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(54) Title: TRICYCLIC KINASE INHIBITORS

(57) Abstract: A series of fused tricyclic thiazole and thiophene derivatives which are substituted in the 2-position of the thiazole or thiophene ring by an optionally substituted morpholin-4-yl moiety, being selective inhibitors of PI3 kinase enzymes, are accordingly of benefit in medicine, for example in the treatment of inflammatory, autoimmune, cardiovascular, neurodegenerative, metabolic, oncological, nociceptive or ophthalmic conditions.

TRICYCLIC KINASE INHIBITORS

The present invention relates to a class of fused tricylic thiazole and thiophene derivatives, and to their use in therapy. More particularly, the invention provides a family of fused tricylic thiazole and thiophene derivatives which are substituted in the 2-position of the thiazole or thiophene ring by an optionally substituted morpholin-4-yl moiety. These compounds are selective inhibitors of phosphoinositide 3-kinase (PI3K) enzymes, and are accordingly of benefit as pharmaceutical agents, especially in the treatment of adverse inflammatory, autoimmune, cardiovascular, neurodegenerative, metabolic, oncological, nociceptive and ophthalmic conditions.

The PI3K pathway is implicated in a variety of physiological and pathological functions that are believed to be operative in a range of human diseases. Thus, PI3Ks provide a critical signal for cell proliferation, cell survival, membrane trafficking, glucose transport, neurite outgrowth, membrane ruffling, superoxide production, actin reorganization and chemotaxis (cf. S. Ward *et al.*, *Chemistry & Biology*, 2003, **10**, 207-213; and S.G. Ward & P. Finan, *Current Opinion in Pharmacology*, 2003, **3**, 426-434); and are known to be involved in the pathology of cancer, and metabolic, inflammatory and cardiovascular diseases (cf. M.P. Wymann *et al.*, *Trends in Pharmacol. Sci.*, 2003, **24**, 366-376). Aberrant upregulation of the PI3K pathway is implicated in a wide variety of human cancers (cf. S. Brader & S.A. Eccles, *Tumori*, 2004, **90**, 2-8).

The compounds in accordance with the present invention, being potent and selective PI3K inhibitors, are therefore beneficial in the treatment and/or prevention of various human ailments. These include autoimmune and inflammatory disorders such as rheumatoid arthritis, multiple sclerosis, asthma, inflammatory bowel disease, psoriasis and transplant rejection; cardiovascular disorders including thrombosis, cardiac hypertrophy, hypertension, and irregular contractility of the heart (e.g. during heart failure); neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, Huntington's disease, stroke, amyotrophic lateral sclerosis, spinal cord injury, head trauma and seizures; metabolic disorders such as obesity and type 2 diabetes; oncological conditions including leukaemia, glioblastoma, lymphoma, melanoma, and human cancers of the liver, bone, skin, brain, pancreas, lung, breast, stomach, colon, rectum, prostate, ovary and cervix; pain and nociceptive disorders; and ophthalmic disorders including age-related macular degeneration (ARMD).

In addition, the compounds in accordance with the present invention may be beneficial as pharmacological standards for use in the development of new biological tests and in the search for new pharmacological agents. Thus, the compounds of this invention may be useful as radioligands in assays for detecting compounds capable of binding to human PI3K enzymes.

Various fused thiazole derivatives are disclosed in *Liebigs Annalen der Chemie*, 1986, 780-784; and in *Russian Journal of General Chemistry* (translation of *Zhurnal Obshchei Khimii*), 2000, **70**[5], 784-787. However, none of the compounds disclosed in either of those publications corresponds to a compound of the present invention; and no therapeutic utility is ascribed to any of the compounds disclosed therein.

WO 2006/040281 describes a class of 4,5-dihydrothiazolo[4,5-*g*]indazoles which are stated to be suitable for use in the treatment of diseases that are characterized by excessive or abnormal cell proliferation. The compounds described in that publication do not, however, possess an optionally substituted morpholin-4-yl moiety at the 2-position of the thiazole ring.

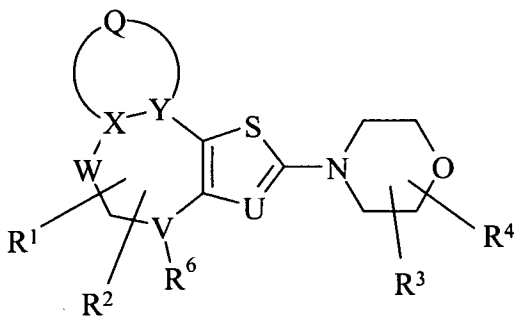
WO 2006/114606 describes a class of fused bicyclic thiazole derivatives which are selective inhibitors of PI3 kinase enzymes and are accordingly of benefit in medicine, for example in the treatment of inflammatory, autoimmune, cardiovascular, neurodegenerative, metabolic, oncological, nociceptive and ophthalmic conditions. A related series of compounds is described in copending international patent application no. PCT/GB2007/002390, published on 3 January 2008 as WO 2008/001076.

Copending international patent application no. PCT/GB2007/002051, published on 13 December 2007 as WO 2007/141504, describes a class of fused bicyclic thiophene derivatives which are selective inhibitors of PI3 kinase enzymes and are accordingly of benefit in medicine, for example in the treatment of inflammatory, autoimmune, cardiovascular, neurodegenerative, metabolic, oncological, nociceptive and ophthalmic conditions.

The compounds in accordance with the present invention are potent and selective PI3K inhibitors having a binding affinity (IC_{50}) for the human PI3Kα and/or PI3Kβ and/or PI3Kγ and/or PI3Kδ isoform of 50 μM or less, generally of 20 μM or less, usually of 5 μM or less, typically of 1 μM or less, suitably of 500 nM or less, ideally of 100 nM or less, and preferably of 20 nM or less (the skilled person will appreciate that a *lower* IC_{50} figure denotes a *more active* compound). The compounds of the invention may possess at least a

10-fold selective affinity, typically at least a 20-fold selective affinity, suitably at least a 50-fold selective affinity, and ideally at least a 100-fold selective affinity, for the human PI3Kα and/or PI3Kβ and/or PI3Kγ and/or PI3Kδ isoform relative to other human kinases.

The present invention provides a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof:



(I)

wherein

U represents N or C-R^5;

V represents a covalent bond or a methylene linkage;

W represents a covalent bond or a methylene linkage;

the moiety X-Y-Q represents an optionally substituted five-membered heteroaromatic ring selected from furyl, thienyl, pyrrolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl and tetrazolyl; or an optionally substituted six-membered heteroaromatic ring selected from pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl and triazinyl;

R^1 and R^2 independently represent hydrogen, hydroxy or amino; or C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, di(C_{1-6})alkylamino, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl(C_{1-6})alkyl, aryl, aryl(C_{1-6})alkyl, C_{3-7} heterocycloalkyl, C_{3-7} heterocycloalkyl(C_{1-6})alkyl, heteroaryl or heteroaryl(C_{1-6})alkyl, any of which groups may be optionally substituted by one or more substituents; or

R^1 and R^2, when both are attached to the same carbon atom, represent, when taken together with the carbon atom to which they are both attached, C_{3-7} cycloalkyl or C_{3-7} heterocycloalkyl, either of which groups may be optionally substituted by one or more substituents; or

R^1 and R^2, when attached to adjacent carbon atoms, represent, when taken together with the carbon atoms to which they are attached, C_{5-7} cycloalkyl, phenyl or heteroaryl, any of which groups may be optionally benzo-fused and/or substituted by one or more substituents;

R^3 and R^4 independently represent hydrogen; or C_{1-6} alkyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl(C_{1-6})alkyl, aryl, aryl(C_{1-6})alkyl, aryl(C_{2-6})alkenyl, aryl(C_{2-6})-alkynyl, biaryl(C_{1-6})alkyl, C_{3-7} heterocycloalkyl, C_{3-7} heterocycloalkyl(C_{1-6})alkyl, C_{3-7} heterocycloalkylcarbonyl, heteroaryl, heteroaryl(C_{1-6})alkyl, heteroaryl-aryl(C_{1-6})alkyl or aryl-heteroaryl(C_{1-6})alkyl, any of which groups may be optionally substituted by one or more substituents; or

R^3 and R^4, when both are attached to the same carbon atom, represent, when taken together with the carbon atom to which they are both attached, C_{3-7} cycloalkyl or C_{3-7} heterocycloalkyl, either of which groups may be optionally substituted by one or more substituents; or

R^3 and R^4, when attached to adjacent carbon atoms, represent, when taken together with the carbon atoms to which they are attached, C_{5-7} cycloalkyl, phenyl or heteroaryl, any of which groups may be optionally benzo-fused and/or substituted by one or more substituents;

R^5 represents hydrogen, halogen, cyano, $-SR^a$, $-COR^e$, $-CO_2R^b$ or $-CONR^cR^d$; or R^5 represents C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkenylcarbonyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl(C_{1-6})alkyl, C_{3-7} cycloalkyl(C_{2-6})alkenyl, C_{3-7} cycloalkyl(C_{2-6})alkynyl, aryl, aryl(C_{1-6})alkyl, aryl(C_{2-6})alkenyl, aryl(C_{2-6})alkynyl, biaryl, C_{3-7} heterocycloalkyl, C_{3-7} heterocycloalkyl(C_{1-6})alkyl, C_{3-7} heterocycloalkyl(C_{2-6})alkenyl, C_{3-7} heterocycloalkyl-(C_{2-6})alkynyl, C_{3-7} heterocycloalkylcarbonyl(C_{2-6})alkynyl, C_{5-9} heterobicycloalkyl-(C_{2-6})alkynyl, C_{3-7} heterocycloalkyl-aryl, C_{3-7} heterocycloalkyl(C_{1-6})alkyl-aryl, C_{3-7} heterocycloalkyl-biaryl, heteroaryl, heteroaryl(C_{1-6})alkyl, heteroaryl(C_{1-6})alkylcarbonyl, heteroaryl(C_{2-6})alkenyl, heteroaryl(C_{2-6})alkynyl, heteroaroylcarbonyl, C_{3-7} heterocycloalkyl-heteroaryl, C_{3-7} heterocycloalkyl-heteroaryl(C_{2-6})alkynyl, heteroaryl-aryl, heteroaryl-aryl(C_{1-6})alkyl, aryl-heteroaryl, aryl-heteroaryl(C_{1-6})alkyl, C_{3-7} heterocycloalkyl-aryl-heteroaryl, C_{3-7} heterocycloalkyl(C_{1-6})alkyl-aryl-heteroaryl, C_{5-9} heterobicycloalkyl(C_{1-6})alkyl-aryl-heteroaryl, heteroaryl-aryl-heteroaryl, bi(heteroaryl), C_{3-7} heterocycloalkylcarbonyl-bi(heteroaryl), aryloxyaryl, aryl(C_{1-6})alkoxyaryl, heteroaryl(C_{1-6})alkoxyaryl, aryl(C_{1-6})alkylaminoaryl, heteroaryl(C_{1-6})alkylaminoaryl, C_{3-7}

cycloalkylcarbonylaminoaryl, arylcarbonylaminoaryl, aryl(C_{1-6})alkylcarbonylaminoaryl, C_{3-7} heterocycloalkylcarbonylaminoaryl, heteroarylcarbonylaminoaryl, aryl-(C_{3-7})heterocycloalkylcarbonylaminoaryl, arylsulphonylaminoaryl, aryl(C_{1-6})alkyl-sulphonylaminoaryl, heteroaryl(C_{1-6})alkylsulphonylaminoaryl, C_{3-7} cycloalkylamino-carbonylaminoaryl, arylaminocarbonylaminoaryl, C_{3-7} heterocycloalkylaminocarbonyl-aminoaryl, C_{3-7} heterocycloalkylaminocarbonylaminoaryl, heteroaryl(C_{1-6})alkyl-aminocarbonylaminoaryl, C_{3-7} heterocycloalkylcarbonylcarbonylaminoaryl, C_{3-7} heterocycloalkyl(C_{1-6})alkylaminocarbonylcarbonylaminoaryl, arylcarbonylaryl, C_{3-7} heterocycloalkylcarbonylaryl, C_{3-7} heterocycloalkylcarbonyl(C_{1-6})alkylaryl, aryl(C_{1-6})-alkylaminocarbonylaryl, C_{3-7} heterocycloalkyl(C_{1-6})alkylaminocarbonylaryl, heteroaryl-aminocarbonylaryl, heteroaryl(C_{1-6})alkylaminocarbonylaryl, C_{3-7} heterocycloalkylamino-carbonyl(C_{1-6})alkylaryl, C_{3-7} heterocycloalkyl(C_{1-6})alkylaminocarbonyl(C_{1-6})alkylaryl, heteroarylaminocarbonyl(C_{1-6})alkylaryl, heteroaryl(C_{1-6})alkylaminocarbonyl(C_{1-6})alkyl-aryl, arylaminoheteroaryl, C_{3-7} heterocycloalkylamino-aryl-heteroaryl, C_{3-7} heterocycloalkylcarbonylamino-aryl-heteroaryl, C_{3-7} heterocycloalkylaminocarbonyl-amino-aryl-heteroaryl, C_{3-7} heterocycloalkylcarbonyl-aryl-heteroaryl, C_{3-7} heterocycloalkyl(C_{1-6})alkylcarbonyl-aryl-heteroaryl, C_{5-9} heterobicycloalkylcarbonyl-aryl-heteroaryl, C_{3-7} heterocycloalkylcarbonyl(C_{1-6})alkyl-aryl-heteroaryl, C_{3-7} heterocycloalkyl-aminocarbonyl-aryl-heteroaryl, C_{3-7} heterocycloalkyl(C_{1-6})alkylaminocarbonyl-aryl-heteroaryl or C_{3-7} heterocycloalkylaminocarbonyl(C_{1-6})alkyl-aryl-heteroaryl, any of which groups may be optionally substituted by one or more substituents;

R^a represents C_{1-6} alkyl, aryl or heteroaryl, any of which groups may be optionally substituted by one or more substituents;

R^b represents hydrogen; or optionally substituted C_{1-6} alkyl;

R^c represents hydrogen; or C_{1-6} alkyl, aryl, aryl(C_{1-6})alkyl, heteroaryl, heteroaryl(C_{1-6})alkyl or (aryl)(heteroaryl)(C_{1-6})alkyl, any of which groups may be optionally substituted by one or more substituents;

R^d represents hydrogen or C_{1-6} alkyl;

R^e represents C_{1-6} alkyl;

R^6 is absent when V represents a covalent bond; or R^6 represents hydrogen, hydroxy, oxo or $-NR^{6a}R^{6b}$; and

R^{6a} and R^{6b} independently represent hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl(C_{1-6})alkyl, aryl, aryl(C_{1-6})alkyl, heteroaryl or heteroaryl(C_{1-6})alkyl, any of which groups may be optionally substituted by one or more substituents.

The present invention also provides a compound of formula (I) as depicted above, or a pharmaceutically acceptable salt or solvate thereof, wherein

R^1 and R^2 independently represent hydrogen; or C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl(C_{1-6})alkyl, aryl, aryl(C_{1-6})alkyl, C_{3-7} heterocycloalkyl, C_{3-7} heterocycloalkyl-(C_{1-6})alkyl, heteroaryl or heteroaryl(C_{1-6})alkyl, any of which groups may be optionally substituted by one or more substituents; or

R^1 and R^2, when both are attached to the same carbon atom, represent, when taken together with the carbon atom to which they are both attached, C_{3-7} cycloalkyl or C_{3-7} heterocycloalkyl, either of which groups may be optionally substituted by one or more substituents; or

R^1 and R^2, when attached to adjacent carbon atoms, represent, when taken together with the carbon atoms to which they are attached, C_{5-7} cycloalkyl, phenyl or heteroaryl, any of which groups may be optionally benzo-fused and/or substituted by one or more substituents; and

U, V, W, the moiety X-Y-Q, R^3, R^4 and R^6 are as defined above.

Where any of the groups in the compounds of formula (I) above is stated to be optionally substituted, this group may be unsubstituted, or substituted, where possible, by one or more substituents. Typically, such groups will be unsubstituted, or substituted, where possible, by one or two substituents. Suitably, such groups will be unsubstituted or, where possible, monosubstituted.

For use in medicine, the salts of the compounds of formula (I) will be pharmaceutically acceptable salts. Other salts may, however, be useful in the preparation of the compounds of the invention or of their pharmaceutically acceptable salts. Suitable pharmaceutically acceptable salts of the compounds of this invention include acid addition salts which may, for example, be formed by mixing a solution of the compound of the invention with a solution of a pharmaceutically acceptable acid such as hydrochloric acid, sulphuric acid, methanesulphonic acid, fumaric acid, maleic acid, succinic acid, acetic acid, benzoic acid, citric acid, tartaric acid or phosphoric acid. Furthermore, where the compounds of the invention carry an acidic moiety, e.g. carboxy, suitable pharmaceutically acceptable salts thereof may include alkali metal salts, e.g. sodium or

potassium salts; alkaline earth metal salts, e.g. calcium or magnesium salts; and salts formed with suitable organic ligands, e.g. quaternary ammonium salts.

The present invention includes within its scope solvates of the compounds of formula (I) above. Such solvates may be formed with common organic solvents, e.g. hydrocarbon solvents such as benzene or toluene; chlorinated solvents such as chloroform or dichloromethane; alcoholic solvents such as methanol, ethanol or isopropanol; ethereal solvents such as diethyl ether or tetrahydrofuran; or ester solvents such as ethyl acetate. Alternatively, the solvates of the compounds of formula (I) may be formed with water, in which case they will be hydrates.

Suitable alkyl groups which may be present on the compounds of the invention include straight-chained and branched C_{1-6} alkyl groups, for example C_{1-4} alkyl groups. Typical examples include methyl and ethyl groups, and straight-chained or branched propyl, butyl and pentyl groups. Particular alkyl groups include methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, *sec*-butyl, isobutyl, *tert*-butyl, 2,2-dimethylpropyl and 3-methylbutyl. Derived expressions such as "C_{1-6} alkoxy", "C_{1-6} alkylthio", "C_{1-6} alkylsulphonyl" and "C_{1-6} alkylamino" are to be construed accordingly.

Typical C_{2-6} alkenyl groups include vinyl and allyl.

Typical C_{2-6} alkynyl groups include ethynyl, prop-1-yn-1-yl, prop-2-yn-1-yl, but-1-yn-1-yl and 3-methylbut-1-yn-1-yl. A specific C_{2-6} alkynyl group is prop-2-yn-1-yl.

Specific C_{3-7} cycloalkyl groups are cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl.

Suitable aryl groups include phenyl and naphthyl, preferably phenyl.

Suitable aryl(C_{1-6})alkyl groups include benzyl, phenylethyl, phenylpropyl and naphthylmethyl.

Specific aryl(C_{2-6})alkenyl groups include 2-phenylethenyl and 3-phenylprop-2-en-1-yl.

Typical aryl(C_{2-6})alkynyl groups include phenylethynyl, 3-phenylprop-1-yn-1-yl and 3-phenylprop-2-yn-1-yl. A specific aryl(C_{2-6})alkynyl group is 3-phenylprop-2-yn-1-yl.

Particular biaryl groups include biphenyl and naphthylphenyl.

Suitable heterocycloalkyl groups, which may comprise benzo-fused analogues thereof, include azetidinyl, tetrahydrofuranyl, dihydrobenzofuranyl, pyrrolidinyl, indolinyl, thiazolidinyl, imidazolidinyl, tetrahydropyranyl, chromanyl, piperidinyl, 1,2,3,4-

tetrahydroquinolinyl, 1,2,3,4-tetrahydroisoquinolinyl, piperazinyl, 1,2,3,4-tetrahydroquinoxalinyl, homopiperazinyl, morpholinyl, benzoxazinyl and thiomorpholinyl.

Typical heterobicycloalkyl groups include quinuclidinyl, 8-azabicyclo[3.2.1]octyl and 3,8-diazabicyclo[3.2.1]octyl.

Suitable heteroaryl groups include furyl, benzofuryl, dibenzofuryl, thienyl, benzothienyl, dibenzothienyl, pyrrolyl, indolyl, pyrrolo[2,3-*b*]pyridinyl, pyrrolo[3,2-*c*]-pyridinyl, pyrazolyl, pyrazolo[1,5-*a*]pyridinyl, indazolyl, oxazolyl, benzoxazolyl, isoxazolyl, thiazolyl, benzothiazolyl, isothiazolyl, imidazolyl, benzimidazolyl, imidazo[1,2-*a*]pyridinyl, imidazo[4,5-*b*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyrazinyl, oxadiazolyl, thiadiazolyl, triazolyl, benzotriazolyl, tetrazolyl, pyridinyl, quinolinyl, isoquinolinyl, pyridazinyl, cinnolinyl, pyrimidinyl, pyrazinyl, quinoxalinyl and chromenyl groups.

The term "halogen" as used herein is intended to include fluorine, chlorine, bromine and iodine atoms, especially fluoro or chloro.

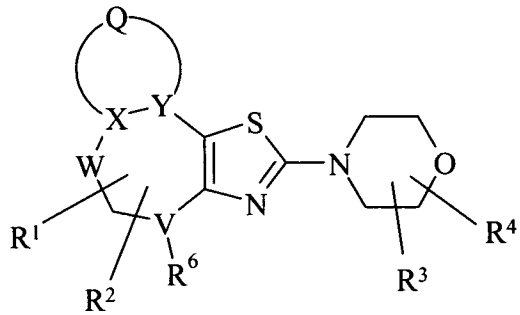
Where the compounds of formula (I) have one or more asymmetric centres, they may accordingly exist as enantiomers. Where the compounds of the invention possess two or more asymmetric centres, they may additionally exist as diastereomers. The invention is to be understood to extend to all such enantiomers and diastereomers, and to mixtures thereof in any proportion, including racemates. Formula (I) and the formulae depicted hereinafter are intended to represent all individual stereoisomers and all possible mixtures thereof, unless stated or shown otherwise. In addition, compounds of formula (I) may exist as tautomers, for example keto ($CH_2C=O$)↔enol (CH=CHOH) tautomers or amide (NHC=O)↔hydroxyimine (N=COH) tautomers. Formula (I) and the formulae depicted hereinafter are intended to represent all individual tautomers and all possible mixtures thereof, unless stated or shown otherwise.

In one embodiment, the moiety X-Y-Q in the compounds of formula (I) above represents an optionally substituted five-membered heteroaromatic ring selected from furyl, thienyl, pyrrolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl and tetrazolyl. In another embodiment, the moiety X-Y-Q in the compounds of formula (I) above represents an optionally substituted six-membered heteroaromatic ring selected from pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl and triazinyl.

Suitably, the moiety X-Y-Q represents a pyrazolyl, isoxazolyl, imidazolyl, triazolyl, tetrazolyl or pyrimidinyl ring, any of which may be optionally substituted, where possible, by one or more substituents.

The five-membered or six-membered heteroaromatic ring represented by the moiety X-Y-Q in the compounds of formula (I) above may be unsubstituted, or may suitably be substituted, where possible, by one more, typically by one or two, substituents. In one embodiment, this ring is unsubstituted. In another embodiment, this ring is monosubstituted. In a further embodiment, this ring is disubstituted. Examples of typical substituents on the five-membered or six-membered heteroaromatic ring as specified for the moiety X-Y-Q include C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl(C_{1-6})alkyl, aryl, aryl(C_{1-6})alkyl, C_{3-7} heterocycloalkyl, C_{3-7} heterocycloalkyl(C_{1-6})alkyl, heteroaryl, heteroaryl(C_{1-6})alkyl, hydroxy, C_{1-6} alkoxy, C_{1-6} alkylthio, C_{1-6} alkylsulphinyl, C_{1-6} alkylsulphonyl, C_{2-6} alkylcarbonyl, amino, C_{1-6} alkylamino, di(C_{1-6})alkylamino, halogen, cyano and trifluoromethyl. Examples of particular substituents include C_{1-6} alkyl, hydroxy and C_{1-6} alkylsulphonyl. Examples of suitable substituents include C_{1-6} alkyl and C_{1-6} alkylsulphonyl.

In one embodiment of the present invention, U represents N. In accordance with that embodiment, the present invention provides a compound of formula (A), or a pharmaceutically acceptable salt or solvate thereof:

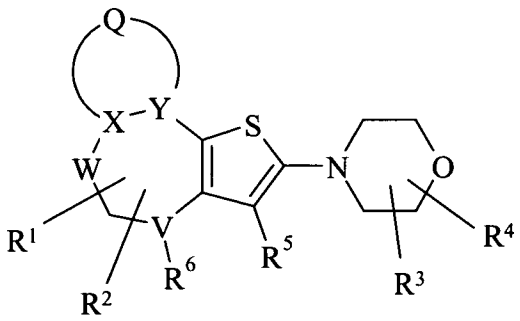


(A)

wherein

V, W, the moiety X-Y-Q, R^1, R^2, R^3, R^4 and R^6 are as defined above.

In another embodiment of the present invention, U represents C-R^5. In accordance with that embodiment, the present invention provides a compound of formula (B), or a pharmaceutically acceptable salt or solvate thereof:

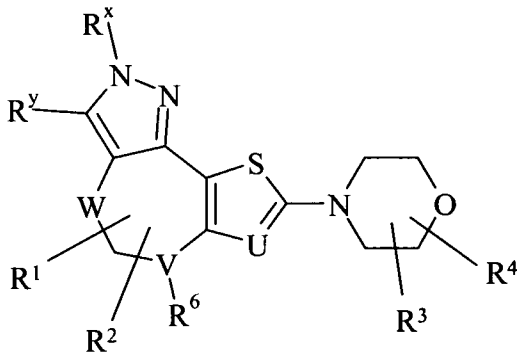


(B)

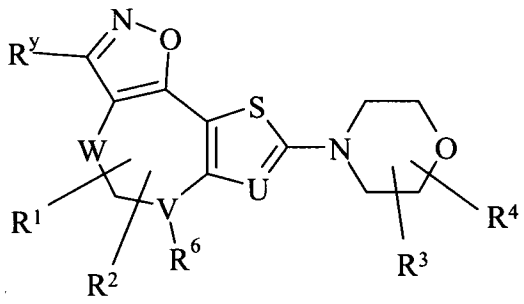
wherein

V, W, the moiety X-Y-Q, R^1, R^2, R^3, R^4, R^5 and R^6 are as defined above.

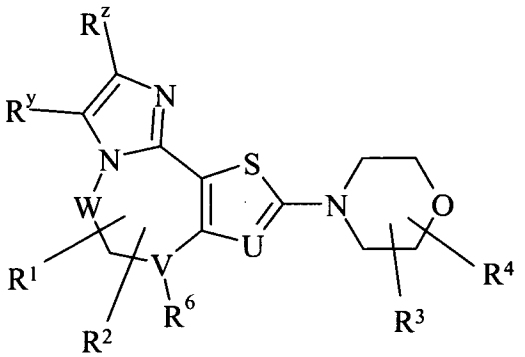
Specific sub-classes of compounds in accordance with the present invention are represented by the compounds of formula (IA), (IB), (IC), (ID), (IE) and (IF):



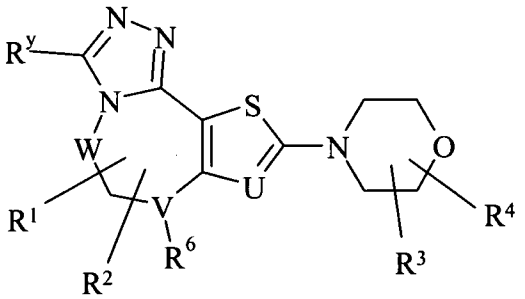
(IA)



(IB)



(IC)



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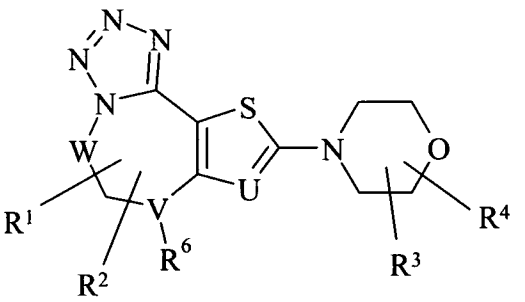
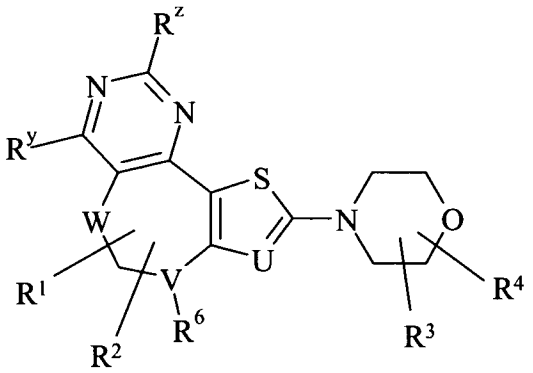


(IE)



(IF)

wherein U, V, W, R^1, R^2, R^3, R^4 and R^6 are as defined above;

R^x represents hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl(C_{1-6})alkyl, aryl, aryl(C_{1-6})alkyl, C_{3-7} heterocycloalkyl, C_{3-7} heterocycloalkyl(C_{1-6})alkyl, heteroaryl, heteroaryl(C_{1-6})alkyl, C_{1-6} alkylsulphonyl or C_{2-6} alkylcarbonyl; and

R^y and R^z independently represent hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl(C_{1-6})alkyl, aryl, aryl(C_{1-6})alkyl, C_{3-7} heterocycloalkyl, C_{3-7} heterocycloalkyl-

(C_{1-6})alkyl, heteroaryl, heteroaryl(C_{1-6})alkyl, hydroxy, C_{1-6} alkoxy, C_{1-6} alkylthio, C_{1-6} alkylsulphinyl, C_{1-6} alkylsulphonyl, C_{2-6} alkylcarbonyl, amino, C_{1-6} alkylamino, di(C_{1-6})alkylamino, halogen, cyano or trifluoromethyl.

Where U represents C-R^5, a particular sub-class of compounds in accordance with the present invention is represented by the compounds of formula (IA) as depicted above. Where U represents N, particular sub-classes of compounds in accordance with the present invention are represented by the compounds of formula (IA), (IB), (IC), (ID), (IE) and (IF) as depicted above.

Suitably, R^x represents hydrogen or C_{1-6} alkylsulphonyl. In one embodiment, R^x represents hydrogen. In another embodiment, R^x represents C_{1-6} alkylsulphonyl, especially methylsulphonyl.

Suitably, R^y and R^z independently represent hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl(C_{1-6})alkyl, aryl, aryl(C_{1-6})alkyl, C_{3-7} heterocycloalkyl, C_{3-7} hetero-cycloalkyl(C_{1-6})alkyl, heteroaryl, heteroaryl(C_{1-6})alkyl, C_{1-6} alkoxy, C_{1-6} alkylthio, C_{1-6} alkylsulphinyl, C_{1-6} alkylsulphonyl, C_{2-6} alkylcarbonyl, amino, C_{1-6} alkylamino, di(C_{1-6})alkylamino, halogen, cyano or trifluoromethyl.

Typical values of R^y and/or R^z include hydrogen, hydroxy and C_{1-6} alkyl.

Suitable values of R^y and/or R^z include hydrogen and C_{1-6} alkyl.

In one embodiment, R^y represents hydrogen. In another embodiment, R^y represents C_{1-6} alkyl, especially methyl. In a further embodiment, R^y represents hydroxy.

In one embodiment, R^z represents hydrogen. In another embodiment, R^z represents C_{1-6} alkyl, especially methyl.

In one embodiment, V represents a covalent bond. In another embodiment, V represents a methylene linkage.

In one embodiment, W represents a covalent bond. In another embodiment, W represents a methylene linkage.

Suitably, R^1 represents hydrogen or C_{1-6} alkyl. Typical values of R^1 include hydrogen, methyl and ethyl. In one embodiment, R^1 is hydrogen. In another embodiment, R^1 is C_{1-6} alkyl. In one aspect of that embodiment, R^1 is methyl. In another aspect of that embodiment, R^1 is ethyl.

Suitably, R^2 represents hydrogen; or C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-7} cycloalkyl or aryl, any of which groups may be optionally substituted by one or more substituents.

Examples of typical substituents on R^1 and/or R^2 include halogen, cyano, nitro, C_{1-6} alkyl, trifluoromethyl, hydroxy, C_{1-6} alkoxy, difluoromethoxy, trifluoromethoxy, aryloxy, C_{1-6} alkylthio, C_{1-6} alkylsulphonyl, amino, C_{1-6} alkylamino, di(C_{1-6})alkylamino, C_{2-6} alkylcarbonylamino, C_{2-6} alkoxycarbonylamino, C_{1-6} alkylsulphonylamino, formyl, C_{2-6} alkylcarbonyl, carboxy, C_{2-6} alkoxycarbonyl, aminocarbonyl, C_{1-6} alkylaminocarbonyl, di(C_{1-6})alkylaminocarbonyl, aminosulphonyl, C_{1-6} alkylaminosulphonyl and di(C_{1-6})alkylaminosulphonyl; especially halogen, C_{1-6} alkoxy or C_{1-6} alkylthio.

Examples of particular substituents on R^1 and/or R^2 include fluoro, chloro, bromo, cyano, nitro, methyl, trifluoromethyl, hydroxy, methoxy, difluoromethoxy, trifluoromethoxy, phenoxy, methylthio, methylsulphonyl, amino, methylamino, dimethylamino, acetylamino, methoxycarbonylamino, methylsulphonylamino, formyl, acetyl, carboxy, methoxycarbonyl, aminocarbonyl, methylaminocarbonyl, dimethylaminocarbonyl, aminosulphonyl, methylaminosulphonyl and dimethylaminosulphonyl; especially chloro, methoxy or methylthio.

Typical values of R^2 include hydrogen, methyl, ethoxy, *n*-propyl, isopropyl, isobutyl, cyclohexyl and phenyl. A particular value of R^2 is methyl.

Alternatively, R^1 and R^2, when both are attached to the same carbon atom, may together form an optionally substituted spiro linkage. Thus, R^1 and R^2, when both are attached to the same carbon atom, may represent, when taken together with the carbon atom to which they are both attached, C_{3-7} cycloalkyl or C_{3-7} heterocycloalkyl, either of which groups may be unsubstituted, or substituted by one or more, typically by one or two, substituents. In this context, R^1 and R^2, when taken together with the carbon atom to which they are both attached, may suitably represent an optionally substituted cyclopentyl, cyclohexyl, pyrrolidine or piperidine ring, especially cyclopentyl or cyclohexyl.

Alternatively, R^1 and R^2, when attached to adjacent carbon atoms, may together form an optionally benzo-fused and/or substituted cycloalkyl, phenyl or heteroaryl (e.g. pyridinyl) ring fused to the ring containing the variable V and/or W. Thus, R^1 and R^2, when attached to adjacent carbon atoms, may represent, when taken together with the carbon atoms to which they are attached, C_{5-7} cycloalkyl, phenyl or heteroaryl (e.g. pyridinyl), any of which groups may be benzo-fused and/or unsubstituted, or substituted by one or more, typically by one or two, substituents. In this context, in one embodiment, R^1 and R^2, when taken together with the adjacent carbon atoms to which they are attached, suitably represent a phenyl ring fused to the ring containing the variable V and/or W. Also

in this context, in another embodiment, R^1 and R^2, when taken together with the adjacent carbon atoms to which they are attached, suitably represent a benzo-fused cyclopentyl ring, i.e. an indanyl moiety fused to the ring containing the variable V and/or W.

Typically, R^3 represents hydrogen; or C_{1-6} alkyl, aryl, aryl(C_{1-6})alkyl, aryl-(C_{2-6})alkynyl, biaryl(C_{1-6})alkyl, C_{3-7} heterocycloalkyl(C_{1-6})alkyl, C_{3-7} heterocycloalkyl-carbonyl, heteroaryl(C_{1-6})alkyl, heteroaryl-aryl(C_{1-6})alkyl or aryl-heteroaryl(C_{1-6})alkyl, any of which groups may be optionally substituted by one or more substituents.

Generally, R^3 represents hydrogen; or C_{2-6} alkynyl, aryl(C_{1-6})alkyl or heteroaryl-(C_{1-6})alkyl, any of which groups may be optionally substituted by one or more substituents. More particularly, R^3 represents aryl(C_{1-6})alkyl or heteroaryl(C_{1-6})alkyl, either of which groups may be optionally substituted by one or more substituents.

In one specific embodiment, R^3 represents hydrogen.

In a representative embodiment, R^3 represents C_{1-6} alkyl, aryl(C_{1-6})alkyl, biaryl-(C_{1-6})alkyl, heteroaryl(C_{1-6})alkyl or heteroaryl-aryl(C_{1-6})alkyl, any of which groups may be optionally substituted by one or more substituents. Preferably, R^3 represents methyl, arylmethyl, biarylmethyl, heteroarylmethyl or heteroaryl-arylmethyl, any of which groups may be optionally substituted by one or more substituents. More particularly, R^3 represents arylmethyl or heteroarylmethyl, either of which groups may be optionally substituted by one or more substituents.

In a particular embodiment, R^3 represents substituted or unsubstituted indolyl-(C_{1-6})alkyl. Advantageously, R^3 represents substituted or unsubstituted indolylmethyl.

In a typical embodiment, R^3 represents substituted or unsubstituted phenyl-(C_{1-6})alkyl. Advantageously, R^3 represents substituted or unsubstituted benzyl.

In another embodiment, R^3 represents substituted or unsubstituted benzofuryl-(C_{1-6})alkyl. Advantageously, R^3 represents substituted or unsubstituted benzofurylmethyl.

Illustratively, R^3 represents hydrogen; or methyl, propynyl, benzyl, phenylethyl, naphthylmethyl, phenylpropynyl, biphenylmethyl, naphthylphenylmethyl, indolinylmethyl, 1,2,3,4-tetrahydroquinolinylmethyl, 1,2,3,4-tetrahydroisoquinolinyl-methyl, piperidinylcarbonyl, 1,2,3,4-tetrahydroquinolinylcarbonyl, 1,2,3,4-tetrahydroisoquinolinylcarbonyl, 1,2,3,4-tetrahydroquinoxalinylcarbonyl, benzofurylmethyl, benzothienylmethyl, indolylmethyl, pyrrolo[2,3-*b*]pyridinylmethyl, pyrrolo[3,2-*c*]pyridinylmethyl, benzimidazolylmethyl, benzotriazolylmethyl, pyridinylmethyl, quinolinylmethyl, isoquinolinylmethyl, benzofurylbenzyl, thienylbenzyl,

benzothienylbenzyl, indolylbenzyl, isoxazolylbenzyl, pyrazolylbenzyl, pyridinylbenzyl, pyrimidinylbenzyl or phenylpyridinylmethyl, any of which groups may be optionally substituted by one or more substituents.

Suitably, R^4 represents hydrogen or optionally substituted C_{1-6} alkyl.

Examples of typical substituents on R^3 and/or R^4 include halogen, cyano, nitro, C_{1-6} alkyl, trifluoromethyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, (C_{1-6})alkylaryl, di(C_{1-6})alkylaryl, piperidinyl(C_{1-6})alkylaryl, piperazinyl(C_{1-6})alkylaryl, (C_{1-6})alkylpiperazinyl(C_{1-6})-alkylaryl, morpholinyl(C_{1-6})alkylaryl, (C_{1-6})alkoxyaryl, cyano(C_{1-6})alkoxyaryl, di(C_{1-6})-alkylamino(C_{1-6})alkylaryl, (C_{1-6})alkylaminocarbonylaryl, aryl(C_{1-6})alkyl, oxazolinyl, azetidinyl, pyrrolidinyl, haloarylpyrrolidinyl, dioxopyrrolidinyl, aminopyrrolidinyl, di-(C_{1-6})alkylaminopyrrolidinyl, indolinyl, oxoindolinyl, arylpiperidinyl, arylcarbonyl-piperidinyl, di(C_{1-6})alkylaminocarbonylpiperidinyl, piperazinyl, (C_{1-6})alkylpiperazinyl, haloarylpiperazinyl, pyridinylpiperazinyl, furoylpiperazinyl, homopiperazinyl, (C_{1-6})alkylhomopiperazinyl, morpholinyl, (C_{1-6})alkylpiperazinyl(C_{1-6})alkyl, morpholinyl(C_{1-6})alkyl, benzofuryl, benzothienyl, pyrazolyl, (C_{1-6})alkylpyrazolyl, di(C_{1-6})-alkylpyrazolyl, tri(C_{1-6})alkylpyrazolyl, [di(C_{1-6})alkyl](trifluoromethyl)pyrazolyl, cyano-(C_{1-6})alkylpyrazolyl, [cyano(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, hydroxy(C_{1-6})alkyl-pyrazolyl, [hydroxy(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, methoxy(C_{1-6})alkylpyrazolyl, [(hydroxy)(methoxy)(C_{1-6})alkyl]pyrazolyl, amino(C_{1-6})alkylpyrazolyl, [(C_{1-6})alkyl][amino-(C_{1-6})alkyl]pyrazolyl, [amino(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, di(C_{1-6})alkylamino(C_{1-6})-alkylpyrazolyl, di(C_{1-6})alkoxyphosphono(C_{1-6})alkylpyrazolyl, (C_{2-6})alkenylpyrazolyl, (C_{3-7})cycloalkyl(C_{1-6})alkylpyrazolyl, [(C_{3-7})cycloalkyl(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, [(C_{1-6})alkyl](aryl)pyrazolyl, (aryl)(trifluoromethyl)pyrazolyl, aryl(C_{1-6})alkylpyrazolyl, aminoaryl(C_{1-6})alkylpyrazolyl, piperidinylpyrazolyl, tetrahydropyranyl(C_{1-6})alkyl-pyrazolyl, [di(C_{1-6})alkyl][tetrahydropyranyl(C_{1-6})alkyl]pyrazolyl, pyrrolidinyl(C_{1-6})alkyl-pyrazolyl, piperidinyl(C_{1-6})alkylpyrazolyl, (C_{1-6})alkylpiperidinyl(C_{1-6})alkylpyrazolyl, morpholinyl(C_{1-6})alkylpyrazolyl, pyridinyl(C_{1-6})alkylpyrazolyl, oxypyridinyl(C_{1-6})alkyl-pyrazolyl, [arylcarbonyl(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, [(C_{1-6})alkyl](piperazinyl-carbonyl)pyrazolyl, [(C_{1-6})alkylaminocarbonyl][(C_{1-6})alkylaryl]pyrazolyl, [(C_{1-6})alkyl]-[amino(C_{1-6})alkylaminocarbonyl]pyrazolyl, aminocarbonyl(C_{1-6})alkylpyrazolyl, [aminocarbonyl(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, di(C_{1-6})alkylaminocarbonyl(C_{1-6})alkyl-pyrazolyl, pyrazolo[1,5-*a*]pyridinyl, di(C_{1-6})alkylisoxazolyl, (amino)[(C_{1-6})alkyl]-isoxazolyl, thiazolyl, di(C_{1-6})alkylthiazolyl, imidazolyl, (C_{1-6})alkylimidazolyl, di(C_{1-6})-

alkylimidazolyl, imidazo[1,2-*a*]pyridinyl, (C_{1-6})alkylimidazo[1,2-*a*]pyridinyl, (C_{1-6})-alkylimidazo[4,5-*b*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyrazinyl, (C_{1-6})-alkylthiadiazolyl, triazolyl, pyridinyl, halopyridinyl, (C_{1-6})alkylpyridinyl, [(C_{1-6})alkyl]-(halo)pyridinyl, di(C_{1-6})alkylpyridinyl, (C_{2-6})alkenylpyridinyl, (C_{1-6})alkylpiperazinyl-pyridinyl, [(C_{1-6})alkyl](piperazinyl)pyridinyl, [(C_{1-6})alkoxycarbonylpiperazinyl][(C_{1-6})-alkyl]pyridinyl, piperidinyl(C_{1-6})alkylpyridinyl, [(C_{1-6})alkyl](oxy)pyridinyl, hydroxypyridinyl, hydroxy(C_{1-6})alkylpyridinyl, (C_{1-6})alkoxypyridinyl, [(C_{1-6})alkoxy]-[(C_{1-6})alkyl]pyridinyl, [(C_{1-6})alkoxy][di(C_{1-6})alkyl]pyridinyl, (C_{1-6})alkoxy(C_{1-6})alkyl-pyridinyl, aminopyridinyl, carboxy(C_{1-6})alkylpyridinyl, (C_{1-6})alkoxycarbonyl(C_{1-6})alkyl-pyridinyl, pyridazinyl, (C_{1-6})alkylpyridazinyl, piperidinylpyridazinyl, oxypyridazinyl, (C_{1-6})alkoxypyridazinyl, aminopyridazinyl, hydroxy(C_{1-6})alkylaminopyridazinyl, di-(C_{1-6})alkylaminopyridazinyl, pyrimidinyl, (C_{1-6})alkylpyrimidinyl, [(C_{1-6})alkyl](halo)-pyrimidinyl, di(C_{1-6})alkylpyrimidinyl, pyrrolidinylpyrimidinyl, (C_{1-6})alkylpiperazinyl-pyrimidinyl, [(C_{1-6})alkyl](piperazinyl)pyrimidinyl, [(C_{1-6})alkoxycarbonyl][(C_{1-6})alkyl]-piperazinylpyrimidinyl, hydroxypyrimidinyl, [(C_{1-6})alkyl](hydroxy)pyrimidinyl, [(C_{1-6})-alkyl][hydroxy(C_{1-6})alkyl]pyrimidinyl, [(C_{1-6})alkyl][hydroxy(C_{2-6})alkynyl]pyrimidinyl, (C_{1-6})alkoxypyrimidinyl, aminopyrimidinyl, di(C_{1-6})alkylaminopyrimidinyl, [di(C_{1-6})alkyl-amino](halo)pyrimidinyl, carboxypyrimidinyl, [(C_{1-6})alkoxycarbonyl(C_{1-6})alkyl][(C_{1-6})-alkyl]pyrimidinyl, aminocarbonylpyrimidinyl, pyrazinyl, (C_{1-6})alkoxypyrazinyl, amino-pyrazinyl, hydroxy, (C_{1-6})alkoxy, difluoromethoxy, trifluoromethoxy, C_{3-7} cycloalkoxy, C_{3-7} cycloalkyl(C_{1-6})alkoxy, aryl(C_{1-6})alkoxycarbonylpiperidinyloxy, morpholinyl(C_{1-6})-alkoxy, aryloxy, haloaryloxy, di(C_{1-6})alkylpyrazolyloxy, halopyridinyloxy, pyrrolidinylpyridinyloxy, (C_{1-6})alkylpiperazinylpyridinyloxy, (C_{1-6})alkylpyrazolyl-pyridinyloxy, (C_{1-6})alkylaminopyridinyloxy, carboxypyridinyloxy, aminocarbonyl-pyridinyloxy, (C_{1-6})alkylpyridazinyloxy, pyrimidinyloxy, (C_{1-6})alkylpyrimidinyloxy, [(C_{1-6})alkyl](halo)pyrimidinyloxy, hydroxy(C_{1-6})alkyl, dihydroxy(C_{1-6})alkyl, pyridinyloxy(C_{1-6})alkyl, methylenedioxy, trifluoromethylenedioxy, amino, (C_{1-6})alkyl-amino, dihydroxy(C_{1-6})alkylamino, (C_{1-6})alkoxy(C_{1-6})alkylamino, di(C_{1-6})alkylamino, *N*-[(C_{1-6})alkoxy(C_{1-6})alkyl]-*N*-[(C_{1-6})alkyl]amino, di(C_{1-6})alkylamino(C_{1-6})alkylamino, *N*-[(C_{1-6})alkyl]-*N*-[di(C_{1-6})alkylamino(C_{1-6})alkyl]amino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{3-7})cycloalkyl]-amino, haloarylamino, *N*-[(C_{1-6})alkyl]-*N*-(haloaryl)amino, methylenedioxyphenylamino, morpholinyl(C_{1-6})alkylphenylamino, oxazolinylphenylamino, [(C_{1-6})alkyl](oxo)pyrazolyl-phenylamino, oxazolylphenylamino, isoxazolylphenylamino, triazolylphenylamino,

(C_{1-6})alkyltriazolylphenylamino, (C_{1-6})alkylpyrimidinylphenylamino, pyrazolyl(C_{1-6})alkylphenylamino, triazolyl(C_{1-6})alkylphenylamino, C_{1-6} alkylsulphonylaminophenylamino, morpholinylcarbonylphenylamino, C_{1-6} alkylsulphonylphenylamino, morpholinylsulphonylphenylamino, *N*-[(C_{1-6})alkyl]-*N*-[aryl(C_{1-6})alkyl]amino, *N*-[di(C_{1-6})alkylamino(C_{1-6})alkyl]-*N*-[aryl(C_{1-6})alkyl]amino, cyanoaryl(C_{1-6})alkylamino, (cyano)(halo)aryl(C_{1-6})alkylamino, methylenedioxyaryl(C_{1-6})alkylamino, dihydrobenzofuranylamino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpyrrolidinyl]amino, C_{1-6} alkylsulphonylindolinylamino, chromanonylamino, piperidinylamino, *N*-[(C_{1-6})alkyl]-*N*-(piperidinyl)amino, *N*-[(C_{3-7})cycloalkyl(C_{1-6})alkyl]-*N*-(piperidinyl)amino, (C_{1-6})alkylpiperidinylamino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpiperidinyl]amino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{3-7})cycloalkylpiperidinyl]amino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{2-6})alkylcarbonylpiperidinyl]-amino, dihydroquinolinonylamino, benzoxazinonylamino, pyrrolidinyl(C_{1-6})alkylamino, *N*-[(C_{1-6})alkyl]-*N*-[pyrrolidinyl(C_{1-6})alkyl]amino, *N*-[(C_{1-6})alkyl]-*N*-[piperidinyl(C_{1-6})-alkyl]amino, benzothienylamino, indolylamino, dioxoindolylamino, (C_{1-6})alkylpyrazolylamino, [(C_{1-6})alkyl](halo)pyrazolylamino, di(C_{1-6})alkylpyrazolylamino, tri(C_{1-6})alkylpyrazolylamino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpyrazolyl]amino, (C_{1-6})alkylindazolylamino, benzoxazolylamino, benzoxazolonylamino, di(C_{1-6})alkylisoxazolylamino, thiazolylamino, benzothiazolylamino, (C_{1-6})alkylisothiazolylamino, imidazolylamino, [(C_{1-6})alkoxycarbonyl][(C_{1-6})alkyl]imidazolylamino, (C_{1-6})alkylbenzimidazolylamino, benzimidazolonylamino, di(C_{1-6})alkylbenzimidazolonylamino, (C_{1-6})alkyloxadiazolylamino, furyloxadiazolylamino, (C_{1-6})alkylthiadiazolylamino, pyridinylamino, halopyridinylamino, (C_{1-6})alkylpyridinylamino, di(C_{1-6})alkylpyridinylamino, trifluoromethylpyridinylamino, hydroxypyridinylamino, hydroxy(C_{1-6})alkylpyridinylamino, dihydroxy(C_{1-6})alkylpyridinylamino, (C_{1-6})alkoxypyridinylamino, dihydroxy(C_{1-6})alkoxypyridinylamino, di(C_{1-6})alkyldioxolanyl(C_{1-6})alkoxypyridinylamino, (C_{1-6})alkoxy(C_{1-6})-alkylpyridinylamino, (C_{1-6})alkoxy(C_{2-6})alkenylpyridinylamino, dihydroxy(C_{1-6})alkylaminopyridinylamino, di(C_{1-6})alkylaminopyridinylamino, (C_{1-6})alkylamino(C_{1-6})alkylpyridinylamino, di(C_{1-6})alkylamino(C_{1-6})alkylpyridinylamino, oxopyridinylamino, carboxypyridinylamino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpyridinyl]amino, bis[(C_{1-6})alkylpyridinyl]amino, bis(trifluoromethylpyridinyl)amino, isoquinolinylamino, (C_{1-6})alkylpyridazinylamino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpyridazinyl]amino, *N*-[aryl(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpyridazinyl]amino, di(C_{1-6})alkylpyridazinylamino, arylpyridazinylamino, piperidinylpyridazinylamino, (C_{1-6})alkoxypyridazinylamino, [(C_{1-6})alkoxy](halo)-

pyridazinylamino, di(C_{1-6})alkylaminopyridazinylamino, bis[(C_{1-6})alkylpyridazinyl]amino, (C_{1-6})alkylcinnolinylamino, oxopyrimidinylamino, thioxopyrimidinylamino, quinoxalinylamino, (C_{1-6})alkylchromenylamino, benzofuryl(C_{1-6})alkylamino, thienyl(C_{1-6})-alkylamino, indolyl(C_{1-6})alkylamino, (C_{1-6})alkylpyrazolyl(C_{1-6})alkylamino, [di(C_{1-6})alkyl]-(halo)pyrazolyl(C_{1-6})alkylamino, di(C_{1-6})alkylisoxazolyl(C_{1-6})alkylamino, thiazolyl(C_{1-6})-alkylamino, imidazolyl(C_{1-6})alkylamino, (C_{1-6})alkylimidazolyl(C_{1-6})alkylamino, pyridinyl(C_{1-6})alkylamino, (C_{1-6})alkylpyridinyl(C_{1-6})alkylamino, *N*-[(C_{1-6})alkyl]-*N*-[pyridinyl(C_{1-6})alkyl]amino, *N*-[dihydroxy(C_{1-6})alkyl]-*N*-[pyridinyl(C_{1-6})alkyl]amino, *N*-[(C_{1-6})alkylpyridinyl(C_{1-6})alkyl]-*N*-[dihydroxy(C_{1-6})alkyl]amino, amino(C_{1-6})alkyl, (C_{1-6})-alkylamino(C_{1-6})alkyl, di(C_{1-6})alkylamino(C_{1-6})alkyl, pyridinylamino(C_{1-6})alkyl, C_{2-6} alkylcarbonylamino, *N*-[(C_{2-6})alkylcarbonyl]-*N*-[(C_{1-6})alkylpyridinyl(C_{1-6})alkyl]amino, di(C_{1-6})alkylamino(C_{1-6})alkylcarbonylamino, C_{2-6} alkylcarbonylaminomethyl, (C_{3-7})-cycloalkylcarbonylamino, (C_{1-6})alkylpiperidinylcarbonylamino, (C_{1-6})alkylimidazolyl-carbonylamino, C_{2-6} alkoxycarbonylamino, [(C_{2-6})alkoxycarbonyl][(C_{1-6})alkyl]amino, C_{1-6} alkylsulphonylamino, formyl, C_{2-6} alkylcarbonyl, C_{2-6} alkylcarbonyl oxime, C_{2-6} alkylcarbonyl *O*-(methyl)oxime, trifluoromethylcarbonyl, carboxy, C_{2-6} alkoxycarbonyl, aminocarbonyl, C_{1-6} alkylaminocarbonyl, [hydroxy(C_{1-6})alkyl]aminocarbonyl, [di(C_{1-6})-alkylamino(C_{1-6})alkyl]aminocarbonyl, di(C_{1-6})alkylaminocarbonyl, [(C_{1-6})alkyl][cyano-(C_{1-6})alkyl]aminocarbonyl, [(C_{1-6})alkyl][hydroxy(C_{1-6})alkyl]aminocarbonyl, [(C_{1-6})alkoxy-(C_{1-6})alkyl][(C_{1-6})alkyl]aminocarbonyl, [di(C_{1-6})alkylamino(C_{1-6})alkyl][(C_{1-6})alkyl]amino-carbonyl, C_{3-7} cycloalkyl(C_{1-6})alkylaminocarbonyl, aryl(C_{1-6})alkylaminocarbonyl, (C_{1-6})-alkylpiperidinylaminocarbonyl, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpiperidinyl]aminocarbonyl, piperidinyl(C_{1-6})alkylaminocarbonyl, heteroarylaminocarbonyl, heteroaryl(C_{1-6})alkyl-aminocarbonyl, azetidinylcarbonyl, hydroxyazetidinylcarbonyl, aminoazetidinylcarbonyl, C_{2-6} alkoxycarbonylaminoazetidinylcarbonyl, pyrrolidinylcarbonyl, (C_{1-6})alkyl-pyrrolidinylcarbonyl, C_{1-6} alkoxy(C_{1-6})alkylpyrrolidinylcarbonyl, di(C_{1-6})alkylamino-pyrrolidinylcarbonyl, thiazolidinylcarbonyl, oxothiazolidinylcarbonyl, piperidinyl-carbonyl, (C_{1-6})alkylpiperazinylcarbonyl, morpholinylcarbonyl, C_{1-6} alkylthio, C_{1-6} alkylsulphinyl, C_{1-6} alkylsulphonyl, C_{1-6} alkylsulphonylmethyl, aminosulphonyl, C_{1-6} alkylaminosulphonyl, di(C_{1-6})alkylaminosulphonyl, C_{2-6} alkoxycarbonyloxy, trimethylsilyl and tetra(C_{1-6})alkyldioxaborolanyl.

Particular examples of typical substituents on R^3 and/or R^4 include halogen, cyano, C_{1-6} alkyl, (C_{1-6})alkylpyrazolyl, C_{2-6} alkoxycarbonyl and di(C_{1-6})alkylaminocarbonyl. A further example is carboxy.

Selected examples of specific substituents on R^3 and/or R^4 include fluoro, chloro, bromo, cyano, nitro, methyl, *n*-propyl, isopropyl, trifluoromethyl, allyl, cyclopropyl, methylphenyl, dimethylphenyl, piperidinylmethylphenyl, piperazinylmethylphenyl, methylpiperazinylmethylphenyl, morpholinylmethylphenyl, methoxyphenyl, cyanomethoxyphenyl, dimethylaminomethylphenyl, methylaminocarbonylphenyl, benzyl, oxazolinyl, azetidinyl, pyrrolidinyl, chlorophenylpyrrolidinyl, dioxopyrrolidinyl, aminopyrrolidinyl, dimethylaminopyrrolidinyl, indolinyl, oxoindolinyl, phenylpiperidinyl, benzoylpiperidinyl, diethylaminocarbonylpiperidinyl, piperazinyl, methylpiperazinyl, chlorophenylpiperazinyl, pyridinylpiperazinyl, furoylpiperazinyl, homopiperazinyl, methylhomopiperazinyl, morpholinyl, methylpiperazinylmethyl, methylpiperazinylethyl, morpholinylmethyl, benzofuryl, benzothienyl, pyrazolyl, methylpyrazolyl, ethylpyrazolyl, propylpyrazolyl, 2-methylpropylpyrazolyl, 3-methylbutylpyrazolyl, dimethylpyrazolyl, trimethylpyrazolyl, (dimethyl)(ethyl)pyrazolyl, (dimethyl)(isopropyl)pyrazolyl, (dimethyl)(2-methylpropyl)pyrazolyl, (dimethyl)(3-methylbutyl)pyrazolyl, (dimethyl)(trifluoromethyl)pyrazolyl, cyanomethylpyrazolyl, (cyanomethyl)(dimethyl)pyrazolyl, hydroxyethylpyrazolyl, hydroxypropylpyrazolyl, 2-hydroxy-2-methylpropylpyrazolyl, (hydroxyethyl)(dimethyl)pyrazolyl, (hydroxypropyl)(dimethyl)pyrazolyl, methoxypropylpyrazolyl, [(hydroxy)-(methoxy)propyl]pyrazolyl, aminoethylpyrazolyl, aminopropylpyrazolyl, (aminopropyl)-(methyl)pyrazolyl, (aminopropyl)(dimethyl)pyrazolyl, dimethylaminoethylpyrazolyl, dimethylaminopropylpyrazolyl, diethoxyphosphonopropylpyrazolyl, allylpyrazolyl, cyclopropylmethylpyrazolyl, (cyclopropylmethyl)(dimethyl)pyrazolyl, (methyl)(phenyl)-pyrazolyl, (phenyl)(trifluoromethyl)pyrazolyl, benzylpyrazolyl, aminobenzylpyrazolyl, piperidinylpyrazolyl, tetrahydropyranylmethylpyrazolyl, (dimethyl)(tetrahydropyranyl-methyl)pyrazolyl, pyrrolidinylethylpyrazolyl, piperidinylethylpyrazolyl, methyl-piperidinylethylpyrazolyl, morpholinylethylpyrazolyl, pyridinylmethylpyrazolyl, oxypyridinylmethylpyrazolyl, (dimethyl)(phenylcarbonylmethyl)pyrazolyl, (ethyl)(piperazinylcarbonyl)pyrazolyl, (methylaminocarbonyl)(methylphenyl)pyrazolyl, (aminoethylaminocarbonyl)(methyl)pyrazolyl, aminocarbonylmethylpyrazolyl, (aminocarbonylmethyl)(dimethyl]pyrazolyl, dimethylaminocarbonylmethylpyrazolyl,

pyrazolo[1,5-*a*]pyridinyl, dimethylisoxazolyl, (amino)(methyl)isoxazolyl, thiazolyl, dimethylthiazolyl, imidazolyl, methylimidazolyl, dimethylimidazolyl, imidazo[1,2-*a*]pyridinyl, methylimidazo[1,2-*a*]pyridinyl, methylimidazo[4,5-*b*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyrazinyl, methylthiadiazolyl, triazolyl, pyridinyl, fluoropyridinyl, methylpyridinyl, (fluoro)(methyl)pyridinyl, dimethylpyridinyl, vinylpyridinyl, (methylpiperazinyl)pyridinyl, (methyl)(piperazinyl)pyridinyl, (*tert*-butoxycarbonylpiperazinyl)(methyl)pyridinyl, piperidinylmethylpyridinyl, (methyl)(oxy)-pyridinyl, hydroxypyridinyl, hydroxymethylpyridinyl, hydroxyethylpyridinyl, methoxypyridinyl, (methoxy)(methyl)pyridinyl, (dimethyl)(methoxy)pyridinyl, methoxymethylpyridinyl, aminopyridinyl, carboxymethylpyridinyl, ethoxycarbonyl-methylpyridinyl, pyridazinyl, methylpyridazinyl, piperidinylpyridazinyl, oxypyridazinyl, methoxypyridazinyl, aminopyridazinyl, hydroxyethylaminopyridazinyl, dimethylamino-pyridazinyl, pyrimidinyl, methylpyrimidinyl, (chloro)(methyl)pyrimidinyl, dimethyl-pyrimidinyl, pyrrolidinylpyrimidinyl, methylpiperazinylpyrimidinyl, (methyl)-(piperazinyl)pyrimidinyl, (*tert*-butoxycarbonylpiperazinyl)(methyl)pyrimidinyl, hydroxypyrimidinyl, (hydroxy)(methyl)pyrimidinyl, (hydroxyethyl)(methyl)pyrimidinyl, (hydroxypropyl)(methyl)pyrimidinyl, (hydroxypropynyl)(methyl)pyrimidinyl, methoxypyrimidinyl, aminopyrimidinyl, dimethylaminopyrimidinyl, (dimethylamino)-(fluoro)pyrimidinyl, carboxypyrimidinyl, (methoxycarbonylmethyl)(methyl)pyrimidinyl, aminocarbonylpyrimidinyl, pyrazinyl, methoxypyrazinyl, aminopyrazinyl, hydroxy, methoxy, isopropoxy, difluoromethoxy, trifluoromethoxy, cyclobutyloxy, cyclopropyl-methoxy, benzyloxycarbonylpiperidinyloxy, morpholinylethoxy, phenoxy, fluorophenoxy, dimethylpyrazolyloxy, bromopyridinyloxy, pyrrolidinylpyridinyloxy, methylpiperazinyl-pyridinyloxy, methylpyrazolylpyridinyloxy, isopropylaminopyridinyloxy, carboxy-pyridinyloxy, aminocarbonylpyridinyloxy, methylpyridazinyloxy, pyrimidinyloxy, methylpyrimidinyloxy, (chloro)(methyl)pyrimidinyloxy, hydroxymethyl, 1-hydroxy-1-methylethyl, dihydroxypropyl, pyridinyloxymethyl, methylenedioxy, difluoromethylenedioxy, amino, isopropylamino, dihydroxypropylamino, methoxyethylamino, methoxypropylamino, dimethylamino, *N*-(methoxyethyl)-*N*-(methyl)amino, *N*-(methoxypropyl)-*N*-(methyl)amino, dimethylaminoethylamino, dimethylaminopropylamino, *N*-(dimethylaminoethyl)-*N*-(methyl)amino, *N*-(diethylaminoethyl)-*N*-(methyl)amino, *N*-(dimethylaminopropyl)-*N*-(methyl)amino, *N*-(dimethylaminoethyl)-*N*-(ethyl)amino, *N*-(dimethylaminopropyl)-*N*-(ethyl)amino, *N*-

(cyclohexyl)-*N*-(methyl)amino, fluorophenylamino, *N*-fluorophenyl-*N*-methylamino, methylenedioxyphenylamino, morpholinylmethylphenylamino, oxazolinylphenylamino, (methyl)(oxo)pyrazolylphenylamino, oxazolylphenylamino, isoxazolylphenylamino, triazolylphenylamino, methyltriazolylphenylamino, methylpyrimidinylphenylamino, pyrazolylmethylphenylamino, triazolylmethylphenylamino, methylsulphonylamino-phenylamino, morpholinylcarbonylphenylamino, methylsulphonylphenylamino, morpholinylsulphonylphenylamino, *N*-benzyl-*N*-methylamino, *N*-(benzyl)-*N*-(dimethyl-aminoethyl)amino, cyanobenzylamino, (cyano)(phenyl)ethylamino, (cyano)(fluoro)-benzylamino, methylenedioxybenzylamino, dihydrobenzofuranylamino, *N*-(methyl)-*N*-(methylpyrrolidinyl)amino, methylsulphonylindolinylamino, chromanonylamino, piperidinylamino, *N*-(methyl)-*N*-(piperidinyl)amino, *N*-(ethyl)-*N*-(piperidinyl)amino, *N*-(cyclopropylmethyl)-*N*-(piperidinyl)amino, methylpiperidinylamino, *N*-(methyl)-*N*-(methylpiperidinyl)amino, *N*-(methyl)-*N*-(2-methylpropylpiperidinyl)amino, *N*-(cyclopentylpiperidinyl)-*N*-(methyl)amino, *N*-(acetylpiperidinyl)-*N*-(methyl)amino, dihydroquinolinonylamino, benzoxazinonylamino, pyrrolidinylethylamino, pyrrolidinylpropylamino, *N*-(methyl)-*N*-(pyrrolidinylethyl)amino, *N*-(methyl)-*N*-(pyrrolidinylpropyl)amino, *N*-(methyl)-*N*-(piperidinylmethyl)amino, benzothienylamino, indolylamino, dioxoindolylamino, methylpyrazolylamino, (bromo)(methyl)pyrazolyl-amino, dimethylpyrazolylamino, trimethylpyrazolylamino, *N*-(ethyl)-*N*-(methylpyrazolyl)-amino, methylindazolylamino, benzoxazolylamino, benzoxazolonylamino, dimethyl-isoxazolylamino, thiazolylamino, benzothiazolylamino, methylisothiazolylamino, imidazolylamino, (ethoxycarbonyl)(methyl)imidazolylamino, methylbenzimidazolyl-amino, benzimidazolonylamino, dimethylbenzimidazolonylamino, methyloxadiazolyl-amino, furyloxadiazolylamino, methylthiadiazolylamino, pyridinylamino, chloropyridinyl-amino, bromopyridinylamino, methylpyridinylamino, dimethylpyridinylamino, trifluoromethylpyridinylamino, hydroxypyridinylamino, hydroxyethylpyridinylamino, dihydroxyethylpyridinylamino, methoxypyridinylamino, dihydroxypropoxypyridinyl-amino, dimethyldioxolanylmethoxypyridinylamino, methoxyethylpyridinylamino, methoxyvinylpyridinylamino, dihydroxypropylaminopyridinylamino, dimethylamino-pyridinylamino, methylaminomethylpyridinylamino, dimethylaminomethylpyridinyl-amino, oxopyridinylamino, carboxypyridinylamino, *N*-(methyl)-*N*-(methylpyridinyl)-amino, *N*-(ethyl)-*N*-(methylpyridinyl)amino, bis(methylpyridinyl)amino, bis(trifluoro-methylpyridinyl)amino, isoquinolinylamino, methylpyridazinylamino, *N*-(methyl)-*N*-

(methylpyridazinyl)amino, *N*-(benzyl)-*N*-(methylpyridazinyl)amino, dimethylpyridazinylamino, phenylpyridazinylamino, piperidinylpyridazinylamino, methoxypyridazinylamino, (chloro)(methoxy)pyridazinylamino, dimethylaminopyridazinylamino, bis(methylpyridazinyl)amino, methylcinnolinylamino, oxopyrimidinylamino, thioxopyrimidinylamino, quinoxalinylamino, methylchromenylamino, benzofurylmethylamino, thienylmethylamino, indolylmethylamino, methylpyrazolylmethylamino, (chloro)(dimethyl)pyrazolylmethylamino, dimethylisoxazolylmethylamino, thiazolylmethylamino, imidazolylmethylamino, methylimidazolylmethylamino, pyridinylmethylamino, methylpyridinylmethylamino, *N*-(methyl)-*N*-(pyridinylethyl)amino, *N*-(dihydroxypropyl)-*N*-(pyridinylmethyl)amino, *N*-(dihydroxypropyl)-*N*-(methylpyridinylmethyl)amino, aminomethyl, methylaminomethyl, dimethylaminomethyl, pyridinylaminomethyl, acetylamino, *N*-(acetyl)-*N*-(methylpyridinyl)amino, dimethylaminoethylcarbonylamino, acetylaminomethyl, cyclohexylcarbonylamino, methylpiperidinylcarbonylamino, methylimidazolylcarbonylamino, methoxycarbonylamino, *N*-methoxycarbonyl-*N*-methylamino, methylsulphonylamino, formyl, acetyl, acetyl oxime, acetyl *O*-(methyl)oxime, trifluoromethylcarbonyl, carboxy, methoxycarbonyl, aminocarbonyl, methylaminocarbonyl, (hydroxyethyl)aminocarbonyl, (dimethylaminoethyl)aminocarbonyl, (1-hydroxyprop-2-yl)aminocarbonyl, dimethylaminocarbonyl, *N*-(cyanomethyl)-*N*-methylaminocarbonyl, *N*-(cyanoethyl)-*N*-methylaminocarbonyl, *N*-(hydroxyethyl)-*N*-methylaminocarbonyl, *N*-(methoxyethyl)-*N*-methylaminocarbonyl, *N*-(dimethylaminoethyl)-*N*-methylaminocarbonyl, *N*-isopropyl-*N*-methylaminocarbonyl, diethylaminocarbonyl, cyclopropylmethylaminocarbonyl, benzylaminocarbonyl, methylpiperidinylaminocarbonyl, *N*-(methyl)-*N*-(methylpiperidinyl)aminocarbonyl, piperidinylethylaminocarbonyl, pyrazolylaminocarbonyl, pyridinylmethylaminocarbonyl, azetidinylcarbonyl, hydroxyazetidinylcarbonyl, aminoazetidinylcarbonyl, *tert*-butoxycarbonylaminoazetidinylcarbonyl, pyrrolidinylcarbonyl, methylpyrrolidinylcarbonyl, methoxymethylpyrrolidinylcarbonyl, dimethylaminopyrrolidinylcarbonyl, thiazolidinylcarbonyl, oxothiazolidinylcarbonyl, piperidinylcarbonyl, methylpiperazinylcarbonyl, morpholinylcarbonyl, isopropylthio, isopropylsulphinyl, methylsulphonyl, isopropylsulphonyl, methylsulphonylmethyl, aminosulphonyl, methylaminosulphonyl, dimethylaminosulphonyl, *tert*-butoxycarbonyloxy, trimethylsilyl and tetramethyldioxaborolanyl.

Particular examples of specific substituents on R^3 and/or R^4 include bromo, cyano, methyl, methylpyrazolyl, methoxycarbonyl and dimethylaminocarbonyl. A further example is carboxy.

Typical values of R^3 include hydrogen, methyl, phenoxymethyl, phenylthiomethyl, aminomethyl, phenylaminomethyl, *N*-methyl-*N*-phenylaminomethyl, pyridinylaminomethyl, benzofurylcarbonylaminomethyl, phenylsulphonylaminomethyl, benzothienylmethylaminocarbonylmethyl, propynyl, trimethylsilylpropynyl, benzyl, chlorobenzyl, bromobenzyl, methylenedioxyphenylaminobenzyl, morpholinylmethylphenylaminobenzyl, oxazolinylphenylaminobenzyl, (methyl)(oxo)pyrazolylphenylaminobenzyl, oxazolylphenylaminobenzyl, isoxazolylphenylaminobenzyl, triazolylphenylaminobenzyl, methyltriazolylphenylaminobenzyl, methylpyrimidinylphenylaminobenzyl, pyrazolylmethylphenylaminobenzyl, triazolylmethylphenylaminobenzyl, methylsulphonylaminophenylaminobenzyl, morpholinylcarbonylphenylaminobenzyl, methylsulphonylphenylaminobenzyl, morpholinylsulphonylphenylaminobenzyl, dihydrobenzofuranylaminobenzyl, methylsulphonylindolinylaminobenzyl, chromanonylaminobenzyl, dihydroquinolinonylaminobenzyl, benzoxazinonylaminobenzyl, benzothienylaminobenzyl, indolylaminobenzyl, dioxoindolylaminobenzyl, (bromo)(methyl)pyrazolylaminobenzyl, trimethylpyrazolylaminobenzyl, methylindazolylaminobenzyl, benzoxazolylaminobenzyl, benzoxazolonylaminobenzyl, dimethylisoxazolylaminobenzyl, benzothiazolylaminobenzyl, methylisothiazolylaminobenzyl, methylbenzimidazolylaminobenzyl, benzimidazolonylaminobenzyl, dimethylbenzimidazolonylaminobenzyl, methyloxadiazolylaminobenzyl, furyloxadiazolylaminobenzyl, pyridinylaminobenzyl, chloropyridinylaminobenzyl, methylpyridinylaminobenzyl, dimethylpyridinylaminobenzyl, methoxypyridinylaminobenzyl, oxopyridinylaminobenzyl, oxopyrimidinylaminobenzyl, thioxopyrimidinylaminobenzyl, (chloro)(methoxy)pyridazinylaminobenzyl, methylcinnolinylaminobenzyl, quinoxalinylaminobenzyl, methylchromenylaminobenzyl, benzofurylmethyl, cyanobenzofurylmethyl, methoxycarbonylbenzofurylmethyl, dimethylaminocarbonylbenzofurylmethyl, azetidinylcarbonylbenzofurylmethyl, indolylmethyl, fluoroindolylmethyl, cyanoindolylmethyl, (cyano)(methyl)indolylmethyl, nitroindolylmethyl, methylindolylmethyl, oxazolinylindolylmethyl, triazolylindolylmethyl, methoxyindolylmethyl, (chloro)(methoxy)indolylmethyl, di(methoxy)indolylmethyl, difluoromethoxyindolylmethyl, trifluoromethoxyindolylmethyl, (chloro)(trifluoro-

methoxy)indolylmethyl, cyclobutyloxyindolylmethyl, cyclopropylmethoxyindolylmethyl, morpholinylethoxyindolylmethyl, methylenedioxyindolylmethyl, difluoromethylenedioxyindolylmethyl, azetidinylindolylmethyl, morpholinylindolylmethyl, acetylaminoindolylmethyl, acetylaminomethylindolylmethyl, methoxycarbonylaminoindolylmethyl, *N*-methoxycarbonyl-*N*-methylaminoindolylmethyl, methylsulphonylaminoindolylmethyl, acetylindolylmethyl, [acetyl oxime]indolylmethyl, [acetyl *O*-(methyl)oxime]-indolylmethyl, trifluoromethylcarbonylindolylmethyl, carboxyindolylmethyl, (carboxy)-(methyl)indolylmethyl, methoxycarbonylindolylmethyl, (methoxycarbonyl)(methyl)-indolylmethyl, (chloro)(methoxycarbonyl)indolylmethyl, aminocarbonylindolylmethyl, (aminocarbonyl)(chloro)indolylmethyl, methylaminocarbonylindolylmethyl, (chloro)-(methylaminocarbonyl)indolylmethyl, (hydroxyethyl)aminocarbonylindolylmethyl, (dimethylaminoethyl)aminocarbonylindolylmethyl, (1-hydroxyprop-2-yl)aminocarbonyl-indolylmethyl, dimethylaminocarbonylindolylmethyl, (dimethylaminocarbonyl)(methyl)-indolylmethyl, (chloro)(dimethylaminocarbonyl)indolylmethyl, bis(dimethylaminocarbonyl)indolylmethyl, *N*-(cyanomethyl)-*N*-methylaminocarbonylindolylmethyl, [*N*-(cyanomethyl)-*N*-methylaminocarbonyl](methyl)indolylmethyl, *N*-(cyanoethyl)-*N*-methylaminocarbonylindolylmethyl, *N*-(hydroxyethyl)-*N*-methylaminocarbonyl-indolylmethyl, *N*-(methoxyethyl)-*N*-methylaminocarbonylindolylmethyl, [*N*-(methoxyethyl)-*N*-methylaminocarbonyl](methyl)indolylmethyl, *N*-(dimethylaminoethyl)-*N*-methylaminocarbonylindolylmethyl, *N*-isopropyl-*N*-methylaminocarbonylindolylmethyl, diethylaminocarbonylindolylmethyl, cyclopropylmethylaminocarbonylindolylmethyl, benzylaminocarbonylindolylmethyl, pyrazolylaminocarbonylindolylmethyl, pyridinylmethylaminocarbonylindolylmethyl, azetidinylcarbonylindolylmethyl, (azetidinylcarbonyl)(methyl)indolylmethyl, hydroxyazetidinylcarbonylindolylmethyl, aminoazetidinylcarbonylindolylmethyl, *tert*-butoxycarbonylaminoazetidinylcarbonyl-indolylmethyl, pyrrolidinylcarbonylindolylmethyl, methylpyrrolidinylcarbonyl-indolylmethyl, methoxymethylpyrrolidinylcarbonylindolylmethyl, dimethylaminopyrrolidinylcarbonylindolylmethyl, thiazolidinylcarbonylindolylmethyl, oxothiazolidinylcarbonylindolylmethyl, piperidinylcarbonylindolylmethyl, methylpiperazinylcarbonyl-indolylmethyl, morpholinylcarbonylindolylmethyl, methylsulphonylindolylmethyl, methylsulphonylmethylindolylmethyl, dimethylaminosulphonylindolylmethyl, trimethylsilylindolylmethyl and pyrrolo[3,2-*c*]pyridinylmethyl.

Representative values of R^3 include hydrogen, bromobenzyl, benzofurylmethyl, indolylmethyl, cyanoindolylmethyl, (cyano)(methyl)indolylmethyl, (carboxy)(methyl)-indolylmethyl, methoxycarbonylindolylmethyl, (methoxycarbonyl)(methyl)indolylmethyl, dimethylaminocarbonylindolylmethyl and (dimethylaminocarbonyl)(methyl)indolyl-methyl.

Particular values of R^3 include hydrogen, bromobenzyl, benzofurylmethyl, indolylmethyl, cyanoindolylmethyl, (cyano)(methyl)indolylmethyl, methoxycarbonyl-indolylmethyl and dimethylaminocarbonylindolylmethyl.

Typical values of R^4 include hydrogen and methyl. In a preferred embodiment, R^4 is hydrogen. In another embodiment, R^4 is C_{1-6} alkyl, especially methyl.

Alternatively, R^3 and R^4, when both are attached to the same carbon atom, may together form an optionally substituted spiro linkage. Thus, R^3 and R^4, when both are attached to the same carbon atom, may represent, when taken together with the carbon atom to which they are both attached, C_{3-7} cycloalkyl or C_{3-7} heterocycloalkyl, either of which groups may be unsubstituted, or substituted by one or more, typically by one or two, substituents. In this context, R^3 and R^4, when taken together with the carbon atom to which they are both attached, may suitably represent an optionally substituted cyclopentyl, cyclohexyl, pyrrolidine or piperidine ring.

Alternatively, R^3 and R^4, when attached to adjacent carbon atoms, may together form an optionally benzo-fused and/or substituted cycloalkyl, phenyl or heteroaryl (e.g. pyridinyl) ring fused to the morpholine ring. Thus, R^3 and R^4, when attached to adjacent carbon atoms, may represent, when taken together with the carbon atoms to which they are attached, C_{5-7} cycloalkyl, phenyl or heteroaryl (e.g. pyridinyl), any of which groups may be benzo-fused and/or unsubstituted, or substituted by one or more, typically by one or two, substituents. In this context, in one embodiment, R^3 and R^4, when taken together with the adjacent carbon atoms to which they are attached, suitably represent a phenyl ring fused to the morpholine ring, which phenyl ring may be unsubstituted, or substituted by one or more, typically by one or two, substituents. Also in this context, in another embodiment, R^3 and R^4, when taken together with the adjacent carbon atoms to which they are attached, suitably represent a benzo-fused cyclopentyl ring, i.e. an indanyl moiety fused to the morpholine ring, which indanyl moiety may be unsubstituted, or substituted by one or more, typically by one or two, substituents.

Examples of typical substituents on the fused rings referred to in the preceding paragraph include halogen, nitro, C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, (C_{1-6})alkylaryl, di(C_{1-6})alkylaryl, piperidinyl(C_{1-6})alkylaryl, piperazinyl(C_{1-6})alkylaryl, (C_{1-6})alkylpiperazinyl(C_{1-6})alkylaryl, morpholinyl(C_{1-6})alkylaryl, (C_{1-6})alkoxyaryl, cyano(C_{1-6})alkoxyaryl, di(C_{1-6})alkylamino(C_{1-6})alkylaryl, (C_{1-6})alkylaminocarbonylaryl, aryl(C_{1-6})alkyl, haloarylpyrrolidinyl, dioxopyrrolidinyl, aminopyrrolidinyl, di(C_{1-6})alkylaminopyrrolidinyl, indolinyl, oxoindolinyl, arylpiperidinyl, arylcarbonylpiperidinyl, di(C_{1-6})alkylaminocarbonylpiperidinyl, piperazinyl, (C_{1-6})alkylpiperazinyl, haloarylpiperazinyl, pyridinylpiperazinyl, furoylpiperazinyl, homopiperazinyl, (C_{1-6})alkylhomopiperazinyl, (C_{1-6})alkylpiperazinyl(C_{1-6})alkyl, morpholinyl(C_{1-6})alkyl, benzofuryl, benzothienyl, pyrazolyl, (C_{1-6})alkylpyrazolyl, di(C_{1-6})alkylpyrazolyl, tri(C_{1-6})alkylpyrazolyl, [di(C_{1-6})alkyl](trifluoromethyl)pyrazolyl, cyano(C_{1-6})alkylpyrazolyl, [cyano-(C_{1-6})alkyl][di(C_{1-6})-alkyl]pyrazolyl, hydroxy(C_{1-6})alkylpyrazolyl, [hydroxy(C_{1-6})-alkyl][di(C_{1-6})alkyl]pyrazolyl, methoxy(C_{1-6})alkylpyrazolyl, [(hydroxy)(methoxy)(C_{1-6})-alkyl]pyrazolyl, amino(C_{1-6})alkylpyrazolyl, [(C_{1-6})alkyl][amino(C_{1-6})alkyl]pyrazolyl, [amino(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, di(C_{1-6})alkylamino(C_{1-6})alkylpyrazolyl, di(C_{1-6})alkoxyphosphono(C_{1-6})alkylpyrazolyl, (C_{2-6})alkenylpyrazolyl, (C_{3-7})cycloalkyl-(C_{1-6})alkylpyrazolyl, [(C_{3-7})cycloalkyl(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, [(C_{1-6})alkyl]-(aryl)pyrazolyl, (aryl)(trifluoromethyl)pyrazolyl, aryl(C_{1-6})alkylpyrazolyl, aminoaryl-(C_{1-6})alkylpyrazolyl, piperidinylpyrazolyl, tetrahydropyranyl(C_{1-6})alkylpyrazolyl, [di-(C_{1-6})alkyl][tetrahydropyranyl(C_{1-6})alkyl]pyrazolyl, pyrrolidinyl(C_{1-6})alkylpyrazolyl, piperidinyl(C_{1-6})alkylpyrazolyl, (C_{1-6})alkylpiperidinyl(C_{1-6})alkylpyrazolyl, morpholinyl(C_{1-6})alkylpyrazolyl, pyridinyl(C_{1-6})alkylpyrazolyl, oxypyridinyl(C_{1-6})alkylpyrazolyl, [arylcarbonyl(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, [(C_{1-6})alkyl](piperazinylcarbonyl)pyrazolyl, [(C_{1-6})alkylaminocarbonyl][(C_{1-6})alkylaryl]pyrazolyl, [(C_{1-6})alkyl]-[amino(C_{1-6})alkylaminocarbonyl]pyrazolyl, aminocarbonyl(C_{1-6})alkylpyrazolyl, [aminocarbonyl(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, di(C_{1-6})alkylaminocarbonyl(C_{1-6})alkylpyrazolyl, pyrazolo[1,5-*a*]pyridinyl, di(C_{1-6})alkylisoxazolyl, (amino)[(C_{1-6})alkyl]-isoxazolyl, thiazolyl, di(C_{1-6})alkylthiazolyl, imidazolyl, (C_{1-6})alkylimidazolyl, di(C_{1-6})-alkylimidazolyl, imidazo[1,2-*a*]pyridinyl, (C_{1-6})alkylimidazo[1,2-*a*]pyridinyl, (C_{1-6})-alkylimidazo[4,5-*b*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyrazinyl, (C_{1-6})-alkylthiadiazolyl, pyridinyl, halopyridinyl, (C_{1-6})alkylpyridinyl, [(C_{1-6})alkyl](halo)-pyridinyl, di(C_{1-6})alkylpyridinyl, (C_{2-6})alkenylpyridinyl, (C_{1-6})alkylpiperazinylpyridinyl,

[(C_{1-6})alkyl](piperazinyl)pyridinyl, [(C_{1-6})alkoxycarbonylpiperazinyl][(C_{1-6})alkyl]-pyridinyl, piperidinyl(C_{1-6})alkylpyridinyl, [(C_{1-6})alkyl](oxy)pyridinyl, hydroxypyridinyl, hydroxy(C_{1-6})alkylpyridinyl, (C_{1-6})alkoxypyridinyl, [(C_{1-6})alkoxy][(C_{1-6})alkyl]pyridinyl, [(C_{1-6})alkoxy][di(C_{1-6})alkyl]pyridinyl, (C_{1-6})alkoxy(C_{1-6})alkylpyridinyl, aminopyridinyl, carboxy(C_{1-6})alkylpyridinyl, (C_{1-6})alkoxycarbonyl(C_{1-6})alkylpyridinyl, pyridazinyl, (C_{1-6})-alkylpyridazinyl, piperidinylpyridazinyl, oxypyridazinyl, (C_{1-6})alkoxypyridazinyl, aminopyridazinyl, hydroxy(C_{1-6})alkylaminopyridazinyl, di(C_{1-6})alkylaminopyridazinyl, pyrimidinyl, (C_{1-6})alkylpyrimidinyl, [(C_{1-6})alkyl](halo)pyrimidinyl, di(C_{1-6})alkyl-pyrimidinyl, pyrrolidinylpyrimidinyl, (C_{1-6})alkylpiperazinylpyrimidinyl, [(C_{1-6})alkyl](piperazinyl)pyrimidinyl, [(C_{1-6})alkoxycarbonyl][(C_{1-6})alkyl]piperazinyl-pyrimidinyl, hydroxypyrimidinyl, [(C_{1-6})alkyl](hydroxy)pyrimidinyl, [(C_{1-6})alkyl]-[hydroxy(C_{1-6})alkyl]pyrimidinyl, [(C_{1-6})alkyl][hydroxy(C_{2-6})alkynyl]pyrimidinyl, (C_{1-6})-alkoxypyrimidinyl, aminopyrimidinyl, di(C_{1-6})alkylaminopyrimidinyl, [di(C_{1-6})alkyl-amino](halo)pyrimidinyl, carboxypyrimidinyl, [(C_{1-6})alkoxycarbonyl(C_{1-6})alkyl][(C_{1-6})-alkyl]pyrimidinyl, aminocarbonylpyrimidinyl, pyrazinyl, (C_{1-6})alkoxypyrazinyl, amino-pyrazinyl, hydroxy, (C_{1-6})alkoxy, aryl(C_{1-6})alkoxycarbonylpiperidinyloxy, morpholinyl-(C_{1-6})alkoxy, aryloxy, haloaryloxy, di(C_{1-6})alkylpyrazolyloxy, halopyridinyloxy, pyrrolidinylpyridinyloxy, (C_{1-6})alkylpiperazinylpyridinyloxy, (C_{1-6})alkylpyrazolyl-pyridinyloxy, (C_{1-6})alkylaminopyridinyloxy, carboxypyridinyloxy, aminocarbonyl-pyridinyloxy, (C_{1-6})alkylpyridazinyloxy, pyrimidinyloxy, (C_{1-6})alkylpyrimidinyloxy, [(C_{1-6})alkyl](halo)pyrimidinyloxy, hydroxy(C_{1-6})alkyl, dihydroxy(C_{1-6})alkyl, pyridinyloxy(C_{1-6})alkyl, amino, (C_{1-6})alkylamino, dihydroxy(C_{1-6})alkylamino, (C_{1-6})-alkoxy(C_{1-6})alkylamino, *N*-[(C_{1-6})alkoxy(C_{1-6})alkyl]-*N*-[(C_{1-6})alkyl]amino, di(C_{1-6})-alkylamino(C_{1-6})alkylamino, *N*-[(C_{1-6})alkyl]-*N*-[di(C_{1-6})alkylamino(C_{1-6})alkyl]amino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{3-7})cycloalkyl]amino, haloarylamino, *N*-[(C_{1-6})alkyl]-*N*-(haloaryl)amino, *N*-[(C_{1-6})alkyl]-*N*-[aryl(C_{1-6})alkyl]amino, *N*-[di(C_{1-6})alkylamino(C_{1-6})alkyl]-*N*-[aryl(C_{1-6})-alkyl]amino, cyanoaryl(C_{1-6})alkylamino, (cyano)(halo)aryl(C_{1-6})alkylamino, methylene-dioxyaryl(C_{1-6})alkylamino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpyrrolidinyl]amino, piperidinyl-amino, *N*-[(C_{1-6})alkyl]-*N*-(piperidinyl)amino, *N*-[(C_{3-7})cycloalkyl(C_{1-6})alkyl]-*N*-(piperidinyl)amino, (C_{1-6})alkylpiperidinylamino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkyl-piperidinyl]amino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{3-7})cycloalkylpiperidinyl]amino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{2-6})alkylcarbonylpiperidinyl]amino, pyrrolidinyl(C_{1-6})alkylamino, *N*-[(C_{1-6})alkyl]-*N*-[pyrrolidinyl(C_{1-6})alkyl]amino, *N*-[(C_{1-6})alkyl]-*N*-[piperidinyl(C_{1-6})alkyl]amino, (C_{1-6})-

alkylpyrazolylamino, di(C_{1-6})alkylpyrazolylamino, tri(C_{1-6})alkylpyrazolylamino, *N*-[(C_{1-6})-alkyl]-*N*-[(C_{1-6})alkylpyrazolyl]amino, thiazolylamino, imidazolylamino, [(C_{1-6})alkoxy-carbonyl][(C_{1-6})alkyl]imidazolylamino, (C_{1-6})alkylthiadiazolylamino, pyridinylamino, halopyridinylamino, (C_{1-6})alkylpyridinylamino, di(C_{1-6})alkylpyridinylamino, trifluoro-methylpyridinylamino, hydroxypyridinylamino, hydroxy(C_{1-6})alkylpyridinylamino, dihydroxy(C_{1-6})alkylpyridinylamino, (C_{1-6})alkoxypyridinylamino, dihydroxy(C_{1-6})alkoxy-pyridinylamino, di(C_{1-6})alkyldioxolanyl(C_{1-6})alkoxypyridinylamino, (C_{1-6})alkoxy(C_{1-6})-alkylpyridinylamino, (C_{1-6})alkoxy(C_{2-6})alkenylpyridinylamino, dihydroxy(C_{1-6})alkyl-aminopyridinylamino, di(C_{1-6})alkylaminopyridinylamino, (C_{1-6})alkylamino(C_{1-6})alkyl-pyridinylamino, di(C_{1-6})alkylamino(C_{1-6})alkylpyridinylamino, carboxypyridinylamino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpyridinyl]amino, bis[(C_{1-6})alkylpyridinyl]amino, bis(trifluoro-methylpyridinyl)amino, isoquinolinylamino, (C_{1-6})alkylpyridazinylamino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpyridazinyl]amino, *N*-[aryl(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpyridazinyl]amino, di(C_{1-6})alkylpyridazinylamino, arylpyridazinylamino, piperidinylpyridazinylamino, (C_{1-6})-alkoxypyridazinylamino, di(C_{1-6})alkylaminopyridazinylamino, bis[(C_{1-6})alkylpyridazinyl]-amino, benzofuryl(C_{1-6})alkylamino, thienyl(C_{1-6})alkylamino, indolyl(C_{1-6})alkylamino, (C_{1-6})alkylpyrazolyl(C_{1-6})alkylamino, [di(C_{1-6})alkyl](halo)pyrazolyl(C_{1-6})alkylamino, di(C_{1-6})alkylisoxazolyl(C_{1-6})alkylamino, thiazolyl(C_{1-6})alkylamino, imidazolyl(C_{1-6})alkyl-amino, (C_{1-6})alkylimidazolyl(C_{1-6})alkylamino, pyridinyl(C_{1-6})alkylamino, (C_{1-6})alkyl-pyridinyl(C_{1-6})alkylamino, *N*-[(C_{1-6})alkyl]-*N*-[pyridinyl(C_{1-6})alkyl]amino, *N*-[dihydroxy-(C_{1-6})alkyl]-*N*-[pyridinyl(C_{1-6})alkyl]amino, *N*-[(C_{1-6})alkylpyridinyl(C_{1-6})alkyl]-*N*-[dihydroxy(C_{1-6})alkyl]amino, amino(C_{1-6})alkyl, (C_{1-6})alkylamino(C_{1-6})alkyl, di(C_{1-6})alkyl-amino(C_{1-6})alkyl, pyridinylamino(C_{1-6})alkyl, *N*-[(C_{2-6})alkylcarbonyl]-*N*-[(C_{1-6})alkyl-pyridinyl(C_{1-6})alkyl]amino, di(C_{1-6})alkylamino(C_{1-6})alkylcarbonylamino, (C_{3-7})cycloalkyl-carbonylamino, (C_{1-6})alkylpiperidinylcarbonylamino, (C_{1-6})alkylimidazolylcarbonylamino, formyl, C_{2-6} alkylcarbonyl, (C_{1-6})alkylpiperidinylaminocarbonyl, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})-alkylpiperidinyl]aminocarbonyl, piperidinyl(C_{1-6})alkylaminocarbonyl, (C_{1-6})alkyl-piperazinylcarbonyl, C_{1-6} alkylthio, C_{1-6} alkylsulphinyl, C_{1-6} alkylsulphonyl, C_{2-6} alkoxycarbonyloxy and tetra(C_{1-6})alkyldioxaborolanyl.

A particular example of a typical substituent on the fused rings referred to in the two preceding paragraphs is (C_{1-6})alkylpyrazolyl.

Selected examples of specific substituents on the fused rings referred to in the three preceding paragraphs include bromo, nitro, methyl, *n*-propyl, isopropyl, allyl, cyclopropyl,

methylphenyl, dimethylphenyl, piperidinylmethylphenyl, piperazinylmethylphenyl, methylpiperazinylmethylphenyl, morpholinylmethylphenyl, methoxyphenyl, cyanomethoxyphenyl, dimethylaminomethylphenyl, methylaminocarbonylphenyl, benzyl, chlorophenylpyrrolidinyl, dioxopyrrolidinyl, aminopyrrolidinyl, dimethylamino-pyrrolidinyl, indolinyl, oxoindolinyl, phenylpiperidinyl, benzoylpiperidinyl, diethylamino-carbonylpiperidinyl, piperazinyl, methylpiperazinyl, chlorophenylpiperazinyl, pyridinylpiperazinyl, furoylpiperazinyl, homopiperazinyl, methylhomopiperazinyl, methylpiperazinylmethyl, methylpiperazinylethyl, morpholinylmethyl, benzofuryl, benzothienyl, pyrazolyl, methylpyrazolyl, ethylpyrazolyl, propylpyrazolyl, 2-methyl-propylpyrazolyl, 3-methylbutylpyrazolyl, dimethylpyrazolyl, trimethylpyrazolyl, (dimethyl)(ethyl)pyrazolyl, (dimethyl)(isopropyl)pyrazolyl, (dimethyl)(2-methylpropyl)-pyrazolyl, (dimethyl)(3-methylbutyl)pyrazolyl, (dimethyl)(trifluoromethyl)pyrazolyl, cyanomethylpyrazolyl, (cyanomethyl)(dimethyl)pyrazolyl, hydroxyethylpyrazolyl, hydroxypropylpyrazolyl, 2-hydroxy-2-methylpropylpyrazolyl, (hydroxyethyl)(dimethyl)-pyrazolyl, (hydroxypropyl)(dimethyl)pyrazolyl, methoxypropylpyrazolyl, [(hydroxy)-(methoxy)propyl]pyrazolyl, aminoethylpyrazolyl, aminopropylpyrazolyl, (aminopropyl)-(methyl)pyrazolyl, (aminopropyl)(dimethyl)pyrazolyl, dimethylaminoethylpyrazolyl, dimethylaminopropylpyrazolyl, diethoxyphosphonopropylpyrazolyl, allylpyrazolyl, cyclopropylmethylpyrazolyl, (cyclopropylmethyl)(dimethyl)pyrazolyl, (methyl)(phenyl)-pyrazolyl, (phenyl)(trifluoromethyl)pyrazolyl, benzylpyrazolyl, aminobenzylpyrazolyl, piperidinylpyrazolyl, tetrahydropyranylmethylpyrazolyl, (dimethyl)(tetrahydropyranyl-methyl)pyrazolyl, pyrrolidinylethylpyrazolyl, piperidinylethylpyrazolyl, methyl-piperidinylethylpyrazolyl, morpholinylethylpyrazolyl, pyridinylmethylpyrazolyl, oxypyridinylmethylpyrazolyl, (dimethyl)(phenylcarbonylmethyl)pyrazolyl, (ethyl)(piperazinylcarbonyl)pyrazolyl, (methylaminocarbonyl)(methylphenyl)pyrazolyl, (aminoethylaminocarbonyl)(methyl)pyrazolyl, aminocarbonylmethylpyrazolyl, (aminocarbonylmethyl)(dimethyl]pyrazolyl, dimethylaminocarbonylmethylpyrazolyl, pyrazolo[1,5-*a*]pyridinyl, dimethylisoxazolyl, (amino)(methyl)isoxazolyl, thiazolyl, dimethylthiazolyl, imidazolyl, methylimidazolyl, dimethylimidazolyl, imidazo[1,2-*a*]pyridinyl, methylimidazo[1,2-*a*]pyridinyl, methylimidazo[4,5-*b*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyrazinyl, methylthiadiazolyl, pyridinyl, fluoropyridinyl, methylpyridinyl, (fluoro)(methyl)pyridinyl, dimethylpyridinyl, vinylpyridinyl, (methyl-piperazinyl)pyridinyl, (methyl)(piperazinyl)pyridinyl, (*tert*-butoxycarbonylpiperazinyl)-

(methyl)pyridinyl, piperidinylmethylpyridinyl, (methyl)(oxy)pyridinyl, hydroxypyridinyl, hydroxymethylpyridinyl, hydroxyethylpyridinyl, methoxypyridinyl, (methoxy)(methyl)-pyridinyl, (dimethyl)(methoxy)pyridinyl, methoxymethylpyridinyl, aminopyridinyl, carboxymethylpyridinyl, ethoxycarbonylmethylpyridinyl, pyridazinyl, methylpyridazinyl, piperidinylpyridazinyl, oxypyridazinyl, methoxypyridazinyl, aminopyridazinyl, hydroxyethylaminopyridazinyl, dimethylaminopyridazinyl, pyrimidinyl, methyl-pyrimidinyl, (chloro)(methyl)pyrimidinyl, dimethylpyrimidinyl, pyrrolidinylpyrimidinyl, methylpiperazinylpyrimidinyl, (methyl)(piperazinyl)pyrimidinyl, (*tert*-butoxycarbonyl-piperazinyl)(methyl)pyrimidinyl, hydroxypyrimidinyl, (hydroxy)(methyl)pyrimidinyl, (hydroxyethyl)(methyl)pyrimidinyl, (hydroxypropyl)(methyl)pyrimidinyl, (hydroxy-propynyl)(methyl)pyrimidinyl, methoxypyrimidinyl, aminopyrimidinyl, dimethylamino-pyrimidinyl, (dimethylamino)(fluoro)pyrimidinyl, carboxypyrimidinyl, (methoxycarbonyl-methyl)(methyl)pyrimidinyl, aminocarbonylpyrimidinyl, pyrazinyl, methoxypyrazinyl, aminopyrazinyl, hydroxy, methoxy, isopropoxy, benzyloxycarbonylpiperidinyloxy, morpholinylethoxy, phenoxy, fluorophenoxy, dimethylpyrazolyloxy, bromopyridinyloxy, pyrrolidinylpyridinyloxy, methylpiperazinylpyridinyloxy, methylpyrazolylpyridinyloxy, isopropylaminopyridinyloxy, carboxypyridinyloxy, aminocarbonylpyridinyloxy, methylpyridazinyloxy, pyrimidinyloxy, methylpyrimidinyloxy, (chloro)(methyl)-pyrimidinyloxy, hydroxymethyl, 1-hydroxy-1-methylethyl, dihydroxypropyl, pyridinyloxymethyl, amino, isopropylamino, dihydroxypropylamino, methoxyethylamino, methoxypropylamino, *N*-(methoxyethyl)-*N*-(methyl)amino, *N*-(methoxypropyl)-*N*-(methyl)amino, dimethylaminoethylamino, dimethylaminopropylamino, *N*-(dimethylaminoethyl)-*N*-(methyl)amino, *N*-(diethylaminoethyl)-*N*-(methyl)amino, *N*-(dimethylaminopropyl)-*N*-(methyl)amino, *N*-(dimethylaminoethyl)-*N*-(ethyl)amino, *N*-(dimethylaminopropyl)-*N*-(ethyl)amino, *N*-(cyclohexyl)-*N*-(methyl)amino, fluorophenyl-amino, *N*-fluorophenyl-*N*-methylamino, *N*-benzyl-*N*-methylamino, *N*-(benzyl)-*N*-(dimethylaminoethyl)amino, cyanobenzylamino, (cyano)(phenyl)ethylamino, (cyano)(fluoro)benzylamino, methylenedioxybenzylamino, *N*-(methyl)-*N*-(methyl-pyrrolidinyl)amino, piperidinylamino, *N*-(methyl)-*N*-(piperidinyl)amino, *N*-(ethyl)-*N*-(piperidinyl)amino, *N*-(cyclopropylmethyl)-*N*-(piperidinyl)amino, methylpiperidinyl-amino, *N*-(methyl)-*N*-(methylpiperidinyl)amino, *N*-(methyl)-*N*-(2-methylpropyl-piperidinyl)amino, *N*-(cyclopentylpiperidinyl)-*N*-(methyl)amino, *N*-(acetylpiperidinyl)-*N*-(methyl)amino, pyrrolidinylethylamino, pyrrolidinylpropylamino, *N*-(methyl)-*N*-

(pyrrolidinylethyl)amino, *N*-(methyl)-*N*-(pyrrolidinylpropyl)amino, *N*-(methyl)-*N*-(piperidinylmethyl)amino, methylpyrazolylamino, dimethylpyrazolylamino, trimethylpyrazolylamino, *N*-(ethyl)-*N*-(methylpyrazolyl)amino, thiazolylamino, imidazolylamino, (ethoxycarbonyl)(methyl)imidazolylamino, methylthiadiazolylamino, pyridinylamino, bromopyridinylamino, methylpyridinylamino, dimethylpyridinylamino, trifluoromethylpyridinylamino, hydroxypyridinylamino, hydroxyethylpyridinylamino, dihydroxyethylpyridinylamino, methoxypyridinylamino, dihydroxypropoxypyridinylamino, dimethyldioxolanylmethoxypyridinylamino, methoxyethylpyridinylamino, methoxyvinylpyridinylamino, dihydroxypropylaminopyridinylamino, dimethylaminopyridinylamino, methylaminomethylpyridinylamino, dimethylaminomethylpyridinylamino, carboxypyridinylamino, *N*-(methyl)-*N*-(methylpyridinyl)amino, *N*-(ethyl)-*N*-(methylpyridinyl)amino, bis(methylpyridinyl)amino, bis(trifluoromethylpyridinyl)amino, isoquinolinylamino, methylpyridazinylamino, *N*-(methyl)-*N*-(methylpyridazinyl)amino, *N*-(benzyl)-*N*-(methylpyridazinyl)amino, dimethylpyridazinylamino, phenylpyridazinylamino, piperidinylpyridazinylamino, methoxypyridazinylamino, dimethylaminopyridazinylamino, bis(methylpyridazinyl)amino, benzofurylmethylamino, thienylmethylamino, indolylmethylamino, methylpyrazolylmethylamino, (chloro)(dimethyl)pyrazolylmethylamino, dimethylisoxazolylmethylamino, thiazolylmethylamino, imidazolylmethylamino, methylimidazolylmethylamino, pyridinylmethylamino, methylpyridinylmethylamino, *N*-(methyl)-*N*-(pyridinylethyl)amino, *N*-(dihydroxypropyl)-*N*-(pyridinylmethyl)amino, *N*-(dihydroxypropyl)-*N*-(methylpyridinylmethyl)amino, aminomethyl, methylaminomethyl, dimethylaminomethyl, pyridinylaminomethyl, *N*-(acetyl)-*N*-(methylpyridinyl)amino, dimethylaminoethylcarbonylamino, cyclohexylcarbonylamino, methylpiperidinylcarbonylamino, methylimidazolylcarbonylamino, formyl, acetyl, methylpiperidinylaminocarbonyl, *N*-(methyl)-*N*-(methylpiperidinyl)aminocarbonyl, piperidinylethylaminocarbonyl, methylpiperazinylcarbonyl, isopropylthio, isopropylsulphinyl, isopropylsulphonyl, *tert*-butoxycarbonyloxy and tetramethyldioxaborolanyl.

A particular example of such a substituent is methylpyrazolyl.

Suitably, R^a represents substituted or unsubstituted aryl.

Suitably, R^c represents hydrogen; or aryl, aryl(C_{1-6})alkyl, heteroaryl(C_{1-6})alkyl or (aryl)(heteroaryl)(C_{1-6})alkyl, any of which groups may be optionally substituted by one or more substituents.

Examples of typical substituents on R^a and/or R^b and/or R^c include halogen, cyano, nitro, C_{1-6} alkyl, trifluoromethyl, hydroxy, C_{1-6} alkoxy, difluoromethoxy, trifluoromethoxy, aryloxy, C_{1-6} alkylthio, C_{1-6} alkylsulphonyl, amino, C_{1-6} alkylamino, di(C_{1-6})alkylamino, C_{2-6} alkylcarbonylamino, C_{2-6} alkoxycarbonylamino, C_{1-6} alkylsulphonylamino, formyl, C_{2-6} alkylcarbonyl, carboxy, C_{2-6} alkoxycarbonyl, aminocarbonyl, C_{1-6} alkylamino-carbonyl, di(C_{1-6})alkylaminocarbonyl, aminosulphonyl, C_{1-6} alkylaminosulphonyl and di(C_{1-6})alkylaminosulphonyl.

Examples of particular substituents on R^a and/or R^b and/or R^c include fluoro, chloro, bromo, cyano, nitro, methyl, trifluoromethyl, hydroxy, methoxy, difluoromethoxy, trifluoromethoxy, phenoxy, methylthio, methylsulphonyl, amino, methylamino, dimethylamino, acetylamino, methoxycarbonylamino, methylsulphonylamino, formyl, acetyl, carboxy, methoxycarbonyl, aminocarbonyl, methylaminocarbonyl, dimethylaminocarbonyl, aminosulphonyl, methylaminosulphonyl and dimethylaminosulphonyl.

A particular value of R^a is phenyl.

In one embodiment, R^b represents hydrogen. In another embodiment, R^b represents C_{1-6} alkyl, especially methyl or ethyl.

Particular values of R^c include hydrogen, phenyl, benzyl, pyridinylmethyl and (phenyl)(pyridinyl)methyl.

In one embodiment, R^d represents hydrogen. In another embodiment, R^d represents C_{1-6} alkyl, especially methyl or ethyl, particularly ethyl.

Suitably, R^e represents methyl.

Generally, R^5 represents hydrogen, halogen, cyano, $-SR^a$, $-COR^e$, $-CO_2R^b$ or $-CONR^cR^d$; or R^5 represents C_{1-6} alkyl, C_{2-6} alkenylcarbonyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl(C_{2-6})alkynyl, aryl, aryl(C_{1-6})alkyl, aryl(C_{2-6})alkenyl, aryl(C_{2-6})alkynyl, biaryl, C_{3-7} heterocycloalkyl(C_{1-6})alkyl, C_{3-7} heterocycloalkyl(C_{2-6})alkynyl, C_{3-7} heterocycloalkylcarbonyl(C_{2-6})alkynyl, C_{5-9} heterobicycloalkyl(C_{2-6})alkynyl, C_{3-7} heterocycloalkyl-aryl, C_{3-7} heterocycloalkyl(C_{1-6})alkyl-aryl, C_{3-7} heterocycloalkyl-biaryl, heteroaryl, heteroaryl(C_{1-6})alkyl, heteroaryl(C_{1-6})alkylcarbonyl, heteroaryl(C_{2-6})alkenyl, heteroaryl(C_{2-6})alkynyl, heteroaroylcarbonyl, C_{3-7} heterocycloalkyl-heteroaryl, C_{3-7} heterocycloalkyl-heteroaryl(C_{2-6})alkynyl, heteroaryl-aryl, aryl-heteroaryl, C_{3-7} heterocycloalkyl-aryl-heteroaryl, C_{3-7} heterocycloalkyl(C_{1-6})alkyl-aryl-heteroaryl, C_{5-9} heterobicycloalkyl(C_{1-6})alkyl-aryl-heteroaryl, heteroaryl-aryl-heteroaryl, bi(heteroaryl),

C_{3-7} heterocycloalkylcarbonyl-bi(heteroaryl), aryloxyaryl, aryl(C_{1-6})alkoxyaryl, heteroaryl(C_{1-6})alkoxyaryl, aryl(C_{1-6})alkylaminoaryl, heteroaryl(C_{1-6})alkylaminoaryl, C_{3-7} cycloalkylcarbonylaminoaryl, arylcarbonylaminoaryl, aryl(C_{1-6})alkylcarbonylaminoaryl, C_{3-7} heterocycloalkylcarbonylaminoaryl, heteroarylcarbonylaminoaryl, aryl-(C_{3-7})heterocycloalkylcarbonylaminoaryl, arylsulphonylaminoaryl, aryl(C_{1-6})alkyl-sulphonylaminoaryl, heteroaryl(C_{1-6})alkylsulphonylaminoaryl, C_{3-7} cycloalkylamino-carbonylaminoaryl, arylaminocarbonylaminoaryl, C_{3-7} heterocycloalkylaminocarbonyl-aminoaryl, C_{3-7} heterocycloalkylaminocarbonylaminoaryl, heteroaryl(C_{1-6})alkyl-aminocarbonylaminoaryl, C_{3-7} heterocycloalkylcarbonylcarbonylaminoaryl, C_{3-7} heterocycloalkyl(C_{1-6})alkylaminocarbonylcarbonylaminoaryl, arylcarbonylaryl, C_{3-7} heterocycloalkylcarbonylaryl, C_{3-7} heterocycloalkylcarbonyl(C_{1-6})alkylaryl, aryl(C_{1-6})-alkylaminocarbonylaryl, C_{3-7} heterocycloalkyl(C_{1-6})alkylaminocarbonylaryl, heteroaryl-aminocarbonylaryl, heteroaryl(C_{1-6})alkylaminocarbonylaryl, C_{3-7} heterocycloalkylamino-carbonyl(C_{1-6})alkylaryl, C_{3-7} heterocycloalkyl(C_{1-6})alkylaminocarbonyl(C_{1-6})alkylaryl, heteroarylaminocarbonyl(C_{1-6})alkylaryl, heteroaryl(C_{1-6})alkylaminocarbonyl(C_{1-6})alkyl-aryl, arylaminoheteroaryl, C_{3-7} heterocycloalkylamino-aryl-heteroaryl, C_{3-7} heterocycloalkylcarbonylamino-aryl-heteroaryl, C_{3-7} heterocycloalkylaminocarbonyl-amino-aryl-heteroaryl, C_{3-7} heterocycloalkylcarbonyl-aryl-heteroaryl, C_{3-7} heterocycloalkyl(C_{1-6})alkylcarbonyl-aryl-heteroaryl, C_{5-9} heterobicycloalkylcarbonyl-aryl-heteroaryl, C_{3-7} heterocycloalkylcarbonyl(C_{1-6})alkyl-aryl-heteroaryl, C_{3-7} heterocycloalkyl-aminocarbonyl-aryl-heteroaryl, C_{3-7} heterocycloalkyl(C_{1-6})alkylaminocarbonyl-aryl-heteroaryl or C_{3-7} heterocycloalkylaminocarbonyl(C_{1-6})alkyl-aryl-heteroaryl, any of which groups may be optionally substituted by one or more substituents.

Typically, R^5 represents hydrogen; or optionally substituted aryl(C_{2-6})alkynyl.

Suitably, R^5 represents hydrogen, halogen, cyano, $-SR^a$, $-COR^e$, $-CO_2R^b$ or $-CONR^cR^d$; or R^5 represents methyl, propyl, ethenylcarbonyl, ethynyl, propynyl, butynyl, 3-methylbutynyl, cyclopropylethynyl, cyclohexylethynyl, phenyl, naphthyl, benzyl, phenylethyl, phenylethenyl, phenylethynyl, phenylpropynyl, biphenyl, piperidinylethyl, pyrrolidinylethynyl, piperidinylethynyl, 1,2,3,4-tetrahydroisoquinolinylpropynyl, piperazinylpropynyl, pyrrolidinylcarbonylethynyl, quinuclidinylethynyl, piperazinyl-phenyl, morpholinylphenyl, piperidinylmethylphenyl, piperazinyl-biphenyl, benzofuryl, dibenzofuryl, benzothienyl, dibenzothienyl, pyridinyl, isoquinolinyl, imidazolylethyl, imidazolylmethylcarbonyl, imidazolylethenyl, indolylethynyl, pyrazolylethynyl,

imidazolylethynyl, pyridinylethynyl, pyrimidinylethynyl, imidazo[1,2-*a*]pyridinylethynyl, imidazolylcarbonylcarbonyl, benzomorpholinyl-pyridinyl, pyrrolidinylpyridinylethynyl, pyrazolylphenyl, pyridinylphenyl, phenylisoxazolyl, phenylthiazolyl, phenylpyridinyl, phenylpyrimidinyl, azetidinylphenylpyridinyl, pyrrolidinylphenylpyridinyl, piperidinylphenylpyridinyl, piperazinylphenylpyridinyl, morpholinylphenylpyridinyl, piperazinylphenylpyrimidinyl, pyrrolidinylmethylphenylpyridinyl, piperidinylmethylphenylpyridinyl, piperazinylmethylphenylpyridinyl, homopiperazinylmethylphenylpyridinyl, morpholinylmethylphenylpyridinyl, azabicyclo[3.2.1]octylmethylphenylpyridinyl, diazabicyclo[3.2.1]octylmethylphenylpyridinyl, tetrazolylphenylpyridinyl, benzofurylpyridinyl, benzothienylpyridinyl, indolylpyridinyl, isoxazolylpyridinyl, bi(pyridinyl), isoquinolinylpyridinyl, morpholinylcarbonylbi(pyridinyl), phenoxyphenyl, benzyloxyphenyl, pyridinylmethoxyphenyl, benzylaminophenyl, furylmethylaminophenyl, pyridinylmethylaminophenyl, cyclopentylcarbonylaminophenyl, phenylcarbonylaminophenyl, benzylcarbonylaminophenyl, pyrrolidinylcarbonylaminophenyl, piperidinylcarbonylaminophenyl, piperazinylcarbonylaminophenyl, morpholinylcarbonylaminophenyl, indolylcarbonylaminophenyl, isoxazolylcarbonylaminophenyl, pyridinylcarbonylaminophenyl, phenylpyrrolidinylcarbonylaminophenyl, phenylsulphonylaminophenyl, benzylsulphonylaminophenyl, isoxazolylsulphonylaminophenyl, cyclopentylaminocarbonylaminophenyl, phenylaminocarbonylaminophenyl, azetidinylaminocarbonylaminophenyl, morpholinylethylaminocarbonylaminophenyl, imidazolylmethylaminocarbonylaminophenyl, morpholinylcarbonylcarbonylaminophenyl, pyrrolidinylethylaminocarbonylcarbonylaminophenyl, phenylcarbonylphenyl, morpholinylcarbonylphenyl, pyrrolidinylcarbonylmethylphenyl, piperidinylcarbonylmethylphenyl, benzylaminocarbonylphenyl, morpholinylethylaminocarbonylphenyl, imidazolylaminocarbonylphenyl, imidazolylmethylaminocarbonylphenyl, pyridinylmethylaminocarbonylphenyl, azetidinylaminocarbonylmethylphenyl, pyrrolidinylmethylaminocarbonylmethylphenyl, pyridinylaminocarbonylmethylphenyl, pyridinylmethylaminocarbonylmethylphenyl, phenylaminopyridinyl, azetidinylaminophenylpyridinyl, pyrrolidinylaminophenylpyridinyl, piperazinylcarbonylaminophenylpyridinyl, piperidinylaminocarbonylaminophenylpyridinyl, azetidinylcarbonylphenylpyridinyl, pyrrolidinylcarbonylphenylpyridinyl, piperidinylcarbonylphenylpyridinyl, piperazinylcarbonylphenylpyridinyl, morpholinylcarbonylphenylpyridinyl, piperidinylcarbonylphenylpyrimidinyl, morpholinylmethylcarbonylphenylpyridinyl,

azabicyclo[3.2.1]octylcarbonylphenylpyridinyl, azetidinylcarbonylmethylphenylpyridinyl, pyrrolidinylcarbonylmethylphenylpyridinyl, piperidinylcarbonylmethylphenylpyridinyl, piperazinylcarbonylmethylphenylpyridinyl, azetidinylaminocarbonylphenylpyridinyl, pyrrolidinylaminocarbonylphenylpyridinyl, piperidinylaminocarbonylphenylpyridinyl, piperidinylmethylaminocarbonylphenylpyridinyl or azetidinylaminocarbonylmethylphenylpyridinyl, any of which groups may be optionally substituted by one or more substituents.

Illustratively, R^5 represents hydrogen; or optionally substituted phenylethynyl.

Examples of representative substituents on R^5 include halogen, cyano, nitro, oxo, C_{1-6} alkyl, trifluoromethyl, hydroxy, hydroxy(C_{1-6})alkyl, C_{1-6} alkoxy, dihydroxy(C_{1-6})alkoxy, aryl(C_{1-6})alkoxy, methoxyaryl(C_{1-6})alkoxy, amino, C_{1-6} alkylamino, di(C_{1-6})alkylamino, amino(C_{1-6})alkyl, C_{1-6} alkylamino(C_{1-6})alkyl, di(C_{1-6})alkylamino(C_{1-6})alkyl, di(C_{1-6})alkylamino(C_{1-6})alkylamino, methoxyaryl(C_{1-6})alkylamino, C_{1-6} alkylcarbonylamino, C_{1-6} alkoxycarbonyl(C_{1-6})alkylcarbonylamino, C_{1-6} alkylcarbonylamino(C_{1-6})alkyl, C_{1-6} alkoxycarbonylamino, *N*-(C_{1-6} alkoxycarbonyl)-*N*-(C_{1-6} alkyl)amino, C_{1-6} alkoxycarbonylamino(C_{1-6})alkyl, *N*-(C_{1-6} alkoxycarbonyl)-*N*-(C_{1-6} alkyl)amino(C_{1-6})alkyl, C_{1-6} alkylsulphonylamino, C_{1-6} alkylsulphonylamino(C_{1-6})alkyl, C_{1-6} alkylaminocarbonylamino, di(C_{1-6})alkylamino(C_{1-6})alkylaminocarbonylamino, *N*-(C_{1-6} alkyl)-*N*-[di(C_{1-6})alkylamino-(C_{1-6})alkyl]aminocarbonylamino, carboxycarbonylamino, C_{1-6} alkoxycarbonylcarbonylamino, C_{1-6} alkylaminocarbonylcarbonylamino, di(C_{1-6})alkylamino(C_{1-6})alkylaminocarbonylcarbonylamino, di(C_{1-6})alkylaminosulphonylamino, formyl, C_{1-6} alkylcarbonyl, di(C_{1-6})alkylamino(C_{1-6})alkylcarbonyl, carboxy, carboxy(C_{1-6})alkyl, C_{1-6} alkoxycarbonyl, C_{1-6} alkoxycarbonyl(C_{1-6})alkyl, aminocarbonyl, C_{1-6} alkylaminocarbonyl, di(C_{1-6})alkylaminocarbonyl, cyano(C_{1-6})alkylaminocarbonyl, di(C_{1-6})alkylamino(C_{1-6})alkylaminocarbonyl, dihydroxy(C_{1-6})alkylaminocarbonyl, *N*-(C_{1-6} alkyl)-*N*-[amino(C_{1-6})alkyl]aminocarbonyl, *N*-(C_{1-6} alkyl)-*N*-[di(C_{1-6})alkylamino(C_{1-6})alkyl]aminocarbonyl, di(C_{1-6})alkylaminocarbonyl(C_{1-6})alkyl, *N*-(C_{1-6} alkyl)-*N*-[di(C_{1-6})alkylamino(C_{1-6})alkyl]-aminocarbonyl(C_{1-6})alkyl, aminocarbonyl(C_{1-6})alkoxy, C_{1-6} alkoxyaminocarbonyl, *N*-(C_{1-6} alkoxy)-*N*-(C_{1-6} alkyl)aminocarbonyl, C_{1-6} alkylsulphonyl, C_{1-6} alkylsulphonyloxy(C_{1-6})alkyl, trifluoromethylsulphonyloxy and tri(C_{1-6})alkylsilyl.

Examples of specific substituents on R^5 include fluoro, chloro, bromo, cyano, nitro, oxo, methyl, ethyl, isopropyl, trifluoromethyl, hydroxy, hydroxymethyl, methoxy, ethoxy, dihydroxypropoxy, isobutoxy, benzyloxy, methoxybenzyloxy, amino, methylamino,

dimethylamino, diethylamino, aminomethyl, methylaminomethyl, dimethylaminomethyl, *N*-isopropyl-*N*-methylaminomethyl, dimethylaminoethylamino, methoxybenzylamino, acetylamino, ethoxycarbonylacetylamino, ethylcarbonylamino, methoxycarbonylethylcarbonylamino, acetylaminomethyl, *tert*-butoxycarbonylamino, *N*-(*tert*-butoxycarbonyl)-*N*-(methyl)amino, *tert*-butoxycarbonylaminomethyl, *N*-(*tert*-butoxycarbonyl)-*N*-(methyl)aminomethyl, methylsulphonylamino, ethylsulphonylamino, methylsulphonylaminomethyl, ethylaminocarbonylamino, dimethylaminoethylaminocarbonylamino, *N*-(dimethylaminoethyl)-*N*-(methyl)aminocarbonylamino, carboxycarbonylamino, ethoxycarbonylcarbonylamino, ethylaminocarbonylcarbonylamino, dimethylaminoethylaminocarbonylcarbonylamino, dimethylaminosulphonylamino, formyl, acetyl, dimethylaminoacetyl, ethylcarbonyl, carboxy, carboxymethyl, methoxycarbonyl, ethoxycarbonyl, *tert*-butoxycarbonyl, methoxycarbonylmethyl, *tert*-butoxycarbonylmethyl, aminocarbonyl, methylaminocarbonyl, cyanomethylaminocarbonyl, ethylaminocarbonyl, dimethylaminoethylaminocarbonyl, dihydroxypropylaminocarbonyl, isopropylaminocarbonyl, dimethylaminocarbonyl, *N*-ethyl-*N*-methylaminocarbonyl, *N*-(aminoethyl)-*N*-(methyl)aminocarbonyl, *N*-(dimethylaminoethyl)-*N*-(methyl)aminocarbonyl, diethylaminocarbonyl, dimethylaminocarbonylmethyl, *N*-(diethylaminoethyl)-*N*-(methyl)aminocarbonylmethyl, aminocarbonylmethoxy, methoxyaminocarbonyl, *N*-(methoxy)-*N*-(methyl)aminocarbonyl, methylsulphonyl, methylsulphonyloxymethyl, trifluoromethylsulphonyloxy and tri(C_{1-6})alkylsilyl.

Specific values of R^5 include hydrogen, fluoro, chloro, bromo, iodo, cyano, phenylthio, acetyl, carboxy, methoxycarbonyl, ethoxycarbonyl, aminocarbonyl, phenylaminocarbonyl, benzylaminocarbonyl, pyridinylmethylaminocarbonyl, (phenyl)(pyridinyl)methylaminocarbonyl, *N*-ethyl-*N*-pyridinylmethylaminocarbonyl, dimethylaminomethyl, dimethylaminosulphonylaminopropyl, dimethylaminoethenylcarbonyl, ethynyl, triethylsilylethynyl, diethylaminopropynyl, methylsulphonylaminopropynyl, dimethylaminosulphonylaminopropynyl, hydroxybutynyl, 3-hydroxy-3-methylbutynyl, cyclopropylethynyl, hydroxycyclohexylethynyl, aminocyclohexylethynyl, phenyl, bromophenyl, (bromo)(nitro)phenyl, hydroxyphenyl, methoxyphenyl, ethoxyphenyl, isobutoxyphenyl, (benzyloxy)(chloro)phenyl, aminophenyl, (amino)(bromo)phenyl, aminomethylphenyl, acetylaminophenyl, ethoxycarbonylacetylaminophenyl, ethylcarbonylaminophenyl, methoxycarbonylethylcarbonylaminophenyl, methylsulphonylaminophenyl, ethylsulphonylaminophenyl,

ethylaminocarbonylaminophenyl, dimethylaminoethylaminocarbonylaminophenyl, *N*-(dimethylaminoethyl)-*N*-(methyl)aminocarbonylaminophenyl, carboxycarbonylaminophenyl, ethoxycarbonylcarbonylaminophenyl, ethylaminocarbonylcarbonylaminophenyl, dimethylaminoethylaminocarbonylcarbonylaminophenyl, acetylphenyl, carboxyphenyl, carboxymethylphenyl, methoxycarbonylphenyl, (chloro)(methoxycarbonyl)phenyl, ethoxycarbonylphenyl, methoxycarbonylmethylphenyl, aminocarbonylphenyl, methylaminocarbonylphenyl, cyanomethylaminocarbonylphenyl, ethylaminocarbonylphenyl, dihydroxypropylaminocarbonylphenyl, isopropylaminocarbonylphenyl, dimethylaminocarbonylphenyl, dimethylaminocarbonylmethylphenyl, *N*-(diethylaminoethyl)-*N*-(methyl)aminocarbonylmethylphenyl, naphthyl, benzyl, phenylethyl, phenylethenyl, phenylethynyl, fluorophenylethynyl, nitrophenylethynyl, hydroxyphenylethynyl, methoxyphenylethynyl, dimethylaminophenylethynyl, phenylpropynyl, biphenyl, (bromo)(dinitro)biphenyl, methoxybiphenyl, aminobiphenyl, dimethylaminobiphenyl, dimethylaminomethylbiphenyl, (dimethylaminocarbonyl)-(methyl)biphenyl, acetylpiperidinylethyl, *tert*-butoxycarbonylpyrrolidinylethynyl, piperidinylethynyl, acetylpiperidinylethynyl, *tert*-butoxycarbonylpiperidinylethynyl, methylsulphonylpiperidinylethynyl, 1,2,3,4-tetrahydroisoquinolinylpropynyl, methylpiperazinylpropynyl, pyrrolidinylcarbonylethynyl, hydroxyquinuclidinylethynyl, piperazinylphenyl, *tert*-butoxycarbonylpiperazinylphenyl, morpholinylphenyl, piperidinylmethylphenyl, piperazinylbiphenyl, *tert*-butoxycarbonylpiperazinylbiphenyl, benzofuryl, dibenzofuryl, benzothienyl, dibenzothienyl, pyridinyl, chloropyridinyl, dichloropyridinyl, bromopyridinyl, carboxypyridinyl, ethoxycarbonylpyridinyl, isoquinolinyl, methylimidazolylethyl, methylimidazolylmethylcarbonyl, methylimidazolylethenyl, indolylethynyl, methylindolylethynyl, pyrazolylethynyl, methylpyrazolylethynyl, methylimidazolylethynyl, dimethylimidazolylethynyl, pyridinylethynyl, chloropyridinylethynyl, aminopyridinylethynyl, dimethylaminoethylaminopyridinylethynyl, aminopyrimidinylethynyl, imidazo[1,2-*a*]pyridinylethynyl, dimethylaminomethylimidazo[1,2-*a*]pyridinylethynyl, methylimidazolylcarbonylcarbonyl, methylbenzomorpholinylpyridinyl, hydroxymethylpyrrolidinylpyridinylethynyl, pyrazolylphenyl, methylpyrazolylphenyl, pyridinylphenyl, (amino)(chloropyridinyl)phenyl, phenylisoxazolyl, phenylthiazolyl, (methyl)(trifluoromethylphenyl)thiazolyl, phenylpyridinyl, fluorophenylpyridinyl, chlorophenylpyridinyl, cyanophenylpyridinyl, methylphenylpyridinyl, (bromo)(methyl)phenylpyridinyl, ethylphenylpyridinyl, hydroxyphenyl-

pyridinyl, hydroxymethylphenylpyridinyl, methoxyphenylpyridinyl, aminocarbonyl-methoxyphenylpyridinyl, dihydroxypropoxyphenylpyridinyl, methoxybenzyloxy-phenylpyridinyl, trifluoromethylsulphonyloxyphenylpyridinyl, methylsulphonyl-oxymethylphenylpyridinyl, aminophenylpyridinyl, (amino)(cyano)phenylpyridinyl, dimethylaminophenylpyridinyl, aminomethylphenylpyridinyl, (aminomethyl)(fluoro)-phenylpyridinyl, methylaminomethylphenylpyridinyl, dimethylaminomethylphenyl-pyridinyl, *N*-isopropyl-*N*-methylaminomethylphenylpyridinyl, methoxybenzylamino-phenylpyridinyl, acetylaminophenylpyridinyl, acetylaminomethylphenylpyridinyl, *tert*-butoxycarbonylaminomethylphenylpyridinyl, *N*-(*tert*-butoxycarbonyl)-*N*-(methyl)-aminomethylphenylpyridinyl, methylsulphonylaminomethylphenylpyridinyl, formylphenylpyridinyl, acetylphenylpyridinyl, dimethylaminomethylcarbonyl-phenylpyridinyl, carboxyphenylpyridinyl, (amino)(carboxy)phenylpyridinyl, ethoxycarbonylphenylpyridinyl, *tert*-butoxycarbonylphenylpyridinyl, methoxycarbonyl-methylphenylpyridinyl, aminocarbonylphenylpyridinyl, methylaminocarbonylphenyl-pyridinyl, dimethylaminoethylaminocarbonylphenylpyridinyl, dihydroxypropylamino-carbonylphenylpyridinyl, dimethylaminocarbonylphenylpyridinyl, (dimethylamino-carbonyl)(fluoro)phenylpyridinyl, (dimethylaminocarbonyl)(nitro)phenylpyridinyl, (amino)(dimethylaminocarbonyl)phenylpyridinyl, *N*-ethyl-*N*-methylaminocarbonyl-phenylpyridinyl, *N*-(aminoethyl)-*N*-(methyl)aminocarbonylphenylpyridinyl, *N*-(dimethylaminoethyl)-*N*-(methyl)aminocarbonylphenylpyridinyl, diethylaminocarbonyl-phenylpyridinyl, methoxyaminocarbonylphenylpyridinyl, *N*-methoxy-*N*-methylamino-carbonylphenylpyridinyl, dimethylaminocarbonylmethylphenylpyridinyl, *N*-(diethyl-aminoethyl)-*N*-(methyl)aminocarbonylmethylphenylpyridinyl, methylsulphonylphenyl-pyridinyl, phenylpyrimidinyl, bromophenylpyrimidinyl, aminoazetidinylphenylpyridinyl, methylaminoazetidinylphenylpyridinyl, aminopyrrolidinylphenylpyridinyl, amino-piperidinylphenylpyridinyl, methylaminopiperidinylphenylpyridinyl, piperazinyl-phenylpyridinyl, *tert*-butoxycarbonylpiperazinylphenylpyridinyl, *tert*-butoxycarbonyl-methylpiperazinylphenylpyridinyl, morpholinylphenylpyridinyl, piperazinylphenyl-pyrimidinyl, pyrrolidinylmethylphenylpyridinyl, hydroxypyrrolidinylmethylphenyl-pyridinyl, dioxopyrrolidinylmethylphenylpyridinyl, aminopyrrolidinylmethylphenyl-pyridinyl, carboxypyrrolidinylmethylphenylpyridinyl, *tert*-butoxycarbonylpyrrolidinyl-methylphenylpyridinyl, aminopiperidinylmethylphenylpyridinyl, methylaminopiperidinyl-methylphenylpyridinyl, piperazinylmethylphenylpyridinyl, methylpiperazinylmethyl-

phenylpyridinyl, oxopiperazinylmethylphenylpyridinyl, homopiperazinylmethylphenylpyridinyl, morpholinylmethylphenylpyridinyl, dimethylmorpholinylmethylphenylpyridinyl, aminoazabicyclo[3.2.1]octylmethylphenylpyridinyl, diazabicyclo[3.2.1]octylmethylphenylpyridinyl, tetrazolylphenylpyridinyl, benzofurylpyridinyl, benzothienylpyridinyl, indolylpyridinyl, dimethylisoxazolylpyridinyl, bi(pyridinyl), chlorobi(pyridinyl), carboxybi(pyridinyl), methoxycarbonylbi(pyridinyl), isoquinolinylpyridinyl, morpholinylcarbonylbi(pyridinyl), phenoxyphenyl, benzyloxyphenyl, methoxybenzyloxyphenyl, pyridinylmethoxyphenyl, *N*-(benzyl)-*N*-(ethylcarbonyl)aminophenyl, methylfurylmethylaminophenyl, pyridinylmethylaminophenyl, cyclopentylcarbonylaminophenyl, phenylcarbonylaminophenyl, benzylcarbonylaminophenyl, hydroxypyrrolidinylcarbonylaminophenyl, aminopyrrolidinylcarbonylaminophenyl, *tert*-butoxycarbonylaminopyrrolidinylcarbonylaminophenyl, (isopropyl)-(oxo)pyrrolidinylcarbonylaminophenyl, *tert*-butoxycarbonylpiperidinylcarbonylaminophenyl, piperazinylcarbonylaminophenyl, methylpiperazinylcarbonylaminophenyl, *tert*-butoxycarbonylpiperazinylcarbonylaminophenyl, morpholinylcarbonylaminophenyl, indolylcarbonylaminophenyl, methylisoxazolylcarbonylaminophenyl, pyridinylcarbonylaminophenyl, hydroxypyridinylcarbonylaminophenyl, (oxo)(phenyl)pyrrolidinylcarbonylaminophenyl, phenylsulphonylaminophenyl, benzylsulphonylaminophenyl, dimethylisoxazolylsulphonylaminophenyl, cyclopentylaminocarbonylaminophenyl, phenylaminocarbonylaminophenyl, methylazetidinylaminocarbonylaminophenyl, morpholinylethylaminocarbonylaminophenyl, methylimidazolylmethylaminocarbonylaminophenyl, morpholinylcarbonylcarbonylaminophenyl, pyrrolidinylethylaminocarbonylcarbonylaminophenyl, phenylcarbonylphenyl, morpholinylcarbonylphenyl, aminopyrrolidinylcarbonylmethylphenyl, *tert*-butoxycarbonylaminopyrrolidinylcarbonylmethylphenyl, aminopiperidinylcarbonylmethylphenyl, methylaminopiperidinylcarbonylmethylphenyl, *tert*-butoxycarbonylaminopiperidinylcarbonylmethylphenyl, *N*-(*tert*-butoxycarbonyl)-*N*-(methyl)aminopiperidinylcarbonylmethylphenyl, benzylaminocarbonylphenyl, morpholinylethylaminocarbonylphenyl, imidazolylaminocarbonylphenyl, methylimidazolylmethylaminocarbonylphenyl, pyridinylmethylaminocarbonylphenyl, azetidinylaminocarbonylmethylphenyl, *tert*-butoxycarbonylazetidinylaminocarbonylmethylphenyl, pyrrolidinylmethylaminocarbonylmethylphenyl, *tert*-butoxycarbonylpyrrolidinylmethylaminocarbonylmethylphenyl, pyridinylaminocarbonylmethylphenyl, pyridinylmethylaminocarbonylmethylphenyl, phenylaminopyridinyl, *N*-methyl-*N*-

phenylaminopyridinyl, azetidinylaminophenylpyridinyl, pyrrolidinylaminophenylpyridinyl, *tert*-butoxycarbonylpyrrolidinylaminophenylpyridinyl, piperazinylcarbonylaminophenylpyridinyl, piperidinylaminocarbonylaminophenylpyridinyl, aminoazetidinylcarbonylphenylpyridinyl, methylaminoazetidinylcarbonylphenylpyridinyl, *tert*-butoxycarbonylaminoazetidinylcarbonylphenylpyridinyl, *N*-(*tert*-butoxycarbonyl)-*N*-(methyl)aminoazetidinylcarbonylphenylpyridinyl, pyrrolidinylcarbonylphenylpyridinyl, hydroxypyrrolidinylcarbonylphenylpyridinyl, aminopyrrolidinylcarbonylphenylpyridinyl, aminopyrrolidinylcarbonylphenyl(amino)pyridinyl, methylaminopyrrolidinylcarbonylphenylpyridinyl, *tert*-butoxycarbonylaminopyrrolidinylcarbonylphenylpyridinyl, *tert*-butoxycarbonylaminopyrrolidinylcarbonylphenyl(methoxybenzylamino)pyridinyl, piperidinylcarbonylphenylpyridinyl, aminopiperidinylcarbonylphenylpyridinyl, methylaminopiperidinylcarbonylphenylpyridinyl, *tert*-butoxycarbonylaminopiperidinylcarbonylphenylpyridinyl, dimethylaminopiperidinylcarbonylphenylpyridinyl, *N*-(*tert*-butoxycarbonyl)-*N*-(methyl)aminopiperidinylcarbonylphenylpyridinyl, piperazinylcarbonylphenylpyridinyl, methylpiperazinylcarbonylphenylpyridinyl, *tert*-butoxycarbonylpiperazinylcarbonylphenylpyridinyl, morpholinylcarbonylphenylpyridinyl, methylaminopiperidinylcarbonylphenylpyrimidinyl, dimethylaminopiperidinylcarbonylphenylpyrimidinyl, morpholinylmethylcarbonylphenylpyridinyl, aminoazabicyclo[3.2.1]octylcarbonylphenylpyridinyl, aminoazetidinylcarbonylmethylphenylpyridinyl, *tert*-butoxycarbonylaminoazetidinylcarbonylmethylphenylpyridinyl, pyrrolidinylcarbonylmethylphenylpyridinyl, aminopyrrolidinylcarbonylmethylphenylpyridinyl, *tert*-butoxycarbonylaminopyrrolidinylcarbonylmethylphenylpyridinyl, methylaminopiperidinylcarbonylmethylphenylpyridinyl, *N*-(*tert*-butoxycarbonyl)-*N*-(methyl)aminopiperidinylcarbonylmethylphenylpyridinyl, methylpiperazinylcarbonylmethylphenylpyridinyl, azetidinylaminocarbonylphenylpyridinyl, *tert*-butoxycarbonylazetidinylaminocarbonylphenylpyridinyl, *N*-(*tert*-butoxycarbonylazetidinyl)-*N*-(ethyl)aminocarbonylphenylpyridinyl, *tert*-butoxycarbonylpyrrolidinylaminocarbonylphenylpyridinyl, *N*-(methylpyrrolidinyl)-*N*-(methyl)aminocarbonylphenylpyridinyl, *N*-(methylpiperidinyl)-*N*-(methyl)aminocarbonylphenylpyridinyl, piperidinylmethylaminocarbonylphenylpyridinyl, *tert*-butoxycarbonylpiperidinylmethylaminocarbonylphenylpyridinyl, azetidinylaminocarbonylmethylphenylpyridinyl and *tert*-butoxycarbonylazetidinylaminocarbonylmethylphenylpyridinyl.

Particular values of R^5 include hydrogen and phenylethynyl.

Suitably, when R^3 and R^4 in the compounds of formula (B) above are both hydrogen, then R^5 is other than hydrogen.

Suitably, when R^5 in the compounds of formula (B) above is hydrogen, then R^3 and/or R^4 is other than hydrogen.

Suitably, R^6, when present, represents hydrogen, hydroxy or $-NR^{6a}R^{6b}$. In a preferred embodiment, R^6 represents hydrogen. In an alternative embodiment, R^6 represents hydroxy. In another embodiment, R^6 represents $-NR^{6a}R^{6b}$. In a further embodiment, R^6 represents oxo.

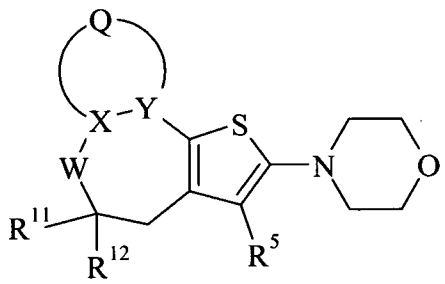
Suitably, R^{6a} represents C_{1-6} alkyl, C_{3-7} cycloalkyl, aryl or aryl(C_{1-6})alkyl, any of which groups may be optionally substituted by one or more substituents.

Examples of suitable substituents on R^{6a} and R^{6b} include halogen, cyano, trifluoromethyl, hydroxy, C_{1-6} alkoxy and trifluoromethoxy, especially hydroxy.

Typical values of R^{6a} include methyl, hydroxyethyl, cyclopropyl, phenyl and benzyl.

Suitably, R^{6b} represents hydrogen or C_{1-6} alkyl. In one embodiment, R^{6b} represents hydrogen. In another embodiment, R^{6b} represents C_{1-6} alkyl, especially methyl.

One sub-class of compounds according to the invention is represented by the compounds of formula (BA), and pharmaceutically acceptable salts and solvates thereof:



(BA)

wherein

W, the moiety X-Y-Q and R^5 are as defined above;

R^{11} represents hydrogen or C_{1-6} alkyl; and

R^{12} represents hydrogen; or C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl(C_{1-6})alkyl, aryl, aryl(C_{1-6})alkyl, C_{3-7} heterocycloalkyl, C_{3-7} heterocycloalkyl-

(C_{1-6})alkyl, heteroaryl or heteroaryl(C_{1-6})alkyl, any of which groups may be optionally substituted by one or more substituents; or

R^{11} and R^{12}, when taken together with the carbon atom to which they are both attached, represent C_{3-7} cycloalkyl or C_{3-7} heterocycloalkyl, either of which groups may be optionally substituted by one or more substituents.

Suitably, R^5 in the compounds of formula (BA) is other than hydrogen.

Where any of the groups in the compounds of formula (BA) above is stated to be optionally substituted, this group may be unsubstituted, or substituted by one or more substituents. Typically, such groups will be unsubstituted, or substituted by one or two substituents. Suitably, such groups will be unsubstituted or monosubstituted.

Typical values of R^{11} include hydrogen, methyl and ethyl. In one embodiment, R^{11} is hydrogen. In another embodiment, R^{11} is C_{1-6} alkyl, especially methyl.

Suitably, R^{12} represents hydrogen; or C_{1-6} alkyl, C_{3-7} cycloalkyl or aryl, any of which groups may be optionally substituted by one or more substituents.

Examples of typical substituents on R^{12} include halogen, cyano, nitro, C_{1-6} alkyl, trifluoromethyl, hydroxy, C_{1-6} alkoxy, difluoromethoxy, trifluoromethoxy, aryloxy, C_{1-6} alkylthio, C_{1-6} alkylsulphonyl, amino, C_{1-6} alkylamino, di(C_{1-6})alkylamino, C_{2-6} alkylcarbonylamino, C_{2-6} alkoxycarbonylamino, C_{1-6} alkylsulphonylamino, formyl, C_{2-6} alkylcarbonyl, carboxy, C_{2-6} alkoxycarbonyl, aminocarbonyl, C_{1-6} alkylaminocarbonyl, di(C_{1-6})alkylaminocarbonyl, aminosulphonyl, C_{1-6} alkylaminosulphonyl and di(C_{1-6})alkylaminosulphonyl; especially halogen, C_{1-6} alkoxy or C_{1-6} alkylthio.

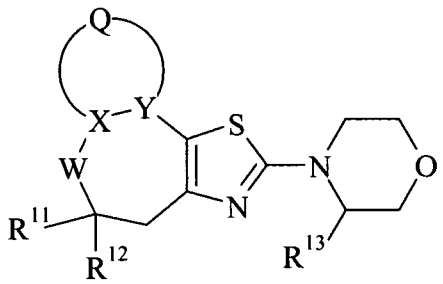
Examples of particular substituents on R^{12} include fluoro, chloro, bromo, cyano, nitro, methyl, trifluoromethyl, hydroxy, methoxy, difluoromethoxy, trifluoromethoxy, phenoxy, methylthio, methylsulphonyl, amino, methylamino, dimethylamino, acetylamino, methoxycarbonylamino, methylsulphonylamino, formyl, acetyl, carboxy, methoxycarbonyl, aminocarbonyl, methylaminocarbonyl, dimethylaminocarbonyl, aminosulphonyl, methylaminosulphonyl and dimethylaminosulphonyl; especially chloro, methoxy or methylthio.

Typical values of R^{12} include hydrogen, methyl, *n*-propyl, isopropyl, isobutyl, cyclohexyl and phenyl. A particular value of R^{12} is methyl.

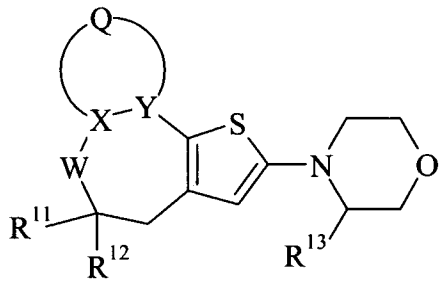
Alternatively, R^{11} and R^{12} may together form an optionally substituted spiro linkage. Thus, R^{11} and R^{12}, when taken together with the carbon atom to which they are both attached, may represent C_{3-7} cycloalkyl or C_{3-7} heterocycloalkyl, either of which

groups may be unsubstituted, or substituted by one or more, typically by one or two, substituents. In this context, R^{11} and R^{12}, when taken together with the carbon atom to which they are both attached, may suitably represent an optionally substituted cyclopentyl, cyclohexyl, pyrrolidine or piperidine ring.

Other sub-classes of compounds according to the invention are represented by the compounds of formula (IIA-A) and (IIA-B), and pharmaceutically acceptable salts and solvates thereof:



(IIA-A)



(IIA-B)

wherein

W, the moiety X-Y-Q, R^{11} and R^{12} are as defined above; and

R^{13} represents hydrogen; or C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl(C_{1-6})alkyl, aryl, aryl(C_{1-6})alkyl, aryl(C_{2-6})alkenyl, aryl(C_{2-6})alkynyl, biaryl(C_{1-6})alkyl, C_{3-7} heterocycloalkyl, C_{3-7} heterocycloalkyl(C_{1-6})alkyl, C_{3-7} heterocycloalkylcarbonyl, heteroaryl, heteroaryl(C_{1-6})alkyl, heteroaryl-aryl(C_{1-6})alkyl or aryl-heteroaryl(C_{1-6})alkyl, any of which groups may be optionally substituted by one or more substituents.

Where any of the groups in the compounds of formula (IIA-A) or (IIA-B) above is stated to be optionally substituted, this group may be unsubstituted, or substituted by one or more substituents. Typically, such groups will be unsubstituted, or substituted by one or two substituents. Suitably, such groups will be unsubstituted or monosubstituted.

Typically, R^{13} represents hydrogen; or C_{1-6} alkyl, aryl(C_{1-6})alkyl, aryl(C_{2-6})alkynyl, biaryl(C_{1-6})alkyl, C_{3-7} heterocycloalkyl(C_{1-6})alkyl, C_{3-7} heterocycloalkylcarbonyl,

heteroaryl(C_{1-6})alkyl, heteroaryl-aryl(C_{1-6})alkyl or aryl-heteroaryl(C_{1-6})alkyl, any of which groups may be optionally substituted by one or more substituents.

Generally, R^{13} represents hydrogen; or C_{2-6} alkynyl, aryl(C_{1-6})alkyl or heteroaryl-(C_{1-6})alkyl, any of which groups may be optionally substituted by one or more substituents. More particularly, R^{13} represents aryl(C_{1-6})alkyl or heteroaryl(C_{1-6})alkyl, either of which groups may be optionally substituted by one or more substituents.

In one specific embodiment, R^{13} represents hydrogen.

Typically, R^{13} is other than hydrogen.

In a representative embodiment, R^{13} represents C_{1-6} alkyl, aryl(C_{1-6})alkyl, biaryl-(C_{1-6})alkyl, heteroaryl(C_{1-6})alkyl or heteroaryl-aryl(C_{1-6})alkyl, any of which groups may be optionally substituted by one or more substituents. Preferably, R^{13} represents methyl, arylmethyl, biarylmethyl, heteroarylmethyl or heteroaryl-arylmethyl, any of which groups may be optionally substituted by one or more substituents. More particularly, R^{13} represents arylmethyl or heteroarylmethyl, either of which groups may be optionally substituted by one or more substituents.

In a particular embodiment, R^{13} represents substituted or unsubstituted indolyl-(C_{1-6})alkyl. Advantageously, R^{13} represents substituted or unsubstituted indolylmethyl.

In a typical embodiment, R^{13} represents substituted or unsubstituted phenyl-(C_{1-6})alkyl. Advantageously, R^{13} represents substituted or unsubstituted benzyl.

In another embodiment, R^{13} represents substituted or unsubstituted benzofuryl-(C_{1-6})alkyl. Advantageously, R^{13} represents substituted or unsubstituted benzofurylmethyl.

Illustratively, R^{13} represents hydrogen; or methyl, propynyl, benzyl, phenylethyl, naphthylmethyl, phenylpropynyl, biphenylmethyl, naphthylphenylmethyl, indolinylmethyl, 1,2,3,4-tetrahydroquinolinylmethyl, 1,2,3,4-tetrahydroisoquinolinyl-methyl, piperidinylcarbonyl, 1,2,3,4-tetrahydroquinolinylcarbonyl, 1,2,3,4-tetrahydroisoquinolinylcarbonyl, 1,2,3,4-tetrahydroquinoxalinylcarbonyl, benzofurylmethyl, benzothienylmethyl, indolylmethyl, pyrrolo[2,3-*b*]pyridinylmethyl, pyrrolo[3,2-*c*]pyridinylmethyl, benzimidazolylmethyl, benzotriazolylmethyl, pyridinylmethyl, quinolinylmethyl, isoquinolinylmethyl, benzofurylbenzyl, thienylbenzyl, benzothienylbenzyl, indolylbenzyl, isoxazolylbenzyl, pyrazolylbenzyl, pyridinylbenzyl, pyrimidinylbenzyl or phenylpyridinylmethyl, any of which groups may be optionally substituted by one or more substituents.

Examples of typical substituents on R^{13} include halogen, cyano, nitro, C_{1-6} alkyl, trifluoromethyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, (C_{1-6})alkylaryl, di(C_{1-6})alkylaryl, piperidinyl-(C_{1-6})alkylaryl, piperazinyl(C_{1-6})alkylaryl, (C_{1-6})alkylpiperazinyl(C_{1-6})alkylaryl, morpholinyl(C_{1-6})alkylaryl, (C_{1-6})alkoxyaryl, cyano(C_{1-6})alkoxyaryl, di(C_{1-6})alkyl-amino(C_{1-6})alkylaryl, (C_{1-6})alkylaminocarbonylaryl, aryl(C_{1-6})alkyl, oxazolinyl, azetidinyl, haloarylpyrrolidinyl, dioxopyrrolidinyl, aminopyrrolidinyl, di(C_{1-6})alkylaminopyrrolidinyl, indolinyl, oxoindolinyl, arylpiperidinyl, arylcarbonylpiperidinyl, di(C_{1-6})alkylamino-carbonylpiperidinyl, piperazinyl, (C_{1-6})alkylpiperazinyl, haloarylpiperazinyl, pyridinylpiperazinyl, furoylpiperazinyl, homopiperazinyl, (C_{1-6})alkylhomopiperazinyl, morpholinyl, (C_{1-6})alkylpiperazinyl(C_{1-6})alkyl, morpholinyl(C_{1-6})alkyl, benzofuryl, benzothienyl, pyrazolyl, (C_{1-6})alkylpyrazolyl, di(C_{1-6})alkylpyrazolyl, tri(C_{1-6})alkyl-pyrazolyl, [di(C_{1-6})alkyl](trifluoromethyl)pyrazolyl, cyano(C_{1-6})alkylpyrazolyl, [cyano-(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, hydroxy(C_{1-6})alkylpyrazolyl, [hydroxy(C_{1-6})-alkyl][di(C_{1-6})alkyl]pyrazolyl, methoxy(C_{1-6})alkylpyrazolyl, [(hydroxy)(methoxy)(C_{1-6})-alkyl]pyrazolyl, amino(C_{1-6})alkylpyrazolyl, [(C_{1-6})alkyl][amino(C_{1-6})alkyl]pyrazolyl, [amino(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, di(C_{1-6})alkylamino(C_{1-6})alkylpyrazolyl, di(C_{1-6})alkoxyphosphono(C_{1-6})alkylpyrazolyl, (C_{2-6})alkenylpyrazolyl, (C_{3-7})cycloalkyl-(C_{1-6})alkylpyrazolyl, [(C_{3-7})cycloalkyl(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, [(C_{1-6})alkyl]-(aryl)pyrazolyl, (aryl)(trifluoromethyl)pyrazolyl, aryl(C_{1-6})alkylpyrazolyl, aminoaryl-(C_{1-6})alkylpyrazolyl, piperidinylpyrazolyl, tetrahydropyranyl(C_{1-6})alkylpyrazolyl, [di-(C_{1-6})alkyl][tetrahydropyranyl(C_{1-6})alkyl]pyrazolyl, pyrrolidinyl(C_{1-6})alkylpyrazolyl, piperidinyl(C_{1-6})alkylpyrazolyl, (C_{1-6})alkylpiperidinyl(C_{1-6})alkylpyrazolyl, morpholinyl(C_{1-6})alkylpyrazolyl, pyridinyl(C_{1-6})alkylpyrazolyl, oxypyridinyl(C_{1-6})alkyl-pyrazolyl, [arylcarbonyl(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, [(C_{1-6})alkyl](piperazinyl-carbonyl)pyrazolyl, [(C_{1-6})alkylaminocarbonyl][(C_{1-6})alkylaryl]pyrazolyl, [(C_{1-6})alkyl]-[amino(C_{1-6})alkylaminocarbonyl]pyrazolyl, aminocarbonyl(C_{1-6})alkylpyrazolyl, [aminocarbonyl(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, di(C_{1-6})alkylaminocarbonyl(C_{1-6})alkyl-pyrazolyl, pyrazolo[1,5-*a*]pyridinyl, di(C_{1-6})alkylisoxazolyl, (amino)[(C_{1-6})alkyl]-isoxazolyl, thiazolyl, di(C_{1-6})alkylthiazolyl, imidazolyl, (C_{1-6})alkylimidazolyl, di(C_{1-6})-alkylimidazolyl, imidazo[1,2-*a*]pyridinyl, (C_{1-6})alkylimidazo[1,2-*a*]pyridinyl, (C_{1-6})-alkylimidazo[4,5-*b*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyrazinyl, (C_{1-6})-alkylthiadiazolyl, triazolyl, pyridinyl, halopyridinyl, (C_{1-6})alkylpyridinyl, [(C_{1-6})alkyl]-(halo)pyridinyl, di(C_{1-6})alkylpyridinyl, (C_{2-6})alkenylpyridinyl, (C_{1-6})alkylpiperazinyl-

pyridinyl, [(C_{1-6})alkyl](piperazinyl)pyridinyl, [(C_{1-6})alkoxycarbonylpiperazinyl][(C_{1-6})-alkyl]pyridinyl, piperidinyl(C_{1-6})alkylpyridinyl, [(C_{1-6})alkyl](oxy)pyridinyl, hydroxypyridinyl, hydroxy(C_{1-6})alkylpyridinyl, (C_{1-6})alkoxypyridinyl, [(C_{1-6})alkoxy]-[(C_{1-6})alkyl]pyridinyl, [(C_{1-6})alkoxy][di(C_{1-6})alkyl]pyridinyl, (C_{1-6})alkoxy(C_{1-6})alkyl-pyridinyl, aminopyridinyl, carboxy(C_{1-6})alkylpyridinyl, (C_{1-6})alkoxycarbonyl(C_{1-6})alkyl-pyridinyl, pyridazinyl, (C_{1-6})alkylpyridazinyl, piperidinylpyridazinyl, oxypyridazinyl, (C_{1-6})alkoxypyridazinyl, aminopyridazinyl, hydroxy(C_{1-6})alkylaminopyridazinyl, di-(C_{1-6})alkylaminopyridazinyl, pyrimidinyl, (C_{1-6})alkylpyrimidinyl, [(C_{1-6})alkyl](halo)-pyrimidinyl, di(C_{1-6})alkylpyrimidinyl, pyrrolidinylpyrimidinyl, (C_{1-6})alkylpiperazinyl-pyrimidinyl, [(C_{1-6})alkyl](piperazinyl)pyrimidinyl, [(C_{1-6})alkoxycarbonyl][(C_{1-6})alkyl]-piperazinylpyrimidinyl, hydroxypyrimidinyl, [(C_{1-6})alkyl](hydroxy)pyrimidinyl, [(C_{1-6})-alkyl][hydroxy(C_{1-6})alkyl]pyrimidinyl, [(C_{1-6})alkyl][hydroxy(C_{2-6})alkynyl]pyrimidinyl, (C_{1-6})alkoxypyrimidinyl, aminopyrimidinyl, di(C_{1-6})alkylaminopyrimidinyl, [di(C_{1-6})alkyl-amino](halo)pyrimidinyl, carboxypyrimidinyl, [(C_{1-6})alkoxycarbonyl(C_{1-6})alkyl][(C_{1-6})-alkyl]pyrimidinyl, aminocarbonylpyrimidinyl, pyrazinyl, (C_{1-6})alkoxypyrazinyl, amino-pyrazinyl, hydroxy, (C_{1-6})alkoxy, difluoromethoxy, trifluoromethoxy, C_{3-7} cycloalkoxy, C_{3-7} cycloalkyl(C_{1-6})alkoxy, aryl(C_{1-6})alkoxycarbonylpiperidinyloxy, morpholinyl(C_{1-6})-alkoxy, aryloxy, haloaryloxy, di(C_{1-6})alkylpyrazolyloxy, halopyridinyloxy, pyrrolidinylpyridinyloxy, (C_{1-6})alkylpiperazinylpyridinyloxy, (C_{1-6})alkylpyrazolyl-pyridinyloxy, (C_{1-6})alkylaminopyridinyloxy, carboxypyridinyloxy, aminocarbonyl-pyridinyloxy, (C_{1-6})alkylpyridazinyloxy, pyrimidinyloxy, (C_{1-6})alkylpyrimidinyloxy, [(C_{1-6})alkyl](halo)pyrimidinyloxy, hydroxy(C_{1-6})alkyl, dihydroxy(C_{1-6})alkyl, pyridinyloxy(C_{1-6})alkyl, methylenedioxy, difluoromethylenedioxy, amino, (C_{1-6})alkyl-amino, dihydroxy(C_{1-6})alkylamino, (C_{1-6})alkoxy(C_{1-6})alkylamino, di(C_{1-6})alkylamino, *N*-[(C_{1-6})alkoxy(C_{1-6})alkyl]-*N*-[(C_{1-6})alkyl]amino, di(C_{1-6})alkylamino(C_{1-6})alkylamino, *N*-[(C_{1-6})alkyl]-*N*-[di(C_{1-6})alkylamino(C_{1-6})alkyl]amino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{3-7})cycloalkyl]-amino, haloarylamino, *N*-[(C_{1-6})alkyl]-*N*-(haloaryl)amino, methylenedioxyphenylamino, morpholinyl(C_{1-6})alkylphenylamino, oxazolinylphenylamino, [(C_{1-6})alkyl](oxo)pyrazolyl-phenylamino, oxazolylphenylamino, isoxazolylphenylamino, triazolylphenylamino, (C_{1-6})alkyltriazolylphenylamino, (C_{1-6})alkylpyrimidinylphenylamino, pyrazolyl(C_{1-6})alkyl-phenylamino, triazolyl(C_{1-6})alkylphenylamino, C_{1-6} alkylsulphonylaminophenylamino, morpholinylcarbonylphenylamino, C_{1-6} alkylsulphonylphenylamino, morpholinylsulphonylphenylamino, *N*-[(C_{1-6})alkyl]-*N*-[aryl(C_{1-6})alkyl]amino,

N-[di(C_{1-6})alkylamino(C_{1-6})alkyl]-*N*-[aryl(C_{1-6})alkyl]amino, cyanoaryl(C_{1-6})alkylamino, (cyano)(halo)aryl(C_{1-6})alkylamino, methylenedioxyaryl(C_{1-6})alkylamino, dihydrobenzofuranylamino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpyrrolidinyl]amino, C_{1-6} alkylsulphonylindolinylamino, chromanonylamino, piperidinylamino, *N*-[(C_{1-6})alkyl]-*N*-(piperidinyl)amino, *N*-[(C_{3-7})cycloalkyl(C_{1-6})alkyl]-*N*-(piperidinyl)amino, (C_{1-6})alkylpiperidinylamino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpiperidinyl]amino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{3-7})cycloalkylpiperidinyl]amino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{2-6})alkylcarbonylpiperidinyl]-amino, dihydroquinolinonylamino, benzoxazinonylamino, pyrrolidinyl(C_{1-6})alkylamino, *N*-[(C_{1-6})alkyl]-*N*-[pyrrolidinyl(C_{1-6})alkyl]amino, *N*-[(C_{1-6})alkyl]-*N*-[piperidinyl(C_{1-6})-alkyl]amino, benzothienylamino, indolylamino, dioxoindolylamino, (C_{1-6})alkylpyrazolylamino, [(C_{1-6})alkyl](halo)pyrazolylamino, di(C_{1-6})alkylpyrazolylamino, tri(C_{1-6})alkylpyrazolylamino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpyrazolyl]amino, (C_{1-6})alkylindazolylamino, benzoxazolylamino, benzoxazolonylamino, di(C_{1-6})alkylisoxazolylamino, thiazolylamino, benzothiazolylamino, (C_{1-6})alkylisothiazolylamino, imidazolylamino, [(C_{1-6})alkoxycarbonyl][(C_{1-6})alkyl]imidazolylamino, (C_{1-6})alkylbenzimidazolylamino, benzimidazolonylamino, di(C_{1-6})alkylbenzimidazolonylamino, (C_{1-6})alkyloxadiazolylamino, furyloxadiazolylamino, (C_{1-6})alkylthiadiazolylamino, pyridinylamino, halopyridinylamino, (C_{1-6})alkylpyridinylamino, di(C_{1-6})alkylpyridinylamino, trifluoromethylpyridinylamino, hydroxypyridinylamino, hydroxy(C_{1-6})alkylpyridinylamino, dihydroxy(C_{1-6})alkylpyridinylamino, (C_{1-6})alkoxypyridinylamino, dihydroxy(C_{1-6})alkoxypyridinylamino, di(C_{1-6})alkyldioxolanyl(C_{1-6})alkoxypyridinylamino, (C_{1-6})alkoxy(C_{1-6})-alkylpyridinylamino, (C_{1-6})alkoxy(C_{2-6})alkenylpyridinylamino, dihydroxy(C_{1-6})alkylaminopyridinylamino, di(C_{1-6})alkylaminopyridinylamino, (C_{1-6})alkylamino(C_{1-6})alkylpyridinylamino, di(C_{1-6})alkylamino(C_{1-6})alkylpyridinylamino, oxopyridinylamino, carboxypyridinylamino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpyridinyl]amino, bis[(C_{1-6})alkylpyridinyl]amino, bis(trifluoromethylpyridinyl)amino, isoquinolinylamino, (C_{1-6})alkylpyridazinylamino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpyridazinyl]amino, *N*-[aryl(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpyridazinyl]amino, di(C_{1-6})alkylpyridazinylamino, arylpyridazinylamino, piperidinylpyridazinylamino, (C_{1-6})alkoxypyridazinylamino, [(C_{1-6})alkoxy](halo)-pyridazinylamino, di(C_{1-6})alkylaminopyridazinylamino, bis[(C_{1-6})alkylpyridazinyl]amino, (C_{1-6})alkylcinnolinylamino, oxopyrimidinylamino, thioxopyrimidinylamino, quinoxalinylamino, (C_{1-6})alkylchromenylamino, benzofuryl(C_{1-6})alkylamino, thienyl(C_{1-6})-alkylamino, indolyl(C_{1-6})alkylamino, (C_{1-6})alkylpyrazolyl(C_{1-6})alkylamino, [di(C_{1-6})alkyl]-

(halo)pyrazolyl(C_{1-6})alkylamino, di(C_{1-6})alkylisoxazolyl(C_{1-6})alkylamino, thiazolyl(C_{1-6})-alkylamino, imidazolyl(C_{1-6})alkylamino, (C_{1-6})alkylimidazolyl(C_{1-6})alkylamino, pyridinyl(C_{1-6})alkylamino, (C_{1-6})alkylpyridinyl(C_{1-6})alkylamino, *N*-[(C_{1-6})alkyl]-*N*-[pyridinyl(C_{1-6})alkyl]amino, *N*-[dihydroxy(C_{1-6})alkyl]-*N*-[pyridinyl(C_{1-6})alkyl]amino, *N*-[(C_{1-6})alkylpyridinyl(C_{1-6})alkyl]-*N*-[dihydroxy(C_{1-6})alkyl]amino, amino(C_{1-6})alkyl, (C_{1-6})-alkylamino(C_{1-6})alkyl, di(C_{1-6})alkylamino(C_{1-6})alkyl, pyridinylamino(C_{1-6})alkyl, C_{2-6} alkylcarbonylamino, *N*-[(C_{2-6})alkylcarbonyl]-*N*-[(C_{1-6})alkylpyridinyl(C_{1-6})alkyl]amino, di(C_{1-6})alkylamino(C_{1-6})alkylcarbonylamino, C_{2-6} alkylcarbonylaminomethyl, (C_{3-7})-cycloalkylcarbonylamino, (C_{1-6})alkylpiperidinylcarbonylamino, (C_{1-6})alkylimidazolyl-carbonylamino, C_{2-6} alkoxycarbonylamino, [(C_{2-6})alkoxycarbonyl][(C_{1-6})alkyl]amino, C_{1-6} alkylsulphonylamino, formyl, C_{2-6} alkylcarbonyl, C_{2-6} alkylcarbonyl oxime, C_{2-6} alkylcarbonyl *O*-(methyl)oxime, trifluoromethylcarbonyl, carboxy, C_{2-6} alkoxycarbonyl, aminocarbonyl, C_{1-6} alkylaminocarbonyl, [hydroxy(C_{1-6})alkyl]aminocarbonyl, [di(C_{1-6})-alkylamino(C_{1-6})alkyl]aminocarbonyl, di(C_{1-6})alkylaminocarbonyl, [(C_{1-6})alkyl][cyano-(C_{1-6})alkyl]aminocarbonyl, [(C_{1-6})alkyl][hydroxy(C_{1-6})alkyl]aminocarbonyl, [(C_{1-6})alkoxy-(C_{1-6})alkyl][(C_{1-6})alkyl]aminocarbonyl, [di(C_{1-6})alkylamino(C_{1-6})alkyl][(C_{1-6})alkyl]amino-carbonyl, C_{3-7} cycloalkyl(C_{1-6})alkylaminocarbonyl, aryl(C_{1-6})alkylaminocarbonyl, (C_{1-6})-alkylpiperidinylaminocarbonyl, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})-alkylpiperidinyl]aminocarbonyl, piperidinyl(C_{1-6})alkylaminocarbonyl, heteroarylaminocarbonyl, heteroaryl(C_{1-6})alkyl-aminocarbonyl, azetidinylcarbonyl, hydroxyazetidinylcarbonyl, aminoazetidinylcarbonyl, C_{2-6} alkoxycarbonylaminoazetidinylcarbonyl, pyrrolidinylcarbonyl, (C_{1-6})alkyl-pyrrolidinylcarbonyl, C_{1-6} alkoxy(C_{1-6})alkylpyrrolidinylcarbonyl, di(C_{1-6})alkylamino-pyrrolidinylcarbonyl, thiazolidinylcarbonyl, oxothiazolidinylcarbonyl, piperidinyl-carbonyl, (C_{1-6})alkylpiperazinylcarbonyl, morpholinylcarbonyl, C_{1-6} alkylthio, C_{1-6} alkylsulphinyl, C_{1-6} alkylsulphonyl, C_{1-6} alkylsulphonylmethyl, aminosulphonyl, C_{1-6} alkylaminosulphonyl, di(C_{1-6})alkylaminosulphonyl, C_{2-6} alkoxycarbonyloxy, trimethylsilyl and tetra(C_{1-6})alkyldioxaborolanyl.

Particular examples of typical substituents on R^{13} include halogen, cyano, C_{1-6} alkyl, C_{2-6} alkoxycarbonyl and di(C_{1-6})alkylaminocarbonyl. A further example is carboxy.

Selected examples of specific substituents on R^{13} include fluoro, chloro, bromo, cyano, nitro, methyl, *n*-propyl, isopropyl, trifluoromethyl, allyl, cyclopropyl, methylphenyl, dimethylphenyl, piperidinylmethylphenyl, piperazinylmethylphenyl, methylpiperazinylmethylphenyl, morpholinylmethylphenyl, methoxyphenyl,

cyanomethoxyphenyl, dimethylaminomethylphenyl, methylaminocarbonylphenyl, benzyl, oxazolinyl, azetidinyl, pyrrolidinyl, chlorophenylpyrrolidinyl, dioxopyrrolidinyl, aminopyrrolidinyl, dimethylaminopyrrolidinyl, indolinyl, oxoindolinyl, phenylpiperidinyl, benzoylpiperidinyl, diethylaminocarbonylpiperidinyl, piperazinyl, methylpiperazinyl, chlorophenylpiperazinyl, pyridinylpiperazinyl, furoylpiperazinyl, homopiperazinyl, methylhomopiperazinyl, morpholinyl, methylpiperazinylmethyl, methylpiperazinylethyl, morpholinylmethyl, benzofuryl, benzothienyl, pyrazolyl, methylpyrazolyl, ethylpyrazolyl, propylpyrazolyl, 2-methylpropylpyrazolyl, 3-methylbutylpyrazolyl, dimethylpyrazolyl, trimethylpyrazolyl, (dimethyl)(ethyl)pyrazolyl, (dimethyl)(isopropyl)pyrazolyl, (dimethyl)(2-methylpropyl)pyrazolyl, (dimethyl)(3-methylbutyl)pyrazolyl, (dimethyl)(trifluoromethyl)pyrazolyl, cyanomethylpyrazolyl, (cyanomethyl)(dimethyl)pyrazolyl, hydroxyethylpyrazolyl, hydroxypropylpyrazolyl, 2-hydroxy-2-methylpropylpyrazolyl, (hydroxyethyl)(dimethyl)pyrazolyl, (hydroxypropyl)(dimethyl)pyrazolyl, methoxypropylpyrazolyl, [(hydroxy)-(methoxy)propyl]pyrazolyl, aminoethylpyrazolyl, aminopropylpyrazolyl, (aminopropyl)-(methyl)pyrazolyl, (aminopropyl)(dimethyl)pyrazolyl, dimethylaminoethylpyrazolyl, dimethylaminopropylpyrazolyl, diethoxyphosphonopropylpyrazolyl, allylpyrazolyl, cyclopropylmethylpyrazolyl, (cyclopropylmethyl)(dimethyl)pyrazolyl, (methyl)(phenyl)-pyrazolyl, (phenyl)(trifluoromethyl)pyrazolyl, benzylpyrazolyl, aminobenzylpyrazolyl, piperidinylpyrazolyl, tetrahydropyranylmethylpyrazolyl, (dimethyl)(tetrahydropyranyl-methyl)pyrazolyl, pyrrolidinylethylpyrazolyl, piperidinylethylpyrazolyl, methyl-piperidinylethylpyrazolyl, morpholinylethylpyrazolyl, pyridinylmethylpyrazolyl, oxypyridinylmethylpyrazolyl, (dimethyl)(phenylcarbonylmethyl)pyrazolyl, (ethyl)(piperazinylcarbonyl)pyrazolyl, (methylaminocarbonyl)(methylphenyl)pyrazolyl, (aminoethylaminocarbonyl)(methyl)pyrazolyl, aminocarbonylmethylpyrazolyl, (aminocarbonylmethyl)(dimethyl]pyrazolyl, dimethylaminocarbonylmethylpyrazolyl, pyrazolo[1,5-*a*]pyridinyl, dimethylisoxazolyl, (amino)(methyl)isoxazolyl, thiazolyl, dimethylthiazolyl, imidazolyl, methylimidazolyl, dimethylimidazolyl, imidazo[1,2-*a*]pyridinyl, methylimidazo[1,2-*a*]pyridinyl, methylimidazo[4,5-*b*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyrazinyl, methylthiadiazolyl, triazolyl, pyridinyl, fluoropyridinyl, methylpyridinyl, (fluoro)(methyl)pyridinyl, dimethylpyridinyl, vinylpyridinyl, (methylpiperazinyl)pyridinyl, (methyl)(piperazinyl)pyridinyl, (*tert*-butoxycarbonylpiperazinyl)(methyl)pyridinyl, piperidinylmethylpyridinyl, (methyl)(oxy)-

pyridinyl, hydroxypyridinyl, hydroxymethylpyridinyl, hydroxyethylpyridinyl, methoxypyridinyl, (methoxy)(methyl)pyridinyl, (dimethyl)(methoxy)pyridinyl, methoxymethylpyridinyl, aminopyridinyl, carboxymethylpyridinyl, ethoxycarbonylmethylpyridinyl, pyridazinyl, methylpyridazinyl, piperidinylpyridazinyl, oxypyridazinyl, methoxypyridazinyl, aminopyridazinyl, hydroxyethylaminopyridazinyl, dimethylaminopyridazinyl, pyrimidinyl, methylpyrimidinyl, (chloro)(methyl)pyrimidinyl, dimethylpyrimidinyl, pyrrolidinylpyrimidinyl, methylpiperazinylpyrimidinyl, (methyl)(piperazinyl)pyrimidinyl, (*tert*-butoxycarbonylpiperazinyl)(methyl)pyrimidinyl, hydroxypyrimidinyl, (hydroxy)(methyl)pyrimidinyl, (hydroxyethyl)(methyl)pyrimidinyl, (hydroxypropyl)(methyl)pyrimidinyl, (hydroxypropynyl)(methyl)pyrimidinyl, methoxypyrimidinyl, aminopyrimidinyl, dimethylaminopyrimidinyl, (dimethylamino)(fluoro)pyrimidinyl, carboxypyrimidinyl, (methoxycarbonylmethyl)(methyl)pyrimidinyl, aminocarbonylpyrimidinyl, pyrazinyl, methoxypyrazinyl, aminopyrazinyl, hydroxy, methoxy, isopropoxy, difluoromethoxy, trifluoromethoxy, cyclobutyloxy, cyclopropylmethoxy, benzyloxycarbonylpiperidinyloxy, morpholinylethoxy, phenoxy, fluorophenoxy, dimethylpyrazolyloxy, bromopyridinyloxy, pyrrolidinylpyridinyloxy, methylpiperazinylpyridinyloxy, methylpyrazolylpyridinyloxy, isopropylaminopyridinyloxy, carboxypyridinyloxy, aminocarbonylpyridinyloxy, methylpyridazinyloxy, pyrimidinyloxy, methylpyrimidinyloxy, (chloro)(methyl)pyrimidinyloxy, hydroxymethyl, 1-hydroxy-1-methylethyl, dihydroxypropyl, pyridinyloxymethyl, methylenedioxy, difluoromethylenedioxy, amino, isopropylamino, dihydroxypropylamino, methoxyethylamino, methoxypropylamino, dimethylamino, *N*-(methoxyethyl)-*N*-(methyl)amino, *N*-(methoxypropyl)-*N*-(methyl)amino, dimethylaminoethylamino, dimethylaminopropylamino, *N*-(dimethylaminoethyl)-*N*-(methyl)amino, *N*-(diethylaminoethyl)-*N*-(methyl)amino, *N*-(dimethylaminopropyl)-*N*-(methyl)amino, *N*-(dimethylaminoethyl)-*N*-(ethyl)amino, *N*-(dimethylaminopropyl)-*N*-(ethyl)amino, *N*-(cyclohexyl)-*N*-(methyl)amino, fluorophenylamino, *N*-fluorophenyl-*N*-methylamino, methylenedioxyphenylamino, morpholinylmethylphenylamino, oxazolinylphenylamino, (methyl)(oxo)pyrazolylphenylamino, oxazolylphenylamino, isoxazolylphenylamino, triazolylphenylamino, methyltriazolylphenylamino, methylpyrimidinylphenylamino, pyrazolylmethylphenylamino, triazolylmethylphenylamino, methylsulphonylaminophenylamino, morpholinylcarbonylphenylamino, methylsulphonylphenylamino, morpholinylsulphonylphenylamino, *N*-benzyl-*N*-methylamino, *N*-(benzyl)-*N*-(dimethyl-

aminoethyl)amino, cyanobenzylamino, (cyano)(phenyl)ethylamino, (cyano)(fluoro)-benzylamino, methylenedioxybenzylamino, dihydrobenzofuranylamino, *N*-(methyl)-*N*-(methylpyrrolidinyl)amino, methylsulphonylindolinylamino, chromanonylamino, piperidinylamino, *N*-(methyl)-*N*-(piperidinyl)amino, *N*-(ethyl)-*N*-(piperidinyl)amino, *N*-(cyclopropylmethyl)-*N*-(piperidinyl)amino, methylpiperidinylamino, *N*-(methyl)-*N*-(methylpiperidinyl)amino, *N*-(methyl)-*N*-(2-methylpropylpiperidinyl)amino, *N*-(cyclopentylpiperidinyl)-*N*-(methyl)amino, *N*-(acetylpiperidinyl)-*N*-(methyl)amino, dihydroquinolinonylamino, benzoxazinonylamino, pyrrolidinylethylamino, pyrrolidinylpropylamino, *N*-(methyl)-*N*-(pyrrolidinylethyl)amino, *N*-(methyl)-*N*-(pyrrolidinylpropyl)amino, *N*-(methyl)-*N*-(piperidinylmethyl)amino, benzothienylamino, indolylamino, dioxoindolylamino, methylpyrazolylamino, (bromo)(methyl)pyrazolylamino, dimethylpyrazolylamino, trimethylpyrazolylamino, *N*-(ethyl)-*N*-(methylpyrazolyl)-amino, methylindazolylamino, benzoxazolylamino, benzoxazolonylamino, dimethylisoxazolylamino, thiazolylamino, benzothiazolylamino, methylisothiazolylamino, imidazolylamino, (ethoxycarbonyl)(methyl)imidazolylamino, methylbenzimidazolylamino, benzimidazolonylamino, dimethylbenzimidazolonylamino, methyloxadiazolylamino, furyloxadiazolylamino, methylthiadiazolylamino, pyridinylamino, chloropyridinylamino, bromopyridinylamino, methylpyridinylamino, dimethylpyridinylamino, trifluoromethylpyridinylamino, hydroxypyridinylamino, hydroxyethylpyridinylamino, dihydroxyethylpyridinylamino, methoxypyridinylamino, dihydroxypropoxypyridinylamino, dimethyldioxolanylmethoxypyridinylamino, methoxyethylpyridinylamino, methoxyvinylpyridinylamino, dihydroxypropylaminopyridinylamino, dimethylaminopyridinylamino, methylaminomethylpyridinylamino, dimethylaminomethylpyridinylamino, oxopyridinylamino, carboxypyridinylamino, *N*-(methyl)-*N*-(methylpyridinyl)-amino, *N*-(ethyl)-*N*-(methylpyridinyl)amino, bis(methylpyridinyl)amino, bis(trifluoromethylpyridinyl)amino, isoquinolinylamino, methylpyridazinylamino, *N*-(methyl)-*N*-(methylpyridazinyl)amino, *N*-(benzyl)-*N*-(methylpyridazinyl)amino, dimethylpyridazinylamino, phenylpyridazinylamino, piperidinylpyridazinylamino, methoxypyridazinylamino, (chloro)(methoxy)pyridazinylamino, dimethylaminopyridazinylamino, bis(methylpyridazinyl)amino, methylcinnolinylamino, oxopyrimidinylamino, thioxopyrimidinylamino, quinoxalinylamino, methylchromenylamino, benzofurylmethylamino, thienylmethylamino, indolylmethylamino, methylpyrazolylmethylamino, (chloro)(dimethyl)pyrazolylmethylamino, dimethylisoxazolylmethylamino,

thiazolylmethylamino, imidazolylmethylamino, methylimidazolylmethylamino, pyridinylmethylamino, methylpyridinylmethylamino, *N*-(methyl)-*N*-(pyridinylethyl)-amino, *N*-(dihydroxypropyl)-*N*-(pyridinylmethyl)amino, *N*-(dihydroxypropyl)-*N*-(methylpyridinylmethyl)amino, aminomethyl, methylaminomethyl, dimethylaminomethyl, pyridinylaminomethyl, acetylamino, *N*-(acetyl)-*N*-(methylpyridinyl)amino, dimethylaminoethylcarbonylamino, acetylaminomethyl, cyclohexylcarbonylamino, methylpiperidinylcarbonylamino, methylimidazolylcarbonylamino, methoxycarbonyl-amino, *N*-methoxycarbonyl-*N*-methylamino, methylsulphonylamino, formyl, acetyl, acetyl oxime, acetyl *O*-(methyl)oxime, trifluoromethylcarbonyl, carboxy, methoxycarbonyl, aminocarbonyl, methylaminocarbonyl, (hydroxyethyl)aminocarbonyl, (dimethyl-aminoethyl)aminocarbonyl, (1-hydroxyprop-2-yl)aminocarbonyl, dimethylamino-carbonyl, *N*-(cyanomethyl)-*N*-methylaminocarbonyl, *N*-(cyanoethyl)-*N*-methylamino-carbonyl, *N*-(hydroxyethyl)-*N*-methylaminocarbonyl, *N*-(methoxyethyl)-*N*-methyl-aminocarbonyl, *N*-(dimethylaminoethyl)-*N*-methylaminocarbonyl, *N*-isopropyl-*N*-methyl-aminocarbonyl, diethylaminocarbonyl, cyclopropylmethylaminocarbonyl, benzylamino-carbonyl, methylpiperidinylaminocarbonyl, *N*-(methyl)-*N*-(methylpiperidinyl)amino-carbonyl, piperidinylethylaminocarbonyl, pyrazolylaminocarbonyl, pyridinylmethylamino-carbonyl, azetidinylcarbonyl, hydroxyazetidinylcarbonyl, aminoazetidinylcarbonyl, *tert*-butoxycarbonylaminoazetidinylcarbonyl, pyrrolidinylcarbonyl, methylpyrrolidinyl-carbonyl, methoxymethylpyrrolidinylcarbonyl, dimethylaminopyrrolidinylcarbonyl, thiazolidinylcarbonyl, oxothiazolidinylcarbonyl, piperidinylcarbonyl, methylpiperazinyl-carbonyl, morpholinylcarbonyl, isopropylthio, isopropylsulphinyl, methylsulphonyl, isopropylsulphonyl, methylsulphonylmethyl, aminosulphonyl, methylaminosulphonyl, dimethylaminosulphonyl, *tert*-butoxycarbonyloxy, trimethylsilyl and tetramethyl-dioxaborolanyl.

Particular examples of specific substituents on R^{13} include bromo, cyano, methyl, methoxycarbonyl and dimethylaminocarbonyl. A further example is carboxy.

Typical values of R^{13} include hydrogen, methyl, phenoxymethyl, phenylthiomethyl, aminomethyl, phenylaminomethyl, *N*-methyl-*N*-phenylaminomethyl, pyridinylaminomethyl, benzofurylcarbonylaminomethyl, phenylsulphonylaminomethyl, benzothienylmethylaminocarbonylmethyl, propynyl, trimethylsilylpropynyl, benzyl, chlorobenzyl, bromobenzyl, methylenedioxyphenylaminobenzyl, morpholinylmethylphenylaminobenzyl, oxazolinylphenylaminobenzyl,

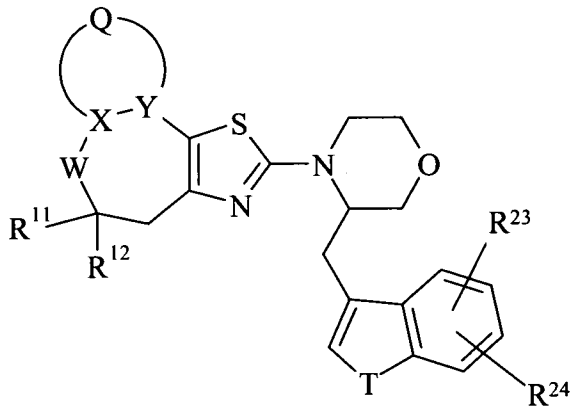
(methyl)(oxo)pyrazolylphenylaminobenzyl, oxazolylphenylaminobenzyl, isoxazolylphenylaminobenzyl, triazolylphenylaminobenzyl, methyltriazolylphenylaminobenzyl, methylpyrimidinylphenylaminobenzyl, pyrazolylmethylphenylaminobenzyl, triazolylmethylphenylaminobenzyl, methylsulphonylaminophenylaminobenzyl, morpholinylcarbonylphenylaminobenzyl, methylsulphonylphenylaminobenzyl, morpholinylsulphonylphenylaminobenzyl, dihydrobenzofuranylaminobenzyl, methylsulphonylindolinylaminobenzyl, chromanonylaminobenzyl, dihydroquinolinonylaminobenzyl, benzoxazinonylaminobenzyl, benzothienylaminobenzyl, indolylaminobenzyl, dioxoindolylaminobenzyl, (bromo)(methyl)pyrazolylaminobenzyl, trimethylpyrazolylaminobenzyl, methylindazolylaminobenzyl, benzoxazolylaminobenzyl, benzoxazolonylaminobenzyl, dimethylisoxazolylaminobenzyl, benzothiazolylaminobenzyl, methylisothiazolylaminobenzyl, methylbenzimidazolylaminobenzyl, benzimidazolonylaminobenzyl, dimethylbenzimidazolonylaminobenzyl, methyloxadiazolylaminobenzyl, furyloxadiazolylaminobenzyl, pyridinylaminobenzyl, chloropyridinylaminobenzyl, methylpyridinylaminobenzyl, dimethylpyridinylaminobenzyl, methoxypyridinylaminobenzyl, oxopyridinylaminobenzyl, oxopyrimidinylaminobenzyl, thioxopyrimidinylaminobenzyl, (chloro)(methoxy)pyridazinylaminobenzyl, methylcinnolinylaminobenzyl, quinoxalinylaminobenzyl, methylchromenylaminobenzyl, benzofurylmethyl, cyanobenzofurylmethyl, methoxycarbonylbenzofurylmethyl, dimethylaminocarbonylbenzofurylmethyl, azetidinylcarbonylbenzofurylmethyl, indolylmethyl, fluoroindolylmethyl, cyanoindolylmethyl, (cyano)(methyl)indolylmethyl, nitroindolylmethyl, methylindolylmethyl, oxazolinylindolylmethyl, triazolylindolylmethyl, methoxyindolylmethyl, (chloro)(methoxy)indolylmethyl, di(methoxy)indolylmethyl, difluoromethoxyindolylmethyl, trifluoromethoxyindolylmethyl, (chloro)(trifluoromethoxy)indolylmethyl, cyclobutyloxyindolylmethyl, cyclopropylmethoxyindolylmethyl, morpholinylethoxyindolylmethyl, methylenedioxyindolylmethyl, difluoromethylenedioxyindolylmethyl, azetidinylindolylmethyl, morpholinylindolylmethyl, acetylaminoindolylmethyl, acetylaminomethylindolylmethyl, methoxycarbonylaminoindolylmethyl, *N*-methoxycarbonyl-*N*-methylaminoindolylmethyl, methylsulphonylaminoindolylmethyl, acetylindolylmethyl, [acetyl oxime]indolylmethyl, [acetyl *O*-(methyl)oxime]indolylmethyl, trifluoromethylcarbonylindolylmethyl, carboxyindolylmethyl, (carboxy)(methyl)indolylmethyl, methoxycarbonylindolylmethyl, (methoxycarbonyl)(methyl)-

indolylmethyl, (chloro)(methoxycarbonyl)indolylmethyl, aminocarbonylindolylmethyl, (aminocarbonyl)(chloro)indolylmethyl, methylaminocarbonylindolylmethyl, (chloro)-(methylaminocarbonyl)indolylmethyl, (hydroxyethyl)aminocarbonylindolylmethyl, (dimethylaminoethyl)aminocarbonylindolylmethyl, (1-hydroxyprop-2-yl)aminocarbonyl-indolylmethyl, dimethylaminocarbonylindolylmethyl, (dimethylaminocarbonyl)(methyl)-indolylmethyl, (chloro)(dimethylaminocarbonyl)indolylmethyl, bis(dimethylamino-carbonyl)indolylmethyl, *N*-(cyanomethyl)-*N*-methylaminocarbonylindolylmethyl, [*N*-(cyanomethyl)-*N*-methylaminocarbonyl](methyl)indolylmethyl, *N*-(cyanoethyl)-*N*-methylaminocarbonylindolylmethyl, *N*-(hydroxyethyl)-*N*-methylaminocarbonyl-indolylmethyl, *N*-(methoxyethyl)-*N*-methylaminocarbonylindolylmethyl, [*N*-(methoxy-ethyl)-*N*-methylaminocarbonyl](methyl)indolylmethyl, *N*-(dimethylaminoethyl)-*N*-methylaminocarbonylindolylmethyl, *N*-isopropyl-*N*-methylaminocarbonylindolylmethyl, diethylaminocarbonylindolylmethyl, cyclopropylmethylaminocarbonylindolylmethyl, benzylaminocarbonylindolylmethyl, pyrazolylaminocarbonylindolylmethyl, pyridinylmethylaminocarbonylindolylmethyl, azetidinylcarbonylindolylmethyl, (azetidinylcarbonyl)(methyl)indolylmethyl, hydroxyazetidinylcarbonylindolylmethyl, aminoazetidinylcarbonylindolylmethyl, *tert*-butoxycarbonylaminoazetidinylcarbonyl-indolylmethyl, pyrrolidinylcarbonylindolylmethyl, methylpyrrolidinylcarbonyl-indolylmethyl, methoxymethylpyrrolidinylcarbonylindolylmethyl, dimethylamino-pyrrolidinylcarbonylindolylmethyl, thiazolidinylcarbonylindolylmethyl, oxothiazolidinyl-carbonylindolylmethyl, piperidinylcarbonylindolylmethyl, methylpiperazinylcarbonyl-indolylmethyl, morpholinylcarbonylindolylmethyl, methylsulphonylindolylmethyl, methylsulphonylmethylindolylmethyl, dimethylaminosulphonylindolylmethyl, trimethylsilylindolylmethyl and pyrrolo[3,2-*c*]pyridinylmethyl.

Representative values of R^{13} include hydrogen, bromobenzyl, benzofurylmethyl, indolylmethyl, cyanoindolylmethyl, (cyano)(methyl)indolylmethyl, (carboxy)(methyl)-indolylmethyl, methoxycarbonylindolylmethyl, (methoxycarbonyl)(methyl)indolylmethyl, dimethylaminocarbonylindolylmethyl and (dimethylaminocarbonyl)(methyl)indolyl-methyl.

Particular values of R^{13} include hydrogen, bromobenzyl, benzofurylmethyl, indolylmethyl, cyanoindolylmethyl, (cyano)(methyl)indolylmethyl, methoxycarbonyl-indolylmethyl and dimethylaminocarbonylindolylmethyl.

One particular sub-group of the compounds of formula (IIA-A) is represented by the compounds of formula (IIB), and pharmaceutically acceptable salts and solvates thereof:



(IIB)

wherein

W, the moiety X-Y-Q, R^{11} and R^{12} are as defined above;

T represents oxygen or N-R^{25};

R^{23} represents hydrogen, halogen, cyano, nitro, C_{1-6} alkyl, hydroxy(C_{1-6})alkyl, trifluoromethyl, aryl(C_{1-6})alkyl, oxazolinyl, triazolyl, hydroxy, C_{1-6} alkoxy, difluoromethoxy, trifluoromethoxy, C_{3-7} cycloalkoxy, C_{3-7} cycloalkyl(C_{1-6})alkoxy, morpholinyl(C_{1-6})alkoxy, aryloxy, aryl(C_{1-6})alkoxy, C_{1-6} alkylthio, C_{1-6} alkylsulphinyl, arylsulphinyl, arylsulphonyl, C_{1-6} alkylsulphonyloxy, amino, azetidinyl, morpholinyl, C_{2-6} alkylcarbonylamino, C_{2-6} alkylcarbonylaminomethyl, C_{2-6} alkoxycarbonylamino, [(C_{2-6})alkoxycarbonyl][(C_{1-6})alkyl]amino, C_{1-6} alkylsulphonylamino, C_{2-6} alkylcarbonyl, C_{2-6} alkylcarbonyl oxime, C_{2-6} alkylcarbonyl *O*-(methyl)oxime, trifluoromethylcarbonyl, carboxy, C_{2-6} alkoxycarbonyl, aminocarbonyl, C_{1-6} alkylaminocarbonyl, [hydroxy(C_{1-6})-alkyl]aminocarbonyl, [di(C_{1-6})alkylamino(C_{1-6})alkyl]aminocarbonyl, di(C_{1-6})alkyl-aminocarbonyl, [(C_{1-6})alkyl][cyano(C_{1-6})alkyl]aminocarbonyl, [(C_{1-6})alkyl][hydroxy(C_{1-6})-alkyl]aminocarbonyl, [(C_{1-6})alkoxy(C_{1-6})alkyl][(C_{1-6})alkyl]aminocarbonyl, [di(C_{1-6})alkyl-amino(C_{1-6})alkyl][(C_{1-6})alkyl]aminocarbonyl, C_{3-7} cycloalkyl(C_{1-6})alkylaminocarbonyl, aryl(C_{1-6})alkylaminocarbonyl, heteroarylaminocarbonyl, heteroaryl(C_{1-6})alkylamino-carbonyl, azetidinylcarbonyl, hydroxyazetidinylcarbonyl, aminoazetidinylcarbonyl, C_{2-6} alkoxycarbonylaminoazetidinylcarbonyl, pyrrolidinylcarbonyl, (C_{1-6})alkylpyrrolidinyl-carbonyl, C_{1-6} alkoxy(C_{1-6})alkylpyrrolidinylcarbonyl, di(C_{1-6})alkylaminopyrrolidinyl-

carbonyl, thiazolidinylcarbonyl, oxothiazolidinylcarbonyl, piperidinylcarbonyl, (C_{1-6})-alkylpiperazinylcarbonyl, morpholinylcarbonyl, C_{1-6} alkylsulphonyl, C_{1-6} alkylsulphonylmethyl or di(C_{1-6})alkylaminosulphonyl; and

R^{24} represents hydrogen, halogen, C_{1-6} alkoxy or di(C_{1-6})alkylaminocarbonyl; or

R^{23} and R^{24}, when situated on adjacent carbon atoms, together represent methylenedioxy or difluoromethylenedioxy; and

R^{25} represents hydrogen or C_{1-6} alkyl.

In a preferred embodiment, T is N-R^{25}. In another embodiment, T is oxygen.

Typical values of R^{23} include hydrogen, cyano, carboxy, C_{2-6} alkoxycarbonyl and di(C_{1-6})alkylaminocarbonyl.

Suitable values of R^{23} include hydrogen, cyano, C_{2-6} alkoxycarbonyl and di(C_{1-6})alkylaminocarbonyl.

Illustrative values of R^{23} include hydrogen, fluoro, chloro, cyano, nitro, oxazolinyl, triazolyl, methoxy, difluoromethoxy, trifluoromethoxy, cyclobutyloxy, cyclopropylmethoxy, morpholinylethoxy, azetidinyl, morpholinyl, acetylamino, acetylaminomethyl, methoxycarbonylamino, *N*-methoxycarbonyl-*N*-methylamino, methylsulphonylamino, acetyl, acetyl oxime, acetyl *O*-(methyl)oxime, trifluoromethylcarbonyl, carboxy, methoxycarbonyl, aminocarbonyl, methylaminocarbonyl, (hydroxyethyl)aminocarbonyl, (dimethylaminoethyl)aminocarbonyl, (1-hydroxyprop-2-yl)aminocarbonyl, dimethylaminocarbonyl, *N*-(cyanomethyl)-*N*-methylaminocarbonyl, *N*-(cyanoethyl)-*N*-methylaminocarbonyl, *N*-(hydroxyethyl)-*N*-methylaminocarbonyl, *N*-(methoxyethyl)-*N*-methylaminocarbonyl, *N*-(dimethylaminoethyl)-*N*-methylaminocarbonyl, *N*-isopropyl-*N*-methylaminocarbonyl, diethylaminocarbonyl, cyclopropylmethylaminocarbonyl, benzylaminocarbonyl, pyrazolylaminocarbonyl, pyridinylmethylaminocarbonyl, azetidinylcarbonyl, hydroxyazetidinylcarbonyl, aminoazetidinylcarbonyl, *tert*-butoxycarbonylaminoazetidinylcarbonyl, pyrrolidinylcarbonyl, methylpyrrolidinylcarbonyl, methoxymethylpyrrolidinylcarbonyl, dimethylaminopyrrolidinylcarbonyl, thiazolidinylcarbonyl, oxothiazolidinylcarbonyl, piperidinylcarbonyl, methylpiperazinylcarbonyl, morpholinylcarbonyl, methylsulphonyl, methylsulphonylmethyl and dimethylaminosulphonyl.

Representative values of R^{23} include hydrogen, cyano, carboxy, methoxycarbonyl and dimethylaminocarbonyl.

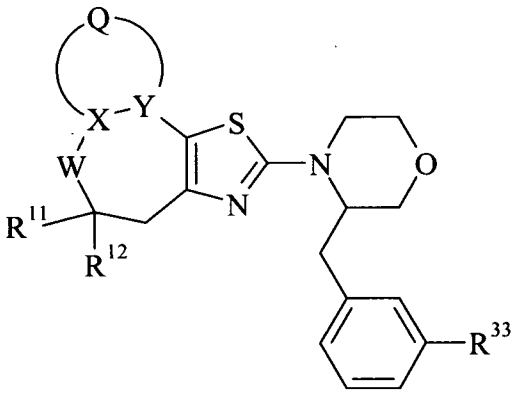
Selected values of R^{23} include hydrogen, cyano, methoxycarbonyl and dimethylaminocarbonyl.

A particular value of R^{23} is hydrogen.

Definitive values of R^{24} include hydrogen, chloro, methoxy and dimethylaminocarbonyl. A particular value of R^{24} is hydrogen.

In one embodiment, R^{25} is hydrogen. In another embodiment, R^{25} is C_{1-6} alkyl, especially methyl.

Another particular sub-group of the compounds of formula (IIA-A) is represented by the compounds of formula (IIC), and pharmaceutically acceptable salts and solvates thereof:



(IIC)

wherein

W, the moiety X-Y-Q, R^{11} and R^{12} are as defined above;

R^{33} represents halogen or -NHR^{34}; or aryl or heteroaryl, either of which groups may be optionally substituted by one or more substituents; and

R^{34} represents methylenedioxyphenyl, morpholinyl(C_{1-6})alkylphenyl, oxazolinylphenyl, [(C_{1-6})alkyl](oxo)pyrazolylphenyl, oxazolylphenyl, isoxazolylphenyl, triazolylphenyl, (C_{1-6})alkyltriazolylphenyl, (C_{1-6})alkylpyrimidinylphenyl, pyrazolyl(C_{1-6})alkylphenyl, triazolyl(C_{1-6})alkylphenyl, C_{1-6} alkylsulphonylaminophenyl, morpholinylcarbonylphenyl, C_{1-6} alkylsulphonylphenyl, morpholinylsulphonylphenyl, dihydrobenzofuranyl, C_{1-6} alkylsulphonylindolinyl, chromanonyl, dihydroquinolinonyl, benzoxazinonyl, benzothienyl, indolyl, dioxoindolyl, [(C_{1-6})alkyl](halo)pyrazolyl, tri(C_{1-6})alkylpyrazolyl, (C_{1-6})alkylindazolyl, benzoxazolyl, benzoxazolonyl, di(C_{1-6})alkylisoxazolyl, benzothiazolyl, (C_{1-6})alkylisothiazolyl, (C_{1-6})alkylbenzimidazolyl, benzimidazolonyl,

di(C_{1-6})alkylbenzimidazolonyl, (C_{1-6})alkyloxadiazolyl, furyloxadiazolyl, pyridinyl, halopyridinyl, (C_{1-6})alkylpyridinyl, di(C_{1-6})alkylpyridinyl, (C_{1-6})alkoxypyridinyl, oxopyridinyl, oxopyrimidinyl, thioxopyrimidinyl, [(C_{1-6})alkoxy](halo)pyridazinyl, (C_{1-6})alkylcinnolinyl, quinoxalinyl or (C_{1-6})alkylchromenyl.

Suitably, R^{33} represents halogen or -NHR^{34}, in which R^{34} is as defined above. In one embodiment, R^{33} represents halogen, especially bromo. In another embodiment, R^{33} represents -NHR^{34}, in which R^{34} is as defined above.

In one embodiment, R^{33} represents unsubstituted or substituted aryl. In another embodiment, R^{33} represents unsubstituted or substituted heteroaryl.

Typical values of R^{34} include pyridinyl, halopyridinyl, (C_{1-6})alkylpyridinyl, di(C_{1-6})alkylpyridinyl and (C_{1-6})alkoxypyridinyl.

Particular values of R^{34} include methylenedioxyphenyl, morpholinylmethylphenyl, oxazolinylphenyl, (methyl)(oxo)pyrazolylphenyl, oxazolylphenyl, isoxazolylphenyl, triazolylphenyl, methyltriazolylphenyl, methylpyrimidinylphenyl, pyrazolylmethylphenyl, triazolylmethylphenyl, methylsulphonylaminophenyl, morpholinylcarbonylphenyl, methylsulphonylphenyl, morpholinylsulphonylphenyl, dihydrobenzofuranyl, methylsulphonylindolinyl, chromanonyl, dihydroquinolinonyl, benzoxazinonyl, benzothienyl, indolyl, dioxoindolyl, (bromo)(methyl)pyrazolyl, trimethylpyrazolyl, methylindazolyl, benzoxazolyl, benzoxazolonyl, dimethylisoxazolyl, benzothiazolyl, methylisothiazolyl, methylbenzimidazolyl, benzimidazolonyl, dimethylbenzimidazolonyl, methyloxadiazolyl, furyloxadiazolyl, pyridinyl, chloropyridinyl, methylpyridinyl, dimethylpyridinyl, methoxypyridinyl, oxopyridinyl, oxopyrimidinyl, thioxopyrimidinyl, (chloro)(methoxy)pyridazinyl, methylcinnolinyl, quinoxalinyl and methylchromenyl.

Suitable values of R^{34} include pyridinyl, chloropyridinyl, methylpyridinyl, dimethylpyridinyl and methoxypyridinyl.

Illustratively, R^{33} represents halogen or -NHR^{34}, in which R^{34} is as defined above. Additionally, R^{33} represents phenyl, naphthyl, benzofuryl, thienyl, benzothienyl, indolyl, isoxazolyl, pyrazolyl, pyridinyl or pyrimidinyl, any of which groups may be optionally substituted by one or more substituents.

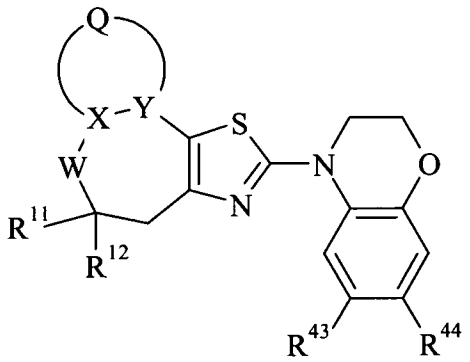
Selected examples of suitable substituents on R^{33} include halogen, cyano, C_{1-6} alkyl, hydroxy(C_{1-6})alkyl, trifluoromethyl, C_{1-6} alkoxy, trifluoromethoxy, aryloxy, methylenedioxy, C_{1-6} alkylthio, arylsulphonyl, amino, C_{2-6} alkylcarbonylamino, C_{1-6} alkylsulphonylamino, C_{2-6} alkylcarbonyl and aminocarbonyl.

Selected examples of representative substituents on R^{33} include fluoro, chloro, bromo, cyano, methyl, hydroxymethyl, trifluoromethyl, methoxy, ethoxy, trifluoromethoxy, phenoxy, methylenedioxy, methylthio, phenylsulphonyl, amino, acetylamino, methylsulphonylamino, acetyl and aminocarbonyl.

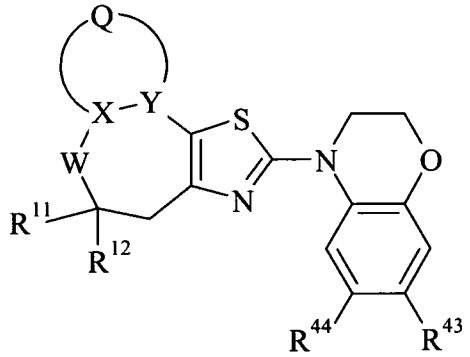
Specific values of R^{33} include bromo, methylenedioxyphenylamino, morpholinylmethylphenylamino, oxazolinylphenylamino, (methyl)(oxo)pyrazolylphenylamino, oxazolylphenylamino, isoxazolylphenylamino, triazolylphenylamino, methyltriazolylphenylamino, methylpyrimidinylphenylamino, pyrazolylmethylphenylamino, triazolylmethylphenylamino, methylsulphonylaminophenylamino, morpholinylcarbonylphenylamino, methylsulphonylphenylamino, morpholinylsulphonylphenylamino, dihydrobenzofuranylamino, methylsulphonylindolinylamino, chromanonylamino, dihydroquinolinonylamino, benzoxazinonylamino, benzothienylamino, indolylamino, dioxoindolylamino, (bromo)(methyl)pyrazolylamino, trimethylpyrazolylamino, methylindazolylamino, benzoxazolylamino, benzoxazolonylamino, dimethylisoxazolylamino, benzothiazolylamino, methylisothiazolylamino, methylbenzimidazolylamino, benzimidazolonylamino, dimethylbenzimidazolonylamino, methyloxadiazolylamino, furyloxadiazolylamino, pyridinylamino, chloropyridinylamino, methylpyridinylamino, dimethylpyridinylamino, methoxypyridinylamino, oxopyridinylamino, oxopyrimidinylamino, thioxopyrimidinylamino, (chloro)(methoxy)pyridazinylamino, methylcinnolinylamino, quinoxalinylamino, methylchromenylamino, phenyl, fluorophenyl, difluorophenyl, chlorophenyl, dichlorophenyl, bromophenyl, cyanophenyl, methylphenyl, (fluoro)(methyl)phenyl, dimethylphenyl, hydroxymethylphenyl, trifluoromethylphenyl, bis(trifluoromethyl)phenyl, methoxyphenyl, dimethoxyphenyl, ethoxyphenyl, methylenedioxyphenyl, trifluoromethoxyphenyl, phenoxyphenyl, methylthiophenyl, aminophenyl, acetylamino-phenyl, methylsulphonylaminophenyl, acetylphenyl, aminocarbonylphenyl, naphthyl, benzofuryl, thienyl, methylthienyl, acetylthienyl, benzothienyl, phenylsulphonylindolyl, dimethylisoxazolyl, methylpyrazolyl, benzylpyrazolyl, pyridinyl, fluoropyridinyl, chloropyridinyl, methoxypyridinyl and pyrimidinylbenzyl.

A particular value of R^{33} is bromo.

Further sub-classes of compounds according to the invention are represented by the compounds of formula (IID-1) and (IID-2), and pharmaceutically acceptable salts and solvates thereof:



(IID-1)



(IID-2)

wherein

W, the moiety X-Y-Q, R^{11} and R^{12} are as defined above;

R^{43} represents hydrogen, halogen, nitro, C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, (C_{1-6})alkylaryl, di(C_{1-6})alkylaryl, piperidinyl(C_{1-6})alkylaryl, piperazinyl(C_{1-6})alkylaryl, (C_{1-6})alkylpiperazinyl(C_{1-6})alkylaryl, morpholinyl(C_{1-6})alkylaryl, (C_{1-6})alkoxyaryl, cyano(C_{1-6})alkoxyaryl, di(C_{1-6})alkylamino(C_{1-6})alkylaryl, (C_{1-6})alkylaminocarbonylaryl, aryl(C_{1-6})alkyl, haloarylpyrrolidinyl, dioxopyrrolidinyl, aminopyrrolidinyl, di(C_{1-6})alkylaminopyrrolidinyl, indolinyl, oxoindolinyl, arylpiperidinyl, arylcarbonylpiperidinyl, di-(C_{1-6})alkylaminocarbonylpiperidinyl, piperazinyl, (C_{1-6})alkylpiperazinyl, haloarylpiperazinyl, pyridinylpiperazinyl, furoylpiperazinyl, homopiperazinyl, (C_{1-6})alkylhomopiperazinyl, (C_{1-6})alkylpiperazinyl(C_{1-6})alkyl, morpholinyl(C_{1-6})alkyl, benzofuryl, benzothienyl, pyrazolyl, (C_{1-6})alkylpyrazolyl, di(C_{1-6})alkylpyrazolyl, tri(C_{1-6})alkylpyrazolyl, [di(C_{1-6})alkyl](trifluoromethyl)pyrazolyl, cyano(C_{1-6})alkylpyrazolyl, [cyano-(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, hydroxy(C_{1-6})alkylpyrazolyl, [hydroxy(C_{1-6})-alkyl][di(C_{1-6})alkyl]pyrazolyl, methoxy(C_{1-6})alkylpyrazolyl, [(hydroxy)(methoxy)(C_{1-6})-alkyl]pyrazolyl, amino(C_{1-6})alkylpyrazolyl, [(C_{1-6})alkyl][amino(C_{1-6})alkyl]pyrazolyl, [amino(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, di(C_{1-6})alkylamino(C_{1-6})alkylpyrazolyl,

di(C_{1-6})alkoxyphosphono(C_{1-6})alkylpyrazolyl, (C_{2-6})alkenylpyrazolyl, (C_{3-7})cycloalkyl-(C_{1-6})alkylpyrazolyl, [(C_{3-7})cycloalkyl(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, [(C_{1-6})alkyl]-(aryl)pyrazolyl, (aryl)(trifluoromethyl)pyrazolyl, aryl(C_{1-6})alkylpyrazolyl, aminoaryl-(C_{1-6})alkylpyrazolyl, piperidinylpyrazolyl, tetrahydropyranyl(C_{1-6})alkylpyrazolyl, [di-(C_{1-6})alkyl][tetrahydropyranyl(C_{1-6})alkyl]pyrazolyl, pyrrolidinyl(C_{1-6})alkylpyrazolyl, piperidinyl(C_{1-6})alkylpyrazolyl, (C_{1-6})alkylpiperidinyl(C_{1-6})alkylpyrazolyl, morpholinyl(C_{1-6})alkylpyrazolyl, pyridinyl(C_{1-6})alkylpyrazolyl, oxypyridinyl(C_{1-6})alkyl-pyrazolyl, [arylcarbonyl(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, [(C_{1-6})alkyl](piperazinyl-carbonyl)pyrazolyl, [(C_{1-6})alkylaminocarbonyl][(C_{1-6})alkylaryl]pyrazolyl, [(C_{1-6})alkyl]-[amino(C_{1-6})alkylaminocarbonyl]pyrazolyl, aminocarbonyl(C_{1-6})alkylpyrazolyl, [aminocarbonyl(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, di(C_{1-6})alkylaminocarbonyl(C_{1-6})alkyl-pyrazolyl, pyrazolo[1,5-*a*]pyridinyl, di(C_{1-6})alkylisoxazolyl, (amino)[(C_{1-6})alkyl]-isoxazolyl, thiazolyl, di(C_{1-6})alkylthiazolyl, imidazolyl, (C_{1-6})alkylimidazolyl, di(C_{1-6})-alkylimidazolyl, imidazo[1,2-*a*]pyridinyl, (C_{1-6})alkylimidazo[1,2-*a*]pyridinyl, (C_{1-6})-alkylimidazo[4,5-*b*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyrazinyl, (C_{1-6})-alkylthiadiazolyl, pyridinyl, halopyridinyl, (C_{1-6})alkylpyridinyl, [(C_{1-6})alkyl](halo)-pyridinyl, di(C_{1-6})alkylpyridinyl, (C_{2-6})alkenylpyridinyl, (C_{1-6})alkylpiperazinylpyridinyl, [(C_{1-6})alkyl](piperazinyl)pyridinyl, [(C_{1-6})alkoxycarbonylpiperazinyl][(C_{1-6})alkyl]-pyridinyl, piperidinyl(C_{1-6})alkylpyridinyl, [(C_{1-6})alkyl](oxy)pyridinyl, hydroxypyridinyl, hydroxy(C_{1-6})alkylpyridinyl, (C_{1-6})alkoxypyridinyl, [(C_{1-6})alkoxy][(C_{1-6})alkyl]pyridinyl, [(C_{1-6})alkoxy][di(C_{1-6})alkyl]pyridinyl, (C_{1-6})alkoxy(C_{1-6})alkylpyridinyl, aminopyridinyl, carboxy(C_{1-6})alkylpyridinyl, (C_{1-6})alkoxycarbonyl(C_{1-6})alkylpyridinyl, pyridazinyl, (C_{1-6})-alkylpyridazinyl, piperidinylpyridazinyl, oxypyridazinyl, (C_{1-6})alkoxypyridazinyl, aminopyridazinyl, hydroxy(C_{1-6})alkylaminopyridazinyl, di(C_{1-6})alkylaminopyridazinyl, pyrimidinyl, (C_{1-6})alkylpyrimidinyl, [(C_{1-6})alkyl](halo)pyrimidinyl, di(C_{1-6})alkyl-pyrimidinyl, pyrrolidinylpyrimidinyl, (C_{1-6})alkylpiperazinylpyrimidinyl, [(C_{1-6})alkyl](piperazinyl)pyrimidinyl, [(C_{1-6})alkoxycarbonyl][(C_{1-6})alkyl]piperazinyl-pyrimidinyl, hydroxypyrimidinyl, [(C_{1-6})alkyl](hydroxy)pyrimidinyl, [(C_{1-6})alkyl]-[hydroxy(C_{1-6})alkyl]pyrimidinyl, [(C_{1-6})alkyl][hydroxy(C_{2-6})alkynyl]pyrimidinyl, (C_{1-6})-alkoxypyrimidinyl, aminopyrimidinyl, di(C_{1-6})alkylaminopyrimidinyl, [di(C_{1-6})alkyl-amino](halo)pyrimidinyl, carboxypyrimidinyl, [(C_{1-6})alkoxycarbonyl(C_{1-6})alkyl][(C_{1-6})-alkyl]pyrimidinyl, aminocarbonylpyrimidinyl, pyrazinyl, (C_{1-6})alkoxypyrazinyl, amino-pyrazinyl, hydroxy, (C_{1-6})alkoxy, aryl(C_{1-6})alkoxycarbonylpiperidinyloxy, morpholinyl-

(C_{1-6})alkoxy, aryloxy, haloaryloxy, di(C_{1-6})alkylpyrazolyloxy, halopyridinyloxy, pyrrolidinylpyridinyloxy, (C_{1-6})alkylpiperazinylpyridinyloxy, (C_{1-6})alkylpyrazolylpyridinyloxy, (C_{1-6})alkylaminopyridinyloxy, carboxypyridinyloxy, aminocarbonylpyridinyloxy, (C_{1-6})alkylpyridazinyloxy, pyrimidinyloxy, (C_{1-6})alkylpyrimidinyloxy, [(C_{1-6})alkyl](halo)pyrimidinyloxy, hydroxy(C_{1-6})alkyl, dihydroxy(C_{1-6})alkyl, pyridinyloxy(C_{1-6})alkyl, amino, (C_{1-6})alkylamino, dihydroxy(C_{1-6})alkylamino, (C_{1-6})-alkoxy(C_{1-6})alkylamino, *N*-[(C_{1-6})alkoxy(C_{1-6})alkyl]-*N*-[(C_{1-6})alkyl]amino, di(C_{1-6})-alkylamino(C_{1-6})alkylamino, *N*-[(C_{1-6})alkyl]-*N*-[di(C_{1-6})alkylamino(C_{1-6})alkyl]amino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{3-7})cycloalkyl]amino, haloarylamino, *N*-[(C_{1-6})alkyl]-*N*-(haloaryl)amino, *N*-[(C_{1-6})alkyl]-*N*-[aryl(C_{1-6})alkyl]amino, *N*-[di(C_{1-6})alkylamino(C_{1-6})alkyl]-*N*-[aryl(C_{1-6})-alkyl]amino, cyanoaryl(C_{1-6})alkylamino, (cyano)(halo)aryl(C_{1-6})alkylamino, methylenedioxyaryl(C_{1-6})alkylamino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpyrrolidinyl]amino, piperidinylamino, *N*-[(C_{1-6})alkyl]-*N*-(piperidinyl)amino, *N*-[(C_{3-7})cycloalkyl(C_{1-6})alkyl]-*N*-(piperidinyl)amino, (C_{1-6})alkylpiperidinylamino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpiperidinyl]amino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{3-7})cycloalkylpiperidinyl]amino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{2-6})alkylcarbonylpiperidinyl]amino, pyrrolidinyl(C_{1-6})alkylamino, *N*-[(C_{1-6})alkyl]-*N*-[pyrrolidinyl(C_{1-6})alkyl]amino, *N*-[(C_{1-6})alkyl]-*N*-[piperidinyl(C_{1-6})alkyl]amino, (C_{1-6})-alkylpyrazolylamino, di(C_{1-6})alkylpyrazolylamino, tri(C_{1-6})alkylpyrazolylamino, *N*-[(C_{1-6})-alkyl]-*N*-[(C_{1-6})alkylpyrazolyl]amino, thiazolylamino, imidazolylamino, [(C_{1-6})alkoxycarbonyl][(C_{1-6})alkyl]imidazolylamino, (C_{1-6})alkylthiadiazolylamino, pyridinylamino, halopyridinylamino, (C_{1-6})alkylpyridinylamino, di(C_{1-6})alkylpyridinylamino, trifluoromethylpyridinylamino, hydroxypyridinylamino, hydroxy(C_{1-6})alkylpyridinylamino, dihydroxy(C_{1-6})alkylpyridinylamino, (C_{1-6})alkoxypyridinylamino, dihydroxy(C_{1-6})alkoxypyridinylamino, di(C_{1-6})alkyldioxolanyl(C_{1-6})alkoxypyridinylamino, (C_{1-6})alkoxy(C_{1-6})-alkylpyridinylamino, (C_{1-6})alkoxy(C_{2-6})alkenylpyridinylamino, dihydroxy(C_{1-6})alkylaminopyridinylamino, di(C_{1-6})alkylaminopyridinylamino, (C_{1-6})alkylamino(C_{1-6})alkylpyridinylamino, di(C_{1-6})alkylamino(C_{1-6})alkylpyridinylamino, carboxypyridinylamino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpyridinyl]amino, bis[(C_{1-6})alkylpyridinyl]amino, bis(trifluoromethylpyridinyl)amino, isoquinolinylamino, (C_{1-6})alkylpyridazinylamino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpyridazinyl]amino, *N*-[aryl(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpyridazinyl]amino, di(C_{1-6})alkylpyridazinylamino, arylpyridazinylamino, piperidinylpyridazinylamino, (C_{1-6})-alkoxypyridazinylamino, di(C_{1-6})alkylaminopyridazinylamino, bis[(C_{1-6})alkylpyridazinyl]-amino, benzofuryl(C_{1-6})alkylamino, thienyl(C_{1-6})alkylamino, indolyl(C_{1-6})alkylamino,

(C_{1-6})alkylpyrazolyl(C_{1-6})alkylamino, [di(C_{1-6})alkyl](halo)pyrazolyl(C_{1-6})alkylamino, di(C_{1-6})alkylisoxazolyl(C_{1-6})alkylamino, thiazolyl(C_{1-6})alkylamino, imidazolyl(C_{1-6})alkylamino, (C_{1-6})alkylimidazolyl(C_{1-6})alkylamino, pyridinyl(C_{1-6})alkylamino, (C_{1-6})alkylpyridinyl(C_{1-6})alkylamino, *N*-[(C_{1-6})alkyl]-*N*-[pyridinyl(C_{1-6})alkyl]amino, *N*-[dihydroxy(C_{1-6})alkyl]-*N*-[pyridinyl(C_{1-6})alkyl]amino, *N*-[(C_{1-6})alkylpyridinyl(C_{1-6})alkyl]-*N*-[dihydroxy(C_{1-6})alkyl]amino, amino(C_{1-6})alkyl, (C_{1-6})alkylamino(C_{1-6})alkyl, di(C_{1-6})alkylamino(C_{1-6})alkyl, pyridinylamino(C_{1-6})alkyl, *N*-[(C_{2-6})alkylcarbonyl]-*N*-[(C_{1-6})alkylpyridinyl(C_{1-6})alkyl]amino, di(C_{1-6})alkylamino(C_{1-6})alkylcarbonylamino, (C_{3-7})cycloalkylcarbonylamino, (C_{1-6})alkylpiperidinylcarbonylamino, (C_{1-6})alkylimidazolylcarbonylamino, formyl, C_{2-6} alkylcarbonyl, (C_{1-6})alkylpiperidinylaminocarbonyl, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpiperidinyl]aminocarbonyl, piperidinyl(C_{1-6})alkylaminocarbonyl, (C_{1-6})alkylpiperazinylcarbonyl, C_{1-6} alkylthio, C_{1-6} alkylsulphinyl, C_{1-6} alkylsulphonyl, C_{2-6} alkoxycarbonyloxy or tetra(C_{1-6})alkyldioxaborolanyl; and

R^{44} represents hydrogen, halogen, C_{1-6} alkyl or C_{1-6} alkoxy.

A suitable value of R^{43} is (C_{1-6})alkylpyrazolyl.

Specific values of R^{43} include bromo, nitro, methyl, *n*-propyl, isopropyl, allyl, cyclopropyl, methylphenyl, dimethylphenyl, piperidinylmethylphenyl, piperazinylmethylphenyl, methylpiperazinylmethylphenyl, morpholinylmethylphenyl, methoxyphenyl, cyanomethoxyphenyl, dimethylaminomethylphenyl, methylaminocarbonylphenyl, benzyl, chlorophenylpyrrolidinyl, dioxopyrrolidinyl, aminopyrrolidinyl, dimethylaminopyrrolidinyl, indolinyl, oxoindolinyl, phenylpiperidinyl, benzoylpiperidinyl, diethylaminocarbonylpiperidinyl, piperazinyl, methylpiperazinyl, chlorophenylpiperazinyl, pyridinylpiperazinyl, furoylpiperazinyl, homopiperazinyl, methylhomopiperazinyl, methylpiperazinylmethyl, methylpiperazinylethyl, morpholinylmethyl, benzofuryl, benzothienyl, pyrazolyl, methylpyrazolyl, ethylpyrazolyl, propylpyrazolyl, 2-methylpropylpyrazolyl, 3-methylbutylpyrazolyl, dimethylpyrazolyl, trimethylpyrazolyl, (dimethyl)(ethyl)pyrazolyl, (dimethyl)(isopropyl)pyrazolyl, (dimethyl)(2-methylpropyl)pyrazolyl, (dimethyl)(3-methylbutyl)pyrazolyl, (dimethyl)(trifluoromethyl)pyrazolyl, cyanomethylpyrazolyl, (cyanomethyl)(dimethyl)pyrazolyl, hydroxyethylpyrazolyl, hydroxypropylpyrazolyl, 2-hydroxy-2-methylpropylpyrazolyl, (hydroxyethyl)(dimethyl)pyrazolyl, (hydroxypropyl)(dimethyl)pyrazolyl, methoxypropylpyrazolyl, [(hydroxy)(methoxy)propyl]pyrazolyl, aminoethylpyrazolyl, aminopropylpyrazolyl, (aminopropyl)(methyl)pyrazolyl, (aminopropyl)(dimethyl)pyrazolyl, dimethylaminoethylpyrazolyl,

dimethylaminopropylpyrazolyl, diethoxyphosphonopropylpyrazolyl, allylpyrazolyl, cyclopropylmethylpyrazolyl, (cyclopropylmethyl)(dimethyl)pyrazolyl, (methyl)(phenyl)-pyrazolyl, (phenyl)(trifluoromethyl)pyrazolyl, benzylpyrazolyl, aminobenzylpyrazolyl, piperidinylpyrazolyl, tetrahydropyranylmethylpyrazolyl, (dimethyl)(tetrahydropyranyl-methyl)pyrazolyl, pyrrolidinylethylpyrazolyl, piperidinylethylpyrazolyl, methyl-piperidinylethylpyrazolyl, morpholinylethylpyrazolyl, pyridinylmethylpyrazolyl, oxypyridinylmethylpyrazolyl, (dimethyl)(phenylcarbonylmethyl)pyrazolyl, (ethyl)(piperazinylcarbonyl)pyrazolyl, (methylaminocarbonyl)(methylphenyl)pyrazolyl, (aminoethylaminocarbonyl)(methyl)pyrazolyl, aminocarbonylmethylpyrazolyl, (aminocarbonylmethyl)(dimethyl]pyrazolyl, dimethylaminocarbonylmethylpyrazolyl, pyrazolo[1,5-*a*]pyridinyl, dimethylisoxazolyl, (amino)(methyl)isoxazolyl, thiazolyl, dimethylthiazolyl, imidazolyl, methylimidazolyl, dimethylimidazolyl, imidazo[1,2-*a*]pyridinyl, methylimidazo[1,2-*a*]pyridinyl, methylimidazo[4,5-*b*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyrazinyl, methylthiadiazolyl, pyridinyl, fluoropyridinyl, methylpyridinyl, (fluoro)(methyl)pyridinyl, dimethylpyridinyl, vinylpyridinyl, (methyl-piperazinyl)pyridinyl, (methyl)(piperazinyl)pyridinyl, (*tert*-butoxycarbonylpiperazinyl)-(methyl)pyridinyl, piperidinylmethylpyridinyl, (methyl)(oxy)pyridinyl, hydroxypyridinyl, hydroxymethylpyridinyl, hydroxyethylpyridinyl, methoxypyridinyl, (methoxy)(methyl)-pyridinyl, (dimethyl)(methoxy)pyridinyl, methoxymethylpyridinyl, aminopyridinyl, carboxymethylpyridinyl, ethoxycarbonylmethylpyridinyl, pyridazinyl, methylpyridazinyl, piperidinylpyridazinyl, oxypyridazinyl, methoxypyridazinyl, aminopyridazinyl, hydroxyethylaminopyridazinyl, dimethylaminopyridazinyl, pyrimidinyl, methyl-pyrimidinyl, (chloro)(methyl)pyrimidinyl, dimethylpyrimidinyl, pyrrolidinylpyrimidinyl, methylpiperazinylpyrimidinyl, (methyl)(piperazinyl)pyrimidinyl, (*tert*-butoxycarbonyl-piperazinyl)(methyl)pyrimidinyl, hydroxypyrimidinyl, (hydroxy)(methyl)pyrimidinyl, (hydroxyethyl)(methyl)pyrimidinyl, (hydroxypropyl)(methyl)pyrimidinyl, (hydroxy-propynyl)(methyl)pyrimidinyl, methoxypyrimidinyl, aminopyrimidinyl, dimethylamino-pyrimidinyl, (dimethylamino)(fluoro)pyrimidinyl, carboxypyrimidinyl, (methoxycarbonyl-methyl)(methyl)pyrimidinyl, aminocarbonylpyrimidinyl, pyrazinyl, methoxypyrazinyl, aminopyrazinyl, hydroxy, methoxy, isopropoxy, benzyloxycarbonylpiperidinyloxy, morpholinylethoxy, phenoxy, fluorophenoxy, dimethylpyrazolyloxy, bromopyridinyloxy, pyrrolidinylpyridinyloxy, methylpiperazinylpyridinyloxy, methylpyrazolylpyridinyloxy, isopropylaminopyridinyloxy, carboxypyridinyloxy, aminocarbonylpyridinyloxy,

methylpyridazinyloxy, pyrimidinyloxy, methylpyrimidinyloxy, (chloro)(methyl)-pyrimidinyloxy, hydroxymethyl, 1-hydroxy-1-methylethyl, dihydroxypropyl, pyridinyloxymethyl, amino, isopropylamino, dihydroxypropylamino, methoxyethylamino, methoxypropylamino, *N*-(methoxyethyl)-*N*-(methyl)amino, *N*-(methoxypropyl)-*N*-(methyl)amino, dimethylaminoethylamino, dimethylaminopropylamino, *N*-(dimethylaminoethyl)-*N*-(methyl)amino, *N*-(diethylaminoethyl)-*N*-(methyl)amino, *N*-(dimethylaminopropyl)-*N*-(methyl)amino, *N*-(dimethylaminoethyl)-*N*-(ethyl)amino, *N*-(dimethylaminopropyl)-*N*-(ethyl)amino, *N*-(cyclohexyl)-*N*-(methyl)amino, fluorophenylamino, *N*-fluorophenyl-*N*-methylamino, *N*-benzyl-*N*-methylamino, *N*-(benzyl)-*N*-(dimethylaminoethyl)amino, cyanobenzylamino, (cyano)(phenyl)ethylamino, (cyano)(fluoro)benzylamino, methylenedioxybenzylamino, *N*-(methyl)-*N*-(methylpyrrolidinyl)amino, piperidinylamino, *N*-(methyl)-*N*-(piperidinyl)amino, *N*-(ethyl)-*N*-(piperidinyl)amino, *N*-(cyclopropylmethyl)-*N*-(piperidinyl)amino, methylpiperidinylamino, *N*-(methyl)-*N*-(methylpiperidinyl)amino, *N*-(methyl)-*N*-(2-methylpropylpiperidinyl)amino, *N*-(cyclopentylpiperidinyl)-*N*-(methyl)amino, *N*-(acetylpiperidinyl)-*N*-(methyl)amino, pyrrolidinylethylamino, pyrrolidinylpropylamino, *N*-(methyl)-*N*-(pyrrolidinylethyl)amino, *N*-(methyl)-*N*-(pyrrolidinylpropyl)amino, *N*-(methyl)-*N*-(piperidinylmethyl)amino, methylpyrazolylamino, dimethylpyrazolylamino, trimethylpyrazolylamino, *N*-(ethyl)-*N*-(methylpyrazolyl)amino, thiazolylamino, imidazolylamino, (ethoxycarbonyl)(methyl)imidazolylamino, methylthiadiazolylamino, pyridinylamino, bromopyridinylamino, methylpyridinylamino, dimethylpyridinylamino, trifluoromethylpyridinylamino, hydroxypyridinylamino, hydroxyethylpyridinylamino, dihydroxyethylpyridinylamino, methoxypyridinylamino, dihydroxypropoxypyridinylamino, dimethyldioxolanylmethoxypyridinylamino, methoxyethylpyridinylamino, methoxyvinylpyridinylamino, dihydroxypropylaminopyridinylamino, dimethylaminopyridinylamino, methylaminomethylpyridinylamino, dimethylaminomethylpyridinylamino, carboxypyridinylamino, *N*-(methyl)-*N*-(methylpyridinyl)amino, *N*-(ethyl)-*N*-(methylpyridinyl)amino, bis(methylpyridinyl)amino, bis(trifluoromethylpyridinyl)amino, isoquinolinylamino, methylpyridazinylamino, *N*-(methyl)-*N*-(methylpyridazinyl)amino, *N*-(benzyl)-*N*-(methylpyridazinyl)amino, dimethylpyridazinylamino, phenylpyridazinylamino, piperidinylpyridazinylamino, methoxypyridazinylamino, dimethylaminopyridazinylamino, bis(methylpyridazinyl)amino, benzofurylmethylamino, thienylmethylamino, indolylmethylamino, methylpyrazolylmethylamino, (chloro)(dimethyl)pyrazolyl-

methylamino, dimethylisoxazolylmethylamino, thiazolylmethylamino, imidazolylmethylamino, methylimidazolylmethylamino, pyridinylmethylamino, methylpyridinylmethylamino, *N*-(methyl)-*N*-(pyridinylethyl)amino, *N*-(dihydroxypropyl)-*N*-(pyridinylmethyl)amino, *N*-(dihydroxypropyl)-*N*-(methylpyridinylmethyl)amino, aminomethyl, methylaminomethyl, dimethylaminomethyl, pyridinylaminomethyl, *N*-(acetyl)-*N*-(methylpyridinyl)amino, dimethylaminoethylcarbonylamino, cyclohexylcarbonylamino, methylpiperidinylcarbonylamino, methylimidazolylcarbonylamino, formyl, acetyl, methylpiperidinylaminocarbonyl, *N*-(methyl)-*N*-(methylpiperidinyl)aminocarbonyl, piperidinylethylaminocarbonyl, methylpiperazinylcarbonyl, isopropylthio, isopropylsulphinyl, isopropylsulphonyl, *tert*-butoxycarbonyloxy and tetramethyldioxaborolanyl.

A particular value of R^{43} is methylpyrazolyl.

In one embodiment, R^{44} represents hydrogen. In another embodiment, R^{44} represents halogen, especially bromo. In a further embodiment, R^{44} represents C_{1-6} alkyl, especially methyl. In an additional embodiment, R^{44} represents C_{1-6} alkoxy, especially methoxy.

Specific novel compounds in accordance with the present invention include each of the compounds whose preparation is described in the accompanying Examples, and pharmaceutically acceptable salts and solvates thereof.

The present invention also provides a pharmaceutical composition which comprises a compound in accordance with the invention as described above, or a pharmaceutically acceptable salt or solvate thereof, in association with one or more pharmaceutically acceptable carriers.

Pharmaceutical compositions according to the invention may take a form suitable for oral, buccal, parenteral, nasal, topical, ophthalmic or rectal administration, or a form suitable for administration by inhalation or insufflation.

For oral administration, the pharmaceutical compositions may take the form of, for example, tablets, lozenges or capsules prepared by conventional means with pharmaceutically acceptable excipients such as binding agents (e.g. pregelatinised maize starch, polyvinylpyrrolidone or hydroxypropyl methyl cellulose); fillers (e.g. lactose, microcrystalline cellulose or calcium hydrogenphosphate); lubricants (e.g. magnesium stearate, talc or silica); disintegrants (e.g. potato starch or sodium glycollate); or wetting agents (e.g. sodium lauryl sulphate). The tablets may be coated by methods well known in the art. Liquid preparations for oral administration may take the form of, for example,

solutions, syrups or suspensions, or they may be presented as a dry product for constitution with water or other suitable vehicle before use. Such liquid preparations may be prepared by conventional means with pharmaceutically acceptable additives such as suspending agents, emulsifying agents, non-aqueous vehicles or preservatives. The preparations may also contain buffer salts, flavouring agents, colouring agents or sweetening agents, as appropriate.

Preparations for oral administration may be suitably formulated to give controlled release of the active compound.

For buccal administration, the compositions may take the form of tablets or lozenges formulated in conventional manner.

The compounds of formula (I) may be formulated for parenteral administration by injection, e.g. by bolus injection or infusion. Formulations for injection may be presented in unit dosage form, e.g. in glass ampoules or multi-dose containers, e.g. glass vials. The compositions for injection may take such forms as suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilising, preserving and/or dispersing agents. Alternatively, the active ingredient may be in powder form for constitution with a suitable vehicle, e.g. sterile pyrogen-free water, before use.

In addition to the formulations described above, the compounds of formula (I) may also be formulated as a depot preparation. Such long-acting formulations may be administered by implantation or by intramuscular injection.

For nasal administration or administration by inhalation, the compounds according to the present invention may be conveniently delivered in the form of an aerosol spray presentation for pressurised packs or a nebuliser, with the use of a suitable propellant, e.g. dichlorodifluoromethane, fluorotrichloromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas or mixture of gases.

The compositions may, if desired, be presented in a pack or dispenser device which may contain one or more unit dosage forms containing the active ingredient. The pack or dispensing device may be accompanied by instructions for administration.

For topical administration the compounds according to the present invention may be conveniently formulated in a suitable ointment containing the active component suspended or dissolved in one or more pharmaceutically acceptable carriers. Particular carriers include, for example, mineral oil, liquid petroleum, propylene glycol,

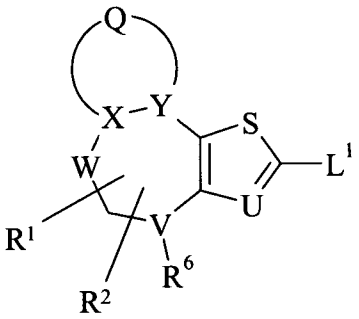
polyoxyethylene, polyoxypropylene, emulsifying wax and water. Alternatively, the compounds according to the present invention may be formulated in a suitable lotion containing the active component suspended or dissolved in one or more pharmaceutically acceptable carriers. Particular carriers include, for example, mineral oil, sorbitan monostearate, polysorbate 60, cetyl esters wax, cetearyl alcohol, benzyl alcohol, 2-octyldodecanol and water.

For ophthalmic administration the compounds according to the present invention may be conveniently formulated as microionized suspensions in isotonic, pH-adjusted sterile saline, either with or without a preservative such as a bactericidal or fungicidal agent, for example phenylmercuric nitrate, benzylalkonium chloride or chlorhexidine acetate. Alternatively, for ophthalmic administration compounds may be formulated in an ointment such as petrolatum.

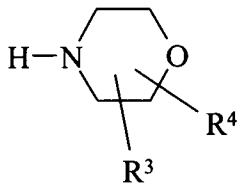
For rectal administration the compounds according to the present invention may be conveniently formulated as suppositories. These can be prepared by mixing the active component with a suitable non-irritating excipient which is solid at room temperature but liquid at rectal temperature and so will melt in the rectum to release the active component. Such materials include, for example, cocoa butter, beeswax and polyethylene glycols.

The quantity of a compound of the invention required for the prophylaxis or treatment of a particular condition will vary depending on the compound chosen and the condition of the patient to be treated. In general, however, daily dosages may range from around 10 ng/kg to 1000 mg/kg, typically from 100 ng/kg to 100 mg/kg, e.g. around 0.01 mg/kg to 40 mg/kg body weight, for oral or buccal administration, from around 10 ng/kg to 50 mg/kg body weight for parenteral administration, and from around 0.05 mg to around 1000 mg, e.g. from around 0.5 mg to around 1000 mg, for nasal administration or administration by inhalation or insufflation.

The compounds of formula (I) above may be prepared by a process which comprises reacting a compound of formula (III) with a compound of formula (IV):



(III)



(IV)

wherein U, V, W, the moiety X-Y-Q, R^1, R^2, R^3, R^4 and R^6 are as defined above, and L^1 represents a suitable leaving group.

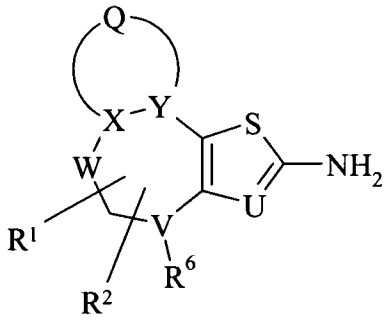
The leaving group L^1 is typically a halogen atom, e.g. bromo.

The reaction is conveniently effected at an elevated temperature in a suitable solvent, e.g. acetonitrile, dimethylsulphoxide, a lower alkanol such as isopropanol, a cyclic ether such as tetrahydrofuran, or a dipolar aprotic solvent such as *N*,*N*-dimethylformamide, optionally under basic conditions, e.g. in the presence of an organic base such as *N*,*N*-diisopropylethylamine or 2,6-lutidine.

Alternatively, the reaction may be effected at an elevated temperature in a solvent such as 2-ethoxyethanol in the presence of a catalytic quantity of a mineral acid, e.g. concentrated hydrochloric acid.

In another alternative, the reaction may be effected at an elevated temperature in a suitable solvent, e.g. a cyclic ether such as tetrahydrofuran, or an aromatic solvent such as toluene, typically under basic conditions, e.g. in the presence of an inorganic base such as sodium *tert*-butoxide, in the presence of a transition metal catalyst. The transition metal catalyst is suitably palladium(II) acetate, in which case the reaction will ideally be performed in the presence of *tert*-butylphosphonium tetrafluoroborate or dicyclohexyl diphenylphosphine.

The intermediates of formula (III) above wherein L^1 is bromo may be prepared from a compound of formula (V):

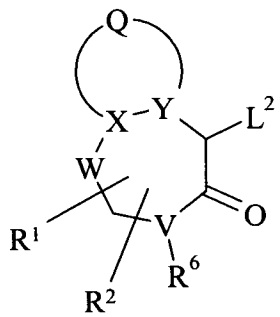


(V)

wherein U, V, W, the moiety X-Y-Q, R^1, R^2 and R^6 are as defined above; by diazotization/ bromination.

The reaction is conveniently effected by stirring compound (V) with *tert*-butyl nitrite and copper(II) bromide in a suitable solvent, e.g. acetonitrile.

The intermediates of formula (V) above wherein U represents N may be prepared by reacting thiourea with a compound of formula (VI):



(VI)

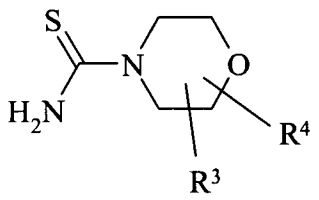
wherein V, W, the moiety X-Y-Q, R^1, R^2 and R^6 are as defined above, and L^2 represents a suitable leaving group.

The leaving group L^2 is typically a halogen atom, e.g. bromo or iodo.

The reaction is conveniently effected at an elevated temperature in a suitable solvent, e.g. a cyclic ether such as tetrahydrofuran, typically under basic conditions, e.g. in the presence of an organic base such as *N,N*-diisopropylethylamine.

Alternatively, the reaction may be accomplished by heating the reactants in a lower alkanol solvent, e.g. a C_{1-6} alkyl alcohol such as ethanol.

In another procedure, the compounds of formula (I) wherein U represents N may be prepared by a process which comprises reacting a compound of formula (VI) as defined above with a compound of formula (VII):



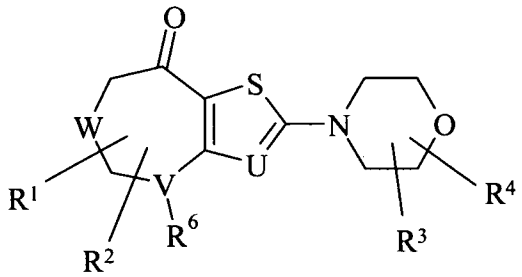
(VII)

wherein R^3 and R^4 are as defined above; under conditions analogous to those described above for the reaction between thiourea and compound (VI).

The reaction may additionally be accomplished by heating the reactants in acetic acid in the presence of sodium acetate.

The intermediates of formula (VII) above may be prepared by reacting a compound of formula (IV) as defined above with 1,1'-thiocarbonyldiimidazole; followed by treatment with ammonia or ammonium hydroxide.

The compounds of formula (IA) above wherein R^x and R^y are both hydrogen may be prepared by a process which comprises reacting a compound of formula (VIII):



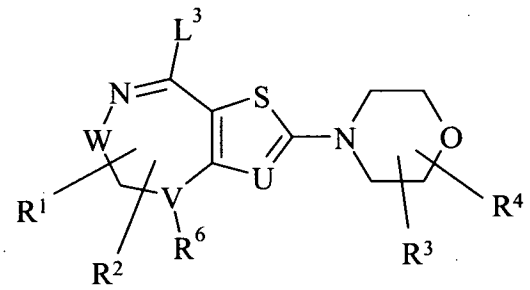
(VIII)

wherein U, V, W, R^1, R^2, R^3, R^4 and R^6 are as defined above; with *tert*-butoxy-bis(dimethylamino)methane (Bredereck's reagent); followed by treatment with hydrazine, typically in the form of its hydrochloride salt, or in the form of its monohydrate.

The reaction between compound (VIII) and Bredereck's reagent may conveniently be effected by heating the reactants together, typically at the reflux temperature. The

subsequent treatment with hydrazine hydrochloride or hydrazine hydrate may conveniently be effected in a suitable solvent, e.g. a lower alkanol solvent such as methanol or ethanol, optionally at an elevated temperature.

The compounds of formula (IC) above wherein R^y and R^z are both hydrogen may be prepared by a process which comprises reacting a compound of formula (IX):



(IX)

wherein U, V, W, R^1, R^2, R^3, R^4 and R^6 are as defined above, and L^3 represents a suitable leaving group; with aminoacetaldehyde dimethyl acetal; followed by treatment with an acid, typically an organic acid such as *p*-toluenesulphonic acid.

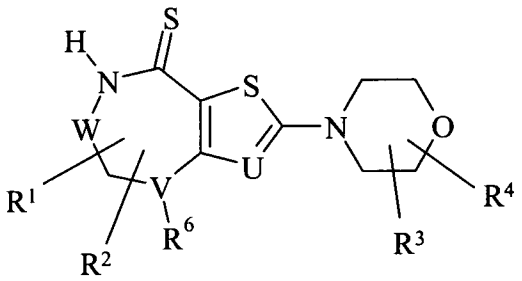
The leaving group L^3 is typically a halogen atom, e.g. chloro, or a methylthio ($-SCH_3$) group.

The reaction between compound (IX) and aminoacetaldehyde dimethyl acetal may conveniently be effected by heating the reactants together. The subsequent acid treatment may conveniently be effected by heating in a suitable solvent, e.g. a hydrocarbon solvent such as toluene, or a lower alkanol solvent such as isopropanol.

The compounds of formula (IC) above wherein R^y is methyl and R^z is hydrogen may be prepared by a process which comprises reacting a compound of formula (IX) as defined above with propargylamine.

The reaction may conveniently be effected at an elevated temperature in a suitable solvent, e.g. a cyclic ether solvent such as tetrahydrofuran.

The intermediates of formula (IX) above wherein L^3 is methylthio may be prepared by reacting a compound of formula (X):

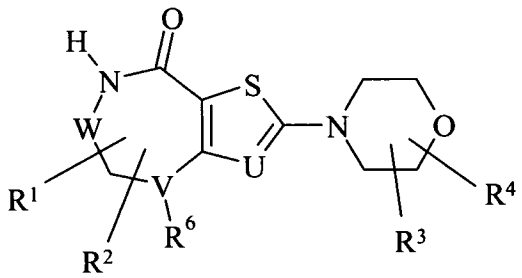


(X)

wherein U, V, W, R^1, R^2, R^3, R^4 and R^6 are as defined above; with a methyl halide, e.g. iodomethane.

The reaction is conveniently effected in a suitable organic solvent, e.g. acetonitrile.

The intermediates of formula (X) above may be prepared by reacting a compound of formula (XI):



(XI)

wherein U, V, W, R^1, R^2, R^3, R^4 and R^6 are as defined above; with 2,4-bis(4-methoxy-phenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulfide (Lawesson's reagent).

The reaction is conveniently effected at an elevated temperature in a suitable solvent, e.g. a hydrocarbon solvent such as toluene.

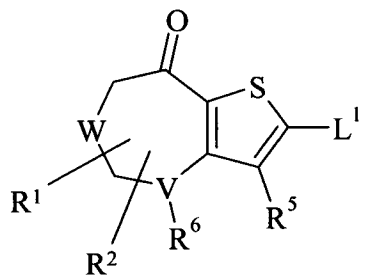
The intermediates of formula (IX) above wherein L^3 is chloro may be prepared by reacting a compound of formula (XI) as defined above with phosphorus oxychloride, typically at an elevated temperature.

The compounds of formula (ID) above may be prepared by a process which comprises reacting a compound of formula (IX) as defined above with a compound of formula R^y-$CONHNH_2$. The reaction may be conveniently accomplished in the presence of an organic acid such as acetic acid.

The compounds of formula (IE) above may be prepared by a process which comprises reacting a compound of formula (IX) as defined above with a metal azide such as sodium azide. The reaction is conveniently accomplished in a suitable solvent, e.g. a lower alkanol solvent such as methanol.

The compounds of formula (VIII) and (XI) above may be prepared by the methods described in WO 2006/114606; in copending international patent application no. PCT/GB2007/002390, published on 3 January 2008 as WO 2008/001076; and in copending international patent application no. PCT/GB2007/002051, published on 13 December 2007 as WO 2007/141504.

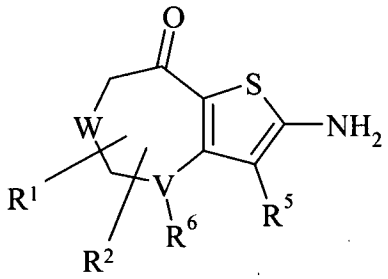
By way of example, the intermediates of formula (VIII) above wherein U represents C-R^5 may be prepared by reacting a compound of formula (IV) as defined above with a compound of formula (XII):



(XII)

wherein V, W, R^1, R^2, R^5, R^6 and L^1 are as defined above; under conditions analogous to those described above for the reaction between compounds (III) and (IV).

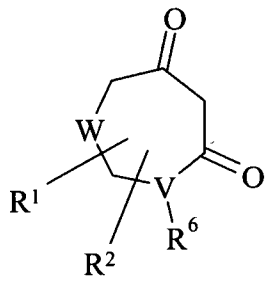
The intermediates of formula (XII) above wherein L^1 is bromo may be prepared from a compound of formula (XIII):



(XIII)

wherein V, W, R^1, R^2, R^5 and R^6 are as defined above; by diazotization/bromination; under conditions analogous to those described above for the diazotization/bromination of compound (V).

The intermediates of formula (XIII) above wherein R^5 represents cyano may be prepared by reacting malononitrile with a compound of formula (XIV):



(XIV)

wherein V, W, R^1, R^2 and R^6 are as defined above; followed by treatment of the resulting compound with sulphur.

The reaction between malononitrile and compound (XIV) is conveniently effected at an elevated temperature in a suitable solvent, e.g. a lower alkanol such as ethanol, typically under basic conditions, e.g. in the presence of piperidine. Treatment of the resulting compound with sulphur is conveniently effected at an elevated temperature in a suitable solvent, e.g. a lower alkanol such as ethanol, typically under basic conditions, e.g. in the presence of morpholine.

Where they are not commercially available, the starting materials of formula (IV), (VI) and (XIV) may be prepared by methods analogous to those described in the accompanying Examples, or by standard methods well known from the art.

It will be understood that any compound of formula (I) initially obtained from any of the above processes may, where appropriate, subsequently be elaborated into a further compound of formula (I) by techniques known from the art. By way of example, a compound of formula (IA) wherein R^x represents hydrogen may be converted into the corresponding compound wherein R^x is an alkylsulphonyl substituent, e.g. methylsulphonyl, by treatment with the appropriate alkylsulphonyl halide, e.g. methanesulphonyl chloride.

A compound of formula (I) wherein R^6 represents hydroxy may be converted into the corresponding compound wherein R^6 represents oxo by treatment with an oxidising agent such as Dess-Martin periodinane.

A compound of formula (I) wherein R^3 and/or R^4 contains an aryl or heteroaryl moiety may be halogenated (e.g. brominated) on the aryl or heteroaryl moiety by treatment with the appropriate *N*-halosuccinimide (e.g. *N*-bromosuccinimide).

A compound of formula (I) wherein R^3 and/or R^4 contains a halogen atom (e.g. bromo) may be converted into the corresponding compound wherein the halogen atom is replaced by amino ($-NH_2$) by treatment with benzophenone imine and tris(dibenzylidene-acetone)dipalladium(0) in the presence of 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP) and a strong base such as sodium *tert*-butoxide.

A compound of formula (I) wherein R^3 contains a halogen atom, e.g. bromo, may be converted into the corresponding compound of formula (I) wherein the halogen atom is replaced by an optionally substituted C_{3-7} cycloalkyl, aryl, aryl(C_{1-6})alkyl or heteroaryl moiety by treatment with, respectively, an appropriately-substituted C_{3-7} cycloalkyl, aryl, aryl(C_{1-6})alkyl or heteroaryl boronic acid or a cyclic ester thereof, e.g. a pinacol ester thereof, in the presence of a catalyst. More particularly, a compound of formula (I) wherein R^3 represents aryl(C_{1-6})alkyl, substituted on the aryl moiety by a halogen atom such as bromo, may be converted into the corresponding compound wherein R^3 represents biaryl(C_{1-6})alkyl or heteroarylaryl(C_{1-6})alkyl by treatment with, respectively, an aryl or heteroaryl boronic acid, in the presence of a catalyst. Similarly, a compound of formula (I) wherein R^3 represents heteroaryl(C_{1-6})alkyl, substituted on the heteroaryl moiety by a halogen atom such as bromo, may be converted into the corresponding compound wherein R^3 represents aryl-heteroaryl(C_{1-6})alkyl by treatment with an aryl boronic acid, in the presence of a catalyst. Furthermore, a compound of formula (I) wherein R^3 contains a cyclic borane moiety, e.g. 4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl, may be converted into the corresponding compound wherein the cyclic borane moiety is replaced by an optionally substituted aryl or heteroaryl moiety by treatment with, respectively, an appropriately-substituted aryl or heteroaryl halide, e.g. chloride, bromide or iodide, in the presence of a catalyst. The catalyst may typically be a transition metal catalyst. A suitable catalyst is tetrakis(triphenylphosphine)palladium(0), in which case the transformation may conveniently be effected at an elevated temperature in the presence of a base such as sodium carbonate, potassium carbonate or potassium phosphate, in an inert solvent such as

1,2-dimethoxyethane, tetrahydrofuran or 1,4-dioxane, optionally in the presence of tetra-*n*-butylammonium bromide. Alternatively, the catalyst may be palladium(II) acetate, in which case the transformation may conveniently be effected at an elevated temperature in the presence of 2-dicyclohexylphosphino-2′,6′-dimethoxybiphenyl and potassium phosphate.

A compound of formula (I) wherein R^3 represents hydroxymethyl may be converted into the corresponding compound wherein R^3 represents a substituted aminomethyl moiety, e.g. phenylaminomethyl, *N*-methyl-*N*-phenylaminomethyl, pyridin-3-ylaminomethyl, indolin-1-ylmethyl, 1,2,3,4-tetrahydroquinolin-1-ylmethyl or 1,2,3,4-tetrahydroisoquinolin-2-ylmethyl, by a two-stage procedure which comprises (i) Swern oxidation of the hydroxymethyl derivative by treatment with oxalyl chloride and dimethyl sulphoxide in the presence of triethylamine; and (ii) reductive amination of the formyl derivative thereby obtained by treatment with the appropriate amine, e.g. aniline, *N*-methylaniline, 3-aminopyridine, indoline, 1,2,3,4-tetrahydroquinoline or 1,2,3,4-tetrahydroisoquinoline, in the presence of a reducing agent such as sodium cyanoborohydride.

In general, any compound of formula (I) which contains a carbonyl-containing functionality, e.g. formyl or a ketone moiety, may be converted into a substituted amino analogue thereof by application of the reductive amination procedure described in step (ii) in the preceding paragraph, which comprises treatment with the appropriately-substituted amine in the presence of a reducing agent, e.g. sodium cyanoborohydride or sodium triacetoxyborohydride.

Any compound of formula (I) wherein R^3 contains an amino moiety can be alkylated on the amino moiety by a reductive amination procedure which comprises treatment with the appropriate aldehyde in the presence of a reducing agent, e.g. sodium cyanoborohydride or sodium triacetoxyborohydride.

A compound of formula (I) wherein R^3 represents hydroxymethyl may be converted into the corresponding compound wherein R^3 represents an optionally substituted C_{3-7} heterocycloalkylcarbonyl moiety, e.g. piperidin-1-ylcarbonyl, 1,2,3,4-tetrahydroquinolin-1-ylcarbonyl, 6-methyl-1,2,3,4-tetrahydroquinolin-1-ylcarbonyl, 6-methoxy-1,2,3,4-tetrahydroquinolin-1-ylcarbonyl, 1,2,3,4-tetrahydroisoquinolin-2-ylcarbonyl or 1,2,3,4-tetrahydroquinoxalin-1-ylcarbonyl, by a two-stage procedure which comprises (i) oxidation of the hydroxymethyl moiety by treatment with potassium

permanganate; and (ii) reaction of the carboxy derivative thereby obtained with the appropriate amine, e.g. piperidine, 1,2,3,4-tetrahydroquinoline, 6-methyl-1,2,3,4-tetrahydroquinoline, 6-methoxy-1,2,3,4-tetrahydroquinoline, 1,2,3,4-tetrahydro-isoquinoline or 1,2,3,4-tetrahydroquinoxaline, in the presence of a condensing agent such as 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide, or *O*-(benzotriazol-1-yl)-*N*,*N*,*N*',*N*'-tetramethyluronium hexafluorophosphate (HBTU).

A compound of formula (I) wherein R^3 contains a phenyl moiety substituted by chloro may be converted into the corresponding compound wherein the phenyl ring is substituted by morpholin-4-yl by treatment with morpholine in the presence of tris(dibenzylideneacetone)dipalladium(0), 2-(di-*tert*-butylphosphino)biphenyl and sodium *tert*-butoxide. A compound of formula (I) wherein R^3 contains a phenyl moiety substituted by bromo may be converted into the corresponding compound wherein the phenyl ring is substituted by pyrrolidin-1-yl by treatment with pyrrolidine in the presence of tris(dibenzylideneacetone)dipalladium(0), 2-dicyclohexylphosphino-2',4',6'-triisopropyl-1,1'-biphenyl and a base such as potassium carbonate. Similarly, a compound of formula (I) wherein R^3 contains a phenyl moiety substituted by bromo may be converted into the corresponding compound wherein the phenyl ring is substituted by an amino moiety (e.g. a group of formula $-NHR^{34}$ as defined above) by treatment with the appropriate amine (e.g. a compound of formula H_2N-R^{34}) in the presence of tris(dibenzylideneacetone)dipalladium(0), 2-(dicyclohexylphosphino)-2',4',6'-tri-isopropyl-1,1'-biphenyl (X-Phos) and a base such as sodium *tert*-butoxide.

A compound of formula (I) wherein R^3/R^4 contains a halogen atom (e.g. bromo) may be converted into the corresponding compound wherein the halogen atom is replaced by carboxy ($-CO_2H$) by treatment with *n*-butyllithium followed by carbon dioxide.

A compound of formula (I) wherein R^3 contains an indole moiety may be methylated on the indole ring by treatment with a methyl halide, e.g. iodomethane, in the presence of a strong base such as sodium hydride. A compound of formula (I) wherein R^3 contains an indole moiety may be acetylated on the indole ring by treatment with acetic anhydride and 4-dimethylamino-pyridine, typically in the presence of an organic base such as triethylamine. A compound of formula (I) wherein R^3 contains an indoline moiety may be converted into the corresponding compound wherein R^3 contains an indole moiety by treatment with an oxidising agent such as manganese dioxide. A compound of formula (I) wherein R^3 contains a hydroxy substituent may be converted into the corresponding

compound wherein R^3 contains a C_{1-6} alkylsulphonyloxy substituent, e.g. methylsulphonyloxy, by treatment with a C_{1-6} alkylsulphonyl halide, e.g. methanesulphonyl chloride. A compound of formula (I) wherein R^3 contains an amino ($-NH_2$) or carboxy ($-CO_2H$) moiety may be converted into the corresponding compound wherein R^3 contains an amido moiety (-NHCO- or -CONH- respectively) by treatment with, respectively, a compound containing a carboxy or amino group, in the presence of *O*-(benzotriazol-1-yl)-*N*,*N*,*N*',*N*'-tetramethyluronium hexafluorophosphate (HBTU), typically in a dipolar aprotic solvent such as *N*,*N*-dimethylformamide; or in the presence of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide and 1-hydroxybenzotriazole. A compound of formula (I) wherein R^3 contains an amino substituent may be converted into the corresponding compound wherein R^3 contains an alkyl- or arylsulphonylamino substituent, e.g. methylsulphonylamino or phenylsulphonylamino, by treatment with an alkyl- or arylsulphonyl halide, e.g. methanesulphonyl chloride or benzenesulphonyl chloride.

A compound of formula (I) wherein R^3 contains an amino moiety may be acylated by treatment with a C_{2-6} alkylcarbonyl halide, e.g. acetyl chloride; or a C_{2-6} alkylcarbonyl anhydride, e.g. acetic anhydride. A compound of formula (I) wherein R^3 contains an amino moiety may be converted into the corresponding carbamate ester by treatment with a C_{1-6} alkyl haloformate, e.g. methyl chloroformate.

A compound of formula (I) wherein R^3 contains a C_{2-6} alkoxycarbonyl substituent, e.g. methoxycarbonyl, may be converted into the corresponding compound wherein R^3 contains a carboxy ($-CO_2H$) substituent under standard saponification conditions, generally by treatment with a base, e.g. an alkali metal hydroxide such as lithium hydroxide or sodium hydroxide. A compound of formula (I) wherein R^3 contains a carboxy ($-CO_2H$) substituent may be converted into the corresponding compound wherein R^3 contains an amido substituent, e.g. methylaminocarbonyl, 2-hydroxyethylaminocarbonyl, dimethylaminocarbonyl, *N*-(2-hydroxyethyl)-*N*-methylaminocarbonyl, benzylaminocarbonyl, azetidin-1-ylcarbonyl, pyrrolidin-1-ylcarbonyl, piperidin-1-ylcarbonyl, 4-methylpiperazin-1-ylcarbonyl or morpholin-4-ylcarbonyl, by a two-stage procedure which comprises (i) treatment of the carboxy derivative with pentafluorophenol in the presence of a condensing agent such as 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide; and (ii) reaction of the pentafluorophenyl ester thereby obtained with the appropriate amine, e.g. methylamine, 2-hydroxyethylamine, dimethylamine, *N*-(2-

hydroxyethyl)-*N*-methylamine, benzylamine, azetidine, pyrrolidine, piperidine, 1-methylpiperazine or morpholine.

A compound of formula (I) wherein R^3/R^4 contains a nitro moiety may be converted into the corresponding compound wherein R^3/R^4 contains an amino ($-NH_2$) moiety by catalytic hydrogenation, typically by treatment with hydrogen in the presence of a hydrogenation catalyst, e.g. palladium on charcoal. A compound of formula (I) wherein R^3/R^4 contains an amino ($-NH_2$) moiety may be converted into the corresponding compound wherein R^3/R^4 contains a heteroaryl-amino moiety, e.g. 6-methylpyridin-3-ylamino, by treatment with the appropriate heteroaryl halide, e.g. 5-bromo-2-methylpyridine, in the presence of palladium(II) acetate, 2-bis(dicyclohexylphosphino)-biphenyl and a base such as sodium *tert*-butoxide.

In general, any compound of formula (I) wherein R^3/R^4 contains a halogen atom, e.g. bromo, may be converted into the corresponding compound wherein the halogen atom is replaced by a substituted amino functionality by treatment with the appropriately-substituted amine derivative and palladium(II) acetate in the presence of a base, e.g. sodium *tert*-butoxide, and tri-*tert*-butylphosphonium tetrafluoroborate. Alternatively, the reaction may be effected by treatment with the appropriately-substituted amine derivative and [1,1'-bis(di-*tert*-butylphosphino)ferrocene]palladium(II) dichloride in the presence of a base, e.g. sodium *tert*-butoxide. Conversely, any compound of formula (I) wherein R^3/R^4 contains an amino functionality may be converted into the corresponding compound wherein the amino functionality is substituted by an optionally substituted aryl or heteroaryl moiety by treatment with an appropriately-substituted aryl or heteroaryl halide (e.g. bromide) and [1,1'-bis(di-*tert*-butylphosphino)ferrocene]palladium(II) dihloride in the presence of a base, e.g. sodium *tert*-butoxide.

A compound of formula (I) wherein R^3/R^4 contains a benzo moiety substituted by a halogen atom, e.g. bromo, may be converted into the corresponding compound wherein R^3/R^4 contains a benzo moiety substituted by a heteroaryl group, e.g. pyrazol-3-yl, 1-methylpyrazol-4-yl, 1-propylpyrazol-4-yl, 1-isobutylpyrazol-4-yl, 1-benzylpyrazol-4-yl, 1-[2-(morpholin-4-yl)ethyl]pyrazol-4-yl, 6-methylpyridin-3-yl or pyrimidin-5-yl, by treatment with the appropriate heteroaryl boronic acid or a cyclic ester thereof formed with an organic diol, e.g. pinacol, in the presence of a catalyst. Similarly, a compound of formula (I) wherein R^3/R^4 contains a benzo moiety substituted by a boronic acid [$-B(OH)_2$] moiety may be converted into the corresponding compound wherein R^3/R^4 contains a

benzo moiety substituted by a heteroaryl group, e.g. methylimidazolyl, by treatment with the appropriate heteroaryl halide, e.g. bromide, derivative in the presence of a catalyst. The catalyst may typically be a transition metal catalyst. A suitable catalyst is tetrakis(triphenylphosphine)palladium(0), in which case the transformation may conveniently be effected at an elevated temperature in the presence of a base such as sodium carbonate, potassium carbonate or potassium phosphate, optionally in the presence of tetrabutylammonium bromide.

A compound of formula (I) wherein R^3/R^4 contains a benzo moiety substituted by a halogen atom, e.g. bromo, may be converted into the corresponding compound wherein R^3/R^4 contains a benzo moiety substituted by a formyl (-CHO) group by treatment with a strong base, e.g. *n*-butyllithium, and *N,N*-dimethylformamide. A compound of formula (I) wherein R^3/R^4 contains a benzo moiety substituted by a formyl (-CHO) group may be converted into the corresponding compound wherein R^3/R^4 contains a benzo moiety substituted by hydroxymethyl by treatment with a reducing agent such as sodium borohydride. A compound of formula (I) wherein R^3/R^4 contains a benzo moiety substituted by a formyl (-CHO) group may be converted into the corresponding compound wherein R^3/R^4 contains a benzo moiety substituted by an aminomethyl moiety (e.g. dimethylaminomethyl, pyridin-3-ylaminomethyl, 4-methylpiperazin-1-ylmethyl or morpholin-4-ylmethyl) by treatment with the appropriate amine (e.g. dimethylamine, pyridin-3-ylamine, 1-methylpiperazine or morpholine) and a reducing agent which typically consists of a mixture of phenylsilane and dibutyltin dichloride. Conversely, a compound of formula (I) wherein R^3/R^4 contains an amino moiety may be converted into the corresponding compound wherein R^3/R^4 is methylated on the amino moiety by treatment with formaldehyde and a reducing agent which typically consists of a mixture of phenylsilane and dibutyltin dichloride. A compound of formula (I) wherein R^3/R^4 contains a benzo moiety substituted by a formyl (-CHO) group may be converted into the corresponding compound wherein R^3/R^4 contains a benzo moiety substituted by a pyridinyloxymethyl moiety by treatment with the appropriate hydroxypyridine in the presence of a mixture of triphenylphosphine and diethyl azodicarboxylate. A compound of formula (I) wherein R^3/R^4 contains a benzo moiety substituted by a C_{2-6} alkoxycarbonyloxy group, e.g. *tert*-butoxycarbonyloxy, may be converted into the corresponding compound wherein R^3/R^4 contains a benzo moiety substituted by hydroxy under standard hydrolytic conditions, e.g. by treatment with trifluoroacetic acid.

A compound of formula (I) wherein R^3/R^4 contains a halogen atom, e.g. bromo, may be converted into the corresponding compound wherein R^3/R^4 contains hydroxy by treatment with sodium hydroxide in the presence of tris(dibenzylideneacetone)-dipalladium(0) and 2-(di-*tert*-butylphosphino)-2',4',6'-triisopropyl-1,1'-biphenyl.

A compound of formula (I) wherein R^3/R^4 contains hydroxy may be converted into the corresponding compound wherein R^3/R^4 contains optionally substituted C_{1-6} alkoxy, C_{3-7} heterocycloalkoxy or C_{3-7} heterocycloalkyl(C_{1-6})alkoxy by treatment with the appropriately substituted C_{1-6} alkyl, C_{3-7} heterocycloalkyl or C_{3-7} heterocycloalkyl(C_{1-6})-alkyl halide, e.g. bromide, ideally at an elevated temperature in the presence of cetyl-ammonium bromide. Alternatively, a compound of formula (I) wherein R^3/R^4 contains hydroxy may be converted into the corresponding compound wherein R^3/R^4 contains optionally substituted pyridinyloxy, pyrimidinyloxy or pyrazinyloxy by treatment with the appropriately substituted pyridinyl, pyrimidinyl or pyrazinyl halide, e.g. fluoride or chloride, typically in the presence of a strong base such as sodium *tert*-butoxide.

A compound of formula (I) wherein R^3/R^4 contains a halogen atom (e.g. bromo) may be converted into the corresponding compound wherein R^3/R^4 contains optionally substituted aryloxy or heteroaryloxy by treatment with an appropriately-substituted hydroxyaryl or hydroxyheteroaryl derivative and a base such as caesium carbonate, ideally in the presence of a copper(I) halide, e.g. copper(I) chloride or copper(I) bromide.

A compound of formula (I) wherein R^3/R^4 contains an amino ($-NH_2$) group may be converted into the corresponding compound wherein R^3/R^4 contains 2,5-dioxopyrrolidin-1-yl by treatment with succinic anhydride.

A compound of formula (I) wherein R^3/R^4 contains an aryl or heteroaryl moiety substituted by a halogen atom, e.g. chloro, may have the halogen atom removed by catalytic hydrogenation.

A compound of formula (I) wherein R^3/R^4 contains a benzo moiety may be alkylated on the aromatic ring by treatment with *n*-butyllithium and an alkyl halide (e.g. iodopropane); or by treatment with an organozinc reagent (e.g. isopropylzinc bromide) in the presence of [1,1'-bis(di-*tert*-butylphosphino)ferrocene]palladium(II) dichloride and copper(I) iodide.

A compound of formula (I) wherein R^3/R^4 contains a halogen atom (e.g. chloro) may be converted into the corresponding compound wherein the halogen atom is replaced by an optionally substituted alkynyl moiety (e.g. 3-hydroxyprop-1-yn-1-yl) by treatment

with an appropriately-substituted alkyne derivative (e.g. 3-hydroxyprop-1-yne) and a catalyst such as tetrakis(triphenylphosphine)palladium(0), typically in the presence of copper(I) iodide and a base such as triethylamine.

A compound of formula (I) wherein R^3/R^4 contains a halogen atom (e.g. bromo) may be converted into the corresponding compound wherein the halogen atom is replaced by acetyl by a two-stage procedure which comprises (i) treatment with butyl vinyl ether and palladium acetate, suitably in the presence of 1,3-bis(diphenylphosphino)propane and an organic base such as triethylamine; and (ii) hydrolysis with a mineral acid such as hydrochloric acid.

A compound of formula (I) wherein R^3/R^4 contains a halogen atom (e.g. bromo) may be converted into the corresponding compound wherein the halogen atom is replaced by 1-hydroxy-1-methylethyl by treatment with *n*-butyllithium and acetone.

A compound of formula (I) wherein R^3/R^4 contains a halogen atom (e.g. bromo) may be converted into the corresponding compound wherein the halogen atom is replaced by C_{1-6} alkylthio (e.g. isopropylthio) by treatment with *n*-butyllithium and the appropriate disulphide derivative (e.g isopropyl disulphide). Conversion of the C_{1-6} alkylthio moiety into C_{1-6} alkylsulphinyl or C_{1-6} alkylsulphonyl may be accomplished by treatment with an oxidising agent, e.g. *m*-chloroperbenzoic acid.

A compound of formula (I) wherein R^3/R^4 contains a pyridinyl moiety may be converted into the corresponding pyridine-*N*-oxide analogue by treatment with peracetic acid.

A compound of formula (I) wherein R^3/R^4 contains a carbonyl-containing moiety (e.g. acetyl) may be converted into the corresponding oxime analogue by treatment with an appropriately-substituted hydroxylamine derivative.

A compound of formula (I) wherein R^3/R^4 contains a formyl moiety may be converted into the corresponding compound wherein R^3/R^4 contains a vinyl moiety by treatment with methyltriphenylphosphonium bromide and a strong base such as sodium hexamethyldisilazide.

A compound of formula (I) wherein R^3/R^4 contains a formyl moiety may be converted into the corresponding compound wherein R^3/R^4 contains a 1-hydroxyethyl moiety by treatment with methyllithium.

A compound of formula (I) wherein R^3/R^4 contains a (2-hydroxyethyl)amino-carbonyl group may be converted into the corresponding compound wherein R^3/R^4 contains an oxazolin-1-yl moiety by treatment with thionyl chloride.

A compound of formula (I) wherein R^3/R^4 contains an ester functionality (e.g. methoxycarbonyl) may be converted into the corresponding compound wherein R^3/R^4 contains an amide functionality (e.g. methylaminocarbonyl or dimethylaminocarbonyl) by treatment with an appropriately-substituted amine (e.g. methylamine or dimethylamine) in the presence of trimethylaluminium.

Alkenyl-containing compounds may be converted into the corresponding *vic*-dihydroxy analogues by treatment with osmium tetroxide.

Alkenyl- and alkynyl-containing compounds may be converted into the corresponding alkyl analogues by catalytic hydrogenation.

A compound of formula (I) wherein R^5 represents $-CO_2R^b$ in which R^b is other than hydrogen may be saponified and then decarboxylated to give the corresponding compounds in which R^5 represents $-CO_2H$ and hydrogen respectively by treatment with a base such as lithium hydroxide. In general, any compound of formula (I) wherein R^5 contains a lower alkyl ester moiety may be converted into the corresponding compound wherein R^5 contains a carboxy ($-CO_2H$) group by treatment with a base such as lithium hydroxide or sodium hydroxide. A compound of formula (I) wherein R^5 represents $-CO_2H$ may be converted into the corresponding compound wherein R^5 represents $-CONR^cR^d$ by treatment with an amine of formula $H-NR^cR^d$ and a condensing agent such as EDC, typically in the presence of an organic base such as triethylamine. In general, any compound of formula (I) wherein R^5 contains a carboxy moiety may be converted into the corresponding compound wherein R^5 contains an amide moiety by treatment with the appropriate amine and a condensing agent such as EDC, typically in the presence of 1-hydroxybenzotriazole (HOBT); alternative condensing agents include isobutyl chloroformate/triethylamine and benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate. Likewise, any compound of formula (I) wherein R^5 contains an amino moiety may be converted into the corresponding compound wherein R^5 contains an amide moiety by treatment with the appropriate carboxylic acid under analogous conditions. A compound of formula (I) wherein R^5 represents cyano may be converted into the corresponding compound wherein R^5 represents $-CONH_2$ by heating under acidic conditions, e.g. in a mixture of acetic acid and sulphuric acid; prolonged treatment leads to

conversion to the corresponding carboxylic acid followed by decarboxylation, i.e. conversion into the corresponding compound wherein R^5 represents hydrogen.

A compound of formula (I) wherein R^5 contains a carboxy moiety may be converted into the corresponding compound containing an arylcarbonyl moiety (e.g. benzoyl) by a two-stage procedure which comprises (i) treatment with *N,O*-dimethylhydroxylamine hydrochloride and a condensing agent such as EDC, typically in the presence of HBTU; and (ii) reaction of the compound thereby obtained with the appropriate aryl lithium derivative, e.g. phenyllithium.

A compound of formula (I) wherein R^5 represents hydrogen may be converted into the corresponding compound wherein R^5 represents fluoro by treatment with Selectfluor™ [i.e. 1-(chloromethyl)-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate)]. A compound of formula (I) wherein R^5 represents hydrogen may be converted into the corresponding compound wherein R^5 represents chloro, bromo or iodo by treatment with *N*-chlorosuccinimide, *N*-bromosuccinimide or *N*-iodosuccinimide respectively. Indeed, the latter procedure is generally applicable for converting any compound of formula (I) wherein R^5 contains an aryl or heteroaryl moiety into the corresponding compound wherein the aryl or heteroaryl moiety is substituted by chloro, bromo or iodo respectively. Alternatively, a compound of formula (I) wherein R^5 represents hydrogen may be converted into the corresponding compound wherein R^5 represents bromo or iodo by treatment with elemental bromine or iodine respectively. A compound of formula (I) wherein R^5 represents hydrogen may be converted into the corresponding compound wherein R^5 represents $-SR^a$ by reaction with a compound of formula R^aS-Cl. A compound of formula (I) wherein R^5 represents hydrogen may be converted into the corresponding compound wherein R^5 represents dimethylaminomethyl by treatment with Eschenmoser's salt (i.e. *N,N*-dimethylmethyleneammonium iodide).

A compound of formula (I) wherein R^5 represents a halogen atom, e.g. iodo or chloro, may be converted into the corresponding compound wherein R^5 represents $-CO_2R^b$ by treatment with carbon monoxide and an alcohol of formula R^b-OH, in the presence of a catalyst. Indeed, this procedure is generally applicable for converting any compound of formula (I) wherein R^5 contains a halogen atom into the corresponding compound containing a lower alkyl ester functionality. The catalyst may typically be a transition metal catalyst. A suitable catalyst is [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II)-dichloromethane complex, in which case the transformation may

conveniently be effected at an elevated temperature and pressure in the presence of an organic base such as triethylamine.

A compound of formula (I) wherein R^5 represents a halogen atom, e.g. bromo or iodo, may be converted into the corresponding compound wherein R^5 represents aryl, biaryl, C_{3-7} heterocycloalkyl-aryl, C_{3-7} heterocycloalkyl(C_{1-6})alkyl-aryl, heteroaryl or heteroaryl-aryl by treatment with, respectively, an aryl, biaryl, C_{3-7} heterocycloalkyl-aryl, C_{3-7} heterocycloalkyl(C_{1-6})alkyl-aryl, heteroaryl or heteroaryl-aryl boronic acid or a cyclic ester thereof formed with an organic diol, e.g. pinacol, in the presence of a catalyst. Similarly, a compound of formula (I) wherein R^5 represents aryl, substituted on the aryl moiety by a halogen atom such as bromo, may be converted into the corresponding compound wherein R^5 represents biaryl or heteroaryl-aryl by treatment with, respectively, an aryl or heteroaryl boronic acid or a cyclic ester thereof formed with an organic diol, e.g. pinacol, in the presence of a catalyst. Likewise, a compound of formula (I) wherein R^5 represents heteroaryl, substituted on the heteroaryl moiety by a halogen atom such as chloro or bromo, may be converted into the corresponding compound wherein R^5 represents aryl-heteroaryl or bi(heteroaryl) by treatment with, respectively, an aryl or heteroaryl boronic acid or a cyclic ester thereof formed with an organic diol, e.g. pinacol or *N*-phenyldiethanolamine, in the presence of a catalyst. The catalyst may typically be a transition metal catalyst. A suitable catalyst is tetrakis(triphenylphosphine)palladium(0), in which case the transformation may conveniently be effected at an elevated temperature in the presence of a base such as sodium carbonate, potassium carbonate, potassium hydroxide or potassium phosphate, in an inert solvent such as 1,2-dimethoxyethane, tetrahydrofuran or 1,4-dioxane. Alternatively, the catalyst may be palladium(II) acetate, in which case the transformation may conveniently be effected at an elevated temperature in the presence of 1,3-bis(diphenylphosphino)propane and potassium phosphate, or in the presence of $PdCl_2$.dppf and potassium phosphate. In general, any compound of formula (I) wherein R^5 represents or contains a halogen atom, e.g. bromo or iodo, may be converted by means of the foregoing procedure into the corresponding compound wherein the halogen atom is replaced by a substituted or unsubstituted aryl, heteroaryl or alkenyl group.

A compound of formula (I) wherein R^5 represents a halogen atom, e.g. iodo, may be converted into the corresponding compound wherein R^5 represents aryl(C_{1-6})alkyl, e.g. benzyl, by treatment with a suitable organozinc reagent, in the presence of a catalyst. The

organozinc reagent may conveniently be prepared by reacting the appropriate aryl(C_{1-6})-alkyl halide, e.g. benzyl bromide, with zinc dust. The catalyst may typically be a transition metal catalyst. A suitable catalyst is dichlorobis(triphenylphosphine)-palladium(II), in which case the transformation may conveniently be effected at an elevated temperature in the presence of an inert solvent such as tetrahydrofuran.

A compound of formula (I) wherein R^5 contains a halogen atom, e.g. chloro, may be converted into the corresponding compound wherein the halogen atom is replaced by an arylamino or heteroarylamino moiety, e.g. phenylamino, by treatment with the appropriate amine, e.g. aniline, and a transition metal catalyst, e.g. palladium acetate, typically in the presence of tributylphosphine tetrafluoroborate and a base such as sodium *tert*-butoxide.

A compound of formula (I) wherein R^5 represents a halogen atom, e.g. iodo, may be converted into the corresponding compound wherein R^5 represents C_{2-6} alkynyl, C_{3-7} cycloalkyl(C_{2-6})alkynyl, aryl(C_{2-6})alkynyl, C_{3-7} heterocycloalkyl(C_{2-6})alkynyl, C_{5-9} heterobicycloalkyl(C_{2-6})alkynyl or heteroaryl(C_{2-6})alkynyl by treatment with, respectively, a suitable C_{2-6} alkyne, C_{3-7} cycloalkyl(C_{2-6})alkyne, aryl(C_{2-6})alkyne, C_{3-7} heterocycloalkyl-(C_{2-6})alkyne, C_{5-9} heterobicycloalkyl(C_{2-6})alkyne or heteroaryl(C_{2-6})alkyne, in the presence of a catalyst. Similarly, a compound of formula (I) wherein R^5 represents C_{2-6} alkynyl, e.g. ethynyl, may be converted into the corresponding compound wherein R^5 represents aryl(C_{2-6})alkynyl, heteroaryl(C_{2-6})alkynyl or C_{3-7} cycloalkyl-heteroaryl(C_{2-6})alkynyl by treatment with, respectively, a suitable aryl, heteroaryl or C_{3-7} cycloalkyl-heteroaryl iodide, in the presence of a catalyst. The catalyst may typically be a transition metal catalyst. A suitable catalyst is dichlorobis(triphenylphosphine)palladium(II), in which case the transformation may conveniently be effected at an elevated temperature in the presence of copper(I) iodide and an organic base such as diisopropylamine.

A compound of formula (I) wherein R^5 represents arylethynyl, e.g. phenylethynyl, may be converted into the corresponding compound wherein R^5 represents arylethyl, e.g. 2-phenylethyl, by catalytic hydrogenation. Indeed, this procedure is generally applicable for converting any compound of formula (I) wherein R^5 contains a -C≡C- moiety into the corresponding compound containing a $-CH_2CH_2-$ moiety. A suitable hydrogenation catalyst is palladium on carbon, in which case the conversion can conveniently be accomplished at an elevated temperature in a suitable solvent, e.g. a lower alkanol such as ethanol, in the presence of a hydrogen donor such as ammonium formate. Under appropriate, generally less forcing, hydrogenation conditions, it is also possible to convert

a compound of formula (I) wherein R^5 contains a -C≡C- moiety into the corresponding compound containing a -CH=CH- moiety.

A compound of formula (I) wherein R^5 contains a -C≡C- moiety may be converted into the corresponding compound containing a $-COCH_2-$ moiety by treatment with a pH 2 buffer solution. Moreover, a compound of formula (I) wherein R^5 contains a -C≡C- moiety may be converted into the corresponding compound containing a -COCO- moiety by treatment with a mineral acid such as hydrochloric acid.

A compound of formula (I) wherein R^5 represents nitro may be converted into the corresponding compound wherein R^5 represents amino by catalytic hydrogenation, which typically comprises reacting the nitro compound with hydrogen in the presence of a catalyst such as palladium on charcoal.

A compound of formula (I) wherein R^5 contains a hydroxy moiety may be converted into the corresponding compound containing a $-OCH_2-$ moiety by treatment with the appropriate alkyl halide, typically in the presence of a base such as potassium carbonate. A compound of formula (I) wherein R^5 contains a hydroxy moiety may be converted into the corresponding compound containing a $-OSO_2-$ moiety by treatment with the appropriate sulphonyl halide, typically in the presence of a base such as triethylamine. A compound of formula (I) wherein R^5 contains a hydroxy moiety may be converted into the corresponding compound containing a trifluoromethylsulphonyloxy moiety by treatment with *N*-phenyltrifluoromethanesulphonimide, typically in the presence of a base such as triethylamine.

A compound of formula (I) wherein R^5 contains a methylsulphonyloxymethyl moiety may be converted into the corresponding compound containing an aminomethyl moiety by treatment with the appropriate amine derivative, typically in the presence of a base such as triethylamine. Similarly, a compound of formula (I) wherein R^5 contains a halomethyl (e.g. chloromethyl) moiety may be converted into the corresponding compound containing an aminomethyl moiety by treatment with the appropriate amine derivative (including cyclic amines), typically in the presence of a base such as potassium carbonate. Furthermore, a compound of formula (I) wherein R^5 contains a hydroxymethyl moiety may be converted into the corresponding compound containing an aminomethyl moiety by treatment with the appropriate amine derivative (including cyclic amines), generally in the presence of triphenylphosphine and diethyl azodicarboxylate.

A compound of formula (I) wherein R^5 contains a trifluoromethylsulphonyloxy moiety may be converted into the corresponding compound wherein the trifluoromethylsulphonyloxy moiety is replaced by an amino functionality by treatment with the appropriate amine derivative (including cyclic amines) and a transition metal catalyst, e.g. acetato(2'-di-*tert*-butylphosphino-1,1'-biphenyl-2-yl)palladium(II), typically at an elevated temperature in the presence of a base such as potassium *tert*-butoxide.

A compound of formula (I) wherein R^5 contains an amino moiety may be alkylated by treatment with the appropriate alkyl halide (e.g. methyl iodide, ethyl bromide, benzyl bromide or *tert*-butyl bromoacetate), typically in the presence of a base such as sodium hydride or triethylamine. A compound of formula (I) wherein R^5 contains an amino moiety may be converted into the corresponding compound containing a $-NCH_2-$ motif by a reductive amination procedure which comprises treatment with the appropriate aldehyde derivative in the presence of a base such as sodium triacetoxyborohydride. A compound of formula (I) wherein R^5 contains an amino moiety may be converted into the corresponding compound containing a carbonylamino moiety by treatment with the appropriate carbonyl halide, typically in the presence of a base such as triethylamine. A compound of formula (I) wherein R^5 contains an amino moiety may be converted into the corresponding compound containing a urea functionality by treatment with the appropriate isocyanate derivative. Alternatively, a compound of formula (I) wherein R^5 contains an amino moiety may be converted into the corresponding compound containing a urea functionality by a two-stage procedure which comprises (i) treatment with triphosgene, typically in the presence of a base such as triethylamine; and (ii) reaction of the compound thereby obtained with the appropriate amine derivative (including cyclic amines). A compound of formula (I) wherein R^5 contains an amino moiety may be converted into the corresponding compound containing a sulphonylamino moiety by treatment with the appropriate sulphonyl halide, typically in the presence of a base such as triethylamine.

A compound of formula (I) wherein R^5 represents a halogen atom, e.g. iodo, may be converted into the corresponding compound wherein R^5 represents acetyl by a two-stage procedure which comprises (i) reaction with butyl vinyl ether and a transition metal catalyst such as tris(dibenzylideneacetone)dipalladium(0), typically in the presence of 1,3-bis(diphenylphosphino)propane and a base such as potassium carbonate; and (ii) hydrolysis of the resulting compound by treatment with a mineral acid, e.g. hydrochloric acid. A compound of formula (I) wherein R^5 represents acetyl may be converted into the

corresponding compound wherein R^5 represents 3-(dimethylamino)-1-oxoprop-2-en-1-yl by treatment with *N,N*-dimethylformamide dimethyl acetal, typically at an elevated temperature. A compound of formula (I) wherein R^5 represents 3-(dimethylamino)-1-oxoprop-2-en-1-yl may be converted into the corresponding compound wherein R^5 represents a substituted or unsubstituted pyrimidinyl moiety by treatment with the appropriate amidine derivative, typically at an elevated temperature in the presence of a base such as sodium ethoxide.

Where a mixture of products is obtained from any of the processes described above for the preparation of compounds according to the invention, the desired product can be separated therefrom at an appropriate stage by conventional methods such as preparative HPLC; or column chromatography utilising, for example, silica and/or alumina in conjunction with an appropriate solvent system.

Where the above-described processes for the preparation of the compounds according to the invention give rise to mixtures of stereoisomers, these isomers may be separated by conventional techniques. In particular, where it is desired to obtain a particular enantiomer of a compound of formula (I) this may be produced from a corresponding mixture of enantiomers using any suitable conventional procedure for resolving enantiomers. Thus, for example, diastereomeric derivatives, e.g. salts, may be produced by reaction of a mixture of enantiomers of formula (I), e.g. a racemate, and an appropriate chiral compound, e.g. a chiral base. The diastereomers may then be separated by any convenient means, for example by crystallisation, and the desired enantiomer recovered, e.g. by treatment with an acid in the instance where the diastereomer is a salt. In another resolution process a racemate of formula (I) may be separated using chiral HPLC. Moreover, if desired, a particular enantiomer may be obtained by using an appropriate chiral intermediate in one of the processes described above. Alternatively, a particular enantiomer may be obtained by performing an enantiomer-specific enzymatic biotransformation, e.g. an ester hydrolysis using an esterase, and then purifying only the enantiomerically pure hydrolysed acid from the unreacted ester antipode. Chromatography, recrystallisation and other conventional separation procedures may also be used with intermediates or final products where it is desired to obtain a particular geometric isomer of the invention.

During any of the above synthetic sequences it may be necessary and/or desirable to protect sensitive or reactive groups on any of the molecules concerned. This may be

achieved by means of conventional protecting groups, such as those described in *Protective Groups in Organic Chemistry*, ed. J.F.W. McOmie, Plenum Press, 1973; and T.W. Greene & P.G.M. Wuts, *Protective Groups in Organic Synthesis*, John Wiley & Sons, 3rd edition, 1999. The protecting groups may be removed at any convenient subsequent stage utilising methods known from the art.

The following Examples illustrate the preparation of compounds according to the invention.

The compounds in accordance with this invention potently inhibit the activity of human PI3Kα and/or PI3Kβ and/or PI3Kγ and/or PI3Kδ.

Enzyme Inhibition Assays

Measurement of the ability of compounds to inhibit the lipid kinase activity of the four class 1 PI3 kinase isoforms (α, β, γ and δ) was performed using a commercially available homogeneous time-resolved fluorescence assay as described by Gray *et al.*, *Anal. Biochem.*, 2003, **313**, 234-245, according to the manufacturer's instructions (Upstate). All assays were performed at 2 μM ATP and a concentration of purified class 1 PI3 kinase known to generate product within the linear range of the assay. Dilutions of inhibitor in DMSO were added to the assay and compared with assays run in the presence of 2% (v/v) DMSO alone (100% activity). The concentration of inhibitor required to inhibit the enzyme activity by 50% is quoted as the IC_{50}.

When tested in the above assay, the compounds of the accompanying Examples were all found to possess IC_{50} values for inhibition of activity of human PI3Kα and/or PI3Kβ and/or PI3Kγ and/or PI3Kδ of 50 μM or better.

EXAMPLES

Abbreviations

DCM: dichloromethane
DMF: *N,N*-dimethylformamide
DMSO: dimethylsulphoxide
MeCN: acetonitrile
Et_2O: diethyl ether
THF: tetrahydrofuran
MeOH: methanol
AcOH: acetic acid
EtOH: ethanol
IPA: isopropyl alcohol

Ac:	acetyl	EtOAc:	ethyl acetate
Me:	methyl	Et:	ethyl
NBS:	*N*-bromosuccinimide	NIS:	*N*-iodoosuccinimide
r.t.:	room temperature	sat.:	saturated
h:	hour	min:	minute
conc.:	concentrated	v:	volume
wt:	weight	M:	mass
SiO_2:	silica	br.:	broad
DIPEA:	*N,N*-diisopropylethylamine	RT:	retention time

EDC: 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride

brine: saturated aqueous sodium chloride solution

HPLC: High Performance Liquid Chromatography

LCMS: Liquid Chromatography Mass Spectrometry

ES+: Electrospray Positive Ionisation

Bredereck's reagent: *tert*-butoxybis(dimethylamino)methane

Lawesson's reagent: 2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulfide

Analytical Conditions

All NMRs were obtained either at 300 MHz or 400 MHz.

Compounds were named with the aid of ACD Labs Name (v. 9.0 or 10.0) supplied by Advanced Chemical Development, Toronto, Canada.

All reactions involving air- or moisture-sensitive reagents were performed under a nitrogen atmosphere using dried solvents and glassware.

INTERMEDIATE 1

3-Bromo-6,6-dimethylpiperidine-2,4-dione

To a stirred suspension of 6,6-dimethylpiperidine-2,4-dione (WO 2005/013986) (10.0 g, 70.92 mmol) in THF (200 mL) at 0°C was added $NaHSO_4$ (2.1 g, 17.73 mmol), followed by NBS (12.6 g, 70.92 mmol) portionwise over 2 h. The reaction mixture was warmed to r.t., stirred for 5 h, and then partitioned between DCM (200 mL) and water (100 mL). The aqueous fraction was separated and extracted with DCM (2 x 100 mL).

The combined organic fractions were washed with water (3 x 200 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Trituration with IPA (3 x 50 mL) gave the *title compound* (10.3 g, 66%) as a white solid. δ_H (DMSO-d_6) 10.80 (1H, br. s), 7.26 (1H, br. s), 2.50 (2H, s) for the main tautomer. LCMS (ES+) 220.0 and 222.0 (1:1 ratio) $(M+H)^+$.

INTERMEDIATE 2 (METHOD A)

6,6-Dimethyl-2-(morpholin-4-yl)-6,7-dihydro[1,3]thiazolo[5,4-*c*]pyridin-4(5*H*)-one

To a stirred solution of *Intermediate 1* (0.16 g, 0.71 mmol) in THF (3 mL) was added morpholine-4-carbothioamide (WO 2006/114606) (0.11 g, 0.71 mmol) and DIPEA (0.25 mL, 1.42 mmol). The reaction mixture was heated to 60°C for 1.5 h, then cooled to r.t. and partitioned between EtOAc (10 mL) and water (10 mL). The aqueous fraction was separated and extracted with EtOAc (3 x 5 mL). The combined organic fractions were washed with water (3 x 10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, 1:1 EtOAc/hexanes) gave the *title compound* (0.07 g, 35%) as a yellow solid. δ_H (DMSO-d_6) 7.30 (1H, br. s), 3.72-3.65 (4H, m), 3.51-3.45 (4H, m), 2.70 (2H, s), 1.24 (6H, s). LCMS (ES+) 268.0 $(M+H)^+$.

INTERMEDIATE 3 (METHOD B)

6,6-Dimethyl-2-(morpholin-4-yl)-6,7-dihydro[1,3]thiazolo[5,4-*c*]pyridine-4(5*H*)-thione

To a stirred solution of *Intermediate 2* (0.80 g, 2.99 mmol) in toluene (20 mL) was added Lawesson's reagent (0.61 g, 1.50 mmol). The reaction mixture was heated to reflux for 30 minutes, then cooled to r.t. and concentrated *in vacuo*. Purification by column chromatography (SiO_2, 1:1 EtOAc/hexanes) gave the *title compound* (0.65 g, 77%) as a yellow solid. δ_H ($CDCl_3$) 6.92 (1H, br. s), 3.84-3.81 (4H, m), 3.61-3.58 (4H, m), 2.80 (2H, s), 1.42 (6H, s). LCMS (ES+) 284.0 $(M+H)^+$.

INTERMEDIATE 4 (METHOD C)

6,6-Dimethyl-4-(methylsulfanyl)-2-(morpholin-4-yl)-6,7-dihydro[1,3]thiazolo[5,4-*c*]pyridine hydroiodide

To a stirred solution of *Intermediate 3* (0.65 g, 2.30 mmol) in MeCN (15 mL) was added methyl iodide (0.17 mL, 2.76 mmol). The reaction mixture was stirred for 16 h, then concentrated *in vacuo*. Trituration with acetone (3 x 3 mL) gave the *title compound* (0.92 g, 94%) as a yellow solid. δ_H ($CDCl_3$) 9.82 (1H, br. s, HI), 3.89-3.83 (4H, m), 3.79-3.74 (4H, m), 3.31 (3H, s), 2.97 (2H, s), 1.85 (6H, s). LCMS (ES+) 298.0 $(M+H)^+$.

INTERMEDIATE 5

tert-Butyl (3*S*)-3-[3-(trimethylsilyl)prop-2-yn-1-yl]morpholine-4-carboxylate

To a stirred solution of (trimethylsilyl)acetylene (9.9 mL, 69.83 mmol) in THF (120 mL) at 0°C was added *n*-butyllithium (28 mL, 2.5M in hexanes, 69.83 mmol) dropwise over 15 minutes. After stirring at this temperature for 30 minutes, a suspension of (3a*R*)-tetrahydro-3*H*-[1,2,3]oxathiazolo[4,3-*c*][1,4]oxazine 1,1-dioxide (WO 2006/114606) (5.0 g, 27.93 mmol) in THF (50 mL) was added dropwise and the reaction mixture stirred at 0°C for 30 minutes, then a further 30 minutes at r.t. Aqueous HCl solution (2M; 80 mL) was added and the reaction mixture stirred vigorously at r.t. MeOH (80 mL) was added and the reaction mixture was stirred at r.t. for 3 h, then concentrated *in vacuo*. The residue was dissolved in DCM (150 mL), and DIPEA (9.7 mL, 55.86 mmol) was added. The reaction mixture was cooled to 0°C and a solution of di-*tert*-butyl dicarbonate (9.2 g, 41.89 mmol) in DCM (50 mL) was added. The reaction mixture was stirred at r.t. for 16 h before addition of water (100 mL). The aqueous layer was separated and extracted with EtOAc (2 x 50 mL). The combined organic fractions were washed with water (3 x 150 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, 0-2% EtOAc/DCM) gave the *title compound* (7.3 g, 88%) as a light orange oil. δ_H (CD_3OD) 3.95-3.88 (1H, m), 3.82 (1H, d, *J* 11.7 Hz), 3.70 (1H, dd, *J* 3.6 and 11.4 Hz), 3.58 (1H, dd, *J* 2.9 and 13.7 Hz), 3.40-3.20 (2H, m), 2.99-2.85 (1H, m), 2.60 (1H, dd, *J* 9.1 and 16.7 Hz), 2.38 (1H, dd, *J* 6.4 and 16.7 Hz), 1.35 (9H, s), 0.00 (9H, s).

INTERMEDIATE 6 (METHOD D)

tert-Butyl (3*S*)-3-[(2-*tert*-butyl-1-benzofuran-3-yl)methyl]morpholine-4-carboxylate

To a stirred solution of *Intermediate 5* (0.83 g, 2.79 mmol) in DMF (25 mL) were added 2-iodophenol (0.61 g, 2.79 mmol), LiCl (0.12 g, 2.79 mmol), Na_2CO_3 (0.53 g, 5.58 mmol) and $Pd(OAc)_2$ (0.025 g, 0.04 mmol). The reaction mixture was stirred at 90°C for 16 h, then cooled to r.t. and concentrated *in vacuo*. Purification by column chromatography (SiO_2, 5-20% EtOAc/hexanes) gave the *title compound* (0.70 g, 64%) as a clear oil. LCMS (ES+) 334.0 $((M-^tBu)+H)^+$.

INTERMEDIATE 7 (METHOD E)

(3*S*)-3-(1-Benzofuran-3-ylmethyl)morpholine

To a solution of *Intermediate 6* (0.70 g, 1.79 mmol) in MeOH (15 mL) at 0°C was added 4M HCl in 1,4-dioxane (10 mL) portionwise. The reaction mixture was warmed to r.t., stirred for 2 h, and then concentrated *in vacuo*. EtOAc (25 mL) and sat. aqueous $NaHCO_3$ solution (5 mL) were added and the layers separated. The organic fraction was washed with water (10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to give the *title compound* (0.29 g, 75%) as a white solid that was used without further purification. LCMS (ES+) 218.1 $(M+H)^+$.

INTERMEDIATE 8 (METHOD F)

(3*S*)-3-(1-Benzofuran-3-ylmethyl)morpholine-4-carbothioamide

To a stirred solution of 1,1'-thiocarbonyldiimidazole (0.26 g, 1.47 mmol) in THF (10 mL) was added *Intermediate 7* (0.29 g, 1.33 mmol). The reaction mixture was stirred at r.t. for 4 h, and then concentrated *in vacuo*. The residue was dissolved in MeCN (15 mL) and aqueous NH_3 (20% v/v, 15 mL) was added. The reaction mixture was stirred at 60°C for 16 h, cooled at r.t., and then concentrated *in vacuo*. Purification by column chromatography (SiO_2, 40% EtOAc/hexanes) gave the *title compound* (0.25 g, 68%) as a yellow solid. LCMS (ES+) 277.1 $(M+H)^+$.

INTERMEDIATE 9

2-[(3*S*)-3-(1-Benzofuran-3-ylmethyl)morpholin-4-yl]-5,5-dimethyl-5,6-dihydro-1,3-benzothiazol-7(4*H*)-one

The *title compound* was prepared from 2-bromo-5,5-dimethylcyclohexane-1,3-dione (WO 2006/114606) and *Intermediate 8* according to *Method A* (after stirring at 60°C for 2 h, additional *Intermediate 8* (1 equivalent) and DIPEA (2 equivalents) were added and the reaction mixture stirred at 60°C for 16 h) and was isolated as a glassy solid (47%) after purification by column chromatography (SiO_2, 50-70% EtOAc/hexanes, followed by SiO_2, 0-1% MeOH/DCM). LCMS (ES+) 485.1 $(M+H)^+$.

INTERMEDIATE 10

Methyl 3-{[(3*S*)-4-(*tert*-butoxycarbonyl)morpholin-3-yl]methyl}-2-(trimethylsilyl)-1*H*-indole-5-carboxylate

The *title compound* was prepared from methyl 4-amino-3-iodobenzoate and *Intermediate 5* according to *Method D* and was isolated as a yellow solid (59%) after purification by column chromatography (SiO_2, 10-25% EtOAc/hexanes). LCMS (ES+) 392.0 $((M-^tBu)+H)^+$.

INTERMEDIATE 11

Methyl 3-[(3*S*)-morpholin-3-ylmethyl]-1*H*-indole-5-carboxylate

The *title compound* was prepared from *Intermediate 10* according to *Method E* and was isolated as a brown gum (quantitative) that was used without further purification. LCMS (ES+) 275.0 $(M+H)^+$.

INTERMEDIATE 12

Methyl 3-{[(3*S*)-4-(aminocarbonothioyl)morpholin-3-yl]methyl}-1*H*-indole-5-carboxylate

The *title compound* was prepared from *Intermediate 11* according to *Method F* and was isolated as a yellow solid (99%) after purification by column chromatography (SiO_2, 0-4% MeOH/DCM). LCMS (ES+) 334.0 $(M+H)^+$.

INTERMEDIATE 13

Methyl 3-{[(3*S*)-4-(6,6-dimethyl-4-oxo-4,5,6,7-tetrahydro[1,3]thiazolo[5,4-*c*]pyridin-2-yl)morpholin-3-yl]methyl}-1*H*-indole-5-carboxylate

The *title compound* was prepared from *Intermediate 12* and *Intermediate 1* according to *Method A* and was isolated as a yellow solid (69%) after purification by column chromatography (SiO_2, 0-5% MeOH/DCM). δ_H (CD_3OD) 8.62 (1H, d, *J* 1.0 Hz), 7.81 (1H, dd, *J* 8.6 and 1.6 Hz), 7.39 (1H, d, *J* 8.6 Hz), 7.24 (1H, s), 4.41-4.35 (1H, m), 4.11-4.05 (1H, m), 3.95 (3H, s), 3.90 (1H, d, *J* 11.7 Hz), 3.73-3.52 (4H, m), 3.45-3.38 (1H, m), 3.18 (1H, dd, *J* 13.9 and 5.4 Hz), 2.87 (1H, d, *J* 16.9 Hz), 2.81 (1H, d, *J* 16.9 Hz), 1.37 (3H, s), 1.36 (3H, s). Exchangeable protons were not observed. LCMS (ES+) 455.0 $(M+H)^+$.

INTERMEDIATE 14

Methyl 3-{[(3*S*)-4-(6,6-dimethyl-4-thioxo-4,5,6,7-tetrahydro[1,3]thiazolo[5,4-*c*]pyridin-2-yl)morpholin-3-yl]methyl}-1*H*-indole-5-carboxylate

The *title compound* was prepared from *Intermediate 13* according to *Method B* and was isolated as a yellow oil (66%) after purification by column chromatography (SiO_2, 1:2 EtOAc/hexanes). δ_H ($CDCl_3$) 8.70 (1H, s), 8.30 (1H, br. s), 7.95 (1H, dd, *J* 8.6 and 1.3 Hz), 7.38 (1H, d, *J* 8.6 Hz), 7.18 (1H, d, *J* 1.6 Hz), 6.87 (1H, br. s), 4.45-4.30 (1H, m), 4.17-4.08 (1H, m), 3.98 (3H, s), 3.88 (1H, d, *J* 11.8 Hz), 3.75-3.61 (3H, m), 3.56 (1H, dd, *J* 11.7 and 2.1 Hz), 3.43 (1H, dd, *J* 13.9 and 10.9 Hz), 3.16 (1H, dd, *J* 13.9 and 4.5 Hz), 2.90 (2H, d, *J* 3.0 Hz), 2.07 (6H, s). LCMS (ES+) 471.1 $(M+H)^+$.

INTERMEDIATE 15

Methyl 3-({(3*S*)-4-[6,6-dimethyl-4-(methylsulfanyl)-6,7-dihydro[1,3]thiazolo[5,4-*c*]pyridin-2-yl]morpholin-3-yl}methyl)-1*H*-indole-5-carboxylate

The *title compound* was prepared from *Intermediate 14* according to *Method C* and was isolated as a yellow solid (quantitative) that was used without further purification. LCMS (ES+) 485.1 $(M+H)^+$.

INTERMEDIATE 16

tert-Butyl (3*S*)-3-{[5-cyano-2-(trimethylsilyl)-1*H*-indol-3-yl]methyl}morpholine-4-carboxylate

The *title compound* was prepared from *Intermediate 5* and 4-amino-3-iodo-benzonitrile according to *Method D* and was isolated as a yellow solid (50%) after work-up (EtOAc and water) and purification by column chromatography (SiO_2, 5-100% EtOAc/hexanes). LCMS (ES+) 414.0 $(M+H)^+$.

INTERMEDIATE 17

3-[(3*S*)-Morpholin-3-ylmethyl]-1*H*-indole-5-carbonitrile

The *title compound* was prepared from *Intermediate 16* according to *Method E* and was isolated as a brown solid (87%) that was used without further purification. LCMS (ES+) 242.0 $(M+H)^+$.

INTERMEDIATE 18

(3*S*)-3-[(5-Cyano-1*H*-indol-3-yl)methyl]morpholine-4-carbothioamide

The *title compound* was prepared from *Intermediate 17* according to *Method F* and was isolated as an off-white solid (39%) after purification by column chromatography (SiO_2, 0-5% MeOH/DCM). LCMS (ES+) 301.0 $(M+H)^+$.

INTERMEDIATE 19

3-{[(3*S*)-4-(6,6-Dimethyl-4-oxo-4,5,6,7-tetrahydro[1,3]thiazolo[5,4-*c*]pyridin-2-yl)morpholin-3-yl]methyl}-1*H*-indole-5-carbonitrile

The *title compound* was prepared from *Intermediate 1* and *Intermediate 18* according to *Method A* and was isolated as a yellow solid (35%) after recrystallisation from MeOH. δ_H (DMSO-d_6) 11.45 (1H, s), 8.44 (1H, s), 7.49 (1H, d, *J* 8.5 Hz), 7.43-7.40 (2H, m), 7.29 (1H, s), 4.33-4.22 (1H, m), 3.99 (1H, d, *J* 7.0 Hz), 3.73 (1H, d, *J* 11.6 Hz), 3.59-3.16 (5H, m), 2.97 (1H, dd, *J* 13.9 and 4.7 Hz), 2.75 (2H, s), 1.25 (6H, s). LCMS (ES+) 422.0 $(M+H)^+$.

INTERMEDIATE 20 (METHOD H)

3-{[(3*S*)-4-(4-Chloro-6,6-dimethyl-6,7-dihydro[1,3]thiazolo[5,4-*c*]pyridin-2-yl)morpholin-3-yl]methyl}-1*H*-indole-5-carbonitrile

A stirred solution of *Intermediate 19* (0.34 g, 0.81 mmol) in phosphorus oxychloride (5 mL) was heated to reflux under nitrogen for 10 minutes, then cooled to r.t. and concentrated *in vacuo*. Water (15 mL) and EtOAc (15 mL) were added, and the layers separated. The organic fraction was washed with brine (15 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the *title compound* (0.25 g, 69%) as a brown solid that was used without further purification. LCMS (ES+) 442.0 and 440.1 $(M+H)^+$.

INTERMEDIATE 21

(3*S*)-3-[3-(Trimethylsilyl)prop-2-yn-1-yl]morpholine hydrochloride

A solution of *Intermediate 5* (25.0 g, 8.40 mmol) in 4N HCl in 1,4-dioxane (200 mL) was stirred at r.t. for 15 minutes, and then concentrated *in vacuo*, azeotroping with toluene. The residue was triturated with hexanes, and then filtered to give the *title compound* (17.5 g, quantitative) as a white solid that was used without further purification. δ_H (CD_3OD) 3.98-3.88 (1H, m), 3.87-3.81 (1H, m), 3.77-3.51 (1H, m), 3.53-3.43 (1H, m), 3.37-3.25 (2H, m), 3.22-3.04 (1H, m), 2.56-2.49 (2H, m), 0.00 (9H, s). Exchangeable proton was not observed.

INTERMEDIATE 22

7,7-Dimethyl-2-{(3*S*)-3-[3-(trimethylsilyl)prop-2-yn-1-yl]morpholin-4-yl}-5,6,7,8-tetrahydro-4*H*-[1,3]thiazolo[5,4-*c*]azepin-4-one

To a stirred solution of 2-bromo-7,7-dimethyl-5,6,7,8-tetrahydro-4*H*-[1,3]thiazolo[5,4-*c*]azepine-4-one (WO 2006/114606) (5.0 g, 18.18 mmol) in DMF (5 mL) was added *Intermediate 21* (3.5 g, 15.09 mmol), followed by DIPEA (7.8 mL, 45.27 mmol). The reaction mixture was heated to 180°C under microwave irradiation, in a sealed tube, then cooled to r.t. EtOAc (10 mL) and brine (10 mL) were added, and the layers separated. The organic fraction was washed with brine (4 x 10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography

(SiO_2, 0-100% EtOAc/DCM), followed by trituration with EtOAc, gave the *title compound* (3.8 g, 65%) as a white solid. δ_H (DMSO-d_6) 5.82-5.73 (1H, m), 4.02 (1H, d, *J* 11.9 Hz), 3.93-3.86 (1H, m), 3.83 (1H, dd, *J* 10.6 and 3.3 Hz), 3.56-3.49 (2H, m), 3.49-3.43 (1H, m), 3.25-3.15 (1H, m), 3.00-2.95 (2H, m), 2.73-2.67 (1H, m), 2.66 (2H, s), 2.50 (1H, dd, *J* 16.4 and 5.3 Hz), 0.96 (6H, s), 0.00 (9H, s). LCMS (ES+) 392.1 $(M+H)^+$.

INTERMEDIATE 23

3-{[(3*S*)-4-(7,7-Dimethyl-4-oxo-5,6,7,8-tetrahydro-4*H*-[1,3]thiazolo[5,4-*c*]azepin-2-yl)morpholin-3-yl]methyl}-2-(trimethylsilyl)-1*H*-indole-5-carbonitrile

The *title compound* was prepared from *Intermediate 22* and 4-amino-3-iodo-benzonitrile according to *Method D* and was isolated as a white solid (79%) after work-up (EtOAc and water) and purification by column chromatography (SiO_2, 33-50% EtOAc/ hexanes). LCMS (ES+) 508.1 $(M+H)^+$.

INTERMEDIATE 24

3-Ethoxy-5,5-dimethylcyclohex-2-en-1-one

To a stirred solution of NaOEt (50 mL, 50.0 mmol), freshly prepared from Na (2.17 g, 50.0 mmol) and EtOH (50 mL), was added 3-chloro-5,5-dimethyl-2-cyclohexene-1-one (3.17 g, 20.0 mmol). The reaction mixture was refluxed for 20 minutes, then cooled to r.t. and partitioned between water (30 mL) and EtOAc (50 mL). The organic fraction was dried (Na_2SO_4), filtered and concentrated *in vacuo* to give the *title compound* (2.74 g, 82%) as a yellow oil that was used without further purification. δ_H ($CDCl_3$) 5.36 (1H, s), 3.92 (2H, q, *J* 6.8 Hz), 2.29 (2H, s), 2.23 (2H, s), 1.39 (3H, t, *J* 7.1 Hz), 1.09 (6H, s). LCMS (ES+) 169.1 $(M+H)^+$.

INTERMEDIATE 25

4-Ethoxy-6,6-dimethyl-2-oxocyclohex-3-ene-1-carbaldehyde

To a stirred suspension of NaH (1.12 g, 60% dispersion in oil, 28.0 mmol) in Et_2O (50 mL) was added a solution of *Intermediate 24* (4.71 g, 28.0 mmol) and ethyl formate (4.5 mL, 56.0 mmol) in Et_2O dropwise over 20 minutes. The reaction mixture was stirred

at r.t. for 18 h. An additional portion of NaH (0.90 g, 60% dispersion in oil, 22.5 mmol) was added and the reaction mixture stirred at r.t. for a further 2 h. Water (100 mL) was added, and the layers were separated. The aqueous fraction was acidified to pH 3 with conc. HCl. The precipitate formed was filtered, washed with water (2 x 30 mL) and dried to give the *title compound* (2.91 g, 53%) as a yellow solid that was used without further purification. δ_H ($CDCl_3$) 14.70 (1H, d, *J* 9.9 Hz), 7.36 (1H, d, *J* 9.9 Hz), 5.35 (1H, s), 3.98 (2H, q, *J* 7.1 Hz), 2.31 (2H, s), 1.40 (3H, t, *J* 7.1 Hz), 1.23 (6H, s). LCMS (ES+) 197.1 $(M+H)^+$.

INTERMEDIATE 26

6-Ethoxy-4,4-dimethyl-4,5-dihydro-1,2-benzisoxazole

To a stirred solution of *Intermediate 25* (3.0 g, 15.30 mmol) in EtOH (50 mL) was added hydroxylamine (1.2 mL, 50% wt. in water, 91.8 mmol). The reaction mixture was stirred at r.t. for 2 h, then concentrated *in vacuo*. AcOH (50 mL) was added. The reaction mixture was refluxed for 20 minutes, then cooled to r.t. and partitioned between EtOAc (50 mL) and aqueous sat. Na_2CO_3 solution (50 mL). The organic fraction was dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, 5-10% EtOAc/hexanes, loading in toluene) gave the *title compound* (1.33 g, 45%) as a white solid. δ_H ($CDCl_3$) 8.00 (1H, s), 5.63 (1H, s), 3.94 (2H, q, *J* 6.8 Hz), 2.41 (2H, s), 1.40 (3H, t, *J* 6.8 Hz), 1.25 (6H, s). LCMS (ES+) 194.1 $(M+H)^+$.

INTERMEDIATE 27

4,4-Dimethyl-4,7-dihydro-1,2-benzisoxazol-6(5*H*)-one

To a stirred solution of *Intermediate 26* (0.46 g, 2.38 mmol) in EtOH (10 mL) was added 4M aqueous HCl (10 mL). The reaction mixture was stirred at r.t. for 2 h, then concentrated to a low volume and partitioned between EtOAc (10 mL) and water (10 mL). The organic fraction was concentrated *in vacuo* to give the *title compound* (0.24 g, 62%) as a yellow oil that was used without further purification. δ_H ($CDCl_3$) 8.24 (1H, s), 3.61 (2H, s), 2.56 (2H, s), 1.33 (6H, s). LCMS (ES+) 166.1 $(M+H)^+$.

INTERMEDIATE 28

7-Iodo-4,4-dimethyl-4,7-dihydro-1,2-benzisoxazol-6(5*H*)-one

To a stirred solution of *Intermediate 27* (0.50 g, 3.00 mmol) in AcOH (10 mL) was added NIS (0.71 g, 3.15 mmol). The reaction mixture was stirred at r.t. for 16 h. Water (10 mL) and EtOAc (15 mL) were added and the layers separated. The aqueous fraction was extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with water (2 x 20 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to give a mixture of the *title compound* and starting material (1:1 ratio, 0.46 g, 33% of *title compound*) that was used without further purification. LCMS (ES+) 291.9 $(M+H)^+$.

INTERMEDIATE 29

(3*S*)-3-(1*H*-Indol-3-ylmethyl)morpholine-4-carbothioamide

The *title compound* was prepared from 3-[(3*S*)-morpholin-3-ylmethyl]-1*H*-indole (WO 2006/114606) according to *Method F* and was isolated as an orange foam (44%) after purification by column chromatography (SiO_2, EtOAc). δ_H (DMSO-d_6) 10.85 (1H, br. s), 7.86 (1H, d, *J* 7.2 Hz), 7.49 (2H, br. s), 7.33 (1H, d, *J* 8.0 Hz), 7.18 (1H, d, *J* 2.2 Hz), 7.09-7.01 (1H, m), 7.00-6.94 (1H, m), 3.87 (1H, m), 3.60 (1H, d, *J* 11.6 Hz), 3.36-3.18 (6H, m), 2.81 (1H, dd, *J* 13.6 and 4.8 Hz). LCMS (ES+) 276.0 $(M+H)^+$.

INTERMEDIATE 30

7-Ethoxy-5,5-dimethyl-5,6-dihydroquinazoline

To boiling formamidine acetate (100 mL) was added *Intermediate 25* (2.0 g, 10.20 mmol). The reaction mixture was refluxed for 15 minutes, then cooled to r.t. and partitioned between DCM (50 mL) and water (50 mL). The aqueous fraction was extracted with DCM (2 x 50 mL). The combined organic fractions were washed with water (2 x 100 mL), dried (Na_2SO_4), filtered, then concentrated *in vacuo*. Purification by column chromatography (SiO_2, 33-50% EtOAc/hexanes) gave the *title compound* (0.45 g, 22%) as a yellow oil. δ_H ($CDCl_3$) 8.83 (1H, s), 8.38 (1H, s), 5.70 (1H, s), 4.04 (2H, q, *J* 6.8 Hz), 2.41 (2H, s), 1.42 (3H, t, *J* 7.3 Hz), 1.37 (6H, s). LCMS (ES+) 194.1 $(M+H)^+$.

INTERMEDIATE 31

5,5-Dimethyl-5,8-dihydroquinazolin-7(6*H*)-one

To a stirred solution of *Intermediate 30* (0.45 g, 2.21 mmol) in EtOH (10 mL) was added 6M aqueous HCl (30 mL). The reaction mixture was stirred at r.t. for 16 h, and then concentrated *in vacuo* (co-distilling with water) to give the *title compound* (0.319 g, 82%) as a yellow oil that was used without further purification. δ_H ($CDCl_3$) 8.99 (1H, s), 8.70 (1H, s), 3.73 (2H, s), 2.53 (2H, s), 1.34 (6H, s). LCMS (ES+) 177.0 $(M+H)^+$.

INTERMEDIATE 32

6-Bromo-4*H*-benzo[1,4]oxazin-3-one

To a stirred solution of 2-amino-4-bromophenol (2.5 g, 13.3 mmol) in THF (80 mL) at 0°C was added NEt_3 (2.4 mL, 17.3 mmol), followed by chloroacetyl chloride (1.12 mL, 14.6 mmol) portionwise. The reaction mixture was stirred at this temperature for 10 minutes, then allowed to warm to r.t. and stirred for a further 2 h. It was then cooled to 0°C and NaH (1.05 g, 60% dispersion in oil, 26 mmol) was added portionwise. The reaction mixture was stirred at 0°C for 20 minutes, then at r.t. for 2 h before being quenched with water (20 mL) and concentrated *in vacuo*. The residue was diluted with water (100 mL). The precipitate formed was filtered, washed with water (3 x 50 mL) and dried *in vacuo* to give the *title compound* (2.14 g, 70%) as a beige solid that was used without further purification. δ_H (DMSO-d_6) 10.81 (1H, br. s), 7.08 (1H, dd, *J* 8.5 and 2.3 Hz), 7.02 (1H, d, *J* 2.3 Hz), 6.92 (1H, d, *J* 8.5 Hz), 4.60 (2H, s).

INTERMEDIATE 33

6-Bromo-3,4-dihydro-2*H*-benzo[1,4]oxazine

To a stirred solution of *Intermediate 32* (2.0 g, 8.0 mmol) in THF (50 mL) was added borane-THF (13.2 mL, 1M solution in THF, 13.2 mmol) portionwise. The reaction mixture was stirred at r.t. for 10 minutes, then heated to reflux for 1 h and allowed to cool to r.t. The reaction mixture was cooled to 0°C and quenched with water (20 mL), then 2M aqueous NaOH (20 mL), and concentrated *in vacuo*. Water (100 mL) and EtOAc (100 mL) were added and the layers separated. The organic fraction was washed with

brine (100 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the *title compound* (2 g, quantitative) as a brown oil. δ_H (DMSO-d_6) 6.68 (3H, m), 4.25-4.18 (2H, m), 3.81 (1H, br. s), 3.44-3.36 (2H, m).

INTERMEDIATE 34

6-Bromo-3,4-dihydro-2*H*-benzo[1,4]oxazine-4-carbothioic acid amide

A solution of *Intermediate 33* (1.7 g, 8 mmol) and 1,1'-thiocarbonyldiimidazole (2.84 g, 16 mmol) in THF (15 mL) was heated to 120°C under microwave irradiation, in a sealed tube, for 15 minutes. After cooling to r.t., NH_3 (40 mL, 7N solution in MeOH, 280 mmol) was added. The reaction mixture was stirred at r.t. for 3 h, concentrated *in vacuo*, and then partitioned between EtOAc (100 mL) and water (100 mL). The organic fraction was washed with water (100 mL), then brine (100 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. Trituration with Et_2O and heptane gave the *title compound* (0.5 g, 23%) as a white solid. δ_H (DMSO-d_6) 8.20 (2H, br. s), 7.60 (1H, d, *J* 2.3 Hz), 7.21 (1H, dd, *J* 8.7 and 2.3 Hz), 6.88 (1H, d, *J* 8.9 Hz), 4.30-4.16 (4H, m).

INTERMEDIATE 35

2-(6-Bromo-2,3-dihydrobenzo[1,4]oxazin-4-yl)-6,6-dimethyl-6,7-dihydro-[1,3]thiazolo[5,4-*c*]pyridin-4(5*H*)-one

Two batches each of *Intermediate 1* (0.25 g, 1.14 mmol), *Intermediate 34* (0.25 g, 0.87 mmol) and DIPEA (0.23 mL, 1.3 mmol) in THF (4 mL) were heated to 120°C under microwave irradiation, in a sealed tube, for 20 minutes. After cooling to r.t., the reaction mixtures were combined and partitioned between EtOAc (100 mL) and water (100 mL). The organic fraction was washed with brine (100 mL) and concentrated *in vacuo*. Purification by preparative HPLC gave the *title compound* (0.10 g, 11%) as an off-white solid. δ_H ($CDCl_3$) 8.18 (1H, d, *J* 2.3 Hz), 7.08 (1H, dd, *J* 8.9 and 2.3 Hz), 6.76 (1H, d, *J* 8.7 Hz), 5.28 (1H, br. s), 4.29-4.22 (2H, m), 4.04-3.98 (2H, m), 2.83 (2H, s), 1.33 (6H, s). LCMS (ES+) 394.0 $(M+H)^+$.

INTERMEDIATE 36

6,6-Dimethyl-2-[6-(1-methyl-1*H*-pyrazol-4-yl)-2,3-dihydrobenzo[1,4]oxazin-4-yl]-6,7-dihydro[1,3]thiazolo[5,4-*c*]pyridin-4(5*H*)-one

A stirred suspension of *Intermediate 35* (0.090 g, 0.23 mmol), 1-methyl-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-1*H*-pyrazole (0.142 g, 0.69 mmol), Na_2CO_3 (0.073 g, 0.69 mmol), tetra-*n*-butylammonium bromide (0.212 g, 0.69 mmol) and tetrakis(triphenylphosphine)palladium(0) (0.026 g, 0.02 mmol) in THF (4 mL) was heated to 150°C under microwave irradiation, in a sealed tube, for 40 minutes. After cooling to r.t., the reaction mixture was partitioned between EtOAc (50 mL) and water (50 mL). The organic fraction was washed with brine (50 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was pre-purified by preparative HPLC, then partitioned between EtOAc (100 mL) and aqueous sat. $NaHCO_3$ solution (100 mL). The combined organic fractions were washed with a mixture of brine and water (100 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was then triturated with EtOAc (100 mL) to give the *title compound* (0.024 g, 27%) as a white solid. δ_H ($CDCl_3$) 7.92 (1H, d, *J* 2.1 Hz), 7.62 (1H, s), 7.49 (1H, s), 7.10 (1H, dd, *J* 8.5 and 2.1 Hz), 6.88 (1H, d, *J* 8.5 Hz), 5.26 (1H, s), 4.30-4.23 (2H, m), 4.16-4.09 (2H, m), 3.88 (3H, s), 2.81 (2H, s), 1.33 (6H, s). LCMS (ES+) 396.0 $(M+H)^+$.

INTERMEDIATE 37

6-Ethoxy-4,4-dimethyl-4,5-dihydro-2*H*-indazole

To a solution of *Intermediate 25* (1.0 g, 5.1 mmol) in ethanol (15 mL) was added hydrazine hydrate (5.61 mmol, 0.272 mL). The reaction mixture was stirred for 5 minutes and allowed to stand for 2 weeks. The reaction mixture was concentrated to an oil *in vacuo* and purified by column chromatography (SiO_2, 66-50% hexanes/EtOAc) to afford the *title compound* as a yellow oil (0.84 g, 86%). δ_H ($CDCl_3$) 7.23 (1H, s), 5.64 (1H, s), 3.92 (2H, q, *J* 7.0 Hz), 2.32 (2H, s), 1.39 (3H, t, *J* 7.0 Hz), 1.27 (6H, s). LCMS (ES+) 193.0 $(M+H)^+$.

INTERMEDIATE 38

4,4-Dimethyl-2,4,5,7-tetrahydro-6*H*-indazol-6-one

To a solution of *Intermediate 37* (0.84 g, 4.38 mmol) in ethanol (10 mL) was added 6N HCl (20 mL) and the reaction mixture stirred for 16 h. The reaction mixture was concentrated to dryness *in vacuo* and the residue was partitioned between ethyl acetate and aqueous sodium bicarbonate. The organic layer was separated, passed through a phase separator and concentrated *in vacuo* to afford the *title compound* as an oil which crystallised on standing (0.708 g, 99%). δ_H ($CDCl_3$) 7.46 (1H, s), 3.61 (2H, s), 2.54 (2H, s), 1.32 (7H, s). LCMS (ES+) 165.0 $(M+H)^+$.

INTERMEDIATE 39

7-Bromo-4,4-dimethyl-2,4,5,7-tetrahydro-6*H*-indazol-6-one

To a stirred solution of *Intermediate 38* (0.53 g, 3.23 mmol) in glacial acetic acid (10 mL) was added *N*-bromosuccinimide (0.575 g, 3.23 mmol). The reaction mixture was stirred for 10 minutes and then water (50 mL) was added. The reaction mixture was extracted with ethyl acetate, the organic fraction washed with water, brine, passed through a phase separator and concentrated *in vacuo* to afford the *title compound* as a brown oil (0.76 g, 97%) which was used without purification. δ_H ($CDCl_3$) 7.53 (1H, s), 5.43 (1H, s), 3.22 (2H, d, *J* 13.7 Hz), 2.46 (1H, d, *J* 13.4 Hz), 1.23 (6H, d).

INTERMEDIATE 40

Pentafluorophenyl 3-{[(3*S*)-4-(5,5-dimethyl-5,6-dihydro[1,3]thiazolo[5,4-*c*]-[1,2,4]triazolo[4,3-*a*]pyridin-8-yl)morpholin-3-yl]methyl}-1-methyl-1*H*-indole-5-carboxylate

Example 23 (0.18 g, 0.4 mmol), pentafluorophenol (0.075 g, 0.44 mmol) and DIPEA (0.08 mL, 0.48 mmol) were dissolved in DMF (2 mL) and cooled to 0°C. EDC (0.08 g, 0.44 mmol) was added and the reaction mixture allowed to warm to r.t. and stirred for 16 h. Water (15 mL) was added, resulting in the precipitation of the crude product which was isolated by filtration and dried *in vacuo*. Purification by column chromatography (SiO_2, EtOAc/MeOH, 0-10%) gave 0.15 g (58%) of the *title compound*. LCMS (ES+) 645.1 $(M+H)^+$.

INTERMEDIATE 41

Methyl 3-iodo-4-(methylamino)benzoate

Methyl 4-amino-3-iodobenzoate (5 g, 18 mmol) was dissolved in formic acid (35 mL) and the reaction mixture heated at reflux for 90 minutes. Volatiles and formic acid were removed by evaporation *in vacuo*. The residue was taken up in DCM (200 mL) and washed with sat. $NaHCO_3$ solution (40 mL). The organic layer was isolated and washed with water (2 x 40 mL), dried ($MgSO_4$) and the solvent removed by evaporation *in vacuo*. The residue was dissolved in THF (200 mL), $BH_3.Me_2S$ (5 mL, 53 mmol) added and the reaction mixture heated at reflux for 90 minutes. Upon cooling the reaction mixture was quenched by the dropwise addition of methanol (20 mL). The solvents were removed by evaporation *in vacuo* and the residue purified by column chromatography (SiO_2, EtOAc/ isohexane, 1:1) to give the *title compound* (5 g, 95%) as a white solid. δ_H ($CDCl_3$) 8.36 (1H, s), 7.93 (1H, d, *J* 8.6 Hz), 6.15 (1H, d, *J* 8.6 Hz), 4.73 (1H, br s), 3.87 (3H, s), 2.96 (3H, d, *J* 5 Hz).

INTERMEDIATE 42

3-Iodo-*N*,*N*-dimethyl-4-(methylamino)benzamide

Me_2NH (1.3 g, 29 mmol) was dissolved in THF (40 mL), the solution cooled to 0°C and Me_3Al (10.2 mL of a 2M solution in toluene, 20.4 mmol) added dropwise. The reaction mixture was stirred at 0°C for 5 minutes. *Intermediate 41* (4 g, 13.7 mmol) was added and the reaction mixture heated at reflux for 2 h. Upon cooling, the reaction mixture was diluted with EtOAc (200 mL) and washed with water (2 x 25 mL), dried ($MgSO_4$) and the solvent removed by evaporation *in vacuo*. The residue was purified by column chromatography (SiO_2, EtOAc/isohexane, 1:1) to give the *title compound* (4.1 g, 98%) as a clear oil. LCMS (ES+) 304.9 $(M+H)^+$.

INTERMEDIATE 43

tert-Butyl (3*S*)-3-{[5-(dimethylcarbamoyl)-1-methyl-2-(trimethylsilyl)-1*H*-indol-3-yl]methyl}morpholine-4-carboxylate

Intermediate 5 (2.2 g, 7.7 mmol), *Intermediate 42* (2.1 g, 7 mmol), LiCl (0.3 g, 7 mmol) and KOAc (1.4 g, 14 mmol) were dissolved in DMF (25 mL) and the solution was

degassed and flushed with nitrogen three times. To this solution was added catalytic $Pd(OAc)_2$ (0.01 g) and the reaction mixture was heated to 105°C for 210 minutes. Upon cooling, the volatiles were removed by evaporation *in vacuo*. The residue was dissolved in EtOAc (50 mL), washed with water (50 mL), dried ($MgSO_4$) and the solvent removed by evaporation *in vacuo*. The residue was purified by column chromatography (SiO_2, EtOAc/isohexane) to give the *title compound* (2.2 g, 66%) as a yellow solid. LCMS (ES+) 474.1 $(M+H)^+$.

INTERMEDIATE 44

N,N,1-Trimethyl-3-[(3*S*)-morpholin-3-ylmethyl]-1*H*-indole-5-carboxamide

Intermediate 43 (2.6 g, 5.5 mmol) was stirred in a solution of 4M HCl in 1,4-dioxane (20 mL) for 60 minutes at r.t. Volatiles and solvent were removed by evaporation *in vacuo*. The residue was dissolved in EtOAc (20 mL) and washed with sat. Na_2CO_3 solution (10 mL). The aqueous layer was saturated with sodium chloride and the organic layer isolated. The aqueous layer was further extracted with EtOAc (3 x 20 mL), the combined organic extracts dried (K_2CO_3) and the solvent removed by evaporation *in vacuo* to afford the *title compound* in quantative yield as a yellow oil. LCMS (ES+) 302.2 $(M+H)^+$.

INTERMEDIATE 45

3-{[(3*S*)-4-Carbamothioylmorpholin-3-yl]methyl}-*N,N*,1-trimethyl-1*H*-indole-5-carboxamide

Intermediate 44 (0.9 g, 3 mmol) and 1,1'-thiocarbonyldiimidazole (0.62 g, 3.6 mmol) were dissolved in THF (20 mL) and stirred for 90 minutes at r.t. Ammonium hydroxide solution (20 mL, 28-30% as NH_3) was added and the reaction mixture stirred for 18 h at r.t. in a stoppered flask. The solvent was removed by evaporation *in vacuo*, and the residue purified by column chromatography (SiO_2, DCM/MeOH, 0-5%) to give the *title compound* (0.7 g, 65%) as a yellow solid. LCMS (ES+) 361.0 $(M+H)^+$.

INTERMEDIATE 46

(3,3-Dimethyl-5-oxocyclohexylidene)malononitrile

To a stirred solution of 5,5-dimethylcyclohexane-1,3-dione (98.0 g, 699.1 mmol) and malononitrile (46.2 g, 699.1 mmol) in EtOH (400 mL) at r.t. was added piperidine (10 mL, 99.9 mmol) dropwise over 15 minutes. The reaction mixture was heated to reflux for 3 days, cooled to r.t. and then concentrated *in vacuo*. The residue was dissolved in EtOAc (500 mL), and the solution was dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, 15% MeOH/ DCM) gave the *title compound* (108.2 g, 82%) as a yellow solid. δ_H (DMSO-d_6) 8.31 (2H, br. s), 2.51 (2H, t, *J* 1.8 Hz), 2.30 (2H, s), 1.04 (6H, s).

INTERMEDIATE 47

2-Amino-5,5-dimethyl-7-oxo-4,5,6,7-tetrahydro-1-benzothiophene-3-carbonitrile

To a stirred solution of *Intermediate 46* (50.8 g, 269.9 mmol) and sulphur (10.3 g, 323.9 mmol) in EtOH (600 mL) at r.t. was added morpholine (47.0 mL, 539.8 mmol) dropwise. The reaction mixture was heated to 80°C for 24 h, and then cooled. The precipitate formed was filtered and washed with cold Et_2O to give the *title compound* (41.2 g, 53%) as a brown solid that was used without further purification. δ_H (DMSO-d_6) 8.31 (2H, br. s), 2.51 (2H, t, *J* 1.8 Hz), 2.30 (2H, s), 1.04 (6H, s). LCMS (ES+) 221.0 $(M+H)^+$.

INTERMEDIATE 48

2-Bromo-5,5-dimethyl-7-oxo-4,5,6,7-tetrahydro-1-benzothiophene-3-carbonitrile

To a stirred solution of $CuBr_2$ (4.2 g, 19.1 mmol) in MeCN (100 mL) at 0°C was added *tert*-butyl nitrite (2 mL, 15.0 mmol) dropwise. The reaction mixture was stirred at this temperature for 10 minutes, and then *Intermediate 47* (3.0 g, 13.6 mmol) was added portionwise. The reaction mixture was allowed to warm to r.t., stirred for 4 h, and then partitioned between 2M aqueous HCl (200 mL) and EtOAc. The aqueous fraction was extracted with EtOAc (2 x 200 mL). The combined organic fractions were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, 25% DCM/hexanes) gave the *title compound* (1.5 g, 40%) as an off-white solid. δ_H (DMSO-d_6) 2.84 (2H, s), 2.51 (2H, s), 1.07 (6H, s).

INTERMEDIATE 49

5,5-Dimethyl-2-(morpholin-4-yl)-7-oxo-4,5,6,7-tetrahydro-1-benzothiophene-3-carbonitrile

To a stirred solution of *Intermediate 48* (18.3 g, 64.4 mmol) in DMSO (150 mL) at r.t. was added morpholine (14.7 mL, 168.0 mmol). The reaction mixture was heated to 100°C for 30 minutes, then cooled to r.t., diluted with water (450 mL) and stirred rigorously. The precipitate formed was filtered, washed with water and dried to give the *title compound* (14.4 g, 77%) as a pale green solid. δ_H (DMSO-d_6) 3.83-3.72 (4H, m), 3.69-3.58 (4H, m), 2.64 (2H, s), 2.35 (2H, s), 1.05 (6H, s). LCMS (ES+) 291.0 $(M+H)^+$.

INTERMEDIATE 50

5,5-Dimethyl-2-(morpholin-4-yl)-5,6-dihydro-1-benzothiophen-7(4*H*)-one

To a stirred solution of *Intermediate 49* (10.0 g, 34.5 mmol) in glacial AcOH (100 mL) at 120°C was added conc. H_2SO_4 (40 mL). The reaction mixture was stirred at this temperature for 24 h, then cooled to r.t. and poured into a well-stirred mixture of EtOAc (950 mL) and water (950 mL) at 0°C. The resulting emulsion was filtered through Celite®. The organic fraction was separated, washed with brine (3 x 100 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, 1:1 EtOAc/hexanes) gave the *title compound* (5.3 g, 58%) as a white powder. δ_H (DMSO-d_6) 6.15 (1H, s), 3.84-3.70 (4H, m), 3.30-3.20 (4H, m), 2.58 (2H, s), 2.26 (2H, s), 1.01 (6H, s). LCMS (ES+) 266.0 $(M+H)^+$.

INTERMEDIATE 51

3-Iodo-5,5-dimethyl-2-(morpholin-4-yl)-5,6-dihydro-1-benzothiophen-7(4*H*)-one

To a stirred solution of *Intermediate 50* (0.20 g, 0.75 mmol) in THF (10 mL) at r.t. was added NIS (0.18 g, 0.82 mmol) portionwise. The reaction mixture was stirred for 30 minutes. EtOAc (100 mL) and sat. aqueous Na_2CO_3 solution (25 ml) were added and the layers separated. The organic fraction was washed with sat. aqueous Na_2CO_3 solution (2 x 25 mL). The combined organic fractions were dried ($MgSO_4$), filtered and concentrated

in vacuo. Purification by column chromatography (SiO_2, 1:1 EtOAc/hexanes) gave the *title compound* (0.26 g, 90%) as a white powder. δ_H (DMSO-d_6) 3.84-3.70 (4H, m), 3.22-3.18 (4H, m), 2.60 (2H, s), 2.41 (2H, s), 1.05 (6H, s).

INTERMEDIATE 52

5,5-Dimethyl-2-(morpholin-4-yl)-3-(phenylethynyl)-5,6-dihydro-1-benzothiophen-7(4*H*)-one

To a stirred solution of *Intermediate 51* (1.63 g, 4.17 mmol) and phenylacetylene (0.64 g, 6.26 mmol) in diisopropylamine (150 mL) at 60°C was added $Pd(PPh_3)_2Cl_2$ (0.20 g, 0.28 mmol) and CuI (0.05 g, 0.26 mmol). The reaction mixture was stirred at this temperature for 45 minutes, and then cooled to r.t. The precipitate formed was filtered and triturated with water to give the *title compound* (1.18 g, 78%) as a fluffy white solid that was used without further purification. δ_H (DMSO-d_6) 7.53-7.48 (2H, m), 7.46-7.38 (3H, m), 3.83-3.75 (4H, m), 3.68-3.60 (4H, m), 2.70 (2H, s), 2.36 (2H, s), 1.07 (6H, s).

EXAMPLE 1 (METHOD G)

7-[(3*S*)-3-(3-Bromobenzyl)morpholin-4-yl]-4,4-dimethyl-4,5-dihydro-2*H*-[1,3]thiazolo[4,5-g]indazole

A stirred solution of 2-[(3*S*)-3-(3-bromobenzyl)morpholin-4-yl]-5,5-dimethyl-5,6-dihydro-1,3-benzothiazol-7(4*H*)-one (WO 2006/114606) (0.50 g, 1.15 mmol) in Bredereck's reagent (5 mL, excess) was heated to reflux for 16 h, then cooled to r.t. and concentrated *in vacuo*. The residue was dissolved in MeOH (5 mL), and hydrazine hydrochloride (0.12 g, 1.72 mmol) was added. The reaction mixture was heated to reflux for 16 h, then cooled to r.t. and concentrated *in vacuo*. Purification by column chromatography (SiO_2, EtOAc) gave the *title compound* (0.20 g, 40%) as a white solid. δ_H (DMSO-d_6) 12.26 (1H, br. s), 7.51-7.46 (2H, m), 7.41-7.36 (1H, m), 7.32-7.21 (2H, m), 4.08-4.00 (1H, m), 4.00-3.91 (1H, m), 3.68-3.44 (5H, m), 3.12-3.02 (1H, m), 3.02-2.92 (1H, m), 2.60 (2H, s), 1.21 (6H, s). LCMS (ES+) 461.1 $(M+H)^+$.

EXAMPLE 2

7-[(3*S*)-3-(1-benzofuran-3-ylmethyl)morpholin-4-yl]-4,4-dimethyl-4,5-dihydro-2*H*-[1,3]thiazolo[4,5-g]indazole

The *title compound* was prepared from *Intermediate 9* according to *Method G* (using hydrazine monohydrate (5 equivalents) and EtOH) and was isolated as a white solid (21%) after purification by column chromatography (SiO_2, 0-5% MeOH/DCM, followed by SiO_2, 2% MeOH/DCM), then by preparative HPLC. δ_H ($CDCl_3$) 8.03-7.98 (1H, m), 7.58 (1H, s), 7.53-7.47 (1H, m), 7.37-7.30 (3H, s), 4.29-4.19 (1H, m), 4.08 (1H, dd, *J* 11.1 and 3.0 Hz), 3.88 (1H, d, *J* 11.6 Hz), 3.81-3.67 (2H, m), 3.65-3.55 (2H, m), 3.41 (1H, *J* 13.9 and 11.4 Hz), 3.07-2.97 (1H, m), 2.84 (2H, s), 1.36 (6H, s). Exchangeable proton was not observed. LCMS (ES+) 421.2 $(M+H)^+$.

EXAMPLE 3

4,4-Dimethyl-7-(morpholin-4-yl)-4,5-dihydro-2*H*-[1,3]thiazolo[4,5-g]indazole

A stirred solution of 5,5-dimethyl-2-(morpholin-4-yl)-5,6-dihydro-1,3-benzothiazol-7(4*H*)-one (WO 2006/114606) (0.63 g, 2.35 mmol) in Bredereck's reagent (5 ml, excess) was heated to reflux for 5 h, then cooled to r.t. and concentrated *in vacuo*. The residue was triturated with toluene, dissolved in MeOH (10 mL), and then hydrazine hydrochloride (0.16 g, 2.35 mmol) was added. The reaction mixture was stirred at r.t. for 24 h, and then concentrated *in vacuo*. Purification by column chromatography (SiO_2, 50% EtOAc/hexanes) gave the *title compound* (0.20 g, 30%) as a pale yellow solid. δ_H (DMSO-d_6) 12.38 (1H, br. s), 7.49 (1H, s), 3.83-3.77 (4H, m), 3.18-3.14 (4H, m), 2.61 (2H, s), 1.20 (6H, s). LCMS (ES+) 291.9 $(M+H)^+$.

EXAMPLE 4

4,4-Dimethyl-2-(methylsulfonyl)-7-(morpholin-4-yl)-4,5-dihydro-2*H*-[1,3]thiazolo[4,5-g]indazole

To a stirred solution of *Example 3* (0.103 g, 0.34 mmol) in DCM (15 mL) was added NEt_3 (0.05 mL, 0.36 mmol), followed by a solution of methanesulfonyl chloride (0.03 mL, 0.36 mmol) in DCM (1 mL) dropwise. The reaction mixture was stirred at r.t. for 24 h under a nitrogen atmosphere. Additional methanesulfonyl chloride (0.01 mL, 0.14 mmol) was added and the reaction mixture stirred for a further 24 h before being

concentrated *in vacuo*. Purification by column chromatography (SiO_2, 50% EtOAc/ hexanes), followed by trituration with a mixture of EtOAc and hexanes (1:1 ratio) then cold hexanes, gave the *title compound* (0.01 g, 7%) as an off-white solid. δ_H (DMSO-d_6) 8.03 (1H, s), 3.75-3.68 (4H, m), 3.55-3.42 (4H, m), 3.45 (3H, s), 2.70 (2H, s), 1.27 (6H, s). LCMS (ES+) 370.0 $(M+H)^+$.

EXAMPLE 5

5,5-Dimethyl-2-(morpholin-4-yl)-4,5-dihydroimidazo[1,2-*a*][1,3]thiazolo[5,4-*c*]pyridine

A stirred solution of *Intermediate 4* (0.24 g, 0.56 mmol) in aminoacetaldehyde dimethyl acetal (2 mL) was heated to reflux for 15 minutes, then cooled to r.t. and concentrated *in vacuo*. The residue was dissolved in toluene (20 mL), and *p*-toluene-sulfonic acid (*ca.* 1 g) was added. The reaction mixture was heated to reflux for 2 h, then cooled to r.t. and concentrated *in vacuo*. Purification by column chromatography (SiO_2, 5-10% MeOH/EtOAc), followed by trituration with EtOAc, gave the *title compound* (0.06 g, 37%) as an off-white solid. δ_H (DMSO-d_6) 7.28 (1H, d, *J* 0.7 Hz), 6.86 (1H, d, *J* 0.6 Hz), 3.73-3.71 (4H, m), 3.46-2.43 (4H, m), 2.93 (2H, s), 1.43 (6H, s). LCMS (ES+) 291.1 $(M+H)^+$.

EXAMPLE 6

5,5-Dimethyl-8-(morpholin-4-yl)-5,6-dihydro[1,3]thiazolo[5,4-*c*][1,2,4]triazolo[4,3-*a*]pyridine

To a stirred solution of *Intermediate 4* (0.08 g, 0.19 mmol) in MeCN (30 mL) were added formic hydrazide (0.11 g, 1.86 mmol) and AcOH (0.1 mL, 1.86 mmol). The reaction mixture was heated to reflux for 4 h. Additional formic hydrazide (0.11 mg, 1.86 mmol) and AcOH (0.1 mL, 1.86 mmol) were added, and the reaction mixture stirred under reflux for 16 h before being concentrated *in vacuo*. Purification by preparative HPLC gave the *title compound* (0.014 g, 26%) as an off-white solid. δ_H (DMSO-d_6) 8.64 (1H, s), 3.75-3.3.72 (4H, m), 3.51-3.49 (4H, m), 2.99 (2H, s), 1.24 (6H, s). LCMS (ES+) 292.1 $(M+H)^+$.

EXAMPLE 7

3,5,5-Trimethyl-8-(morpholin-4-yl)-5,6-dihydro[1,3]thiazolo[5,4-*c*][1,2,4]triazolo[4,3-*a*]pyridine

To a stirred solution of *Intermediate 4* (0.24 g, 0.57 mmol) in AcOH (10 mL) was added acethydrazide (0.42 g, 5.74 mmol). The reaction mixture was heated to reflux for 16 h, then cooled to r.t. and concentrated *in vacuo*. Purification by preparative HPLC gave the *title compound* (0.08 g, 46%) as an off-white solid. δ_H (DMSO-d_6) 3.74-3.71 (4H, m), 3.49-3.47 (4H, m), 3.00 (2H, s), 2.50 (3H, s), 1.54 (6H, s). LCMS (ES+) 306.1 $(M+H)^+$.

EXAMPLE 8

Methyl 3-{[(3*S*)-4-(5,5-dimethyl-4,5-dihydroimidazo[1,2-*a*][1,3]thiazolo[5,4-*c*]pyridin-2-yl)morpholin-3-yl]methyl}-1*H*-indole-5-carboxylate

A solution of *Intermediate 15* (0.37 g, 0.76 mmol) in aminoacetaldehyde dimethyl acetal (3 mL) was stirred at 60°C for 2 h, then cooled to r.t. and concentrated *in vacuo*. The residue was dissolved in MeOH (10 mL), and *p*-toluenesulfonic acid (*ca.* 1 g) and toluene (20 mL) were added. The reaction mixture was heated to reflux for 4 h, then cooled to r.t. and concentrated *in vacuo*. EtOAc (20 mL) and sat. aqueous Na_2CO_3 solution (20 mL) were added, and the layers separated. The organic fraction was dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, 0-5% MeOH/EtOAc) gave the *title compound* (0.23 g, 64%) as a yellow oil. δ_H ($CDCl_3$) 8.76 (1H, s), 8.53 (1H, br. s), 7.94 (1H, dd, *J* 8.6 and 1.3 Hz), 7.38 (1H, d, *J* 8.6 Hz), 7.18 (1H, d, *J* 1.8 Hz), 7.05 (1H, d, *J* 1.0 Hz), 7.01 (1H, d, *J* 1.0 Hz), 4.24 (1H, *J* 7.6 and 2.8 Hz), 4.13-4.07 (1H, m), 3.99 (3H, s), 3.89 (1H, d, *J* 11.6 Hz), 3.78-3.55 (4H, m), 3.45 (1H, dd, *J* 13.9 and 10.9 Hz), 3.16 (1H, dd, *J* 10.4 and 3.8 Hz), 3.10 (2H, d, *J* 7.6 Hz), 1.56 (6H, s). LCMS (ES+) 478.2 $(M+H)^+$.

EXAMPLE 9

3-{[(3*S*)-4-(5,5-Dimethyl-4,5-dihydroimidazo[1,2-*a*][1,3]thiazolo[5,4-*c*]pyridin-2-yl)morpholin-3-yl]methyl}-*N*,*N*-dimethyl-1*H*-indole-5-carboxamide

To a stirred solution of dimethylamine (1 mL, 15.60 mmol) in THF (2 mL) at 0°C was added trimethylaluminium (3.9 mL, 2M in toluene, 7.80 mmol) dropwise, followed by *Example 8* (0.18 g, 0.39 mmol). The reaction mixture was stirred at this temperature for 15 minutes, and then quenched with the addition of water (10 mL), filtered through Celite® and washed with EtOAc (2 x 10 mL). The organic fraction of the filtrate was separated, dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by preparative HPLC gave the *title compound* (0.07 g, 38%) as a white solid. δ_H (DMSO-d_6) 11.10 (1H, s), 8.05 (1H, s), 7.37 (1H, d, *J* 8.3 Hz), 7.29 (2H, s), 7.16 (1H, d, *J* 8.6 Hz), 6.87 (1H, s), 4.21-4.13 (1H, s), 4.04-3.96 (1H, m), 3.75 (1H, d, *J* 11.6 Hz), 3.65-3.45 (4H, m), 3.04 (6H, s), 2.97 (2H, d, *J* 4.5 Hz), 2.89-2.69 (2H, m), 1.47 (3H, s), 1.44 (3H, s). LCMS (ES+) 491.3 $(M+H)^+$.

EXAMPLE 10 (METHOD I)

3-{[(3*S*)-4-(5,5-Dimethyl-4,5-dihydroimidazo[1,2-*a*][1,3]thiazolo[5,4-*c*]pyridin-2-yl)morpholin-3-yl]methyl}-1*H*-indole-5-carbonitrile

A solution of *Intermediate 20* (0.25 g, 0.56 mmol) in aminoacetaldehyde dimethyl acetal (3 mL) was stirred at 100°C for 30 minutes, then cooled to r.t. and concentrated *in vacuo*. The residue was dissolved in warm IPA (25 mL), and a sufficient amount of *p*-toluenesulfonic acid to render the mixture acidic was added. The reaction mixture was heated to reflux for 1 h, then cooled to r.t. and concentrated *in vacuo*. The residue was dissolved in EtOAc (20 mL), and sat. aqueous Na_2CO_3 solution (20 mL) was added. The organic fraction was separated, dried (K_2CO_3), filtered and concentrated *in vacuo*. Trituration with a small volume of MeOH gave the *title compound* (0.12 g, 49%) as an off-white solid. δ_H (DMSO-d_6) 11.48 (1H, s), 8.53 (1H, s), 7.54-7.47 (1H, m), 7.47-7.40 (2H, m), 7.28 (1H, s), 6.86 (1H, s), 4.27-4.19 (1H, m), 4.05-3.96 (1H, m), 3.74 (1H, d, *J* 11.6 Hz), 3.65-3.46 (4H, m), 3.36-3.27 (1H, m), 3.02 (2H, s), 2.97 (1H, dd, *J* 13.6 and 3.5 Hz), 1.47 (3H, s), 1.45 (3H, s). LCMS (ES+) 445.1 $(M+H)^+$.

EXAMPLE 11

3-{[(3*S*)-4-(5,5-Dimethyl-5,6-dihydro-4*H*-imidazo[1,2-*a*][1,3]thiazolo[5,4-*c*]azepin-2-yl)morpholin-3-yl]methyl}-1*H*-indole-5-carbonitrile

The *title compound* was prepared from *Intermediate 23* according to *Method E*, then *Method H*, followed by *Method I*, and was isolated as a yellow solid (41%) after trituration with MeOH. δ_H (DMSO-d_6) 11.47 (1H, s), 8.59 (1H, s), 7.53-7.49 (1H, m), 7.46-7.41 (2H, m), 7.06 (1H, s), 6.80 (1H, s), 4.28-4.19 (1H, m), 4.03-3.94 (3H, m), 3.69 (1H, d, *J* 11.6 Hz), 3.63-3.43 (3H, m), 3.40-3.34 (1H, m), 3.30-3.22 (1H, m), 2.99 (2H, s), 2.92 (1H, dd, *J* 13.4 and 2.3 Hz), 1.02 (6H, s). LCMS (ES+) 459.2 $(M+H)^+$.

EXAMPLE 12 (METHOD J)

3-{[(3*S*)-4-(5,5-Dimethyl-4,5-dihydroimidazo[1,2-*a*][1,3]thiazolo[5,4-*c*]pyridin-2-yl)morpholin-3-yl]methyl}-1-methyl-1*H*-indole-5-carbonitrile

To a stirred solution of *Example 10* (0.20 g, 0.45 mmol) in DMF (5 mL) at 0°C was added methyl iodide (0.5 mL, excess), followed by NaH (50 mg, 60% dispersion in oil, excess). The reaction mixture was stirred at this temperature for 5 minutes, and then partitioned between EtOAc (5 mL) and water (5mL). The organic fraction was dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, 0-5% MeOH/EtOAc) gave the *title compound* (0.03 g, 16%) as a yellow solid. δ_H (DMSO-d_6) 8.54 (1H, s), 7.60 (1H, d, *J* 8.6 Hz), 7.51 (1H, d, *J* 8.6 Hz), 7.45 (1H, s), 7.29 (1H, s), 6.87 (1H, s), 4.24-4.16 (1H, m), 4.05-3.97 (1H, m), 3.80 (3H, s), 3.77-3.70 (1H, m), 3.66-3.45 (5H, m), 3.04 (2H, s), 2.94 (1H, dd, *J* 13.6 and 2.5 Hz), 1.46 (6H, s). LCMS (ES+) 459.2 $(M+H)^+$.

EXAMPLE 13

3-{[(3*S*)-4-(5,5-Dimethyl-5,6-dihydro-4*H*-imidazo[1,2-*a*][1,3]thiazolo[5,4-*c*]azepin-2-yl)morpholin-3-yl]methyl}-1-methyl-1*H*-indole-5-carbonitrile

The *title compound* was prepared from *Example 11* according to *Method J* and was isolated as an off-white solid (84%) after filtration of the solid formed from concentration of the organic fraction to a reduced volume, followed by trituration with EtOAc. δ_H (DMSO-d_6) 8.59 (1H, s), 7.60 (1H, d, *J* 8.6 Hz), 7.51 (1H, d, *J* 8.6 Hz), 7.43 (1H, s), 7.07 (1H, s), 6.81 (1H, s), 4.26-4.16 (1H, m), 4.03-3.94 (3H, m), 3.80 (3H, s), 3.69 (1H, d, *J* 11.6 Hz), 3.64-3.41 (3H, m), 3.39-3.33 (1H, m), 3.31-3.23 (1H, m), 3.00 (2H, s), 2.94-2.85 (1H, m), 1.03 (3H, s), 1.02 (3H, s). LCMS (ES+) 473.3 $(M+H)^+$.

EXAMPLE 14

7-[(3*S*)-3-(1*H*-Indol-3-ylmethyl)morpholin-4-yl]-4,4-dimethyl-4,5-dihydro-[1,3]thiazolo[4,5-*g*][1,2]benzisoxazole

The *title compound* was prepared from *Intermediate 28* and *Intermediate 29* according to *Method A* and was isolated as a yellow oil (65%) after purification by column chromatography (SiO_2, 25-50% EtOAc/hexanes). δ_H ($CDCl_3$) 8.12 (1H, s), 8.10 (1H, br. s), 7.97 (1H, d, *J* 7.6 Hz), 7.40 (1H, d, *J* 7.8 Hz), 7.28-7.19 (2H, m), 7.17-7.14 (1H, m), 4.20-4.11 (2H, m), 3.92 (1H, d, *J* 11.9 Hz), 3.81-3.60 (3H, m), 3.60-3.53 (1H, m), 3.52-3.42 (1H, m), 3.10 (1H, dd, *J* 13.9 and 3.3 Hz), 2.89 (2H, s), 1.35 (6H, d, *J* 2.5 Hz). LCMS (ES+) 421.7 $(M+H)^+$.

EXAMPLE 15

2-[(3*S*)-3-(1*H*-Indol-3-ylmethyl)morpholin-4-yl]-5,5-dimethyl-4,5-dihydro-[1,3]thiazolo[4,5-*h*]quinazoline

To a stirred solution of *Intermediate 31* (0.112 g, 0.64 mmol) in AcOH (5 mL) was added NIS (0.150 g, 0.67 mmol). The reaction mixture was stirred at r.t. for 16 h. *Intermediate 29* (0.176 g, 0.64 mmol) was added, followed by NaOAc (0.16 g, 2.00 mmol). The reaction mixture was heated to 100°C for 30 minutes, then cooled to r.t. and partitioned between EtOAc (20 mL) and water (20 mL). The organic fraction was washed with water (20 mL), then brine (20 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, 33-50% EtOAc/hexanes) gave the *title compound* (0.048 g, 17%) as a yellow solid. δ_H ($CDCl_3$) 8.88 (1H, s), 8.46 (1H, s), 8.11 (1H, s), 7.97 (1H, d, *J* 7.3 Hz), 7.43-7.39 (1H, m), 7.28-7.19 (2H, m), 7.17 (1H, d, *J* 2.0 Hz), 4.26-4.18 (1H, m), 4.16-4.05 (1H, m), 3.92 (1H, d, *J* 11.9 Hz), 3.89-3.80 (1H, m), 3.78-3.62 (2H, m), 3.61-3.44 (2H, m), 3.12 (1H, dd, *J* 13.9 and 3.8 Hz), 2.91 (2H, s), 1.56 (3H, s), 1.32 (3H, s). LCMS (ES+) 432.6 $(M+H)^+$.

EXAMPLE 16

9-[(3*S*)-3-(1*H*-Indol-3-ylmethyl)morpholin-4-yl]-6,6-dimethyl-6,7-dihydro-5*H*-tetrazolo[1,5-*a*][1,3]thiazolo[5,4-*c*]azepine

A stirred solution of 2-[(3*S*)-3-(1*H*-indol-3-ylmethyl)morpholin-4-yl]-7,7-dimethyl-5,6,7,8-tetrahydro-4*H*-[1,3]thiazolo[5,4-*c*]azepin-4-one (WO 2006/114606) (0.41 g, 0.94 mmol) in phosphorus oxychloride (5 mL) was heated to 95°C for 1.5 h, then cooled to r.t. and concentrated *in vacuo*. The residue was dissolved in MeOH (8 mL), and NaN_3 (0.40 g, 6.15 mmol) was added. The reaction mixture was stirred at r.t. for 16 h, then filtered and the filtrate concentrated *in vacuo*. The residue was dissolved in EtOAc, and the solution washed with water (2 x 20 mL), then brine (20 ml), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, 0-50% EtOAc/hexanes), followed by stirring in water at 80°C for 1 h, gave the *title compound* (0.09 g, 22%) as a white solid. δ_H ($CDCl_3$) 8.08 (1H, s), 7.96 (1H, d, *J* 7.6 Hz), 7.40 (1H, d, *J* 8.1 Hz), 7.28-7.18 (2H, m), 7.16 (1H, d, *J* 1.8 Hz), 4.43 (2H, s), 4.24-4.16 (1H, m), 4.13-4.06 (1H, m), 3.92 (1H, d, *J* 11.9 Hz), 3.78-3.63 (3H, m), 3.56 (1H, dd, *J* 11.6 and 1.8 Hz), 3.51-3.42 (1H, m), 3.15-3.10 (1H, m), 3.11-3.03 (2H, m), 1.17 (6H, s). LCMS (ES+) 436.7 $(M+H)^+$.

EXAMPLE 17

5,5-Dimethyl-2-[6-(1-methyl-1*H*-pyrazol-4-yl)-2,3-dihydro-4*H*-1,4-benzoxazin-4-yl]-4,5-dihydroimidazo[1,2-*a*][1,3]thiazolo[5,4-*c*]pyridine

The *title compound* was prepared from *Intermediate 36* according to *Method H*, followed by work-up (EtOAc/water), then according to *Method I*, and was isolated as a pale orange solid (16%) after purification by preparative HPLC. δ_H ($CDCl_3$) 8.01 (1H, d, *J* 1.7 Hz), 7.70 (1H, s), 7.57 (1H, s), 7.14 (1H, dd, *J* 8.5 and 1.9 Hz), 7.02 (2H, d, *J* 7.2 Hz), 6.95 (1H, d, *J* 8.3 Hz), 4.44-4.26 (2H, m), 4.29-4.09 (2H, m), 3.94 (3H, s), 3.02 (2H, s), 1.54 (6H, s). LCMS (ES+) 419.20 $(M+H)^+$.

EXAMPLE 18

5,5-Dimethyl-2-(morpholin-4-yl)-5,6-dihydro-4*H*-imidazo[1,2-*a*][1,3]thiazolo[5,4-*c*]azepine

The *title compound* was prepared from 7,7-dimethyl-2-(morpholin-4-yl)-5,6,7,8-tetrahydro-4*H*-[1,3]thiazolo[5,4-*c*]azepin-4-one (WO 2006/114606) according to *Method H*, followed by *Method I*, and was isolated as a white solid (29%) after purification by column chromatography (SiO_2, 0-10% MeOH/EtOAc), followed by preparative HPLC. δ_H ($CDCl_3$) 6.97 (1H, d, *J* 1.1 Hz), 6.76 (1H, d, *J* 1.1 Hz), 3.88 (2H, s), 3.86-3.80 (4H, m), 3.53-3.46 (4H, m), 2.92 (2H, s), 1.09 (6H, s). LCMS (ES+) 305.6 $(M+H)^+$.

EXAMPLE 19

7-[(3*S*)-3-(1*H*-Indol-3-ylmethyl)morpholin-4-yl]-4,4-dimethyl-4,5-dihydro-2*H*-[1,3]thiazolo[4,5-*g*]indazole

To a solution of *Intermediate 39* (0.729 g, 3.0 mmol) in tetrahydrofuran (20 mL) was added *Intermediate 29* (0.825 g, 3.0 mmol) and DIPEA (2.65 mL, 15 mmol). The reaction mixture was heated at reflux for 2 h, cooled and partitioned between ethyl acetate and water. The organic layer was washed with brine, passed through a phase separator and concentrated *in vacuo* to afford an oil which was purified by column chromatography (SiO_2, 66-50% EtOAc/hexanes) to afford the *title compound* as an off-white solid (0.277 g, 22%). δ_H ($CDCl_3$) 8.14 (1H, s), 8.00 (1H, d, *J* 7.3 Hz), 7.37 (1H, d, *J* 7.3 Hz), 7.33 (1H, s), 7.22 (2H, m), 7.15 (1H, d, *J* 2.0 Hz), 4.08 (2H, m), 3.90 (1H, d, *J* 11.6 Hz), 3.82-3.44 (5H, m), 3.10 (1H, dd, *J* 13.6, 3.3 Hz), 2.84 (2H, s), 1.36 (6H, s). LCMS (ES+) 420.6 $(M+H)^+$.

EXAMPLE 20

9-[(3*S*)-3-(1*H*-Indol-3-ylmethyl)morpholin-4-yl]-6,6-dimethyl-2,5,6,7-tetrahydro-3*H*-[1,3]thiazolo[5,4-*c*][1,2,4]triazolo[4,3-*a*]azepin-3-one

A solution of 2-[(3*S*)-3-(1*H*-indol-3-ylmethyl)morpholin-4-yl]-7,7-dimethyl-5,6,7,8-tetrahydro-4*H*-[1,3]thiazolo[5,4-*c*]azepin-4-one (WO 2006/114606) (0.50 g, 1.1 mmol) in $POCl_3$ (5 mL) was heated at 95°C for 1.5 h. The reaction mixture was concentrated *in vacuo*, and the residue was redissolved in MeCN (10 mL), treated with methyl hydrazinocarboxylate (0.55 g, 6.1 mmol), and stirred at room temperature for 1 h and then at 90°C for a further 1 h. The reaction mixture was partitioned between EtOAc (20 mL) and water (20 mL), then the aqueous layer was separated and extracted into

EtOAc (2 x 10 mL). The organic fractions were combined, washed with water (10 mL), brine (10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* and washed with Et_2O to give a pale yellow solid. A portion of this solid (0.30 g) was dissolved in AcOH (2 mL) and heated by microwave radiation to 140°C for 10 min. The reaction mixture was partitioned between EtOAc (20 mL) and sat. $NaHCO_3$ solution (20 mL). The organics were separated, washed with water (10 mL), brine (10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to give a white foam, which was washed with Et_2O to give the *title compound* as a white solid (0.08 g, 18%). δ_H ($CDCl_3$) 9.42 (1H, br s), 8.13 (1H, br s), 7.95 (1H, d, *J* 7.6 Hz), 7.39 (1H, m), 7.22 (2H, m), 7.14 (1H, d, *J* 2.3 Hz), 4.13 (1H, m), 4.07 (1H, d, *J* 3.3 Hz), 3.90 (1H, d, *J* 11.9 Hz), 3.61-3.71 (5H, m), 3.54 (1H, m), 3.45 (1H, dd, *J* 13.9, 11.1 Hz), 3.09 (1H, dd, *J* 13.9, 3.8 Hz), 2.98 (2H, d, *J* 2.5 Hz), 1.15 (6H, s). LCMS (ES+) 451.7 $(M+H)^+$, RT 2.25 minutes.

EXAMPLE 21

2-[(3*S*)-3-(1*H*-Indol-3-ylmethyl)morpholin-4-yl]-5,5,8-trimethyl-5,6-dihydro-4*H*-imidazo[1,2-*a*][1,3]thiazolo[5,4-*c*]azepine

A solution of 2-[(3*S*)-3-(1*H*-indol-3-ylmethyl)morpholin-4-yl]-7,7-dimethyl-5,6,7,8-tetrahydro-4*H*-[1,3]thiazolo[5,4-*c*]azepin-4-one (WO 2006/114606) (0.40 g, 1.1 mmol) in $POCl_3$ (4 mL) was heated at 95°C for 1.5 h. The mixture was then concentrated *in vacuo* and redissolved in THF (5mL). To this was added propargylamine (1 mL, 16 mmol). The reaction mixture was stirred overnight at room temperature, then at 40°C for 6 h and overnight at 60°C. The reaction mixture was partitioned between EtOAc (20 mL) and water (20 mL), then the organics were separated and washed with water (10 mL), brine (10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to give a crude foam. Purification by column chromatography (SiO_2, EtOAc/hexanes) gave a beige foam. This was further purified by preparative HPLC to give the *title compound* as a white solid (0.21 g, 44%). δ_H ($CDCl_3$) 8.10 (1H, s), 7.99 (1H, m), 7.38 (1H, m), 7.20 (3H, m), 6.78 (1H, d, *J* 1.0 Hz), 4.08 (2H, m), 3.87 (1H, d, *J* 11.6 Hz), 3.75 (2H, s), 3.70 (2H, m), 3.57 (2H, m), 3.45 (1H, dd, *J* 13.6, 11.4 Hz), 3.10 (1H, m), 2.98 (2H, d, *J* 1.5 Hz), 2.22 (3H, d, *J* 0.8 Hz), 1.13 (6H, s). LCMS (ES+) 448.8 $(M+H)^+$, RT 2.75 minutes.

EXAMPLE 22

Methyl 3-{[(3*S*)-4-(5,5-dimethyl-5,6-dihydro[1,3]thiazolo[5,4-*c*][1,2,4]triazolo[4,3-*a*]pyridin-8-yl)morpholin-3-yl]methyl}-1-methyl-1*H*-indole-5-carboxylate

Methyl 3-{[(3*S*)-4-(6,6-dimethyl-4-oxo-4,5,6,7-tetrahydro[1,3]thiazolo[5,4-*c*]-pyridin-2-yl)morpholin-3-yl]methyl}-1-methyl-1*H*-indole-5-carboxylate (WO 2008/001076) (0.24 mg, 0.5 mmol) was heated at 90°C in phosphorus oxychloride (4 mL) for 90 minutes. The reaction mixture was cooled to r.t. and the volatiles and excess phosphorus oxychloride were removed by evaporation *in vacuo*, yielding methyl 3-{[(3*S*)-4-(4-chloro-6,6-dimethyl-6,7-dihydro[1,3]thiazolo[5,4-*c*]pyridin-2-yl)morpholin-3-yl]methyl}-1-methyl-1*H*-indole-5-carboxylate as a yellow solid. This was slurried in MeCN (5 mL) and formyl hydrazide (0.07 g, 1.1 mmol) was added. The resulting mixture was heated at reflux for 16 h. Upon cooling, the solvent was removed by evaporation *in vacuo*. The residue was taken up in EtOAc (20 mL), washed with water (5 mL) twice, dried ($MgSO_4$), filtered and the solvent removed by evaporation *in vacuo*. Purification by column chromatography (SiO_2, EtOAc/MeOH, 0-10%) gave the *title compound* as a white solid (0.10 g, 42%). δ_H ($CDCl_3$) 8.75 (1H, s), 8.19 (1H, s), 7.97-7.95 (1H, d, *J* 8.7 Hz), 7.40-7.20 (1H, m), 7.05 (1H, s), 4.35-4.20 (1H, br s), 4.20-4.09 (1H, m), 3.99 (3H, s), 3.98-3.55 (8H, m),3.50-3.40 (1H, m), 3.30-3.10 (3H, m), 1.64-1.63 (6H, d, *J* 5.7 Hz). LCMS (ES+) 493.1 $(M+H)^+$.

EXAMPLE 23

3-{[(3*S*)-4-(5,5-Dimethyl-5,6-dihydro[1,3]thiazolo[5,4-*c*][1,2,4]triazolo[4,3-*a*]pyridin-8-yl)morpholin-3-yl]methyl}-1-methyl-1*H*-indole-5-carboxylic acid

To a stirred solution of *Example 22* (0.20 g, 0.4 mmol) dissolved in ethanol (5 mL) and water (5 mL) was added sodium hydroxide (0.10 g, 2.5 mmol) and the reaction mixture heated at reflux for 2 h. Upon cooling, the solvents were removed by evaporation *in vacuo* and the residue dissolved in water. The resulting solution was neutralized with citric acid, resulting in the precipitation of the *title compound* which was isolated by filtration, washed with water and dried *in vacuo* (0.19 g, 98%). δ_H (DMSO-d_6) 8.64-8.63 (2H, m), 7.79-7.77 (1H, d, *J* 8.6 Hz), 7.46-7.43 (1H, d, *J* 8.6 Hz), 7.32 (1H, s), 4.27-4.25

(1H, br s), 4.03-4.01 (1H, d, *J* 7.5 Hz), 3.80-3.70 (4H, m), 3.65-3.45 (2H, m), 3.40-3.00 (6H, m), 2.97-2.94 (1H, m), 1.53 (6H, s). LCMS (ES+) 479.0 $(M+H)^+$.

EXAMPLE 24

3-{[(3*S*)-4-(5,5-Dimethyl-5,6-dihydro[1,3]thiazolo[5,4-*c*][1,2,4]triazolo[4,3-*a*]pyridin-8-yl)morpholin-3-yl]methyl}-*N*,*N*,1-trimethyl-1*H*-indole-5-carboxamide

To *Intermediate 40* (0.15 g, 0.23 mmol) in MeCN (4 mL) at 0°C was added excess dimethylamine. The flask was stoppered, allowed to warm to r.t. and stirred for 16 h. The solvent was removed by evaporation *in vacuo* and the residue purified by column chromatography (SiO_2, EtOAc/MeOH, 0-10%) to give the *title compound* (0.06 g, 52%) as a white solid. δ_H (DMSO-d_6) 8.65 (1H, s), 8.03 (1H, s), 7.42 (1H, m), 7.30 (1H, s), 7.21 (1H, m), 4.30-4.10 (1H, br s), 4.00 (1H, br s), 3.76 (1H, s), 3.70-3.50 (4H, m), 3.31 (3H, s), 3.20-2.80 (10H, m), 1.52 (6H, d, *J* 10.3 Hz). LCMS (ES+) 506.1 $(M+H)^+$.

EXAMPLE 25

3-{[(3*S*)-4-(4,4-Dimethyl-4,5-dihydro-3a*H*-[1,3]thiazolo[4,5-g]indazol-7-yl)morpholin-3-yl]methyl}-*N*,*N*,1-trimethyl-1*H*-indole-5-carboxamide

Intermediate 45 (0.12 g, 0.3 mmol), *Intermediate 39* (0.146 g, 0.6 mmol) and DIPEA (0.06 mL, 0.34 mmol) in THF (10 mL) were heated to reflux for 18 h. Upon cooling the *title compound* (0.055 g, 36%) was isolated by filtration, washed with THF followed by EtOAc and dried *in vacuo*. δ_H (DMSO-d_6) 12.30 (1H, s), 8.09 (1H, s), 7.52 (1H, s), 7.43 (1H, d, *J* 8.5 Hz), 7.29 (1H, s), 7.21 (1H, d, *J* 8.4 Hz), 4.20-3.90 (2H, m), 3.77-3.70 (4H, m), 3.70-3.40 (3H, m), 3.40-3.20 (2H, m), 3.03 (6H, s), 2.89-2.86 (1H, m), 2.51 (2H, s), 1.24 (6H, s). LCMS (ES+) 505.3 $(M+H)^+$.

EXAMPLE 26

4,4-Dimethyl-7-(morpholin-4-yl)-4,5-dihydro-2*H*-thieno[3,2-g]indazole

A stirred solution of *Intermediate 50* (0.20 g, 0.75 mmol) in Bredereck's reagent (5 mL, excess) was heated to reflux for 16 h, then cooled to r.t. and concentrated *in vacuo*. The residue was dissolved in MeOH (5 mL) and hydrazine monohydrate (0.056 g,

1.12 mmol) was added. The reaction mixture was stirred at 40°C for 2.5 h, then cooled to r.t. and concentrated *in vacuo*. Purification by preparative HPLC gave the *title compound* (0.06 g, 27%) as a white solid. δ_H (DMSO-d_6) 12.25 (1H, br. s), 7.53 (1H, s), 6.16 (1H, s), 3.83-3.78 (4H, m), 3.17-3.14 (4H, m), 2.60 (2H, s), 1.27 (6H, s). LCMS (ES+) 290.1 $(M+H)^+$.

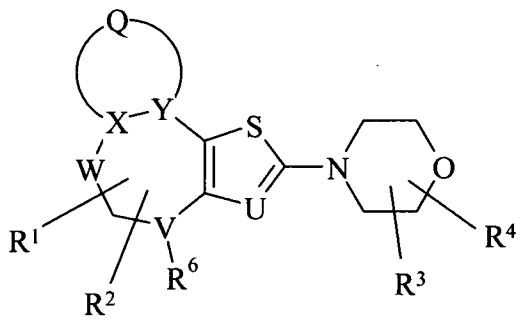
EXAMPLE 27

4,4-Dimethyl-7-(morpholin-4-yl)-6-(phenylethynyl)-4,5-dihydro-2*H*-thieno[3,2-g]indazole

A stirred solution of *Intermediate 52* (0.13 g, 0.35 mmol) in Bredereck's reagent (5 mL, excess) was heated at 90°C for 3 days, then at 100°C for 2 days. The reaction mixture was then cooled to r.t. and partitioned between EtOAc (10 mL) and water (10 mL). The organic fraction was washed with water (10 mL), then brine (10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residue was dissolved in EtOH (10 mL) and hydrazine monohydrate (0.1 mL, 1.75 mmol) was added. The reaction mixture was heated at 60°C for 16 h, then cooled to r.t. and concentrated *in vacuo*. Purification by column chromatography (SiO_2, 30-50% EtOAc/hexanes) gave the *title compound* (0.05 g, 4%) as a white solid. δ_H (DMSO-d_6) 12.38 (1H, br. s), 7.54 (1H, d, *J* 1.1 Hz), 7.51-7.48 (2H, m), 7.45-7.39 (3H, m), 3.81-3.79 (4H, m), 3.35-3.32 (4H, m), 2.66 (2H, s), 1.23 (6H, s). LCMS (ES+) 390.1 $(M+H)^+$.

Claims:

1. A compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof:



(I)

wherein

U represents N or C-R^5;

V represents a covalent bond or a methylene linkage;

W represents a covalent bond or a methylene linkage;

the moiety X-Y-Q represents an optionally substituted five-membered heteroaromatic ring selected from furyl, thienyl, pyrrolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl and tetrazolyl; or an optionally substituted six-membered heteroaromatic ring selected from pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl and triazinyl;

R^1 and R^2 independently represent hydrogen, hydroxy or amino; or C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, di(C_{1-6})alkylamino, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl(C_{1-6})alkyl, aryl, aryl(C_{1-6})alkyl, C_{3-7} heterocycloalkyl, C_{3-7} heterocycloalkyl(C_{1-6})alkyl, heteroaryl or heteroaryl(C_{1-6})alkyl, any of which groups may be optionally substituted by one or more substituents; or

R^1 and R^2, when both are attached to the same carbon atom, represent, when taken together with the carbon atom to which they are both attached, C_{3-7} cycloalkyl or C_{3-7} heterocycloalkyl, either of which groups may be optionally substituted by one or more substituents; or

R^1 and R^2, when attached to adjacent carbon atoms, represent, when taken together with the carbon atoms to which they are attached, C_{5-7} cycloalkyl, phenyl or heteroaryl,

any of which groups may be optionally benzo-fused and/or substituted by one or more substituents;

R^3 and R^4 independently represent hydrogen; or C_{1-6} alkyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl(C_{1-6})alkyl, aryl, aryl(C_{1-6})alkyl, aryl(C_{2-6})alkenyl, aryl(C_{2-6})-alkynyl, biaryl(C_{1-6})alkyl, C_{3-7} heterocycloalkyl, C_{3-7} heterocycloalkyl(C_{1-6})alkyl, C_{3-7} heterocycloalkylcarbonyl, heteroaryl, heteroaryl(C_{1-6})alkyl, heteroaryl-aryl(C_{1-6})alkyl or aryl-heteroaryl(C_{1-6})alkyl, any of which groups may be optionally substituted by one or more substituents; or

R^3 and R^4, when both are attached to the same carbon atom, represent, when taken together with the carbon atom to which they are both attached, C_{3-7} cycloalkyl or C_{3-7} heterocycloalkyl, either of which groups may be optionally substituted by one or more substituents; or

R^3 and R^4, when attached to adjacent carbon atoms, represent, when taken together with the carbon atoms to which they are attached, C_{5-7} cycloalkyl, phenyl or heteroaryl, any of which groups may be optionally benzo-fused and/or substituted by one or more substituents;

R^5 represents hydrogen, halogen, cyano, $-SR^a$, $-COR^e$, $-CO_2R^b$ or $-CONR^cR^d$; or R^5 represents C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkenylcarbonyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl(C_{1-6})alkyl, C_{3-7} cycloalkyl(C_{2-6})alkenyl, C_{3-7} cycloalkyl(C_{2-6})alkynyl, aryl, aryl(C_{1-6})alkyl, aryl(C_{2-6})alkenyl, aryl(C_{2-6})alkynyl, biaryl, C_{3-7} heterocycloalkyl, C_{3-7} heterocycloalkyl(C_{1-6})alkyl, C_{3-7} heterocycloalkyl(C_{2-6})alkenyl, C_{3-7} heterocycloalkyl-(C_{2-6})alkynyl, C_{3-7} heterocycloalkylcarbonyl(C_{2-6})alkynyl, C_{5-9} heterobicycloalkyl-(C_{2-6})alkynyl, C_{3-7} heterocycloalkyl-aryl, C_{3-7} heterocycloalkyl(C_{1-6})alkyl-aryl, C_{3-7} heterocycloalkyl-biaryl, heteroaryl, heteroaryl(C_{1-6})alkyl, heteroaryl(C_{1-6})alkylcarbonyl, heteroaryl(C_{2-6})alkenyl, heteroaryl(C_{2-6})alkynyl, heteroaroylcarbonyl, C_{3-7} heterocycloalkyl-heteroaryl, C_{3-7} heterocycloalkyl-heteroaryl(C_{2-6})alkynyl, heteroaryl-aryl, heteroaryl-aryl(C_{1-6})alkyl, aryl-heteroaryl, aryl-heteroaryl(C_{1-6})alkyl, C_{3-7} heterocycloalkyl-aryl-heteroaryl, C_{3-7} heterocycloalkyl(C_{1-6})alkyl-aryl-heteroaryl, C_{5-9} heterobicycloalkyl(C_{1-6})alkyl-aryl-heteroaryl, heteroaryl-aryl-heteroaryl, bi(heteroaryl), C_{3-7} heterocycloalkylcarbonyl-bi(heteroaryl), aryloxyaryl, aryl(C_{1-6})alkoxyaryl, heteroaryl(C_{1-6})alkoxyaryl, aryl(C_{1-6})alkylaminoaryl, heteroaryl(C_{1-6})alkylaminoaryl, C_{3-7} cycloalkylcarbonylaminoaryl, arylcarbonylaminoaryl, aryl(C_{1-6})alkylcarbonylaminoaryl, C_{3-7} heterocycloalkylcarbonylaminoaryl, heteroarylcarbonylaminoaryl, aryl-

(C_{3-7})heterocycloalkylcarbonylaminoaryl, arylsulphonylaminoaryl, aryl(C_{1-6})alkylsulphonylaminoaryl, heteroaryl(C_{1-6})alkylsulphonylaminoaryl, C_{3-7} cycloalkylaminocarbonylaminoaryl, arylaminocarbonylaminoaryl, C_{3-7} heterocycloalkylaminocarbonylaminoaryl, C_{3-7} heterocycloalkylaminocarbonylaminoaryl, heteroaryl(C_{1-6})alkylaminocarbonylaminoaryl, C_{3-7} heterocycloalkylcarbonylcarbonylaminoaryl, C_{3-7} heterocycloalkyl(C_{1-6})alkylaminocarbonylcarbonylaminoaryl, arylcarbonylaryl, C_{3-7} heterocycloalkylcarbonylaryl, C_{3-7} heterocycloalkylcarbonyl(C_{1-6})alkylaryl, aryl(C_{1-6})alkylaminocarbonylaryl, C_{3-7} heterocycloalkyl(C_{1-6})alkylaminocarbonylaryl, heteroarylaminocarbonylaryl, heteroaryl(C_{1-6})alkylaminocarbonylaryl, C_{3-7} heterocycloalkylaminocarbonyl(C_{1-6})alkylaryl, C_{3-7} heterocycloalkyl(C_{1-6})alkylaminocarbonyl(C_{1-6})alkylaryl, heteroarylaminocarbonyl(C_{1-6})alkylaryl, heteroaryl(C_{1-6})alkylaminocarbonyl(C_{1-6})alkylaryl, arylaminoheteroaryl, C_{3-7} heterocycloalkylamino-aryl-heteroaryl, C_{3-7} heterocycloalkylcarbonylamino-aryl-heteroaryl, C_{3-7} heterocycloalkylaminocarbonylamino-aryl-heteroaryl, C_{3-7} heterocycloalkylcarbonyl-aryl-heteroaryl, C_{3-7} heterocycloalkyl(C_{1-6})alkylcarbonyl-aryl-heteroaryl, C_{5-9} heterobicycloalkylcarbonyl-aryl-heteroaryl, C_{3-7} heterocycloalkylcarbonyl(C_{1-6})alkyl-aryl-heteroaryl, C_{3-7} heterocycloalkylaminocarbonyl-aryl-heteroaryl, C_{3-7} heterocycloalkyl(C_{1-6})alkylaminocarbonyl-aryl-heteroaryl or C_{3-7} heterocycloalkylaminocarbonyl(C_{1-6})alkyl-aryl-heteroaryl, any of which groups may be optionally substituted by one or more substituents;

R^a represents C_{1-6} alkyl, aryl or heteroaryl, any of which groups may be optionally substituted by one or more substituents;

R^b represents hydrogen; or optionally substituted C_{1-6} alkyl;

R^c represents hydrogen; or C_{1-6} alkyl, aryl, aryl(C_{1-6})alkyl, heteroaryl, heteroaryl(C_{1-6})alkyl or (aryl)(heteroaryl)(C_{1-6})alkyl, any of which groups may be optionally substituted by one or more substituents;

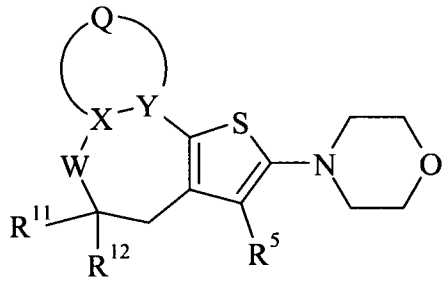
R^d represents hydrogen or C_{1-6} alkyl;

R^e represents C_{1-6} alkyl;

R^6 is absent when V represents a covalent bond; or R^6 represents hydrogen, hydroxy, oxo or $-NR^{6a}R^{6b}$; and

R^{6a} and R^{6b} independently represent hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl(C_{1-6})alkyl, aryl, aryl(C_{1-6})alkyl, heteroaryl or heteroaryl(C_{1-6})alkyl, any of which groups may be optionally substituted by one or more substituents.

2. A compound as claimed in claim 1 represented by formula (BA), or a pharmaceutically acceptable salt or solvate thereof:



(BA)

wherein

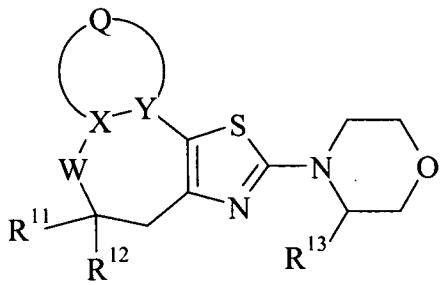
W, the moiety X-Y-Q and R^5 are as defined in claim 1;

R^{11} represents hydrogen or C_{1-6} alkyl; and

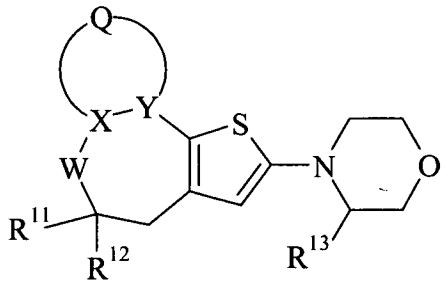
R^{12} represents hydrogen; or C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl(C_{1-6})alkyl, aryl, aryl(C_{1-6})alkyl, C_{3-7} heterocycloalkyl, C_{3-7} heterocycloalkyl-(C_{1-6})alkyl, heteroaryl or heteroaryl(C_{1-6})alkyl, any of which groups may be optionally substituted by one or more substituents; or

R^{11} and R^{12}, when taken together with the carbon atom to which they are both attached, represent C_{3-7} cycloalkyl or C_{3-7} heterocycloalkyl, either of which groups may be optionally substituted by one or more substituents.

3. A compound as claimed in claim 1 represented by formula (IIA-A) or (IIA-B), or a pharmaceutically acceptable salt or solvate thereof:



(IIA-A)



(IIA-B)

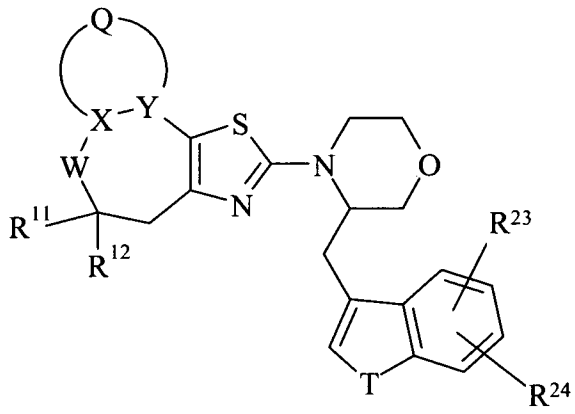
wherein

W and the moiety X-Y-Q are as defined in claim 1;

R^{11} and R^{12} are as defined in claim 2; and

R^{13} represents hydrogen; or C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl(C_{1-6})alkyl, aryl, aryl(C_{1-6})alkyl, aryl(C_{2-6})alkenyl, aryl(C_{2-6})alkynyl, biaryl(C_{1-6})alkyl, C_{3-7} heterocycloalkyl, C_{3-7} heterocycloalkyl(C_{1-6})alkyl, C_{3-7} heterocycloalkylcarbonyl, heteroaryl, heteroaryl(C_{1-6})alkyl, heteroaryl-aryl(C_{1-6})alkyl or aryl-heteroaryl(C_{1-6})alkyl, any of which groups may be optionally substituted by one or more substituents.

4. A compound as claimed in claim 3 represented by formula (IIB), or a pharmaceutically acceptable salt or solvate thereof:



(IIB)

wherein

W and the moiety X-Y-Q are as defined in claim 1;

R^{11} and R^{12} are as defined in claim 2;

T represents oxygen or N-R^{25};

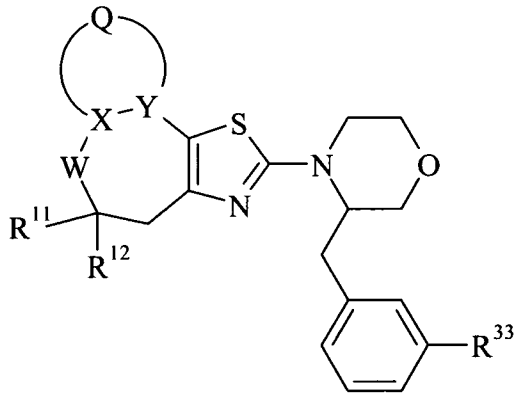
R^{23} represents hydrogen, halogen, cyano, nitro, C_{1-6} alkyl, hydroxy(C_{1-6})alkyl, trifluoromethyl, aryl(C_{1-6})alkyl, oxazolinyl, triazolyl, hydroxy, C_{1-6} alkoxy, difluoromethoxy, trifluoromethoxy, C_{3-7} cycloalkoxy, C_{3-7} cycloalkyl(C_{1-6})alkoxy, morpholinyl(C_{1-6})alkoxy, aryloxy, aryl(C_{1-6})alkoxy, C_{1-6} alkylthio, C_{1-6} alkylsulphinyl, arylsulphinyl, arylsulphonyl, C_{1-6} alkylsulphonyloxy, amino, azetidinyl, morpholinyl, C_{2-6} alkylcarbonylamino, C_{2-6} alkylcarbonylaminomethyl, C_{2-6} alkoxycarbonylamino, [(C_{2-6})alkoxycarbonyl][(C_{1-6})alkyl]amino, C_{1-6} alkylsulphonylamino, C_{2-6} alkylcarbonyl, C_{2-6} alkylcarbonyl oxime, C_{2-6} alkylcarbonyl *O*-(methyl)oxime, trifluoromethylcarbonyl, carboxy, C_{2-6} alkoxycarbonyl, aminocarbonyl, C_{1-6} alkylaminocarbonyl, [hydroxy(C_{1-6})-alkyl]aminocarbonyl, [di(C_{1-6})alkylamino(C_{1-6})alkyl]aminocarbonyl, di(C_{1-6})alkyl-aminocarbonyl, [(C_{1-6})alkyl][cyano(C_{1-6})alkyl]aminocarbonyl, [(C_{1-6})alkyl][hydroxy(C_{1-6})-alkyl]aminocarbonyl, [(C_{1-6})alkoxy(C_{1-6})alkyl][(C_{1-6})alkyl]aminocarbonyl, [di(C_{1-6})alkyl-amino(C_{1-6})alkyl][(C_{1-6})alkyl]aminocarbonyl, C_{3-7} cycloalkyl(C_{1-6})alkylaminocarbonyl, aryl(C_{1-6})alkylaminocarbonyl, heteroarylaminocarbonyl, heteroaryl(C_{1-6})alkylamino-carbonyl, azetidinylcarbonyl, hydroxyazetidinylcarbonyl, aminoazetidinylcarbonyl, C_{2-6} alkoxycarbonylaminoazetidinylcarbonyl, pyrrolidinylcarbonyl, (C_{1-6})alkylpyrrolidinyl-carbonyl, C_{1-6} alkoxy(C_{1-6})alkylpyrrolidinylcarbonyl, di(C_{1-6})alkylaminopyrrolidinyl-carbonyl, thiazolidinylcarbonyl, oxothiazolidinylcarbonyl, piperidinylcarbonyl, (C_{1-6})-alkylpiperazinylcarbonyl, morpholinylcarbonyl, C_{1-6} alkylsulphonyl, C_{1-6} alkylsulphonyl-methyl or di(C_{1-6})alkylaminosulphonyl; and

R^{24} represents hydrogen, halogen, C_{1-6} alkoxy or di(C_{1-6})alkylaminocarbonyl; or

R^{23} and R^{24}, when situated on adjacent carbon atoms, together represent methylenedioxy or difluoromethylenedioxy; and

R^{25} represents hydrogen or C_{1-6} alkyl.

5. A compound as claimed in claim 3 represented by formula (IIC), or a pharmaceutically acceptable salt or solvate thereof:



(IIC)

wherein

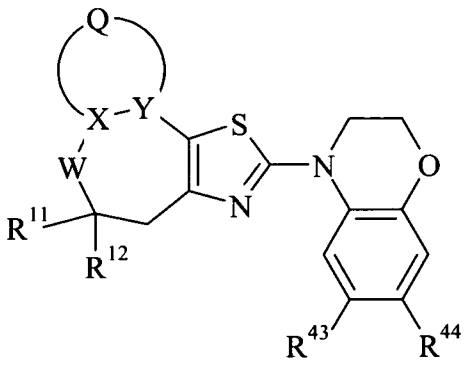
W and the moiety X-Y-Q are as defined in claim 1;

R^{11} and R^{12} are as defined in claim 2;

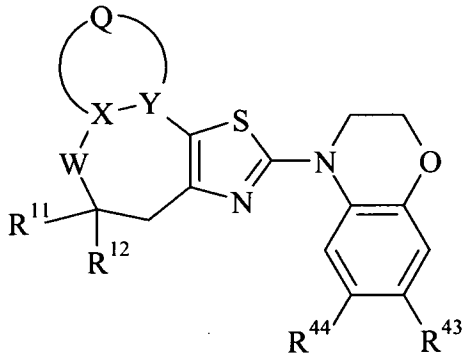
R^{33} represents halogen or $-NHR^{34}$; or aryl or heteroaryl, either of which groups may be optionally substituted by one or more substituents; and

R^{34} represents methylenedioxyphenyl, morpholinyl(C_{1-6})alkylphenyl, oxazolinylphenyl, [(C_{1-6})alkyl](oxo)pyrazolylphenyl, oxazolylphenyl, isoxazolylphenyl, triazolylphenyl, (C_{1-6})alkyltriazolylphenyl, (C_{1-6})alkylpyrimidinylphenyl, pyrazolyl(C_{1-6})alkylphenyl, triazolyl(C_{1-6})alkylphenyl, C_{1-6} alkylsulphonylaminophenyl, morpholinylcarbonylphenyl, C_{1-6} alkylsulphonylphenyl, morpholinylsulphonylphenyl, dihydrobenzofuranyl, C_{1-6} alkylsulphonylindolinyl, chromanonyl, dihydroquinolinonyl, benzoxazinonyl, benzothienyl, indolyl, dioxoindolyl, [(C_{1-6})alkyl](halo)pyrazolyl, tri(C_{1-6})alkylpyrazolyl, (C_{1-6})alkylindazolyl, benzoxazolyl, benzoxazolonyl, di(C_{1-6})alkylisoxazolyl, benzothiazolyl, (C_{1-6})alkylisothiazolyl, (C_{1-6})alkylbenzimidazolyl, benzimidazolonyl, di(C_{1-6})alkylbenzimidazolonyl, (C_{1-6})alkyloxadiazolyl, furyloxadiazolyl, pyridinyl, halopyridinyl, (C_{1-6})alkylpyridinyl, di(C_{1-6})alkylpyridinyl, (C_{1-6})alkoxypyridinyl, oxopyridinyl, oxopyrimidinyl, thioxopyrimidinyl, [(C_{1-6})alkoxy](halo)pyridazinyl, (C_{1-6})alkylcinnolinyl, quinoxalinyl or (C_{1-6})alkylchromenyl.

6. A compound as claimed in claim 1 represented by formula (IID-1) or (IID-2), or a pharmaceutically acceptable salt or solvate thereof:



(IID-1)



(IID-2)

wherein

W and the moiety X-Y-Q are as defined in claim 1;

R^{11} and R^{12} are as defined in claim 2;

R^{43} represents hydrogen, halogen, nitro, C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, (C_{1-6})alkylaryl, di(C_{1-6})alkylaryl, piperidinyl(C_{1-6})alkylaryl, piperazinyl(C_{1-6})alkylaryl, (C_{1-6})alkylpiperazinyl(C_{1-6})alkylaryl, morpholinyl(C_{1-6})alkylaryl, (C_{1-6})alkoxyaryl, cyano(C_{1-6})alkoxyaryl, di(C_{1-6})alkylamino(C_{1-6})alkylaryl, (C_{1-6})alkylaminocarbonylaryl, aryl(C_{1-6})alkyl, haloarylpyrrolidinyl, dioxopyrrolidinyl, aminopyrrolidinyl, di(C_{1-6})alkylaminopyrrolidinyl, indolinyl, oxoindolinyl, arylpiperidinyl, arylcarbonylpiperidinyl, di(C_{1-6})alkylaminocarbonylpiperidinyl, piperazinyl, (C_{1-6})alkylpiperazinyl, haloarylpiperazinyl, pyridinylpiperazinyl, furoylpiperazinyl, homopiperazinyl, (C_{1-6})alkylhomopiperazinyl, (C_{1-6})alkylpiperazinyl(C_{1-6})alkyl, morpholinyl(C_{1-6})alkyl, benzofuryl, benzothienyl, pyrazolyl, (C_{1-6})alkylpyrazolyl, di(C_{1-6})alkylpyrazolyl, tri(C_{1-6})alkylpyrazolyl, [di(C_{1-6})alkyl](trifluoromethyl)pyrazolyl, cyano(C_{1-6})alkylpyrazolyl, [cyano-(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, hydroxy(C_{1-6})alkylpyrazolyl, [hydroxy(C_{1-6})-alkyl][di(C_{1-6})alkyl]pyrazolyl, methoxy(C_{1-6})alkylpyrazolyl, [(hydroxy)(methoxy)(C_{1-6})-alkyl]pyrazolyl, amino(C_{1-6})alkylpyrazolyl, [(C_{1-6})alkyl][amino(C_{1-6})alkyl]pyrazolyl, [amino(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, di(C_{1-6})alkylamino(C_{1-6})alkylpyrazolyl,

di(C_{1-6})alkoxyphosphono(C_{1-6})alkylpyrazolyl, (C_{2-6})alkenylpyrazolyl, (C_{3-7})cycloalkyl-(C_{1-6})alkylpyrazolyl, [(C_{3-7})cycloalkyl(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, [(C_{1-6})alkyl]-(aryl)pyrazolyl, (aryl)(trifluoromethyl)pyrazolyl, aryl(C_{1-6})alkylpyrazolyl, aminoaryl-(C_{1-6})alkylpyrazolyl, piperidinylpyrazolyl, tetrahydropyranyl(C_{1-6})alkylpyrazolyl, [di-(C_{1-6})alkyl][tetrahydropyranyl(C_{1-6})alkyl]pyrazolyl, pyrrolidinyl(C_{1-6})alkylpyrazolyl, piperidinyl(C_{1-6})alkylpyrazolyl, (C_{1-6})alkylpiperidinyl(C_{1-6})alkylpyrazolyl, morpholinyl(C_{1-6})alkylpyrazolyl, pyridinyl(C_{1-6})alkylpyrazolyl, oxypyridinyl(C_{1-6})alkyl-pyrazolyl, [arylcarbonyl(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, [(C_{1-6})alkyl](piperazinyl-carbonyl)pyrazolyl, [(C_{1-6})alkylaminocarbonyl][(C_{1-6})alkylaryl]pyrazolyl, [(C_{1-6})alkyl]-[amino(C_{1-6})alkylaminocarbonyl]pyrazolyl, aminocarbonyl(C_{1-6})alkylpyrazolyl, [aminocarbonyl(C_{1-6})alkyl][di(C_{1-6})alkyl]pyrazolyl, di(C_{1-6})alkylaminocarbonyl(C_{1-6})alkyl-pyrazolyl, pyrazolo[1,5-*a*]pyridinyl, di(C_{1-6})alkylisoxazolyl, (amino)[(C_{1-6})alkyl]-isoxazolyl, thiazolyl, di(C_{1-6})alkylthiazolyl, imidazolyl, (C_{1-6})alkylimidazolyl, di(C_{1-6})-alkylimidazolyl, imidazo[1,2-*a*]pyridinyl, (C_{1-6})alkylimidazo[1,2-*a*]pyridinyl, (C_{1-6})-alkylimidazo[4,5-*b*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyrazinyl, (C_{1-6})-alkylthiadiazolyl, pyridinyl, halopyridinyl, (C_{1-6})alkylpyridinyl, [(C_{1-6})alkyl](halo)-pyridinyl, di(C_{1-6})alkylpyridinyl, (C_{2-6})alkenylpyridinyl, (C_{1-6})alkylpiperazinylpyridinyl, [(C_{1-6})alkyl](piperazinyl)pyridinyl, [(C_{1-6})alkoxycarbonylpiperazinyl][(C_{1-6})alkyl]-pyridinyl, piperidinyl(C_{1-6})alkylpyridinyl, [(C_{1-6})alkyl](oxy)pyridinyl, hydroxypyridinyl, hydroxy(C_{1-6})alkylpyridinyl, (C_{1-6})alkoxypyridinyl, [(C_{1-6})alkoxy][(C_{1-6})alkyl]pyridinyl, [(C_{1-6})alkoxy][di(C_{1-6})alkyl]pyridinyl, (C_{1-6})alkoxy(C_{1-6})alkylpyridinyl, aminopyridinyl, carboxy(C_{1-6})alkylpyridinyl, (C_{1-6})alkoxycarbonyl(C_{1-6})alkylpyridinyl, pyridazinyl, (C_{1-6})-alkylpyridazinyl, piperidinylpyridazinyl, oxypyridazinyl, (C_{1-6})alkoxypyridazinyl, aminopyridazinyl, hydroxy(C_{1-6})alkylaminopyridazinyl, di(C_{1-6})alkylaminopyridazinyl, pyrimidinyl, (C_{1-6})alkylpyrimidinyl, [(C_{1-6})alkyl](halo)pyrimidinyl, di(C_{1-6})alkyl-pyrimidinyl, pyrrolidinylpyrimidinyl, (C_{1-6})alkylpiperazinylpyrimidinyl, [(C_{1-6})alkyl](piperazinyl)pyrimidinyl, [(C_{1-6})alkoxycarbonyl][(C_{1-6})alkyl]piperazinyl-pyrimidinyl, hydroxypyrimidinyl, [(C_{1-6})alkyl](hydroxy)pyrimidinyl, [(C_{1-6})alkyl]-[hydroxy(C_{1-6})alkyl]pyrimidinyl, [(C_{1-6})alkyl][hydroxy(C_{2-6})alkynyl]pyrimidinyl, (C_{1-6})-alkoxypyrimidinyl, aminopyrimidinyl, di(C_{1-6})alkylaminopyrimidinyl, [di(C_{1-6})alkyl-amino](halo)pyrimidinyl, carboxypyrimidinyl, [(C_{1-6})alkoxycarbonyl(C_{1-6})alkyl][(C_{1-6})-alkyl]pyrimidinyl, aminocarbonylpyrimidinyl, pyrazinyl, (C_{1-6})alkoxypyrazinyl, amino-pyrazinyl, hydroxy, (C_{1-6})alkoxy, aryl(C_{1-6})alkoxycarbonylpiperidinyloxy, morpholinyl-

(C_{1-6})alkoxy, aryloxy, haloaryloxy, di(C_{1-6})alkylpyrazolyloxy, halopyridinyloxy, pyrrolidinylpyridinyloxy, (C_{1-6})alkylpiperazinylpyridinyloxy, (C_{1-6})alkylpyrazolylpyridinyloxy, (C_{1-6})alkylaminopyridinyloxy, carboxypyridinyloxy, aminocarbonylpyridinyloxy, (C_{1-6})alkylpyridazinyloxy, pyrimidinyloxy, (C_{1-6})alkylpyrimidinyloxy, [(C_{1-6})alkyl](halo)pyrimidinyloxy, hydroxy(C_{1-6})alkyl, dihydroxy(C_{1-6})alkyl, pyridinyloxy(C_{1-6})alkyl, amino, (C_{1-6})alkylamino, dihydroxy(C_{1-6})alkylamino, (C_{1-6})-alkoxy(C_{1-6})alkylamino, *N*-[(C_{1-6})alkoxy(C_{1-6})alkyl]-*N*-[(C_{1-6})alkyl]amino, di(C_{1-6})-alkylamino(C_{1-6})alkylamino, *N*-[(C_{1-6})alkyl]-*N*-[di(C_{1-6})alkylamino(C_{1-6})alkyl]amino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{3-7})cycloalkyl]amino, haloarylamino, *N*-[(C_{1-6})alkyl]-*N*-(haloaryl)amino, *N*-[(C_{1-6})alkyl]-*N*-[aryl(C_{1-6})alkyl]amino, *N*-[di(C_{1-6})alkylamino(C_{1-6})alkyl]-*N*-[aryl(C_{1-6})-alkyl]amino, cyanoaryl(C_{1-6})alkylamino, (cyano)(halo)aryl(C_{1-6})alkylamino, methylenedioxyaryl(C_{1-6})alkylamino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpyrrolidinyl]amino, piperidinylamino, *N*-[(C_{1-6})alkyl]-*N*-(piperidinyl)amino, *N*-[(C_{3-7})cycloalkyl(C_{1-6})alkyl]-*N*-(piperidinyl)amino, (C_{1-6})alkylpiperidinylamino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpiperidinyl]amino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{3-7})cycloalkylpiperidinyl]amino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{2-6})alkylcarbonylpiperidinyl]amino, pyrrolidinyl(C_{1-6})alkylamino, *N*-[(C_{1-6})alkyl]-*N*-[pyrrolidinyl(C_{1-6})alkyl]amino, *N*-[(C_{1-6})alkyl]-*N*-[piperidinyl(C_{1-6})alkyl]amino, (C_{1-6})-alkylpyrazolylamino, di(C_{1-6})alkylpyrazolylamino, tri(C_{1-6})alkylpyrazolylamino, *N*-[(C_{1-6})-alkyl]-*N*-[(C_{1-6})alkylpyrazolyl]amino, thiazolylamino, imidazolylamino, [(C_{1-6})alkoxycarbonyl][(C_{1-6})alkyl]imidazolylamino, (C_{1-6})alkylthiadiazolylamino, pyridinylamino, halopyridinylamino, (C_{1-6})alkylpyridinylamino, di(C_{1-6})alkylpyridinylamino, trifluoromethylpyridinylamino, hydroxypyridinylamino, hydroxy(C_{1-6})alkylpyridinylamino, dihydroxy(C_{1-6})alkylpyridinylamino, (C_{1-6})alkoxypyridinylamino, dihydroxy(C_{1-6})alkoxypyridinylamino, di(C_{1-6})alkyldioxolanyl(C_{1-6})alkoxypyridinylamino, (C_{1-6})alkoxy(C_{1-6})-alkylpyridinylamino, (C_{1-6})alkoxy(C_{2-6})alkenylpyridinylamino, dihydroxy(C_{1-6})alkylaminopyridinylamino, di(C_{1-6})alkylaminopyridinylamino, (C_{1-6})alkylamino(C_{1-6})alkylpyridinylamino, di(C_{1-6})alkylamino(C_{1-6})alkylpyridinylamino, carboxypyridinylamino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpyridinyl]amino, bis[(C_{1-6})alkylpyridinyl]amino, bis(trifluoromethylpyridinyl)amino, isoquinolinylamino, (C_{1-6})alkylpyridazinylamino, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpyridazinyl]amino, *N*-[aryl(C_{1-6})alkyl]-*N*-[(C_{1-6})alkylpyridazinyl]amino, di(C_{1-6})alkylpyridazinylamino, arylpyridazinylamino, piperidinylpyridazinylamino, (C_{1-6})-alkoxypyridazinylamino, di(C_{1-6})alkylaminopyridazinylamino, bis[(C_{1-6})alkylpyridazinyl]-amino, benzofuryl(C_{1-6})alkylamino, thienyl(C_{1-6})alkylamino, indolyl(C_{1-6})alkylamino,

(C_{1-6})alkylpyrazolyl(C_{1-6})alkylamino, [di(C_{1-6})alkyl](halo)pyrazolyl(C_{1-6})alkylamino, di(C_{1-6})alkylisoxazolyl(C_{1-6})alkylamino, thiazolyl(C_{1-6})alkylamino, imidazolyl(C_{1-6})alkylamino, (C_{1-6})alkylimidazolyl(C_{1-6})alkylamino, pyridinyl(C_{1-6})alkylamino, (C_{1-6})alkylpyridinyl(C_{1-6})alkylamino, *N*-[(C_{1-6})alkyl]-*N*-[pyridinyl(C_{1-6})alkyl]amino, *N*-[dihydroxy(C_{1-6})alkyl]-*N*-[pyridinyl(C_{1-6})alkyl]amino, *N*-[(C_{1-6})alkylpyridinyl(C_{1-6})alkyl]-*N*-[dihydroxy(C_{1-6})alkyl]amino, amino(C_{1-6})alkyl, (C_{1-6})alkylamino(C_{1-6})alkyl, di(C_{1-6})alkylamino(C_{1-6})alkyl, pyridinylamino(C_{1-6})alkyl, *N*-[(C_{2-6})alkylcarbonyl]-*N*-[(C_{1-6})alkylpyridinyl(C_{1-6})alkyl]amino, di(C_{1-6})alkylamino(C_{1-6})alkylcarbonylamino, (C_{3-7})cycloalkylcarbonylamino, (C_{1-6})alkylpiperidinylcarbonylamino, (C_{1-6})alkylimidazolylcarbonylamino, formyl, C_{2-6} alkylcarbonyl, (C_{1-6})alkylpiperidinylaminocarbonyl, *N*-[(C_{1-6})alkyl]-*N*-[(C_{1-6})-alkylpiperidinyl]aminocarbonyl, piperidinyl(C_{1-6})alkylaminocarbonyl, (C_{1-6})alkylpiperazinylcarbonyl, C_{1-6} alkylthio, C_{1-6} alkylsulphinyl, C_{1-6} alkylsulphonyl, C_{2-6} alkoxycarbonyloxy or tetra(C_{1-6})alkyldioxaborolanyl; and

R^{44} represents hydrogen, halogen, C_{1-6} alkyl or C_{1-6} alkoxy.

7. A compound as claimed in claim 1 as herein specifically disclosed in any one of the Examples.

8. A pharmaceutical composition comprising a compound of formula (I) as defined in claim 1, or a pharmaceutically acceptable salt or solvate thereof, in association with a pharmaceutically acceptable carrier.

9. A compound of formula (I) as defined in claim 1, or a pharmaceutically acceptable salt or solvate thereof, for use in therapy.

10. A compound of formula (I) as defined in claim 1, or a pharmaceutically acceptable salt or solvate thereof, for use in the treatment and/or prevention of a disorder for which the administration of a selective PI3K inhibitor is indicated.

11. The use of a compound of formula (I) as defined in claim 1, or a pharmaceutically acceptable salt or solvate thereof, for the manufacture of a medicament for the treatment and/or prevention of a disorder for which the administration of a selective PI3K inhibitor is indicated.

12. A method for the treatment and/or prevention of a disorder for which the administration of a selective PI3K inhibitor is indicated which comprises administering to a patient in need of such treatment an effective amount of a compound of formula (I) as defined in claim 1, or a pharmaceutically acceptable salt or solvate thereof.

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2008/004002

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D513/04 A61K31/425 A61P29/00

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)
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, 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 2005/037843 A (VERTEX PHARMA [US]; JIMENEZ JUAN-MIGUEL [GB]; GREEN JEREMY [US]; GAO H) 28 April 2005 (2005-04-28) page 68; claim 1; examples III-32	1-12
X	KADOYA, S., NAGASAKI, S.: "Synthetic chemotherapeutic agents. V. Antibacterial activities of thiazolo[5,4-f]quinolinecarboxylic acid derivatives" YAKUGAKU ZASSHI, vol. 99, no. 5, 1979, pages 483-492, XP009112737 example 9; table i	1

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[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
27 February 2009	05/03/2009

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Baston, Eckhard

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2008/004002

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KADOYA, S., TAKAMURA, I., SUZUKI, N., DOHMORI, R.: "Synthetic chemotherapeutic agents. II. Synthesis of 2-substituted thiazolo[5,4-f]quinoline derivatives. (2)" CHEMICAL & PHARMACEUTICAL BULLETIN, vol. 24, no. 1, 1976, pages 136-146, XP009112744 example 15f	1
A	WO 2006/114606 A (UCB SA [BE]; ALEXANDER RIKKI PETER [GB]; AUJLA PAVANDEEP [GB]; BATCHEL) 2 November 2006 (2006-11-02) claim 1	1-12
P,A	WO 2008/001076 A (UCB PHARMA SA [BE]; ALEXANDER RIKKI PETER [GB]; AUJLA PAVANDEEP SINGH) 3 January 2008 (2008-01-03) claim 1	1-12
P,A	WO 2007/141504 A (UCB PHARMA SA [BE]; ALEXANDER RIKKI PETER [GB]; BAILEY STUART [GB]; BR) 13 December 2007 (2007-12-13) claim 1	1-12

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/GB2008/004002

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WO 2007141504 A	13-12-2007	NONE	