NOVEL TRICYCLIC COMPOUNDS

CROSS REFERENCE TO RELATED APPLICATION

This application claims priority to U.S. Provisional Application Serial No. 61/265,563 filed on December 1, 2009, and U.S. Provisional Application Serial No. 61/364,116 filed July 14, 2010, the contents of which are incorporated herein.

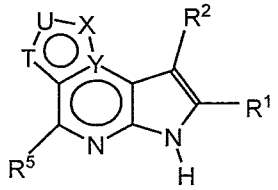
BACKGROUND OF THE INVENTION

The invention provides a novel class of compounds, pharmaceutical compositions comprising such compounds and methods of using such compounds to treat or prevent diseases or disorders associated with abnormal or deregulated kinase activity, particularly diseases or disorders that involve abnormal activation of the Jak1, Jak2, Jak3, Tyk2, KDR, Flt-3, CDK2, CDK4, TANK, Trk, FAK, Abl, Bcr-Abl, cMet, b-RAF, FGFR3, c-kit, PDGF-R, Syk, BTK, CSF1R, PKC kinases or Aurora kinases.

The protein kinases represent a large family of proteins that play a central role in the regulation of a wide variety of cellular processes and maintenance of cellular function. A partial, non-limiting, list of these kinases include: non-receptor tyrosine kinases such as the Janus kinase family (Jak1, Jak2, Jak3 and Tyk2); the fusion kinases, such as BCR-Abl, focal adhesion kinase (FAK), Fes, Lck and Syk; receptor tyrosine kinases such as platelet-derived growth factor receptor kinase (PDGF-R), the receptor kinase for stem cell factor, c-kit, the hepatocyte growth factor receptor, c-Met, and the fibroblast growth factor receptor, FGFR3; and serine/threonine kinases such as b-RAF, mitogen-activated protein kinases (e.g., MKK6) and SAPK2β. Aberrant kinase activity has been observed in many disease states including benign and malignant proliferative disorders as well as diseases resulting from inappropriate activation of the immune and nervous systems. The novel compounds of this invention inhibit the activity of one or more protein kinases and are, therefore, expected to be useful in the treatment of kinase-mediated diseases.

SUMMARY

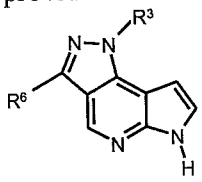
In a first embodiment the disclosure provides a compound of Formula (I)



Formula (I)

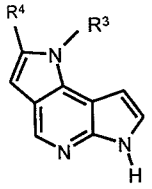
,

provided that when the compound is



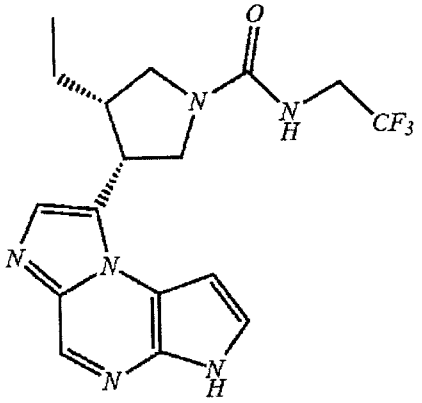
R^3 is defined as above and R^6 is not linked to the pyrazole ring by a nitrogen or oxygen atom; and

provided that when the compound is



when R^3 is H, CH_3 or –C(O)OH then R^4 is not H, -C(O)OCH_2CH_3, -C(O)NH-optionally substituted phenyl, -NHC(O)-optionally substituted phenyl or –$S(O)_2$-phenyl.

In one aspect, there is provided a compound represented by the following structure:



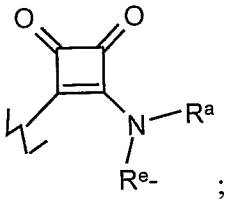
or a pharmaceutically acceptable salt thereof.

In a second embodiment the disclosure provides a compound according to the first embodiment wherein R^3 is -A-D-E-G and A is a bond, optionally substituted (C_1-C_6)alkylene, optionally substituted (C_3-C_{12})cycloalkylene or optionally substituted (C_2-C_6)heterocyclylene.

In a third embodiment the disclosure provides a compound according to the any of the foregoing embodiments wherein R^3 is -A-D-E-G and D is an optionally substituted (C_1-C_8)alkylene, optionally substituted (C_3-C_{10})cycloalkylene, optionally substituted bridged (C_5-C_{10})cycloalkenylene, optionally substituted (C_3-C_{10})bridged heterocyclylene or optionally substituted (C_2-C_{10})heterocyclylene.

In a fourth embodiment the disclosure provides a compound according to the any of the foregoing embodiments 3 wherein D is optionally substituted (C_1-C_6)alkylene, optionally substituted (C_3-C_6)cycloalkylene, optionally substituted bicyclo[2.2.2]octany-1-yl, optionally substituted 2,5-diazabicyclo[2.2.1]heptane, optionally substituted 2,6-diazabicyclo[3.2.1]octane, optionally substituted octahydropyrrolo[3,4-*c*]pyrrole, optionally substituted octahydropyrrolo[3,2-*b*]pyridine, optionally substituted 1,4-diazepane, optionally substituted cubane, optionally substituted 1,4-dioxane-spiro[4.4]nonane, optionally substituted 2,5-diazaspiro[3.5]nonane, optionally substituted piperidine, optionally substituted piperazine, optionally substituted pyrrolidine, optionally substituted tetrahydrofuran or optionally substituted tetrahydropyran.

In a fifth embodiment the disclosure provides a compound according to the any of the foregoing embodiments wherein R^3 is -A-D-E-G and E is a bond, -R^e-, -R^e-C(O)-R^e-, -R^e-O-R^e-, -R^e-$S(O)_2$-R^e-, -R^e-N(R^a)-R^e-, =N-R^e-. -R^e-N(R^a)C(O)-R^e-, -R^e-N(R^a)C(O)O-R^e-, -R^e-N(R^a)C(O)N(R^b)-R^e-, -R^eC(O)N(R^a)R^e-, -R^e-N(R^a)$S(O)_2$-R^e-, -R^e-$S(O)_2$N(R^a)-R^e-, -R^e-



$N(R^a)S(O)_2N(R^a)$-R^e-, -R^e-OC(O)$N(R^a)$-R^e, -R^e-C(O)O-R^e, -R^e-OC(O)-R^e; or ;

wherein

R^a for each occurrence is independently hydrogen, CN, an optionally substituted (C_1-C_{10})alkyl or an optionally substituted -(C_1-C_6)alkylene-(C_3-C_{10})cycloalkyl; and

R^e for each occurrence is independently a bond, an optionally substituted (C_1-C_{10})alkylene, an optionally substituted (C_3-C_{10})cycloalkylene, an optionally substituted (C_6-C_{10})arylene, an optionally substituted (C_1-C_{10})heteroarylene, or an optionally substituted (C_1-C_{10})heterocyclylene.

In a sixth embodiment the disclosure provides a compound according to the any of the foregoing embodiments wherein R^3 is -A-D-E-G and G is hydrogen, deuterium, -$N(R^a)(R^b)$, halogen, -OR^a, -$S(O)_2R^a$, -CN, -C(O)$N(R^a)(R^b)$, -$N(R^a)$C(O)R^b, -CF_3, -$S(O)_2N(R^a)(R^b)$, an optionally substituted -(C_1-C_6)alkyl, an optionally substituted -(C_3-C_{10})cycloalkyl, an optionally substituted -(C_1-C_{10})heteroaryl, an optionally substituted -(C_1-C_{10}) heterocyclyl, or an optionally substituted -(C_6-C_{10})aryl;

wherein in a moiety containing -$N(R^a)(R^b)$, the nitrogen, R^a and R^b may form a ring such that -$N(R^a)(R^b)$ represents an optionally substituted (C_2-C_{10})heterocyclyl or an optionally substituted (C_1-C_{10}) heteroaryl linked through a nitrogen;

R^a is independently hydrogen, CN, an optionally substituted (C_1-C_{10})alkyl, an optionally substituted (C_3-C_{10})cycloalkyl, or an optionally substituted (C_6-C_{10})aryl.

In a seventh embodiment the disclosure provides a compound according to the any of the foregoing embodiments wherein G is hydrogen, deuterium, -$N(R^a)(R^b)$, halogen, -OR^a, -$S(O)_2R^a$, -CN, -C(O)$N(R^a)(R^b)$, -$N(R^a)$C(O)R^b, -CF_3, -$S(O)_2N(R^a)(R^b)$, an optionally substituted -(C_1-C_4)alkyl, an optionally substituted -(C_3-C_6)cycloalkyl, optionally substituted azepanyl, optionally substituted azetidinyl, optionally substituted benzo[d]isoxazolyl, optionally substituted 4,5-dihydroisoxazolyl, optionally substituted isothiazolidinyl, optionally substituted isothiazolyl, optionally substituted isoxazolyl, optionally substituted morpholinyl, optionally substituted oxadiazolyl, optionally substituted oxazolyl, optionally substituted oxetanyl, optionally substitute phenyl, optionally substituted piperazinyl, optionally substituted piperidinyl, optionally substituted pyrazinyl, optionally substituted pyrazolyl, optionally substituted pyridazinyl, optionally substituted pyridinyl, optionally substituted pyrimidinyl, optionally substituted pyrrolidinyl, optionally substituted pyrrolyl, optionally substituted tetrahydrofuranyl, optionally substituted tetrahydropyranyl, optionally substituted tetrahydrothiopyranyl, optionally substituted

thienyl, optionally substituted thiomorpholinyl, optionally substituted 1,1-dioxo-thiomorpholinyl, optionally substituted thiazolyl or optionally substituted triazolyl.

In eighth embodiment the disclosure provides a compound according to the any of the foregoing embodiments wherein R^3 is hydrogen, optionally substituted $(C_1\text{-}C_8)$alkyl, optionally substituted $(C_3\text{-}C_{10})$cycloalkyl, or optionally substituted $(C_2\text{-}C_{10})$heterocyclyl.

In a ninth embodiment the disclosure provides a compound according to the any of the foregoing embodiments wherein R^6 is –J-L-M-Q and J is a bond, optionally substituted $(C_1\text{-}C_6)$alkylene, or an optionally substituted $(C_2\text{-}C_6)$alkenylene.

In a tenth embodiment the disclosure provides a compound according to the any of the foregoing embodiments wherein R^6 is –J-L-M-Q and L is a bond, or an optionally substituted $(C_1\text{-}C_8)$alkylene.

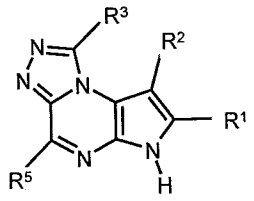
In an eleventh embodiment the disclosure provides a compound according to the any of the foregoing embodiments wherein R^6 is –J-L-M-Q and M is a bond, $-R^e-$, $-R^e\text{-}C(O)\text{-}R^e-$, $-R^e\text{-}O\text{-}R^e-$, $-R^e\text{-}S(O)_2\text{-}R^e-$, $-R^e\text{-}S(O)\text{-}R^e-$, $-R^e\text{-}S\text{-}R^e-$, $-R^e\text{-}N(R^a)\text{-}R^e-$, $-R^e\text{-}N(R^a)C(O)\text{-}R^e-$, $-R^e\text{-}C(O)N(R^a)R^e-$, $-R^e\text{-}N(R^a)C(O)N(R^b)\text{-}R^e-$, $-R^e\text{-}N(R^a)S(O)_2\text{-}R^e-$, or $-R^e\text{-}S(O)_2N(R^a)\text{-}R^e-$; where in all cases, M is linked to either a carbon or a nitrogen atom in L.

In a twelfth embodiment the disclosure provides a compound according to the any of the foregoing embodiments wherein R^6 is –J-L-M-Q and Q is hydrogen, deuterium, $-N(R^a)(R^b)$, halogen, $-OR^a$, $-SR^a$, $-S(O)R^a$, $-S(O)_2R^a$, $-NO_2$, $-C(O)OR^a$, $-CN$, $-C(O)N(R^a)(R^b)$, $-N(R^a)C(O)R^b$, $-N(R^a)C(O)OR^b$, $-N(R^a)C(O)N(R^b)_2$, $-C(O\text{-}R^a)(R^b)_2$, $-C(O)R^a$, $-CF_3$, $-OCF_3$, $-N(R^a)S(O)_2R^b$, $-S(O)_2N(R^a)(R^b)$, $-S(O)_2N(R^a)C(O)R^b$, an optionally substituted $(C_1\text{-}C_6)$alkyl, an optionally substituted $(C_3\text{-}C_{10})$cycloalkyl, an optionally substituted $(C_1\text{-}C_{10})$heteroaryl, an optionally substituted $(C_1\text{-}C_{10})$ heterocyclyl, an optionally substituted $(C_6\text{-}C_{10})$aryl;

wherein in a moiety containing $-N(R^a)(R^b)$, the nitrogen, R^a and R^b may form a ring such that $-N(R^a)(R^b)$ represents an optionally substituted $(C_2\text{-}C_{10})$heterocyclyl or an optionally substituted $(C_1\text{-}C_{10})$ heteroaryl linked through a nitrogen;

R^a and R^b are each independently hydrogen, deuterium, an optionally substituted $(C_1\text{-}C_6)$alkyl, an optionally substituted $(C_2\text{-}C_{10})$alkenyl, an optionally substituted $(C_3\text{-}C_6)$cycloalkyl, an optionally substituted $(C_6\text{-}C_{10})$aryl, an optionally substituted $(C_1\text{-}C_{10})$heteroaryl, or an optionally substituted $(C_1\text{-}C_{10})$heterocyclyl.

In a thirteenth embodiment the disclosure provides a compound according to the any of the foregoing embodiments wherein T is N, U is N, X is CR^3 and Y is N and forms a compound of Formula (Ia)



Formula (Ia)

In a fourteenth embodiment the disclosure provides a compound according to the thirteenth embodiment wherein in the compound is

N-(1-((6*H*-pyrrolo[2,3-*e*][1,2,4]triazolo[4,3-*a*]pyrazin-1-yl)methyl)cyclobutyl)cyclopropanesulfonamide;

N-(1-((6*H*-pyrrolo[2,3-*e*][1,2,4]triazolo[4,3-*a*]pyrazin-1-yl)methyl)cyclobutyl)-2-cyanoacetamide;

(*S*)-1-((1-(cyclopropylsulfonyl)pyrrolidin-3-yl)methyl)-6*H*-pyrrolo[2,3-*e*][1,2,4]triazolo[4,3-*a*]pyrazine;

N-((1*S*,3*R*,4*R*)-4-ethyl-3-fluoro-3-(6*H*-pyrrolo[2,3-*e*][1,2,4]triazolo[4,3-*a*]pyrazin-1-yl)cyclopentyl)cyclopropanesulfonamide;

N-((1*R*,3*S*,4*S*)-4-ethyl-3-fluoro-3-(6*H*-pyrrolo[2,3-*e*][1,2,4]triazolo[4,3-*a*]pyrazin-1-yl)cyclopentyl)cyclopropanesulfonamide;

N-((1*R*,3*R*,4*S*)-4-ethyl-3-fluoro-3-(6*H*-pyrrolo[2,3-*e*][1,2,4]triazolo[4,3-*a*]pyrazin-1-yl)cyclopentyl)cyclopropanesulfonamide;

N-((1*S*,3*S*,4*R*)-4-ethyl-3-fluoro-3-(6*H*-pyrrolo[2,3-*e*][1,2,4]triazolo[4,3-*a*]pyrazin-1-yl)cyclopentyl)cyclopropanesulfonamide;

(1*S*,3*R*)-1-[3-(6*H*-pyrrolo[2,3-*e*][1,2,4]triazolo[4,3-*a*]pyrazin-1-yl)-isothiazolidin-2-yl-1,1-dioxide]cyclopentane;

N-((1*S*,3*R*,4*S*)-3-ethyl-4-(6*H*-pyrrolo[2,3-*e*][1,2,4]triazolo[4,3-*a*]pyrazin-1-yl)cyclopentyl)-*N*-methylcyclopropanesulfonamide;

1-((1*S*,2*R*,4*S*)-2-ethyl-4-(4-methoxybenzyloxy)cyclopentyl)-6*H*-pyrrolo[2,3-*e*][1,2,4]triazolo[4,3-*a*]pyrazine;

(*S*)-5-(3-((6*H*-pyrrolo[2,3-*e*][1,2,4]triazolo[4,3-*a*]pyrazin-1-yl)methyl)pyrrolidin-1-yl)pyrazine-2-carbonitrile;

N-(cyclopropylmethyl)-*N*-((1*S*,3*R*,4*S*)-3-ethyl-4-(6*H*-pyrrolo[2,3-*e*][1,2,4]triazolo[4,3-*a*]pyrazin-1-yl)cyclopentyl)cyclopropanesulfonamide;

N-((1*S*,3*R*)-3-(6*H*-pyrrolo[2,3-*e*][1,2,4]triazolo[4,3-*a*]pyrazin-1-yl)cyclopentyl)-2-(4-cyanophenyl)acetamide;

N-((1*S*,3*R*)-3-(6*H*-pyrrolo[2,3-*e*][1,2,4]triazolo[4,3-*a*]pyrazin-1-yl)cyclopentyl)cyclopropanecarboxamide;

[(1*S*,3*R*,4*S*)-3-Ethyl-4-(6H-pyrrolo[2,3-e][1,2,4]triazolo[4,3-a]pyrazin-1-yl)-cyclopentyl]-(5-methyl-isoxazol-3-ylmethyl)-oxetan-3-yl-amine;

{5-[(1*S*,3*R*,4*S*)-3-Ethyl-4-(6H-pyrrolo[2,3-e][1,2,4]triazolo[4,3-a]pyrazin-1-yl)-cyclopentylmethyl]-[1,2,4]oxadiazol-3-yl}-methanol;

1-[(1*S*,2*R*,4*S*)-4-(3-Cyclopropyl-pyrazol-1-yl)-2-ethyl-cyclopentyl]-6H-pyrrolo[2,3-e][1,2,4]triazolo[4,3-a]pyrazin-1-yl;

1-[(1*S*,2*R*,4*S*)-4-(5-Cyclopropyl-pyrazol-1-yl)-2-ethyl-cyclopentyl]-6H-pyrrolo[2,3-e][1,2,4]triazolo[4,3-a]pyrazin-1-yl;

(3*S*,4*R*)-3-Ethyl-4-(6H-pyrrolo[2,3-e][1,2,4]triazolo[4,3-a]pyrazin-1-yl)-pyrrolidine-1-sulfonic acid (2,2,2-trifluoro-ethyl)-amide;

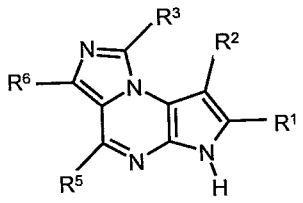
(3*R*,4*S*)-3-Ethyl-4-(6H-pyrrolo[2,3-e][1,2,4]triazolo[4,3-a]pyrazin-1-yl)-pyrrolidine-1-sulfonic acid (2,2,2-trifluoro-ethyl)-amide;

1-[(1*S*,2*R*,4*S*)-4-(3-Cyclopropyl-[1,2,4]triazol-1-yl)-2-ethyl-cyclopentyl]-6H-pyrrolo[2,3-e][1,2,4]triazolo[4,3-a]pyrazin-1-yl;

1-[(1*S*,2*R*,4*S*)-4-(5-Cyclopropyl-[1,2,4]triazol-1-yl)-2-ethyl-cyclopentyl]-6H-pyrrolo[2,3-e][1,2,4]triazolo[4,3-a]pyrazin-1-yl; or

[(1*S*,3*R*,4*S*)-3-Ethyl-4-(6H-pyrrolo[2,3-e][1,2,4]triazolo[4,3-a]pyrazin-1-yl)-cyclopentyl]-oxetan-3-yl-(3,3,3-trifluoro-propyl)-amine.

In a fifteenth embodiment the disclosure provides a compound according to the first through twelfth embodiments wherein T is CR^6, U is N, X is CR^3 and Y is N and forms a compound of Formula (Ib)



Formula (Ib)

In a sixteenth embodiment the disclosure provides a compound according to the fifteenth embodiment wherein the compound is

((cis)-3-(6*H*-imidazo[1,5-*a*]pyrrolo[2,3-*e*]pyrazin-1-yl)-4-methylpiperidin-1-yl)(2,4-difluorophenyl)methanone;

((cis)-3-(6*H*-imidazo[1,5-*a*]pyrrolo[2,3-*e*]pyrazin-1-yl)-4-methylpiperidin-1-yl)(4-(trifluoromethyl)phenyl)methanone;

((cis)-3-(6*H*-imidazo[1,5-*a*]pyrrolo[2,3-*e*]pyrazin-1-yl)-4-methylpiperidin-1-yl)(pyridin-3-yl)methanone;

1-((1*S*,2*R*,4*S*)-4-Cyclopropanesulfonylamino-2-ethyl-cyclopentyl)-6*H*-2,5,6,8b-tetraaza-as-indacene-3-carboxylic acid;

1-((1*R*,2*R*,4*S*)-4-Cyclopropanesulfonylamino-2-ethyl-cyclopentyl)-6*H*-2,5,6,8b-tetraaza-as-indacene-3-carboxylic acid;

Cyclopropanesulfonic acid [(1*S*,3*R*,4*S*)-3-methyl-4-(3-trifluoromethyl-6*H*-2,5,6,8b-tetraaza-as-indacen-1-yl)-cyclopentyl]-amide;

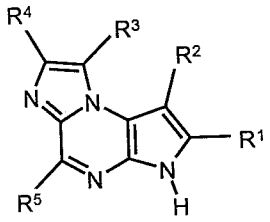
1-[(1*R*,3*R*,4*S*)-3-Ethyl-4-(3-trifluoromethyl-6*H*-2,5,6,8b-tetraaza-as-indacen-1-yl)-cyclopentyl]-2-methyl-propan-2-ol;

Cyclopropanesulfonic acid {(1*S*,3*R*,4*S*)-3-ethyl-4-[3-(2,2,2-trifluoro-ethyl)-6*H*-2,5,6,8b-tetraaza-as-indacen-1-yl]-cyclopentyl}-amide;

[(1*R*,3*R*,4*S*)-3-Ethyl-4-(3-trifluoromethyl-6*H*-2,5,6,8b-tetraaza-as-indacen-1-yl)-cyclopentyl]-acetic acid ethyl ester or

1-[(1*S*,2*R*,4*R*)-2-Ethyl-4-(3-methoxymethyl-[1,2,4]oxadiazol-5-ylmethyl)-cyclopentyl]-3-trifluoromethyl-6*H*-2,5,6,8b-tetraaza-as-indacene.

In a seventeenth embodiment the disclosure provides a compound according to the first through twelfth embodiments wherein T is N, U is CR^4, X is CR^3 and Y is N and forms a compound of Formula (Ic)



Formula (Ic) .

In an eighteenth embodiment the disclosure provides a compound according to the seventeeth embodiment wherein the compound is

3-((3*S*,4*S*)-3-(3*H*-imidazo[1,2-*a*]pyrrolo[2,3-*e*]pyrazin-8-yl)-4-methylpiperidin-1-yl)-3-oxopropanenitrile;

5-(3-(3*H*-imidazo[1,2-*a*]pyrrolo[2,3-*e*]pyrazin-8-yl)piperidin-1-yl)pyrazine-2-carbonitrile;

(*S*)-1-(3-(3*H*-imidazo[1,2-*a*]pyrrolo[2,3-*e*]pyrazin-8-yl)piperidine-1-carbonyl)cyclopropanecarbonitrile;

N-((1*S*,3*R*,4*R*)-3-ethyl-4-(3*H*-imidazo[1,2-*a*]pyrrolo[2,3-*e*]pyrazin-8-yl)cyclopentyl)cyclopropanesulfonamide;

N-((1*R*,3*S*,4*S*)-3-ethyl-4-(3*H*-imidazo[1,2-*a*]pyrrolo[2,3-*e*]pyrazin-8-yl)cyclopentyl)cyclopropanesulfonamide;

Azetidine-1-sulfonic acid [(1*S*,3*R*,4*S*)-3-methyl-4-(3H-imidazo[1,2-a]pyrrolo[2,3-e]pyrazin-8-yl)-cyclopentyl]-amide;

{3-[(1*S*,3*R*,4*S*)-3-Methyl-4-(3H-imidazo[1,2-a]pyrrolo[2,3-e]pyrazin-8-yl)-cyclopentylamino]-oxetan-3-yl}-acetonitrile;

3,3-Difluoro-cyclobutanesulfonic acid [(1*S*,3*R*,4*S*)-3-methyl-4-(3H-imidazo[1,2-a]pyrrolo[2,3-e]pyrazin-8-yl)-cyclopentyl]-amide;

8-[(1*S*,2*R*,4*S*)-2-Methyl-4-(tetrahydro-pyran-4-yloxy)-cyclopentyl]-3*H*-3,4,6,8a-tetraaza-as-indacene;

8-[(1*R*,2*R*)-2-Methyl-4-(tetrahydro-pyran-4-yloxy)-cyclopentyl]-3*H*-3,4,6,8a-tetraaza-as-indacene;

3-Fluoro-azetidine-1-sulfonic acid [(1*S*,3*R*,4*S*)-3-methyl-4-(3H-imidazo[1,2-a]pyrrolo[2,3-e]pyrazin-8-yl)-cyclopentyl]-amide;

3-Fluoro-propane-1-sulfonic acid [(1*S*,3*R*,4*S*)-3-methyl-4-(3H-imidazo[1,2-a]pyrrolo[2,3-e]pyrazin-8-yl)-cyclopentyl]-amide;

Cyclopropanesulfonic acid [(1*S*,3*R*,4*S*)-3-methyl-4-(7-methyl-3H-imidazo[1,2-a]pyrrolo[2,3-e]pyrazin-8-yl)-cyclopentyl]-amide;

Cyclopropanesulfonic acid [(1*R*,3*S*,4*R*)-3-methyl-4-(7-methyl-3H-imidazo[1,2-a]pyrrolo[2,3-e]pyrazin-8-yl)-cyclopentyl]-amide;

2-Cyano-N-[(1*S*,3*R*,4*S*)-3-methyl-4-(3H-imidazo[1,2-a]pyrrolo[2,3-e]pyrazin-8-yl)-cyclopentyl]-acetamide;

8-[(1*S*,2*R*,4*R*)-2-Methyl-4-(tetrahydro-pyran-4-yloxy)-cyclopentyl]-3*H*-3,4,6,8a-tetraaza-as-indacene;

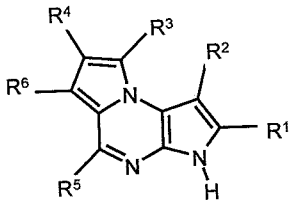
(2-Cyclopropyl-ethyl)-[(1*S*,3*R*,4*S*)-3-methyl-4-(3H-imidazo[1,2-a]pyrrolo[2,3-e]pyrazin-8-yl)-cyclopentyl]-oxetan-3-yl-amine;

Cyclopropylmethyl-[(1*S*,3*R*,4*S*)-3-methyl-4-(3H-imidazo[1,2-a]pyrrolo[2,3-e]pyrazin-8-yl)-cyclopentyl]-oxetan-3-yl-amine;

(3*R*,4*S*)-3-Ethyl-4-(3H-imidazo[1,2-a]pyrrolo[2,3-e]pyrazin-8-yl)-pyrrolidine-1-carboxylic acid (2,2,2-trifluoro-ethyl)-amide; or

(3*S*,4*R*)-3-Ethyl-4-(3H-imidazo[1,2-a]pyrrolo[2,3-e]pyrazin-8-yl)-pyrrolidine-1-carboxylic acid (2,2,2-trifluoro-ethyl)-amide.

In a nineteenth embodiment the disclosure provides a compound according to the first through twelfth embodiments wherein T is CR^6, U is CR^4, X is CR^3 and Y is N and forms a compound of Formula (Id)

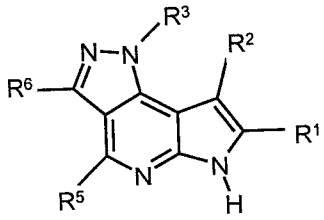


Formula (Id)

In a twentieth embodiment the disclosure provides a compound according to the nineteenth embodiment wherein the compound is

N-(4-(3*H*-dipyrrolo[1,2-*a*:2',3'-*e*]pyrazin-8-yl)bicyclo[2.2.2]octan-1-yl)cyclopropanesulfonamide.

In a twenty-first embodiment the disclosure provides a compound according to the first through twelfth embodiments wherein T is CR^6, U is N, X is NR^3 and Y is C and forms a compound of Formula (Ie)



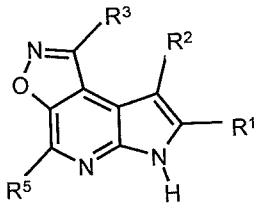
Formula (Ie)

In a twenty-second embodiment the disclosure provides a compound according to the twenty-first embodiment wherein the compound is

(*R*)-1-(3-(pyrazolo[3,4-*d*]pyrrolo[2,3-*b*]pyridin-1(6*H*)-yl)piperidine-1-carbonyl)cyclopropanecarbonitrile; or

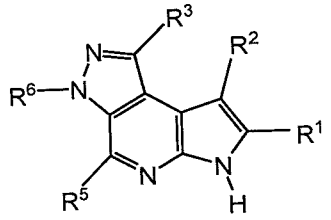
(*S*)-1-(3-(pyrazolo[3,4-*d*]pyrrolo[2,3-*b*]pyridin-1(6*H*)-yl)piperidine-1-carbonyl)cyclopropanecarbonitrile.

In a twenty-third embodiment the disclosure provides a compound according to the first through twelfth embodiments wherein T is O, U is N, X is CR^3 and Y is C and forms a compound of Formula (If)



Formula (If)

In a twenty-fourth embodiment the disclosure provides a compound according to the first through twelfth embodiments wherein T is NR^6, U is N, X is CR^3 and Y is C and forms a compound of Formula (Ig)



Formula (Ig)

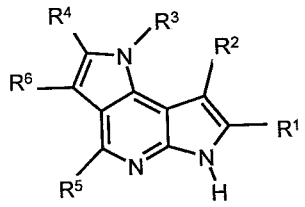
In a twenty-fifth embodiment the disclosure provides a compound according to the twenty-fourth embodiment wherein the compound is

1-((1*R*,2*R*,4*S*)-2-ethyl-4-(4-methoxybenzyloxy)cyclopentyl)-3,6-dihydropyrazolo[4,3-*d*]pyrrolo[2,3-*b*]pyridine;

1-((1*S*,2*S*,4*R*)-2-ethyl-4-(4-methoxybenzyloxy)cyclopentyl)-3,6-dihydropyrazolo[4,3-*d*]pyrrolo[2,3-*b*]pyridine; or

N-(4-(3,6-dihydropyrazolo[4,3-*d*]pyrrolo[2,3-*b*]pyridin-1-yl)bicyclo[2.2.2]octan-1-yl)cyclopropanesulfonamide.

In a twenty-sixth embodiment the disclosure provides a compound according to the first through twelfth embodiments wherein T is CR^6, U is CR^4, X is NR^3 and Y is C and forms a compound of Formula (Ih)



Formula (Ih)

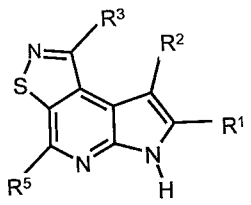
In a twenty-seventh embodiment the disclosure provides a compound according to the twenty-sixth embodiment wherein the compound is

1-cyclohexyl-1,6-dihydroimidazo[4,5-*d*]pyrrolo[2,3-*b*]pyridine;

1-cyclohexyl-2-methyl-1,6-dihydroimidazo[4,5-*d*]pyrrolo[2,3-*b*]pyridine; or

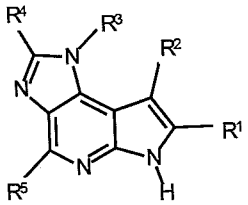
1-cyclohexyl-2-(trifluoromethyl)-1,6-dihydroimidazo[4,5-*d*]pyrrolo[2,3-*b*]pyridine.

In a twenty-eighth embodiment the disclosure provides a compound according to the first through twelfth embodiments wherein T is S, U is N, X is CR^3 and Y is C and forms a compound of Formula (Ii)



Formula (Ii)

In a twenty-ninth embodiment the disclosure provides a compound according to the first through twelfth embodiments wherein T is N, U is CR^4, X is NR^3 and Y is C and forms a compound of formula (Ij)



Formula (Ij)

In a thirtieth embodiment the disclosure provides a compound according to the twenty-ninth embodiment wherein the compound is

N-((1*S*,3*R*,4*S*)-3-ethyl-4-(imidazo[4,5-*d*]pyrrolo[2,3-*b*]pyridin-1(6*H*)-yl)cyclopentyl)cyclopropanesulfonamide;

N-((1*S*,3*S*,4*R*)-3-(imidazo[4,5-*d*]pyrrolo[2,3-*b*]pyridin-1(6*H*)-yl)-4-methylcyclopentyl)cyclopropanesulfonamide;

N-((1*S*,3*S*,4*R*)-3-(2-cyclopropylimidazo[4,5-*d*]pyrrolo[2,3-*b*]pyridin-1(6*H*)-yl)-4-methylcyclopentyl)cyclopropanesulfonamide;

N-((1*S*,3*R*,4*S*)-3-methyl-4-(2-methylimidazo[4,5-*d*]pyrrolo[2,3-*b*]pyridin-1(6*H*)-yl)cyclopentyl)cyclopropanesulfonamide;

Cyclopropanesulfonic acid [(1*S*,3*R*,4*S*)-3-methyl-4-(2-trifluoromethyl- imidazo[4,5-*d*]pyrrolo[2,3-*b*]pyridin-1(6*H*)-yl)-cyclopentyl]-amide;

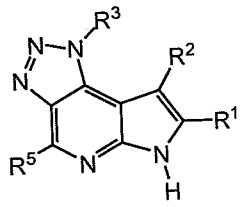
Cyclopropanesulfonic acid [(1*S*,3*R*,4*S*)-3-ethyl-4-(2-trifluoromethyl- imidazo[4,5-*d*]pyrrolo[2,3-*b*]pyridin-1(6*H*)-yl)-cyclopentyl]-amide;

Cyclopropanesulfonic acid [(1*S*,3*S*,4*R*)-3-(2-difluoromethyl- imidazo[4,5-*d*]pyrrolo[2,3-*b*]pyridin-1(6*H*)-yl)-4-ethyl-cyclopentyl]-amide;

Cyclopropanesulfonic acid [(1*S*,3*R*,4*S*)-3-ethyl-4-(2-methyl- imidazo[4,5-*d*]pyrrolo[2,3-*b*]pyridin-1(6*H*)-yl)-cyclopentyl]-amide;

Cyclopropanesulfonic acid [(1*S*,3*S*,4*R*)-3-(2-amino- imidazo[4,5-*d*]pyrrolo[2,3-*b*]pyridin-1(6*H*)-yl)-4-ethyl-cyclopentyl]-amide.

according to the first through twelfth embodiments wherein is N, U is N, X is NR^3 and Y is C and forms a compound of Formula (Ik)

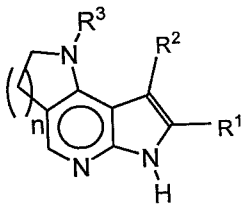


Formula (Ik)

In a thirty-second embodiment the disclosure provides a compound according to the thirty-first embodiment wherein the compound is

Cyclopropanesulfonic acid [(1S,3R,4S)-3-ethyl-4-(*6H*-[1,2,3]triazolo[4,5-*d*]pyrrolo[2,3-*b*]pyridin-1-yl)-cyclopentyl]-amide.

In a thirty-third embodiment the disclosure provides a compound of Formula (II) wherein the compound is



Formula (II)

pharmaceutically acceptable salts, pro-drugs, biologically active metabolites, stereoisomers and isomers thereof wherein

R^1,and R^2 are independently hydrogen, deuterium, $-N(R^a)(R^b)$, halogen, $-OR^a$, $-SR^a$, $-S(O)R^a$, $-S(O)_2R^a$, $-NO_2$, $-C(O)OR^a$, -CN, $-C(O)N(R^a)(R^b)$, $-N(R^a)C(O)(R^b)$, $-C(O)R^a$, $-C(OH)R^aR^b$, $-N(R^a)S(O)_2-R^b$, $-S(O)_2N(R^a)(R^b)$, $-CF_3$, $-OCF_3$, optionally substituted (C_1-C_6)alkyl, optionally substituted (C_2-C_6)alkenyl, optionally substituted (C_2-C_6)alkynyl, optionally substituted (C_3-C_{10})cycloalkyl, optionally substituted (C_1-C_{10})heteroaryl, optionally substituted (C_1-C_{10}) heterocyclyl, or optionally substituted (C_6-C_{10})aryl;

wherein in a moiety containing $-N(R^a)(R^b)$, the nitrogen, R^a and R^b may form a ring such that $-N(R^a)(R^b)$ represents an optionally substituted (C_2-C_{10})heterocyclyl or optionally substituted (C_1-C_{10})heteroaryl linked through a nitrogen;

R^3 is hydrogen, an optionally substituted bridged (C_5-C_{12})cycloalkyl, optionally substituted bridged (C_2-C_{10})heterocyclyl, optionally substituted (C_1-C_8)alkyl, optionally substituted (C_3-C_{10})cycloalkyl, optionally substituted (C_3-C_8)cycloalkenyl, optionally substituted

an optionally substituted (C_6-C_{10})aryl, an optionally substituted (C_1-C_{10})heteroaryl, an optionally substituted (C_1-C_{10})heterocyclyl, an optionally substituted -(C_1-C_6)alkylene-(C_3-C_{10})cycloalkyl, an optionally substituted -(C_1-C_6)alkylene-(C_6-C_{10})aryl, an optionally substituted -(C_1-C_6)alkylene-(C_1-C_{10})heteroaryl, or an optionally substituted -(C_1-C_6)alkylene-(C_1-C_{10})heterocyclyl; and

R^e for each occurrence is independently a bond, an optionally substituted (C_1-C_{10})alkylene, an optionally substituted (C_2-C_{10})alkenylene, an optionally substituted (C_2-C_{10})alkynylene, an optionally substituted -(C_1-C_{10})alkylene-O-(C_1-C_{10})alkylene group, an optionally substituted (C_3-C_{10})cycloalkylene, an optionally substituted (C_6-C_{10})arylene, an optionally substituted (C_1-C_{10})heteroarylene, or an optionally substituted (C_1-C_{10})heterocyclylene.

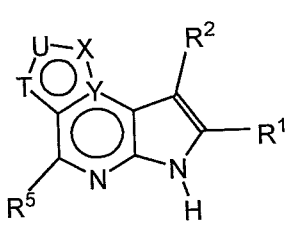
In a thirty-fourth embodiment the disclosure provides a compound according to the thirty-third embodiment wherein the compound is

1-Cyclohexyl-2,3,4,7-tetrahydro-1*H*-pyrrolo[2,3-*h*][1,6]naphthyridine;

Cyclopropanesulfonic acid [(1S,3R,4S)-3-ethyl-4-(3,6,7,8-tetrahydro-3,4,9-triaza-cyclopenta[a]naphthalen-9-yl)-cyclopentyl]-amide; or

Cyclopropanesulfonic acid [(1S,3S,4R)-3-(3,6-dihydro-2H-dipyrrolo[2,3-b;2',3'-d]pyridin-1-yl)-4-ethyl-cyclopentyl]-amide.

In a thirty-fifth embodiment the disclosure provides a pharmaceutical composition comprising a compound of Formula (I) or Formula (II) as defined in any of the foregoing embodiments

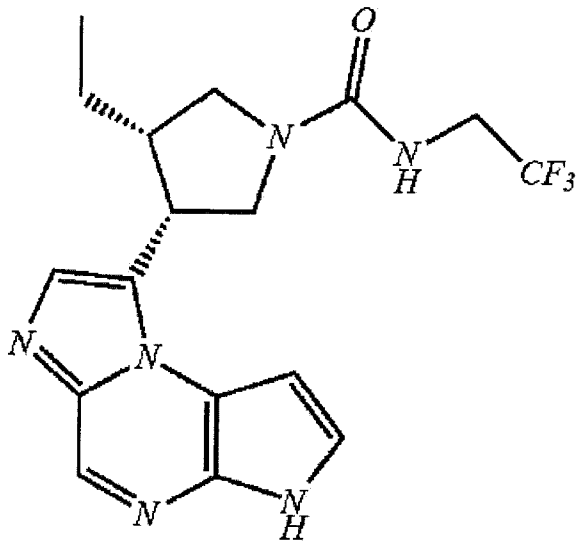


Formula (I) , Formula (II)

a pharmaceutically acceptable carrier and excipient and a second therapeutic agent selected from the group consisting of cytokine suppressive anti-inflammatory drugs, antibodies to or antagonists of other human cytokines or growth factors, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-12, IL-15, IL-16, IL-21, IL-23, interferons, EMAP-II, GM-CSF, FGF, PDGF, CTLA or their ligands including CD154, HUMIRA™, REMICADE™, SIMPONI™ (golimumab), CIMZIA™, ACTEMRA™, CDP 571, soluble p55 or p75 TNF receptors, ENBREL™, Lenercept, TNFα converting enzyme inhibitors, IL-1 inhibitors, Interleukin 11, IL-18 antagonists, IL-12 antagonists, IL-12 antibodies, soluble IL-12 receptors, IL-12 binding proteins, non-depleting anti-CD4 inhibitors FK506, rapamycin, mycophenolate mofetil, leflunomide, NSAIDs, ibuprofen, corticosteroids, phosphodiesterase inhibitors, adensosine agonists, antithrombotic agents, complement inhibitors, adrenergic agents, IL-1β converting enzyme inhibitors, T-cell signalling

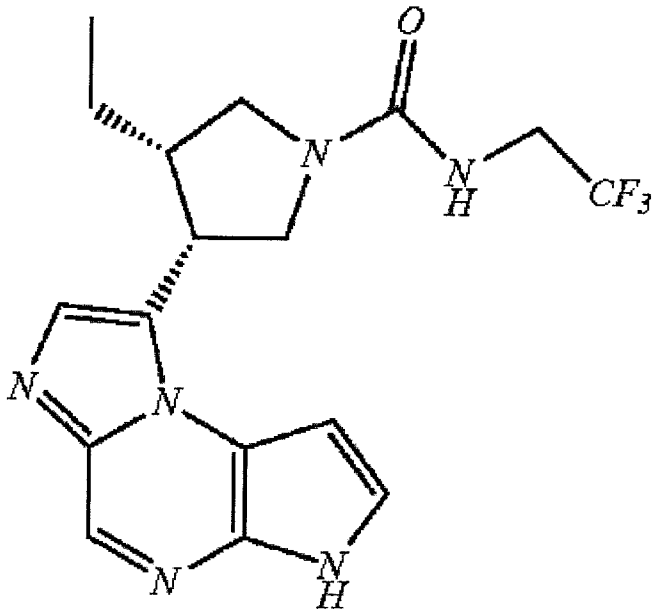
What is claimed:

1. A compound represented by the following structure:



or a pharmaceutically acceptable salt thereof.

2. The compound according to claim 1 represented by the following structure:



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