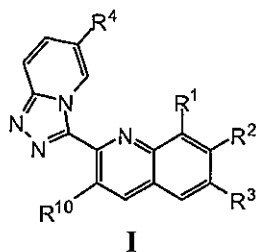


What is claimed is:

1. A compound of general Formula I



- 5 and stereoisomers, pharmaceutically acceptable salts and solvates thereof, wherein:

R^1 is H, halogen, CN, OH, (1-6C)alkyl, fluoro(1-6C)alkyl, difluoro(1-6C)alkyl, trifluoro(1-6C)alkyl, hydroxy(1-6C)alkyl, cyano(1-6C)alkyl, (1-3C alkoxy)(1-6C)alkyl (optionally substituted with hydroxy), di(1-3C alkoxy)(1-6C)alkyl, (1-6C)alkoxy, fluoro(1-6C)alkoxy, difluoro(1-6C)alkoxy, trifluoro(1-6C)alkoxy, hydroxy(2-6C)alkoxy, cyano(1-6C)alkoxy, (1-3C alkoxy)(2-6C)alkoxy, di(1-3C alkoxy)(2-6C)alkoxy, (3-6C cycloalkyl)methoxy, oxetanylmethoxy (optionally substituted with methyl), (1-6C alkyl)sulfanyl, $-C(=O)NR^aR^b$, $-CH_2C(=O)NR^cR^d$, or (3-6C)cycloalkyl optionally substituted with $-CH_2OH$ or $-CH_2O(1-4C\text{ alkyl})$,

R^a , R^b , R^c and R^d are independently selected from H and (1-4C)alkyl;

15 R^2 is H, halogen, CN, OH, (1-6C)alkyl, fluoro(1-6C)alkyl, difluoro(1-6C)alkyl, trifluoro(1-6C)alkyl, hydroxy(1-6C)alkyl, (1-3C alkoxy)(1-6C)alkyl, (1-6C)alkoxy (optionally substituted with (1-6C alkyl) $C(=O)O-$, amino(1-6C alkyl) $C(=O)O-$, or phenyl $C(=O)O-$), fluoro(1-6C)alkoxy, difluoro(1-6C)alkoxy, trifluoro(1-6C)alkoxy, hydroxy(2-6C)alkoxy, (1-3C alkoxy)(2-6C)alkoxy, (3-6C cycloalkyl)methoxy, (3-6C)cycloalkoxy (optionally substituted with OH), oxetanylmethoxy (optionally substituted with methyl), tetrahydropyranyloxy, (1-6C alkyl)sulfanyl, hydroxy(2-6C alkyl)sulfanyl, (1-3C alkylsulfanyl)(2-6C)alkoxy, $-COOH$, $hetAr^1$, $-C(=O)NR^eR^f$, $-NR^eC(=O)R^f$, oxetanyl, or cyclopropyl optionally substituted with $-CH_2OH$ or $-CH_2O(1-6C\text{ alkyl})$;

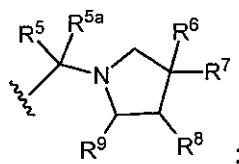
20 or R^1 and R^2 together with the atoms to which they are attached form a 5-6 membered heterocyclic ring having 1 - 2 ring heteroatoms independently selected from O and N, wherein said ring is optionally substituted with (1-4C)alkyl;

$hetAr^1$ is a 5-6 membered heteroaryl ring having one or two ring nitrogen atoms and optionally substituted with one or more groups selected from (1-6C)alkyl;

25 R^e and R^f are independently H, (1-6C)alkyl or cyclopropyl optionally substituted with (1-4C)alkyl;

R^3 is H, halogen or (1-6C)alkyl;

R⁴ is



R⁵ is CF₃, CH₂F, CHF₂, methyl or ethyl;

R^{5a} is H or methyl;

5 or R⁵ and R^{5a} together with the atom to which they are attached form a cyclopropyl ring;

R⁶ is H, NH₂, OH, (1-6C alkyl)NH-, fluoro(1-6C alkyl)NH-, hydroxy(1-6C alkyl)NH-, (3-6C cycloalkyl)CH₂NH-, (1-6C alkyl)C(=O)NH-, (1-6C alkyl)OC(=O)NH- (optionally substituted with 5-methyl-2-oxo-1,3-dioxol-4-yl) or amino(1-6C)alkyl-;

10 R⁷ is H, (1-6C)alkyl, fluoro(1-6C)alkyl or hydroxy(1-6C)alkyl;

or R⁶ and R⁷ together with the atom to which they are attached form a 5-6 membered spirocyclic heterocycle having a ring nitrogen atom;

R⁸ is H, halogen, OH, or (1-6C)alkoxy, or

15 R⁶ and R⁸ together with the carbon atoms to which they are attached form a cyclopropyl ring optionally substituted with NH₂;

R⁹ is H, or

R⁶ and R⁹ together form a linking group having the formula -CH₂NH- which links the carbon atoms to which they are attached; and

R¹⁰ is H or halogen.

20 2. A compound according to claim 1, wherein:

R¹ is H, halogen, CN, OH, (1-6C)alkyl, fluoro(1-6C)alkyl, difluoro(1-6C)alkyl, trifluoro(1-6C)alkyl, hydroxy(1-6C)alkyl, cyano(1-6C)alkyl, (1-3C alkoxy)(1-6C)alkyl (optionally substituted with hydroxy), di(1-3C alkoxy)(1-6C)alkyl, (1-6C)alkoxy, fluoro(1-6C)alkoxy, difluoro(1-6C)alkoxy, trifluoro(1-6C)alkoxy, hydroxy(2-6C)alkoxy, 25 cyano(1-6C)alkoxy, (1-3C alkoxy)(2-6C)alkoxy, di(1-3C alkoxy)(2-6C)alkoxy, (3-6C cycloalkyl)methoxy, oxetanylmethoxy (optionally substituted with methyl), (1-6C alkyl)sulfonyl, -C(=O)NR^aR^b, -CH₂C(=O)NR^cR^d, or (3-6C)cycloalkyl optionally substituted with -CH₂OH or -CH₂O(1-4C alkyl);

R^a, R^b, R^c and R^d are independently selected from H and (1-4C)alkyl;

30 R² is H, halogen, CN, OH, (1-6C)alkyl, fluoro(1-6C)alkyl, difluoro(1-6C)alkyl, trifluoro(1-6C)alkyl, hydroxy(1-6C)alkyl, (1-3C alkoxy)(1-6C)alkyl, (1-6C)alkoxy (optionally substituted with (1-6C alkyl)C(=O)O- or amino(1-6C alkyl)C(=O)O-),

fluoro(1-6C)alkoxy, difluoro(1-6C)alkoxy, trifluoro(1-6C)alkoxy, hydroxy(2-6C)alkoxy, (1-3C alkoxy)(2-6C)alkoxy, (3-6C cycloalkyl)methoxy, oxetanylmethoxy (optionally substituted with methyl), tetrahydropyranyloxy, (1-6C alkyl)sulfanyl, hydroxy(2-6C alkyl)sulfanyl, (1-3C alkylsulfanyl)(2-6C)alkoxy, -COOH, hetAr¹, -C(=O)NR^eR^f,
 5 -NR^eC(=O)R^f, or cyclopropyl optionally substituted with -CH₂OH or -CH₂O(1-6C alkyl);

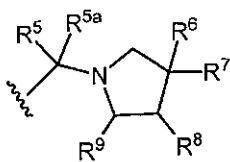
or R¹ and R² together with the atoms to which they are attached form a 5-6 membered heterocyclic ring having 1 - 2 ring heteroatoms independently selected from O and N, wherein said ring is optionally substituted with (1-4C)alkyl;

hetAr¹ is a 5-6 membered heteroaryl ring having one or two ring nitrogen atoms and optionally substituted with one or more groups selected from (1-6C)alkyl;

R^e and R^f are independently H, (1-6C)alkyl or cyclopropyl optionally substituted with (1-4C)alkyl;

R³ is H, halogen or (1-6C)alkyl;

R⁴ is



R⁵ is CF₃, CH₂F, CHF₂, methyl or ethyl;

R^{5a} is H or methyl;

or R⁵ and R^{5a} together with the atom to which they are attached form a cyclopropyl ring;

20 R⁶ is H, -NH₂, OH, (1-6C alkyl)NH-, fluoro(1-6C alkyl)NH-, hydroxy(1-6C alkyl)NH-, (3-6C cycloalkyl)CH₂NH-, (1-6C alkyl)C(=O)NH-, (1-6C alkyl)OC(=O)NH- or amino(1-6C)alkyl-;

R⁷ is H, (1-6C)alkyl, fluoro(1-6C)alkyl or hydroxy(1-6C)alkyl;

25 or R⁶ and R⁷ together with the atom to which they are attached form a 5-6 membered spirocyclic heterocycle having a ring nitrogen atom;

R⁸ is H, halogen, OH, or (1-6C)alkoxy, or

R⁶ and R⁸ together with the carbon atoms to which they are attached form a cyclopropyl ring optionally substituted with NH₂;

R⁹ is H, or

30 R⁶ and R⁹ together form a linking group having the formula -CH₂NH- which links the carbon atoms to which they are attached; and

R¹⁰ is H.

3. A compound of claim 1 or 2, wherein R^1 is selected from H, (1-6C)alkyl, (3-6C)cycloalkyl optionally substituted with $-CH_2OH$ or $-CH_2O(1-4C \text{ alkyl})$, (1-6C)alkoxy, trifluoro(1-6C)alkoxy, hydroxy(2-6C)alkoxy, (1-3C alkoxy)(2-6C)alkoxy, and (3-6C)cycloalkylmethoxy.

4. A compound of claim 3, wherein R^1 is selected from H, methyl, ethyl, isopropyl, tert-butyl, cyclopropyl, methoxy, ethoxy, isopropoxy, trifluoromethoxy, 2-hydroxyethoxy, 2-hydroxypropoxy, 3-hydroxypropoxy, 2-methoxyethoxy, 3-methoxypropoxy, 2-methoxypropoxy, 3-methoxyprop-2-oxy, 2-ethoxyethoxy, 1,3-dimethoxypropan-2-yloxy and cyclopropylmethoxy.

5. A compound of claim 4, wherein R^1 is H.

6. A compound of claim 4, wherein R^1 (1-3C alkoxy)(2-6C)alkoxy.

7. A compound of claim 1, wherein R^1 is selected from halogen, CN, OH, fluoro(1-6C)alkyl, difluoro(1-6C)alkyl, trifluoro(1-6C)alkyl, hydroxy(1-6C)alkyl, cyano(1-6C)alkyl, di(1-3C alkoxy)(1-6C)alkyl, fluoro(1-6C)alkoxy, difluoro(1-6C)alkoxy, trifluoro(1-6C)alkoxy, cyano(1-6C)alkoxy, di(1-3C alkoxy)(2-6C)alkoxy, oxetanylmethoxy (optionally substituted with methyl), (1-6C alkyl)sulfanyl, $-C(=O)NR^aR^b$, and $-CH_2C(=O)NR^cR^d$.

8. A compound according to any of claims 1-7, wherein R^2 is selected from H, (1-3C alkoxy)(1-6C)alkyl, hydroxy(2-6C)alkoxy, and (1-6C)alkoxy which is optionally substituted with (1-6C alkyl) $C(=O)O-$ or amino(1-6C alkyl) $C(=O)O-$.

9. A compound according to claim 8, wherein R^2 is selected from H, 2-methoxyethoxy, 3-methoxyprop-2-oxy, 2-methoxypropoxy, 2-ethoxyethoxy, and 2-hydroxyethoxy.

10. A compound according to claim 9, wherein R^2 is H.

11. A compound according to any of claims 1-7, wherein R^2 is selected from halogen, CN, OH, (1-6C)alkyl, fluoro(1-6C)alkyl, difluoro(1-6C)alkyl, trifluoro(1-6C)alkyl, hydroxy(1-6C)alkyl, fluoro(1-6C)alkoxy, difluoro(1-6C)alkoxy, trifluoro(1-6C)alkoxy, (1-3C alkoxy)(2-6C)alkoxy, (3-6C cycloalkyl)methoxy, oxetanylmethoxy (optionally substituted with methyl), tetrahydropyranyloxy, (1-6C alkyl)sulfanyl, hydroxy(2-6C alkyl)sulfanyl, (1-3C alkylsulfanyl)(2-6C)alkoxy, $-COOH$, $hetAr^1$, $-C(=O)NR^eR^f$, $-NR^eC(=O)R^f$, and cyclopropyl optionally substituted with $-CH_2OH$ or $-CH_2O(1-6C \text{ alkyl})$.

12. A compound according to claim 1 or 2, wherein R^1 and R^2 together with the atoms to which they are attached form a 5-6 membered heterocyclic ring having 1 to 2

ring heteroatoms independently selected from O and N, wherein said ring is optionally substituted with (1-4C)alkyl.

13. A compound according to any of claims 1-12, wherein R³ is selected from H, F and methyl.

5 14. A compound according to claim 13, wherein R³ is H.

15. A compound according to claim 13, wherein R³ is F.

16. A compound according to any of claims 1-15, wherein R⁵ is CF₃, CH₂F, CHF₂, methyl or ethyl and R^{5a} is H.

17. A compound according to claim 16, wherein R⁵ is CF₃ and R^{5a} is H.

10 18. A compound according to any of claims 1-15, wherein R⁵ is CF₃, CH₂F, CHF₂, methyl or ethyl and R^{5a} is methyl.

19. A compound according to claim 15, wherein R⁵ is methyl, and R^{5a} is H.

20. A compound according to any of claims 1-19, wherein R⁶ is selected from H, NH₂, OH, CH₃NH-, (CH₃)₂CHNH-, FCH₂CH₂NH-, HOCH₂CH₂NH-,
15 (cyclopropyl)CH₂NH-, CH₃C(=O)NH-, (CH₃)₃CC(=O)NH- and NH₂CH₂-.

21. A compound according to claim 20, wherein R⁶ is NH₂.

22. A compound according to any of claims 1-21, wherein R⁷ is selected from H, methyl, ethyl, FCH₂- and HOCH₂-.

23. A compound according to claim 22, wherein R⁷ is H.

20 24. A compound according to claim 23, wherein R⁷ is methyl.

25. A compound according to any of claims 1-19, wherein R⁶ and R⁷ together with the atom to which they are attached form a 5-6 membered spirocyclic heterocycle having a ring nitrogen atom.

26. A compound according to any of claims 1-25, wherein R⁸ is selected from
25 H, F, OH or -OMe.

27. A compound according to claim 26, wherein R⁸ is H.

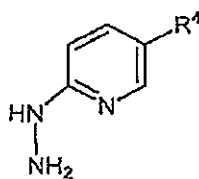
28. A compound according to any of claims 1-19, wherein R⁶ and R⁸ together with the carbon atoms to which they are attached form a cyclopropyl ring optionally substituted with NH₂.

30 29. A compound according to any of claims 1-28, wherein R⁹ is H.

30. A compound according to any of claims 1-19, wherein R⁶ and R⁹ together form a linking group having the formula -CH₂NH- which links the carbon atoms to which they are attached.

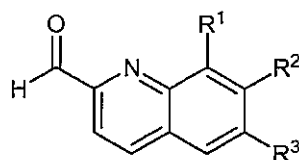
31. A compound according to any of claims 1-30, wherein R¹⁰ is H.

32. A compound according to any of claims 1 or 3-30, wherein R¹⁰ is fluoro.
33. A compound of claim 1, selected from anyone of Examples 1-328.
34. A composition comprising a compound according to any of claims 1-33 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable diluent or carrier.
35. A compound of Formula I as defined in anyone of claims 1 to 33, or a pharmaceutically acceptable salt thereof, for use in the treatment of an inflammatory or autoimmune disease.
36. A compound as defined in claim 35, wherein the inflammatory or autoimmune disease is multiple sclerosis, lupus, inflammatory bowel disease or rheumatoid arthritis.
37. A compound of Formula I as defined in anyone of claims 1 to 33 or a pharmaceutically acceptable salt thereof, for use in the treatment of cancer.
38. A compound of Formula I as defined in anyone of claims 1 to 33, or a pharmaceutically acceptable salt thereof for use in the treatment of PIM-1 and/or PIM-2 and/or PIM-3 kinase-mediated condition.
39. A compound of Formula I as defined in anyone of claims 1 to 33, or a pharmaceutically acceptable salt thereof for use in the treatment of an inflammatory or autoimmune disorder.
40. The compound as defined in claim 39 wherein the inflammatory or autoimmune disease is multiple sclerosis, lupus, inflammatory bowel disease or rheumatoid arthritis.
41. A compound as defined in anyone of claims 1 to 33, or a pharmaceutically acceptable salt thereof for use in the treatment of cancer.
42. A process for the preparation a compound of claim 1, which comprises:
(a) reacting a corresponding compound of formula II or a protected derivative thereof



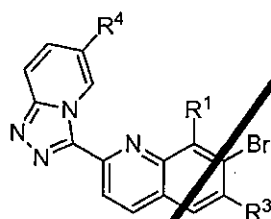
II

where R^4 is as defined for Formula I, with a corresponding compound having the formula **III** or a protected derivative thereof

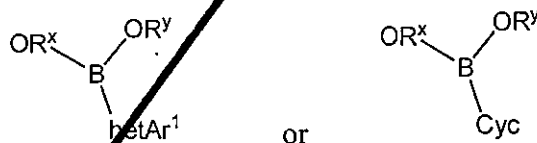
**III**

- 5 where R^1 , R^2 and R^3 are as defined for Formula I, in the presence of an organo hypervalent iodine reagent; or

(b) for a compound of Formula I where R^2 is hetAr¹ or a cyclopropyl ring optionally substituted with -CH₂OH or -CH₂O(1-6C alkyl), reacting a corresponding compound having the formula **IV** or a protected derivative thereof:

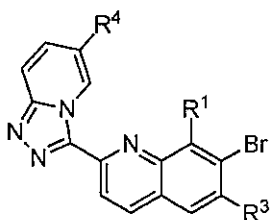
**IV**

where R^1 , R^3 and R^4 are as defined for Formula I, with a reagent having the formula



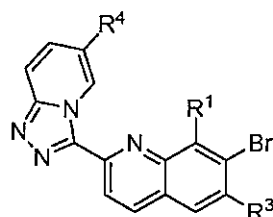
respectively, where hetAr¹ is as defined for Formula I, Cyc is cyclopropyl optionally substituted with -CH₂OH or -CH₂O(1-6C alkyl), and R^x and R^y are H or (1-6C)alkyl, or R^x and R^y together with the atoms to which they are connected form a 5-6 membered ring optionally substituted with 1-4 substituents selected from (1-3C alkyl), wherein said reaction takes place in the presence of a palladium catalyst and optionally in the presence of a base and a ligand; or

(c) for a compound of Formula I where R^2 is -NR^eC(=O)R^f, reacting a corresponding compound having the formula **IV** or a protected derivative thereof:

**IV**

where R^1 , R^3 and R^4 are as defined for Formula I, with a reagent having the formula $\text{HNR}^e\text{C}(=\text{O})\text{R}^f$ in the presence of a base and a metal catalyst; or

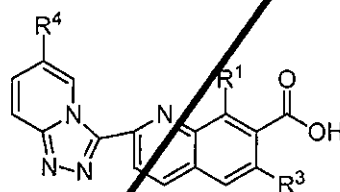
- (d) for a compound of Formula I where R^2 is (1-6C alkyl)sulfanyl or hydroxy(2-6C alkyl)sulfanyl, reacting a corresponding compound having the formula IV or a protected derivative thereof:



IV

where R^1 , R^2 , R^3 and R^4 are as defined for Formula I, with a reagent having the formula $\text{HS}(1-6\text{C alkyl})$ or $\text{HS}(1-6\text{C alkyl})\text{OH}$, respectively, in the presence of a base; or

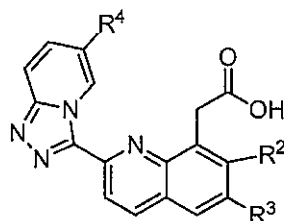
- (e) for a compound of Formula I where R^2 is $-\text{C}(=\text{O})\text{NR}^e\text{R}^f$, coupling a corresponding compound having the formula V or a protected derivative thereof:



V

- where R^1 , R^3 and R^4 are as defined for Formula I, with a reagent having the formula HNR^eR^f , where R^e and R^f are as defined for Formula I, in the presence of a base and a coupling reagent; or

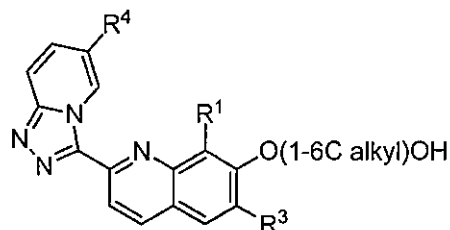
(f) for a compound of Formula I where R^1 is $-\text{CH}_2\text{C}(=\text{O})\text{NR}^e\text{R}^d$, coupling a corresponding compound having the formula VI or a protected derivative thereof



VI

where R^2 , R^3 and R^4 are as defined for Formula I, with a reagent having the formula HNR^eR^d , where R^e and R^d are as defined for Formula I, in the presence of a base and a coupling reagent; or

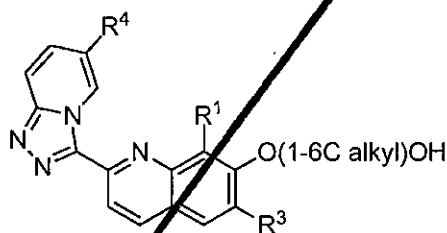
(g) for a compound of Formula I where R^2 is (1-6C)alkoxy substituted with (1-6C alkyl)C(=O)O-, coupling a corresponding compound having the formula VII or a protected derivative thereof



VII

where R^1 , R^3 and R^4 are as defined for Formula I, with a (1-6C)alkyl acid anhydride or a (1-6C)alkyl acid chloride in the presence of a base; or

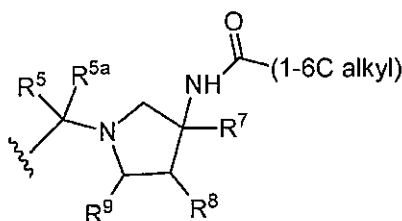
(h) for a compound of Formula I where R^2 is (1-6C)alkoxy substituted with amino(1-6C alkyl)C(=O)O-, coupling a corresponding compound having the formula VII or a protected derivative thereof



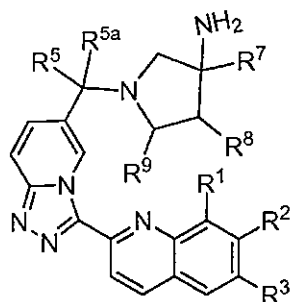
VII

where R^1 , R^3 and R^4 are as defined for Formula I, with a compound having the formula $P^1NH(1-6C\text{ alkyl})C(=O)OH$ where P^1 is H or an amine protecting group, in the presence of a base and a coupling reagent; or

(i) for a compound of Formula I where R^4 is a moiety having the structure



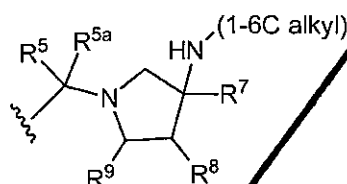
where R^5 , R^{5a} , and R^7 are as defined for Formula I, R^8 is H, halogen, OH, or (1-6C)alkoxy, and R^9 is H, reacting a corresponding compound having the formula VIII



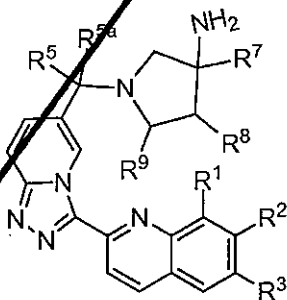
VIII

where R^1 , R^2 , R^3 , R^5 , R^{5a} , and R^7 are as defined for Formula I, R^8 is H, halogen, OH, or (1-6C)alkoxy, and R^9 is H, with a (1-6C)alkylcarboxylic acid anhydride or a (1-6C)alkylcarboxylic acid chloride in the presence of a base; or

(j) for a compound of Formula I where R^4 is a moiety having the structure



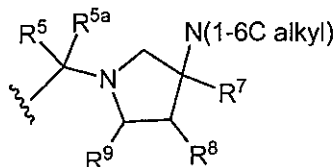
where R^5 , R^{5a} , and R^7 are as defined for Formula I, R^8 is H, halogen, OH, or (1-6C)alkoxy, and R^9 is H, reacting a corresponding compound having the formula VIII



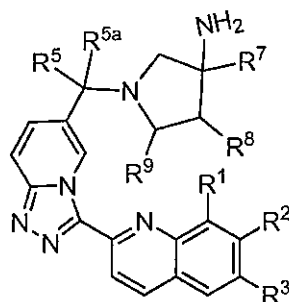
VIII

where R^1 , R^2 , R^3 , R^5 , R^{5a} and R^7 are as defined for Formula I, R^8 is H, halogen, OH, or (1-6C)alkoxy, and R^9 is H, with a (1-6C)aldehyde or a protected (1-6C)aldehyde in the presence of a catalyst and a base followed by treatment with a reducing agent; or

(k) for a compound of Formula I where R^4 is a moiety having the structure



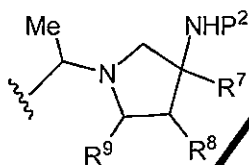
where R^5 , R^{5a} , and R^7 are as defined for Formula I, R^8 is H, halogen, OH, or (1-6C)alkoxy, and R^9 is H, reacting a corresponding compound having the formula VIII



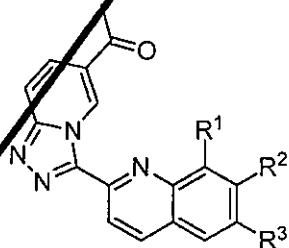
VIII

where R^1 , R^2 , R^3 , R^5 , R^{5a} , and R^7 are as defined for Formula I, R^8 is H, halogen, OH, or (1-6C)alkoxy, and R^9 is H, in the presence of a reagent having the formula $HC(=O)(1-5C$
 5 alkyl) and a reducing agent; or

(l) for a compound of Formula I where R^4 is a moiety having the structure



where R^7 is as defined for Formula I, R^8 is H, halogen, OH, or (1-6C)alkoxy, R^9 is H, and P^2 is H or an amine protecting group, reacting a corresponding compound having the
 10 formula IX

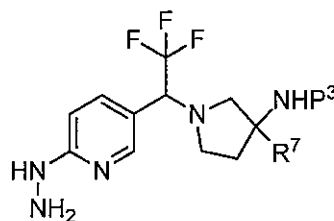


IX

where R^1 , R^2 , and R^3 are as defined for Formula I, in the presence of a Lewis acid, followed by treatment with a reducing agent; and

15 removing any protecting group or groups and, if desired, forming a salt.

43. A compound having the formula II-A



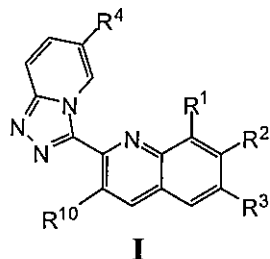
II-A

including enantiomers and diastereomers thereof, where P^3 is H or an amine protecting group and R^7 is H, (1-6C)alkyl, fluoro(1-6C)alkyl or hydroxy(1-6C)alkyl.

44. A compound of claim 43, wherein R^7 is H or (1-6C)alkyl.
45. A compound of claim 44, wherein R^7 is H or methyl.

What is claimed is:

1. A compound of general Formula I



- 5 and stereoisomers, pharmaceutically acceptable salts and solvates thereof, wherein:

R^1 is H, halogen, CN, OH, (1-6C)alkyl, fluoro(1-6C)alkyl, difluoro(1-6C)alkyl, trifluoro(1-6C)alkyl, hydroxy(1-6C)alkyl, cyano(1-6C)alkyl, (1-3C alkoxy)(1-6C)alkyl (optionally substituted with hydroxy), di(1-3C alkoxy)(1-6C)alkyl, (1-6C)alkoxy, fluoro(1-6C)alkoxy, difluoro(1-6C)alkoxy, trifluoro(1-6C)alkoxy, hydroxy(2-6C)alkoxy, cyano(1-6C)alkoxy, (1-3C alkoxy)(2-6C)alkoxy, di(1-3C alkoxy)(2-6C)alkoxy, (3-6C cycloalkyl)methoxy, oxetanylmethoxy (optionally substituted with methyl), (1-6C alkyl)sulfanyl, $-C(=O)NR^aR^b$, $-CH_2C(=O)NR^cR^d$, or (3-6C)cycloalkyl optionally substituted with $-CH_2OH$ or $-CH_2O(1-4C\text{ alkyl})$;

R^a , R^b , R^c and R^d are independently selected from H and (1-4C)alkyl;

15 R^2 is H, halogen, CN, OH, (1-6C)alkyl, fluoro(1-6C)alkyl, difluoro(1-6C)alkyl, trifluoro(1-6C)alkyl, hydroxy(1-6C)alkyl, (1-3C alkoxy)(1-6C)alkyl, (1-6C)alkoxy (optionally substituted with (1-6C alkyl) $C(=O)O-$, amino(1-6C alkyl) $C(=O)O-$, or phenyl($C(=O)O-$), fluoro(1-6C)alkoxy, difluoro(1-6C)alkoxy, trifluoro(1-6C)alkoxy, hydroxy(2-6C)alkoxy, (1-3C alkoxy)(2-6C)alkoxy, (3-6C cycloalkyl)methoxy, (3-6C)cycloalkoxy (optionally substituted with OH), oxetanylmethoxy (optionally substituted with methyl), tetrahydropyranyloxy, (1-6C alkyl)sulfanyl, hydroxy(2-6C alkyl)sulfanyl, (1-3C alkylsulfanyl)(2-6C)alkoxy, $-COOH$, $hetAr^1$, $-C(=O)NR^eR^f$, $-NR^eC(=O)R^f$, oxetanyl, or cyclopropyl optionally substituted with $-CH_2OH$ or $-CH_2O(1-6C\text{ alkyl})$;

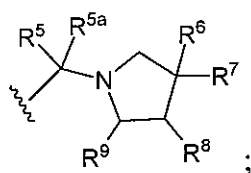
25 or R^1 and R^2 together with the atoms to which they are attached form a 5-6 membered heterocyclic ring having 1 - 2 ring heteroatoms independently selected from O and N, wherein said ring is optionally substituted with (1-4C)alkyl;

$hetAr^1$ is a 5-6 membered heteroaryl ring having one or two ring nitrogen atoms and optionally substituted with one or more groups selected from (1-6C)alkyl;

30 R^e and R^f are independently H, (1-6C)alkyl or cyclopropyl optionally substituted with (1-4C)alkyl;

R^3 is H, halogen or (1-6C)alkyl;

R⁴ is



R⁵ is CF₃, CH₂F, CHF₂, methyl or ethyl;

R^{5a} is H or methyl;

5 or R⁵ and R^{5a} together with the atom to which they are attached form a cyclopropyl ring;

R⁶ is H, NH₂, OH, (1-6C alkyl)NH-, fluoro(1-6C alkyl)NH-, hydroxy(1-6C alkyl)NH-, (3-6C cycloalkyl)CH₂NH-, (1-6C alkyl)C(=O)NH-, (1-6C alkyl)OC(=O)NH- (optionally substituted with 5-methyl-2-oxo-1,3-dioxol-4-yl) or amino(1-6C)alkyl-;

10 R⁷ is H, (1-6C)alkyl, fluoro(1-6C)alkyl or hydroxy(1-6C)alkyl;

or R⁶ and R⁷ together with the atom to which they are attached form a 5-6 membered spirocyclic heterocycle having a ring nitrogen atom;

R⁸ is H, halogen, OH, or (1-6C)alkoxy, or

15 R⁶ and R⁸ together with the carbon atoms to which they are attached form a cyclopropyl ring optionally substituted with NH₂;

R⁹ is H, or

R⁶ and R⁹ together form a linking group having the formula -CH₂NH- which links the carbon atoms to which they are attached; and

R¹⁰ is H or halogen.

20 2. A compound according to claim 1, wherein:

R¹ is H, halogen, CN, OH, (1-6C)alkyl, fluoro(1-6C)alkyl, difluoro(1-6C)alkyl, trifluoro(1-6C)alkyl, hydroxy(1-6C)alkyl, cyano(1-6C)alkyl, (1-3C alkoxy)(1-6C)alkyl (optionally substituted with hydroxy), di(1-3C alkoxy)(1-6C)alkyl, (1-6C)alkoxy, fluoro(1-6C)alkoxy, difluoro(1-6C)alkoxy, trifluoro(1-6C)alkoxy, hydroxy(2-6C)alkoxy, 25 cyano(1-6C)alkoxy, (1-3C alkoxy)(2-6C)alkoxy, di(1-3C alkoxy)(2-6C)alkoxy, (3-6C cycloalkyl)methoxy, oxetanylmethoxy (optionally substituted with methyl), (1-6C alkyl)sulfanyl, -C(=O)NR^aR^b, -CH₂C(=O)NR^cR^d, or (3-6C)cycloalkyl optionally substituted with -CH₂OH or -CH₂O(1-4C alkyl);

R^a, R^b, R^c and R^d are independently selected from H and (1-4C)alkyl;

30 R² is H, halogen, CN, OH, (1-6C)alkyl, fluoro(1-6C)alkyl, difluoro(1-6C)alkyl, trifluoro(1-6C)alkyl, hydroxy(1-6C)alkyl, (1-3C alkoxy)(1-6C)alkyl, (1-6C)alkoxy (optionally substituted with (1-6C alkyl)C(=O)O- or amino(1-6C alkyl)C(=O)O-),

fluoro(1-6C)alkoxy, difluoro(1-6C)alkoxy, trifluoro(1-6C)alkoxy, hydroxy(2-6C)alkoxy, (1-3C alkoxy)(2-6C)alkoxy, (3-6C cycloalkyl)methoxy, oxetanylmethoxy (optionally substituted with methyl), tetrahydropyranyloxy, (1-6C alkyl)sulfanyl, hydroxy(2-6C alkyl)sulfanyl, (1-3C alkylsulfanyl)(2-6C)alkoxy, -COOH, hetAr¹, -C(=O)NR^eR^f,
 5 -NR^eC(=O)R^f, or cyclopropyl optionally substituted with -CH₂OH or -CH₂O(1-6C alkyl);

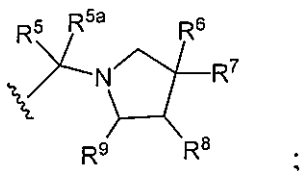
or R¹ and R² together with the atoms to which they are attached form a 5-6 membered heterocyclic ring having 1 - 2 ring heteroatoms independently selected from O and N, wherein said ring is optionally substituted with (1-4C)alkyl;

hetAr¹ is a 5-6 membered heteroaryl ring having one or two ring nitrogen atoms
 10 and optionally substituted with one or more groups selected from (1-6C)alkyl;

R^e and R^f are independently H, (1-6C)alkyl or cyclopropyl optionally substituted with (1-4C)alkyl;

R³ is H, halogen or (1-6C)alkyl;

R⁴ is



R⁵ is CF₃, CH₂F, CHF₂, methyl or ethyl;

R^{5a} is H or methyl;

or R⁵ and R^{5a} together with the atom to which they are attached form a cyclopropyl ring;

20 R⁶ is H, -NH₂, OH, (1-6C alkyl)NH-, fluoro(1-6C alkyl)NH-, hydroxy(1-6C alkyl)NH-, (3-6C cycloalkyl)CH₂NH-, (1-6C alkyl)C(=O)NH-, (1-6C alkyl)OC(=O)NH- or amino(1-6C)alkyl-;

R⁷ is H, (1-6C)alkyl, fluoro(1-6C)alkyl or hydroxy(1-6C)alkyl;

or R⁶ and R⁷ together with the atom to which they are attached form a 5-6
 25 membered spirocyclic heterocycle having a ring nitrogen atom;

R⁸ is H, halogen, OH, or (1-6C)alkoxy, or

R⁶ and R⁸ together with the carbon atoms to which they are attached form a cyclopropyl ring optionally substituted with NH₂;

R⁹ is H, or

30 R⁶ and R⁹ together form a linking group having the formula -CH₂NH- which links the carbon atoms to which they are attached; and

R¹⁰ is H.

3. A compound of claim 1 or 2, wherein R^1 is selected from H, (1-6C)alkyl, (3-6C)cycloalkyl optionally substituted with $-CH_2OH$ or $-CH_2O(1-4C \text{ alkyl})$, (1-6C)alkoxy, trifluoro(1-6C)alkoxy, hydroxy(2-6C)alkoxy, (1-3C alkoxy)(2-6C)alkoxy, and (3-6C)cycloalkylmethoxy.
- 5 4. A compound of claim 3, wherein R^1 is selected from H, methyl, ethyl, isopropyl, tert-butyl, cyclopropyl, methoxy, ethoxy, isopropoxy, trifluoromethoxy, 2-hydroxyethoxy, 2-hydroxypropoxy, 3-hydroxypropoxy, 2-methoxyethoxy, 3-methoxypropoxy, 2-methoxypropoxy, 3-methoxyprop-2-oxy, 2-ethoxyethoxy, 1,3-dimethoxypropan-2-yloxy and cyclopropylmethoxy.
- 10 5. A compound of claim 4, wherein R^1 is H.
6. A compound of claim 4, wherein R^1 (1-3C alkoxy)(2-6C)alkoxy.
7. A compound of claim 1, wherein R^1 is selected from halogen, CN, OH, fluoro(1-6C)alkyl, difluoro(1-6C)alkyl, trifluoro(1-6C)alkyl, hydroxy(1-6C)alkyl, cyano(1-6C)alkyl, di(1-3C alkoxy)(1-6C)alkyl, fluoro(1-6C)alkoxy, difluoro(1-6C)alkoxy, 15 trifluoro(1-6C)alkoxy, cyano(1-6C)alkoxy, di(1-3C alkoxy)(2-6C)alkoxy, oxetanylmethoxy (optionally substituted with methyl), (1-6C alkyl)sulfanyl, $-C(=O)NR^aR^b$, and $-CH_2C(=O)NR^cR^d$.
8. A compound according to any of claims 1-7, wherein R^2 is selected from H, (1-3C alkoxy)(1-6C)alkyl, hydroxy(2-6C)alkoxy, and (1-6C)alkoxy which is optionally 20 substituted with (1-6C alkyl) $C(=O)O-$ or amino(1-6C alkyl) $C(=O)O-$.
9. A compound according to claim 8, wherein R^2 is selected from H, 2-methoxyethoxy, 3-methoxyprop-2-oxy, 2-methoxypropoxy, 2-ethoxyethoxy, and 2-hydroxyethoxy.
10. A compound according to claim 9, wherein R^2 is H.
- 25 11. A compound according to any of claims 1-7, wherein R^2 is selected from halogen, CN, OH, (1-6C)alkyl, fluoro(1-6C)alkyl, difluoro(1-6C)alkyl, trifluoro(1-6C)alkyl, hydroxy(1-6C)alkyl, fluoro(1-6C)alkoxy, difluoro(1-6C)alkoxy, trifluoro(1-6C)alkoxy, (1-3C alkoxy)(2-6C)alkoxy, (3-6C cycloalkyl)methoxy, oxetanylmethoxy (optionally substituted with methyl), tetrahydropyranyloxy, (1-6C alkyl)sulfanyl, 30 hydroxy(2-6C alkyl)sulfanyl, (1-3C alkylsulfanyl)(2-6C)alkoxy, $-COOH$, $hetAr^1$, $-C(=O)NR^eR^f$, $-NR^eC(=O)R^f$, and cyclopropyl optionally substituted with $-CH_2OH$ or $-CH_2O(1-6C \text{ alkyl})$.
12. A compound according to claim 1 or 2, wherein R^1 and R^2 together with the atoms to which they are attached form a 5-6 membered heterocyclic ring having 1 to 2

ring heteroatoms independently selected from O and N, wherein said ring is optionally substituted with (1-4C)alkyl.

13. A compound according to any of claims 1-12, wherein R^3 is selected from H, F and methyl.

5 14. A compound according to claim 13, wherein R^3 is H.

15. A compound according to claim 13, wherein R^3 is F.

16. A compound according to any of claims 1-15, wherein R^5 is CF_3 , CH_2F , CHF_2 , methyl or ethyl and R^{5a} is H.

17. A compound according to claim 16, wherein R^5 is CF_3 and R^{5a} is H.

10 18. A compound according to any of claims 1-15, wherein R^5 is CF_3 , CH_2F , CHF_2 , methyl or ethyl and R^{5a} is methyl.

19. A compound according to claim 15, wherein R^5 is methyl, and R^{5a} is H.

20. A compound according to any of claims 1-19, wherein R^6 is selected from H, NH_2 , OH, CH_3NH- , $(CH_3)_2CHNH-$, FCH_2CH_2NH- , $HOCH_2CH_2NH-$,
15 (cyclopropyl) CH_2NH- , $CH_3C(=O)NH-$, $(CH_3)_3COC(=O)NH-$ and NH_2CH_2- .

21. A compound according to claim 20, wherein R^6 is NH_2 .

22. A compound according to any of claims 1-21, wherein R^7 is selected from H, methyl, ethyl, FCH_2- and $HOCH_2-$.

23. A compound according to claim 22, wherein R^7 is H.

20 24. A compound according to claim 22, wherein R^7 is methyl.

25. A compound according to any of claims 1-19, wherein R^6 and R^7 together with the atom to which they are attached form a 5-6 membered spirocyclic heterocycle having a ring nitrogen atom.

26. A compound according to any of claims 1-25, wherein R^8 is selected from
25 H, F, OH or -OMe.

27. A compound according to claim 26, wherein R^8 is H.

28. A compound according to any of claims 1-19, wherein R^6 and R^8 together with the carbon atoms to which they are attached form a cyclopropyl ring optionally substituted with NH_2 .

30 29. A compound according to any of claims 1-28, wherein R^9 is H.

30. A compound according to any of claims 1-19, wherein R^6 and R^9 together form a linking group having the formula $-CH_2NH-$ which links the carbon atoms to which they are attached.

31. A compound according to any of claims 1-30, wherein R^{10} is H.

32. A compound according to any of claims 1 or 3-30, wherein R¹⁰ is fluoro.

33. A compound of claim 1, selected from anyone of Examples 1-328.

34. A composition comprising a compound according to any of claims 1-33 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable diluent or carrier.

35. A compound of Formula I as defined in anyone of claims 1 to 33, or a pharmaceutically acceptable salt thereof, for use in the treatment of an inflammatory or autoimmune disease.

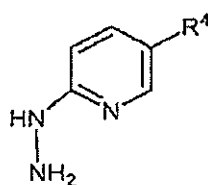
36. A compound as defined in claim 35, wherein the inflammatory or autoimmune disease is multiple sclerosis, lupus, inflammatory bowel disease or rheumatoid arthritis.

37. A compound of Formula I as defined in anyone of claims 1 to 33 or a pharmaceutically acceptable salt thereof, for use in the treatment of cancer.

38. A compound of Formula I as defined in anyone of claims 1 to 33, or a pharmaceutically acceptable salt thereof for use in the treatment of PIM-1 and/or PIM-2 and/or PIM-3 kinase-mediated condition.

39. A process for the preparation a compound of claim 1, which comprises:

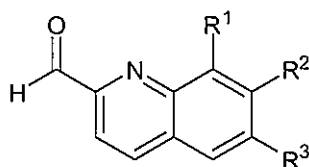
(a) reacting a corresponding compound of formula II or a protected derivative thereof



II

where R⁴ is as defined for Formula I, with a corresponding compound having the formula

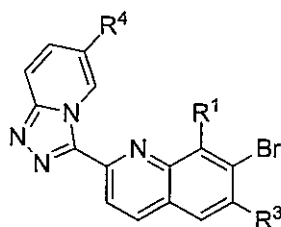
III or a protected derivative thereof



III

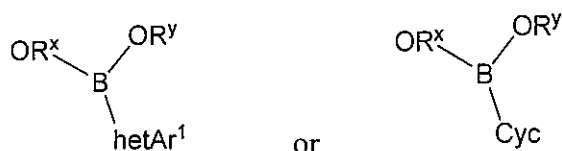
where R¹, R² and R³ are as defined for Formula I, in the presence of an organo hypervalent iodine reagent; or

(b) for a compound of Formula I where R^2 is hetAr^1 or a cyclopropyl ring optionally substituted with $-\text{CH}_2\text{OH}$ or $-\text{CH}_2\text{O}(1-6\text{C alkyl})$, reacting a corresponding compound having the formula IV or a protected derivative thereof:



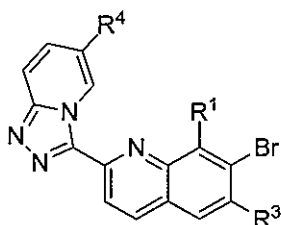
IV

where R^1 , R^3 and R^4 are as defined for Formula I, with a reagent having the formula



respectively, where hetAr^1 is as defined for Formula I, Cyc is cyclopropyl optionally substituted with $-\text{CH}_2\text{OH}$ or $-\text{CH}_2\text{O}(1-6\text{C alkyl})$, and R^x and R^y are H or (1-6C)alkyl, or R^x and R^y together with the atoms to which they are connected form a 5-6 membered ring optionally substituted with 1-4 substituents selected from (1-3C alkyl), wherein said reaction takes place in the presence of a palladium catalyst and optionally in the presence of a base and a ligand; or

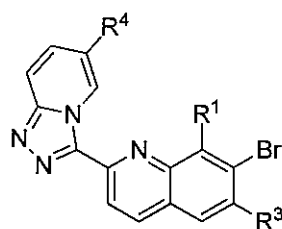
(c) for a compound of Formula I where R^2 is $-\text{NR}^e\text{C}(=\text{O})\text{R}^f$, reacting a corresponding compound having the formula IV or a protected derivative thereof:



IV

where R^1 , R^3 and R^4 are as defined for Formula I, with a reagent having the formula $\text{HNR}^e\text{C}(=\text{O})\text{R}^f$ in the presence of a base and a metal catalyst; or

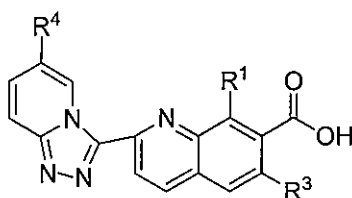
(d) for a compound of Formula I where R^2 is (1-6C alkyl)sulfanyl or hydroxy(2-6C alkyl)sulfanyl, reacting a corresponding compound having the formula IV or a protected derivative thereof:



IV

where R^1 , R^2 , R^3 and R^4 are as defined for Formula I, with a reagent having the formula $HS(1-6C \text{ alkyl})$ or $HS(1-6C \text{ alkyl})OH$, respectively, in the presence of a base; or

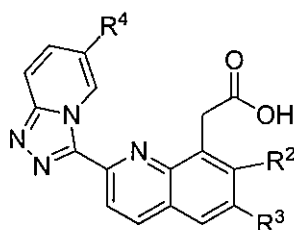
- 5 (e) for a compound of Formula I where R^2 is $-C(=O)NR^eR^f$, coupling a corresponding compound having the formula V or a protected derivative thereof:



V

- 10 where R^1 , R^3 and R^4 are as defined for Formula I, with a reagent having the formula HNR^eR^f , where R^e and R^f are as defined for Formula I, in the presence of a base and a coupling reagent; or

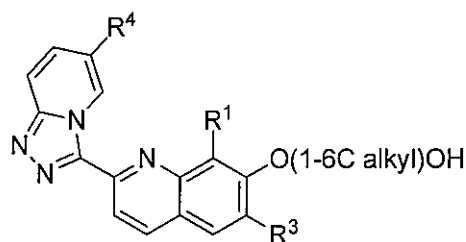
(f) for a compound of Formula I where R^1 is $-CH_2C(=O)NR^eR^d$, coupling a corresponding compound having the formula VI or a protected derivative thereof



VI

- 15 where R^2 , R^3 and R^4 are as defined for Formula I, with a reagent having the formula HNR^eR^d , where R^e and R^d are as defined for Formula I, in the presence of a base and a coupling reagent; or

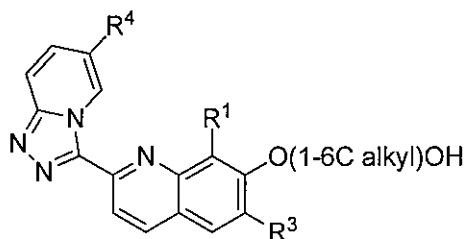
- 20 (g) for a compound of Formula I where R^2 is (1-6C)alkoxy substituted with (1-6C alkyl) $C(=O)O-$, coupling a corresponding compound having the formula VII or a protected derivative thereof



VII

where R^1 , R^3 and R^4 are as defined for Formula I, with a (1-6C)alkyl acid anhydride or a (1-6C)alkyl acid chloride in the presence of a base; or

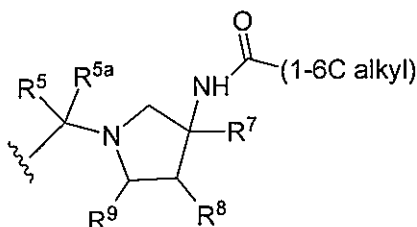
- 5 (h) for a compound of Formula I where R^2 is (1-6C)alkoxy substituted with amino(1-6C alkyl)C(=O)O-, coupling a corresponding compound having the formula **VII** or a protected derivative thereof



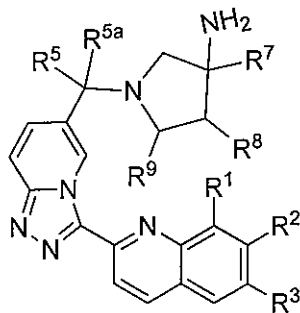
VII

- 10 where R^1 , R^3 and R^4 are as defined for Formula I, with a compound having the formula $P^1NH(1-6C \text{ alkyl})C(=O)OH$ where P^1 is H or an amine protecting group, in the presence of a base and a coupling reagent; or

- (i) for a compound of Formula I where R^4 is a moiety having the structure



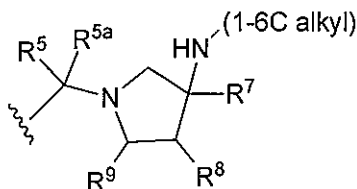
- 15 where R^5 , R^{5a} , and R^7 are as defined for Formula I, R^8 is H, halogen, OH, or (1-6C)alkoxy, and R^9 is H, reacting a corresponding compound having the formula **VIII**



VIII

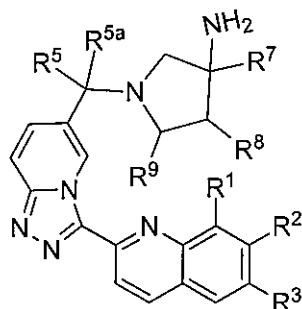
where R^1 , R^2 , R^3 , R^5 , R^{5a} , and R^7 are as defined for Formula I, R^8 is H, halogen, OH, or (1-6C)alkoxy, and R^9 is H, with a (1-6C)alkylcarboxylic acid anhydride or a (1-6C)alkylcarboxylic acid chloride in the presence of a base; or

(j) for a compound of Formula I where R^4 is a moiety having the structure



5

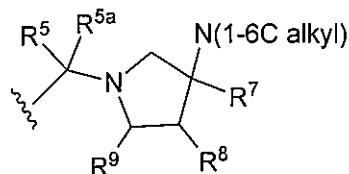
where R^5 , R^{5a} , and R^7 are as defined for Formula I, R^8 is H, halogen, OH, or (1-6C)alkoxy, and R^9 is H, reacting a corresponding compound having the formula VIII



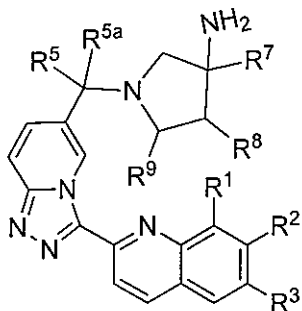
VIII

10 where R^1 , R^2 , R^3 , R^5 , R^{5a} and R^7 are as defined for Formula I, R^8 is H, halogen, OH, or (1-6C)alkoxy, and R^9 is H, with a (1-6C)aldehyde or a protected (1-6C)aldehyde in the presence of a catalyst and a base followed by treatment with a reducing agent; or

(k) for a compound of Formula I where R^4 is a moiety having the structure



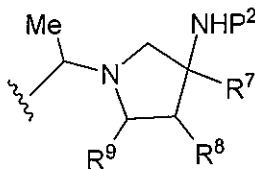
15 where R^5 , R^{5a} , and R^7 are as defined for Formula I, R^8 is H, halogen, OH, or (1-6C)alkoxy, and R^9 is H, reacting a corresponding compound having the formula VIII



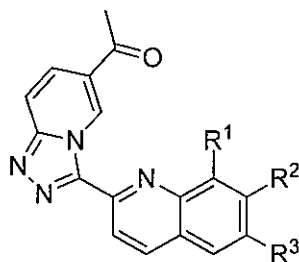
VIII

where R^1 , R^2 , R^3 , R^5 , R^{5a} , and R^7 are as defined for Formula I, R^8 is H, halogen, OH, or (1-6C)alkoxy, and R^9 is H, in the presence of a reagent having the formula $HC(=O)(1-5C\text{ alkyl})$ and a reducing agent; or

(l) for a compound of Formula I where R^4 is a moiety having the structure



where R^7 is as defined for Formula I, R^8 is H, halogen, OH, or (1-6C)alkoxy, R^9 is H, and P^2 is H or an amine protecting group, reacting a corresponding compound having the formula IX

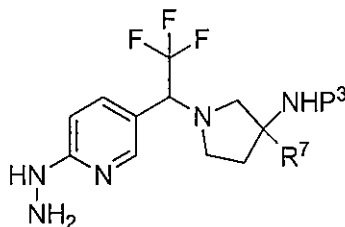


IX

where R^1 , R^2 , and R^3 are as defined for Formula I, in the presence of a Lewis acid, followed by treatment with a reducing agent; and

removing any protecting group or groups and, if desired, forming a salt.

40. A compound having the formula II-A



II-A

including enantiomers and diastereomers thereof, where P^3 is H or an amine protecting group and R^7 is H, (1-6C)alkyl, fluoro(1-6C)alkyl or hydroxy(1-6C)alkyl.

41. A compound of claim 40, wherein R^7 is H or (1-6C)alkyl.

42. A compound of claim 41, wherein R^7 is H or methyl.