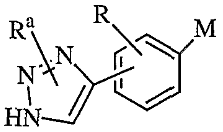
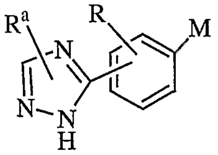
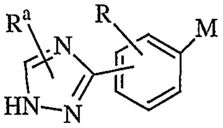
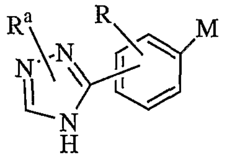
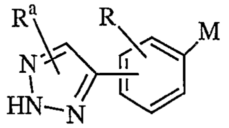
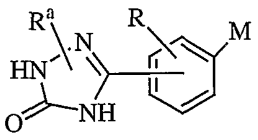
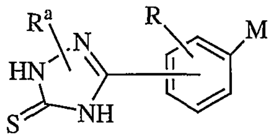



























or a stereoisomer or pharmaceutically acceptable salt thereof.

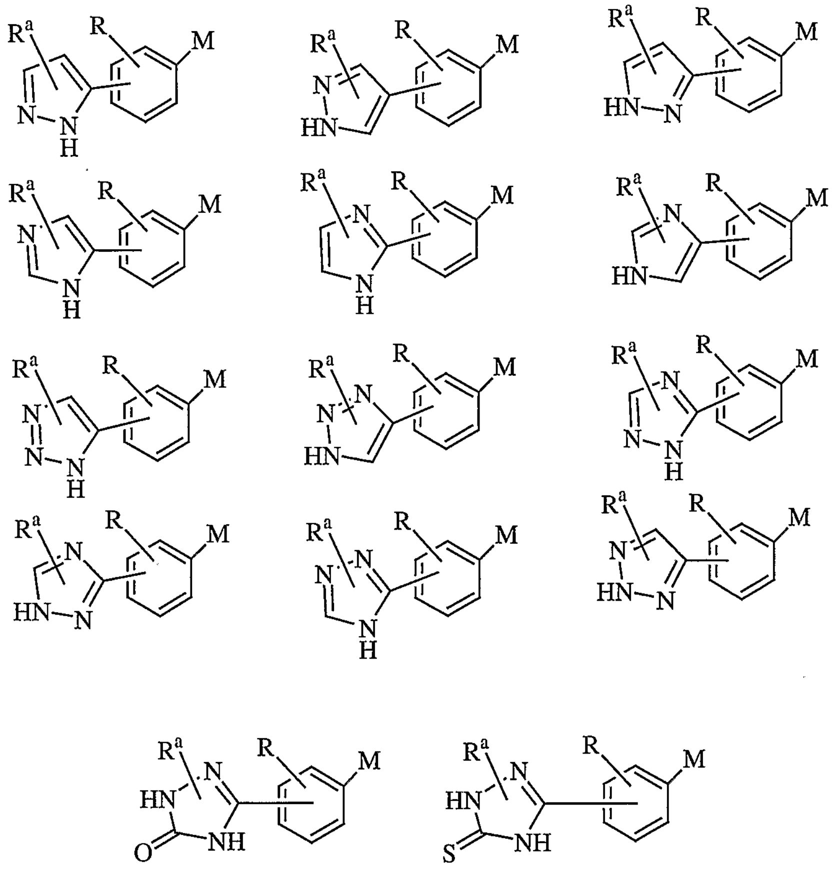
In another embodiment, the present invention provides a novel compound selected from one of the formulas:

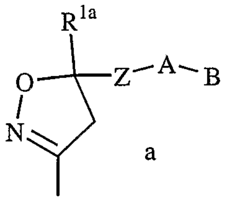
or a stereoisomer or pharmaceutically acceptable salt thereof.

In another embodiment, the present invention provides a novel compound selected from one of the formulas:



or a stereoisomer or pharmaceutically acceptable salt thereof.

In another embodiment, the present invention provides a novel compound wherein M is selected from the group:



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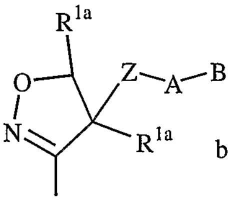

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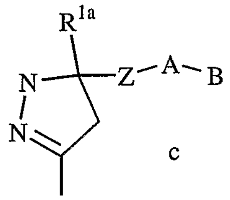

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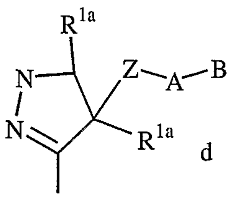

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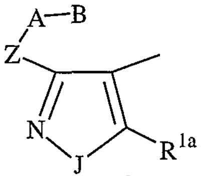

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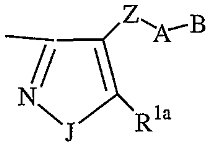

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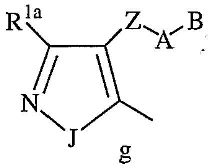

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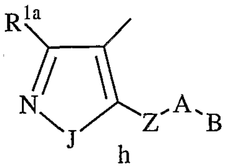

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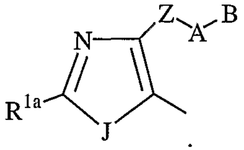

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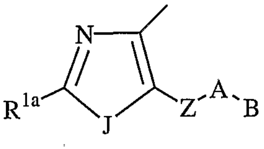

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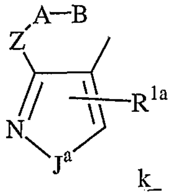

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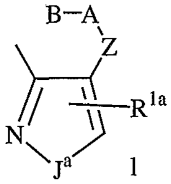

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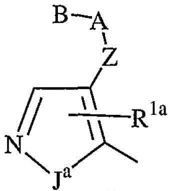

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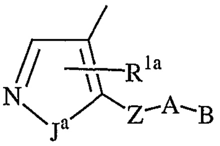

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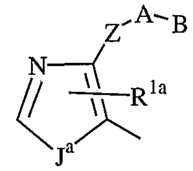

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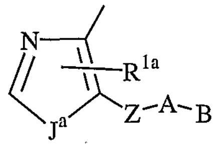

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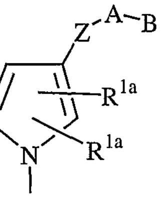

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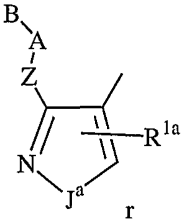

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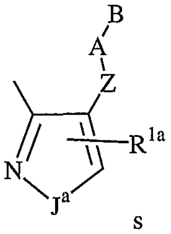

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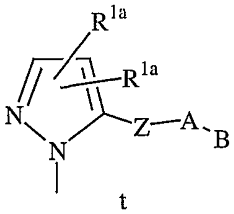

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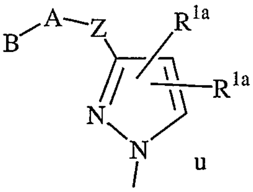

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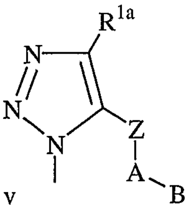

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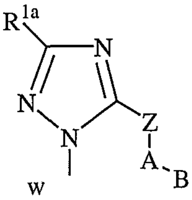

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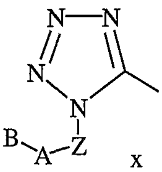

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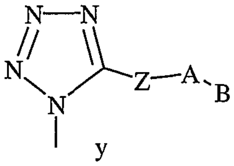

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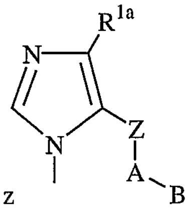

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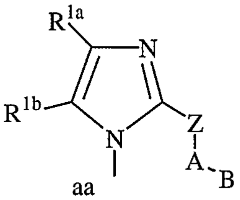

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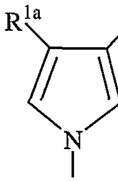

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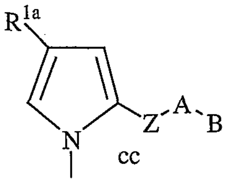

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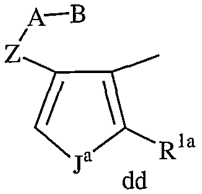

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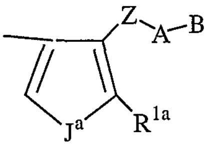

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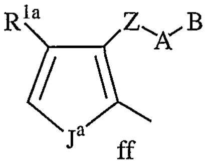

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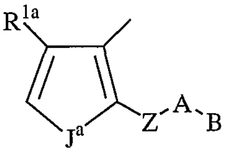

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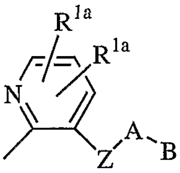

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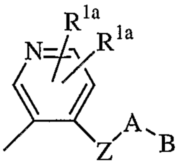

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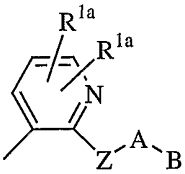

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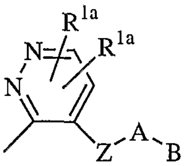

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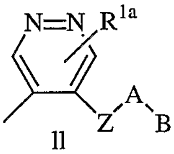

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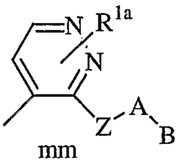

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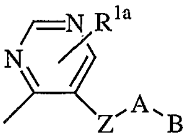

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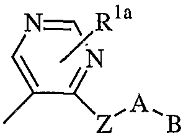

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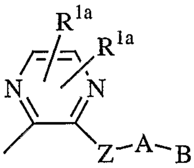

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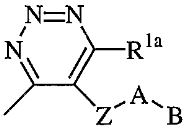

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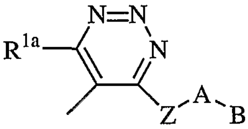

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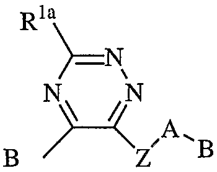

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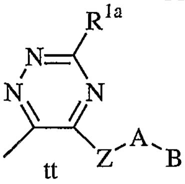

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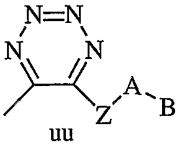

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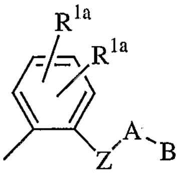

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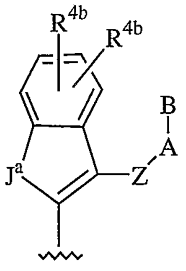

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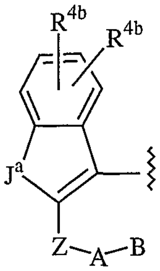

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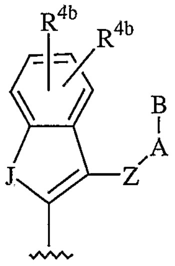

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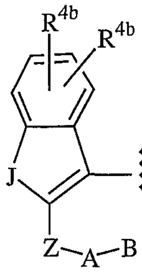

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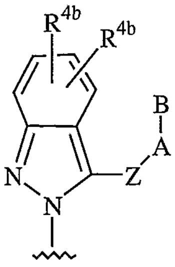

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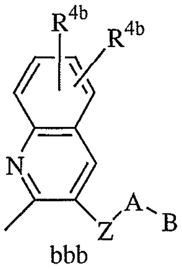

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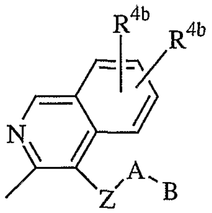

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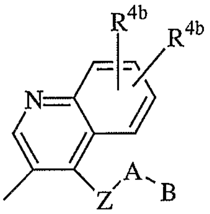

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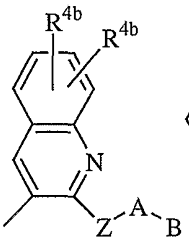

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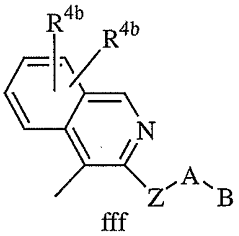

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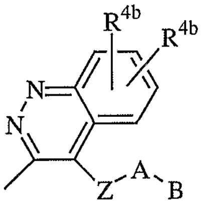

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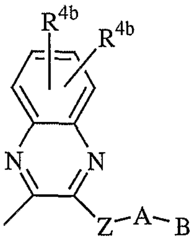

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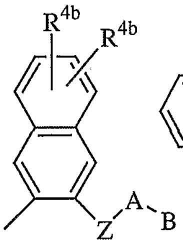

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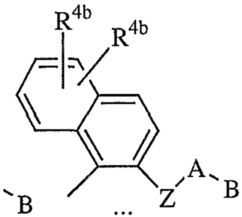

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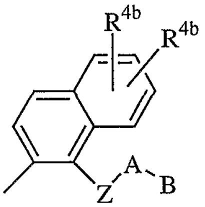
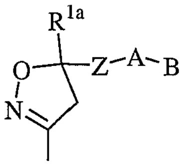


kkk

J is O or S; and,

J^a is NH or NR^{1a}.

In another embodiment, the present invention provides a novel compound wherein M is selected from the group: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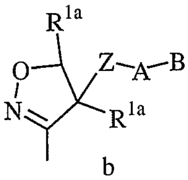
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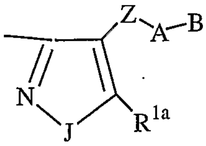
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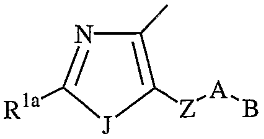
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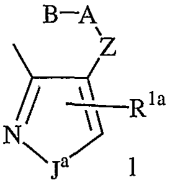
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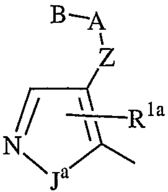
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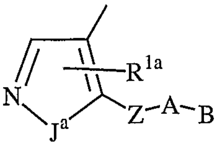
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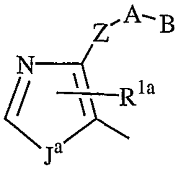
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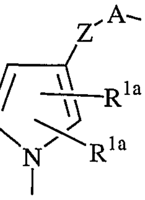
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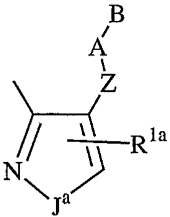
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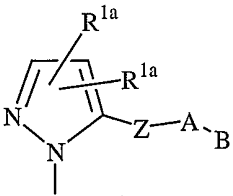
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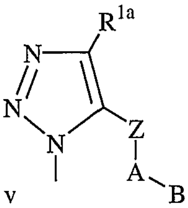
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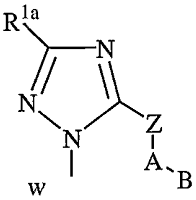
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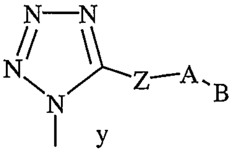
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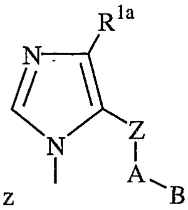
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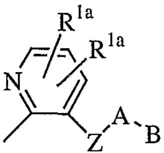
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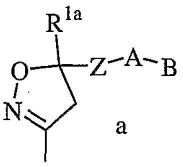
In another embodiment, the present invention provides a novel compound wherein M is selected from the group: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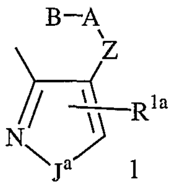
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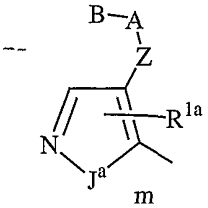
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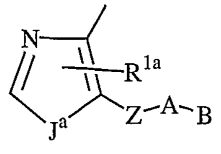
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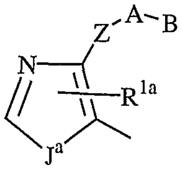
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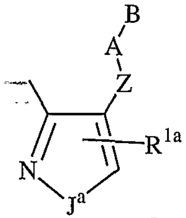
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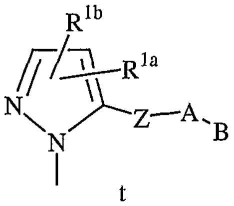
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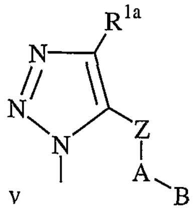
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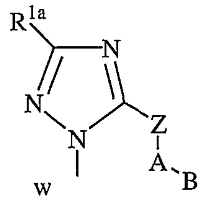
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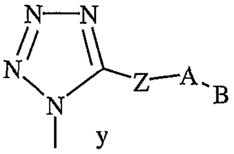
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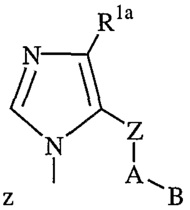
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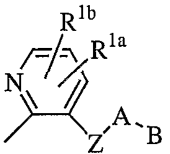

hh.

In another embodiment, the present invention provides a novel compound wherein A is selected from one of the following carbocyclic and heterocyclic systems that are substituted with 0-2 R^4;

phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, benzoxazolyl, benzthiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, and isoindazolyl;

In another embodiment, the present invention provides a novel compound wherein A is selected from phenyl, piperidinyl, pyridyl, and pyrimidyl, and is substituted with 0-2 R^4.

In another embodiment, the present invention provides a novel compound wherein A is selected from the group: phenyl, piperidinyl, 2-pyridyl, 3-pyridyl, 2-pyrimidyl, 2-Cl-phenyl, 3-Cl-phenyl, 2-F-phenyl, 3-F-phenyl, 2-methylphenyl, 2-aminophenyl, and 2-methoxyphenyl.

In another embodiment, the present invention provides a novel compound wherein:

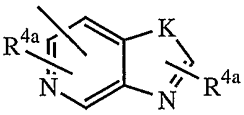
B is selected from: H, Y, and X-Y, provided that Z and B are attached to different atoms on A;

X is selected from $-(CR^2R^{2a})_{1-4}-$, $-C(O)-$, $-C(=NR^{1c})-$, $-CR^2(NR^{1c}R^2)-$, $-C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)$, $-C(O)NR^2-$, $-NR^2C(O)-$, $-C(O)NR^2CR^2R^{2a}-$, $-NR^2C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)NR^2-$, $-CR^2R^{2a}NR^2C(O)-$, $-NR^2C(O)NR^2-$, $-NR^2-$, $-NR^2CR^2R^{2a}-$, $-CR^2R^{2a}NR^2-$, O, $-CR^2R^{2a}O-$, and $-OCR^2R^{2a}-$;

Y is selected from one of the following carbocyclic and heterocyclic systems that are substituted with 0-2 R^{4a};

cyclopropyl, cyclopentyl, cyclohexyl, phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, isoxazolinyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, benzoxazolyl, benzthiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, and isoindazolyl;

alternatively, Y is selected from the following bicyclic heteroaryl ring systems:



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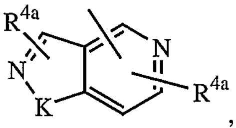

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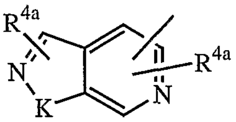

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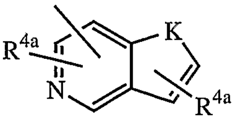

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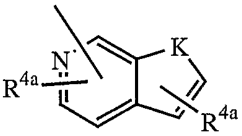

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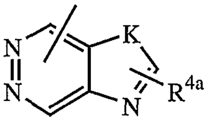

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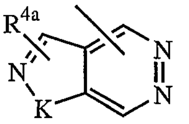

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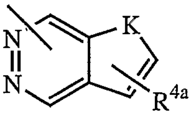


;

K is selected from O, S, NH, and N.

In another embodiment, the present invention provides a novel compound wherein:

Y is selected from one of the following carbocyclic and heterocyclic systems which are substituted with 0-2 R^{4a};

phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazole, thiadiazole, triazole, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole, 1,3,4-thiadiazole, 1,2,3-triazole, 1,2,4-triazole, 1,2,5-triazole, 1,3,4-triazole, benzofuran, benzothiofuran, indole, benzimidazole, benzimidazolone, benzoxazole, benzthiazole, indazole, benzisoxazole, benzisothiazole, and isoindazole.

In another embodiment, the present invention provides a novel compound wherein B is selected from phenyl, pyrrolidino, N-pyrrolidino-carbonyl, morpholino, N-morpholino-carbonyl, 1,2,3-triazolyl, imidazolyl, and benzimidazolyl, and is substituted with 0-1 R^{4a}.

In another embodiment, the present invention provides a novel compound wherein B is selected from the group: 2-(aminosulfonyl)phenyl, 2-(methylaminosulfonyl)phenyl, 1-pyrrolidinocarbonyl, 2-(methylsulfonyl)phenyl, 2-(N,N-dimethylaminomethyl)phenyl, 2-(N-methylaminomethyl)phenyl, 2-(N-ethyl-N-methylaminomethyl)phenyl, 2-(N-pyrrolidinylmethyl)phenyl, 1-methyl-2-imidazolyl, 2-methyl-1-imidazolyl, 2-(dimethylaminomethyl)-1-imidazolyl, 2-(methylaminomethyl)-1-imidazolyl, 2-(N-(cyclopropylmethyl)aminomethyl)phenyl, 2-(N-(cyclobutyl)aminomethyl)phenyl, 2-(N-(cyclopentyl)aminomethyl)phenyl, 2-(N-(4-hydroxypiperidinyl)methyl)phenyl, and 2-(N-(3-hydroxypyrrolidinyl)methyl)phenyl.

In another embodiment, the present invention provides novel pharmaceutical compositions, comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of the present invention or a pharmaceutically acceptable salt form thereof.

In another embodiment, the present invention provides a novel method for treating or preventing a thromboembolic disorder, comprising: administering to a patient in need thereof a therapeutically effective amount of a compound of the present invention or a pharmaceutically acceptable salt form thereof.

In another embodiment, the present invention provides a compound of the present invention as described above for use in therapy.

In another embodiment, the present invention provides the use of the present invention as described above for the manufacture of a medicament for the treatment of a thromboembolic disorder.

DEFINITIONS

The compounds herein described may have asymmetric centers. Compounds of the present invention containing an asymmetrically substituted atom may be isolated in optically active or racemic forms. It is well known in the art how to prepare optically active forms, such as by resolution of racemic forms or by synthesis from optically active starting materials. Many geometric isomers of olefins, C=N double bonds, and the like can also be present in the compounds described herein, and all such stable isomers are contemplated in the present invention. Cis and trans geometric isomers of the compounds of the present invention are described and may be isolated as a mixture of isomers or as separated isomeric forms. All chiral, diastereomeric, racemic forms and all geometric isomeric forms of a structure are intended, unless the specific stereochemistry or isomeric form is specifically indicated. All processes used to prepare compounds of the present invention and intermediates made therein are considered to be part of the present invention. All tautomers of shown or described compounds are also considered to be part of the present invention.

The term "substituted," as used herein, means that any one or more hydrogens on the designated atom is replaced with a selection from the indicated group, provided that the designated atom's normal valency is not exceeded, and that the substitution results in a stable compound. When a substituent is keto (i.e., =O), then 2 hydrogens on the atom are replaced. Keto substituents are not present on aromatic moieties.

The present invention is intended to include all isotopes of atoms occurring in the present compounds. Isotopes include those atoms having the same atomic number but different mass numbers. By way of general example and without limitation, isotopes of hydrogen include tritium and deuterium. Isotopes of carbon include C-13 and C-14.

When any variable (e.g., R^6) occurs more than one time in any constituent or formula for a compound, its definition at each occurrence is independent of its definition at every other occurrence. Thus, for example, if a group is shown to be substituted with 0-2 R^6, then said group may optionally be substituted with up to two R^6 groups and R^6 at each occurrence is selected independently from the definition of R^6. Also, combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

When a bond to a substituent is shown to cross a bond connecting two atoms in a ring, then such substituent may be bonded to any atom on the ring. When a substituent is listed without indicating the atom via which such substituent is bonded to the rest of the compound of a given formula, then such substituent may be bonded via any atom in such substituent. Combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

As used herein, "alkyl" is intended to include both branched and straight-chain saturated aliphatic hydrocarbon groups having the specified number of carbon atoms. C_{1-10} alkyl, is intended to include C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, and C_{10} alkyl groups. Examples of alkyl include, but are not limited to, methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, and s-pentyl. "Haloalkyl" is intended to include both branched and straight-chain saturated aliphatic hydrocarbon groups having the specified number of carbon atoms, substituted with 1 or more halogen (for example $-C_vF_w$ where v = 1 to 3 and w = 1 to (2v+1)). Examples of haloalkyl include, but are not limited to, trifluoromethyl, trichloromethyl, pentafluoroethyl, and pentachloroethyl. "Alkoxy" represents an alkyl group as defined above with the indicated number of carbon atoms attached through an oxygen bridge. C_{1-10} alkoxy, is intended to include C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, and C_{10} alkoxy groups. Examples of alkoxy include, but are not limited to, methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, s-butoxy, t-butoxy, n-pentoxy, and s-pentoxy. "Cycloalkyl" is intended to include saturated ring groups, such as cyclopropyl, cyclobutyl, or cyclopentyl. C_{3-7} cycloalkyl is intended to include C_3, C_4, C_5, C_6, and C_7 cycloalkyl groups. Alkenyl" is intended to include hydrocarbon chains of either straight or branched configuration and one or more unsaturated carbon-carbon bonds that may occur in any stable point along the chain, such as ethenyl and propenyl. C_{2-10} alkenyl is intended to include C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, and C_{10} alkenyl groups. "Alkynyl" is intended to include hydrocarbon chains of either straight or branched configuration and one or more triple carbon-carbon bonds that may occur in any stable point along the chain, such as ethynyl and propynyl. C_{2-10} Alkynyl is intended to include C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, and C_{10} alkynyl groups.

"Halo" or "halogen" as used herein refers to fluoro, chloro, bromo, and iodo; and "counterion" is used to represent a small, negatively charged species such as chloride, bromide, hydroxide, acetate, and sulfate.

As used herein, "carbocycle" or "carbocyclic residue" is intended to mean any stable 3, 4, 5, 6, or 7-membered monocyclic or bicyclic or 7, 8, 9, 10, 11, 12, or 13-membered bicyclic or tricyclic, any of which may be saturated, partially unsaturated, or aromatic. Examples of such carbocycles include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, adamantyl, cyclooctyl, [3.3.0]bicyclooctane, [4.3.0]bicyclononane, [4.4.0]bicyclodecane, [2.2.2]bicyclooctane, fluorenyl, phenyl, naphthyl, indanyl, adamantyl, and tetrahydronaphthyl.

As used herein, the term "heterocycle" or "heterocyclic system" is intended to mean a stable 5, 6, or 7-membered monocyclic or bicyclic or 7, 8, 9, or 10-membered bicyclic heterocyclic ring which is saturated, partially unsaturated or unsaturated (aromatic), and which consists of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, NH, O and S and including any bicyclic group in which any of the above-defined heterocyclic rings is fused to a benzene ring. The nitrogen and sulfur heteroatoms may optionally be oxidized. The heterocyclic ring may be attached to its pendant group at any heteroatom or carbon atom that results in a stable structure. The heterocyclic rings described herein may be substituted on carbon or on a nitrogen atom if the resulting compound is stable. A nitrogen in the heterocycle may optionally be quaternized. It is preferred that when the total number of S and O atoms in the heterocycle exceeds 1, then these heteroatoms are not adjacent to one another. It is preferred that the total number of S and O atoms in the heterocycle is not more than 1. As used herein, the term "aromatic heterocyclic system" or "heteroaryl" is intended to mean a stable 5, 6, or 7-membered monocyclic or bicyclic or 7, 8, 9, or 10-membered bicyclic heterocyclic aromatic ring which consists of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, NH, O and S. It is to be noted that total number of S and O atoms in the aromatic heterocycle is not more than 1.

Examples of heterocycles include, but are not limited to, acridinyl, azocinyl, benzimidazolyl, benzofuranyl, benzothiofuranyl, benzothiophenyl, benzoxazolyl, benzoxazolinyl, benzthiazolyl, benztriazolyl, benztetrazolyl, benzisoxazolyl, benzisothiazolyl, benzimidazolinyl, carbazolyl, 4a*H*-carbazolyl, carbolinyl, chromanyl, chromenyl, cinnolinyl, decahydroquinolinyl, 2*H*,6*H*-1,5,2-dithiazinyl, dihydrofuro[2,3-*b*]tetrahydrofuran, furanyl, furazanyl, imidazolidinyl, imidazolinyl, imidazolyl, 1*H*-indazolyl, indolenyl, indolinyl, indolizinyl, indolyl, 3H-indolyl, isatinoyl, isobenzofuranyl, isochromanyl, isoindazolyl, isoindolinyl, isoindolyl, isoquinolinyl, isothiazolyl, isoxazolyl, methylenedioxyphenyl, morpholinyl, naphthyridinyl, octahydroisoquinolinyl, oxadiazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, oxazolidinyl, oxazolyl, oxindolyl, pyrimidinyl, phenanthridinyl, phenanthrolinyl, phenazinyl, phenothiazinyl, phenoxathinyl, phenoxazinyl, phthalazinyl, piperazinyl, piperidinyl, piperidonyl, 4-piperidonyl, piperonyl, pteridinyl, purinyl, pyranyl, pyrazinyl, pyrazolidinyl, pyrazolinyl, pyrazolyl, pyridazinyl, pyridooxazole, pyridoimidazole, pyridothiazole, pyridinyl, pyridyl, pyrimidinyl, pyrrolidinyl, pyrrolinyl, 2H-pyrrolyl, pyrrolyl, quinazolinyl, quinolinyl, 4*H*-quinolizinyl, quinoxalinyl, quinuclidinyl, tetrahydrofuranyl, tetrahydroisoquinolinyl, tetrahydroquinolinyl, tetrazolyl, 6*H*-1,2,5-thiadiazinyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, thianthrenyl, thiazolyl, thienyl, thienothiazolyl, thienooxazolyl, thienoimidazolyl, thiophenyl, triazinyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, and xanthenyl. Also included are fused ring and spiro compounds containing, for example, the above heterocycles.

The phrase "pharmaceutically acceptable" is employed herein to refer to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

As used herein, "pharmaceutically acceptable salts" refer to derivatives of the disclosed compounds wherein the parent compound is modified by making acid or base salts thereof. Examples of pharmaceutically acceptable salts include, but are not limited to, mineral or organic acid salts of basic residues such as amines; alkali or organic salts of acidic residues such as carboxylic acids; and the like. The pharmaceutically acceptable salts include the conventional non-toxic salts or the quaternary ammonium salts of the parent compound formed, for example, from non-toxic inorganic or organic acids. For example, such conventional non-toxic salts include those derived from inorganic acids such as hydrochloric, hydrobromic, sulfuric, sulfamic, phosphoric, nitric and the like; and the salts prepared from organic acids such as acetic, propionic, succinic, glycolic, stearic, lactic, malic, tartaric, citric, ascorbic, pamoic, maleic, hydroxymaleic, phenylacetic, glutamic, benzoic, salicylic, sulfanilic, 2-acetoxybenzoic, fumaric, toluenesulfonic, methanesulfonic, ethane disulfonic, oxalic, isethionic, and the like.

The pharmaceutically acceptable salts of the present invention can be synthesized from the parent compound that contains a basic or acidic moiety by conventional chemical methods. Generally, such salts can be prepared by reacting the free acid or base forms of these compounds with a stoichiometric amount of the appropriate base or acid in water or in an organic solvent, or in a mixture of the two; generally, non-aqueous media like ether, ethyl acetate, ethanol, isopropanol, or acetonitrile are preferred. Lists of suitable salts are found in *Remington's Pharmaceutical Sciences*, 17th ed., Mack Publishing Company, Easton, PA, 1985, p. 1418, the disclosure of which is hereby incorporated by reference.

Since prodrugs are known to enhance numerous desirable qualities of pharmaceuticals (e.g., solubility, bioavailability, manufacturing, etc...) the compounds of the present invention may be delivered in prodrug form. Thus, the present invention is intended to cover prodrugs of the presently claimed compounds, methods of delivering the same and compositions containing the same. "Prodrugs" are intended to include any covalently bonded carriers that release an active parent drug of the present invention *in vivo* when such prodrug is administered to a mammalian subject. Prodrugs the present invention are prepared by modifying functional groups present in the compound in such a way that the modifications are cleaved, either in routine manipulation or *in vivo*, to the parent compound. Prodrugs include compounds of the present invention wherein a hydroxy, amino, or sulfhydryl group is bonded to any group that, when the prodrug of the present invention is administered to a mammalian subject, it cleaves to form a free hydroxyl, free amino, or free sulfhydryl group, respectively. Examples of prodrugs include, but are not limited to, acetate, formate and benzoate derivatives of alcohol and amine functional groups in the compounds of the present invention.

"Stable compound" and "stable structure" are meant to indicate a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture, and formulation into an efficacious therapeutic agent.

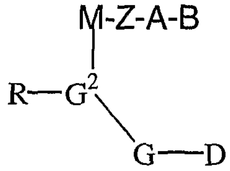
"Substituted" is intended to indicate that one or more hydrogens on the atom indicated in the expression using "substituted" is replaced with a selection from the indicated group(s), provided that the indicated atom's normal valency is not exceeded, and that the substitution results in a stable compound. When a substituent is keto (i.e., =O) group, then 2 hydrogens on the atom are replaced.

"Therapeutically effective amount" is intended to include an amount of a compound of the present invention or an amount of the combination of compounds claimed effective to inhibit factor Xa. The combination of compounds is preferably a synergistic combination. Synergy, as described, for example, by Chou and Talalay, *Adv. Enzyme Regul.* **1984**, *22*:27-55, occurs when the effect (in this case, inhibition of factor Xa) of the compounds when administered in combination is greater than the additive effect of the compounds when administered alone as a single agent. In general, a synergistic effect is most clearly demonstrated at sub-optimal concentrations of the compounds. Synergy can be in terms of lower cytotoxicity, increased antiviral effect, or some other beneficial effect of the combination compared with the individual components.

SYNTHESIS

The compounds of the present invention can be prepared in a number of ways known to one skilled in the art of organic synthesis. The compounds of the present invention can be synthesized using the methods described below, together with synthetic methods known in the art of synthetic organic chemistry, or by variations thereon as appreciated by those skilled in the art. Preferred methods include, but are not limited to, those described below. The reactions are performed in a solvent appropriate to the reagents and materials employed and suitable for the transformations being effected. It will be understood by those skilled in the art of organic synthesis that the functionality present on the molecule should be consistent with the transformations proposed. This will sometimes require a judgment to modify the order of the synthetic steps or to select one particular process scheme over another in order to obtain a desired compound of the invention. It will also be recognized that another major consideration in the planning of any synthetic route in this field is the judicious choice of the protecting group used for protection of the reactive functional groups present in the compounds described in this invention. An authoritative account describing the many alternatives to the trained practitioner is Greene and Wuts (*Protective Groups In Organic Synthesis*, Wiley and Sons, **1991**). All references cited herein are hereby incorporated in their entirety herein by reference.

Scheme 1

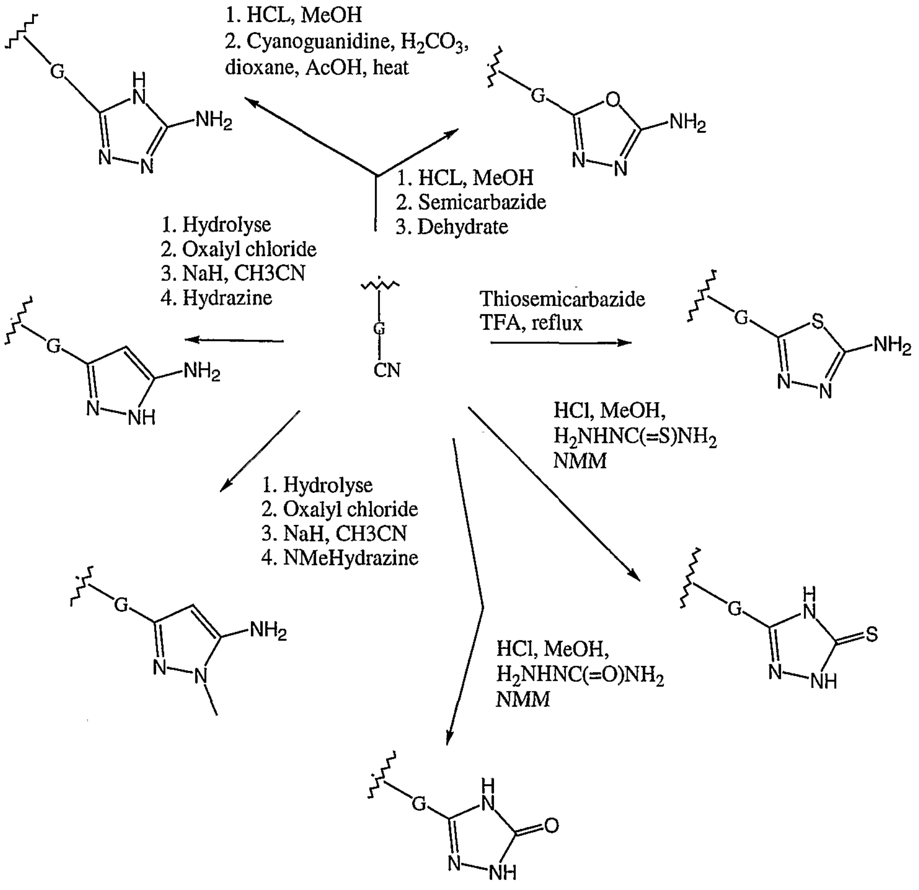


The heterocyclic system shown in Scheme 1 (wherein G-D can be -CN or halo) can be prepared according to the schemes shown in PCT applications WO98/28269, WO98/28282, WO/9857934 and

WO99/32454. In Scheme 1 and the schemes that follow, -G-D represents rings D1, D2, or D3 attached to linker G or precursor to this moiety.

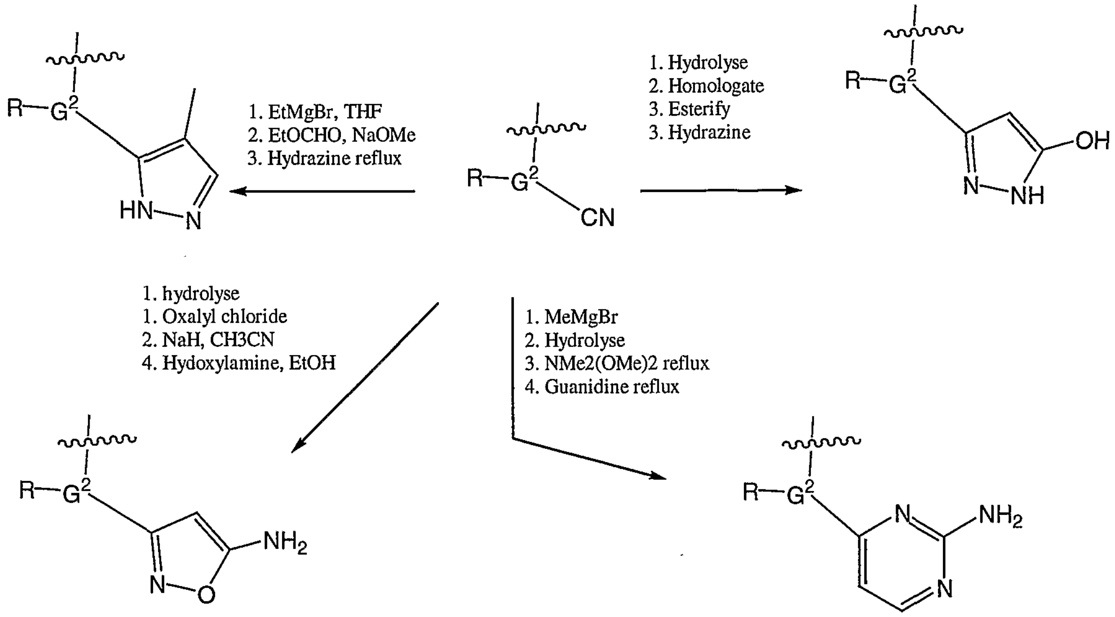
Compounds of this invention wherein G-D is a cyano group can be manipulated to afford thiadiazoles, oxadiazoles, aminooxadiazoles, pyrazoles, triazoles, and triazolones as outlined in Scheme 2.

Scheme 2



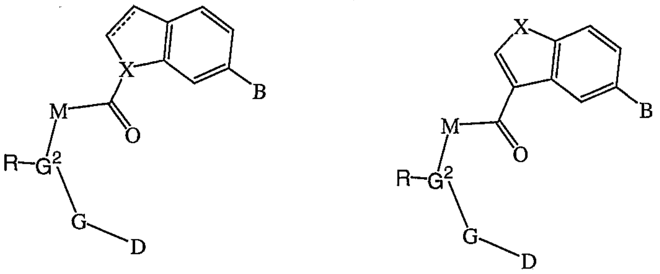
Other heterocycles contained in this invention can also be obtained via methods shown in Scheme 3

Scheme 3



Scheme 4

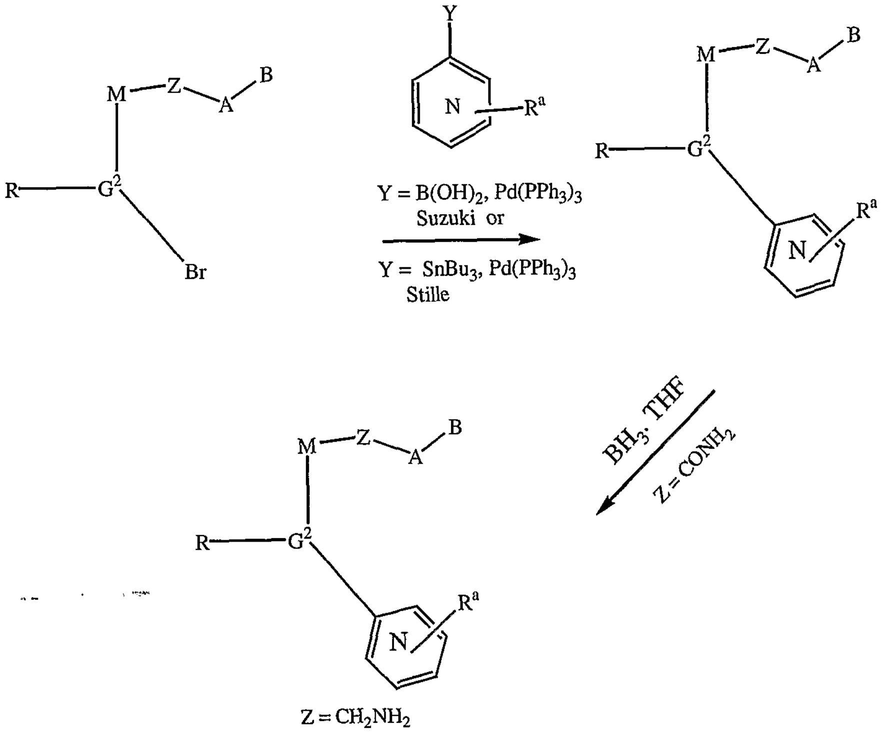
x = N, NH, O or S



Various analogs of the compounds contained in Scheme 4 can be made following the methodologies outlined in Schemes 1-3 and WO01/05784.

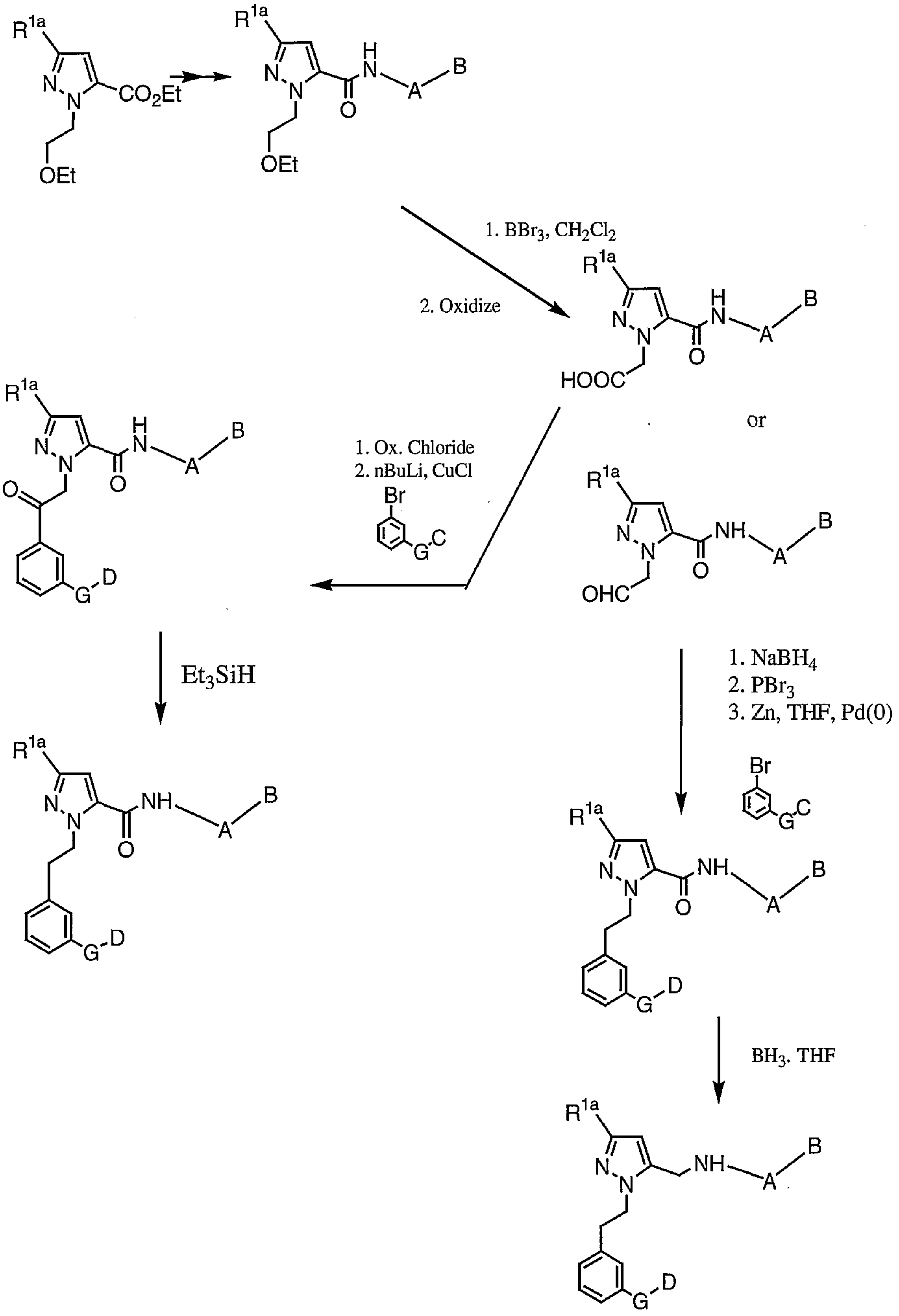
Compounds of this invention wherein ring D is a pyridyl, pyrimidyl, pyridazine, or other heterocyclic ring systems can also be prepared via the Suzuki and or the Stille coupling techniques from easily accessible bromo-phenyl precursors shown in Scheme 5.

Scheme 5



Additionally, other compounds of this invention can also be prepared by those knowledgeable in the art following the methodology outlined in Scheme 6.

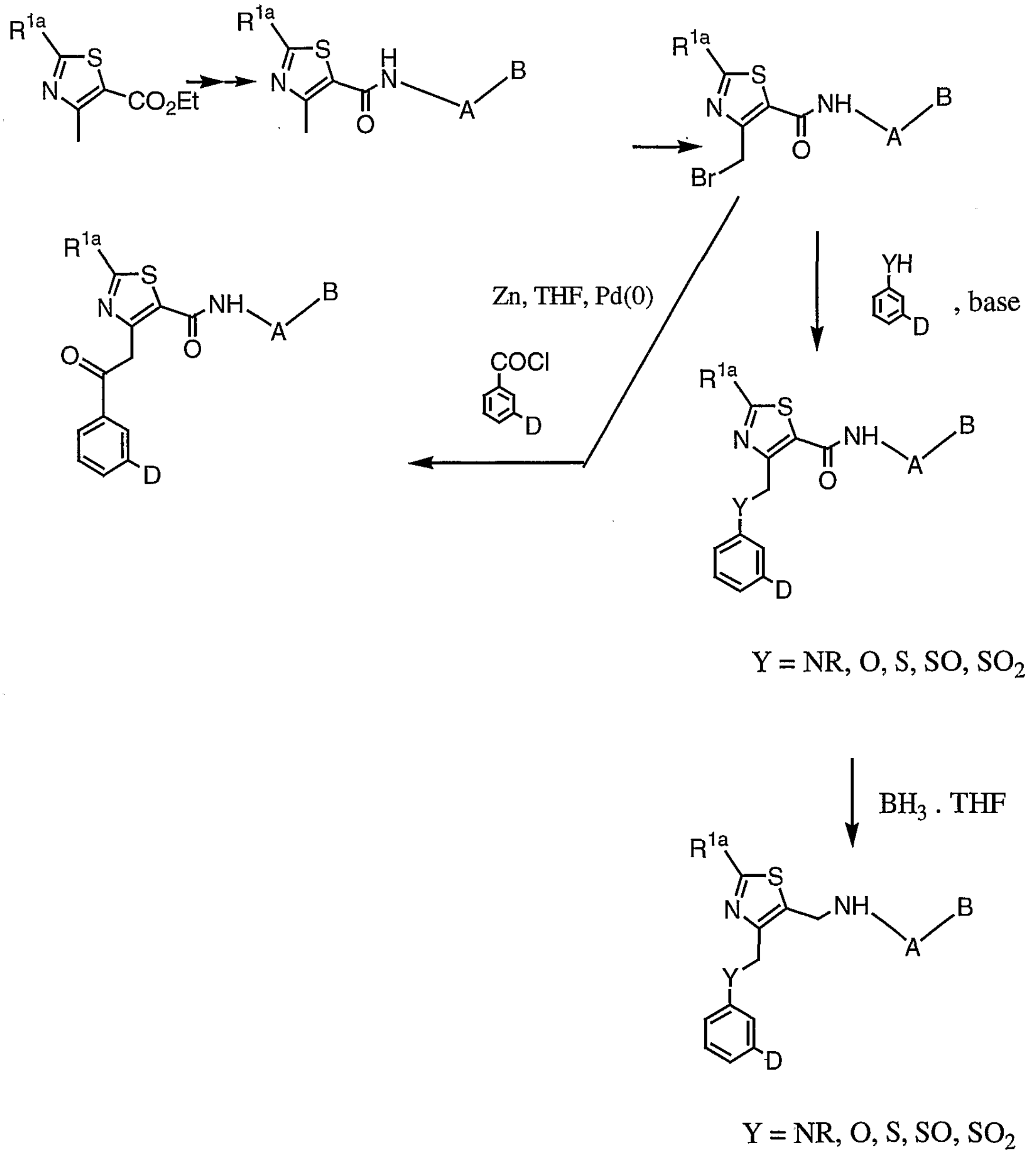
Scheme 6



The compounds prepared via Scheme 6 can be used to prepare similar analogs with other five membered heterocyclic core systems or other linker G^1. These can then be further elaborated via the methodologies shown in earlier schemes to obtain compounds of this invention.

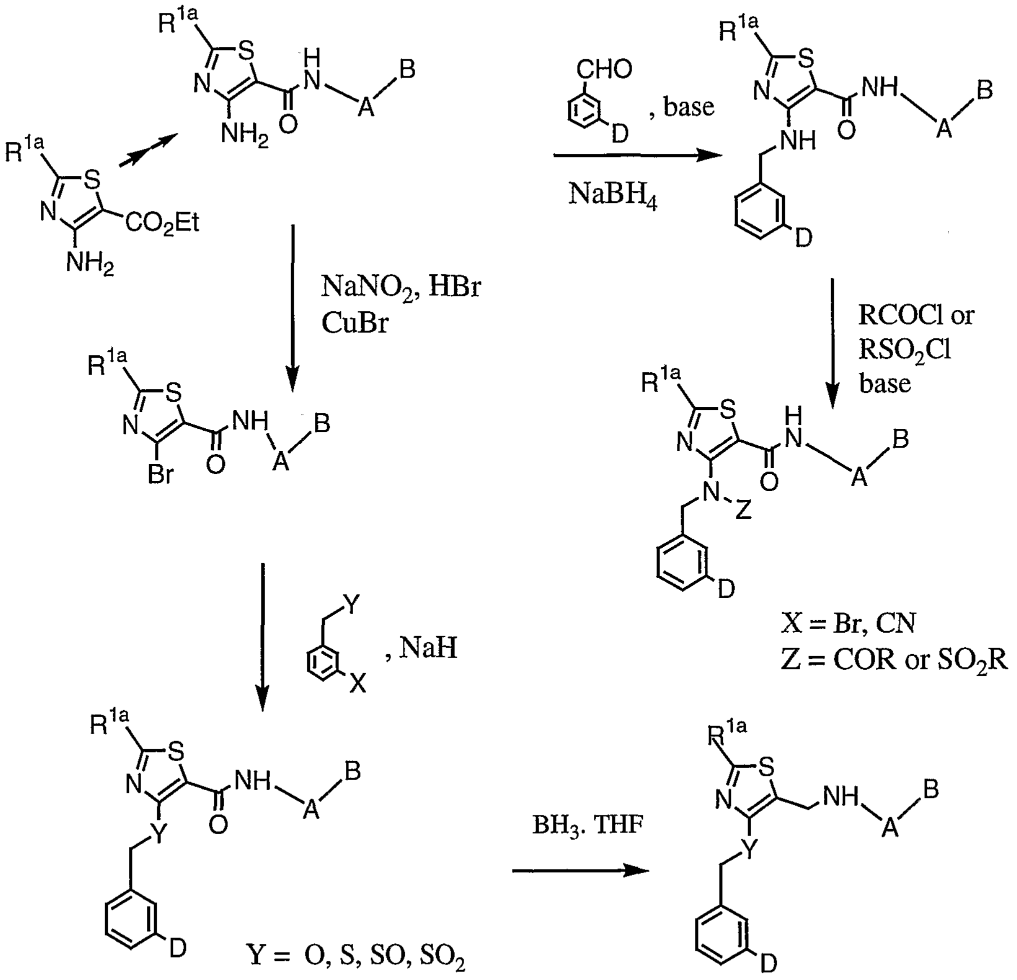
For other carbon based heterocyclic or aryl core systems the above methodologies apply but can be further modified via the method outlined in Scheme 7

Scheme 7



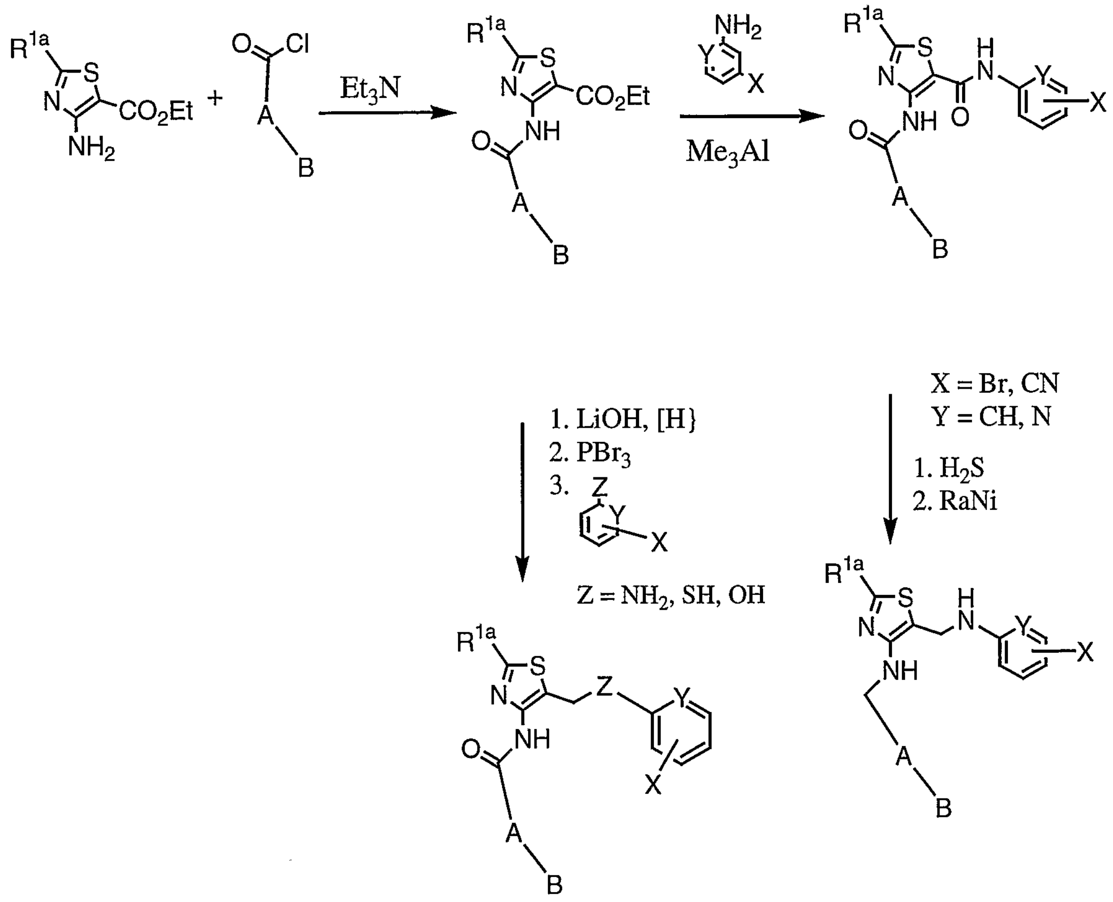
The synthesis shown in Scheme 7 can be adopted for other carbon based heterocycles or aryl rings. In addition to the above other compounds of this invention can also be prepared via the method outlined in Scheme 8.

Scheme 8



Alternatively, compounds of these inventions can also be prepared via the methodology outlined in Scheme 9.

Scheme 9



The synthetic methodology applied in Scheme 9 can also be applied to all other heterocyclic or aryl systems. In all the cases and schemes provided the intermediates wherein X (or D-G-) is a halogen or cyano group these in turn can be manipulated to the heterocyclic systems contained in this invention.

The compounds of the present invention have a group "A-B" attached to ring M directly or via Z. Preparations of some of the rings M and the "A-B" moieties can follow the same methods described in WO97/23212, WO97/30971, WO97/38984, WO98/01428, WO98/06694, WO98/28269, WO98/28282, WO98/57934, WO98/57937, and WO98/57951, the contents of which are incorporated herein by reference

UTILITY

The compounds of this invention are useful as anticoagulants for the treatment or prevention of thromboembolic disorders in mammals. The term "thromboembolic disorders" as used herein includes arterial or venous cardiovascular or cerebrovascular thromboembolic disorders, including, for example, unstable angina, first or recurrent myocardial infarction, ischemic sudden death, transient ischemic attack, stroke, atherosclerosis, venous thrombosis, deep vein thrombosis, thrombophlebitis, arterial embolism, coronary and cerebral arterial thrombosis, cerebral embolism, kidney embolisms, and pulmonary embolisms. The anticoagulant effect of compounds of the present invention is believed to be due to inhibition of factor Xa or thrombin.

The effectiveness of compounds of the present invention as inhibitors of factor Xa was determined using purified human factor Xa and synthetic substrate. The rate of factor Xa hydrolysis of chromogenic substrate S2222 (Kabi Pharmacia, Franklin, OH) was measured both in the absence and presence of compounds of the present invention. Hydrolysis of the substrate resulted in the release of pNA, which was monitored spectrophotometrically by measuring the increase in absorbance at 405 nM. A decrease in the rate of absorbance change at 405 nm in the presence of inhibitor is indicative of enzyme inhibition. The results of this assay are expressed as inhibitory constant, K_i.

Factor Xa determinations were made in 0.10 M sodium phosphate buffer, pH 7.5, containing 0.20 M NaCl, and 0.5% PEG 8000. The Michaelis constant, K_m, for substrate hydrolysis was determined at 25°C using the method of Lineweaver and Burk. Values of K_i were determined by allowing 0.2-0.5 nM human factor Xa (Enzyme Research Laboratories, South Bend, IN) to react with the substrate

(0.20 mM-1 mM) in the presence of inhibitor. Reactions were allowed to go for 30 minutes and the velocities (rate of absorbance change vs time) were measured in the time frame of 25-30 minutes. The following relationship was used to calculate K_i values:

$$(v_o - v_s)/v_s = I/(K_i\ (1 + S/K_m))$$

where:

v_o is the velocity of the control in the absence of inhibitor;

v_s is the velocity in the presence of inhibitor;

I is the concentration of inhibitor;

K_i is the dissociation constant of the enzyme:inhibitor complex;

S is the concentration of substrate;

K_m is the Michaelis constant.

Using the methodology described above, some compounds of the present invention were found to exhibit a K_i of $\leq$10 μM, thereby confirming the utility of the compounds of the present invention as effective Xa inhibitors.

Compounds tested in the above assay are considered to be active if they exhibit a K_i of $\leq$10 μM. Preferred compounds of the present invention have K_i's of $\leq$1 μM. More preferred compounds of the present invention have K_i's of $\leq$0.1 μM. Even more preferred compounds of the present invention have K_i's of $\leq$0.01 μM. Still more preferred compounds of the present invention have K_i's of $\leq$0.001 μM.

The antithrombotic effect of compounds of the present invention can be demonstrated in a rabbit arterio-venous (AV) shunt thrombosis model. In this model, rabbits weighing 2-3 kg anesthetized with a mixture of xylazine (10 mg/kg i.m.) and ketamine (50 mg/kg i.m.) are used. A saline-filled AV shunt device is connected between the femoral arterial and the femoral venous cannulae. The AV shunt device consists of a piece of 6-cm tygon tubing that contains a piece of silk thread. Blood will flow from the femoral artery via the AV-shunt into the femoral vein. The exposure of flowing blood to a silk thread will induce the formation of a significant thrombus. After forty minutes, the shunt is disconnected and the silk thread covered with thrombus is weighed. Test agents or vehicle will be given (i.v., i.p., s.c., or orally) prior to the opening of the AV shunt. The percentage inhibition of thrombus formation is determined for each treatment group. The ID50 values (dose which produces 50% inhibition of thrombus formation) are estimated by linear regression.

The compounds of the present invention may also be useful as inhibitors of serine proteases, notably human thrombin, plasma kallikrein and plasmin. Because of their inhibitory action, these compounds are indicated for use in the prevention or treatment of physiological reactions, blood coagulation and inflammation, catalyzed by the aforesaid class of enzymes. Specifically, the compounds have utility as drugs for the treatment of diseases arising from elevated thrombin activity such as myocardial infarction, and as reagents used as anticoagulants in the processing of blood to plasma for diagnostic and other commercial purposes.

Some compounds of the present invention were shown to be direct acting inhibitors of the serine protease thrombin by their ability to inhibit the cleavage of small molecule substrates by thrombin in a purified system. *In vitro* inhibition constants were determined by the method described by Kettner et al. in *J. Biol. Chem.* **1990**, *265*, 18289-18297, herein incorporated by reference. In these assays, thrombin-mediated hydrolysis of the chromogenic substrate S2238 (Helena Laboratories, Beaumont, TX) was monitored spectrophotometrically. Addition of an inhibitor to the assay mixture results in decreased absorbance and is indicative of thrombin inhibition. Human thrombin (Enzyme

Research Laboratories, Inc., South Bend, IN) at a concentration of 0.2 nM in 0.10 M sodium phosphate buffer, pH 7.5, 0.20 M NaCl, and 0.5% PEG 6000, was incubated with various substrate concentrations ranging from 0.20 to 0.02 mM. After 25 to 30 minutes of incubation, thrombin activity was assayed by monitoring the rate of increase in absorbance at 405 nm that arises owing to substrate hydrolysis. Inhibition constants were derived from reciprocal plots of the reaction velocity as a function of substrate concentration using the standard method of Lineweaver and Burk. Using the methodology described above, some compounds of this invention were evaluated and found to exhibit a K_i of less than 10 µm, thereby confirming the utility of the compounds of the present invention as effective thrombin inhibitors.

The compounds of the present invention can be administered alone or in combination with one or more additional therapeutic agents. These include other anti-coagulant or coagulation inhibitory agents, anti-platelet or platelet inhibitory agents, thrombin inhibitors, or thrombolytic or fibrinolytic agents.

The compounds are administered to a mammal in a therapeutically effective amount. By "therapeutically effective amount" it is meant an amount of a compound of the present invention that, when administered alone or in combination with an additional therapeutic agent to a mammal, is effective to prevent or ameliorate the thromboembolic disease condition or the progression of the disease.

By "administered in combination" or "combination therapy" it is meant that the compound of the present invention and one or more additional therapeutic agents are administered concurrently to the mammal being treated. When administered in combination each component may be administered at the same time or sequentially in any order at different points in time. Thus, each component may be administered separately but sufficiently closely in time so as to provide the desired therapeutic effect. Other anticoagulant agents (or coagulation inhibitory agents) that may be used in combination with the compounds of this invention include warfarin and heparin, as well as other factor Xa inhibitors such as those described in the publications identified above under Background of the Invention.

The term anti-platelet agents (or platelet inhibitory agents), as used herein, denotes agents that inhibit platelet function such as by inhibiting the aggregation, adhesion or granular secretion of platelets. Such agents include, but are not limited to, the various known non-steroidal anti-inflammatory drugs (NSAIDS) such as aspirin, ibuprofen, naproxen, sulindac, indomethacin, mefenamate, droxicam, diclofenac, sulfinpyrazone, and piroxicam, including pharmaceutically acceptable salts or prodrugs thereof. Of the NSAIDS, aspirin (acetylsalicyclic acid or ASA), and piroxicam are preferred. Other suitable anti-platelet agents include ticlopidine, including pharmaceutically acceptable salts or prodrugs thereof. Ticlopidine is also a preferred compound since it is known to be gentle on the gastro-intestinal tract in use. Still other suitable platelet inhibitory agents include IIb/IIIa antagonists, thromboxane-A2-receptor antagonists and thromboxane-A2-synthetase inhibitors, as well as pharmaceutically acceptable salts or prodrugs thereof.

The term thrombin inhibitors (or anti-thrombin agents), as used herein, denotes inhibitors of the serine protease thrombin. By inhibiting thrombin, various thrombin-mediated processes, such as thrombin-mediated platelet activation (that is, for example, the aggregation of platelets, and/or the granular secretion of plasminogen activator inhibitor-1 and/or serotonin) and/or fibrin formation are disrupted. A number of thrombin inhibitors are known to one of skill in the art and these inhibitors are contemplated to be used in combination with the present compounds. Such inhibitors include, but are not limited to, boroarginine derivatives, boropeptides, heparins, hirudin and argatroban, including pharmaceutically acceptable salts and prodrugs thereof. Boroarginine derivatives and boropeptides include N-acetyl and peptide derivatives of boronic acid, such as C-terminal a-aminoboronic acid derivatives of lysine, ornithine, arginine, homoarginine and corresponding isothiouronium analogs thereof. The term hirudin, as used herein, includes suitable derivatives or analogs of hirudin, referred to herein as hirulogs, such as disulfatohirudin. Boropeptide thrombin inhibitors include compounds described in Kettner et al., U.S. Patent No. 5,187,157 and European Patent Application Publication Number 293 881 A2, the disclosures of which are hereby incorporated herein by reference. Other suitable boroarginine derivatives and boropeptide thrombin inhibitors include those disclosed in PCT Application Publication Number 92/07869 and European Patent Application Publication Number 471,651 A2, the disclosures of which are hereby incorporated herein by reference.

The term thrombolytics (or fibrinolytic) agents (or thrombolytics or fibrinolytics), as used herein, denotes agents that lyse blood clots (thrombi). Such agents include tissue plasminogen activator, anistreplase, urokinase or streptokinase, including pharmaceutically acceptable salts or prodrugs thereof. The term anistreplase, as used herein, refers to anisoylated plasminogen streptokinase activator complex, as described, for example, in European Patent Application No. 028,489, the disclosure of which is hereby incorporated herein by reference herein. The term urokinase, as used herein, is intended to denote both dual and single chain urokinase, the latter also being referred to herein as prourokinase.

Administration of the compounds of the present invention in combination with such additional therapeutic agent, may afford an efficacy advantage over the compounds and agents alone, and may do so while permitting the use of lower doses of each. A lower dosage minimizes the potential of side effects, thereby providing an increased margin of safety.

The compounds of the present invention are also useful as standard or reference compounds, for example as a quality standard or control, in tests or assays involving the inhibition of factor Xa. Such compounds may be provided in a commercial kit, for example, for use in pharmaceutical research involving factor Xa. For example, a compound of the present invention could be used as a reference in an assay to compare its known activity to a compound with an unknown activity. This would ensure the experimenter that the assay was being performed properly and provide a basis for comparison, especially if the test compound was a derivative of the reference compound. When developing new assays or protocols, compounds according to the present invention could be used to test their effectiveness.

The compounds of the present invention may also be used in diagnostic assays involving factor Xa. For example, the presence of factor Xa in an unknown sample could be determined by addition of chromogenic substrate S2222 to a series of solutions containing test sample and optionally one of the compounds of the present invention. If production of pNA is observed in the solutions containing test sample, but not in the presence of a compound of the present invention, then one would conclude factor Xa was present.

Dosage and Formulation

The compounds of this invention can be administered in such oral dosage forms as tablets, capsules (each of which includes sustained release or timed release formulations), pills, powders, granules, elixirs, tinctures, suspensions, syrups, and emulsions. They may also be administered in intravenous (bolus or infusion), intraperitoneal, subcutaneous, or intramuscular form, all using dosage forms well known to those of ordinary skill in the pharmaceutical arts. They can be administered alone, but generally will be administered with a pharmaceutical carrier selected on the basis of the chosen route of administration and standard pharmaceutical practice.

The dosage regimen for the compounds of the present invention will, of course, vary depending upon known factors, such as the pharmacodynamic characteristics of the particular agent and its mode and route of administration; the species, age, sex, health, medical condition, and weight of the recipient; the nature and extent of the symptoms; the kind of concurrent treatment; the frequency of treatment; the route of administration, the renal and hepatic function of the patient,and the effect desired. A physician or veterinarian can determine and prescribe the effective amount of the drug required to prevent, counter, or arrest the progress of the thromboembolic disorder.

By way of general guidance, the daily oral dosage of each active ingredient, when used for the indicated effects, will range between about 0.001 to 1000 mg/kg of body weight, preferably between about 0.01 to 100 mg/kg of body weight per day, and most preferably between about 1.0 to 20 mg/kg/day. Intravenously, the most preferred doses will range from about 1 to about 10 mg/kg/minute during a constant rate infusion. Compounds of this invention may be administered in a single daily dose, or the total daily dosage may be administered in divided doses of two, three, or four times daily.

Compounds of this invention can be administered in intranasal form via topical use of suitable intranasal vehicles, or via transdermal routes, using transdermal skin patches. When administered in the form of a transdermal delivery system, the dosage administration will, of course, be continuous rather than intermittent throughout the dosage regimen.

The compounds are typically administered in admixture with suitable pharmaceutical diluents, excipients, or carriers (collectively referred to herein as pharmaceutical carriers) suitably selected with respect to the intended form of administration, that is, oral tablets, capsules, elixirs, syrups and the like, and consistent with conventional pharmaceutical practices.

For instance, for oral administration in the form of a tablet or capsule, the active drug component can be combined with an oral, non-toxic, pharmaceutically acceptable, inert carrier such as lactose, starch, sucrose, glucose, methyl callulose, magnesium stearate, dicalcium phosphate, calcium sulfate, mannitol, sorbitol and the like; for oral administration in liquid form, the oral drug components can be combined with any oral, non-toxic, pharmaceutically acceptable inert carrier such as ethanol, glycerol, water, and the like. Moreover, when desired or necessary, suitable binders, lubricants, disintegrating agents, and coloring agents can also be incorporated into the mixture. Suitable binders include starch, gelatin, natural sugars such as glucose or beta-lactose, corn sweeteners, natural and synthetic gums such as acacia, tragacanth, or sodium alginate, carboxymethylcellulose, polyethylene glycol, waxes, and the like. Lubricants used in these dosage forms include sodium oleate, sodium stearate, magnesium stearate, sodium benzoate, sodium acetate, sodium chloride, and the like. Disintegrators include, without limitation, starch, methyl cellulose, agar, bentonite, xanthan gum, and the like.

The compounds of the present invention can also be administered in the form of liposome delivery systems, such as small unilamellar vesicles, large unilamellar vesicles, and multilamellar vesicles. Liposomes can be formed from a variety of phospholipids, such as cholesterol, stearylamine, or phosphatidylcholines.

Compounds of the present invention may also be coupled with soluble polymers as targetable drug carriers. Such polymers can include polyvinylpyrrolidone, pyran copolymer, polyhydroxypropylmethacrylamide-phenol, polyhydroxyethylaspartamidephenol, or polyethyleneoxide-polylysine substituted with palmitoyl residues. Furthermore, the compounds of the present invention may be coupled to a class of biodegradable polymers useful in achieving controlled release of a drug, for example, polylactic acid, polyglycolic acid, copolymers of polylactic and polyglycolic acid, polyepsilon caprolactone, polyhydroxy butyric acid, polyorthoesters, polyacetals, polydihydropyrans, polycyanoacylates, and crosslinked or amphipathic block copolymers of hydrogels.

Dosage forms (pharmaceutical compositions) suitable for administration may contain from about 1 milligram to about 100 milligrams of active ingredient per dosage unit. In these pharmaceutical compositions the active ingredient will ordinarily be present in an amount of about 0.5-95% by weight based on the total weight of the composition.

Gelatin capsules may 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 glycols 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 propyl-paraben, and chlorobutanol.

Suitable pharmaceutical carriers are described in Remington's Pharmaceutical Sciences, Mack Publishing Company, a standard reference text in this field.

Representative useful pharmaceutical dosage-forms for administration of the compounds of this invention can be illustrated as follows:

Capsules

A large number of unit capsules can be 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.

Soft Gelatin Capsules

A mixture of active ingredient in a digestable oil such as soybean oil, cottonseed oil or olive oil may be 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 should be washed and dried.

Tablets

Tablets may be 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.

Injectable

A parenteral composition suitable for administration by injection may be prepared by stirring 1.5% by weight of active ingredient in 10% by volume propylene glycol and water. The solution should be made isotonic with sodium chloride and sterilized.

Suspension

An aqueous suspension can be prepared for oral administration so that each 5 mL contain 100 mg of finely divided active ingredient, 200 mg of sodium carboxymethyl cellulose, 5 mg of sodium benzoate, 1.0 g of sorbitol solution, U.S.P., and 0.025 mL of vanillin.

Where the compounds of this invention are combined with other anticoagulant agents, for example, a daily dosage may be about 0.1 to 100 milligrams of the compound of the present invention and about 1 to 7.5 milligrams of the second anticoagulant, per kilogram of patient body weight. For a tablet dosage form, the compounds of this invention generally may be present in an amount of about 5 to 10 milligrams per dosage unit, and the second anti-coagulant in an amount of about 1 to 5 milligrams per dosage unit.

Where the compounds of the present invention are administered in combination with an anti-platelet agent, by way of general guidance, typically a daily dosage may be about 0.01 to 25 milligrams of the compound of the present invention and about 50 to 150 milligrams of the anti-platelet agent, preferably about 0.1 to 1 milligrams of the compound of the present invention and about 1 to 3 milligrams of anti-platelet agents, per kilogram of patient body weight.

Where the compounds of the present invention are adminstered in combination with thrombolytic agent, typically a daily dosage may be about 0.1 to 1 milligrams of the compound of the present invention, per kilogram of patient body weight and, in the case of the thrombolytic agents, the usual dosage of the thrombolyic agent when administered alone may be reduced by about 70-80% when administered with a compound of the present invention.

Where two or more of the foregoing second therapeutic agents are administered with the compound of the present invention, generally the amount of each component in a typical daily dosage and typical dosage form may be reduced relative to the usual dosage of the agent when administered alone, in view of the additive or synergistic effect of the therapeutic agents when administered in combination.

Particularly when provided as a single dosage unit, the potential exists for a chemical interaction between the combined active ingredients. For this reason, when the compound of the present invention and a second therapeutic agent are combined in a single dosage unit they are formulated such that although the active ingredients are combined in a single dosage unit, the physical contact between the active ingredients is minimized (that is, reduced). For example, one active ingredient may be enteric coated. By enteric coating one of the active ingredients, it is possible not only to minimize the contact between the combined active ingredients, but also, it is possible to control the release of one of these components in the gastrointestinal tract such that one of these components is not released in the stomach but rather is released in the intestines. One of the active ingredients may also be coated with a material that effects a sustained-release throughout the gastrointestinal tract and also serves to minimize physical contact between the combined active ingredients. Furthermore, the sustained-released component can be additionally enteric coated such that the release of this component occurs only in the intestine. Still another approach would involve the formulation of a combination product in which the one component is coated with a sustained and/or enteric release polymer, and the other component is also coated with a polymer such as a low-viscosity grade of hydroxypropyl methylcellulose (HPMC) or other appropriate materials as known in the art, in order to further separate the active components. The polymer coating serves to form an additional barrier to interaction with the other component.

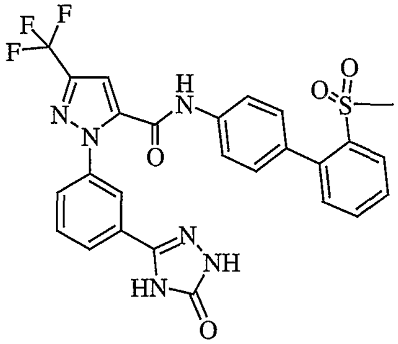
These as well as other ways of minimizing contact between the components of combination products of the present invention, whether administered in a single dosage form or administered in separate forms but at the same time by the same manner, will be readily apparent to those skilled in the art, once armed with the present disclosure.

Other features of the invention will become apparent in the course of the following descriptions of exemplary embodiments that are given for illustration of the invention and are not intended to be limiting thereof.

EXAMPLES

Example 1

1-[3-(1′,3′,4′-Triazol-2′-on-5′-yl)phenyl]-3-trifluoromethyl-5-[(2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole

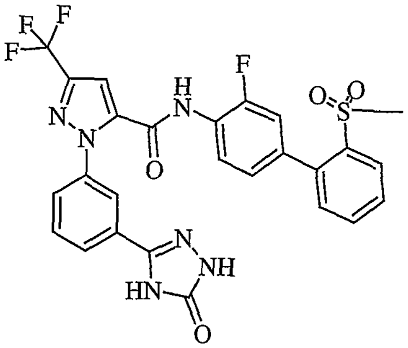


Part A: The starting nitrile, 1-(3-cyanophenyl)-3-trifluoromethyl-5-[(2′-sulfonylmethyl-[1,1′]-biphen-4-yl)aminocarbonyl]pyrazole, was prepared according to the methodology described in WO98/28269 (see Example 73). To 0.54 g (1.06 mmol) of this nitrile in anhydrous ethanol was bubbled HCl gas for 0.5h. The reaction mixture was capped and allowed to stir at room temperature for 18h. The ethanol was evaporated to afford the crude ethoxyimidate intermediate. LRMS (NH_3-CI) m/z (relative intensity) 557 (M=H, 100).

Part B: To the crude product in dioxane (10 mL) from part A was added N-Methyl morpholine (0.6 mL, 5.03 mmol). To this mixture was added semicarbazide hydrochloride (0.13 g, 1.06 mmol) and the reaction mixture was refluxed gently for 72h. The mixture was cooled, poured in water (100 mL) and the organics were extracted with ethyl acetate (2x50 mL), dried and evaporated to a brown mass. The crude mixture was purified via reverse-phase HPLC to afford the title compound. ^1H NMR (DMSO-d_6, 300MHz) δ: 12.91 (s, 1H), 11.81 (s, 1H), 10.90 (s, 1H), 8.08 (d, 1H, J=7.7Hz), 7.98 (s, 1H), 7.92-7.90 (m, 1H), 7.78-7.64 (m, 7H), 7.41-7.38 (m, 3H), 2.84 (s, 3H) ppm. LRMS (ES+): m/z 591 (M+Na). HRMS (ESI): for $C_{26}H_{20}SF_3O_4N_6$ Mass= 569.1206.

Example 2

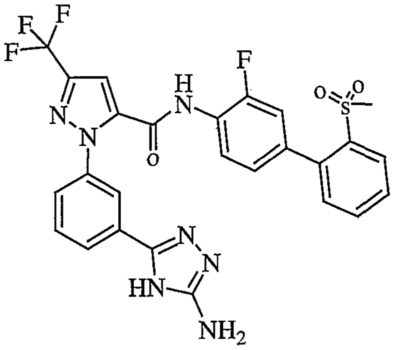
1-[3-(1′,3′,4′-Triazol-2′-on-5′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole



The starting nitrile, 1-(3-cyanophenyl)-3-trifluoromethyl-5-[(3-fluoro-2′-sulfonylmethyl-[1,1′]-biphen-4-yl)aminocarbonyl]pyrazole, was prepared according to the methodology described in *WO98/28269* (see Example 206). The title compound was prepared from this nitrile in a similar method to that described for Example 1. ^{1}HNMR (DMSO-d_6, 300MHz) δ: 12.17 (s, 1H), 11.81 (s, 1H), 10.73 (s, 1H), 8.09 (dd, 1H, J_1=J_2=8.0Hz), 7.99 (s, 1H), 7.93-7.90 (m, 1H), 7.81-7.64 (m, 6H), 7.43 (dd, 1H, J_1=J_2=7.0Hz), 7.38 (dd, 1H, J_1=J_2=11.0Hz), 7.24 (d, 1H, J=8.0Hz), 2.92 (s, 3H) ppm. LRMS (ES+): m/z 587 (M+H) 609 (M+Na). HRMS (ESI): for $C_{26}H_{19}SF_4O_4N_6$ Mass= 587.1123.

Example 3

1-[3-(2′-Amino-1′,3′,4′-triazol-5′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole trifluoroacetic acid salt

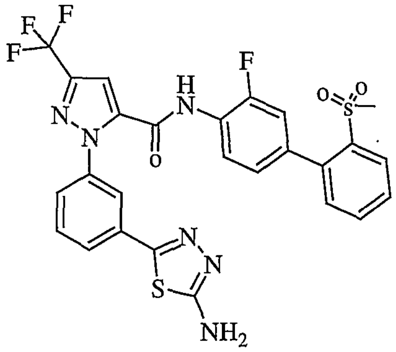


Part A: The nitrile employed for Example 2 was utilized for the preparation of Example 3. Hydrogen chloride was bubbled into an ice-cooled solution of the nitrile (0.52 g, 0.98 mmol) in anhydrous ethanol (50 mL) for 0.5h. The reaction mixture was allowed to warm to ambient temperature overnight and then concentrated *in vacuo*. The crude ethyl imidate hydrochloride was placed under high vacuum and used directly in the next step.

Part B: Acetic acid (1.0 mL) was added to a suspension of crude imidate hydrochloride (0.98 mmol) obtained in part A and aminoguanidine bicarbonate (0.18 g, 1.31 mmol) in 1,4-dioxane (25 mL). The reaction mixture was refluxed for 48h and then concentrated under reduced pressure. The crude solid was purified by reverse phase HPLC. ^{1}HNMR (DMSO-d_6, 300MHz) δ: 10.74 (s, 1H), 8.88-7.99 (m, 3H), 7.80-7.69 (m, 4H), 7.62-7.60 (m, 2H), 7.44-7.36 (m, 2H), 7.24-7.22 (m, 1H), 2.92 (s, 3H) ppm. LRMS (ES+): m/z 586 (M+H) 608 (M+Na). HRMS (ESI): for $C_{26}H_{20}SF_4O_3N_6$ Mass= 586.1280.

Example 4

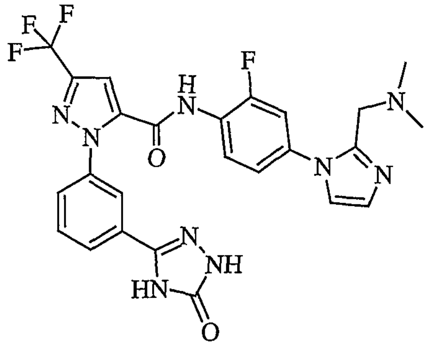
1-[3-(2′-Amino-3′,4′-thiadiazol-5′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole trifluoroacetic acid salt



The nitrile employed for Example 2 was dissolved in TFA (2 mL). To this mixture was added thiosemicarbazide (0.13 g, 1.42 mmol) and the reaction mixture was gently refluxed for 2h. The reaction was then concentrated and the crude oil was purified via reverse phase HPLC to afford the title compound. ^{1}HNMR (DMSO-d_6, 300MHz) δ: 10.73 (s, 1H), 8.10 (d, 1H, J=8.0Hz), 7.95 (s, 1H), 7.87-7.86 (m, 1H), 7.80-7.62 (m, 8H), 7.44 (d, 1H, J=8.0Hz), 7.38 (d, 1H, J=11.0Hz), 7.24 (d, 1H, J=8.0Hz), 2.92 (s, 3H) ppm. LRMS (ES+): m/z 625 (M+Na). HRMS (ESI): for $C_{26}H_{19}S_2F_4O_3N_6$ Mass= 603.0889.

Example 5

1-[3-(1′,3′,4′-Triazol-2′-on-5′-yl)phenyl]-3-trifluoromethyl-5-[4-(2′-(N,N-dimethylamino)methylimidazol-1′-yl)-2-fluorophenyl)aminocarbonyl]pyrazole trifluoroacetic acid salt

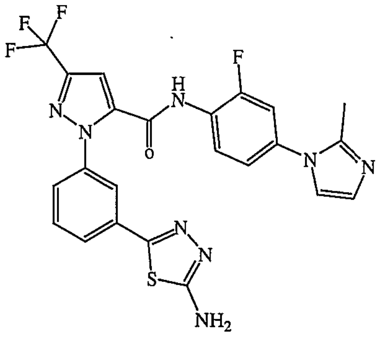


Part A: 1-(3-Cyanophenyl)-3-trifluoromethylpyrazole-5-carboxylic acid was prepared according the methods of WO98/28269 (see Example 14). The pyrazole acid chloride (2.48 mmol) was coupled with 2-fluoro-N,N-dimethyl-2-aminomethyl-4-imidazoloaniline (1.04 g, 2.25 mmol) using DMAP (1.38 g, 11.26 mmol) in dichloromethane. After 48h the reaction mixture was concentrated, dissolved in EtOAc, and washed three times with brine. Then the organics were dried over $MgSO_4$ and concentrated under reduced pressure. The crude material was purified by flash chromatograghy. ^{1}HNMR (DMSO-d_6, 300MHz) δ: 10.72 (s, 1H), 8.16 (s, 1H), 8.01 (d, 1H, J=8Hz), 7.93 (d, 1H, J=8Hz), 7.77-7.69 (m, 4H), 7.51-7.47 (m, 2H), 7.00 (s, 1H), 3.38 (s, 2H), 2.13 (s, 6H) ppm; LRMS: m/z 496 (M-H).

Part B: The coupling product was converted to its corresponding methylimidate via the Pinner reaction. The imidate (1.62 mmol) was then treated with semicarbazide (0.22 g, 1.94 mmol) in refluxing 1,4-dioxane (40 mL) for 48h. The reaction mixture was concentrated to give the crude aminooxadiazole. The product was purified by HPLC. LRMS: m/z 556 (M+H).

Example 6

1-[3-(2′-Amino-3′,4′-thiadiazol-5′-yl)phenyl]-3-trifluoromethyl-5-[4-(2′-methylimidazol-1′-yl)-2-fluorophenyl)aminocarbonyl]pyrazole trifluoroacetic acid salt

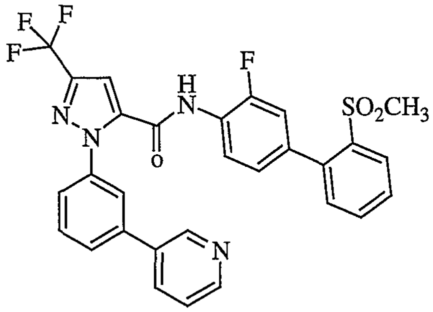


Part A: 1-(3-Cyanophenyl)-3-trifluoromethylpyrazole-5-carboxylic acid was prepared according the methods of WO98/28269 (see Example 14). The pyrazole acid chloride (0.51 mmol) was coupled with 2-methyl-4-imidazoloaniline (1.04 g, 2.25 mmol) using DMAP (0.31 g, 2.49 mmol) in 10 mL dichloromethane. After 24H the reaction mixture was concentrated. The resulting concentrate was dissolved in EtOAc and washed three times with brine. The organics were dried over $MgSO_4$ and concentrated under reduced pressure. The crude coupling product was used directly. LRMS: m/z 437 (M+H).

Part B: The crude benzonitrile was treated with thiosemicarbazide (0.04 g, 0.45 mmol) in 5 mL refluxing TFA for 4h. The reaction mixture was concentrated and purified by HPLC to give the aminothiadiazole. ^{1}HNMR (DMSO, 300MHz) δ: 11.07 (s, 1H), 7.95 (s, 1H), 7.89-7.84 (m, 4H), 7.77 (d, 1H, J=2Hz), 7.71 (s, 1H), 7.63-7.55 (m, 4H), 2.50 (s, 3H)ppm; LRMS: m/z 256 (M/2+H), 511 (M+H); HRMS: calc'd for C2 3H18 S O F3 N8=511.1288.

Example 7

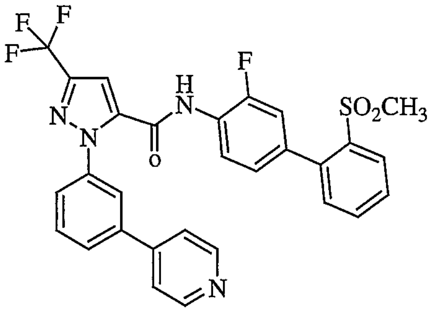
1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole trifluoroacetic acid salt



1-(Bromophenyl)-5-(2'-methylsulfonyl-[1,1']-biphen-4-yl)-3-trifluoromethyl-pyrazole was prepared according to the methods of WO98/28269 (see Example 10, except that 3-methoxy-trichloroacetyl-4,4,4-trifluorocrotonate was used in place of 3-methoxy-trichloroacetylcrotonate). 3-Pyridylboronate (0.112 g, 0.75 mmol) was added to 1-(bromophenyl)-5-(2′-methylsulfonyl-[1,1′]-biphen-4-yl)-3-trifluoromethyl-pyrazole (0.366 g, 0.62 mmol) in a solution of Toluene:EtOH (4:1, 50 mL). Sodium carbonate (2M, 0.4 mL) was added and the solution was degassed for 0.5h. To this solution was added Pd(PPh_3)$_4$ and the solution was gently refluxed for 18h. The solution was concentrated and purified via reverse phase HPLC to afford 0.050g of colorless product. LRMS 581 m/z (rel. intensity), 581 (M+H, 100).

Example 8

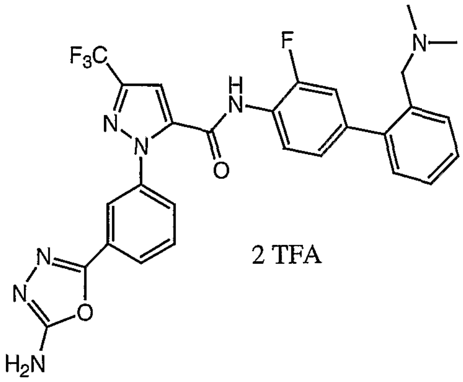
1-[3-(Pyrid-4′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole trifluoroacetic acid salt



Prepared via the Stille coupling methodology using 4-tributyltinpyridine and the bromophenyl-pyrazole intermediate used in Example 8. The title compound was obtained as colorless crystals (20% yield) after purification by reverse phase HPLC. LRMS m/z (rel. intensity) 581 (M+H, 100).

Example 9

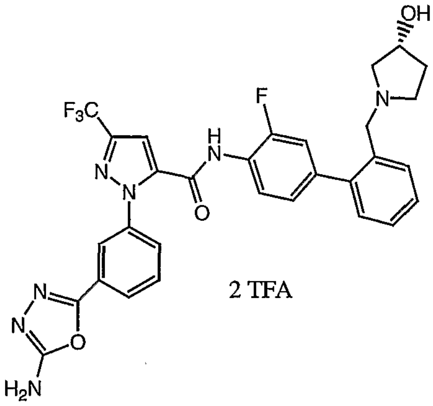
1-[3-(5-Amino-1,3,4-oxadiazol-2-yl)phenyl]-N-{2′-[(dimethylamino)methyl]-3-fluoro-1,1′-biphenyl-4-yl}-3-(trifluoromethyl)-1H-pyrazole-5-carboxamide



This compound was prepared by the methods described in Example 1-6. LRMS (ES$^+$), 566.2 $(M+H)^+$.

Example 10

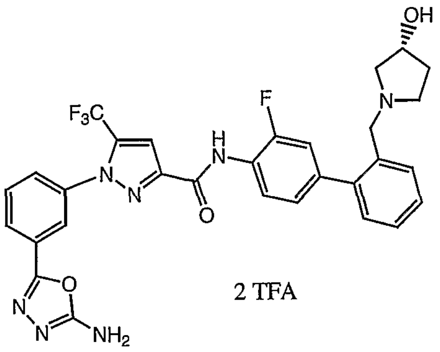
1-[3-(5-Amino-1,3,4-oxadiazol-2-yl)phenyl]-N-(3-fluoro-2'-{[(3S)-3-hydroxy-1-pyrrolidinyl]methyl}-1,1'-biphenyl-4-yl)-3-(trifluoromethyl)-1H-pyrazole-5-carboxamide



This compound was prepared by the methods described in Example 1-6. LRMS (ES$^+$), 608.4 $(M+H)^+$.

Example 11

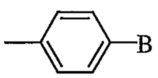
1-[3-(5-Amino-1,3,4-oxadiazol-2-yl)phenyl]-N-(3-fluoro-2'-{[(3S)-3-hydroxy-1-pyrrolidinyl]methyl}-1,1'-biphenyl-4-yl)-5-(trifluoromethyl)-1H-pyrazole-3-carboxamide



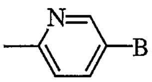
This compound was prepared by the methods described in Example 1-6. LRMS (ES^+), 608.1 $(M+H)^+$.

The following tables contain representative examples of the present invention. Each entry in each table is intended to be paired with each formulas at the start of the table. For example, in Tables 1 and 2, example 1 is intended to be paired with each of the formulas.

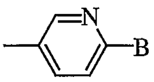
The following nomenclature is intended for group A in the following tables.



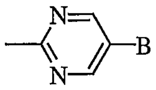
phenyl



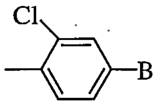
2-pyridyl



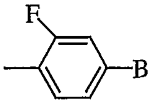
3-pyridyl



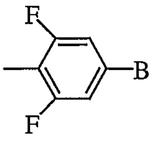
2-pyrimidyl



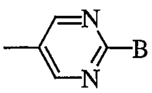
2-Cl-phenyl



2-F-phenyl

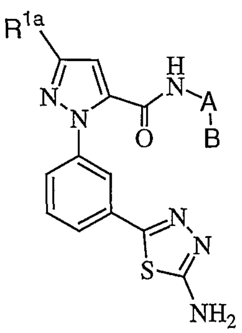


2,6-diF-phenyl



5-pyrimidyl

Table 1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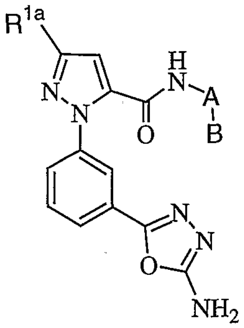
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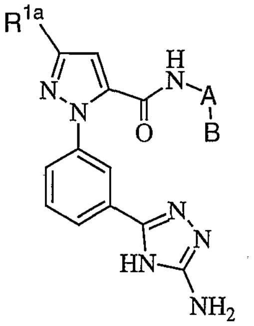
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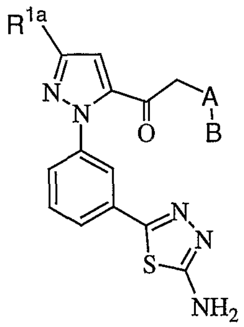
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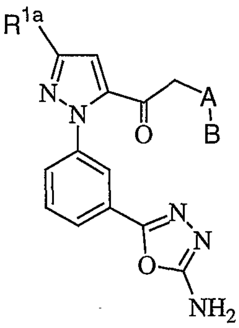
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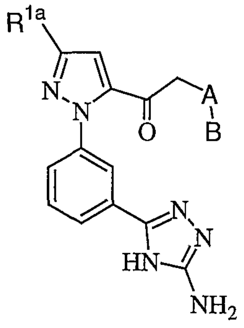
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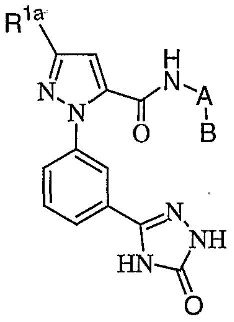
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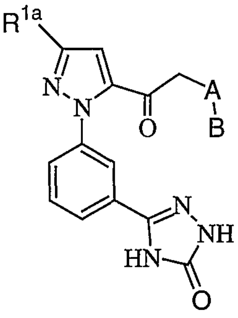
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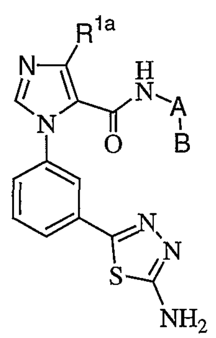
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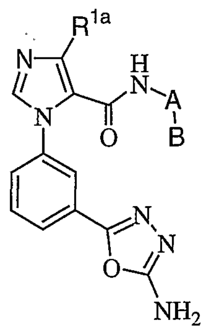
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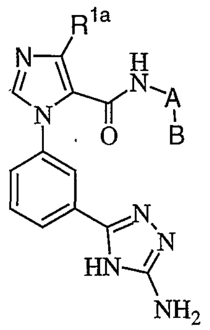
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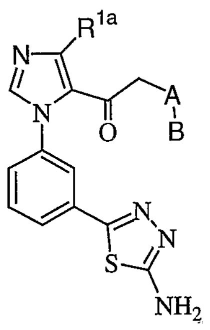
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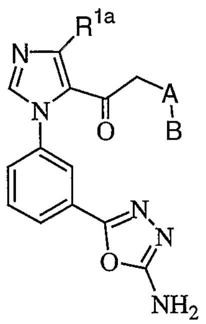
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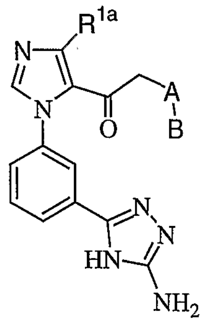
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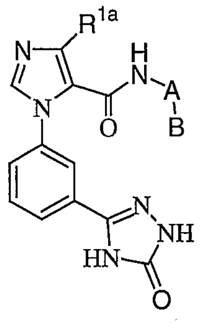
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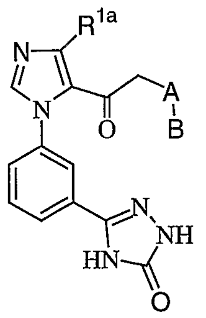
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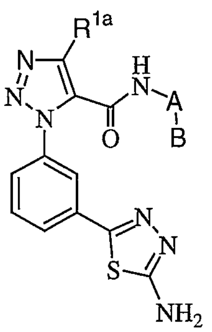
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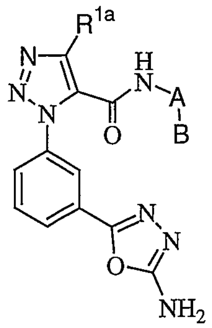
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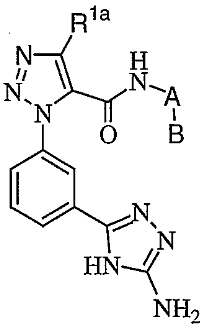
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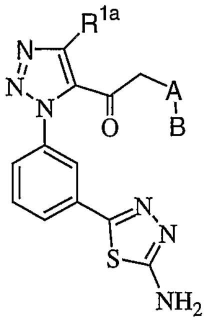
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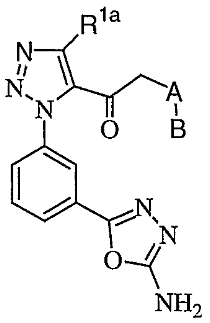
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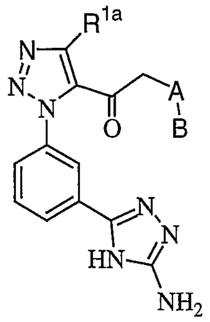
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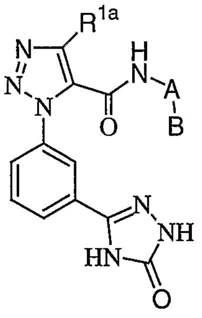
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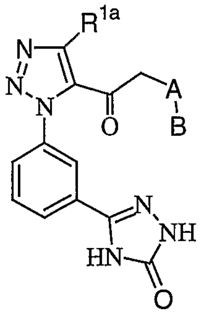
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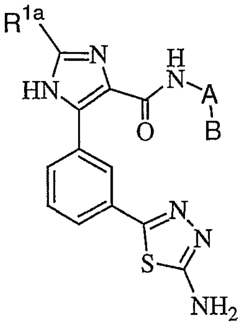
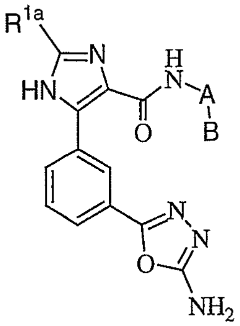
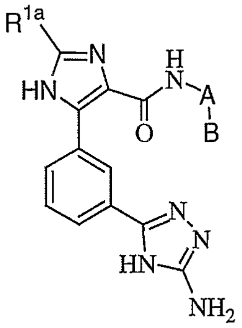

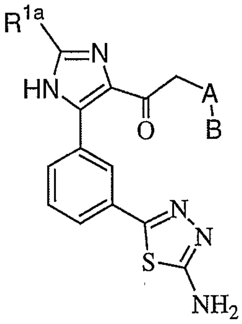
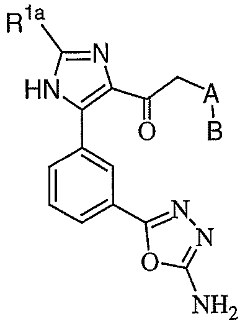
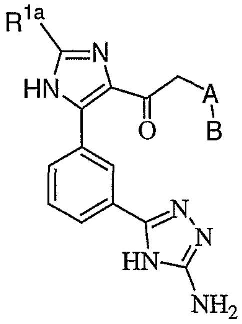

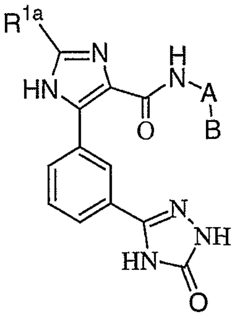
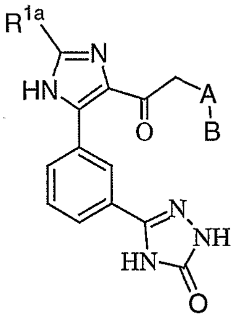

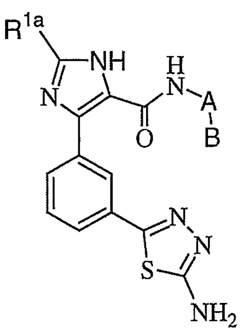
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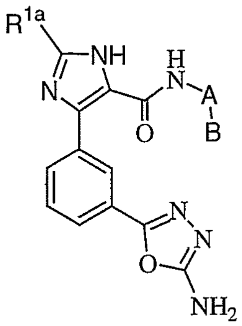
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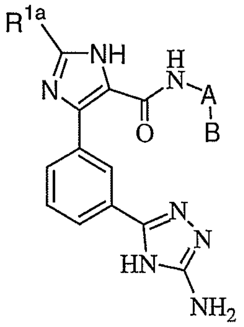
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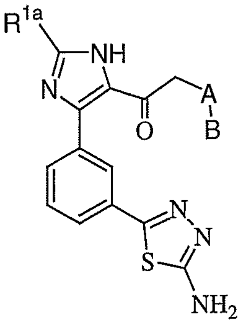
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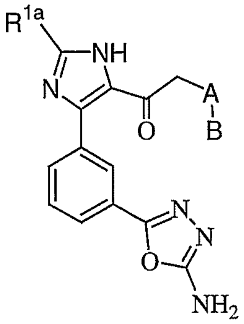
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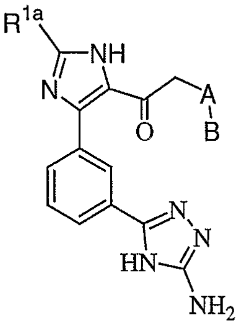
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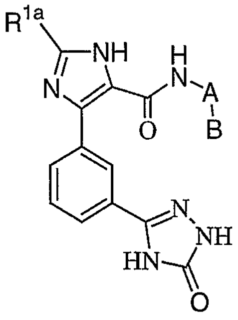
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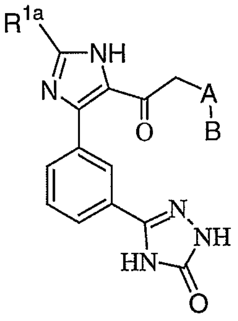
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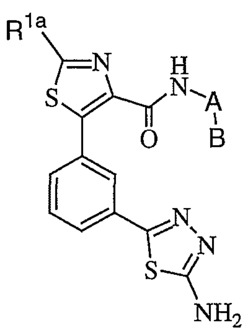
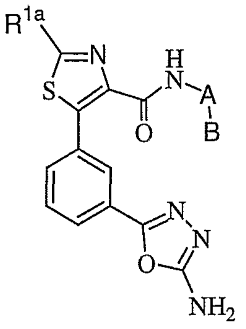
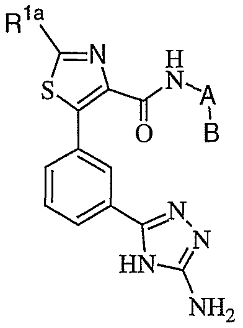
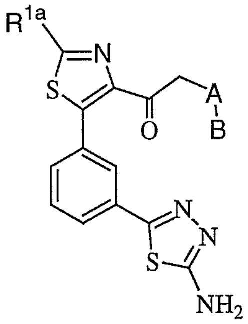
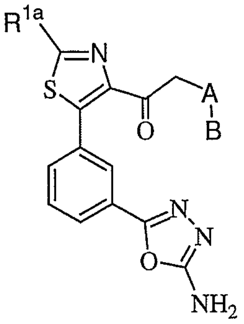
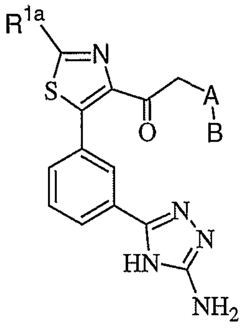
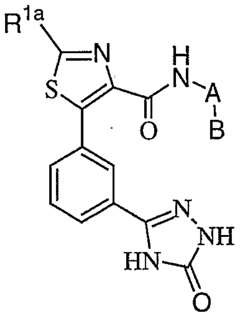
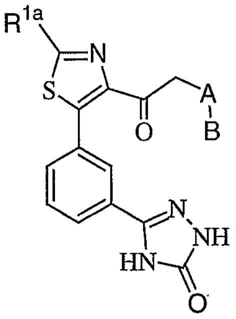
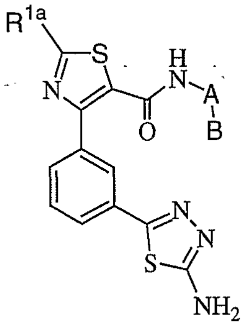
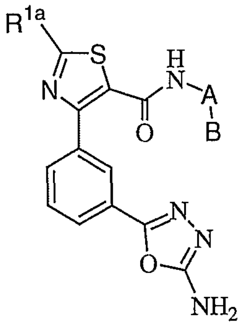
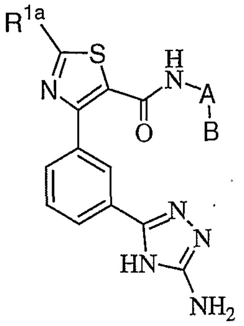
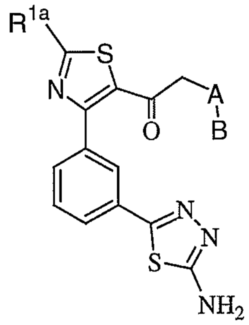
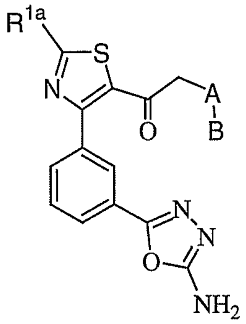









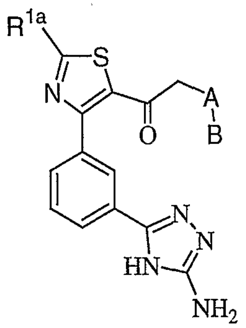


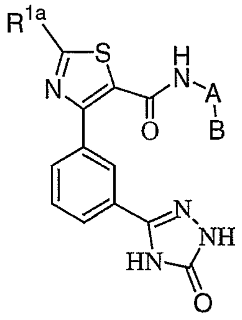


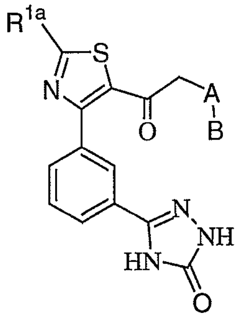












R^{1a} is CH_3;

Ex#	**A**	**B**
1.	phenyl	2-(NH_2SO_2)phenyl
2.	phenyl	2-(CH_3SO_2)phenyl
3.	phenyl	3-NH_2SO_2-4-pyridyl
4.	phenyl	3-CH_3SO_2-4-pyridyl
5.	phenyl	2-(CH_3NH)phenyl
6.	phenyl	3-((CH_3)$_2$$NCH_2$)-4-pyridyl
7.	phenyl	2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
8.	phenyl	2-(N-(4-HO-piperidinyl)CH_2)phenyl
9.	phenyl	2-((CH_3)$_2$$NCH_2$)phenyl
10.	phenyl	2-((CH_3)$NHCH_2$)phenyl
11.	phenyl	2-((CH_3CH_2)$NHCH_2$)phenyl
12.	phenyl	2-((CH_3CH_2)$_2$$NCH_2$)phenyl
13.	phenyl	2-((CH_3CH_2)N(CH_3)CH_2)phenyl
14.	phenyl	2-(((CH_3)$_2$CH)$NHCH_2$)phenyl
15.	phenyl	2-(((CH_3)$_2$CH)$_2$$NCH_2$)phenyl
16.	phenyl	2-((cyclopropyl)$NHCH_2$)phenyl

17.	phenyl	2-((cyclopropyl)$_2$NCH$_2$)phenyl
18.	phenyl	2-((cyclobutyl)NHCH$_2$)phenyl
19.	phenyl	2-((cyclobutyl)$_2$NCH$_2$)phenyl
20.	phenyl	2-((cyclopentyl)NHCH$_2$)phenyl
21.	phenyl	2-((cyclopentyl)$_2$NCH$_2$)phenyl
22.	phenyl	2-((cyclohexyl)NHCH$_2$)phenyl
23.	phenyl	2-((cyclohexyl)$_2$NCH$_2$)phenyl
24.	phenyl	1-CH$_3$-2-imidazolyl
25.	phenyl	2-CH$_3$-1-imidazolyl
26.	phenyl	2-((CH$_3$)$_2$NCH$_2$)-1-imidazolyl
27.	phenyl	2-((CH$_3$)NHCH$_2$)-1-imidazolyl
28.	phenyl	2-((CH$_3$CH$_2$)NHCH$_2$)-1-imidazolyl
29.	phenyl	2-((CH$_3$CH$_2$)$_2$NCH$_2$)-1-imidazolyl
30.	phenyl	2-((CH$_3$CH$_2$)N(CH$_3$)CH$_2$)-1-imidazolyl
31.	phenyl	2-(((CH$_3$)$_2$CH)NHCH$_2$)-1-imidazolyl
32.	phenyl	2-(((CH$_3$)$_2$CH)$_2$NCH$_2$)-1-imidazolyl
33.	phenyl	2-((cyclopropyl)NHCH$_2$)-1-imidazolyl
34.	phenyl	2-((cyclopropyl)$_2$NCH$_2$)-1-imidazolyl
35.	phenyl	2-((cyclobutyl)NHCH$_2$)-1-imidazolyl
36.	phenyl	2-((cyclobutyl)$_2$NCH$_2$)-1-imidazolyl
37.	phenyl	2-((cyclopentyl)NHCH$_2$)-1-imidazolyl
38.	phenyl	2-((cyclopentyl)$_2$NCH$_2$)-1-imidazolyl
39.	phenyl	2-((cyclohexyl)NHCH$_2$)-1-imidazolyl
40.	phenyl	2-((cyclohexyl)$_2$NCH$_2$)-1-imidazolyl
41.	2-pyridyl	2-(NH$_2$SO$_2$)phenyl
42.	2-pyridyl	2-(CH$_3$SO$_2$)phenyl
43.	2-pyridyl	3-NH$_2$SO$_2$-4-pyridyl
44.	2-pyridyl	3-CH$_3$SO$_2$-4-pyridyl
45.	2-pyridyl	2-(CH$_3$NH)phenyl
46.	2-pyridyl	3-((CH$_3$)$_2$NCH$_2$)-4-pyridyl
47.	2-pyridyl	2-(N-(3-R-HO-pyrrolidinyl)CH$_2$)phenyl
48.	2-pyridyl	2-(N-(4-HO-piperidinyl)CH$_2$)phenyl
49.	2-pyridyl	2-((CH$_3$)$_2$NCH$_2$)phenyl
50.	2-pyridyl	2-((CH$_3$)NHCH$_2$)phenyl
51.	2-pyridyl	2-((CH$_3$CH$_2$)NHCH$_2$)phenyl
52.	2-pyridyl	2-((CH$_3$CH$_2$)$_2$NCH$_2$)phenyl
53.	2-pyridyl	2-((CH$_3$CH$_2$)N(CH$_3$)CH$_2$)phenyl
54.	2-pyridyl	2-(((CH$_3$)$_2$CH)NHCH$_2$)phenyl
55.	2-pyridyl	2-(((CH$_3$)$_2$CH)$_2$NCH$_2$)phenyl
56.	2-pyridyl	2-((cyclopropyl)NHCH$_2$)phenyl
57.	2-pyridyl	2-((cyclopropyl)$_2$NCH$_2$)phenyl
58.	2-pyridyl	2-((cyclobutyl)NHCH$_2$)phenyl
59.	2-pyridyl	2-((cyclobutyl)$_2$NCH$_2$)phenyl
60.	2-pyridyl	2-((cyclopentyl)NHCH$_2$)phenyl
61.	2-pyridyl	2-((cyclopentyl)$_2$NCH$_2$)phenyl
62.	2-pyridyl	2-((cyclohexyl)NHCH$_2$)phenyl
63.	2-pyridyl	2-((cyclohexyl)$_2$NCH$_2$)phenyl
64.	2-pyridyl	1-CH$_3$-2-imidazolyl
65.	2-pyridyl	2-CH$_3$-1-imidazolyl
66.	2-pyridyl	2-((CH$_3$)$_2$NCH$_2$)-1-imidazolyl
67.	2-pyridyl	2-((CH$_3$)NHCH$_2$)-1-imidazolyl
68.	2-pyridyl	2-((CH$_3$CH$_2$)NHCH$_2$)-1-imidazolyl
69.	2-pyridyl	2-((CH$_3$CH$_2$)$_2$NCH$_2$)-1-imidazolyl

70.	2-pyridyl	2-((CH_3CH_2)N(CH_3)CH_2)-1-imidazolyl
71.	2-pyridyl	2-(((CH_3)$_2$CH)$NHCH_2$)-1-imidazolyl
72.	2-pyridyl	2-(((CH_3)$_2$CH)$_2$$NCH_2$)-1-imidazolyl
73.	2-pyridyl	2-((cyclopropyl)$NHCH_2$)-1-imidazolyl
74.	2-pyridyl	2-((cyclopropyl)$_2$$NCH_2$)-1-imidazolyl
75.	2-pyridyl	2-((cyclobutyl)$NHCH_2$)-1-imidazolyl
76.	2-pyridyl	2-((cyclobutyl)$_2$$NCH_2$)-1-imidazolyl
77.	2-pyridyl	2-((cyclopentyl)$NHCH_2$)-1-imidazolyl
78.	2-pyridyl	2-((cyclopentyl)$_2$$NCH_2$)-1-imidazolyl
79.	2-pyridyl	2-((cyclohexyl)$NHCH_2$)-1-imidazolyl
80.	2-pyridyl	2-((cyclohexyl)$_2$$NCH_2$)-1-imidazolyl
81.	3-pyridyl	2-(NH_2SO_2)phenyl
82.	3-pyridyl	2-(CH_3SO_2)phenyl
83.	3-pyridyl	3-NH_2SO_2-4-pyridyl
84.	3-pyridyl	3-CH_3SO_2-4-pyridyl
85.	3-pyridyl	2-(CH_3NH)phenyl
86.	3-pyridyl	3-((CH_3)$_2$$NCH_2$)-4-pyridyl
87.	3-pyridyl	2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
88.	3-pyridyl	2-(N-(4-HO-piperidinyl)CH_2)phenyl
89.	3-pyridyl	2-((CH_3)$_2$$NCH_2$)phenyl
90.	3-pyridyl	2-((CH_3)$NHCH_2$)phenyl
91.	3-pyridyl	2-((CH_3CH_2)$NHCH_2$)phenyl
92.	3-pyridyl	2-((CH_3CH_2)$_2$$NCH_2$)phenyl
93.	3-pyridyl	2-((CH_3CH_2)N(CH_3)CH_2)phenyl
94.	3-pyridyl	2-(((CH_3)$_2$CH)$NHCH_2$)phenyl
95.	3-pyridyl	2-(((CH_3)$_2$CH)$_2$$NCH_2$)phenyl
96.	3-pyridyl	2-((cyclopropyl)$NHCH_2$)phenyl
97.	3-pyridyl	2-((cyclopropyl)$_2$$NCH_2$)phenyl
98.	3-pyridyl	2-((cyclobutyl)$NHCH_2$)phenyl
99.	3-pyridyl	2-((cyclobutyl)$_2$$NCH_2$)phenyl
100.	3-pyridyl	2-((cyclopentyl)$NHCH_2$)phenyl
101.	3-pyridyl	2-((cyclopentyl)$_2$$NCH_2$)phenyl
102.	3-pyridyl	2-((cyclohexyl)$NHCH_2$)phenyl
103.	3-pyridyl	2-((cyclohexyl)$_2$$NCH_2$)phenyl
104.	3-pyridyl	1-CH_3-2-imidazolyl
105.	3-pyridyl	2-CH_3-1-imidazolyl
106.	3-pyridyl	2-((CH_3)$_2$$NCH_2$)-1-imidazolyl
107.	3-pyridyl	2-((CH_3)$NHCH_2$)-1-imidazolyl
108.	3-pyridyl	2-((CH_3CH_2)$NHCH_2$)-1-imidazolyl
109.	3-pyridyl	2-((CH_3CH_2)$_2$$NCH_2$)-1-imidazolyl
110.	3-pyridyl	2-((CH_3CH_2)N(CH_3)CH_2)-1-imidazolyl
111.	3-pyridyl	2-(((CH_3)$_2$CH)$NHCH_2$)-1-imidazolyl
112.	3-pyridyl	2-(((CH_3)$_2$CH)$_2$$NCH_2$)-1-imidazolyl
113.	3-pyridyl	2-((cyclopropyl)$NHCH_2$)-1-imidazolyl
114.	3-pyridyl	2-((cyclopropyl)$_2$$NCH_2$)-1-imidazolyl
115.	3-pyridyl	2-((cyclobutyl)$NHCH_2$)-1-imidazolyl
116.	3-pyridyl	2-((cyclobutyl)$_2$$NCH_2$)-1-imidazolyl
117.	3-pyridyl	2-((cyclopentyl)$NHCH_2$)-1-imidazolyl
118.	3-pyridyl	2-((cyclopentyl)$_2$$NCH_2$)-1-imidazolyl
119.	3-pyridyl	2-((cyclohexyl)$NHCH_2$)-1-imidazolyl
120.	3-pyridyl	2-((cyclohexyl)$_2$$NCH_2$)-1-imidazolyl
121.	2-pyrimidyl	2-(NH_2SO_2)phenyl
122.	2-pyrimidyl	2-(CH_3SO_2)phenyl

123.	2-pyrimidyl	3-NH_2SO_2-4-pyridyl
124.	2-pyrimidyl	3-CH_3SO_2-4-pyridyl
125.	2-pyrimidyl	2-(CH_3NH)phenyl
126.	2-pyrimidyl	3-((CH_3)$_2NCH_2$)-4-pyridyl
127.	2-pyrimidyl	2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
128.	2-pyrimidyl	2-(N-(4-HO-piperidinyl)CH_2)phenyl
129.	2-pyrimidyl	2-((CH_3)$_2NCH_2$)phenyl
130.	2-pyrimidyl	2-((CH_3)$NHCH_2$)phenyl
131.	2-pyrimidyl	2-((CH_3CH_2)$NHCH_2$)phenyl
132.	2-pyrimidyl	2-((CH_3CH_2)$_2NCH_2$)phenyl
133.	2-pyrimidyl	2-((CH_3CH_2)N(CH_3)CH_2)phenyl
134.	2-pyrimidyl	2-(((CH_3)$_2CH$)$NHCH_2$)phenyl
135.	2-pyrimidyl	2-(((CH_3)$_2CH$)$_2NCH_2$)phenyl
136.	2-pyrimidyl	2-((cyclopropyl)$NHCH_2$)phenyl
137.	2-pyrimidyl	2-((cyclopropyl)$_2NCH_2$)phenyl
138.	2-pyrimidyl	2-((cyclobutyl)$NHCH_2$)phenyl
139.	2-pyrimidyl	2-((cyclobutyl)$_2NCH_2$)phenyl
140.	2-pyrimidyl	2-((cyclopentyl)$NHCH_2$)phenyl
141.	2-pyrimidyl	2-((cyclopentyl)$_2NCH_2$)phenyl
142.	2-pyrimidyl	2-((cyclohexyl)$NHCH_2$)phenyl
143.	2-pyrimidyl	2-((cyclohexyl)$_2NCH_2$)phenyl
144.	2-pyrimidyl	1-CH_3-2-imidazolyl
145.	2-pyrimidyl	2-CH_3-1-imidazolyl
146.	2-pyrimidyl	2-((CH_3)$_2NCH_2$)-1-imidazolyl
147.	2-pyrimidyl	2-((CH_3)$NHCH_2$)-1-imidazolyl
148.	2-pyrimidyl	2-((CH_3CH_2)$NHCH_2$)-1-imidazolyl
149.	2-pyrimidyl	2-((CH_3CH_2)$_2NCH_2$)-1-imidazolyl
150.	2-pyrimidyl	2-((CH_3CH_2)N(CH_3)CH_2)-1-imidazolyl
151.	2-pyrimidyl	2-(((CH_3)$_2CH$)$NHCH_2$)-1-imidazolyl
152.	2-pyrimidyl	2-(((CH_3)$_2CH$)$_2NCH_2$)-1-imidazolyl
153.	2-pyrimidyl	2-((cyclopropyl)$NHCH_2$)-1-imidazolyl
154.	2-pyrimidyl	2-((cyclopropyl)$_2NCH_2$)-1-imidazolyl
155.	2-pyrimidyl	2-((cyclobutyl)$NHCH_2$)-1-imidazolyl
156.	2-pyrimidyl	2-((cyclobutyl)$_2NCH_2$)-1-imidazolyl
157.	2-pyrimidyl	2-((cyclopentyl)$NHCH_2$)-1-imidazolyl
158.	2-pyrimidyl	2-((cyclopentyl)$_2NCH_2$)-1-imidazolyl
159.	2-pyrimidyl	2-((cyclohexyl)$NHCH_2$)-1-imidazolyl
160.	2-pyrimidyl	2-((cyclohexyl)$_2NCH_2$)-1-imidazolyl
161.	5-pyrimidyl	2-(NH_2SO_2)phenyl
162.	5-pyrimidyl	2-(CH_3SO_2)phenyl
163.	5-pyrimidyl	3-NH_2SO_2-4-pyridyl
164.	5-pyrimidyl	3-CH_3SO_2-4-pyridyl
165.	5-pyrimidyl	2-(CH_3NH)phenyl
166.	5-pyrimidyl	3-((CH_3)$_2NCH_2$)-4-pyridyl
167.	5-pyrimidyl	2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
168.	5-pyrimidyl	2-(N-(4-HO-piperidinyl)CH_2)phenyl
169.	5-pyrimidyl	2-((CH_3)$_2NCH_2$)phenyl
170.	5-pyrimidyl	2-((CH_3)$NHCH_2$)phenyl
171.	5-pyrimidyl	2-((CH_3CH_2)$NHCH_2$)phenyl
172.	5-pyrimidyl	2-((CH_3CH_2)$_2NCH_2$)phenyl
173.	5-pyrimidyl	2-((CH_3CH_2)N(CH_3)CH_2)phenyl
174.	5-pyrimidyl	2-(((CH_3)$_2CH$)$NHCH_2$)phenyl
175.	5-pyrimidyl	2-(((CH_3)$_2CH$)$_2NCH_2$)phenyl

176.	5-pyrimidyl	2-((cyclopropyl)$NHCH_2$)phenyl
177.	5-pyrimidyl	2-((cyclopropyl)$_2NCH_2$)phenyl
178.	5-pyrimidyl	2-((cyclobutyl)$NHCH_2$)phenyl
179.	5-pyrimidyl	2-((cyclobutyl)$_2NCH_2$)phenyl
180.	5-pyrimidyl	2-((cyclopentyl)$NHCH_2$)phenyl
181.	5-pyrimidyl	2-((cyclopentyl)$_2NCH_2$)phenyl
182.	5-pyrimidyl	2-((cyclohexyl)$NHCH_2$)phenyl
183.	5-pyrimidyl	2-((cyclohexyl)$_2NCH_2$)phenyl
184.	5-pyrimidyl	1-CH_3-2-imidazolyl
185.	5-pyrimidyl	2-CH_3-1-imidazolyl
186.	5-pyrimidyl	2-((CH_3)$_2NCH_2$)-1-imidazolyl
187.	5-pyrimidyl	2-((CH_3)$NHCH_2$)-1-imidazolyl
188.	5-pyrimidyl	2-((CH_3CH_2)$NHCH_2$)-1-imidazolyl
189.	5-pyrimidyl	2-((CH_3CH_2)$_2NCH_2$)-1-imidazolyl
190.	5-pyrimidyl	2-((CH_3CH_2)N(CH_3)CH_2)-1-imidazolyl
191.	5-pyrimidyl	2-(((CH_3)$_2CH$)$NHCH_2$)-1-imidazolyl
192.	5-pyrimidyl	2-(((CH_3)$_2CH$)$_2NCH_2$)-1-imidazolyl
193.	5-pyrimidyl	2-((cyclopropyl)$NHCH_2$)-1-imidazolyl
194.	5-pyrimidyl	2-((cyclopropyl)$_2NCH_2$)-1-imidazolyl
195.	5-pyrimidyl	2-((cyclobutyl)$NHCH_2$)-1-imidazolyl
196.	5-pyrimidyl	2-((cyclobutyl)$_2NCH_2$)-1-imidazolyl
197.	5-pyrimidyl	2-((cyclopentyl)$NHCH_2$)-1-imidazolyl
198.	5-pyrimidyl	2-((cyclopentyl)$_2NCH_2$)-1-imidazolyl
199.	5-pyrimidyl	2-((cyclohexyl)$NHCH_2$)-1-imidazolyl
200.	5-pyrimidyl	2-((cyclohexyl)$_2NCH_2$)-1-imidazolyl
201.	2-Cl-phenyl	2-(NH_2SO_2)phenyl
202.	2-Cl-phenyl	2-(CH_3SO_2)phenyl
203.	2-Cl-phenyl	3-NH_2SO_2-4-pyridyl
204.	2-Cl-phenyl	3-CH_3SO_2-4-pyridyl
205.	2-Cl-phenyl	2-(CH_3NH)phenyl
206.	2-Cl-phenyl	3-((CH_3)$_2NCH_2$)-4-pyridyl
207.	2-Cl-phenyl	2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
208.	2-Cl-phenyl	2-(N-(4-HO-piperidinyl)CH_2)phenyl
209.	2-Cl-phenyl	2-((CH_3)$_2NCH_2$)phenyl
210.	2-Cl-phenyl	2-((CH_3)$NHCH_2$)phenyl
211.	2-Cl-phenyl	2-((CH_3CH_2)$NHCH_2$)phenyl
212.	2-Cl-phenyl	2-((CH_3CH_2)$_2NCH_2$)phenyl
213.	2-Cl-phenyl	2-((CH_3CH_2)N(CH_3)CH_2)phenyl
214.	2-Cl-phenyl	2-(((CH_3)$_2CH$)$NHCH_2$)phenyl
215.	2-Cl-phenyl	2-(((CH_3)$_2CH$)$_2NCH_2$)phenyl
216.	2-Cl-phenyl	2-((cyclopropyl)$NHCH_2$)phenyl
217.	2-Cl-phenyl	2-((cyclopropyl)$_2NCH_2$)phenyl
218.	2-Cl-phenyl	2-((cyclobutyl)$NHCH_2$)phenyl
219.	2-Cl-phenyl	2-((cyclobutyl)$_2NCH_2$)phenyl
220.	2-Cl-phenyl	2-((cyclopentyl)$NHCH_2$)phenyl
221.	2-Cl-phenyl	2-((cyclopentyl)$_2NCH_2$)phenyl
222.	2-Cl-phenyl	2-((cyclohexyl)$NHCH_2$)phenyl
223.	2-Cl-phenyl	2-((cyclohexyl)$_2NCH_2$)phenyl
224.	2-Cl-phenyl	1-CH_3-2-imidazolyl
225.	2-Cl-phenyl	2-CH_3-1-imidazolyl
226.	2-Cl-phenyl	2-((CH_3)$_2NCH_2$)-1-imidazolyl
227.	2-Cl-phenyl	2-((CH_3)$NHCH_2$)-1-imidazolyl
228.	2-Cl-phenyl	2-((CH_3CH_2)$NHCH_2$)-1-imidazolyl

229.	2-Cl-phenyl	2-((CH_3CH_2)$_2$$NCH_2$)-1-imidazolyl
230.	2-Cl-phenyl	2-((CH_3CH_2)N(CH_3)CH_2)-1-imidazolyl
231.	2-Cl-phenyl	2-(((CH_3)$_2$CH)$NHCH_2$)-1-imidazolyl
232.	2-Cl-phenyl	2-(((CH_3)$_2$CH)$_2$$NCH_2$)-1-imidazolyl
233.	2-Cl-phenyl	2-((cyclopropyl)$NHCH_2$)-1-imidazolyl
234.	2-Cl-phenyl	2-((cyclopropyl)$_2$$NCH_2$)-1-imidazolyl
235.	2-Cl-phenyl	2-((cyclobutyl)$NHCH_2$)-1-imidazolyl
236.	2-Cl-phenyl	2-((cyclobutyl)$_2$$NCH_2$)-1-imidazolyl
237.	2-Cl-phenyl	2-((cyclopentyl)$NHCH_2$)-1-imidazolyl
238.	2-Cl-phenyl	2-((cyclopentyl)$_2$$NCH_2$)-1-imidazolyl
239.	2-Cl-phenyl	2-((cyclohexyl)$NHCH_2$)-1-imidazolyl
240.	2-Cl-phenyl	2-((cyclohexyl)$_2$$NCH_2$)-1-imidazolyl
241.	2-F-phenyl	2-(NH_2SO_2)phenyl
242.	2-F-phenyl	2-(CH_3SO_2)phenyl
243.	2-F-phenyl	3-NH_2SO_2-4-pyridyl
244.	2-F-phenyl	3-CH_3SO_2-4-pyridyl
245.	2-F-phenyl	2-(CH_3NH)phenyl
246.	2-F-phenyl	3-((CH_3)$_2$$NCH_2$)-4-pyridyl
247.	2-F-phenyl	2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
248.	2-F-phenyl	2-(N-(4-HO-piperidinyl)CH_2)phenyl
249.	2-F-phenyl	2-((CH_3)$_2$$NCH_2$)phenyl
250.	2-F-phenyl	2-((CH_3)$NHCH_2$)phenyl
251.	2-F-phenyl	2-((CH_3CH_2)$NHCH_2$)phenyl
252.	2-F-phenyl	2-((CH_3CH_2)$_2$$NCH_2$)phenyl
253.	2-F-phenyl	2-((CH_3CH_2)N(CH_3)CH_2)phenyl
254.	2-F-phenyl	2-(((CH_3)$_2$CH)$NHCH_2$)phenyl
255.	2-F-phenyl	2-(((CH_3)$_2$CH)$_2$$NCH_2$)phenyl
256.	2-F-phenyl	2-((cyclopropyl)$NHCH_2$)phenyl
257.	2-F-phenyl	2-((cyclopropyl)$_2$$NCH_2$)phenyl
258.	2-F-phenyl	2-((cyclobutyl)$NHCH_2$)phenyl
259.	2-F-phenyl	2-((cyclobutyl)$_2$$NCH_2$)phenyl
260.	2-F-phenyl	2-((cyclopentyl)$NHCH_2$)phenyl
261.	2-F-phenyl	2-((cyclopentyl)$_2$$NCH_2$)phenyl
262.	2-F-phenyl	2-((cyclohexyl)$NHCH_2$)phenyl
263.	2-F-phenyl	2-((cyclohexyl)$_2$$NCH_2$)phenyl
264.	2-F-phenyl	1-CH_3-2-imidazolyl
265.	2-F-phenyl	2-CH_3-1-imidazolyl
266.	2-F-phenyl	2-((CH_3)$_2$$NCH_2$)-1-imidazolyl
267.	2-F-phenyl	2-((CH_3)$NHCH_2$)-1-imidazolyl
268.	2-F-phenyl	2-((CH_3CH_2)$NHCH_2$)-1-imidazolyl
269.	2-F-phenyl	2-((CH_3CH_2)$_2$$NCH_2$)-1-imidazolyl
270.	2-F-phenyl	2-((CH_3CH_2)N(CH_3)CH_2)-1-imidazolyl
271.	2-F-phenyl	2-(((CH_3)$_2$CH)$NHCH_2$)-1-imidazolyl
272.	2-F-phenyl	2-(((CH_3)$_2$CH)$_2$$NCH_2$)-1-imidazolyl
273.	2-F-phenyl	2-((cyclopropyl)$NHCH_2$)-1-imidazolyl
274.	2-F-phenyl	2-((cyclopropyl)$_2$$NCH_2$)-1-imidazolyl
275.	2-F-phenyl	2-((cyclobutyl)$NHCH_2$)-1-imidazolyl
276.	2-F-phenyl	2-((cyclobutyl)$_2$$NCH_2$)-1-imidazolyl
277.	2-F-phenyl	2-((cyclopentyl)$NHCH_2$)-1-imidazolyl
278.	2-F-phenyl	2-((cyclopentyl)$_2$$NCH_2$)-1-imidazolyl
279.	2-F-phenyl	2-((cyclohexyl)$NHCH_2$)-1-imidazolyl
280.	2-F-phenyl	2-((cyclohexyl)$_2$$NCH_2$)-1-imidazolyl
281.	2,6-diF-phenyl	2-(NH_2SO_2)phenyl

282.	2,6-diF-phenyl	2-(CH_3SO_2)phenyl
283.	2,6-diF-phenyl	3-NH_2SO_2-4-pyridyl
284.	2,6-diF-phenyl	3-CH_3SO_2-4-pyridyl
285.	2,6-diF-phenyl	2-(CH_3NH)phenyl
286.	2,6-diF-phenyl	3-($(CH_3)_2NCH_2$)-4-pyridyl
287.	2,6-diF-phenyl	2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
288.	2,6-diF-phenyl	2-(N-(4-HO-piperidinyl)CH_2)phenyl
289.	2,6-diF-phenyl	2-($(CH_3)_2NCH_2$)phenyl
290.	2,6-diF-phenyl	2-($(CH_3)NHCH_2$)phenyl
291.	2,6-diF-phenyl	2-($(CH_3CH_2)NHCH_2$)phenyl
292.	2,6-diF-phenyl	2-($(CH_3CH_2)_2NCH_2$)phenyl
293.	2,6-diF-phenyl	2-($(CH_3CH_2)N(CH_3)CH_2$)phenyl
294.	2,6-diF-phenyl	2-($((CH_3)_2CH)NHCH_2$)phenyl
295.	2,6-diF-phenyl	2-($((CH_3)_2CH)_2NCH_2$)phenyl
296.	2,6-diF-phenyl	2-((cyclopropyl)$NHCH_2$)phenyl
297.	2,6-diF-phenyl	2-((cyclopropyl)$_2NCH_2$)phenyl
298.	2,6-diF-phenyl	2-((cyclobutyl)$NHCH_2$)phenyl
299.	2,6-diF-phenyl	2-((cyclobutyl)$_2NCH_2$)phenyl
300.	2,6-diF-phenyl	2-((cyclopentyl)$NHCH_2$)phenyl
301.	2,6-diF-phenyl	2-((cyclopentyl)$_2NCH_2$)phenyl
302.	2,6-diF-phenyl	2-((cyclohexyl)$NHCH_2$)phenyl
303.	2,6-diF-phenyl	2-((cyclohexyl)$_2NCH_2$)phenyl
304.	2,6-diF-phenyl	1-CH_3-2-imidazolyl
305.	2,6-diF-phenyl	2-CH_3-1-imidazolyl
306.	2,6-diF-phenyl	2-($(CH_3)_2NCH_2$)-1-imidazolyl
307.	2,6-diF-phenyl	2-($(CH_3)NHCH_2$)-1-imidazolyl
308.	2,6-diF-phenyl	2-($(CH_3CH_2)NHCH_2$)-1-imidazolyl
309.	2,6-diF-phenyl	2-($(CH_3CH_2)_2NCH_2$)-1-imidazolyl
310.	2,6-diF-phenyl	2-($(CH_3CH_2)N(CH_3)CH_2$)-1-imidazolyl
311.	2,6-diF-phenyl	2-($((CH_3)_2CH)NHCH_2$)-1-imidazolyl
312.	2,6-diF-phenyl	2-($((CH_3)_2CH)_2NCH_2$)-1-imidazolyl
313.	2,6-diF-phenyl	2-((cyclopropyl)$NHCH_2$)-1-imidazolyl
314.	2,6-diF-phenyl	2-((cyclopropyl)$_2NCH_2$)-1-imidazolyl
315.	2,6-diF-phenyl	2-((cyclobutyl)$NHCH_2$)-1-imidazolyl
316.	2,6-diF-phenyl	2-((cyclobutyl)$_2NCH_2$)-1-imidazolyl
317.	2,6-diF-phenyl	2-((cyclopentyl)$NHCH_2$)-1-imidazolyl
318.	2,6-diF-phenyl	2-((cyclopentyl)$_2NCH_2$)-1-imidazolyl
319.	2,6-diF-phenyl	2-((cyclohexyl)$NHCH_2$)-1-imidazolyl
320.	2,6-diF-phenyl	2-((cyclohexyl)$_2NCH_2$)-1-imidazolyl
321.	piperidinyl	2-(NH_2SO_2)phenyl
322.	piperidinyl	2-(CH_3SO_2)phenyl
323.	piperidinyl	3-NH_2SO_2-4-pyridyl
324.	piperidinyl	3-CH_3SO_2-4-pyridyl
325.	piperidinyl	2-(CH_3NH)phenyl
326.	piperidinyl	3-($(CH_3)_2NCH_2$)-4-pyridyl
327.	piperidinyl	2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
328.	piperidinyl	2-(N-(4-HO-piperidinyl)CH_2)phenyl
329.	piperidinyl	2-($(CH_3)_2NCH_2$)phenyl
330.	piperidinyl	2-($(CH_3)NHCH_2$)phenyl
331.	piperidinyl	2-($(CH_3CH_2)NHCH_2$)phenyl
332.	piperidinyl	2-($(CH_3CH_2)_2NCH_2$)phenyl
333.	piperidinyl	2-($(CH_3CH_2)N(CH_3)CH_2$)phenyl
334.	piperidinyl	2-($((CH_3)_2CH)NHCH_2$)phenyl

335.	piperidinyl	2-($((CH_3)_2CH)_2NCH_2$)phenyl
336.	piperidinyl	2-((cyclopropyl)$NHCH_2$)phenyl
337.	piperidinyl	2-((cyclopropyl)$_2NCH_2$)phenyl
338.	piperidinyl	2-((cyclobutyl)$NHCH_2$)phenyl
339.	piperidinyl	2-((cyclobutyl)$_2NCH_2$)phenyl
340.	piperidinyl	2-((cyclopentyl)$NHCH_2$)phenyl
341.	piperidinyl	2-((cyclopentyl)$_2NCH_2$)phenyl
342.	piperidinyl	2-((cyclohexyl)$NHCH_2$)phenyl
343.	piperidinyl	2-((cyclohexyl)$_2NCH_2$)phenyl
344.	piperidinyl	1-CH_3-2-imidazolyl
345.	piperidinyl	2-CH_3-1-imidazolyl
346.	piperidinyl	2-($(CH_3)_2NCH_2$)-1-imidazolyl
347.	piperidinyl	2-($(CH_3)NHCH_2$)-1-imidazolyl
348.	piperidinyl	2-($(CH_3CH_2)NHCH_2$)-1-imidazolyl
349.	piperidinyl	2-($(CH_3CH_2)_2NCH_2$)-1-imidazolyl
350.	piperidinyl	2-($(CH_3CH_2)N(CH_3)CH_2$)-1-imidazolyl
351.	piperidinyl	2-($((CH_3)_2CH)NHCH_2$)-1-imidazolyl
352.	piperidinyl	2-($((CH_3)_2CH)_2NCH_2$)-1-imidazolyl
353.	piperidinyl	2-((cyclopropyl)$NHCH_2$)-1-imidazolyl
354.	piperidinyl	2-((cyclopropyl)$_2NCH_2$)-1-imidazolyl
355.	piperidinyl	2-((cyclobutyl)$NHCH_2$)-1-imidazolyl
356.	piperidinyl	2-((cyclobutyl)$_2NCH_2$)-1-imidazolyl
357.	piperidinyl	2-((cyclopentyl)$NHCH_2$)-1-imidazolyl
358.	piperidinyl	2-((cyclopentyl)$_2NCH_2$)-1-imidazolyl
359.	piperidinyl	2-((cyclohexyl)$NHCH_2$)-1-imidazolyl
360.	piperidinyl	2-((cyclohexyl)$_2NCH_2$)-1-imidazolyl

Table 2

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

R^{1a} is CH_2CH_3.

Table 3

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

R^{1a} is CF_3.

Table 4

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

R^{1a} is SCH_3.

Table 5

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

R^{1a} is $SOCH_3$.

Table 6

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

R^{1a} is SO_2CH_3.

Table 7

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

R^{1a} is Cl.

Table 8

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

R^{1a} is F.

Table 9

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

R^{1a} is CO_2CH_3.

Table 10

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

R^{1a} is CH_2OCH_3.

Table 11

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

R^{1a} is $CONH_2$.

Table 12

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

R^{1a} is CN.

Table 13

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

R^{1a} is CH_2NH_2.

Table 14

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

R^{1a} is $CH_2NHSO_2CH_3$.

Table 15

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

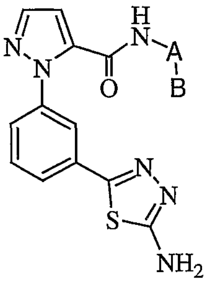
R^{1a} is 1-imidazolyl-CH_2.

Table 16

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

R^{1a} is 1-tetrazolyl-CH_2-.

Table 17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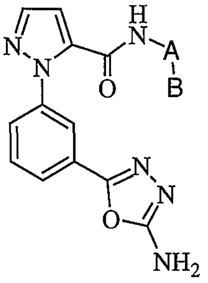
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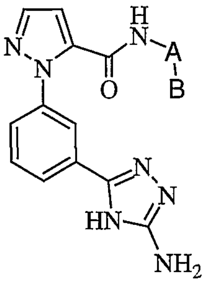
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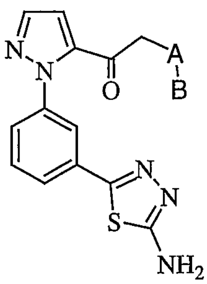
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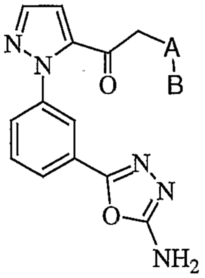
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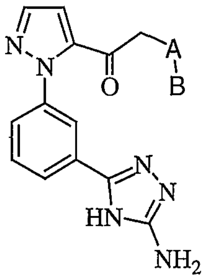
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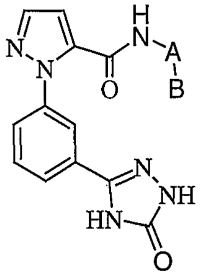
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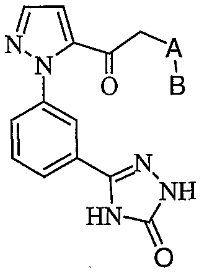
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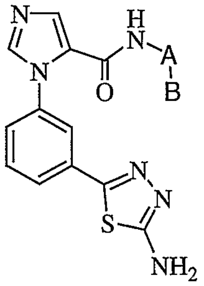

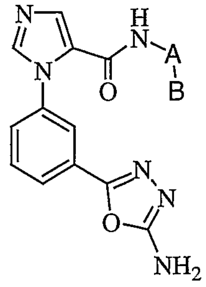

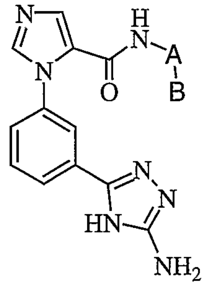

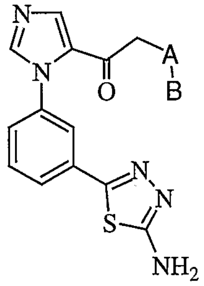

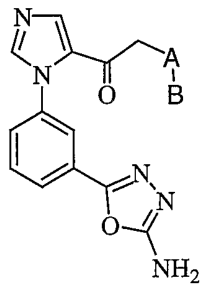

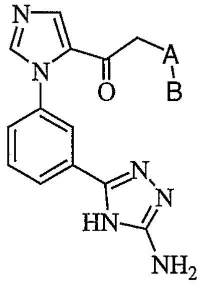

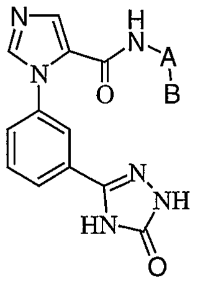

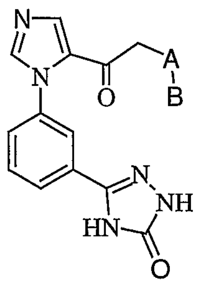

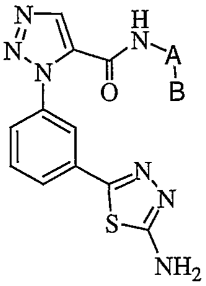

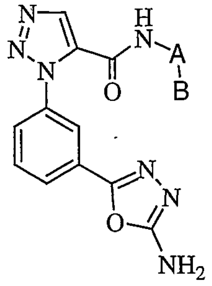

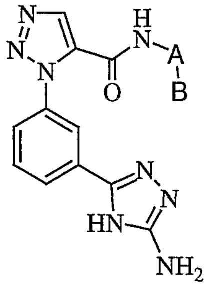

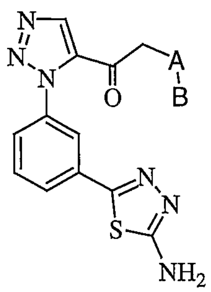

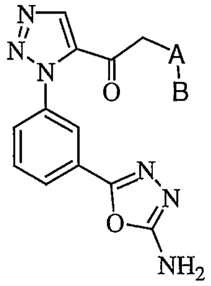

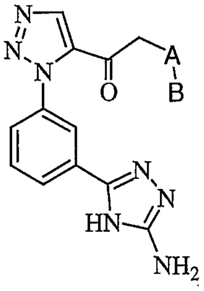

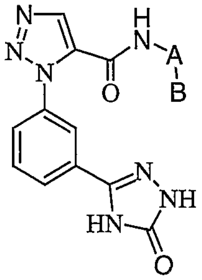

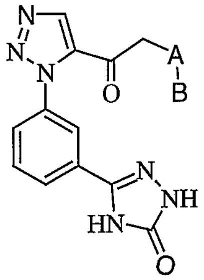

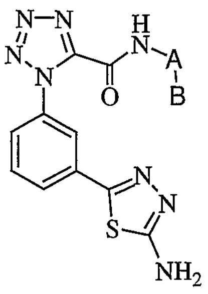

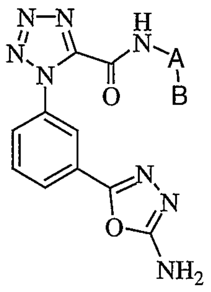

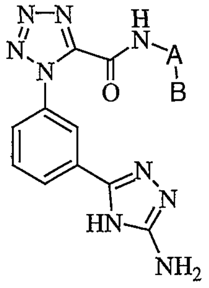

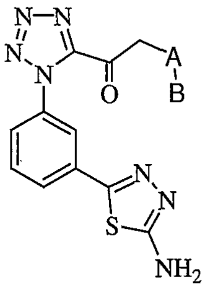

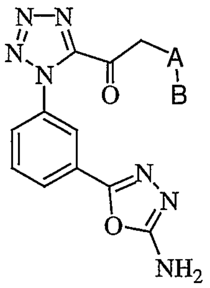

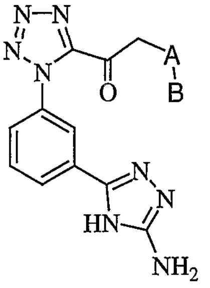

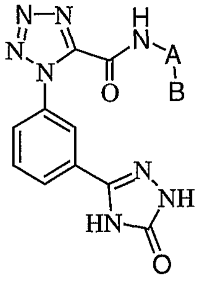

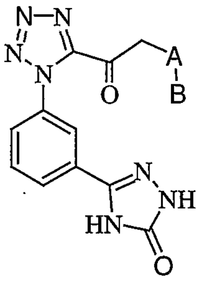

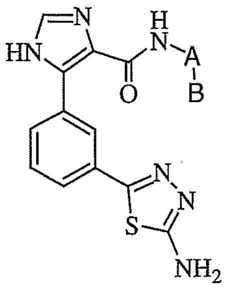
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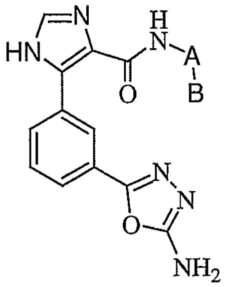
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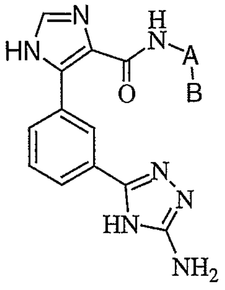
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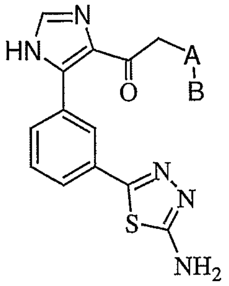
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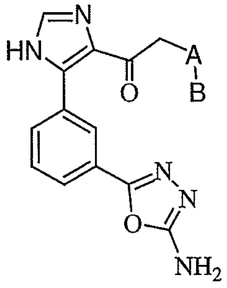
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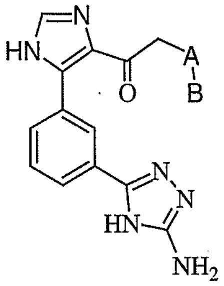
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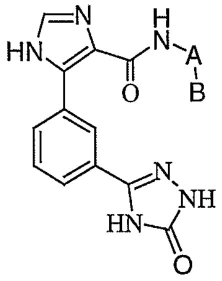
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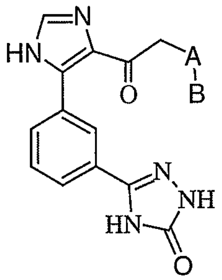
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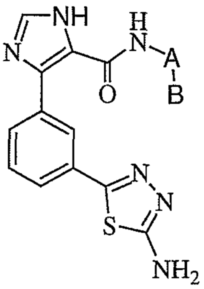

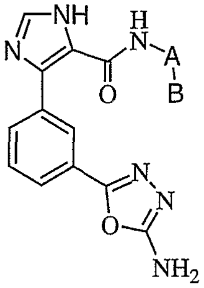

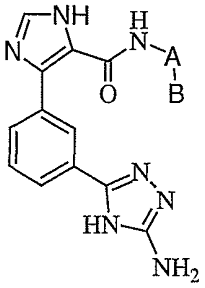

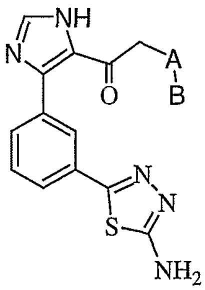

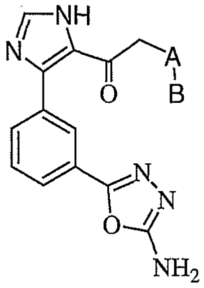

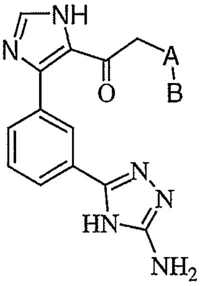

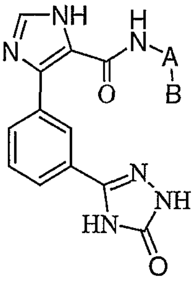

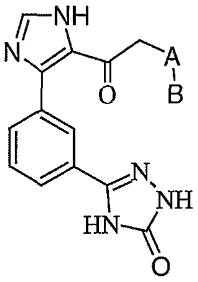

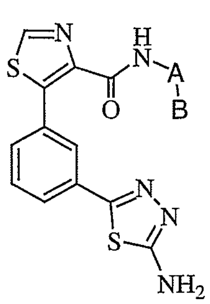

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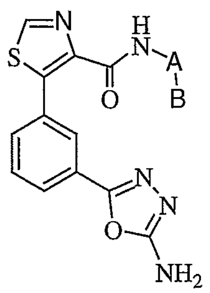

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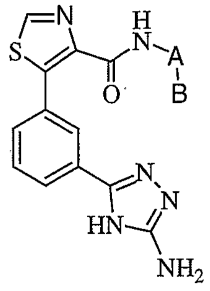

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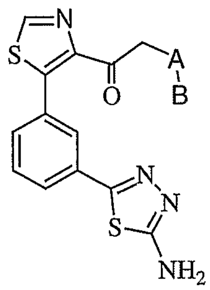

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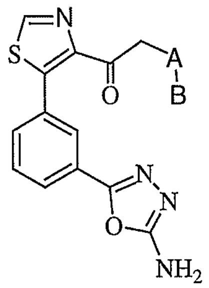

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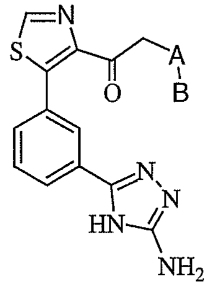

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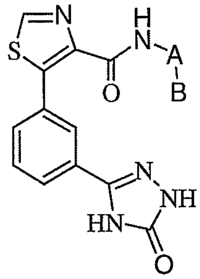

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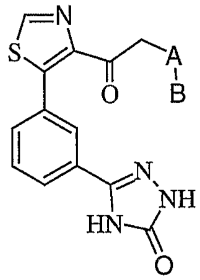

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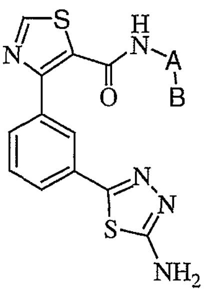
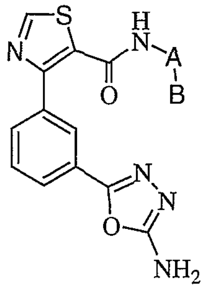
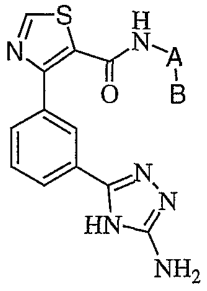
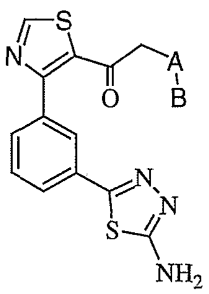
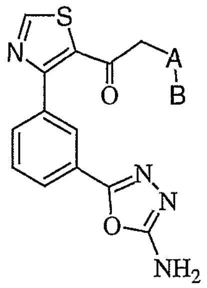
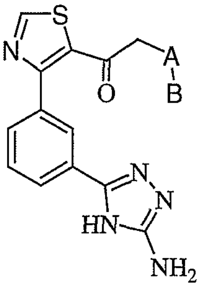
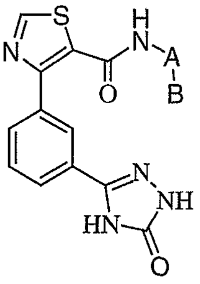
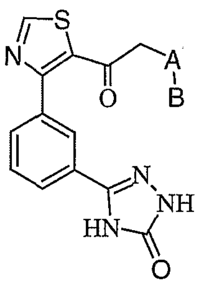




Ex#	**A**	**B**
1.	phenyl	2-(NH_2SO_2)phenyl
2.	phenyl	2-(CH_3SO_2)phenyl
3.	phenyl	3-NH_2SO_2-4-pyridyl
4.	phenyl	3-CH_3SO_2-4-pyridyl
5.	phenyl	2-(CH_3NH)phenyl
6.	phenyl	3-($(CH_3)_2NCH_2$)-4-pyridyl
7.	phenyl	2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
8.	phenyl	2-(N-(4-HO-piperidinyl)CH_2)phenyl
9.	phenyl	2-($(CH_3)_2NCH_2$)phenyl
10.	phenyl	2-($(CH_3)NHCH_2$)phenyl
11.	phenyl	2-($(CH_3CH_2)NHCH_2$)phenyl
12.	phenyl	2-($(CH_3CH_2)_2NCH_2$)phenyl
13.	phenyl	2-($(CH_3CH_2)N(CH_3)CH_2$)phenyl
14.	phenyl	2-($((CH_3)_2CH)NHCH_2$)phenyl
15.	phenyl	2-($((CH_3)_2CH)_2NCH_2$)phenyl
16.	phenyl	2-((cyclopropyl)$NHCH_2$)phenyl
17.	phenyl	2-((cyclopropyl)$_2NCH_2$)phenyl
18.	phenyl	2-((cyclobutyl)$NHCH_2$)phenyl
19.	phenyl	2-((cyclobutyl)$_2NCH_2$)phenyl
20.	phenyl	2-((cyclopentyl)$NHCH_2$)phenyl
21.	phenyl	2-((cyclopentyl)$_2NCH_2$)phenyl

22.	phenyl	2-((cyclohexyl)$NHCH_2$)phenyl
23.	phenyl	2-((cyclohexyl)$_2NCH_2$)phenyl
24.	phenyl	1-CH_3-2-imidazolyl
25.	phenyl	2-CH_3-1-imidazolyl
26.	phenyl	2-((CH_3)$_2NCH_2$)-1-imidazolyl
27.	phenyl	2-((CH_3)$NHCH_2$)-1-imidazolyl
28.	phenyl	2-((CH_3CH_2)$NHCH_2$)-1-imidazolyl
29.	phenyl	2-((CH_3CH_2)$_2NCH_2$)-1-imidazolyl
30.	phenyl	2-((CH_3CH_2)N(CH_3)CH_2)-1-imidazolyl
31.	phenyl	2-(((CH_3)$_2CH$)$NHCH_2$)-1-imidazolyl
32.	phenyl	2-(((CH_3)$_2CH$)$_2NCH_2$)-1-imidazolyl
33.	phenyl	2-((cyclopropyl)$NHCH_2$)-1-imidazolyl
34.	phenyl	2-((cyclopropyl)$_2NCH_2$)-1-imidazolyl
35.	phenyl	2-((cyclobutyl)$NHCH_2$)-1-imidazolyl
36.	phenyl	2-((cyclobutyl)$_2NCH_2$)-1-imidazolyl
37.	phenyl	2-((cyclopentyl)$NHCH_2$)-1-imidazolyl
38.	phenyl	2-((cyclopentyl)$_2NCH_2$)-1-imidazolyl
39.	phenyl	2-((cyclohexyl)$NHCH_2$)-1-imidazolyl
40.	phenyl	2-((cyclohexyl)$_2NCH_2$)-1-imidazolyl
41.	2-pyridyl	2-(NH_2SO_2)phenyl
42.	2-pyridyl	2-(CH_3SO_2)phenyl
43.	2-pyridyl	3-NH_2SO_2-4-pyridyl
44.	2-pyridyl	3-CH_3SO_2-4-pyridyl
45.	2-pyridyl	2-(CH_3NH)phenyl
46.	2-pyridyl	3-((CH_3)$_2NCH_2$)-4-pyridyl
47.	2-pyridyl	2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
48.	2-pyridyl	2-(N-(4-HO-piperidinyl)CH_2)phenyl
49.	2-pyridyl	2-((CH_3)$_2NCH_2$)phenyl
50.	2-pyridyl	2-((CH_3)$NHCH_2$)phenyl
51.	2-pyridyl	2-((CH_3CH_2)$NHCH_2$)phenyl
52.	2-pyridyl	2-((CH_3CH_2)$_2NCH_2$)phenyl
53.	2-pyridyl	2-((CH_3CH_2)N(CH_3)CH_2)phenyl
54.	2-pyridyl	2-(((CH_3)$_2CH$)$NHCH_2$)phenyl
55.	2-pyridyl	2-(((CH_3)$_2CH$)$_2NCH_2$)phenyl
56.	2-pyridyl	2-((cyclopropyl)$NHCH_2$)phenyl
57.	2-pyridyl	2-((cyclopropyl)$_2NCH_2$)phenyl
58.	2-pyridyl	2-((cyclobutyl)$NHCH_2$)phenyl
59.	2-pyridyl	2-((cyclobutyl)$_2NCH_2$)phenyl
60.	2-pyridyl	2-((cyclopentyl)$NHCH_2$)phenyl
61.	2-pyridyl	2-((cyclopentyl)$_2NCH_2$)phenyl
62.	2-pyridyl	2-((cyclohexyl)$NHCH_2$)phenyl
63.	2-pyridyl	2-((cyclohexyl)$_2NCH_2$)phenyl
64.	2-pyridyl	1-CH_3-2-imidazolyl
65.	2-pyridyl	2-CH_3-1-imidazolyl
66.	2-pyridyl	2-((CH_3)$_2NCH_2$)-1-imidazolyl
67.	2-pyridyl	2-((CH_3)$NHCH_2$)-1-imidazolyl
68.	2-pyridyl	2-((CH_3CH_2)$NHCH_2$)-1-imidazolyl
69.	2-pyridyl	2-((CH_3CH_2)$_2NCH_2$)-1-imidazolyl
70.	2-pyridyl	2-((CH_3CH_2)N(CH_3)CH_2)-1-imidazolyl
71.	2-pyridyl	2-(((CH_3)$_2CH$)$NHCH_2$)-1-imidazolyl
72.	2-pyridyl	2-(((CH_3)$_2CH$)$_2NCH_2$)-1-imidazolyl
73.	2-pyridyl	2-((cyclopropyl)$NHCH_2$)-1-imidazolyl
74.	2-pyridyl	2-((cyclopropyl)$_2NCH_2$)-1-imidazolyl

75.	2-pyridyl	2-((cyclobutyl)$NHCH_2$)-1-imidazolyl
76.	2-pyridyl	2-((cyclobutyl)$_2NCH_2$)-1-imidazolyl
77.	2-pyridyl	2-((cyclopentyl)$NHCH_2$)-1-imidazolyl
78.	2-pyridyl	2-((cyclopentyl)$_2NCH_2$)-1-imidazolyl
79.	2-pyridyl	2-((cyclohexyl)$NHCH_2$)-1-imidazolyl
80.	2-pyridyl	2-((cyclohexyl)$_2NCH_2$)-1-imidazolyl
81.	3-pyridyl	2-(NH_2SO_2)phenyl
82.	3-pyridyl	2-(CH_3SO_2)phenyl
83.	3-pyridyl	3-NH_2SO_2-4-pyridyl
84.	3-pyridyl	3-CH_3SO_2-4-pyridyl
85.	3-pyridyl	2-(CH_3NH)phenyl
86.	3-pyridyl	3-((CH_3)$_2NCH_2$)-4-pyridyl
87.	3-pyridyl	2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
88.	3-pyridyl	2-(N-(4-HO-piperidinyl)CH_2)phenyl
89.	3-pyridyl	2-((CH_3)$_2NCH_2$)phenyl
90.	3-pyridyl	2-((CH_3)$NHCH_2$)phenyl
91.	3-pyridyl	2-((CH_3CH_2)$NHCH_2$)phenyl
92.	3-pyridyl	2-((CH_3CH_2)$_2NCH_2$)phenyl
93.	3-pyridyl	2-((CH_3CH_2)N(CH_3)CH_2)phenyl
94.	3-pyridyl	2-(((CH_3)$_2CH$)$NHCH_2$)phenyl
95.	3-pyridyl	2-(((CH_3)$_2CH$)$_2NCH_2$)phenyl
96.	3-pyridyl	2-((cyclopropyl)$NHCH_2$)phenyl
97.	3-pyridyl	2-((cyclopropyl)$_2NCH_2$)phenyl
98.	3-pyridyl	2-((cyclobutyl)$NHCH_2$)phenyl
99.	3-pyridyl	2-((cyclobutyl)$_2NCH_2$)phenyl
100.	3-pyridyl	2-((cyclopentyl)$NHCH_2$)phenyl
101.	3-pyridyl	2-((cyclopentyl)$_2NCH_2$)phenyl
102.	3-pyridyl	2-((cyclohexyl)$NHCH_2$)phenyl
103.	3-pyridyl	2-((cyclohexyl)$_2NCH_2$)phenyl
104.	3-pyridyl	1-CH_3-2-imidazolyl
105.	3-pyridyl	2-CH_3-1-imidazolyl
106.	3-pyridyl	2-((CH_3)$_2NCH_2$)-1-imidazolyl
107.	3-pyridyl	2-((CH_3)$NHCH_2$)-1-imidazolyl
108.	3-pyridyl	2-((CH_3CH_2)$NHCH_2$)-1-imidazolyl
109.	3-pyridyl	2-((CH_3CH_2)$_2NCH_2$)-1-imidazolyl
110.	3-pyridyl	2-((CH_3CH_2)N(CH_3)CH_2)-1-imidazolyl
111.	3-pyridyl	2-(((CH_3)$_2CH$)$NHCH_2$)-1-imidazolyl
112.	3-pyridyl	2-(((CH_3)$_2CH$)$_2NCH_2$)-1-imidazolyl
113.	3-pyridyl	2-((cyclopropyl)$NHCH_2$)-1-imidazolyl
114.	3-pyridyl	2-((cyclopropyl)$_2NCH_2$)-1-imidazolyl
115.	3-pyridyl	2-((cyclobutyl)$NHCH_2$)-1-imidazolyl
116.	3-pyridyl	2-((cyclobutyl)$_2NCH_2$)-1-imidazolyl
117.	3-pyridyl	2-((cyclopentyl)$NHCH_2$)-1-imidazolyl
118.	3-pyridyl	2-((cyclopentyl)$_2NCH_2$)-1-imidazolyl
119.	3-pyridyl	2-((cyclohexyl)$NHCH_2$)-1-imidazolyl
120.	3-pyridyl	2-((cyclohexyl)$_2NCH_2$)-1-imidazolyl
121.	2-pyrimidyl	2-(NH_2SO_2)phenyl
122.	2-pyrimidyl	2-(CH_3SO_2)phenyl
123.	2-pyrimidyl	3-NH_2SO_2-4-pyridyl
124.	2-pyrimidyl	3-CH_3SO_2-4-pyridyl
125.	2-pyrimidyl	2-(CH_3NH)phenyl
126.	2-pyrimidyl	3-((CH_3)$_2NCH_2$)-4-pyridyl
127.	2-pyrimidyl	2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl

128.	2-pyrimidyl	2-(N-(4-HO-piperidinyl)CH$_2$)phenyl
129.	2-pyrimidyl	2-((CH$_3$)$_2$NCH$_2$)phenyl
130.	2-pyrimidyl	2-((CH$_3$)NHCH$_2$)phenyl
131.	2-pyrimidyl	2-((CH$_3$CH$_2$)NHCH$_2$)phenyl
132.	2-pyrimidyl	2-((CH$_3$CH$_2$)$_2$NCH$_2$)phenyl
133.	2-pyrimidyl	2-((CH$_3$CH$_2$)N(CH$_3$)CH$_2$)phenyl
134.	2-pyrimidyl	2-(((CH$_3$)$_2$CH)NHCH$_2$)phenyl
135.	2-pyrimidyl	2-(((CH$_3$)$_2$CH)$_2$NCH$_2$)phenyl
136.	2-pyrimidyl	2-((cyclopropyl)NHCH$_2$)phenyl
137.	2-pyrimidyl	2-((cyclopropyl)$_2$NCH$_2$)phenyl
138.	2-pyrimidyl	2-((cyclobutyl)NHCH$_2$)phenyl
139.	2-pyrimidyl	2-((cyclobutyl)$_2$NCH$_2$)phenyl
140.	2-pyrimidyl	2-((cyclopentyl)NHCH$_2$)phenyl
141.	2-pyrimidyl	2-((cyclopentyl)$_2$NCH$_2$)phenyl
142.	2-pyrimidyl	2-((cyclohexyl)NHCH$_2$)phenyl
143.	2-pyrimidyl	2-((cyclohexyl)$_2$NCH$_2$)phenyl
144.	2-pyrimidyl	1-CH$_3$-2-imidazolyl
145.	2-pyrimidyl	2-CH$_3$-1-imidazolyl
146.	2-pyrimidyl	2-((CH$_3$)$_2$NCH$_2$)-1-imidazolyl
147.	2-pyrimidyl	2-((CH$_3$)NHCH$_2$)-1-imidazolyl
148.	2-pyrimidyl	2-((CH$_3$CH$_2$)NHCH$_2$)-1-imidazolyl
149.	2-pyrimidyl	2-((CH$_3$CH$_2$)$_2$NCH$_2$)-1-imidazolyl
150.	2-pyrimidyl	2-((CH$_3$CH$_2$)N(CH$_3$)CH$_2$)-1-imidazolyl
151.	2-pyrimidyl	2-(((CH$_3$)$_2$CH)NHCH$_2$)-1-imidazolyl
152.	2-pyrimidyl	2-(((CH$_3$)$_2$CH)$_2$NCH$_2$)-1-imidazolyl
153.	2-pyrimidyl	2-((cyclopropyl)NHCH$_2$)-1-imidazolyl
154.	2-pyrimidyl	2-((cyclopropyl)$_2$NCH$_2$)-1-imidazolyl
155.	2-pyrimidyl	2-((cyclobutyl)NHCH$_2$)-1-imidazolyl
156.	2-pyrimidyl	2-((cyclobutyl)$_2$NCH$_2$)-1-imidazolyl
157.	2-pyrimidyl	2-((cyclopentyl)NHCH$_2$)-1-imidazolyl
158.	2-pyrimidyl	2-((cyclopentyl)$_2$NCH$_2$)-1-imidazolyl
159.	2-pyrimidyl	2-((cyclohexyl)NHCH$_2$)-1-imidazolyl
160.	2-pyrimidyl	2-((cyclohexyl)$_2$NCH$_2$)-1-imidazolyl
161.	5-pyrimidyl	2-(NH$_2$SO$_2$)phenyl
162.	5-pyrimidyl	2-(CH$_3$SO$_2$)phenyl
163.	5-pyrimidyl	3-NH$_2$SO$_2$-4-pyridyl
164.	5-pyrimidyl	3-CH$_3$SO$_2$-4-pyridyl
165.	5-pyrimidyl	2-(CH$_3$NH)phenyl
166.	5-pyrimidyl	3-((CH$_3$)$_2$NCH$_2$)-4-pyridyl
167.	5-pyrimidyl	2-(N-(3-R-HO-pyrrolidinyl)CH$_2$)phenyl
168.	5-pyrimidyl	2-(N-(4-HO-piperidinyl)CH$_2$)phenyl
169.	5-pyrimidyl	2-((CH$_3$)$_2$NCH$_2$)phenyl
170.	5-pyrimidyl	2-((CH$_3$)NHCH$_2$)phenyl
171.	5-pyrimidyl	2-((CH$_3$CH$_2$)NHCH$_2$)phenyl
172.	5-pyrimidyl	2-((CH$_3$CH$_2$)$_2$NCH$_2$)phenyl
173.	5-pyrimidyl	2-((CH$_3$CH$_2$)N(CH$_3$)CH$_2$)phenyl
174.	5-pyrimidyl	2-(((CH$_3$)$_2$CH)NHCH$_2$)phenyl
175.	5-pyrimidyl	2-(((CH$_3$)$_2$CH)$_2$NCH$_2$)phenyl
176.	5-pyrimidyl	2-((cyclopropyl)NHCH$_2$)phenyl
177.	5-pyrimidyl	2-((cyclopropyl)$_2$NCH$_2$)phenyl
178.	5-pyrimidyl	2-((cyclobutyl)NHCH$_2$)phenyl
179.	5-pyrimidyl	2-((cyclobutyl)$_2$NCH$_2$)phenyl
180.	5-pyrimidyl	2-((cyclopentyl)NHCH$_2$)phenyl

181.	5-pyrimidyl	2-((cyclopentyl)$_2$NCH$_2$)phenyl
182.	5-pyrimidyl	2-((cyclohexyl)NHCH$_2$)phenyl
183.	5-pyrimidyl	2-((cyclohexyl)$_2$NCH$_2$)phenyl
184.	5-pyrimidyl	1-CH$_3$-2-imidazolyl
185.	5-pyrimidyl	2-CH$_3$-1-imidazolyl
186.	5-pyrimidyl	2-((CH$_3$)$_2$NCH$_2$)-1-imidazolyl
187.	5-pyrimidyl	2-((CH$_3$)NHCH$_2$)-1-imidazolyl
188.	5-pyrimidyl	2-((CH$_3$CH$_2$)NHCH$_2$)-1-imidazolyl
189.	5-pyrimidyl	2-((CH$_3$CH$_2$)$_2$NCH$_2$)-1-imidazolyl
190.	5-pyrimidyl	2-((CH$_3$CH$_2$)N(CH$_3$)CH$_2$)-1-imidazolyl
191.	5-pyrimidyl	2-(((CH$_3$)$_2$CH)NHCH$_2$)-1-imidazolyl
192.	5-pyrimidyl	2-(((CH$_3$)$_2$CH)$_2$NCH$_2$)-1-imidazolyl
193.	5-pyrimidyl	2-((cyclopropyl)NHCH$_2$)-1-imidazolyl
194.	5-pyrimidyl	2-((cyclopropyl)$_2$NCH$_2$)-1-imidazolyl
195.	5-pyrimidyl	2-((cyclobutyl)NHCH$_2$)-1-imidazolyl
196.	5-pyrimidyl	2-((cyclobutyl)$_2$NCH$_2$)-1-imidazolyl
197.	5-pyrimidyl	2-((cyclopentyl)NHCH$_2$)-1-imidazolyl
198.	5-pyrimidyl	2-((cyclopentyl)$_2$NCH$_2$)-1-imidazolyl
199.	5-pyrimidyl	2-((cyclohexyl)NHCH$_2$)-1-imidazolyl
200.	5-pyrimidyl	2-((cyclohexyl)$_2$NCH$_2$)-1-imidazolyl
201.	2-Cl-phenyl	2-(NH$_2$SO$_2$)phenyl
202.	2-Cl-phenyl	2-(CH$_3$SO$_2$)phenyl
203.	2-Cl-phenyl	3-NH$_2$SO$_2$-4-pyridyl
204.	2-Cl-phenyl	3-CH$_3$SO$_2$-4-pyridyl
205.	2-Cl-phenyl	2-(CH$_3$NH)phenyl
206.	2-Cl-phenyl	3-((CH$_3$)$_2$NCH$_2$)-4-pyridyl
207.	2-Cl-phenyl	2-(N-(3-R-HO-pyrrolidinyl)CH$_2$)phenyl
208.	2-Cl-phenyl	2-(N-(4-HO-piperidinyl)CH$_2$)phenyl
209.	2-Cl-phenyl	2-((CH$_3$)$_2$NCH$_2$)phenyl
210.	2-Cl-phenyl	2-((CH$_3$)NHCH$_2$)phenyl
211.	2-Cl-phenyl	2-((CH$_3$CH$_2$)NHCH$_2$)phenyl
212.	2-Cl-phenyl	2-((CH$_3$CH$_2$)$_2$NCH$_2$)phenyl
213.	2-Cl-phenyl	2-((CH$_3$CH$_2$)N(CH$_3$)CH$_2$)phenyl
214.	2-Cl-phenyl	2-(((CH$_3$)$_2$CH)NHCH$_2$)phenyl
215.	2-Cl-phenyl	2-(((CH$_3$)$_2$CH)$_2$NCH$_2$)phenyl
216.	2-Cl-phenyl	2-((cyclopropyl)NHCH$_2$)phenyl
217.	2-Cl-phenyl	2-((cyclopropyl)$_2$NCH$_2$)phenyl
218.	2-Cl-phenyl	2-((cyclobutyl)NHCH$_2$)phenyl
219.	2-Cl-phenyl	2-((cyclobutyl)$_2$NCH$_2$)phenyl
220.	2-Cl-phenyl	2-((cyclopentyl)NHCH$_2$)phenyl
221.	2-Cl-phenyl	2-((cyclopentyl)$_2$NCH$_2$)phenyl
222.	2-Cl-phenyl	2-((cyclohexyl)NHCH$_2$)phenyl
223.	2-Cl-phenyl	2-((cyclohexyl)$_2$NCH$_2$)phenyl
224.	2-Cl-phenyl	1-CH$_3$-2-imidazolyl
225.	2-Cl-phenyl	2-CH$_3$-1-imidazolyl
226.	2-Cl-phenyl	2-((CH$_3$)$_2$NCH$_2$)-1-imidazolyl
227.	2-Cl-phenyl	2-((CH$_3$)NHCH$_2$)-1-imidazolyl
228.	2-Cl-phenyl	2-((CH$_3$CH$_2$)NHCH$_2$)-1-imidazolyl
229.	2-Cl-phenyl	2-((CH$_3$CH$_2$)$_2$NCH$_2$)-1-imidazolyl
230.	2-Cl-phenyl	2-((CH$_3$CH$_2$)N(CH$_3$)CH$_2$)-1-imidazolyl
231.	2-Cl-phenyl	2-(((CH$_3$)$_2$CH)NHCH$_2$)-1-imidazolyl
232.	2-Cl-phenyl	2-(((CH$_3$)$_2$CH)$_2$NCH$_2$)-1-imidazolyl
233.	2-Cl-phenyl	2-((cyclopropyl)NHCH$_2$)-1-imidazolyl

234.	2-Cl-phenyl	2-((cyclopropyl)$_2$NCH$_2$)-1-imidazolyl
235.	2-Cl-phenyl	2-((cyclobutyl)NHCH$_2$)-1-imidazolyl
236.	2-Cl-phenyl	2-((cyclobutyl)$_2$NCH$_2$)-1-imidazolyl
237.	2-Cl-phenyl	2-((cyclopentyl)NHCH$_2$)-1-imidazolyl
238.	2-Cl-phenyl	2-((cyclopentyl)$_2$NCH$_2$)-1-imidazolyl
239.	2-Cl-phenyl	2-((cyclohexyl)NHCH$_2$)-1-imidazolyl
240.	2-Cl-phenyl	2-((cyclohexyl)$_2$NCH$_2$)-1-imidazolyl
241.	2-F-phenyl	2-(NH_2SO_2)phenyl
242.	2-F-phenyl	2-(CH_3SO_2)phenyl
243.	2-F-phenyl	3-NH_2SO_2-4-pyridyl
244.	2-F-phenyl	3-CH_3SO_2-4-pyridyl
245.	2-F-phenyl	2-(CH_3NH)phenyl
246.	2-F-phenyl	3-((CH_3)$_2$NCH$_2$)-4-pyridyl
247.	2-F-phenyl	2-(N-(3-R-HO-pyrrolidinyl)CH$_2$)phenyl
248.	2-F-phenyl	2-(N-(4-HO-piperidinyl)CH$_2$)phenyl
249.	2-F-phenyl	2-((CH_3)$_2$NCH$_2$)phenyl
250.	2-F-phenyl	2-((CH_3)NHCH$_2$)phenyl
251.	2-F-phenyl	2-((CH_3CH_2)NHCH$_2$)phenyl
252.	2-F-phenyl	2-((CH_3CH_2)$_2$NCH$_2$)phenyl
253.	2-F-phenyl	2-((CH_3CH_2)N(CH_3)CH$_2$)phenyl
254.	2-F-phenyl	2-(((CH_3)$_2$CH)NHCH$_2$)phenyl
255.	2-F-phenyl	2-(((CH_3)$_2$CH)$_2$NCH$_2$)phenyl
256.	2-F-phenyl	2-((cyclopropyl)NHCH$_2$)phenyl
257.	2-F-phenyl	2-((cyclopropyl)$_2$NCH$_2$)phenyl
258.	2-F-phenyl	2-((cyclobutyl)NHCH$_2$)phenyl
259.	2-F-phenyl	2-((cyclobutyl)$_2$NCH$_2$)phenyl
260.	2-F-phenyl	2-((cyclopentyl)NHCH$_2$)phenyl
261.	2-F-phenyl	2-((cyclopentyl)$_2$NCH$_2$)phenyl
262.	2-F-phenyl	2-((cyclohexyl)NHCH$_2$)phenyl
263.	2-F-phenyl	2-((cyclohexyl)$_2$NCH$_2$)phenyl
264.	2-F-phenyl	1-CH_3-2-imidazolyl
265.	2-F-phenyl	2-CH_3-1-imidazolyl
266.	2-F-phenyl	2-((CH_3)$_2$NCH$_2$)-1-imidazolyl
267.	2-F-phenyl	2-((CH_3)NHCH$_2$)-1-imidazolyl
268.	2-F-phenyl	2-((CH_3CH_2)NHCH$_2$)-1-imidazolyl
269.	2-F-phenyl	2-((CH_3CH_2)$_2$NCH$_2$)-1-imidazolyl
270.	2-F-phenyl	2-((CH_3CH_2)N(CH_3)CH$_2$)-1-imidazolyl
271.	2-F-phenyl	2-(((CH_3)$_2$CH)NHCH$_2$)-1-imidazolyl
272.	2-F-phenyl	2-(((CH_3)$_2$CH)$_2$NCH$_2$)-1-imidazolyl
273.	2-F-phenyl	2-((cyclopropyl)NHCH$_2$)-1-imidazolyl
274.	2-F-phenyl	2-((cyclopropyl)$_2$NCH$_2$)-1-imidazolyl
275.	2-F-phenyl	2-((cyclobutyl)NHCH$_2$)-1-imidazolyl
276.	2-F-phenyl	2-((cyclobutyl)$_2$NCH$_2$)-1-imidazolyl
277.	2-F-phenyl	2-((cyclopentyl)NHCH$_2$)-1-imidazolyl
278.	2-F-phenyl	2-((cyclopentyl)$_2$NCH$_2$)-1-imidazolyl
279.	2-F-phenyl	2-((cyclohexyl)NHCH$_2$)-1-imidazolyl
280.	2-F-phenyl	2-((cyclohexyl)$_2$NCH$_2$)-1-imidazolyl
281.	2,6-diF-phenyl	2-(NH_2SO_2)phenyl
282.	2,6-diF-phenyl	2-(CH_3SO_2)phenyl
283.	2,6-diF-phenyl	3-NH_2SO_2-4-pyridyl
284.	2,6-diF-phenyl	3-CH_3SO_2-4-pyridyl
285.	2,6-diF-phenyl	2-(CH_3NH)phenyl
286.	2,6-diF-phenyl	3-((CH_3)$_2$NCH$_2$)-4-pyridyl

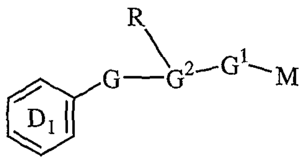
287.	2,6-diF-phenyl	2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
288.	2,6-diF-phenyl	2-(N-(4-HO-piperidinyl)CH_2)phenyl
289.	2,6-diF-phenyl	2-((CH_3)$_2$$NCH_2$)phenyl
290.	2,6-diF-phenyl	2-((CH_3)$NHCH_2$)phenyl
291.	2,6-diF-phenyl	2-((CH_3CH_2)$NHCH_2$)phenyl
292.	2,6-diF-phenyl	2-((CH_3CH_2)$_2$$NCH_2$)phenyl
293.	2,6-diF-phenyl	2-((CH_3CH_2)N(CH_3)CH_2)phenyl
294.	2,6-diF-phenyl	2-(((CH_3)$_2$CH)$NHCH_2$)phenyl
295.	2,6-diF-phenyl	2-(((CH_3)$_2$CH)$_2$$NCH_2$)phenyl
296.	2,6-diF-phenyl	2-((cyclopropyl)$NHCH_2$)phenyl
297.	2,6-diF-phenyl	2-((cyclopropyl)$_2$$NCH_2$)phenyl
298.	2,6-diF-phenyl	2-((cyclobutyl)$NHCH_2$)phenyl
299.	2,6-diF-phenyl	2-((cyclobutyl)$_2$$NCH_2$)phenyl
300.	2,6-diF-phenyl	2-((cyclopentyl)$NHCH_2$)phenyl
301.	2,6-diF-phenyl	2-((cyclopentyl)$_2$$NCH_2$)phenyl
302.	2,6-diF-phenyl	2-((cyclohexyl)$NHCH_2$)phenyl
303.	2,6-diF-phenyl	2-((cyclohexyl)$_2$$NCH_2$)phenyl
304.	2,6-diF-phenyl	1-CH_3-2-imidazolyl
305.	2,6-diF-phenyl	2-CH_3-1-imidazolyl
306.	2,6-diF-phenyl	2-((CH_3)$_2$$NCH_2$)-1-imidazolyl
307.	2,6-diF-phenyl	2-((CH_3)$NHCH_2$)-1-imidazolyl
308.	2,6-diF-phenyl	2-((CH_3CH_2)$NHCH_2$)-1-imidazolyl
309.	2,6-diF-phenyl	2-((CH_3CH_2)$_2$$NCH_2$)-1-imidazolyl
310.	2,6-diF-phenyl	2-((CH_3CH_2)N(CH_3)CH_2)-1-imidazolyl
311.	2,6-diF-phenyl	2-(((CH_3)$_2$CH)$NHCH_2$)-1-imidazolyl
312.	2,6-diF-phenyl	2-(((CH_3)$_2$CH)$_2$$NCH_2$)-1-imidazolyl
313.	2,6-diF-phenyl	2-((cyclopropyl)$NHCH_2$)-1-imidazolyl
314.	2,6-diF-phenyl	2-((cyclopropyl)$_2$$NCH_2$)-1-imidazolyl
315.	2,6-diF-phenyl	2-((cyclobutyl)$NHCH_2$)-1-imidazolyl
316.	2,6-diF-phenyl	2-((cyclobutyl)$_2$$NCH_2$)-1-imidazolyl
317.	2,6-diF-phenyl	2-((cyclopentyl)$NHCH_2$)-1-imidazolyl
318.	2,6-diF-phenyl	2-((cyclopentyl)$_2$$NCH_2$)-1-imidazolyl
319.	2,6-diF-phenyl	2-((cyclohexyl)$NHCH_2$)-1-imidazolyl
320.	2,6-diF-phenyl	2-((cyclohexyl)$_2$$NCH_2$)-1-imidazolyl
321.	piperidinyl	2-(NH_2SO_2)phenyl
322.	piperidinyl	2-(CH_3SO_2)phenyl
323.	piperidinyl	3-NH_2SO_2-4-pyridyl
324.	piperidinyl	3-CH_3SO_2-4-pyridyl
325.	piperidinyl	2-(CH_3NH)phenyl
326.	piperidinyl	3-((CH_3)$_2$$NCH_2$)-4-pyridyl
327.	piperidinyl	2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
328.	piperidinyl	2-(N-(4-HO-piperidinyl)CH_2)phenyl
329.	piperidinyl	2-((CH_3)$_2$$NCH_2$)phenyl
330.	piperidinyl	2-((CH_3)$NHCH_2$)phenyl
331.	piperidinyl	2-((CH_3CH_2)$NHCH_2$)phenyl
332.	piperidinyl	2-((CH_3CH_2)$_2$$NCH_2$)phenyl
333.	piperidinyl	2-((CH_3CH_2)N(CH_3)CH_2)phenyl
334.	piperidinyl	2-(((CH_3)$_2$CH)$NHCH_2$)phenyl
335.	piperidinyl	2-(((CH_3)$_2$CH)$_2$$NCH_2$)phenyl
336.	piperidinyl	2-((cyclopropyl)$NHCH_2$)phenyl
337.	piperidinyl	2-((cyclopropyl)$_2$$NCH_2$)phenyl
338.	piperidinyl	2-((cyclobutyl)$NHCH_2$)phenyl
339.	piperidinyl	2-((cyclobutyl)$_2$$NCH_2$)phenyl

340.	piperidinyl	2-((cyclopentyl)NHCH$_2$)phenyl
341.	piperidinyl	2-((cyclopentyl)$_2$NCH$_2$)phenyl
342.	piperidinyl	2-((cyclohexyl)NHCH$_2$)phenyl
343.	piperidinyl	2-((cyclohexyl)$_2$NCH$_2$)phenyl
344.	piperidinyl	1-CH$_3$-2-imidazolyl
345.	piperidinyl	2-CH$_3$-1-imidazolyl
346.	piperidinyl	2-((CH$_3$)$_2$NCH$_2$)-1-imidazolyl
347.	piperidinyl	2-((CH$_3$)NHCH$_2$)-1-imidazolyl
348.	piperidinyl	2-((CH$_3$CH$_2$)NHCH$_2$)-1-imidazolyl
349.	piperidinyl	2-((CH$_3$CH$_2$)$_2$NCH$_2$)-1-imidazolyl
350.	piperidinyl	2-((CH$_3$CH$_2$)N(CH$_3$)CH$_2$)-1-imidazolyl
351.	piperidinyl	2-(((CH$_3$)$_2$CH)NHCH$_2$)-1-imidazolyl
352.	piperidinyl	2-(((CH$_3$)$_2$CH)$_2$NCH$_2$)-1-imidazolyl
353.	piperidinyl	2-((cyclopropyl)NHCH$_2$)-1-imidazolyl
354.	piperidinyl	2-((cyclopropyl)$_2$NCH$_2$)-1-imidazolyl
355.	piperidinyl	2-((cyclobutyl)NHCH$_2$)-1-imidazolyl
356.	piperidinyl	2-((cyclobutyl)$_2$NCH$_2$)-1-imidazolyl
357.	piperidinyl	2-((cyclopentyl)NHCH$_2$)-1-imidazolyl
358.	piperidinyl	2-((cyclopentyl)$_2$NCH$_2$)-1-imidazolyl
359.	piperidinyl	2-((cyclohexyl)NHCH$_2$)-1-imidazolyl
360.	piperidinyl	2-((cyclohexyl)$_2$NCH$_2$)-1-imidazolyl

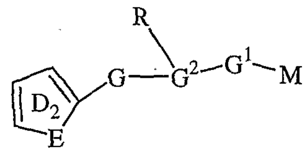
Numerous modifications and variations of the present invention are possible in light of the above teachings. It is therefore to be understood that within the scope of the appended claims, the invention may be practiced otherwise that as specifically described herein.

WHAT IS CLAIMED IS:

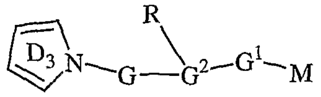
1. A compound of formula Ia, Ib, or Ic:



Ia



Ib



Ic

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

ring D_1 is selected from pyridine, pyrazine, pyridazine, and pyrimidine and is substituted with 1 R^a and 0-1 R^b;

ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-3 N atoms, wherein E is selected from O, S, and N-R^c and ring D_2 is substituted with 1 R^a and 0-1 R^b;

ring D_3 is a 5-membered heteroaromatic ring system comprising carbon atoms and from 0-3 additional N atoms and ring D_3 is substituted with 1 R^a and 0-1 R^b;

R is selected from H, C_{1-4} alkyl, F, Cl, Br, I, OH, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, CN, $C(=NR^8)NR^7R^9$, $NHC(=NR^8)NR^7R^9$, $NR^8CH(=NR^7)$, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, $C(=NH)NH_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl$)_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), $CH_2CH_2N(C_{1-3}$ alkyl$)_2$, $(CR^8R^9)_tNR^7R^8$, $(CR^8R^9)_tC(O)NR^7R^8$, and OCF_3;

R^a is selected from H, C_{1-4} alkyl, F, Cl, Br, I, OH, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, CN, $C(=NR^8)NR^7R^9$, $NHC(=NR^8)NR^7R^9$, $NR^8CH(=NR^7)$, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$

alkyl)$_2$, C(=NH)NH$_2$, CH$_2$NH$_2$, CH$_2$NH(C$_{1-3}$ alkyl), CH$_2$N(C$_{1-3}$ alkyl)$_2$, CH$_2$CH$_2$NH$_2$, CH$_2$CH$_2$NH(C$_{1-3}$ alkyl), CH$_2$CH$_2$N(C$_{1-3}$ alkyl)$_2$, (CR^{8}R^9)$_t$NR^{7}R^8, (CR^{8}R^9)$_t$C(O)NR^{7}R^8, and OCF$_3$;

R^b is selected from H, C$_{1-4}$ alkyl, F, Cl, Br, I, OH, OCH$_3$, OCH$_2$CH$_3$, OCH(CH$_3$)$_2$, OCH$_2$CH$_2$CH$_3$, CN, C(=NR^8)NR^{7}R^9, NHC(=NR^8)NR^{7}R^9, NR^{8}CH(=NR^7), NH$_2$, NH(C$_{1-3}$ alkyl), N(C$_{1-3}$ alkyl)$_2$, C(=NH)NH$_2$, CH$_2$NH$_2$, CH$_2$NH(C$_{1-3}$ alkyl), CH$_2$N(C$_{1-3}$ alkyl)$_2$, CH$_2$CH$_2$NH$_2$, CH$_2$CH$_2$NH(C$_{1-3}$ alkyl), CH$_2$CH$_2$N(C$_{1-3}$ alkyl)$_2$, (CR^{8}R^9)$_t$NR^{7}R^8, (CR^{8}R^9)$_t$C(O)NR^{7}R^8, and OCF$_3$;

R^c is selected from H, C$_{1-4}$ alkyl, OCH$_3$, OCH$_2$CH$_3$, OCH(CH$_3$)$_2$, OCH$_2$CH$_2$CH$_3$, NH$_2$, NH(C$_{1-3}$ alkyl), N(C$_{1-3}$ alkyl)$_2$, C(=NH)NH$_2$, CH$_2$NH$_2$, CH$_2$NH(C$_{1-3}$ alkyl), CH$_2$N(C$_{1-3}$ alkyl)$_2$, CH$_2$CH$_2$NH$_2$, CH$_2$CH$_2$NH(C$_{1-3}$ alkyl), CH$_2$CH$_2$N(C$_{1-3}$ alkyl)$_2$, (CR^{8}R^9)$_t$NR^{7}R^8, (CR^{8}R^9)$_t$C(O)NR^{7}R^8, and OCF$_3$;

G is absent or is selected from CH$_2$, C(O), O, NR^3, S(O)$_p$, CH$_2$CH$_2$, C(O)CH$_2$, CH$_2$C(O), OCH$_2$, CH$_2$O, NR^{3}CH$_2$, CH$_2$NR^3, S(O)$_p$CH$_2$, CH$_2$S(O)$_p$, CH$_2$CH$_2$CH$_2$, C(O)CH$_2$CH$_2$, CH$_2$C(O)CH$_2$, CH$_2$CH$_2$C(O), OCH$_2$CH$_2$, CH$_2$OCH$_2$, CH$_2$CH$_2$O, NR^{3}CH$_2$CH$_2$, CH$_2$NR^{3}CH$_2$, CH$_2$CH$_2$NR^3, S(O)$_p$CH$_2$CH$_2$, CH$_2$S(O)$_p$CH$_2$, and CH$_2$CH$_2$S(O)$_p$;

G$_1$ is absent or is selected from (CR^{3}R^{3a})$_{1-5}$, (CR^{3}R^{3a})$_{0-2}$CR^3=CR^3(CR^{3}R^{3a})$_{0-2}$, (CR^{3}R^{3a})$_{0-2}$C≡C(CR^{3}R^{3a})$_{0-2}$, (CR^{3}R^{3a})$_u$C(O)(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$C(O)O(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$OC(O)(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$O(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$NR^3(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$C(O)NR^3(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$NR^{3}C(O)(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$OC(O)NR^3(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$NR^{3}C(O)O(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$NR^{3}C(O)NR^3(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$NR^{3}C(S)NR^3(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$S(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$S(O)(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$S(O)$_2$(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$S(O)NR^3(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$NR^{3}S(O)$_2$(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$S(O)$_2$NR^3(CR^{3}R^{3a})$_w$, and (CR^{3}R^{3a})$_u$NR^{3}S(O)$_2$NR^3(CR^{3}R^{3a})$_w$, wherein u + w total 0, 1, 2, 3, or 4, provided that G_1 does not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached;

G^2 is phenyl, naphthyl, or a 5-10 membered heteroaryl consisting of carbon atoms and from 1-3 heteroatoms selected from N, O, and S;

M is isoxazoline, pyrazoline, isothiazoline, triazoline, tetrazoline, phenyl, or a 5-6 membered aromatic heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from O, N, and S, and is substituted with -Z-A-B;

M is also substituted with 0-2 R^{1a};

Z is selected from a bond, $-(CR^2R^{2a})_{1-4}-$, $(CR^2R^{2a})_qO(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qNR^3(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qC(O)(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qC(O)O(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qOC(O)(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qC(O)NR^3(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qNR^3C(O)(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qOC(O)O(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qOC(O)NR^3(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qNR^3C(O)O(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qNR^3C(O)NR^3(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qS(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qS(O)(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qS(O)_2(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qSO_2NR^3(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qNR^3SO_2(CR^2R^{2a})_{q^1}$, and $(CR^2R^{2a})_qNR^3SO_2NR^3(CR^2R^{2a})_{q^1}$, wherein q + q^1 total 0, 1, or 2, provided that Z does not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached;

R^{1a} is selected from H, $-(CH_2)_r-R^{1b}$, $-CH=CH-R^{1b}$, NCH_2R^{1c}, OCH_2R^{1c}, SCH_2R^{1c}, $NH(CH_2)_2(CH_2)_tR^{1b}$, $O(CH_2)_2(CH_2)_tR^{1b}$, $S(CH_2)_2(CH_2)_tR^{1b}$, $S(O)_p(CH_2)_rR^{1d}$, $O(CH_2)_rR^{1d}$, $NR^3(CH_2)_rR^{1d}$, $OC(O)NR^3(CH_2)_rR^{1d}$, $NR^3C(O)NR^3(CH_2)_rR^{1d}$, $NR^3C(O)O(CH_2)_rR^{1d}$, and $NR^3C(O)(CH_2)_rR^{1d}$, provided that R^{1a} forms other than an N-halo, N-N, N-S, N-O, or N-CN bond;

alternatively, when two R^{1a}'s are attached to adjacent atoms, together with the atoms to which they are attached they form a 5-7 membered ring consisting of: carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and $S(O)_p$, this ring being substituted with 0-2 R^{4b} and comprising: 0-3 double bonds;

R^{1b} is selected from H, C_{1-3} alkyl, F, Cl, Br, I, -CN, -CHO, $(CF_2)_rCF_3$, $(CH_2)_rOR^2$, NR^2R^{2a}, $C(O)R^{2c}$, $OC(O)R^2$, $(CF_2)_rCO_2R^{2a}$, $S(O)_pR^{2b}$, $NR^2(CH_2)_rOR^2$, $C(=NR^{2c})NR^2R^{2a}$, $NR^2C(O)R^{2b}$, $NR^2C(O)NHR^{2b}$, $NR^2C(O)_2R^{2a}$, $OC(O)NR^{2a}R^{2b}$, $C(O)NR^2R^{2a}$, $C(O)NR^2(CH_2)_rOR^2$, $SO_2NR^2R^{2a}$, $NR^2SO_2R^{2b}$, C_{3-6} carbocycle substituted with 0-2 R^{4a}, and 5-10 membered heterocycle consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-2 R^{4a}, provided that R^{1b} forms other than an N-halo, N-N, N-S, N-O, or N-CN bond;

R^{1c} is selected from H, $CH(CH_2OR^2)_2$, $C(O)R^{2c}$, $C(O)NR^2R^{2a}$, $S(O)R^{2b}$, $S(O)_2R^{2b}$, and $SO_2NR^2R^{2a}$;

R^{1d} is selected from C_{3-13} carbocycle substituted with 0-2 R^{4a}, and 5-13 membered heterocycle consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-2 R^{4a}, provided that R^{1d} forms other than an N-N, N-S, or N-O bond;

R^2, at each occurrence, is selected from H, CF_3, C_{1-6} alkyl, benzyl, C_{3-6} carbocyclic residue substituted with 0-2

R^{4b}, and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4b};

R^{2a}, at each occurrence, is selected from H, CF_3, C_{1-6} alkyl, benzyl, phenethyl, C_{3-6} carbocyclic residue substituted with 0-2 R^{4b}, and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4b};

R^{2b}, at each occurrence, is selected from CF_3, C_{1-4} alkoxy, C_{1-6} alkyl, benzyl, C_{3-6} carbocyclic residue substituted with 0-2 R^{4b}, and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4b};

R^{2c}, at each occurrence, is selected from CF_3, OH, C_{1-4} alkoxy, C_{1-6} alkyl, benzyl, C_{3-6} carbocyclic residue substituted with 0-2 R^{4b}, and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4b};

alternatively, R^2 and R^{2a}, together with the atom to which they are attached, combine to form a 5 or 6 membered saturated, partially saturated or unsaturated ring substituted with 0-2 R^{4b} and comprising carbon atoms and from 0-1 additional heteroatoms selected from the group consisting of N, O, and S;

R^3, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

R^{3a}, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

R^{3b}, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

R^{3c}, at each occurrence, is selected from C_{1-4} alkyl, and phenyl;

R^{3d}, at each occurrence, is selected from H, C_{1-4} alkyl, C_{1-4} alkyl-phenyl, and $C(=O)R^{3c}$;

A is selected from:

C_{3-10} carbocyclic residue substituted with 0-2 R^4, and

5-12 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^4;

B is selected from: H, Y, and X-Y, provided that Z and B are attached to different atoms on A;

X is selected from $-(CR^2R^{2a})_{1-4}-$, $-CR^2(CR^2R^{2b})(CH_2)_t-$, $-C(O)-$, $-C(=NR^{1c})-$, $-CR^2(NR^{1c}R^2)-$, $-CR^2(OR^2)-$, $-CR^2(SR^2)-$, $-C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)$, $-S-$, $-S(O)-$, $-S(O)_2-$, $-SCR^2R^{2a}-$, $-S(O)CR^2R^{2a}-$, $-S(O)_2CR^2R^{2a}-$, $-CR^2R^{2a}S-$, $-CR^2R^{2a}S(O)-$, $-CR^2R^{2a}S(O)_2-$, $-S(O)_2NR^2-$, $-NR^2S(O)_2-$, $-NR^2S(O)_2CR^2R^{2a}-$, $-CR^2R^{2a}S(O)_2NR^2-$, $-NR^2S(O)_2NR^2-$, $-C(O)NR^2-$, $-NR^2C(O)-$, $-C(O)NR^2CR^2R^{2a}-$, $-NR^2C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)NR^2-$, $-CR^2R^{2a}NR^2C(O)-$, $-NR^2C(O)O-$, $-OC(O)NR^2-$,

$-NR^2C(O)NR^2-$, $-NR^2-$, $-NR^2CR^2R^{2a}-$, $-CR^2R^{2a}NR^2-$, O, $-CR^2R^{2a}O-$, and $-OCR^2R^{2a}-$;

Y is selected from:

C_{3-10} carbocyclic residue substituted with 0-2 R^{4a}, and

5-12 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4a};

R^4, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, $(CH_2)_rF$, $(CH_2)_rCl$, $(CH_2)_rBr$, $(CH_2)_rI$, C_{1-4} alkyl, $(CH_2)_rCN$, $(CH_2)_rNO_2$, $(CH_2)_rNR^2R^{2a}$, $C(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $C(=NS(O)_2R^5)NR^2R^{2a}$, $NHC(=NR^2)NR^2R^{2a}$, $C(O)NHC(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, $NR^2SO_2-C_{1-4}$ alkyl, $NR^2SO_2R^5$, $S(O)_pR^5$, $(CF_2)_rCF_3$, $(CH_2)_r-CF_3$, NCH_2R^{1c}, OCH_2R^{1c}, SCH_2R^{1c}, $N(CH_2)_2(CH_2)_tR^{1b}$, $O(CH_2)_2(CH_2)_tR^{1b}$, $S(CH_2)_2(CH_2)_tR^{1b}$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5;

R^{4a}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, $(CF_2)_rCF_3$, $(CH_2)_r-CF_3$, $(CH_2)_r-F$, $(CH_2)_r-Br$, $(CH_2)_r-Cl$, C_{1-4} alkyl, $(CH_2)_rCN$, $(CH_2)_rNO_2$, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $(CH_2)_rN=CHOR^3$, $C(O)NH(CH_2)_2NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $NHC(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, $NR^2SO_2-C_{1-4}$ alkyl, $NR^2SO_2R^5$, $C(O)NHSO_2-C_{1-4}$ alkyl, $S(O)_pR^5$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5;

R^{4b}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^3$, $(CH_2)_r$-F, $(CH_2)_r$-Cl, $(CH_2)_r$-Br, $(CH_2)_r$-I, C_{1-4} alkyl, $(CH_2)_r$-CN, $(CH_2)_r$-NO_2, $(CH_2)_rNR^3R^{3a}$, $(CH_2)_rC(O)R^3$, $(CH_2)_rC(O)OR^{3c}$, $NR^3C(O)R^{3a}$, $C(O)NR^3R^{3a}$, $NR^3C(O)NR^3R^{3a}$, $C(=NR^3)NR^3R^{3a}$, $NR^3C(=NR^3)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, $NR^3SO_2NR^3R^{3a}$, NR^3SO_2-C_{1-4} alkyl, $NR^3SO_2CF_3$, NR^3SO_2-phenyl, $S(O)_pCF_3$, $S(O)_p$-C_{1-4} alkyl, $S(O)_p$-phenyl, $(CH_2)_rCF_3$, and $(CF_2)_rCF_3$;

R^5, at each occurrence, is selected from H, C_{1-6} alkyl, =O, $(CH_2)_rOR^3$, F, Cl, Br, I, -CN, NO_2, $(CH_2)_rNR^3R^{3a}$, $(CH_2)_rC(O)R^3$, $(CH_2)_rC(O)OR^{3c}$, $NR^3C(O)R^{3a}$, $C(O)NR^3R^{3a}$, $NR^3C(O)NR^3R^{3a}$, $CH(=NOR^{3d})$, $C(=NR^3)NR^3R^{3a}$, $NR^3C(=NR^3)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, $NR^3SO_2NR^3R^{3a}$, NR^3SO_2-C_{1-4} alkyl, $NR^3SO_2CF_3$, NR^3SO_2-phenyl, $S(O)_pCF_3$, $S(O)_p$-C_{1-4} alkyl, $S(O)_p$-phenyl, $(CF_2)_rCF_3$, phenyl substituted with 0-2 R^6, naphthyl substituted with 0-2 R^6, and benzyl substituted with 0-2 R^6;

R^6, at each occurrence, is selected from H, OH, $(CH_2)_rOR^2$, halo, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2b}$, $NR^2C(O)R^{2b}$, $NR^2C(O)NR^2R^{2a}$, $C(=NH)NH_2$, $NHC(=NH)NH_2$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, and $NR^2SO_2C_{1-4}$ alkyl;

R^7, at each occurrence, is selected from H, OH, C_{1-4} alkoxycarbonyl, C_{6-10} aryloxy, C_{6-10} aryloxycarbonyl, C_{6-10} arylmethylcarbonyl, C_{1-4} alkylcarbonyloxy C_{1-4} alkoxycarbonyl, C_{6-10} arylcarbonyloxy C_{1-4} alkoxycarbonyl, C_{1-6} alkylaminocarbonyl, phenylaminocarbonyl, and phenyl C_{1-4} alkoxycarbonyl;

R^8, at each occurrence, is selected from H, C_{1-6} alkyl, and $(CH_2)_n$-phenyl;

alternatively, R^7 and R^8, when attached to the same nitrogen, combine to form a 5-6 membered heterocyclic ring consisting of carbon atoms and 0-2 additional heteroatoms selected from the group consisting of N, O, and $S(O)_p$;

R^9, at each occurrence, is selected from H, C_{1-6} alkyl, and $(CH_2)_n$-phenyl;

n, at each occurrence, is selected from 0, 1, 2, and 3;

m, at each occurrence, is selected from 0, 1, and 2;

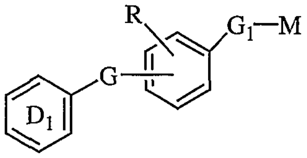
p, at each occurrence, is selected from 0, 1, and 2;

r, at each occurrence, is selected from 0, 1, 2, and 3;

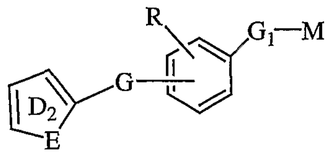
s, at each occurrence, is selected from 0, 1, and 2; and,

t, at each occurrence, is selected from 0, 1, 2, and 3.

2. A compound according to Claim 1, wherein the compound is of formula Ia_1-Ic_1, wherein:



Ia_1



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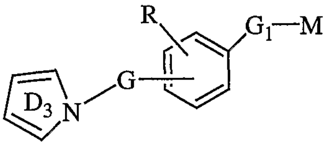


Ic_1

ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N-R^c and ring D_2 is substituted with 1 R^a and 0-1 R^b;

ring D_3 is a 5-membered heteroaromatic ring system comprising carbon atoms and from 0-3 additional N atoms and ring D_3 is substituted with 1 R^a and 0-1 R^b;

R is selected from H, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl$)_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl$)_2$;

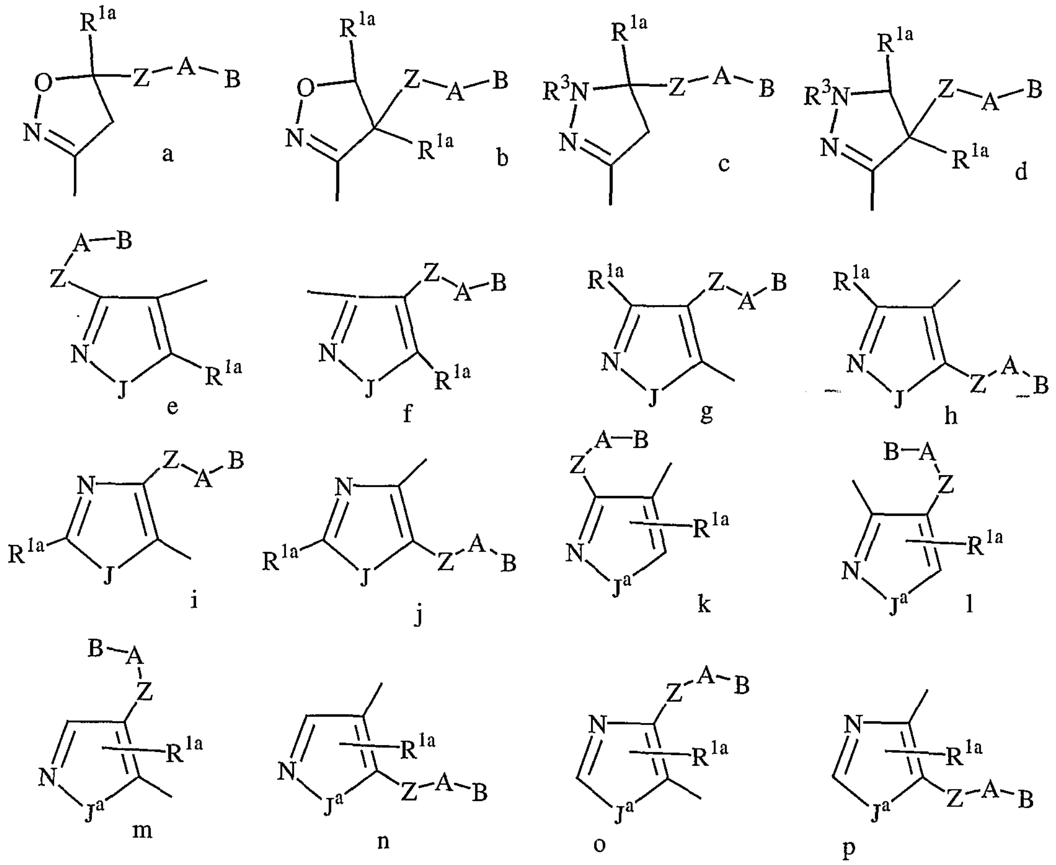
R^a is selected from H, OH, SH, C_{1-3} alkoxy, C_{1-3} thioalkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl$)_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl$)_2$;

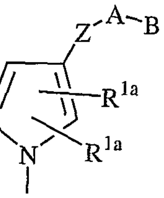
R^b is selected from H, C_{1-4} alkyl, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl$)_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl$)_2$;

R^c is selected from H, C_{1-4} alkyl, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl$)_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl$)_2$;

G_1 is absent or is selected from CH_2, C(O), O, NR^3, $S(O)_p$, CH_2CH_2, $C(O)CH_2$, $CH_2C(O)$, OCH_2, CH_2O, NR^3CH_2, CH_2NR^3, $S(O)_pCH_2$, $CH_2S(O)_p$, $CH_2CH_2CH_2$, $C(O)CH_2CH_2$, $CH_2C(O)CH_2$, $CH_2CH_2C(O)$, OCH_2CH_2, CH_2OCH_2, CH_2CH_2O, $NR^3CH_2CH_2$, $CH_2NR^3CH_2$, $CH_2CH_2NR^3$, $S(O)_pCH_2CH_2$, $CH_2S(O)_pCH_2$, and $CH_2CH_2S(O)_p$, and provided that G_1-M form other than a N-N, O-N, or S-N bond;

M is selected from the group:





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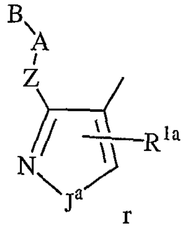

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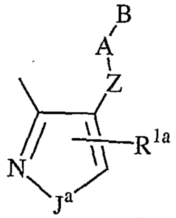

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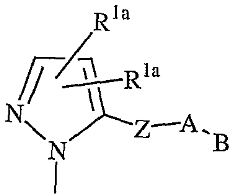

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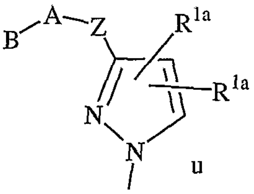

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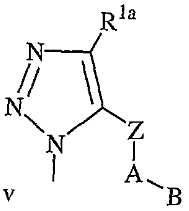

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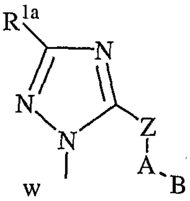

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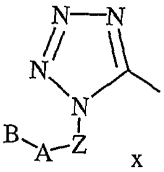

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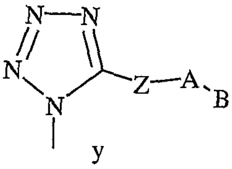

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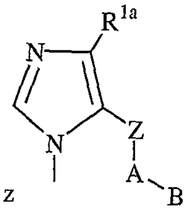

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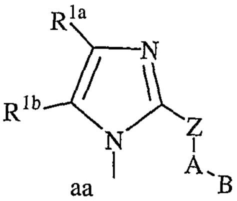

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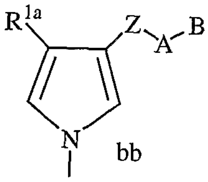

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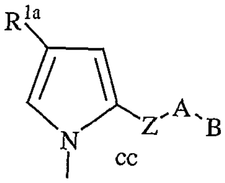

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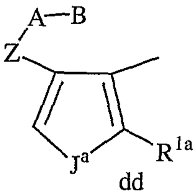

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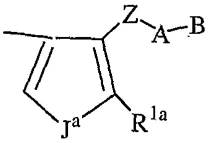

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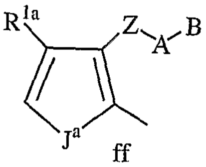

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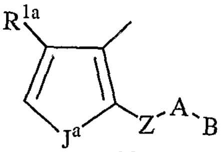

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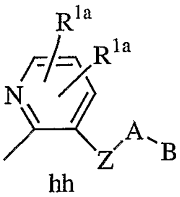
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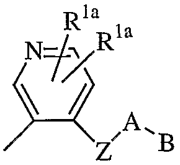
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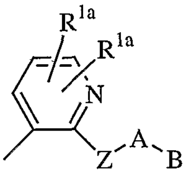
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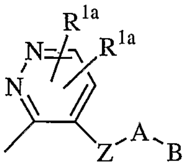
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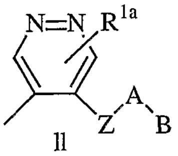
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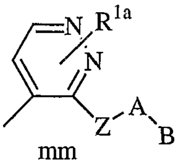
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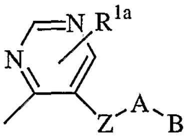
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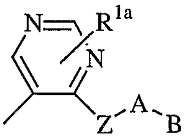
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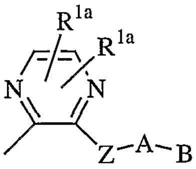
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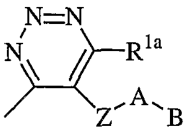
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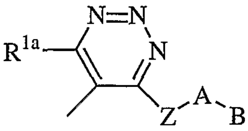
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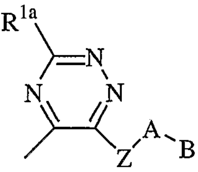
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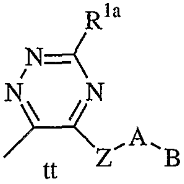
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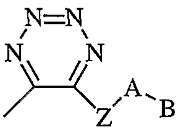
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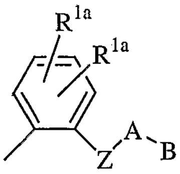
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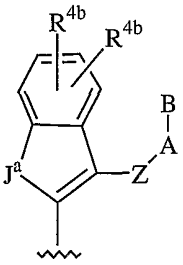
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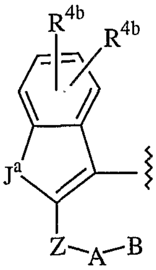
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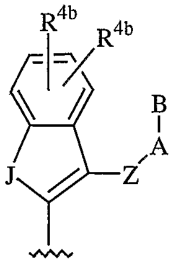
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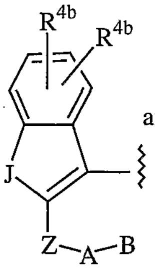
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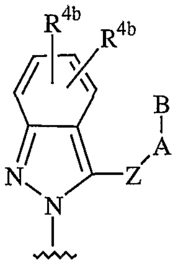
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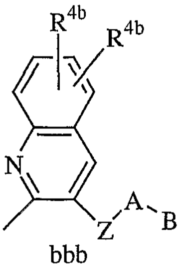
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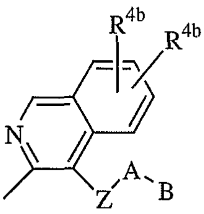
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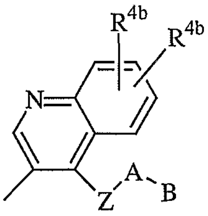
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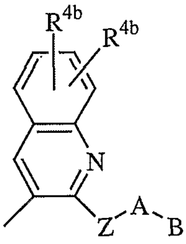
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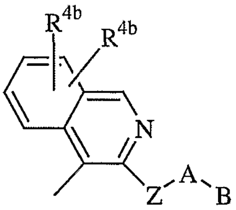
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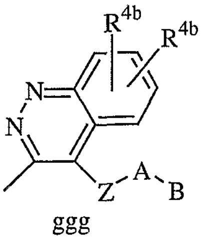
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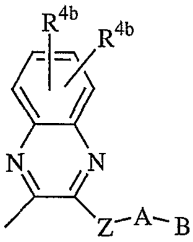
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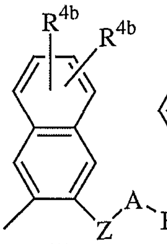
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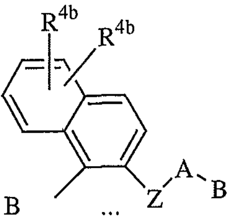
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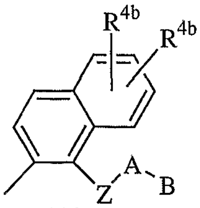

kkk

J is O or S;

J^a is NH or NR^{1a};

G_1 is absent or is selected from $(CR^3R^{3a})_{1-3}$, $(CR^3R^{3a})_uC(O)(CR^3R^{3a})_w$, $(CR^3R^{3a})_uO(CR^3R^{3a})_w$, $(CR^3R^{3a})_uNR^3(CR^3R^{3a})_w$, $(CR^3R^{3a})_uC(O)NR^3(CR^3R^{3a})_w$, $(CR^3R^{3a})_uNR^3C(O)(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(O)(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(O)_2(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(O)NR^3(CR^3R^{3a})_w$, and $(CR^3R^{3a})_uS(O)_2NR^3(CR^3R^{3a})_w$, wherein u + w total 0, 1, or 2, provided that G_1 does not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached;

A is selected from one of the following carbocyclic and heterocyclic systems which are substituted with 0-2 R^4;

phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, benzoxazolyl, benzthiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, and isoindazolyl;

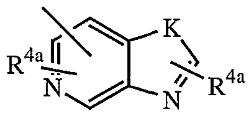
X is selected from $-(CR^2R^{2a})_{1-4}-$, $-C(O)-$, $-C(=NR^{1c})-$, $-CR^2(NR^{1c}R^2)-$, $-C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)$, $-C(O)NR^2-$, $-NR^2C(O)-$, $-C(O)NR^2CR^2R^{2a}-$, $-NR^2C(O)CR^2R^{2a}-$,

$-CR^2R^{2a}C(O)NR^2-$, $-CR^2R^{2a}NR^2C(O)-$, $-NR^2C(O)NR^2-$, $-NR^2-$, $-NR^2CR^2R^{2a}-$, $-CR^2R^{2a}NR^2-$, O, $-CR^2R^{2a}O-$, and $-OCR^2R^{2a}-$;

Y is selected from one of the following carbocyclic and heterocyclic systems that are substituted with 0-2 R^{4a};

cyclopropyl, cyclopentyl, cyclohexyl, phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, isoxazolinyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, benzoxazolyl, benzthiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, and isoindazolyl;

alternatively, Y is selected from the following bicyclic heteroaryl ring systems: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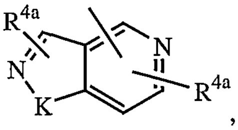
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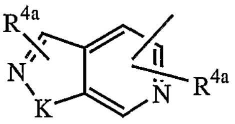
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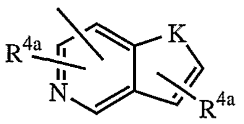
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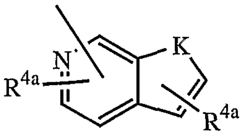
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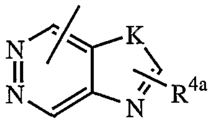
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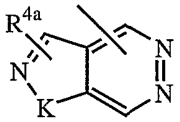
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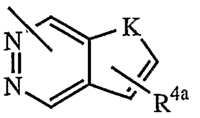

;

K is selected from O, S, NH, and N;

Z is selected from a bond, CH_2O, OCH_2, NH, CH_2NH, $NHCH_2$, $CH_2C(O)$, $C(O)CH_2$, $C(O)NH$, $NHC(O)$, $CH_2S(O)_2$, $S(O)_2(CH_2)$, SO_2NH, and $NHSO_2$, provided that Z does not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached;

R^4, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, F, Cl, Br, I, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $C(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, NR^2SO_2-C_{1-4} alkyl, $NR^2SO_2R^5$, $S(O)_pR^5$, CF_3, NCH_2R^{1c}, OCH_2R^{1c}, SCH_2R^{1c}, $N(CH_2)_2(CH_2)_tR^{1b}$, $O(CH_2)_2(CH_2)_tR^{1b}$, $S(CH_2)_2(CH_2)_tR^{1b}$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5; and,

R^{4a}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, CF_3, F, Br, Cl, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $NHC(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, NR^2SO_2-C_{1-4} alkyl, $NR^2SO_2R^5$, $C(O)NHSO_2$-C_{1-4} alkyl, $S(O)_pR^5$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5.

3. A compound according to Claim 2, wherein the compound is of formula Ib_1 or Ic_1, wherein:

ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N-R^c and ring D_2 is substituted with 1 R^a and 0-1 R^b;

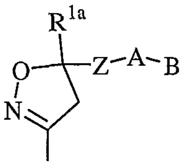
R is selected from H, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl$)_2$;

R^a is selected from H, OH, SH, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl$)_2$;

R^b is selected from H, C_{1-4} alkyl, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl$)_2$;

R^c is selected from H, C_{1-4} alkyl, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl$)_2$;

M is selected from the group:



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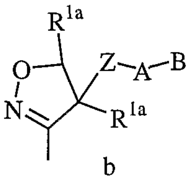

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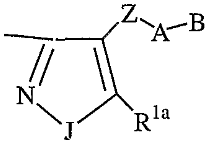

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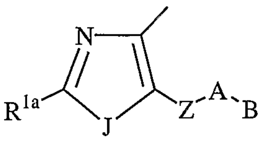

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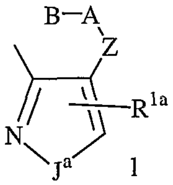

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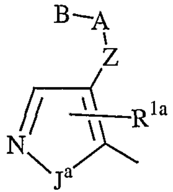

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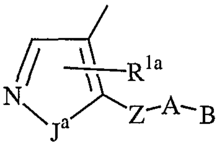

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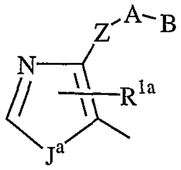

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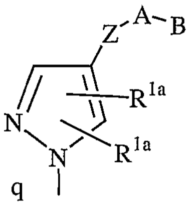

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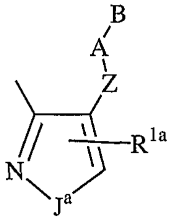

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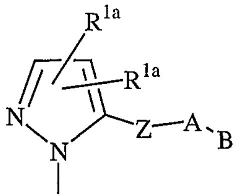

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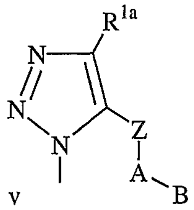

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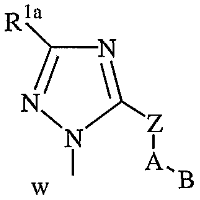

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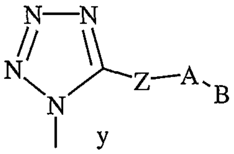

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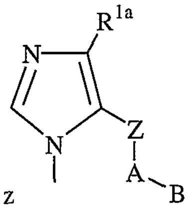

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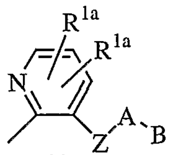

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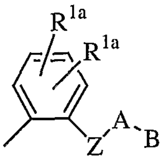
and



vv

Y is selected from one of the following carbocyclic and heterocyclic systems which are substituted with 0-2 R^{4a};

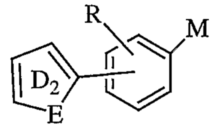
phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazole, thiadiazole, triazole, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole, 1,3,4-thiadiazole, 1,2,3-triazole, 1,2,4-triazole, 1,2,5-triazole, 1,3,4-triazole, benzofuran, benzothiofuran, indole, benzimidazole, benzimidazolone, benzoxazole, benzthiazole, indazole, benzisoxazole, benzisothiazole, and isoindazole;

Z is selected from a bond, CH_2O, OCH_2, NH, CH_2NH, $NHCH_2$, $CH_2C(O)$, $C(O)CH_2$, C(O)NH, NHC(O), $CH_2S(O)_2$, $S(O)_2(CH_2)$, SO_2NH, and $NHSO_2$, provided that Z does not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached;

R^4, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, F, Cl, Br, I, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $C(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, NR^2SO_2-C_{1-4} alkyl, $NR^2SO_2R^5$, $S(O)_pR^5$, CF_3, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5; and,

R^{4a}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, CF_3, F, Br, Cl, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $C(O)NHSO_2$-C_{1-4} alkyl, $S(O)_pR^5$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5.

4. A compound according to Claim 3, wherein the compound is of formula Ib_2:



Ib_2

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

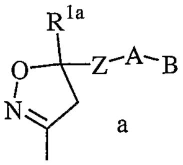
ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N-R^c and ring D_2 is substituted with 1 R^a and 0-1 R^b;

R is selected from H, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, NH(C_{1-3} alkyl), N(C_{1-3} alkyl)$_2$, CH_2NH_2, CH_2NH(C_{1-3} alkyl), and CH_2N(C_{1-3} alkyl)$_2$;

R^a is selected from H, OH, SH, NH_2, NH(C_{1-3} alkyl), and N(C_{1-3} alkyl)$_2$;

R^b is selected from H, C_{1-4} alkyl, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, NH(C_{1-3} alkyl), N(C_{1-3} alkyl)$_2$, CH_2NH_2, CH_2NH(C_{1-3} alkyl), and CH_2N(C_{1-3} alkyl)$_2$;

M is selected from the group: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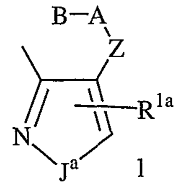
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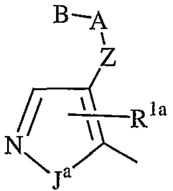
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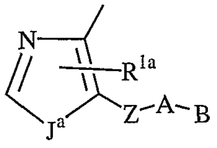
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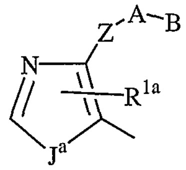
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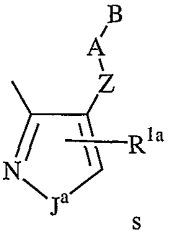
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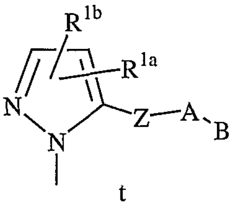
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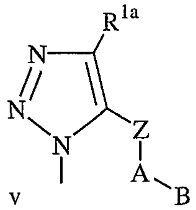
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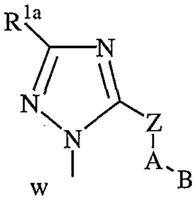
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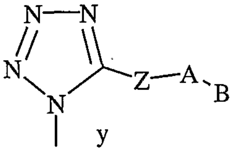
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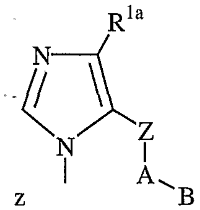
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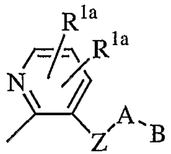
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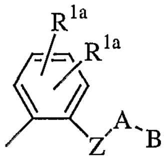
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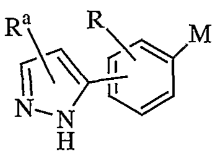
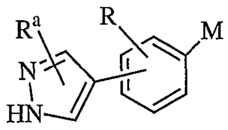
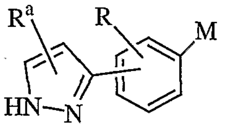
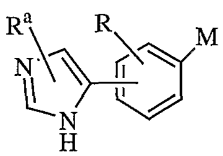
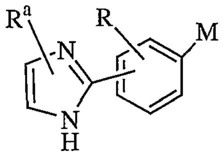
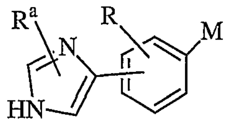
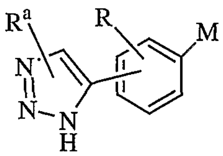
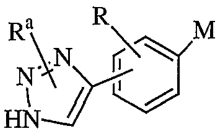
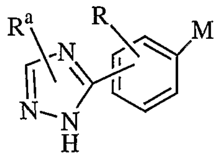
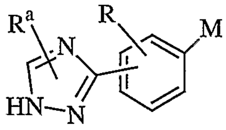
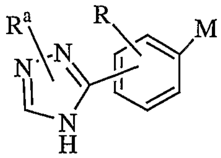
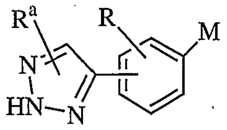
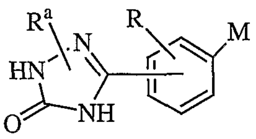
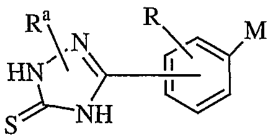
G_1 is absent or is selected from CH_2, CH_2CH_2, CH_2O, OCH_2, NH, CH_2NH, $NHCH_2$, $CH_2C(O)$, $C(O)CH_2$, C(O)NH, NHC(O), $CH_2S(O)_2$, $S(O)_2(CH_2)$, SO_2NH, and $NHSO_2$, provided that G_1 does not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached.

5. A compound according to Claim 4, wherein the compound is selected from one of the formulas:

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

G_1 is absent;

A is selected from phenyl, piperidinyl, pyridyl, and pyrimidyl, and is substituted with 0-2 R^4; and,

B is selected from phenyl, pyrrolidino, N-pyrrolidino-carbonyl, morpholino, N-morpholino-carbonyl, 1,2,3-triazolyl, imidazolyl, and benzimidazolyl, and is substituted with 0-1 R^{4a};

R^2, at each occurrence, is selected from H, CH_3, CH_2CH_3, cyclopropylmethyl, cyclobutyl, and cyclopentyl;

R^{2a}, at each occurrence, is selected from H, CH_3, and CH_2CH_3;

alternatively, R^2 and R^{2a}, together with the atom to which they are attached, combine to form pyrrolidine substituted with 0-2 R^{4b} or piperidine substituted with 0-2 R^{4b};

R^4, at each occurrence, is selected from OH, OR^2, $(CH_2)OR^2$, $(CH_2)_2OR^2$, F, Br, Cl, I, C_{1-4} alkyl, NR^2R^{2a}, $(CH_2)NR^2R^{2a}$, $(CH_2)_2NR^2R^{2a}$, CF_3, and $(CF_2)CF_3$;

R^{4a} is selected from C_{1-4} alkyl, CF_3, OR^2, $(CH_2)OR^2$, $(CH_2)_2OR^2$, NR^2R^{2a}, $(CH_2)NR^2R^{2a}$, $(CH_2)_2NR^2R^{2a}$, SR^5, $S(O)R^5$, $S(O)_2R^5$, $SO_2NR^2R^{2a}$, and 1-CF_3-tetrazol-2-yl;

R^{4b}, at each occurrence, is selected from H, CH_3, and OH;

R^5, at each occurrence, is selected from CF_3, C_{1-6} alkyl, phenyl, and benzyl; and,

r, at each occurrence, is selected from 0, 1, and 2.

6. A compound according to Claim 5, wherein:

A is selected from the group: phenyl, piperidinyl, 2-pyridyl, 3-pyridyl, 2-pyrimidyl, 2-Cl-phenyl, 3-Cl-phenyl, 2-F-phenyl, 3-F-phenyl, 2-methylphenyl, 2-aminophenyl, and 2-methoxyphenyl; and,

B is selected from the group: 2-(aminosulfonyl)phenyl, 2-(methylaminosulfonyl)phenyl, 1-pyrrolidinocarbonyl, 2-(methylsulfonyl)phenyl, 2-(N,N-dimethylaminomethyl)phenyl, 2-(N-methylaminomethyl)phenyl, 2-(N-ethyl-N-methylaminomethyl)phenyl, 2-(N-pyrrolidinylmethyl)phenyl, 1-methyl-2-imidazolyl, 2-methyl-1-imidazolyl, 2-(dimethylaminomethyl)-1-imidazolyl, 2-(methylaminomethyl)-1-imidazolyl, 2-(N-(cyclopropylmethyl)aminomethyl)phenyl, 2-(N-(cyclobutyl)aminomethyl)phenyl, 2-(N-(cyclopentyl)aminomethyl)phenyl, 2-(N-(4-hydroxypiperidinyl)methyl)phenyl, and 2-(N-(3-hydroxypyrrolidinyl)methyl)phenyl.

7. A compound according to Claim 1, wherein the compound is selected from the group:

1-[3-(1′,3′,4′-Triazol-2′-on-5′-yl)phenyl]-3-trifluoromethyl-5-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(1′,3′,4′-Triazol-2′-on-5′-yl)phenyl]-3-trifluoromethyl-5-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(1′,3′,4′-Triazol-2′-on-5′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(1′,3′,4′-Triazol-2′-on-5′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(1′,3′,4′-Triazol-2′-on-5′-yl)phenyl]-3-trifluoromethyl-5-[(2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(1′,3′,4′-Triazol-2′-on-5′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(2′-Amino-1′,3′,4′-triazol-5′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(2′-Amino-1′,3′,4′-triazol-5′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(2′-Amino-1′,3′,4′-triazol-5′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(2′-Amino-3′,4′-thiadiazol-5′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(2′-Amino-3′,4′-thiadiazol-5′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(2′-Amino-3′,4′-thiadiazol-5′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(1′,3′,4′-Triazol-2′-on-5′-yl)phenyl]-3-trifluoromethyl-5-[4-(2′-(N,N-dimethylamino)methylimidazol-1′-yl)-2-fluorophenyl)aminocarbonyl]pyrazole;

1-[3-(1′,3′,4′-Triazol-2′-on-5′-yl)phenyl]-3-trifluoromethyl-5-[4-(2′-methylimidazol-1′-yl)-2-fluorophenyl)aminocarbonyl]pyrazole;

1-[3-(Pyrid-3′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(Pyrid-3′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(Pyrid-3′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(Pyrid-4′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(Pyrid-4′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(Pyrid-4′-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(5-Amino-1,3,4-oxadiazol-2-yl)phenyl]-N-{2′-[(dimethylamino)methyl]-3-fluoro-1,1′-biphenyl-4-yl}-3-(trifluoromethyl)-1H-pyrazole-5-carboxamide;

1-[3-(5-Amino-1,3,4-oxadiazol-2-yl)phenyl]-N-(3-fluoro-2′-{[(3S)-3-hydroxy-1-pyrrolidinyl]methyl}-1,1′-biphenyl-

4-yl)-3-(trifluoromethyl)-1H-pyrazole-5-carboxamide; and,

1-[3-(5-Amino-1,3,4-oxadiazol-2-yl)phenyl]-N-(3-fluoro-2'-{[(3S)-3-hydroxy-1-pyrrolidinyl]methyl}-1,1'-biphenyl-4-yl)-5-(trifluoromethyl)-1H-pyrazole-3-carboxamide;

or a pharmaceutically acceptable salt thereof.

8. A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 1, 2, 3, 4, 5, 6, or 7 or a pharmaceutically acceptable salt form thereof.

9. A method for treating or preventing a thromboembolic disorder, comprising: administering to a patient in need thereof a therapeutically effective amount of a compound of Claim 1, 2, 3, 4, 5, 6, or 7 or a pharmaceutically acceptable salt form thereof.

10. A compound of Claim 1, 2, 3, 4, 5, 6, or 7 for use in therapy.

11. Use of a compound of Claim 1, 2, 3, 4, 5, 6, or 7 for the manufacture of a medicament for the treatment of a thromboembolic disorder.

INTERNATIONAL SEARCH REPORT

In tional Application No
PCT/US 01/20112

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D403/10 C07D417/10 C07D403/14 C07D417/14 C07D401/10
C07D413/10 C07D413/14 A61K31/41 A61K31/44 A61P7/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 28269 A (DUPONT MERCK) 2 July 1998 (1998-07-02) page 1, line 1 -page 3, line 33; claims; examples ---	1,8-11
X	US 6 020 357 A (PINTO ET. AL.) 1 February 2000 (2000-02-01) column 1, line 1 -column 2, line 65; claims; examples ---	1,8-11
P,X	WO 00 59902 A (DU PONT) 12 October 2000 (2000-10-12) page 78, line 1 - line 27; claims; examples ---	1,8-11
P,X	WO 00 53264 A (DU PONT) 14 September 2000 (2000-09-14) page 4, line 10 -page 5, line 25; claims --- -/--	1,8-11

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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"&" document member of the same patent family

Date of the actual completion of the international search 15 November 2001	Date of mailing of the international search report 22/11/2001
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Helps, I

INTERNATIONAL SEARCH REPORT

In tional Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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A	US 5 939 418 A (QUAN ET. AL.) 17 August 1999 (1999-08-17) claims; examples ---	1-11
A	DE 198 19 548 A (MERCK PATENT GMBH) 4 November 1999 (1999-11-04) page 2, line 44 - line 69; claims; examples -----	1-11

INTERNATIONAL SEARCH REPORT

Information on patent family members

Ir itional Application No

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