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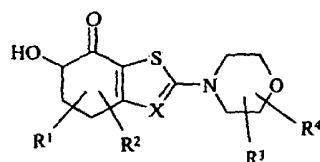
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(54) Title: FUSED THIOPHENE AND THIAZOLE DERIVATIVES AS PI3K KINASE INHIBITORS



(I)

(57) Abstract: A series of fused bicyclic thiophene and thiazole derivatives (I) which are substituted in the 2-position by an optionally substituted morpholin-4-yl moiety, and wherein the thiophene or thiazole ring is fused to a six-membered carbocyclic ring containing an alpha-hydroxyketone functionality, 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.

FUSED THIOPHENE AND THIAZOLE DERIVATIVES AS PI3K KINASE INHIBITORS

The present invention relates to a class of fused thiophene and thiazole derivatives, 5 and to their use in therapy. More particularly, the invention provides a family of fused bicyclic thiophene and thiazole derivatives which are substituted in the 2-position of the thiophene or thiazole 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 10 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 15 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**, 20 366-376). 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 25 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 30 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 Obshchey 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 2006/114606 and WO 2008/001076 describe related classes of fused bicyclic thiazole derivatives; as also does copending international patent application no.

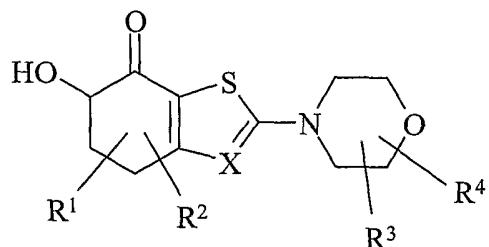
15 PCT/GB2007/003853, which was published on 17 April 2008 as WO 2008/044022.

WO 2007/141504 describes a class of fused bicyclic thiophene derivatives. The compounds disclosed in all of those patent filings 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 PI3K α and/or PI3K β and/or PI3K γ and/or PI3K δ isoform of 50 μ M or less, generally of 20 μ M or less, usually of 5 μ M or less, typically of 1 μ M or less, suitably of 500 nM or less, ideally of 100 nM or less, and 25 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 PI3K α and/or PI3K β and/or PI3K γ and/or PI3K δ isoform relative to other human kinases.

30 The compounds of the present invention possess markedly improved affinity for PI3K isoforms relative to their structurally closest prior art analogues; and also display interesting pharmacokinetic properties owing to their improved solubility and clearance.

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



(I)

5

wherein

X represents N or C-R⁵;

R¹ and R² independently represent hydrogen; or C₁₋₆ alkyl, C₃₋₇ cycloalkyl, C₃₋₇ cycloalkyl(C₁₋₆)alkyl, aryl, aryl(C₁₋₆)alkyl, C₃₋₇ heterocycloalkyl, C₃₋₇ heterocycloalkyl-(C₁₋₆)alkyl, heteroaryl or heteroaryl(C₁₋₆)alkyl, any of which groups may be optionally substituted by one or more substituents; or

R¹ and R², when both are attached to the same carbon atom, represent, when taken together with the carbon atom to which they are both attached, C₃₋₇ cycloalkyl or C₃₋₇ heterocycloalkyl, either of which groups may be optionally substituted by one or more substituents; or

R¹ and R², when attached to adjacent carbon atoms, represent, when taken together with the carbon atoms to which they are attached, C₅₋₇ cycloalkyl, phenyl or heteroaryl, any of which groups may be optionally benzo-fused and/or substituted by one or more substituents;

R³ and R⁴ independently represent hydrogen; or C₁₋₆ alkyl, C₂₋₆ alkynyl, C₃₋₇ cycloalkyl, C₃₋₇ cycloalkyl(C₁₋₆)alkyl, aryl, aryl(C₁₋₆)alkyl, aryl(C₂₋₆)alkenyl, aryl(C₂₋₆)-alkynyl, biaryl(C₁₋₆)alkyl, C₃₋₇ heterocycloalkyl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkyl, C₃₋₇ heterocycloalkylcarbonyl, heteroaryl, heteroaryl(C₁₋₆)alkyl, heteroaryl-aryl(C₁₋₆)alkyl or aryl-heteroaryl(C₁₋₆)alkyl, any of which groups may be optionally substituted by one or more substituents; or

R³ and R⁴, when both are attached to the same carbon atom, represent, when taken together with the carbon atom to which they are both attached, C₃₋₇ cycloalkyl or C₃₋₇

heterocycloalkyl, either of which groups may be optionally substituted by one or more substituents; or

R³ and R⁴, when attached to adjacent carbon atoms, represent, when taken together with the carbon atoms to which they are attached, C₅₋₇ cycloalkyl, phenyl or heteroaryl,

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

R⁵ represents hydrogen, halogen, cyano, -SR^a, -COR^c, -CO₂R^b, -CONR^cR^d or -C(=N-OR^f)R^e; or R⁵ represents C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkenylcarbonyl, C₂₋₆ alkynyl, C₃₋₇ cycloalkyl, C₃₋₇ cycloalkyl(C₁₋₆)alkyl, C₃₋₇ cycloalkyl(C₂₋₆)alkenyl, C₃₋₇ cycloalkyl-

- 10 (C₂₋₆)alkynyl, aryl, aryl(C₁₋₆)alkyl, aryl(C₂₋₆)alkenyl, aryl(C₂₋₆)alkynyl, biaryl, C₃₋₇ heterocycloalkyl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkyl, C₃₋₇ heterocycloalkyl(C₂₋₆)alkenyl, C₃₋₇ heterocycloalkyl(C₂₋₆)alkynyl, C₃₋₇ heterocycloalkylcarbonyl(C₂₋₆)alkynyl, C₅₋₉ heterobicycloalkyl(C₂₋₆)alkynyl, C₃₋₇ heterocycloalkyl-aryl, C₃₋₇ heterocycloalkyl(C₁₋₆)-alkyl-aryl, C₃₋₇ heterocycloalkyl-biaryl, heteroaryl, heteroaryl(C₁₋₆)alkyl, heteroaryl(C₁₋₆)-alkylcarbonyl, heteroaryl(C₂₋₆)alkenyl, heteroaryl(C₂₋₆)alkynyl, heteroaroylcarbonyl, C₃₋₇ heterocycloalkyl-heteroaryl, C₃₋₇ heterocycloalkyl-heteroaryl(C₂₋₆)alkynyl, heteroaryl-aryl, heteroaryl-aryl(C₁₋₆)alkyl, aryl-heteroaryl, aryl-heteroaryl(C₁₋₆)alkyl, C₃₋₇ heterocycloalkyl-aryl-heteroaryl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkyl-aryl-heteroaryl, C₅₋₉ heterobicycloalkyl(C₁₋₆)alkyl-aryl-heteroaryl, heteroaryl-aryl-heteroaryl, bi(heteroaryl),

- 20 C₃₋₇ heterocycloalkylcarbonyl-bi(heteroaryl), aryloxyaryl, aryl(C₁₋₆)alkoxyaryl, heteroaryl(C₁₋₆)alkoxyaryl, aryl(C₁₋₆)alkylaminoaryl, heteroaryl(C₁₋₆)alkylaminoaryl, C₃₋₇ cycloalkylcarbonylaminoaryl, arylcarbonylaminoaryl, aryl(C₁₋₆)alkylcarbonylaminoaryl, C₃₋₇ heterocycloalkylcarbonylaminoaryl, heteroarylcarbonylaminoaryl, aryl-(C₃₋₇)heterocycloalkylcarbonylaminoaryl, arylsulphonylaminoaryl, aryl(C₁₋₆)alkyl-

- 25 sulphonylaminoaryl, heteroaryl(C₁₋₆)alkylsulphonylaminoaryl, C₃₋₇ cycloalkylamino-carbonylaminoaryl, arylaminocarbonylaminoaryl, C₃₋₇ heterocycloalkylaminocarbonyl-aminoaryl, C₃₋₇ heterocycloalkylaminocarbonylaminoaryl, heteroaryl(C₁₋₆)alkyl-aminocarbonylaminoaryl, C₃₋₇ heterocycloalkylcarbonylcarbonylaminoaryl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkylaminocarbonylcarbonylaminoaryl, arylcarbonylaryl, C₃₋₇ heterocycloalkylcarbonylaryl, C₃₋₇ heterocycloalkylcarbonyl(C₁₋₆)alkylaryl, aryl(C₁₋₆)-

- 30 alkylaminocarbonylaryl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkylaminocarbonylaryl, heteroaryl-aminocarbonylaryl, heteroaryl(C₁₋₆)alkylaminocarbonylaryl, C₃₋₇ heterocycloalkylaminocarbonyl(C₁₋₆)alkylaryl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkylaminocarbonyl(C₁₋₆)alkylaryl,

heteroarylaminocarbonyl(C₁₋₆)alkylaryl, heteroaryl(C₁₋₆)alkylaminocarbonyl(C₁₋₆)alkyl-aryl, arylaminoheteroaryl, C₃₋₇ heterocycloalkylamino-aryl-heteroaryl, C₃₋₇ heterocycloalkylcarbonylamino-aryl-heteroaryl, C₃₋₇ heterocycloalkylaminocarbonyl-amino-aryl-heteroaryl, C₃₋₇ cycloalkylcarbonyl-aryl-heteroaryl, C₃₋₇ heterocycloalkyl-carbonyl-aryl-heteroaryl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkylcarbonyl-aryl-heteroaryl, C₅₋₉ heterobicycloalkylcarbonyl-aryl-heteroaryl, C₃₋₇ heterocycloalkylcarbonyl(C₁₋₆)alkyl-aryl-heteroaryl, C₃₋₇ heterocycloalkyl-aminocarbonyl-aryl-heteroaryl, C₃₋₇ heterocycloalkyl-(C₁₋₆)alkylaminocarbonyl-aryl-heteroaryl or C₃₋₇ heterocycloalkylaminocarbonyl(C₁₋₆)-alkyl-aryl-heteroaryl, any of which groups may be optionally substituted by one or more substituents;

R^a represents C₁₋₆ alkyl, aryl or heteroaryl, any of which groups may be optionally substituted by one or more substituents;

R^b represents hydrogen; or optionally substituted C₁₋₆ alkyl;

R^c represents hydrogen; or C₁₋₆ alkyl, aryl, aryl(C₁₋₆)alkyl, heteroaryl,

heteroaryl(C₁₋₆)alkyl or (aryl)(heteroaryl)(C₁₋₆)alkyl, any of which groups may be optionally substituted by one or more substituents;

R^d represents hydrogen or C₁₋₆ alkyl;

R^e represents C₁₋₆ alkyl; and

R^f represents C₁₋₆ alkyl, aryl, aryl(C₁₋₆)alkyl, heteroaryl or heteroaryl(C₁₋₆)alkyl,

any of which groups may be optionally substituted by one or more substituents.

Where any of the groups in the compounds of formula (I) 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.

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 C₁₋₆ alkyl groups, for example C₁₋₄ 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 "C₁₋₆ alkoxy", "C₁₋₆ alkylthio", "C₁₋₆ alkylsulphonyl" and "C₁₋₆ alkylamino" are to be construed accordingly.

Typical C₂₋₆ alkenyl groups include vinyl and allyl.

Typical C₂₋₆ alkynyl groups include ethynyl, prop-1-yn-1-yl, but-1-yn-1-yl and 3-methylbut-1-yn-1-yl.

Specific C₃₋₇ cycloalkyl groups are cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl.

Suitable aryl groups include phenyl and naphthyl, preferably phenyl.

Suitable aryl(C₁₋₆)alkyl groups include benzyl, phenylethyl, phenylpropyl and naphthylmethyl.

Specific aryl(C₂₋₆)alkenyl groups include 2-phenylethenyl and 3-phenylprop-2-en-1-yl.

Specific aryl(C₂₋₆)alkynyl groups include phenylethynyl, 3-phenylprop-1-yn-1-yl and 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-tetrahydroquinoxaliny, homopiperazinyl, morpholinyl, benzoxazinyl and thiomorpholinyl.

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

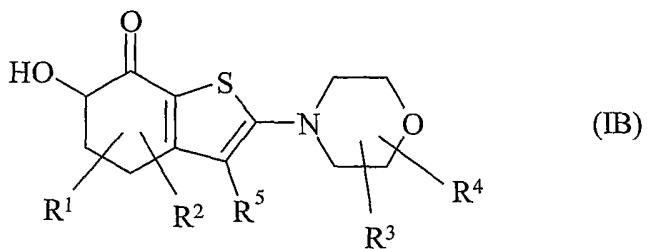
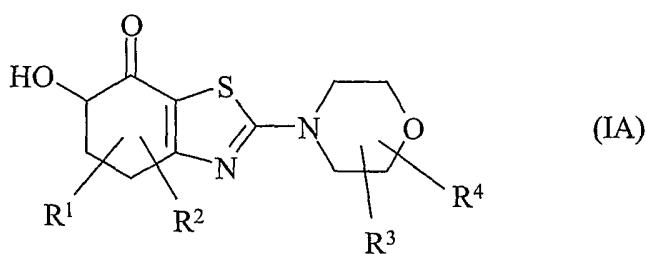
5 Suitable heteroaryl groups include furyl, benzofuryl, dibenzofuryl, thienyl, benzothienyl, dibenzothienyl, pyrrolyl, indolyl, pyrrolo[2,3-*b*]pyridinyl, pyrrolo[3,2-*c*]pyridinyl, pyrazolyl, pyrazolo[1,5-*a*]pyridinyl, indazolyl, oxazolyl, benzoxazolyl, isoxazolyl, thiazolyl, benzothiazolyl, isothiazolyl, imidazolyl, benzimidazolyl, imidazo[1,2-*a*]pyridinyl, imidazo[4,5-*b*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, 10 imidazo[1,2-*a*]pyrazinyl, oxadiazolyl, thiadiazolyl, triazolyl, benzotriazolyl, tetrazolyl, pyridinyl, quinolinyl, isoquinolinyl, pyridazinyl, cinnolinyl, pyrimidinyl, pyrazinyl, quinoxalinyl and chromenyl groups.

Typical bi(heteroaryl) groups include benzofuryl-pyridinyl, benzothienyl-pyridinyl, indolyl-pyridinyl, isoxazolyl-pyridinyl, bipyridinyl and isoquinolinyl-pyridinyl.

15 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 20 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 ($\text{CH}_2\text{C}=\text{O}$)↔enol ($\text{CH}=\text{CHOH}$) tautomers or amide 25 ($\text{NHC}=\text{O}$)↔hydroxyimine ($\text{N}=\text{COH}$) 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.

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



wherein R¹, R², R³, R⁴ and R⁵ are as defined above.

5 In one embodiment, X represents N. In another embodiment, X represents C-R⁵.

Suitably, R¹ represents hydrogen or C₁₋₆ alkyl. Typical values of R¹ include hydrogen, methyl and ethyl. In one embodiment, R¹ is hydrogen. In another embodiment, R¹ is C₁₋₆ alkyl. In one aspect of that embodiment, R¹ is methyl. In another aspect of that embodiment, R¹ is ethyl.

10 Suitably, R² represents hydrogen; or C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₇ cycloalkyl or aryl, any of which groups may be optionally substituted by one or more substituents.

Examples of typical substituents on R¹ and/or R² include halogen, cyano, nitro, C₁₋₆ alkyl, trifluoromethyl, hydroxy, C₁₋₆ alkoxy, difluoromethoxy, trifluoromethoxy, aryloxy, C₁₋₆ alkylthio, C₁₋₆ alkylsulphonyl, amino, C₁₋₆ alkylamino, di(C₁₋₆)alkylamino, C₂₋₆ 15 alkylcarbonylamino, C₂₋₆ alkoxy carbonylamino, C₁₋₆ alkylsulphonylamino, formyl, C₂₋₆ alkylcarbonyl, carboxy, C₂₋₆ alkoxy carbonyl, aminocarbonyl, C₁₋₆ alkylaminocarbonyl, di(C₁₋₆)alkylaminocarbonyl, aminosulphonyl, C₁₋₆ alkylaminosulphonyl and di(C₁₋₆)alkylaminosulphonyl; especially halogen, C₁₋₆ alkoxy or C₁₋₆ alkylthio.

Examples of particular substituents on R¹ and/or R² include fluoro, chloro, bromo, 20 cyano, nitro, methyl, trifluoromethyl, hydroxy, methoxy, difluoromethoxy, trifluoromethoxy, phenoxy, methylthio, methylsulphonyl, amino, methylamino, dimethylamino, acetyl amine, methoxycarbonylamino, methylsulphonylamino, formyl, acetyl, carboxy, methoxycarbonyl, aminocarbonyl, methylaminocarbonyl, dimethylaminocarbonyl, aminosulphonyl, methylaminosulphonyl and 25 dimethylaminosulphonyl; especially chloro, methoxy or methylthio.

Typical values of R² include hydrogen, methyl, ethoxy, *n*-propyl, isopropyl, isobutyl, cyclohexyl and phenyl. A particular value of R² is methyl.

Alternatively, R¹ and R², when both are attached to the same carbon atom, may together form an optionally substituted spiro linkage. Thus, R¹ and R², when both are attached to the same carbon atom, may represent, when taken together with the carbon atom to which they are both attached, C₃₋₇ cycloalkyl or C₃₋₇ heterocycloalkyl, either of which groups may be unsubstituted, or substituted by one or more, typically by one or two, substituents. In this context, R¹ and R², 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, R¹ and R², 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 α -hydroxyketone moiety. Thus, R¹ and R², when attached to adjacent carbon atoms, may represent, when taken together with the carbon atoms to which they are attached, C₅₋₇ 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, R¹ and R², when taken together with the adjacent carbon atoms to which they are attached, suitably represent a phenyl ring fused to the ring containing the α -hydroxyketone moiety.

Also in this context, in another embodiment, R¹ and R², 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 α -hydroxyketone moiety.

Typically, R³ represents hydrogen; or C₁₋₆ alkyl, aryl, aryl(C₁₋₆)alkyl, aryl-(C₂₋₆)alkynyl, biaryl(C₁₋₆)alkyl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkyl, C₃₋₇ heterocycloalkyl-carbonyl, heteroaryl(C₁₋₆)alkyl, heteroaryl-aryl(C₁₋₆)alkyl or aryl-heteroaryl(C₁₋₆)alkyl, any of which groups may be optionally substituted by one or more substituents.

Generally, R³ represents hydrogen; or C₂₋₆ alkynyl, aryl(C₁₋₆)alkyl or heteroaryl-(C₁₋₆)alkyl, any of which groups may be optionally substituted by one or more substituents. More particularly, R³ represents aryl(C₁₋₆)alkyl or heteroaryl(C₁₋₆)alkyl, either of which groups may be optionally substituted by one or more substituents.

In one specific embodiment, R³ represents hydrogen.

In a representative embodiment, R³ represents C₁₋₆ alkyl, aryl(C₁₋₆)alkyl, biaryl-(C₁₋₆)alkyl, heteroaryl(C₁₋₆)alkyl or heteroaryl-aryl(C₁₋₆)alkyl, any of which groups may be optionally substituted by one or more substituents. Preferably, R³ represents methyl, arylmethyl, biaryl methyl, heteroarylmethyl or heteroaryl-arylmethyl, any of which groups 5 may be optionally substituted by one or more substituents. More particularly, R³ represents arylmethyl or heteroarylmethyl, either of which groups may be optionally substituted by one or more substituents.

In a particular embodiment, R³ represents substituted or unsubstituted indolyl-(C₁₋₆)alkyl. Advantageously, R³ represents substituted or unsubstituted indolylmethyl.

10 In a typical embodiment, R³ represents substituted or unsubstituted phenyl-(C₁₋₆)alkyl. Advantageously, R³ represents substituted or unsubstituted benzyl.

In another embodiment, R³ represents substituted or unsubstituted benzofuryl-(C₁₋₆)alkyl. Advantageously, R³ represents substituted or unsubstituted benzofurylmethyl.

15 Illustratively, R³ represents hydrogen; or methyl, propynyl, benzyl, phenylethyl, naphthylmethyl, phenylpropynyl, biphenylmethyl, naphthylphenylmethyl, indolinylmethyl, 1,2,3,4-tetrahydroquinolinylmethyl, 1,2,3,4-tetrahydroisoquinolinylmethyl, piperidinylcarbonyl, 1,2,3,4-tetrahydroquinolinylcarbonyl, 1,2,3,4-tetrahydroisoquinolinylcarbonyl, 1,2,3,4-tetrahydroquinoxalinylcarbonyl, benzofurylmethyl, benzothienylmethyl, indolymethyl, pyrrolo[2,3-*b*]pyridinylmethyl, 20 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.

25 Suitably, R⁴ represents hydrogen or optionally substituted C₁₋₆ alkyl.

Examples of typical substituents on R³ and/or R⁴ include halogen, cyano, nitro, C₁₋₆ alkyl, trifluoromethyl, C₂₋₆ alkenyl, C₃₋₇ cycloalkyl, (C₁₋₆)alkylaryl, di(C₁₋₆)alkylaryl, piperidinyl(C₁₋₆)alkylaryl, piperazinyl(C₁₋₆)alkylaryl, (C₁₋₆)alkylpiperazinyl(C₁₋₆)-alkylaryl, morpholinyl(C₁₋₆)alkylaryl, (C₁₋₆)alkoxyaryl, cyano(C₁₋₆)alkoxyaryl, di(C₁₋₆)-30 alkylamino(C₁₋₆)alkylaryl, (C₁₋₆)alkylaminocarbonylaryl, aryl(C₁₋₆)alkyl, oxazolinyl, azetidinyl, pyrrolidinyl, haloarylpyrrolidinyl, dioxopyrrolidinyl, aminopyrrolidinyl, di-(C₁₋₆)alkylaminopyrrolidinyl, indolinyl, oxoindolinyl, arylpiperidinyl, arylcarbonylpiperidinyl, di(C₁₋₆)alkylaminocarbonylpiperidinyl, piperazinyl, (C₁₋₆)alkylpiperazinyl,

haloarylpirazinyl, pyridinylpirazinyl, furoylpirazinyl, homopiperazinyl,
(C₁₋₆)alkylhomopiperazinyl, morpholinyl, (C₁₋₆)alkylpirazinyl(C₁₋₆)alkyl,
morpholinyl(C₁₋₆)alkyl, benzofuryl, benzothienyl, pyrazolyl, (C₁₋₆)alkylpyrazolyl, di(C₁₋₆)-
alkylpyrazolyl, tri(C₁₋₆)alkylpyrazolyl, [di(C₁₋₆)alkyl](trifluoromethyl)pyrazolyl, cyano-
5 (C₁₋₆)alkylpyrazolyl, [cyano(C₁₋₆)alkyl][di(C₁₋₆)alkyl]pyrazolyl, hydroxy(C₁₋₆)alkyl-
pyrazolyl, [hydroxy(C₁₋₆)alkyl][di(C₁₋₆)alkyl]pyrazolyl, methoxy(C₁₋₆)alkylpyrazolyl,
[dihydroxy(C₁₋₆)alkyl]pyrazolyl, [(hydroxy)(methoxy)(C₁₋₆)alkyl]pyrazolyl, amino-
(C₁₋₆)alkylpyrazolyl, [(C₁₋₆)alkyl][amino(C₁₋₆)alkyl]pyrazolyl, [amino(C₁₋₆)alkyl][di-
(C₁₋₆)alkyl]pyrazolyl, di(C₁₋₆)alkylamino(C₁₋₆)alkylpyrazolyl, di(C₁₋₆)alkoxypyrophono-
10 (C₁₋₆)alkylpyrazolyl, (C₂₋₆)alkenylpyrazolyl, (C₃₋₇)cycloalkyl(C₁₋₆)alkylpyrazolyl,
[(C₃₋₇)cycloalkyl(C₁₋₆)alkyl][di(C₁₋₆)alkyl]pyrazolyl, [(C₁₋₆)alkyl](aryl)pyrazolyl,
(aryl)(trifluoromethyl)pyrazolyl, aryl(C₁₋₆)alkylpyrazolyl, aminoaryl(C₁₋₆)alkylpyrazolyl,
piperidinylpyrazolyl, tetrahydropyran(C₁₋₆)alkylpyrazolyl, [di(C₁₋₆)alkyl]-
15 [tetrahydropyran(C₁₋₆)alkyl]pyrazolyl, pyrrolidinyl(C₁₋₆)alkylpyrazolyl, piperidinyl-
(C₁₋₆)alkylpyrazolyl, (C₁₋₆)alkylpiperidinyl(C₁₋₆)alkylpyrazolyl, morpholinyl(C₁₋₆)alkyl-
pyrazolyl, pyridinyl(C₁₋₆)alkylpyrazolyl, oxypyridinyl(C₁₋₆)alkylpyrazolyl,
[arylcarbonyl(C₁₋₆)alkyl][di(C₁₋₆)alkyl]pyrazolyl, [(C₁₋₆)alkyl](piperazinyl-
carbonyl)pyrazolyl, [(C₁₋₆)alkylaminocarbonyl][(C₁₋₆)alkylaryl]pyrazolyl, [(C₁₋₆)alkyl]-
20 [amino(C₁₋₆)alkylaminocarbonyl]pyrazolyl, aminocarbonyl(C₁₋₆)alkylpyrazolyl,
[aminocarbonyl(C₁₋₆)alkyl][di(C₁₋₆)alkyl]pyrazolyl, di(C₁₋₆)alkylaminocarbonyl(C₁₋₆)alkyl-
pyrazolyl, pyrazolo[1,5-*a*]pyridinyl, di(C₁₋₆)alkylisoxazolyl, (amino)[(C₁₋₆)alkyl]-
isoxazolyl, thiazolyl, di(C₁₋₆)alkylthiazolyl, imidazolyl, (C₁₋₆)alkylimidazolyl, di(C₁₋₆)-
alkylimidazolyl, imidazo[1,2-*a*]pyridinyl, (C₁₋₆)alkylimidazo[1,2-*a*]pyridinyl, (C₁₋₆)-
alkylimidazo[4,5-*b*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyrazinyl, (C₁₋₆)-
25 alkylthiadiazolyl, triazolyl, pyridinyl, halopyridinyl, (C₁₋₆)alkylpyridinyl, [(C₁₋₆)alkyl]-
(halo)pyridinyl, di(C₁₋₆)alkylpyridinyl, (C₂₋₆)alkenylpyridinyl, (C₁₋₆)alkylpirazinyl-
pyridinyl, [(C₁₋₆)alkyl](piperazinyl)pyridinyl, [(C₁₋₆)alkoxycarbonylpiperazinyl][(C₁₋₆)-
alkyl]pyridinyl, piperidinyl(C₁₋₆)alkylpyridinyl, [(C₁₋₆)alkyl](oxy)pyridinyl,
hydroxypyridinyl, hydroxy(C₁₋₆)alkylpyridinyl, (C₁₋₆)alkoxypyridinyl, [(C₁₋₆)alkoxy]-
30 [(C₁₋₆)alkyl]pyridinyl, [(C₁₋₆)alkoxy][di(C₁₋₆)alkyl]pyridinyl, (C₁₋₆)alkoxy(C₁₋₆)alkyl-
pyridinyl, aminopyridinyl, carboxy(C₁₋₆)alkylpyridinyl, (C₁₋₆)alkoxycarbonyl(C₁₋₆)alkyl-
pyridinyl, pyridazinyl, (C₁₋₆)alkylpyridazinyl, piperidinylpyridazinyl, oxypyridazinyl,
(C₁₋₆)alkoxypyridazinyl, aminopyridazinyl, hydroxy(C₁₋₆)alkylaminopyridazinyl, di-

(C₁₋₆)alkylaminopyridazinyl, pyrimidinyl, (C₁₋₆)alkylpyrimidinyl, [(C₁₋₆)alkyl](halo)-pyrimidinyl, di(C₁₋₆)alkylpyrimidinyl, pyrrolidinylpyrimidinyl, (C₁₋₆)alkylpiperazinyl-pyrimidinyl, [(C₁₋₆)alkyl](piperazinyl)pyrimidinyl, [(C₁₋₆)alkoxycarbonyl][(C₁₋₆)alkyl]-piperazinylpyrimidinyl, hydroxypyrimidinyl, [(C₁₋₆)alkyl](hydroxy)pyrimidinyl, [(C₁₋₆)alkyl][hydroxy(C₁₋₆)alkyl]pyrimidinyl, [(C₁₋₆)alkyl][hydroxy(C₂₋₆)alkynyl]pyrimidinyl, 5 (C₁₋₆)alkoxypyrimidinyl, aminopyrimidinyl, di(C₁₋₆)alkylaminopyrimidinyl, [di(C₁₋₆)alkyl-amino](halo)pyrimidinyl, carboxypyrimidinyl, [(C₁₋₆)alkoxycarbonyl(C₁₋₆)alkyl][(C₁₋₆)-alkyl]pyrimidinyl, aminocarbonylpyrimidinyl, pyrazinyl, (C₁₋₆)alkoxypyrazinyl, amino-pyrazinyl, hydroxy, (C₁₋₆)alkoxy, difluoromethoxy, trifluoromethoxy, C₃₋₇ cycloalkoxy, 10 C₃₋₇ cycloalkyl(C₁₋₆)alkoxy, aryl(C₁₋₆)alkoxycarbonylpiperidinyloxy, morpholinyl(C₁₋₆)-alkoxy, aryloxy, haloaryloxy, di(C₁₋₆)alkylpyrazolylloxy, halopyridinyloxy, pyrrolidinylpyridinyloxy, (C₁₋₆)alkylpiperazinylpyridinyloxy, (C₁₋₆)alkylpyrazolyl-pyridinyloxy, (C₁₋₆)alkylaminopyridinyloxy, carboxypyridinyloxy, aminocarbonyl-pyridinyloxy, (C₁₋₆)alkylpyridazinylloxy, pyrimidinyloxy, (C₁₋₆)alkylpyrimidinyloxy, 15 [(C₁₋₆)alkyl](halo)pyrimidinyloxy, hydroxy(C₁₋₆)alkyl, dihydroxy(C₁₋₆)alkyl, pyridinyloxy(C₁₋₆)alkyl, methylenedioxy, trifluoromethylenedioxy, amino, (C₁₋₆)alkyl-amino, dihydroxy(C₁₋₆)alkylamino, (C₁₋₆)alkoxy(C₁₋₆)alkylamino, di(C₁₋₆)alkylamino, N-[(C₁₋₆)alkoxy(C₁₋₆)alkyl]-N-[(C₁₋₆)alkyl]amino, di(C₁₋₆)alkylamino(C₁₋₆)alkylamino, N-[(C₁₋₆)alkyl]-N-[di(C₁₋₆)alkylamino(C₁₋₆)alkyl]amino, N-[(C₁₋₆)alkyl]-N-[(C₃₋₇)cycloalkyl]-20 amino, haloarylarnino, N-[(C₁₋₆)alkyl]-N-(haloaryl)amino, methylenedioxyphenylamino, morpholinyl(C₁₋₆)alkylphenylamino, oxazolinylphenylamino, [(C₁₋₆)alkyl](oxo)pyrazolyl-phenylamino, oxazolylphenylamino, isoxazolylphenylamino, triazolylphenylamino, (C₁₋₆)alkyltriazolylphenylamino, (C₁₋₆)alkylpyrimidinylphenylamino, pyrazolyl(C₁₋₆)alkyl-phenylamino, triazolyl(C₁₋₆)alkylphenylamino, C₁₋₆ alkylsulphonylaminophenylamino, 25 morpholinylcarbonylphenylamino, C₁₋₆ alkylsulphonylphenylamino, morpholinylsulphonylphenylamino, N-[(C₁₋₆)alkyl]-N-[aryl(C₁₋₆)alkyl]amino, N-[di(C₁₋₆)alkylamino(C₁₋₆)alkyl]-N-[aryl(C₁₋₆)alkyl]amino, cyanoaryl(C₁₋₆)alkylamino, (cyano)(halo)aryl(C₁₋₆)alkylamino, methylenedioxyaryl(C₁₋₆)alkylamino, dihydrobenzofuranylarnino, N-[(C₁₋₆)alkyl]-N-[(C₁₋₆)alkylpyrrolidinyl]amino, C₁₋₆ 30 alkylsulphonylindolinylamino, chromanonylarnino, piperidinylarnino, N-[(C₁₋₆)alkyl]-N-(piperidinyl)arnino, N-[(C₃₋₇)cycloalkyl(C₁₋₆)alkyl]-N-(piperidinyl)arnino, (C₁₋₆)alkyl-piperidinylarnino, N-[(C₁₋₆)alkyl]-N-[(C₁₋₆)alkylpiperidinyl]arnino, N-[(C₁₋₆)alkyl]-N-[(C₃₋₇)cycloalkylpiperidinyl]arnino, N-[(C₁₋₆)alkyl]-N-[(C₂₋₆)alkylcarbonylpiperidinyl]-

amino, dihydroquinolinonylamino, benzoxazinonylamino, pyrrolidinyl(C₁₋₆)alkylamino,
N-[(C₁₋₆)alkyl]-N-[pyrrolidinyl(C₁₋₆)alkyl]amino, N-[(C₁₋₆)alkyl]-N-[piperidinyl(C₁₋₆)-
alkyl]amino, benzothienylamino, indolylamino, dioxoindolylamino, (C₁₋₆)alkylpyrazolyl-
amino, [(C₁₋₆)alkyl](halo)pyrazolylamino, di(C₁₋₆)alkylpyrazolylamino, tri(C₁₋₆)alkyl-
5 pyrazolylamino, N-[(C₁₋₆)alkyl]-N-[(C₁₋₆)alkylpyrazolyl]amino, (C₁₋₆)alkylindazolylamino,
benzoxazolylamino, benzoxazolonylamino, di(C₁₋₆)alkylisoxazolylamino, thiazolylamino,
benzothiazolylamino, (C₁₋₆)alkylisothiazolylamino, imidazolylamino, [(C₁₋₆)alkoxy-
carbonyl][(C₁₋₆)alkyl]imidazolylamino, (C₁₋₆)alkylbenzimidazolylamino,
benzimidazolonylamino, di(C₁₋₆)alkylbenzimidazolonylamino, (C₁₋₆)alkyloxadiazolyl-
10 amino, furyloxadiazolylamino, (C₁₋₆)alkylthiadiazolylamino, pyridinylamino,
halopyridinylamino, (C₁₋₆)alkylpyridinylamino, di(C₁₋₆)alkylpyridinylamino, trifluoro-
methylpyridinylamino, hydroxypyridinylamino, hydroxy(C₁₋₆)alkylpyridinylamino,
dihydroxy(C₁₋₆)alkylpyridinylamino, (C₁₋₆)alkoxypyridinylamino, dihydroxy(C₁₋₆)alkoxy-
pyridinylamino, di(C₁₋₆)alkyldioxolanyl(C₁₋₆)alkoxypyridinylamino, (C₁₋₆)alkoxy(C₁₋₆)-
15 alkylpyridinylamino, (C₁₋₆)alkoxy(C₂₋₆)alkenylpyridinylamino, dihydroxy(C₁₋₆)alkyl-
aminopyridinylamino, di(C₁₋₆)alkylaminopyridinylamino, (C₁₋₆)alkylamino(C₁₋₆)alkyl-
pyridinylamino, di(C₁₋₆)alkylamino(C₁₋₆)alkylpyridinylamino, oxypyridinylamino,
carboxypyridinylamino, N-[(C₁₋₆)alkyl]-N-[(C₁₋₆)alkylpyridinyl]amino, bis[(C₁₋₆)alkyl-
pyridinyl]amino, bis(trifluoromethylpyridinyl)amino, isoquinolinylamino, (C₁₋₆)alkyl-
20 pyridazinylamino, N-[(C₁₋₆)alkyl]-N-[(C₁₋₆)alkylpyridazinyl]amino, N-[aryl(C₁₋₆)alkyl]-N-
[(C₁₋₆)alkylpyridazinyl]amino, di(C₁₋₆)alkylpyridazinylamino, arylpyridazinylamino,
piperidinylpyridazinylamino, (C₁₋₆)alkoxypyridazinylamino, [(C₁₋₆)alkoxy](halo)-
pyridazinylamino, di(C₁₋₆)alkylaminopyridazinylamino, bis[(C₁₋₆)alkylpyridazinyl]amino,
(C₁₋₆)alkylcinnolinylamino, oxopyrimidinylamino, thioxopyrimidinylamino,
25 quinoxalinylamino, (C₁₋₆)alkylchromenylamino, benzofuryl(C₁₋₆)alkylamino, thieryl(C₁₋₆)-
alkylamino, indolyl(C₁₋₆)alkylamino, (C₁₋₆)alkylpyrazolyl(C₁₋₆)alkylamino, [di(C₁₋₆)alkyl]-
(halo)pyrazolyl(C₁₋₆)alkylamino, di(C₁₋₆)alkylisoxazolyl(C₁₋₆)alkylamino, thiazolyl(C₁₋₆)-
alkylamino, imidazolyl(C₁₋₆)alkylamino, (C₁₋₆)alkylimidazolyl(C₁₋₆)alkylamino,
pyridinyl(C₁₋₆)alkylamino, (C₁₋₆)alkylpyridinyl(C₁₋₆)alkylamino, N-[(C₁₋₆)alkyl]-N-
30 [pyridinyl(C₁₋₆)alkyl]amino, N-[dihydroxy(C₁₋₆)alkyl]-N-[pyridinyl(C₁₋₆)alkyl]amino, N-
[(C₁₋₆)alkylpyridinyl(C₁₋₆)alkyl]-N-[dihydroxy(C₁₋₆)alkyl]amino, amino(C₁₋₆)alkyl, (C₁₋₆)-
alkylamino(C₁₋₆)alkyl, di(C₁₋₆)alkylamino(C₁₋₆)alkyl, pyridinylamino(C₁₋₆)alkyl, C₂₋₆
alkylcarbonylamino, N-[(C₂₋₆)alkylcarbonyl]-N-[(C₁₋₆)alkylpyridinyl(C₁₋₆)alkyl]amino,

di(C₁₋₆)alkylamino(C₁₋₆)alkylcarbonylamino, C₂₋₆ alkylcarbonylaminomethyl, (C₃₋₇)-cycloalkylcarbonylamino, (C₁₋₆)alkylpiperidinylcarbonylamino, (C₁₋₆)alkylimidazolylcarbonylamino, C₂₋₆ alkoxy carbonylamino, [(C₂₋₆)aloxycarbonyl][(C₁₋₆)alkyl]amino, C₁₋₆ alkylsulphonylamino, formyl, C₂₋₆ alkylcarbonyl, C₂₋₆ alkylcarbonyl oxime, C₂₋₆

5 alkylcarbonyl O-(methyl)oxime, trifluoromethylcarbonyl, carboxy, C₂₋₆ alkoxy carbonyl, aminocarbonyl, C₁₋₆ alkylaminocarbonyl, [hydroxy(C₁₋₆)alkyl]aminocarbonyl, [di(C₁₋₆)-alkylamino(C₁₋₆)alkyl]aminocarbonyl, di(C₁₋₆)alkylaminocarbonyl, [(C₁₋₆)alkyl][cyano-C₁₋₆)alkyl]aminocarbonyl, [(C₁₋₆)alkyl][hydroxy(C₁₋₆)alkyl]aminocarbonyl, [(C₁₋₆)alkoxy-C₁₋₆)alkyl][(C₁₋₆)alkyl]aminocarbonyl, [di(C₁₋₆)alkylamino(C₁₋₆)alkyl][(C₁₋₆)alkyl]amino-

10 carbonyl, C₃₋₇ cycloalkyl(C₁₋₆)alkylaminocarbonyl, aryl(C₁₋₆)alkylaminocarbonyl, (C₁₋₆)-alkylpiperidinylaminocarbonyl, N-[(C₁₋₆)alkyl]-N-[(C₁₋₆)-alkylpiperidinyl]aminocarbonyl, piperidinyl(C₁₋₆)alkylaminocarbonyl, heteroarylaminocarbonyl, heteroaryl(C₁₋₆)alkyl-aminocarbonyl, azetidinylcarbonyl, hydroxyazetidinylcarbonyl, aminoazetidinylcarbonyl, C₂₋₆ alkoxy carbonylaminoazetidinylcarbonyl, pyrrolidinylcarbonyl, (C₁₋₆)alkyl-

15 pyrrolidinylcarbonyl, C₁₋₆ alkoxy(C₁₋₆)alkylpyrrolidinylcarbonyl, di(C₁₋₆)alkylamino-pyrrolidinylcarbonyl, thiazolidinylcarbonyl, oxothiazolidinylcarbonyl, piperidinyl-carbonyl, (C₁₋₆)alkylpiperazinylcarbonyl, morpholinylcarbonyl, C₁₋₆ alkylthio, C₁₋₆ alkylsulphanyl, C₁₋₆ alkylsulphonyl, C₁₋₆ alkylsulphonylmethyl, aminosulphonyl, C₁₋₆ alkylaminosulphonyl, di(C₁₋₆)alkylaminosulphonyl, C₂₋₆ alkoxy carbonyloxy, trimethylsilyl

20 and tetra(C₁₋₆)alkyldioxaborolanyl.

Particular examples of typical substituents on R³ and/or R⁴ include C₁₋₆ alkyl and di(C₁₋₆)alkylaminocarbonyl.

Selected examples of specific substituents on R³ and/or R⁴ include fluoro, chloro, bromo, cyano, nitro, methyl, n-propyl, isopropyl, trifluoromethyl, allyl, cyclopropyl, methylphenyl, dimethylphenyl, piperidinylmethylphenyl, piperazinylmethylphenyl, 25 methylpiperazinylmethylphenyl, morpholinylmethylphenyl, methoxyphenyl, cyanomethoxyphenyl, dimethylaminomethylphenyl, methylaminocarbonylphenyl, benzyl, oxazolinyl, azetidinyl, pyrrolidinyl, chlorophenylpyrrolidinyl, dioxopyrrolidinyl, aminopyrrolidinyl, dimethylaminopyrrolidinyl, indolinyl, oxoindolinyl, phenylpiperidinyl, 30 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,

5 (cyanomethyl)(dimethyl)pyrazolyl, hydroxyethylpyrazolyl, hydroxypropylpyrazolyl, 2-hydroxy-2-methylpropylpyrazolyl, (hydroxyethyl)(dimethyl)pyrazolyl, (hydroxypropyl)-(dimethyl)pyrazolyl, methoxypropylpyrazolyl, (dihydroxypropyl)pyrazolyl, [(hydroxy)-(methoxy)propyl]pyrazolyl, aminoethylpyrazolyl, aminopropylpyrazolyl, (aminopropyl)-(methyl)pyrazolyl, (aminopropyl)(dimethyl)pyrazolyl, dimethylaminoethylpyrazolyl,

10 10 dimethylaminopropylpyrazolyl, diethoxyphosphonopropylpyrazolyl, allylpyrazolyl, cyclopropylmethylpyrazolyl, (cyclopropylmethyl)(dimethyl)pyrazolyl, (methyl)(phenyl)-pyrazolyl, (phenyl)(trifluoromethyl)pyrazolyl, benzylpyrazolyl, aminobenzylpyrazolyl, piperidinylpyrazolyl, tetrahydropyranymethylpyrazolyl, (dimethyl)(tetrahydropyranymethyl)pyrazolyl, pyrrolidinylethylpyrazolyl, piperidinylethylpyrazolyl, methyl-

15 15 piperidinylethylpyrazolyl, morpholinylethylpyrazolyl, pyridinylmethylpyrazolyl, oxypyridinylmethylpyrazolyl, (dimethyl)(phenylcarbonylmethyl)pyrazolyl, (ethyl)(piperazinylcarbonyl)pyrazolyl, (methylaminocarbonyl)(methylphenyl)pyrazolyl, (aminoethylaminocarbonyl)(methyl)pyrazolyl, aminocarbonylmethylpyrazolyl, (aminocarbonylmethyl)(dimethyl)pyrazolyl, dimethylaminocarbonylmethylpyrazolyl,

20 20 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,

25 25 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, 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)-
5 (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-
10 pyridinyloxy, methylpyrazolylpyridinyloxy, isopropylaminopyridinyloxy, carboxy-
pyridinyloxy, aminocarbonylpyridinyloxy, methylpyridazinyloxy, pyrimidinyloxy,
methylpyrimidinyloxy, (chloro)(methyl)pyrimidinyloxy, hydroxymethyl, 1-hydroxy-1-
methylethyl, dihydroxypropyl, pyridinyloxymethyl, methylenedioxy,
difluoromethylenedioxy, amino, isopropylamino, dihydroxypropylamino,
15 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*-
20 (cyclohexyl)-*N*-(methyl)amino, fluorophenylamino, *N*-fluorophenyl-*N*-methylamino,
methylenedioxypyhenylamino, morpholinylmethylphenylamino, oxazolinylphenylamino,
(methyl)(oxo)pyrazolylphenylamino, oxazolylphenylamino, isoxazolylphenylamino,
triazolylphenylamino, methyltriazolylphenylamino, methylpyrimidinylphenylamino,
pyrazolylmethylphenylamino, triazolylmethylphenylamino, methylsulphonylamino-
25 phenylamino, morpholinylcarbonylphenylamino, methylsulphonylphenylamino,
morpholinylsulphonylphenylamino, *N*-benzyl-*N*-methylamino, *N*-(benzyl)-*N*-(dimethyl-
aminoethyl)amino, cyanobenzylamino, (cyano)(phenyl)ethylamino, (cyano)(fluoro)-
benzylamino, methylenedioxypyhenylamino, dihydrobenzofuranylarnino, *N*-(methyl)-*N*-
(methylpyrrolidinyl)amino, methylsulphonylindolinylamino, chromanonylamino,
30 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*-(acetyl)piperidinyl)-*N*-(methyl)amino,

dihydroquinolinylamino, benzoxazinylamino, pyrrolidinylethylamino,
pyrrolidinylpropylamino, *N*-(methyl)-*N*-(pyrrolidinylethyl)amino, *N*-(methyl)-*N*-
(pyrrolidinylpropyl)amino, *N*-(methyl)-*N*-(piperidinylmethyl)amino, benzothienylamino,
indolylamino, dioxoindolylamino, methylpyrazolylamino, (bromo)(methyl)pyrazolyl-
5 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-
10 amino, furyloxadiazolylamino, methylthiadiazolylamino, pyridinylamino, chloropyridinyl-
amino, bromopyridinylamino, methylpyridinylamino, dimethylpyridinylamino,
trifluoromethylpyridinylamino, hydroxypyridinylamino, hydroxyethylpyridinylamino,
dihydroxyethylpyridinylamino, methoxypyridinylamino, dihydroxypropoxypyridinyl-
amino, dimethyldioxolanylmethoxypyridinylamino, methoxyethylpyridinylamino,
15 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*-
20 (methylpyridazinyl)amino, *N*-(benzyl)-*N*-(methylpyridazinyl)amino, dimethyl-
pyridazinylamino, phenylpyridazinylamino, piperidinylpyridazinylamino,
methoxypyridazinylamino, (chloro)(methoxy)pyridazinylamino, dimethylamino-
pyridazinylamino, bis(methylpyridazinyl)amino, methylcinnolinylamino, oxopyrimidinyl-
amino, thioxopyrimidinylamino, quinoxalinylamino, methylchromenylamino,
25 benzofurylmethylamino, thienylmethylamino, indolymethylamino, methylpyrazolyl-
methylamino, (chloro)(dimethyl)pyrazolylmethylamino, dimethylisoxazolylmethylamino,
thiazolymethylamino, imidazolymethylamino, methylimidazolymethylamino,
pyridinylmethylamino, methylpyridinylmethylamino, *N*-(methyl)-*N*-(pyridinylethyl)-
amino, *N*-(dihydroxypropyl)-*N*-(pyridinylmethyl)amino, *N*-(dihydroxypropyl)-*N*-
30 (methylpyridinylmethyl)amino, aminomethyl, methylaminomethyl, dimethylaminomethyl,
pyridinylaminomethyl, acetylarnino, *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, (dimethylaminoethyl)aminocarbonyl, (1-hydroxyprop-2-yl)aminocarbonyl, dimethylamino-
5 carbonyl, *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)amino-
10 carbonyl, piperidinylethylaminocarbonyl, pyrazolylaminocarbonyl, pyridinylmethylaminocarbonyl, azetidinylcarbonyl, hydroxyazetidinylcarbonyl, aminoazetidinylcarbonyl, *tert*-butoxycarbonylaminoazetidinylcarbonyl, pyrrolidinylcarbonyl, methylpyrrolidinylcarbonyl, methoxymethylpyrrolidinylcarbonyl, dimethylaminopyrrolidinylcarbonyl, thiazolidinylcarbonyl, oxothiazolidinylcarbonyl, piperidinylcarbonyl, methylpiperazinyl-
15 carbonyl, morpholinylcarbonyl, isopropylthio, isopropylsulphanyl, methylsulphonyl, isopropylsulphonyl, methylsulphonylmethyl, aminosulphonyl, methylaminosulphonyl, dimethylaminosulphonyl, *tert*-butoxycarbonyloxy, trimethylsilyl and tetramethyl-dioxaborolanyl.

Particular examples of specific substituents on R³ and/or R⁴ include methyl and
20 dimethylaminocarbonyl.

Typical values of R³ include hydrogen, methyl, phenoxyethyl, phenylthiomethyl, aminomethyl, phenylaminomethyl, *N*-methyl-*N*-phenylaminomethyl, pyridinylaminomethyl, benzofurylcarbonylaminomethyl, phenylsulphonylaminomethyl, benzothienyl-methylaminocarbonylmethyl, propynyl, trimethylsilylpropynyl, benzyl, chlorobenzyl,
25 bromobenzyl, methylenedioxypyrenylaminobenzyl, morpholinylmethylphenylaminobenzyl, oxazolinylphenylaminobenzyl, (methyl)(oxo)pyrazolylphenylaminobenzyl, oxazolyl-phenylaminobenzyl, isoxazolylphenylaminobenzyl, triazolylphenylaminobenzyl, methyltriazolylphenylaminobenzyl, methylpyrimidinylphenylaminobenzyl, pyrazolylmethylphenylaminobenzyl, triazolylmethylphenylaminobenzyl,
30 methylsulphonylaminophenylaminobenzyl, morpholinylcarbonylphenylaminobenzyl, methylsulphonylphenylaminobenzyl, morpholinylsulphonylphenylaminobenzyl, dihydrobenzofuranylaminobenzyl, methylsulphonylindolinylaminobenzyl, chromanonylaminobenzyl, dihydroquinolinonylaminobenzyl, benzoxazinonyl-

aminobenzyl, benzothienylaminobenzyl, indolylaminobenzyl, dioxoindolylaminobenzyl, (bromo)(methyl)pyrazolylaminobenzyl, trimethylpyrazolylaminobenzyl, methylindazolylaminobenzyl, benzoxazolylaminobenzyl, benzoxazolonylaminobenzyl, dimethylisoxazolylaminobenzyl, benzothiazolylaminobenzyl, methylisothiazolylaminobenzyl,

5 methylbenzimidazolylaminobenzyl, benzimidazolonylaminobenzyl, dimethylbenzimidazolonylaminobenzyl, methyloxadiazolylaminobenzyl, furyloxadiazolylaminobenzyl, pyridinylaminobenzyl, chloropyridinylaminobenzyl, methylpyridinylaminobenzyl, dimethylpyridinylaminobenzyl, methoxypyridinylaminobenzyl, oxopyridinylaminobenzyl, oxopyrimidinylaminobenzyl, thioxopyrimidinylaminobenzyl, (chloro)-(methoxy)pyridazinylaminobenzyl, methylcinnolinylaminobenzyl, quinoxalinylaminobenzyl, methylchromenylaminobenzyl, benzofurylmethyl, cyanobenzofurylmethyl, methoxycarbonylbenzofurylmethyl, dimethylaminocarbonylbenzofurylmethyl, azetidinylcarbonylbenzofurylmethyl, indolymethyl, fluoroindolymethyl, cyanoindolymethyl, (cyano)(methyl)indolymethyl, nitroindolymethyl,

10 methylindolymethyl, oxazolinylindolymethyl, triazolylindolymethyl, methoxyindolymethyl, (chloro)(methoxy)indolymethyl, di(methoxy)indolymethyl, difluoromethoxyindolymethyl, trifluoromethoxyindolymethyl, (chloro)(trifluoromethoxy)indolymethyl, cyclobutyloxyindolymethyl, cyclopropylmethoxyindolymethyl, morpholinylethoxyindolymethyl, methylenedioxyindolymethyl, difluoromethylenedioxyindolymethyl, azetidinylindolymethyl, morpholinylindolymethyl, acetylaminindolymethyl, acetylaminomethylindolymethyl, methoxycarbonylaminoindolymethyl, N-methoxycarbonyl-N-methylaminoindolymethyl, methylsulphonylaminoindolymethyl, acetylindolymethyl, [acetyl oxime]indolymethyl, [acetyl O-(methyl)oxime]-indolymethyl, trifluoromethylcarbonylindolymethyl, carboxyindolymethyl, (carboxy)-(methyl)indolymethyl, methoxycarbonylindolymethyl, (methoxycarbonyl)(methyl)indolymethyl, (chloro)(methoxycarbonyl)indolymethyl, aminocarbonylindolymethyl, (aminocarbonyl)(chloro)indolymethyl, methylaminocarbonylindolymethyl, (chloro)(methylaminocarbonyl)indolymethyl, (hydroxyethyl)aminocarbonylindolymethyl, (dimethylaminoethyl)aminocarbonylindolymethyl, (1-hydroxyprop-2-yl)aminocarbonylindolymethyl, dimethylaminocarbonylindolymethyl, (dimethylaminocarbonyl)(methyl)indolymethyl, (chloro)(dimethylaminocarbonyl)indolymethyl, bis(dimethylamino-carbonyl)indolymethyl, N-(cyanomethyl)-N-methylaminocarbonylindolymethyl, [N-(cyanomethyl)-N-methylaminocarbonyl](methyl)indolymethyl, N-(cyanoethyl)-N-

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methylaminocarbonylindolylmethyl, *N*-(hydroxyethyl)-*N*-methylaminocarbonyl-indolylmethyl, *N*-(methoxyethyl)-*N*-methylaminocarbonylindolylmethyl, [*N*-(methoxyethyl)-*N*-methylaminocarbonyl](methyl)indolylmethyl, *N*-(dimethylaminoethyl)-*N*-methylaminocarbonylindolylmethyl, *N*-isopropyl-*N*-methylaminocarbonylindolylmethyl,
5 diethylaminocarbonylindolylmethyl, cyclopropylmethylaminocarbonylindolylmethyl, benzylaminocarbonylindolylmethyl, pyrazolylaminocarbonylindolylmethyl, pyridinylmethylaminocarbonylindolylmethyl, azetidinylcarbonylindolylmethyl, (azetidinylcarbonyl)(methyl)indolylmethyl, hydroxyazetidinylcarbonylindolylmethyl, aminoazetidinylcarbonylindolylmethyl, *tert*-butoxycarbonylaminoazetidinylcarbonyl-
10 indolylmethyl, pyrrolidinylcarbonylindolylmethyl, methylpyrrolidinylcarbonyl-indolylmethyl, methoxymethylpyrrolidinylcarbonylindolylmethyl, dimethylamino-pyrrolidinylcarbonylindolylmethyl, thiazolidinylcarbonylindolylmethyl, oxothiazolidinyl-carbonylindolylmethyl, piperidinylcarbonylindolylmethyl, methylpiperazinylcarbonyl-indolylmethyl, morpholinylcarbonylindolylmethyl, methylsulphonylindolylmethyl,
15 methylsulphonylmethylindolylmethyl, dimethylaminosulphonylindolylmethyl, trimethylsilylindolylmethyl and pyrrolo[3,2-*c*]pyridinylmethyl.

A particular value of R³ is (dimethylaminocarbonyl)(methyl)indolylmethyl.

Typical values of R⁴ include hydrogen and methyl. In a preferred embodiment, R⁴ is hydrogen. In another embodiment, R⁴ is C₁₋₆ alkyl, especially methyl.

20 Alternatively, R³ and R⁴, when both are attached to the same carbon atom, may together form an optionally substituted spiro linkage. Thus, R³ and R⁴, when both are attached to the same carbon atom, may represent, when taken together with the carbon atom to which they are both attached, C₃₋₇ cycloalkyl or C₃₋₇ heterocycloalkyl, either of which groups may be unsubstituted, or substituted by one or more, typically by one or two, 25 substituents. In this context, R³ and R⁴, 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.

30 Alternatively, R³ and R⁴, 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, R³ and R⁴, when attached to adjacent carbon atoms, may represent, when taken together with the carbon atoms to which they are attached, C₅₋₇ 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, R³ and R⁴, 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 5 embodiment, R³ and R⁴, 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 10 paragraph include halogen, nitro, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₃₋₇ cycloalkyl, (C₁₋₆)alkylaryl, di(C₁₋₆)alkylaryl, piperidinyl(C₁₋₆)alkylaryl, piperazinyl(C₁₋₆)alkylaryl, (C₁₋₆)alkylpiperazinyl(C₁₋₆)alkylaryl, morpholinyl(C₁₋₆)alkylaryl, (C₁₋₆)alkoxyaryl, cyano(C₁₋₆)alkoxyaryl, di(C₁₋₆)alkylamino(C₁₋₆)alkylaryl, (C₁₋₆)alkylaminocarbonylaryl, aryl(C₁₋₆)alkyl, haloarylpyrrolidinyl, dioxopyrrolidinyl, aminopyrrolidinyl, di(C₁₋₆)alkyl- 15 aminopyrrolidinyl, indolinyl, oxoindolinyl, arylpiperidinyl, arylcarbonylpiperidinyl, di(C₁₋₆)alkylaminocarbonylpiperidinyl, piperazinyl, (C₁₋₆)alkylpiperazinyl, haloaryl-piperazinyl, pyridinylpiperazinyl, furoylpiperazinyl, homopiperazinyl, (C₁₋₆)alkyl-homopiperazinyl, (C₁₋₆)alkylpiperazinyl(C₁₋₆)alkyl, morpholinyl(C₁₋₆)alkyl, benzofuryl, benzothienyl, pyrazolyl, (C₁₋₆)alkylpyrazolyl, di(C₁₋₆)alkylpyrazolyl, tri(C₁₋₆)alkyl- 20 pyrazolyl, (difluoromethyl)pyrazolyl, [di(C₁₋₆)alkyl](trifluoromethyl)pyrazolyl, cyano(C₁₋₆)alkylpyrazolyl, [cyano(C₁₋₆)alkyl][di(C₁₋₆)alkyl]pyrazolyl, hydroxy(C₁₋₆)alkyl-pyrazolyl, [hydroxy(C₁₋₆)alkyl][di(C₁₋₆)alkyl]pyrazolyl, methoxy(C₁₋₆)alkylpyrazolyl, [dihydroxy(C₁₋₆)alkyl]pyrazolyl, [(hydroxy)(methoxy)(C₁₋₆)alkyl]pyrazolyl, amino(C₁₋₆)-alkylpyrazolyl, [(C₁₋₆)alkyl][amino(C₁₋₆)alkyl]pyrazolyl, [amino(C₁₋₆)alkyl][di(C₁₋₆)alkyl]- 25 pyrazolyl, di(C₁₋₆)alkylamino(C₁₋₆)alkylpyrazolyl, di(C₁₋₆)alkoxyphosphono(C₁₋₆)alkyl-pyrazolyl, (C₂₋₆)alkenylpyrazolyl, (C₃₋₇)cycloalkyl(C₁₋₆)alkylpyrazolyl, [(C₃₋₇)cycloalkyl-(C₁₋₆)alkyl][di(C₁₋₆)alkyl]pyrazolyl, [(C₁₋₆)alkyl](aryl)pyrazolyl, (aryl)(trifluoromethyl)-pyrazolyl, aryl(C₁₋₆)alkylpyrazolyl, aminoaryl(C₁₋₆)alkylpyrazolyl, piperidinylpyrazolyl, tetrahydropyranyl(C₁₋₆)alkylpyrazolyl, [di(C₁₋₆)alkyl][tetrahydropyranyl(C₁₋₆)alkyl]- 30 pyrazolyl, pyrrolidinyl(C₁₋₆)alkylpyrazolyl, piperidinyl(C₁₋₆)alkylpyrazolyl, (C₁₋₆)alkyl-piperidinyl(C₁₋₆)alkylpyrazolyl, morpholinyl(C₁₋₆)alkylpyrazolyl, pyridinyl(C₁₋₆)alkyl-pyrazolyl, oxypyridinyl(C₁₋₆)alkylpyrazolyl, [arylcarbonyl(C₁₋₆)alkyl][di(C₁₋₆)alkyl]-pyrazolyl, [(C₁₋₆)alkyl](piperazinylcarbonyl)pyrazolyl, [(C₁₋₆)alkylaminocarbonyl][(C₁₋₆)-

alkylaryl]pyrazolyl, [(C₁₋₆)alkyl][amino(C₁₋₆)alkylaminocarbonyl]pyrazolyl, aminocarbonyl(C₁₋₆)alkylpyrazolyl, [aminocarbonyl(C₁₋₆)alkyl][di(C₁₋₆)alkyl]pyrazolyl, di(C₁₋₆)alkylaminocarbonyl(C₁₋₆)alkylpyrazolyl, pyrazolo[1,5-*a*]pyridinyl, di(C₁₋₆)alkyl-isoxazolyl, (amino)[(C₁₋₆)alkyl]isoxazolyl, thiazolyl, di(C₁₋₆)alkylthiazolyl, imidazolyl,

5 (C₁₋₆)alkylimidazolyl, di(C₁₋₆)alkylimidazolyl, imidazo[1,2-*a*]pyridinyl, (C₁₋₆)alkyl-imidazo[1,2-*a*]pyridinyl, (C₁₋₆)alkylimidazo[4,5-*b*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyrazinyl, (C₁₋₆)alkylthiadiazolyl, pyridinyl, halopyridinyl, (C₁₋₆)alkyl-pyridinyl, [(C₁₋₆)alkyl](halo)pyridinyl, di(C₁₋₆)alkylpyridinyl, (C₂₋₆)alkenylpyridinyl, (C₁₋₆)alkylpiperazinylpyridinyl, [(C₁₋₆)alkyl](piperazinyl)pyridinyl, [(C₁₋₆)alkoxycarbonyl-10 piperazinyl][(C₁₋₆)alkyl]pyridinyl, piperidinyl(C₁₋₆)alkylpyridinyl, [(C₁₋₆)alkyl]-oxy)pyridinyl, hydroxypyridinyl, hydroxy(C₁₋₆)alkylpyridinyl, (C₁₋₆)alkoxypyridinyl, [(C₁₋₆)alkoxy][(C₁₋₆)alkyl]pyridinyl, [(C₁₋₆)alkoxy][di(C₁₋₆)alkyl]pyridinyl, (C₁₋₆)alkoxy(C₁₋₆)alkylpyridinyl, aminopyridinyl, carboxy(C₁₋₆)alkylpyridinyl, (C₁₋₆)alkoxycarbonyl(C₁₋₆)alkylpyridinyl, pyridazinyl, (C₁₋₆)alkylpyridazinyl,

15 piperidinylpyridazinyl, oxypyridazinyl, (C₁₋₆)alkoxypyridazinyl, aminopyridazinyl, hydroxy(C₁₋₆)alkylaminopyridazinyl, di(C₁₋₆)alkylaminopyridazinyl, pyrimidinyl, (C₁₋₆)alkylpyrimidinyl, [(C₁₋₆)alkyl](halo)pyrimidinyl, di(C₁₋₆)alkylpyrimidinyl, pyrrolidinylpyrimidinyl, (C₁₋₆)alkylpiperazinylpyrimidinyl, [(C₁₋₆)alkyl](piperazinyl)-pyrimidinyl, [(C₁₋₆)alkoxycarbonyl][(C₁₋₆)alkyl]piperazinylpyrimidinyl,

20 hydroxypyrimidinyl, [(C₁₋₆)alkyl](hydroxy)pyrimidinyl, [(C₁₋₆)alkyl][hydroxy(C₁₋₆)alkyl]-pyrimidinyl, [(C₁₋₆)alkyl][hydroxy(C₂₋₆)alkynyl]pyrimidinyl, (C₁₋₆)alkoxypyrimidinyl, aminopyrimidinyl, di(C₁₋₆)alkylaminopyrimidinyl, [di(C₁₋₆)alkylamino](halo)pyrimidinyl, carboxypyrimidinyl, [(C₁₋₆)alkoxycarbonyl(C₁₋₆)alkyl][(C₁₋₆)alkyl]pyrimidinyl, aminocarbonylpyrimidinyl, pyrazinyl, (C₁₋₆)alkoxypyrazinyl, aminopyrazinyl, hydroxy,

25 (C₁₋₆)alkoxy, aryl(C₁₋₆)alkoxycarbonylpiperidinyloxy, morpholinyl(C₁₋₆)alkoxy, aryloxy, haloaryloxy, di(C₁₋₆)alkylpyrazolinyloxy, halopyridinyloxy, pyrrolidinylpyridinyloxy, (C₁₋₆)alkylpiperazinylpyridinyloxy, (C₁₋₆)alkylpyrazolylpyridinyloxy, (C₁₋₆)alkylaminopyridinyloxy, carboxypyridinyloxy, aminocarbonylpyridinyloxy, pyridazinyloxy, (C₁₋₆)alkylpyridazinyloxy, pyrimidinyloxy, (C₁₋₆)alkylpyrimidinyloxy,

30 [(C₁₋₆)alkyl](halo)pyrimidinyloxy, hydroxy(C₁₋₆)alkyl, dihydroxy(C₁₋₆)alkyl, pyridinyloxy(C₁₋₆)alkyl, amino, (C₁₋₆)alkylamino, dihydroxy(C₁₋₆)alkylamino, (C₁₋₆)-alkoxy(C₁₋₆)alkylamino, *N*-[(C₁₋₆)alkoxy(C₁₋₆)alkyl]-*N*-[(C₁₋₆)alkyl]amino, di(C₁₋₆)-alkylamino(C₁₋₆)alkylamino, *N*-[(C₁₋₆)alkyl]-*N*-[di(C₁₋₆)alkylamino(C₁₋₆)alkyl]amino, *N*-

[(C₁₋₆)alkyl]-N-[(C₃₋₇)cycloalkyl]amino, haloaryl amino, N-[(C₁₋₆)alkyl]-N-(haloaryl)amino, N-[(C₁₋₆)alkyl]-N-[aryl(C₁₋₆)alkyl]amino, N-[di(C₁₋₆)alkylamino(C₁₋₆)alkyl]-N-[aryl(C₁₋₆)alkyl]amino, cyanoaryl(C₁₋₆)alkylamino, (cyano)(halo)aryl(C₁₋₆)alkylamino, methylene-dioxyaryl(C₁₋₆)alkylamino, N-[(C₁₋₆)alkyl]-N-[(C₁₋₆)alkylpyrrolidinyl]amino, piperidinyl-amino, N-[(C₁₋₆)alkyl]-N-(piperidinyl)amino, N-[(C₃₋₇)cycloalkyl(C₁₋₆)alkyl]-N-(piperidinyl)amino, (C₁₋₆)alkylpiperidinylamino, N-[(C₁₋₆)alkyl]-N-[(C₁₋₆)alkyl-piperidinyl]amino, N-[(C₁₋₆)alkyl]-N-[(C₃₋₇)cycloalkylpiperidinyl]amino, N-[(C₁₋₆)alkyl]-N-[(C₂₋₆)alkylcarbonylpiperidinyl]amino, pyrrolidinyl(C₁₋₆)alkylamino, N-[(C₁₋₆)alkyl]-N-[pyrrolidinyl(C₁₋₆)alkyl]amino, N-[(C₁₋₆)alkyl]-N-[piperidinyl(C₁₋₆)alkyl]amino, (C₁₋₆)-alkylpyrazolylamino, di(C₁₋₆)alkylpyrazolylamino, tri(C₁₋₆)alkylpyrazolylamino, N-[(C₁₋₆)-alkyl]-N-[(C₁₋₆)alkylpyrazolyl]amino, thiazolylamino, imidazolylamino, [(C₁₋₆)alkoxy-carbonyl][(C₁₋₆)alkyl]imidazolylamino, (C₁₋₆)alkylthiadiazolylamino, pyridinylamino, halopyridinylamino, (C₁₋₆)alkylpyridinylamino, di(C₁₋₆)alkylpyridinylamino, trifluoro-methylpyridinylamino, hydroxypyridinylamino, hydroxy(C₁₋₆)alkylpyridinylamino, dihydroxy(C₁₋₆)alkylpyridinylamino, (C₁₋₆)alkoxypyridinylamino, dihydroxy(C₁₋₆)alkoxy-pyridinylamino, di(C₁₋₆)alkyldioxolanyl(C₁₋₆)alkoxypyridinylamino, (C₁₋₆)alkoxy(C₁₋₆)-alkylpyridinylamino, (C₁₋₆)alkoxy(C₂₋₆)alkenylpyridinylamino, dihydroxy(C₁₋₆)alkyl-aminopyridinylamino, di(C₁₋₆)alkylaminopyridinylamino, (C₁₋₆)alkylamino(C₁₋₆)alkyl-pyridinylamino, di(C₁₋₆)alkylamino(C₁₋₆)alkylpyridinylamino, carboxypyridinylamino, N-[(C₁₋₆)alkyl]-N-[(C₁₋₆)alkylpyridinyl]amino, bis[(C₁₋₆)alkylpyridinyl]amino, bis(trifluoro-methylpyridinyl)amino, isoquinolinylamino, (C₁₋₆)alkylpyridazinylamino, N-[(C₁₋₆)alkyl]-N-[(C₁₋₆)alkylpyridazinyl]amino, N-[aryl(C₁₋₆)alkyl]-N-[(C₁₋₆)alkylpyridazinyl]amino, di(C₁₋₆)alkylpyridazinylamino, arylpyridazinylamino, piperidinylpyridazinylamino, (C₁₋₆)-alkoxypyridazinylamino, di(C₁₋₆)alkylaminopyridazinylamino, bis[(C₁₋₆)alkylpyridazinyl]-amino, benzofuryl(C₁₋₆)alkylamino, thienyl(C₁₋₆)alkylamino, indolyl(C₁₋₆)alkylamino, (C₁₋₆)alkylpyrazolyl(C₁₋₆)alkylamino, [di(C₁₋₆)alkyl](halo)pyrazolyl(C₁₋₆)alkylamino, di(C₁₋₆)alkylisoxazolyl(C₁₋₆)alkylamino, thiazolyl(C₁₋₆)alkylamino, imidazolyl(C₁₋₆)alkyl-amino, (C₁₋₆)alkylimidazolyl(C₁₋₆)alkylamino, pyridinyl(C₁₋₆)alkylamino, (C₁₋₆)alkyl-pyridinyl(C₁₋₆)alkylamino, N-[(C₁₋₆)alkyl]-N-[pyridinyl(C₁₋₆)alkyl]amino, N-[dihydroxy-(C₁₋₆)alkyl]-N-[pyridinyl(C₁₋₆)alkyl]amino, N-[(C₁₋₆)alkylpyridinyl(C₁₋₆)alkyl]-N-[dihydroxy(C₁₋₆)alkyl]amino, amino(C₁₋₆)alkyl, (C₁₋₆)alkylamino(C₁₋₆)alkyl, di(C₁₋₆)alkyl-amino(C₁₋₆)alkyl, pyridinylamino(C₁₋₆)alkyl, N-[(C₂₋₆)alkylcarbonyl]-N-[(C₁₋₆)alkyl-pyridinyl(C₁₋₆)alkyl]amino, di(C₁₋₆)alkylamino(C₁₋₆)alkylcarbonylamino, (C₃₋₇)cycloalkyl-

carbonylamino, (C₁₋₆)alkylpiperidinylcarbonylamino, (C₁₋₆)alkylimidazolylcarbonylamino, formyl, C₂₋₆ alkylcarbonyl, (C₁₋₆)alkylpiperidinylaminocarbonyl, N-[(C₁₋₆)alkyl]-N-[(C₁₋₆)-alkylpiperidinyl]aminocarbonyl, piperidinyl(C₁₋₆)alkylaminocarbonyl, (C₁₋₆)alkyl-piperazinylcarbonyl, C₁₋₆ alkylthio, C₁₋₆ alkylsulphanyl, C₁₋₆ alkylsulphonyl, C₂₋₆

5 alkoxy carbonyloxy and tetra(C₁₋₆)alkyldioxaborolanyl.

Particular examples of typical substituents on the fused rings referred to in the two preceding paragraphs include halogen, hydroxy(C₁₋₆)alkylpyrazolyl and [dihydroxy(C₁₋₆)-alkyl]pyrazolyl.

Selected examples of specific substituents on the fused rings referred to in the three preceding paragraphs include fluoro, chloro, bromo, nitro, methyl, *n*-propyl, isopropyl, allyl, cyclopropyl, methylphenyl, dimethylphenyl, piperidinylmethylphenyl, piperazinylmethylphenyl, methylpiperazinylmethylphenyl, morpholinylmethylphenyl, methoxyphenyl, cyanomethoxyphenyl, dimethylaminomethylphenyl, methylaminocarbonylphenyl, benzyl, chlorophenylpyrrolidinyl, dioxopyrrolidinyl, 15 aminopyrrolidinyl, dimethylaminopyrrolidinyl, indolinyl, oxoindolinyl, phenylpiperidinyl, benzoylpiperidinyl, diethylaminocarbonylpiperidinyl, piperazinyl, methylpiperazinyl, chlorophenylpiperazinyl, pyridinylpiperazinyl, furoylpiperazinyl, homopiperazinyl, methylhomopiperazinyl, methylpiperazinylmethyl, methylpiperazinylethyl, morpholinylmethyl, benzofuryl, benzothienyl, pyrazolyl, methylpyrazolyl, ethylpyrazolyl, 20 propylpyrazolyl, 2-methylpropylpyrazolyl, 3-methylbutylpyrazolyl, dimethylpyrazolyl, trimethylpyrazolyl, (dimethyl)(ethyl)pyrazolyl, (dimethyl)(isopropyl)pyrazolyl, (dimethyl)(2-methylpropyl)pyrazolyl, (dimethyl)(3-methylbutyl)pyrazolyl, (difluoromethyl)pyrazolyl, (dimethyl)(trifluoromethyl)pyrazolyl, cyanomethylpyrazolyl, (cyanomethyl)(dimethyl)pyrazolyl, hydroxyethylpyrazolyl, hydroxypropylpyrazolyl, 2- 25 hydroxy-2-methylpropylpyrazolyl, (hydroxymethyl)(isopropyl)(methyl)pyrazolyl, (hydroxyethyl)(dimethyl)pyrazolyl, (hydroxypropyl)(dimethyl)pyrazolyl, methoxypropylpyrazolyl, (dihydroxypropyl)pyrazolyl, [(hydroxy)(methoxy)propyl]-pyrazolyl, aminoethylpyrazolyl, aminopropylpyrazolyl, (aminopropyl)(methyl)pyrazolyl, (aminopropyl)(dimethyl)pyrazolyl, dimethylaminoethylpyrazolyl, 30 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,

5 (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, (1-hydroxy-1-methylethyl)pyridinyl,

10 15 methoxypyridinyl, (methoxy)(methyl)pyridinyl, (dimethyl)(methoxy)pyridinyl, methoxymethylpyridinyl, aminopyridinyl, carboxymethylpyridinyl, ethoxycarbonylmethylpyridinyl, pyridazinyl, methylpyridazinyl, piperidinylpyridazinyl, oxypyridazinyl, methoxypyridazinyl, aminopyridazinyl, hydroxyethylaminopyridazinyl, dimethylaminopyridazinyl, pyrimidinyl, methylpyrimidinyl, (chloro)(methyl)pyrimidinyl,

20 25 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, (methoxycarbonyl-methyl)(methyl)pyrimidinyl, aminocarbonylpyrimidinyl, pyrazinyl, methoxypyrazinyl, aminopyrazinyl, hydroxy, methoxy, isopropoxy, benzyloxycarbonylpiperidinyloxy, morpholinylethoxy, phenoxy, fluorophenoxy, dimethylpyrazolyloxy, bromopyridinyloxy, pyrrolidinylpyridinyloxy, methylpiperazinylpyridinyloxy, methylpyrazolylpyridinyloxy,

30 35 isopropylaminopyridinyloxy, carboxypyridinyloxy, aminocarbonylpyridinyloxy, pyridazinyloxy, 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*-
5 (*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*-
10 (*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*-(acetyl)piperidinyl)-*N*-(methyl)amino, pyrrolidinylethylamino,
pyrrolidinylpropylamino, *N*-(methyl)-*N*-(pyrrolidinylethyl)amino, *N*-(methyl)-*N*-
15 (*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,
20 trifluoromethylpyridinylamino, hydroxypyridinylamino, hydroxyethylpyridinylamino,
dihydroxyethylpyridinylamino, methoxypyridinylamino, dihydroxypropoxypyridinyl-
amino, dimethyldioxolanylmethoxypyridinylamino, methoxyethylpyridinylamino,
methoxyvinylpyridinylamino, dihydroxypropylaminopyridinylamino, dimethylamino-
pyridinylamino, methylaminomethylpyridinylamino, dimethylaminomethylpyridinyl-
25 amino, 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, phenylpyridazinyl-
amino, piperidinylpyridazinylamino, methoxypyridazinylamino, dimethylamino-
30 pyridazinylamino, bis(methylpyridazinyl)amino, benzofurylmethylamino, thienylmethyl-
amino, indolylmethylamino, methylpyrazolylmethylamino, (chloro)(dimethyl)pyrazolyl-
methylamino, dimethylisoxazolylmethylamino, thiazolylmethylamino, imidazolylmethyl-
amino, methylimidazolylmethylamino, pyridinylmethylamino, methylpyridinylmethyl-

amino, *N*-(methyl)-*N*-(pyridinylethyl)amino, *N*-(dihydroxypropyl)-*N*-(pyridinylmethyl)-amino, *N*-(dihydroxypropyl)-*N*-(methylpyridinylmethyl)amino, aminomethyl, methylaminomethyl, dimethylaminomethyl, pyridinylaminomethyl, *N*-(acetyl)-*N*-(methyl-pyridinyl)amino, dimethylaminoethylcarbonylamino, cyclohexylcarbonylamino,

5 methylpiperidinylcarbonylamino, methylimidazolylcarbonylamino, formyl, acetyl, methylpiperidinylaminocarbonyl, *N*-(methyl)-*N*-(methylpiperidinyl)aminocarbonyl, piperidinylethylaminocarbonyl, methylpiperazinylcarbonyl, isopropylthio, isopropyl-sulphanyl, isopropylsulphonyl, *tert*-butoxycarbonyloxy and tetramethyldioxaborolanyl.

Particular examples of such substituents include bromo, hydroxyethylpyrazolyl and
10 (dihydroxypropyl)pyrazolyl.

Suitably, R^a represents substituted or unsubstituted aryl.

Suitably, R^c represents hydrogen; or aryl, aryl(C₁₋₆)alkyl, heteroaryl(C₁₋₆)alkyl or (aryl)(heteroaryl)(C₁₋₆)alkyl, any of which groups may be optionally substituted by one or more substituents.

15 Examples of typical substituents on R^a and/or R^b and/or R^c and/or R^f include halogen, cyano, nitro, C₁₋₆ alkyl, trifluoromethyl, hydroxy, C₁₋₆ alkoxy, difluoromethoxy, trifluoromethoxy, aryloxy, C₁₋₆ alkylthio, C₁₋₆ alkylsulphonyl, amino, C₁₋₆ alkylamino, di(C₁₋₆)alkylamino, C₂₋₆ alkylcarbonylamino, C₂₋₆ alkoxy carbonylamino, C₁₋₆ alkylsulphonylamino, formyl, C₂₋₆ alkylcarbonyl, carboxy, C₂₋₆ alkoxy carbonyl, 20 aminocarbonyl, C₁₋₆ alkylaminocarbonyl, di(C₁₋₆)alkylaminocarbonyl, aminosulphonyl, C₁₋₆ alkylaminosulphonyl and di(C₁₋₆)alkylaminosulphonyl.

Examples of particular substituents on R^a and/or R^b and/or R^c and/or R^f include fluoro, chloro, bromo, cyano, nitro, methyl, trifluoromethyl, hydroxy, methoxy, difluoromethoxy, trifluoromethoxy, phenoxy, methylthio, methylsulphonyl, amino, 25 methylamino, dimethylamino, acetyl amine, methoxycarbonylamino, methylsulphonylamino, formyl, acetyl, carboxy, methoxycarbonyl, aminocarbonyl, methylaminocarbonyl, dimethylaminocarbonyl, aminosulphonyl, methylaminosulphonyl and dimethylaminosulphonyl.

A particular value of R^a is phenyl.

30 In one embodiment, R^b represents hydrogen. In another embodiment, R^b represents C₁₋₆ 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 C₁₋₆ alkyl, especially methyl or ethyl, particularly ethyl.

Suitably, R^e represents methyl.

Suitably, R^f represents optionally substituted aryl, especially phenyl.

- 5 Generally, R⁵ represents hydrogen, halogen, cyano, -SR^a, -COR^e, -CO₂R^b,
-CONR^cR^d or -C(=N-OR^f)R^e; or R⁵ represents C₁₋₆ alkyl, C₂₋₆ alkenylcarbonyl, C₂₋₆
alkynyl, C₃₋₇ cycloalkyl(C₂₋₆)alkynyl, aryl, aryl(C₁₋₆)alkyl, aryl(C₂₋₆)alkenyl, aryl(C₂₋₆)
alkynyl, biaryl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkyl, C₃₋₇ heterocycloalkyl(C₂₋₆)alkynyl, C₃₋₇
heterocycloalkylcarbonyl(C₂₋₆)alkynyl, C₅₋₉ heterobicycloalkyl(C₂₋₆)alkynyl, C₃₋₇
10 heterocycloalkyl-aryl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkyl-aryl, C₃₋₇ heterocycloalkyl-biaryl,
heteroaryl, heteroaryl(C₁₋₆)alkyl, heteroaryl(C₁₋₆)alkylcarbonyl, heteroaryl(C₂₋₆)alkenyl,
heteroaryl(C₂₋₆)alkynyl, heteroaroylcarbonyl, C₃₋₇ heterocycloalkyl-heteroaryl, C₃₋₇
heterocycloalkyl-heteroaryl(C₂₋₆)alkynyl, heteroaryl-aryl, aryl-heteroaryl, C₃₋₇
heterocycloalkyl-aryl-heteroaryl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkyl-aryl-heteroaryl, C₅₋₉
15 heterobicycloalkyl(C₁₋₆)alkyl-aryl-heteroaryl, heteroaryl-aryl-heteroaryl, bi(heteroaryl),
C₃₋₇ heterocycloalkylcarbonyl-bi(heteroaryl), aryloxyaryl, aryl(C₁₋₆)alkoxyaryl,
heteroaryl(C₁₋₆)alkoxyaryl, aryl(C₁₋₆)alkylaminoaryl, heteroaryl(C₁₋₆)alkylaminoaryl, C₃₋₇
cycloalkylcarbonylaminoaryl, arylcarbonylaminoaryl, aryl(C₁₋₆)alkylcarbonylaminoaryl,
C₃₋₇ heterocycloalkylcarbonylaminoaryl, heteroarylcarbonylaminoaryl, aryl-
20 (C₃₋₇)heterocycloalkylcarbonylaminoaryl, arylsulphonylaminoaryl, aryl(C₁₋₆)alkyl-
sulphonylaminoaryl, heteroaryl(C₁₋₆)alkylsulphonylaminoaryl, C₃₋₇ cycloalkylamino-
carbonylaminoaryl, arylaminocarbonylaminoaryl, C₃₋₇ heterocycloalkylaminocarbonyl-
aminoaryl, C₃₋₇ heterocycloalkylaminocarbonylaminoaryl, heteroaryl(C₁₋₆)alkyl-
aminocarbonylaminoaryl, C₃₋₇ heterocycloalkylcarbonylcarbonylaminoaryl, C₃₋₇
25 heterocycloalkyl(C₁₋₆)alkylaminocarbonylcarbonylaminoaryl, arylcarbonylaryl, C₃₋₇
heterocycloalkylcarbonylaryl, C₃₋₇ heterocycloalkylcarbonyl(C₁₋₆)alkylaryl, aryl(C₁₋₆)-
alkylaminocarbonylaryl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkylaminocarbonylaryl, heteroaryl-
aminocarbonylaryl, heteroaryl(C₁₋₆)alkylaminocarbonylaryl, C₃₋₇ heterocycloalkylamino-
carbonyl(C₁₋₆)alkylaryl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkylaminocarbonyl(C₁₋₆)alkylaryl,
30 heteroarylaminocarbonyl(C₁₋₆)alkylaryl, heteroaryl(C₁₋₆)alkylaminocarbonyl(C₁₋₆)alkyl-
aryl, arylaminoheteroaryl, C₃₋₇ heterocycloalkylamino-aryl-heteroaryl, C₃₋₇
heterocycloalkylcarbonylamino-aryl-heteroaryl, C₃₋₇ heterocycloalkylaminocarbonyl-
amino-aryl-heteroaryl, C₃₋₇ cycloalkylcarbonyl-aryl-heteroaryl, C₃₋₇ heterocycloalkyl-

carbonyl-aryl-heteroaryl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkylcarbonyl-aryl-heteroaryl, C₅₋₉ heterobicycloalkylcarbonyl-aryl-heteroaryl, C₃₋₇ heterocycloalkylcarbonyl(C₁₋₆)alkyl-aryl-heteroaryl, C₃₋₇ heterocycloalkyl-aminocarbonyl-aryl-heteroaryl, C₃₋₇ heterocycloalkyl-(C₁₋₆)alkylaminocarbonyl-aryl-heteroaryl or C₃₋₇ heterocycloalkylaminocarbonyl(C₁₋₆)-

- 5 alkyl-aryl-heteroaryl, any of which groups may be optionally substituted by one or more substituents.

Suitably, R⁵ represents hydrogen, halogen, cyano, -SR^a, -COR^e, -CO₂R^b or -CONR^cR^d; or R⁵ represents methyl, propyl, ethenylcarbonyl, ethynyl, propynyl, butynyl, 3-methylbutynyl, cyclopropylethynyl, cyclohexylethynyl, phenyl, naphthyl, benzyl, 10 phenylethyl, phenylethenyl, phenylethynyl, phenylpropynyl, biphenyl, piperidinylethyl, pyrrolidinylethynyl, piperidinylethynyl, 1,2,3,4-tetrahydroisoquinolinylpropynyl, piperazinylpropynyl, pyrrolidinylcarbonylethynyl, quinuclidinylethynyl, piperazinyl-phenyl, morpholinylphenyl, piperidinylmethylphenyl, piperazinylbiphenyl, benzofuryl, dibenzofuryl, benzothienyl, dibenzothienyl, pyridinyl, isoquinolinyl, imidazolylethyl, 15 imidazolylmethylcarbonyl, imidazolylethenyl, indolylethynyl, pyrazolylethynyl, imidazolylethynyl, pyridinylethynyl, pyrimidinylethynyl, imidazo[1,2-a]pyridinylethynyl, imidazolylcarbonylcarbonyl, benzomorpholinylpyridinyl, pyrrolidinylpyridinylethynyl, pyrazolylphenyl, pyridinylphenyl, phenylisoxazolyl, phenylthiazolyl, phenylpyridinyl, phenylpyrimidinyl, azetidinylphenylpyridinyl, pyrrolidinylphenylpyridinyl, 20 piperidinylphenylpyridinyl, piperazinylphenylpyridinyl, morpholinylphenylpyridinyl, piperazinylphenylpyrimidinyl, pyrrolidinylmethylphenylpyridinyl, piperidinylmethyl-phenylpyridinyl, piperazinylmethylphenylpyridinyl, homopiperazinylmethylphenyl-pyridinyl, morpholinylmethylphenylpyridinyl, azabicyclo[3.2.1]octylmethylphenyl-pyridinyl, diazabicyclo[3.2.1]octylmethylphenylpyridinyl, tetrazolylphenylpyridinyl, 25 benzofurylpyridinyl, benzothienylpyridinyl, indolylpyridinyl, isoxazolylpyridinyl, bi(pyridinyl), isoquinolinylpyridinyl, morpholinylcarbonylbi(pyridinyl), phenoxyphenyl, benzyloxyphenyl, pyridinylmethoxyphenyl, benzylaminophenyl, furylmethylaminophenyl, pyridinylmethylaminophenyl, cyclopentylcarbonylaminophenyl, phenylcarbonylamino-phenyl, benzylcarbonylaminophenyl, pyrrolidinylcarbonylaminophenyl, piperidinyl-30 carbonylaminophenyl, piperazinylcarbonylaminophenyl, morpholinylcarbonylamino-phenyl, indolylcarbonylaminophenyl, isoxazolylcarbonylaminophenyl, pyridinylcarbonyl-aminophenyl, phenylpyrrolidinylcarbonylaminophenyl, phenylsulphonylaminophenyl, benzylsulphonylaminophenyl, isoxazolylsulphonylaminophenyl, cyclopentylamino-

carbonylaminophenyl, phenylaminocarbonylaminophenyl, azetidinylaminocarbonylaminophenyl, morpholinylethylaminocarbonylaminophenyl, imidazolylmethylaminocarbonylaminophenyl, morpholinylcarbonylcarbonylaminophenyl, pyrrolidinylethylaminocarbonylcarbonylaminophenyl, phenylcarbonylphenyl, morpholinylcarbonylphenyl, pyrrolidinylcarbonylmethylphenyl, piperidinylcarbonylmethylphenyl, benzylaminocarbonylphenyl, morpholinylethylaminocarbonylphenyl, imidazolylaminocarbonylphenyl, imidazolylmethylaminocarbonylphenyl, pyridinylmethylaminocarbonylphenyl, azetidinylaminocarbonylmethylphenyl, pyrrolidinylmethylaminocarbonylmethylphenyl, pyridinylaminocarbonylmethylphenyl, pyridinylmethylaminocarbonylmethylphenyl, phenylaminopyridinyl, azetidinylaminophenylpyridinyl, pyrrolidinylaminophenylpyridinyl, piperazinylcarbonylaminophenylpyridinyl, piperidinylaminocarbonylaminophenylpyridinyl, cyclopropylcarbonylphenylpyridinyl, pyrrolidinylcarbonylphenylpyridinyl, piperidinylcarbonylphenylpyridinyl, piperazinylcarbonylphenylpyridinyl, morpholinylcarbonylphenylpyridinyl, piperidinylcarbonylphenylpyrimidinyl, morpholinylmethylcarbonylphenylpyridinyl, azabicyclo[3.2.1]octylcarbonylphenylpyridinyl, azetidinylcarbonylmethylphenylpyridinyl, pyrrolidinylcarbonylmethylphenylpyridinyl, piperidinylcarbonylmethylphenylpyridinyl, piperazinylcarbonylmethylphenylpyridinyl, azetidinylaminocarbonylphenylpyridinyl, pyrrolidinylaminocarbonylphenylpyridinyl, 20 piperidinylaminocarbonylphenylpyridinyl, piperidinylmethylaminocarbonylphenylpyridinyl or azetidinylaminocarbonylmethylphenylpyridinyl, any of which groups may be optionally substituted by one or more substituents.

Examples of representative substituents on R⁵ include halogen, cyano, nitro, oxo, C₁₋₆ alkyl, trifluoromethyl, hydroxy, hydroxy(C₁₋₆)alkyl, C₁₋₆ alkoxy, dihydroxy(C₁₋₆)-alkoxy, aryl(C₁₋₆)alkoxy, methoxyaryl(C₁₋₆)alkoxy, amino, C₁₋₆ alkylamino, di(C₁₋₆)-alkylamino, amino(C₁₋₆)alkyl, C₁₋₆ alkylamino(C₁₋₆)alkyl, di(C₁₋₆)alkylamino(C₁₋₆)alkyl, di(C₁₋₆)alkylamino(C₁₋₆)alkylamino, methoxyaryl(C₁₋₆)alkylamino, C₁₋₆ alkylcarbonyl-amino, C₁₋₆ alkoxy carbonyl(C₁₋₆)alkylcarbonylamino, C₁₋₆ alkylcarbonylamino(C₁₋₆)alkyl, C₁₋₆ alkoxy carbonyl-amino, N-(C₁₋₆ alkoxy carbonyl)-N-(C₁₋₆ alkyl)amino, C₁₋₆ alkoxy carbonyl-amino(C₁₋₆)alkyl, N-(C₁₋₆ alkoxy carbonyl)-N-(C₁₋₆ alkyl)amino(C₁₋₆)alkyl, C₁₋₆ alkylsulphonylamino, C₁₋₆ alkylsulphonylamino(C₁₋₆)alkyl, C₁₋₆ alkylaminocarbonylamino, di(C₁₋₆)alkylamino(C₁₋₆)alkylaminocarbonylamino, N-(C₁₋₆ alkyl)-N-[di(C₁₋₆)alkylamino-(C₁₋₆)alkyl]aminocarbonylamino, carboxycarbonylamino, C₁₋₆ alkoxy carbonyl-

carbonylamino, C₁₋₆ alkylaminocarbonylcarbonylamino, di(C₁₋₆)alkylamino(C₁₋₆)alkylaminocarbonylcarbonylamino, di(C₁₋₆)alkylaminosulphonylamino, formyl, C₁₋₆ alkylcarbonyl, di(C₁₋₆)alkylamino(C₁₋₆)alkylcarbonyl, carboxy, carboxy(C₁₋₆)alkyl, C₁₋₆ alkoxy carbonyl, C₁₋₆ alkoxy carbonyl(C₁₋₆)alkyl, aminocarbonyl, C₁₋₆ alkylaminocarbonyl,
5 di(C₁₋₆)alkylaminocarbonyl, cyano(C₁₋₆)alkylaminocarbonyl, di(C₁₋₆)alkylamino(C₁₋₆)-alkylaminocarbonyl, dihydroxy(C₁₋₆)alkylaminocarbonyl, N-(C₁₋₆ alkyl)-N-[amino(C₁₋₆)-alkyl]aminocarbonyl, N-(C₁₋₆ alkyl)-N-[di(C₁₋₆)alkylamino(C₁₋₆)alkyl]aminocarbonyl, di(C₁₋₆)alkylaminocarbonyl(C₁₋₆)alkyl, N-(C₁₋₆ alkyl)-N-[di(C₁₋₆)alkylamino(C₁₋₆)alkyl]-aminocarbonyl(C₁₋₆)alkyl, aminocarbonyl(C₁₋₆)alkoxy, C₁₋₆ alkoxyaminocarbonyl, N-(C₁₋₆ 10 alkoxy)-N-(C₁₋₆ alkyl)aminocarbonyl, C₁₋₆ alkylsulphonyl, C₁₋₆ alkylsulphonyloxy(C₁₋₆)-alkyl, trifluoromethylsulphonyloxy and tri(C₁₋₆)alkylsilyl; especially halogen or di(C₁₋₆)-alkylaminocarbonyl.

Examples of specific substituents on R⁵ include fluoro, chloro, bromo, cyano, nitro, oxo, methyl, ethyl, isopropyl, trifluoromethyl, hydroxy, hydroxymethyl, methoxy, ethoxy, 15 dihydroxypropoxy, isobutoxy, benzyloxy, methoxybenzyloxy, amino, methylamino, dimethylamino, diethylamino, aminomethyl, methylaminomethyl, dimethylaminomethyl, N-isopropyl-N-methylaminomethyl, dimethylaminoethylamino, methoxybenzylamino, acetylamino, ethoxycarbonylacetyl amine, ethylcarbonylamino, methoxycarbonyl-ethylcarbonylamino, 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, dimethylaminoethyl-aminocarbonylcarbonylamino, dimethylaminosulphonylamino, formyl, acetyl, dimethyl-aminoacetyl, ethylcarbonyl, carboxy, carboxymethyl, methoxycarbonyl, ethoxycarbonyl, *tert*-butoxycarbonyl, methoxycarbonylmethyl, *tert*-butoxycarbonylmethyl, aminocarbonyl, methylaminocarbonyl, cyanomethylaminocarbonyl, ethylaminocarbonyl, dimethylaminoethylaminocarbonyl, dihydroxypropylaminocarbonyl, isopropylaminocarbonyl, 25 dimethylaminocarbonyl, N-ethyl-N-methylaminocarbonyl, N-(aminoethyl)-N-(methyl)aminocarbonyl, N-(dimethylaminoethyl)-N-(methyl)aminocarbonyl, diethylamino-carbonyl, dimethylaminocarbonylmethyl, N-(diethylaminoethyl)-N-(methyl)aminocarbonylmethyl, aminocarbonylmethoxy, methoxyaminocarbonyl, N-(methoxy)-N-30

(methyl)aminocarbonyl, methylsulphonyl, methylsulphonyloxymethyl, trifluoromethylsulphonyloxy and tri(C₁₋₆)alkylsilyl; especially fluoro or dimethylaminocarbonyl.

Specific values of R⁵ include hydrogen, fluoro, chloro, bromo, iodo, cyano, phenylthio, acetyl, carboxy, methoxycarbonyl, ethoxycarbonyl, aminocarbonyl, phenylaminocarbonyl, benzylaminocarbonyl, pyridinylmethyldimethylaminocarbonyl, (phenyl)(pyridinyl)methylaminocarbonyl, N-ethyl-N-pyridinylmethylaminocarbonyl, dimethylaminomethyl, dimethylaminosulphonylaminopropyl, dimethylaminoethenylcarbonyl, ethynyl, triethylsilylethynyl, diethylaminopropynyl, methylsulphonylaminopropynyl, dimethylaminosulphonylaminopropynyl, hydroxybutynyl, 3-hydroxy-3-methylbutynyl, cyclopropylethynyl, hydroxycyclohexyl-ethynyl, aminocyclohexylethynyl, phenyl, bromophenyl, (bromo)(nitro)phenyl, hydroxyphenyl, methoxyphenyl, ethoxyphenyl, isobutoxyphenyl, (benzyloxy)(chlorophenyl, aminophenyl, (amino)(bromo)phenyl, aminomethylphenyl, acetylaminophenyl, ethoxycarbonylacetylaminophenyl, ethylcarbonylaminophenyl, methoxycarbonyl-ethylcarbonylaminophenyl, methylsulphonylaminophenyl, ethylsulphonylaminophenyl, ethylaminocarbonylaminophenyl, dimethylaminoethylaminocarbonylaminophenyl, N-(dimethylaminoethyl)-N-(methyl)aminocarbonylaminophenyl, carboxycarbonylamino-phenyl, ethoxycarbonylcarbonylaminophenyl, ethylaminocarbonylcarbonylaminophenyl, dimethylaminoethylaminocarbonylcarbonylaminophenyl, acetylphenyl, carboxyphenyl, carboxymethylphenyl, methoxycarbonylphenyl, (chloro)(methoxycarbonyl)phenyl, ethoxycarbonylphenyl, methoxycarbonylmethylphenyl, aminocarbonylphenyl, methylaminocarbonylphenyl, cyanomethylaminocarbonylphenyl, ethylaminocarbonyl-phenyl, 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, acetylperidinylethyl, *tert*-butoxycarbonylpiperidinylethynyl, piperidinylethynyl, acetylperidinylethynyl, *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, ethoxycarbonylpypyridinyl,
5 isoquinoliny, methylimidazolylethyl, methylimidazolymethylcarbonyl, methyl-
imidazolylethenyl, indolylethynyl, methylindolylethynyl, pyrazolylethynyl, methyl-
pyrazolylethynyl, methylimidazolylethynyl, dimethylimidazolylethynyl, pyridinylethynyl,
chloropyridinylethynyl, aminopyridinylethynyl, dimethylaminoethylaminopyridinyl-
ethynyl, aminopyrimidinylethynyl, imidazo[1,2-*a*]pyridinylethynyl, dimethylamino-
10 methylimidazo[1,2-*a*]pyridinylethynyl, methylimidazolylcarbonylcarbonyl, methyl-
benzomorpholinylpyridinyl, hydroxymethylpyrrolidinylpyridinylethynyl, pyrazolylphenyl,
methylpyrazolylphenyl, pyridinylphenyl, (amino)(chloropyridinyl)phenyl, phenyl-
isoxazolyl, phenylthiazolyl, (methyl)(trifluoromethylphenyl)thiazolyl, phenylpyridinyl,
fluorophenylpyridinyl, chlorophenylpyridinyl, cyanophenylpyridinyl, methylphenyl-
15 pyridinyl, (bromo)(methyl)phenylpyridinyl, ethylphenylpyridinyl, hydroxyphenyl-
pyridinyl, hydroxymethylphenylpyridinyl, methoxyphenylpyridinyl, aminocarbonyl-
methoxyphenylpyridinyl, dihydroxypropoxyphenylpyridinyl, methoxybenzyloxy-
phenylpyridinyl, trifluoromethylsulphonyloxyphenylpyridinyl, methylsulphonyl-
oxymethylphenylpyridinyl, aminophenylpyridinyl, (amino)(cyano)phenylpyridinyl,
20 dimethylaminophenylpyridinyl, aminomethylphenylpyridinyl, (aminomethyl)(fluoro)-
phenylpyridinyl, methylaminomethylphenylpyridinyl, dimethylaminomethylphenyl-
pyridinyl, *N*-isopropyl-*N*-methylaminomethylphenylpyridinyl, methoxybenzylamino-
phenylpyridinyl, acetylaminophenylpyridinyl, acetylaminomethylphenylpyridinyl, *tert*-
butoxycarbonylaminomethylphenylpyridinyl, *N*-(*tert*-butoxycarbonyl)-*N*-(methyl)-
25 aminomethylphenylpyridinyl, methylsulphonylaminomethylphenylpyridinyl,
formylphenylpyridinyl, acetylphenylpyridinyl, dimethylaminomethylcarbonyl-
phenylpyridinyl, carboxyphenylpyridinyl, (amino)(carboxy)phenylpyridinyl,
ethoxycarbonylphenylpyridinyl, *tert*-butoxycarbonylphenylpyridinyl, methoxycarbonyl-
methylphenylpyridinyl, aminocarbonylphenylpyridinyl, methylaminocarbonylphenyl-
30 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-
5 aminoethyl)-*N*-(methyl)aminocarbonylmethylphenylpyridinyl, methylsulphonylphenyl-
pyridinyl, phenylpyrimidinyl, bromophenylpyrimidinyl, aminoazetidinylphenylpyridinyl,
methylaminoazetidinylphenylpyridinyl, aminopyrrolidinylphenylpyridinyl, amino-
piperidinylphenylpyridinyl, methylaminopiperidinylphenylpyridinyl, piperazinyl-
phenylpyridinyl, *tert*-butoxycarbonylpiperazinylphenylpyridinyl, *tert*-butoxycarbonyl-
10 methylpiperazinylphenylpyridinyl, morpholinylphenylpyridinyl, piperazinylphenyl-
pyrimidinyl, pyrrolidinylmethylphenylpyridinyl, hydroxypyrrrolidinylmethylphenyl-
pyridinyl, dioxopyrrolidinylmethylphenylpyridinyl, aminopyrrolidinylmethylphenyl-
pyridinyl, carboxypyrrrolidinylmethylphenylpyridinyl, *tert*-butoxycarbonylprrrolidinyl-
methylphenylpyridinyl, aminopiperidinylmethylphenylpyridinyl, methylaminopiperidinyl-
15 methylphenylpyridinyl, piperazinylmethylphenylpyridinyl, methylpiperazinylmethyl-
phenylpyridinyl, oxopiperazinylmethylphenylpyridinyl, homopiperazinylmethylphenyl-
pyridinyl, morpholinylmethylphenylpyridinyl, dimethylmorpholinylmethylphenyl-
pyridinyl, aminoazabicyclo[3.2.1]octylmethylphenylpyridinyl, diazabicyclo[3.2.1]octyl-
methylphenylpyridinyl, tetrazolylphenylpyridinyl, benzofurylpyridinyl,
20 benzothienylpyridinyl, indolylpyridinyl, dimethylisoxazolylpyridinyl, bi(pyridinyl),
chlorobi(pyridinyl), carboxybi(pyridinyl), methoxycarbonylbi(pyridinyl),
isoquinolinylpyridinyl, morpholinylcarbonylbi(pyridinyl), phenoxyphenyl,
benzyloxyphenyl, methoxybenzyloxyphenyl, pyridinylmethoxyphenyl, *N*-(benzyl)-*N*-
(ethylcarbonyl)aminophenyl, methylfurylmethylaminophenyl, pyridinylmethylamino-
25 phenyl, cyclopentylcarbonylaminophenyl, phenylcarbonylaminophenyl, benzylcarbonyl-
aminophenyl, hydroxypyrrrolidinylcarbonylaminophenyl, aminopyrrolidinylcarbonyl-
aminophenyl, *tert*-butoxycarbonylaminopyrrolidinylcarbonylaminophenyl, (isopropyl)-
(oxo)pyrrolidinylcarbonylaminophenyl, *tert*-butoxycarbonylpiperidinylcarbonylaminophenyl,
30 piperazinylcarbonylaminophenyl, methylpiperazinylcarbonylaminophenyl, *tert*-
butoxycarbonylpiperazinylcarbonylaminophenyl, morpholinylcarbonylaminophenyl,
indolylcarbonylaminophenyl, methylisoxazolylcarbonylaminophenyl, pyridinylcarbonyl-
aminophenyl, hydroxypyridinylcarbonylaminophenyl, (oxo)(phenyl)pyrrolidinylcarbonyl-
aminophenyl, phenylsulphonylaminophenyl, benzylsulphonylaminophenyl, dimethyl-

isoxazolylsulphonylaminophenyl, cyclopentylaminocarbonylaminophenyl, phenylamino-
carbonylaminophenyl, methylazetidinylaminocarbonylaminophenyl, morpholinylethyl-
aminocarbonylaminophenyl, methylimidazolylmethylaminocarbonylaminophenyl,
morpholinylcarbonylcarbonylaminophenyl, pyrrolidinylethylaminocarbonylcarbonyl-
5 aminophenyl, phenylcarbonylphenyl, morpholinylcarbonylphenyl, aminopyrrolidinyl-
carbonylmethylphenyl, *tert*-butoxycarbonylaminopyrrolidinylcarbonylmethylphenyl,
aminopiperidinylcarbonylmethylphenyl, methylaminopiperidinylcarbonylmethylphenyl,
tert-butoxycarbonylaminopiperidinylcarbonylmethylphenyl, *N*-(*tert*-butoxycarbonyl)-*N*-
(methyl)aminopiperidinylcarbonylmethylphenyl, benzylaminocarbonylphenyl,
10 morpholinylethylaminocarbonylphenyl, imidazolylaminocarbonylphenyl, methyl-
imidazolylmethylaminocarbonylphenyl, pyridinylmethylaminocarbonylphenyl,
azetidinylaminocarbonylmethylphenyl, *tert*-butoxycarbonylazetidinylaminocarbonyl-
methylphenyl, pyrrolidinylmethylaminocarbonylmethylphenyl, *tert*-butoxycarbonyl-
pyrrolidinylmethylaminocarbonylmethylphenyl, pyridinylaminocarbonylmethylphenyl,
15 pyridinylmethylaminocarbonylmethylphenyl, phenylaminopyridinyl, *N*-methyl-*N*-
phenylaminopyridinyl, azetidinylaminophenylpyridinyl, pyrrolidinylaminophenyl-
pyridinyl, *tert*-butoxycarbonylpvrrolidinylaminophenylpyridinyl, piperazinylcarbonyl-
aminophenylpyridinyl, piperidinylaminocarbonylaminophenylpyridinyl,
(cyclopropylcarbonyl)(fluoro)phenylpyridinyl, aminoazetidinylcarbonylphenylpyridinyl,
20 methylaminoazetidinylcarbonylphenylpyridinyl, *tert*-butoxycarbonylaminoazetidinyl-
carbonylphenylpyridinyl, *N*-(*tert*-butoxycarbonyl)-*N*-(methyl)aminoazetidinylcarbonyl-
phenylpyridinyl, pyrrolidinylcarbonylphenylpyridinyl, hydroxypyrrrolidinylcarbonyl-
phenylpyridinyl, aminopyrrolidinylcarbonylphenylpyridinyl, aminopyrrolidinylcarbonyl-
phenyl(amino)pyridinyl, methylaminopyrrolidinylcarbonylphenylpyridinyl, *tert*-
25 butoxycarbonylaminopyrrolidinylcarbonylphenylpyridinyl, *tert*-butoxycarbonyl-
aminopyrrolidinylcarbonylphenyl(methoxybenzylamino)pyridinyl,
piperidinylcarbonylphenylpyridinyl, aminopiperidinylcarbonylphenylpyridinyl, methyl-
aminopiperidinylcarbonylphenylpyridinyl, *tert*-butoxycarbonylaminopiperidinylcarbonyl-
phenylpyridinyl, dimethylaminopiperidinylcarbonylphenylpyridinyl, *N*-(*tert*-butoxy-
30 carbonyl)-*N*-(methyl)aminopiperidinylcarbonylphenylpyridinyl, piperazinylcarbonyl-
phenylpyridinyl, methylpiperazinylcarbonylphenylpyridinyl, *tert*-butoxycarbonyl-
piperazinylcarbonylphenylpyridinyl, morpholinylcarbonylphenylpyridinyl, (fluoro)-
(morpholinylcarbonyl)phenylpyridinyl, methylaminopiperidinylcarbonylphenyl-

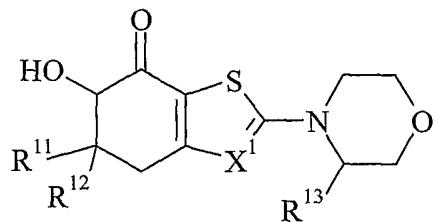
pyrimidinyl, dimethylaminopiperidinylcarbonylphenylpyrimidinyl, morpholinylmethylcarbonylphenylpyridinyl, aminoazabicyclo[3.2.1]octylcarbonylphenylpyridinyl, aminoazetidinylcarbonylmethylphenylpyridinyl, *tert*-butoxy-carbonylaminoazetidinylcarbonylmethylphenylpyridinyl, pyrrolidinylcarbonylmethyl-phenylpyridinyl, aminopyrrolidinylcarbonylmethylphenylpyridinyl, *tert*-butoxycarbonylaminopyrrolidinylcarbonylmethylphenylpyridinyl, methylaminopiperidinylcarbonylmethylphenylpyridinyl, *N*-(*tert*-butoxycarbonyl)-*N*-(methyl)aminopiperidinylcarbonylmethylphenylpyridinyl, methylpiperazinylcarbonylmethylphenylpyridinyl, azetidinyl-aminocarbonylphenylpyridinyl, *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.

In one embodiment, R⁵ is hydrogen.

Suitably, when R³ and R⁴ are both hydrogen, then R⁵ is other than hydrogen.

Suitably, when R⁵ is hydrogen, then R³ and/or R⁴ is other than hydrogen.

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



(IIA)

wherein

X¹ represents N or CH;
R¹¹ represents hydrogen or C₁₋₆ alkyl; and
R¹² represents hydrogen; or C₁₋₆ alkyl, C₃₋₇ cycloalkyl, C₃₋₇ cycloalkyl(C₁₋₆)alkyl, aryl, aryl(C₁₋₆)alkyl, C₃₋₇ heterocycloalkyl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkyl, heteroaryl or

heteroaryl(C₁₋₆)alkyl, any of which groups may be optionally substituted by one or more substituents; or

R¹¹ and R¹², when taken together with the carbon atom to which they are both attached, represent C₃₋₇ cycloalkyl or C₃₋₇ heterocycloalkyl, either of which groups may be

5 optionally substituted by one or more substituents; and

R¹³ represents hydrogen; or C₁₋₆ alkyl, C₃₋₇ cycloalkyl, C₃₋₇ cycloalkyl(C₁₋₆)alkyl, aryl, aryl(C₁₋₆)alkyl, aryl(C₂₋₆)alkenyl, aryl(C₂₋₆)alkynyl, biaryl(C₁₋₆)alkyl, C₃₋₇ heterocycloalkyl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkyl, C₃₋₇ heterocycloalkylcarbonyl, heteroaryl, heteroaryl(C₁₋₆)alkyl, heteroaryl-aryl(C₁₋₆)alkyl or aryl-heteroaryl(C₁₋₆)alkyl,

10 any of which groups may be optionally substituted by one or more substituents.

In one embodiment, X¹ represents N. In another embodiment, X¹ represents CH.

Where any of the groups in the compounds of formula (IIA) 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.

15 Typical values of R¹¹ include hydrogen, methyl and ethyl. In one embodiment, R¹¹ is hydrogen. In another embodiment, R¹¹ is C₁₋₆ alkyl, especially methyl.

Suitably, R¹² represents hydrogen; or C₁₋₆ alkyl, C₃₋₇ cycloalkyl or aryl, any of which groups may be optionally substituted by one or more substituents.

20 Examples of typical substituents on R¹² include halogen, cyano, nitro, C₁₋₆ alkyl, trifluoromethyl, hydroxy, C₁₋₆ alkoxy, difluoromethoxy, trifluoromethoxy, aryloxy, C₁₋₆ alkylthio, C₁₋₆ alkylsulphonyl, amino, C₁₋₆ alkylamino, di(C₁₋₆)alkylamino, C₂₋₆ alkylcarbonylamino, C₂₋₆ alkoxy carbonylamino, C₁₋₆ alkylsulphonylamino, formyl, C₂₋₆ alkylcarbonyl, carboxy, C₂₋₆ alkoxy carbonyl, aminocarbonyl, C₁₋₆ alkylaminocarbonyl, 25 di(C₁₋₆)alkylaminocarbonyl, aminosulphonyl, C₁₋₆ alkylaminosulphonyl and di(C₁₋₆)alkylaminosulphonyl; especially halogen, C₁₋₆ alkoxy or C₁₋₆ alkylthio.

Examples of particular substituents on R¹² include fluoro, chloro, bromo, cyano, nitro, methyl, trifluoromethyl, hydroxy, methoxy, difluoromethoxy, trifluoromethoxy, phenoxy, methylthio, methylsulphonyl, amino, methylamino, dimethylamino, acetylamino, 30 methoxycarbonylamino, methylsulphonylamino, formyl, acetyl, carboxy, methoxycarbonyl, aminocarbonyl, methylaminocarbonyl, dimethylaminocarbonyl, aminosulphonyl, methylaminosulphonyl and dimethylaminosulphonyl; especially chloro, methoxy or methylthio.

Typical values of R¹² include hydrogen, methyl, *n*-propyl, isopropyl, isobutyl, cyclohexyl and phenyl. A particular value of R¹² is methyl.

Alternatively, R¹¹ and R¹² may together form an optionally substituted spiro linkage. Thus, R¹¹ and R¹², when taken together with the carbon atom to which they are both attached, may represent C₃₋₇ cycloalkyl or C₃₋₇ heterocycloalkyl, either of which groups may be unsubstituted, or substituted by one or more, typically by one or two, substituents. In this context, R¹¹ and R¹², 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.

Typically, R¹³ represents hydrogen; or C₁₋₆ alkyl, aryl(C₁₋₆)alkyl, aryl(C₂₋₆)alkynyl, biaryl(C₁₋₆)alkyl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkyl, C₃₋₇ heterocycloalkylcarbonyl, heteroaryl(C₁₋₆)alkyl, heteroaryl-aryl(C₁₋₆)alkyl or aryl-heteroaryl(C₁₋₆)alkyl, any of which groups may be optionally substituted by one or more substituents.

Generally, R¹³ represents hydrogen; or C₂₋₆ alkynyl, aryl(C₁₋₆)alkyl or heteroaryl-(C₁₋₆)alkyl, any of which groups may be optionally substituted by one or more substituents. More particularly, R¹³ represents aryl(C₁₋₆)alkyl or heteroaryl(C₁₋₆)alkyl, either of which groups may be optionally substituted by one or more substituents.

In one specific embodiment, R¹³ represents hydrogen.

In a representative embodiment, R¹³ represents C₁₋₆ alkyl, aryl(C₁₋₆)alkyl, biaryl-(C₁₋₆)alkyl, heteroaryl(C₁₋₆)alkyl or heteroaryl-aryl(C₁₋₆)alkyl, any of which groups may be optionally substituted by one or more substituents. Preferably, R¹³ represents methyl, arylmethyl, biaryl methyl, heteroarylmethyl or heteroaryl-aryl methyl, any of which groups may be optionally substituted by one or more substituents. More particularly, R¹³ represents arylmethyl or heteroarylmethyl, either of which groups may be optionally substituted by one or more substituents.

In a particular embodiment, R¹³ represents substituted or unsubstituted indolyl-(C₁₋₆)alkyl. Advantageously, R¹³ represents substituted or unsubstituted indolylmethyl.

In a typical embodiment, R¹³ represents substituted or unsubstituted phenyl-(C₁₋₆)alkyl. Advantageously, R¹³ represents substituted or unsubstituted benzyl.

In another embodiment, R¹³ represents substituted or unsubstituted benzofuryl-(C₁₋₆)alkyl. Advantageously, R¹³ represents substituted or unsubstituted benzofurylmethyl.

Illustratively, R¹³ represents hydrogen; or methyl, propynyl, benzyl, phenylethyl, naphthylmethyl, phenylpropynyl, biphenylmethyl, naphthylphenylmethyl,

indolinylmethyl, 1,2,3,4-tetrahydroquinolinylmethyl, 1,2,3,4-tetrahydroisoquinolinylmethyl, piperidinylcarbonyl, 1,2,3,4-tetrahydroquinolinylcarbonyl, 1,2,3,4-tetrahydroisoquinolinylcarbonyl, 1,2,3,4-tetrahydroquinoxalinylcarbonyl, benzofurylmethyl, benzothienylmethyl, indolymethyl, pyrrolo[2,3-*b*]pyridinylmethyl, 5 pyrrolo[3,2-*c*]pyridinylmethyl, benzimidazolymethyl, benzotriazolymethyl, 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.

- 10 Examples of typical substituents on R¹³ include halogen, cyano, nitro, C₁₋₆ alkyl, trifluoromethyl, C₂₋₆ alkenyl, C₃₋₇ cycloalkyl, (C₁₋₆)alkylaryl, di(C₁₋₆)alkylaryl, piperidinyl-(C₁₋₆)alkylaryl, piperazinyl(C₁₋₆)alkylaryl, (C₁₋₆)alkylpiperazinyl(C₁₋₆)alkylaryl, morpholinyl(C₁₋₆)alkylaryl, (C₁₋₆)alkoxyaryl, cyano(C₁₋₆)alkoxyaryl, di(C₁₋₆)alkyl-amino(C₁₋₆)alkylaryl, (C₁₋₆)alkylaminocarbonylaryl, aryl(C₁₋₆)alkyl, oxazolinyl, azetidinyl, 15 haloarylpyrrolidinyl, dioxopyrrolidinyl, aminopyrrolidinyl, di(C₁₋₆)alkylaminopyrrolidinyl, indolinyl, oxoindolinyl, arylpiperidinyl, arylcarbonylpiperidinyl, di(C₁₋₆)alkylamino-carbonylpiperidinyl, piperazinyl, (C₁₋₆)alkylpiperazinyl, haloarylpirazinyl, pyridinylpiperazinyl, furoylpiperazinyl, homopiperazinyl, (C₁₋₆)alkylhomopiperazinyl, morpholinyl, (C₁₋₆)alkylpiperazinyl(C₁₋₆)alkyl, morpholinyl(C₁₋₆)alkyl, benzofuryl, 20 benzothienyl, pyrazolyl, (C₁₋₆)alkylpyrazolyl, di(C₁₋₆)alkylpyrazolyl, tri(C₁₋₆)alkyl-pyrazolyl, [di(C₁₋₆)alkyl](trifluoromethyl)pyrazolyl, cyano(C₁₋₆)alkylpyrazolyl, [cyano-(C₁₋₆)alkyl][di(C₁₋₆)alkyl]pyrazolyl, hydroxy(C₁₋₆)alkylpyrazolyl, [hydroxy(C₁₋₆)-alkyl][di(C₁₋₆)alkyl]pyrazolyl, methoxy(C₁₋₆)alkylpyrazolyl, [dihydroxy(C₁₋₆)alkyl]-pyrazolyl, [(hydroxy)(methoxy)(C₁₋₆)alkyl]pyrazolyl, amino(C₁₋₆)alkylpyrazolyl, 25 [(C₁₋₆)alkyl][amino(C₁₋₆)alkyl]pyrazolyl, [amino(C₁₋₆)alkyl][di(C₁₋₆)alkyl]pyrazolyl, di(C₁₋₆)alkylamino(C₁₋₆)alkylpyrazolyl, di(C₁₋₆)alkoxyphosphono(C₁₋₆)alkylpyrazolyl, (C₂₋₆)alkenylpyrazolyl, (C₃₋₇)cycloalkyl(C₁₋₆)alkylpyrazolyl, [(C₃₋₇)cycloalkyl(C₁₋₆)alkyl]-[di(C₁₋₆)alkyl]pyrazolyl, [(C₁₋₆)alkyl](aryl)pyrazolyl, (aryl)(trifluoromethyl)pyrazolyl, aryl(C₁₋₆)alkylpyrazolyl, aminoaryl(C₁₋₆)alkylpyrazolyl, piperidinylpyrazolyl, 30 tetrahydropyranyl(C₁₋₆)alkylpyrazolyl, [di(C₁₋₆)alkyl][tetrahydropyranyl(C₁₋₆)alkyl]-pyrazolyl, pyrrolidinyl(C₁₋₆)alkylpyrazolyl, piperidinyl(C₁₋₆)alkylpyrazolyl, (C₁₋₆)alkyl-piperidinyl(C₁₋₆)alkylpyrazolyl, morpholinyl(C₁₋₆)alkylpyrazolyl, pyridinyl(C₁₋₆)alkyl-pyrazolyl, oxypyridinyl(C₁₋₆)alkylpyrazolyl, [arylcarbonyl(C₁₋₆)alkyl][di(C₁₋₆)alkyl]-

pyrazolyl, [(C₁₋₆)alkyl](piperazinylcarbonyl)pyrazolyl, [(C₁₋₆)alkylaminocarbonyl]-[(C₁₋₆)alkylaryl]pyrazolyl, [(C₁₋₆)alkyl][amino(C₁₋₆)alkylaminocarbonyl]pyrazolyl, aminocarbonyl(C₁₋₆)alkylpyrazolyl, [aminocarbonyl(C₁₋₆)alkyl][di(C₁₋₆)alkyl]pyrazolyl, di(C₁₋₆)alkylaminocarbonyl(C₁₋₆)alkylpyrazolyl, pyrazolo[1,5-*a*]pyridinyl, di(C₁₋₆)alkyl-5 isoxazolyl, (amino)[(C₁₋₆)alkyl]isoxazolyl, thiazolyl, di(C₁₋₆)alkylthiazolyl, imidazolyl, (C₁₋₆)alkylimidazolyl, di(C₁₋₆)alkylimidazolyl, imidazo[1,2-*a*]pyridinyl, (C₁₋₆)alkyl-imidazo[1,2-*a*]pyridinyl, (C₁₋₆)alkylimidazo[4,5-*b*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyrazinyl, (C₁₋₆)alkylthiadiazolyl, triazolyl, pyridinyl, halopyridinyl, (C₁₋₆)alkylpyridinyl, [(C₁₋₆)alkyl](halo)pyridinyl, di(C₁₋₆)alkylpyridinyl, (C₂₋₆)alkenyl-10 pyridinyl, (C₁₋₆)alkylpiperazinylpyridinyl, [(C₁₋₆)alkyl](piperazinyl)pyridinyl, [(C₁₋₆)alkoxycarbonylpiperazinyl][(C₁₋₆)alkyl]pyridinyl, piperidinyl(C₁₋₆)alkylpyridinyl, [(C₁₋₆)alkyl](oxy)pyridinyl, hydroxypyridinyl, hydroxy(C₁₋₆)alkylpyridinyl, (C₁₋₆)alkoxy-pyridinyl, [(C₁₋₆)alkoxy][(C₁₋₆)alkyl]pyridinyl, [(C₁₋₆)alkoxy][di(C₁₋₆)alkyl]pyridinyl, (C₁₋₆)alkoxy(C₁₋₆)alkylpyridinyl, aminopyridinyl, carboxy(C₁₋₆)alkylpyridinyl, 15 (C₁₋₆)alkoxycarbonyl(C₁₋₆)alkylpyridinyl, pyridazinyl, (C₁₋₆)alkylpyridazinyl, piperidinylpyridazinyl, oxypyridazinyl, (C₁₋₆)alkoxypyridazinyl, aminopyridazinyl, hydroxy(C₁₋₆)alkylaminopyridazinyl, di(C₁₋₆)alkylaminopyridazinyl, pyrimidinyl, (C₁₋₆)alkylpyrimidinyl, [(C₁₋₆)alkyl](halo)pyrimidinyl, di(C₁₋₆)alkylpyrimidinyl, pyrrolidinylpyrimidinyl, (C₁₋₆)alkylpiperazinylpyrimidinyl, [(C₁₋₆)alkyl](piperazinyl)-20 pyrimidinyl, [(C₁₋₆)alkoxycarbonyl][(C₁₋₆)alkyl]piperazinylpyrimidinyl, hydroxypyrimidinyl, [(C₁₋₆)alkyl](hydroxy)pyrimidinyl, [(C₁₋₆)alkyl][hydroxy(C₁₋₆)alkyl]-pyrimidinyl, [(C₁₋₆)alkyl][hydroxy(C₂₋₆)alkynyl]pyrimidinyl, (C₁₋₆)alkoxypyrimidinyl, aminopyrimidinyl, di(C₁₋₆)alkylaminopyrimidinyl, [di(C₁₋₆)alkylamino](halo)pyrimidinyl, carboxypyrimidinyl, [(C₁₋₆)alkoxycarbonyl(C₁₋₆)alkyl][(C₁₋₆)alkyl]pyrimidinyl, 25 aminocarbonylpyrimidinyl, pyrazinyl, (C₁₋₆)alkoxypyrazinyl, aminopyrazinyl, hydroxy, (C₁₋₆)alkoxy, difluoromethoxy, trifluoromethoxy, C₃₋₇ cycloalkoxy, C₃₋₇ cycloalkyl-(C₁₋₆)alkoxy, aryl(C₁₋₆)alkoxycarbonylpiperidinyloxy, morpholinyl(C₁₋₆)alkoxy, aryloxy, haloaryloxy, di(C₁₋₆)alkylpyrazolyl, halopyridinyl, pyrrolidinylpyridinyl, (C₁₋₆)alkylpiperazinylpyridinyl, (C₁₋₆)alkylpyrazolylpyridinyl, (C₁₋₆)alkylamino-30 pyridinyl, carboxypyridinyl, aminocarbonylpyridinyl, (C₁₋₆)alkyl-pyridazinyl, pyrimidinyl, (C₁₋₆)alkylpyrimidinyl, [(C₁₋₆)alkyl](halo)-pyrimidinyl, hydroxy(C₁₋₆)alkyl, dihydroxy(C₁₋₆)alkyl, pyridinyl, (C₁₋₆)alkyl, methylenedioxy, difluoromethylenedioxy, amino, (C₁₋₆)alkylamino, dihydroxy(C₁₋₆)alkyl-

amino, (C₁₋₆)alkoxy(C₁₋₆)alkylamino, di(C₁₋₆)alkylamino, N-[(C₁₋₆)alkoxy(C₁₋₆)alkyl]-N-[(C₁₋₆)alkyl]amino, di(C₁₋₆)alkylamino(C₁₋₆)alkylamino, N-[(C₁₋₆)alkyl]-N-[di(C₁₋₆)alkyl-amino(C₁₋₆)alkyl]amino, N-[(C₁₋₆)alkyl]-N-[(C₃₋₇)cycloalkyl]amino, haloaryl amino, N-[(C₁₋₆)alkyl]-N-(haloaryl)amino, methylenedioxypyrenylamino, morpholinyl(C₁₋₆)alkyl-phenylamino, oxazolinylphenylamino, [(C₁₋₆)alkyl](oxo)pyrazolylphenylamino, oxazolylphenylamino, isoxazolylphenylamino, triazolylphenylamino, (C₁₋₆)alkyltriazolylphenylamino, (C₁₋₆)alkylpyrimidinylphenylamino, pyrazolyl(C₁₋₆)alkyl-phenylamino, triazolyl(C₁₋₆)alkylphenylamino, C₁₋₆ alkylsulphonylaminophenylamino, morpholinylcarbonylphenylamino, C₁₋₆ alkylsulphonylphenylamino,

5 morpholinylsulphonylphenylamino, N-[(C₁₋₆)alkyl]-N-[aryl(C₁₋₆)alkyl]amino, N-[di(C₁₋₆)alkylamino(C₁₋₆)alkyl]-N-[aryl(C₁₋₆)alkyl]amino, cyanoaryl(C₁₋₆)alkylamino, (cyano)(halo)aryl(C₁₋₆)alkylamino, methylenedioxyaryl(C₁₋₆)alkylamino, dihydrobenzofuranylamino, N-[(C₁₋₆)alkyl]-N-[(C₁₋₆)alkylpyrrolidinyl]amino, C₁₋₆ alkylsulphonylindolinylamino, chromanonylamino, piperidinylamino, N-[(C₁₋₆)alkyl]-N-

10 (piperidinyl)amino, N-[(C₃₋₇)cycloalkyl(C₁₋₆)alkyl]-N-(piperidinyl)amino, (C₁₋₆)alkyl-piperidinylamino, N-[(C₁₋₆)alkyl]-N-[(C₁₋₆)alkylpiperidinyl]amino, N-[(C₁₋₆)alkyl]-N-[(C₃₋₇)cycloalkylpiperidinyl]amino, N-[(C₁₋₆)alkyl]-N-[(C₂₋₆)alkylcarbonylpiperidinyl]-amino, dihydroquinolinonylamino, benzoxazinonylamino, pyrrolidinyl(C₁₋₆)alkylamino, N-[(C₁₋₆)alkyl]-N-[pyrrolidinyl(C₁₋₆)alkyl]amino, N-[(C₁₋₆)alkyl]-N-[piperidinyl(C₁₋₆)-

15 alkyl]amino, benzothienylamino, indolylamino, dioxoindolylamino, (C₁₋₆)alkylpyrazolyl-amino, [(C₁₋₆)alkyl](halo)pyrazolylamino, di(C₁₋₆)alkylpyrazolylamino, tri(C₁₋₆)alkyl-pyrazolylamino, N-[(C₁₋₆)alkyl]-N-[(C₁₋₆)alkylpyrazolyl]amino, (C₁₋₆)alkylindazolylamino, benzoxazolylamino, benzoxazolonylamino, di(C₁₋₆)alkylisoxazolylamino, thiazolylamino, benzothiazolylamino, (C₁₋₆)alkylisothiazolylamino, imidazolylamino, [(C₁₋₆)alkoxy-carbonyl][(C₁₋₆)alkyl]imidazolylamino, (C₁₋₆)alkylbenzimidazolylamino,

20 benzimidazolonylamino, di(C₁₋₆)alkylbenzimidazolonylamino, (C₁₋₆)alkyloxadiazolyl-amino, furyloxadiazolylamino, (C₁₋₆)alkylthiadiazolylamino, pyridinylamino, halopyridinylamino, (C₁₋₆)alkylpyridinylamino, di(C₁₋₆)alkylpyridinylamino, trifluoro-methylpyridinylamino, hydroxypyridinylamino, hydroxy(C₁₋₆)alkylpyridinylamino,

25 dihydroxy(C₁₋₆)alkylpyridinylamino, (C₁₋₆)alkoxypyridinylamino, dihydroxy(C₁₋₆)alkoxy-pyridinylamino, di(C₁₋₆)alkyldioxolanyl(C₁₋₆)alkoxypyridinylamino, (C₁₋₆)alkoxy(C₁₋₆)-alkylpyridinylamino, (C₁₋₆)alkoxy(C₂₋₆)alkenylpyridinylamino, dihydroxy(C₁₋₆)alkyl-aminopyridinylamino, di(C₁₋₆)alkylaminopyridinylamino, (C₁₋₆)alkylamino(C₁₋₆)alkyl-

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pyridinylamino, di(C₁₋₆)alkylamino(C₁₋₆)alkylpyridinylamino, oxopyridinylamino, carboxypyridinylamino, *N*-[(C₁₋₆)alkyl]-*N*-[(C₁₋₆)alkylpyridinyl]amino, bis[(C₁₋₆)alkylpyridinyl]amino, bis(trifluoromethylpyridinyl)amino, isoquinolinylamino, (C₁₋₆)alkylpyridazinylamino, *N*-[(C₁₋₆)alkyl]-*N*-[(C₁₋₆)alkylpyridazinyl]amino, *N*-[aryl(C₁₋₆)alkyl]-*N*-[(C₁₋₆)alkylpyridazinyl]amino, di(C₁₋₆)alkylpyridazinylamino, arylpyridazinylamino, piperidinylpyridazinylamino, (C₁₋₆)alkoxypyridazinylamino, [(C₁₋₆)alkoxy](halo)-pyridazinylamino, di(C₁₋₆)alkylaminopyridazinylamino, bis[(C₁₋₆)alkylpyridazinyl]amino, (C₁₋₆)alkylcinnolinylamino, oxopyrimidinylamino, thioxopyrimidinylamino, quinoxalinylamino, (C₁₋₆)alkylchromenylamino, benzofuryl(C₁₋₆)alkylamino, thienyl(C₁₋₆)-alkylamino, indolyl(C₁₋₆)alkylamino, (C₁₋₆)alkylpyrazolyl(C₁₋₆)alkylamino, [di(C₁₋₆)alkyl]- (halo)pyrazolyl(C₁₋₆)alkylamino, di(C₁₋₆)alkylisoxazolyl(C₁₋₆)alkylamino, thiazolyl(C₁₋₆)-alkylamino, imidazolyl(C₁₋₆)alkylamino, (C₁₋₆)alkylimidazolyl(C₁₋₆)alkylamino, pyridinyl(C₁₋₆)alkylamino, (C₁₋₆)alkylpyridinyl(C₁₋₆)alkylamino, *N*-[(C₁₋₆)alkyl]-*N*-[pyridinyl(C₁₋₆)alkyl]amino, *N*-[(C₁₋₆)alkylpyridinyl(C₁₋₆)alkyl]-*N*-[dihydroxy(C₁₋₆)alkyl]amino, amino(C₁₋₆)alkyl, (C₁₋₆)-alkylamino(C₁₋₆)alkyl, di(C₁₋₆)alkylamino(C₁₋₆)alkyl, pyridinylamino(C₁₋₆)alkyl, C₂₋₆ alkylcarbonylamino, *N*-[(C₂₋₆)alkylcarbonyl]-*N*-[(C₁₋₆)alkylpyridinyl(C₁₋₆)alkyl]amino, di(C₁₋₆)alkylamino(C₁₋₆)alkylcarbonylamino, C₂₋₆ alkylcarbonylaminomethyl, (C₃₋₇)-cycloalkylcarbonylamino, (C₁₋₆)alkylpiperidinylcarbonylamino, (C₁₋₆)alkylimidazolyl-carbonylamino, C₂₋₆ alkoxycarbonylamino, [(C₂₋₆)alkoxycarbonyl][(C₁₋₆)alkyl]amino, C₁₋₆ alkylsulphonylamino, formyl, C₂₋₆ alkylcarbonyl, C₂₋₆ alkylcarbonyl oxime, C₂₋₆ alkylcarbonyl *O*-(methyl)oxime, trifluoromethylcarbonyl, carboxy, C₂₋₆ alkoxycarbonyl, aminocarbonyl, C₁₋₆ alkylaminocarbonyl, [hydroxy(C₁₋₆)alkyl]aminocarbonyl, [di(C₁₋₆)-alkylamino(C₁₋₆)alkyl]aminocarbonyl, di(C₁₋₆)alkylaminocarbonyl, [(C₁₋₆)alkyl][cyano-(C₁₋₆)alkyl]aminocarbonyl, [(C₁₋₆)alkyl][hydroxy(C₁₋₆)alkyl]aminocarbonyl, [(C₁₋₆)alkoxy-(C₁₋₆)alkyl][(C₁₋₆)alkyl]aminocarbonyl, [di(C₁₋₆)alkylamino(C₁₋₆)alkyl][(C₁₋₆)alkyl]aminocarbonyl, C₃₋₇ cycloalkyl(C₁₋₆)alkylaminocarbonyl, aryl(C₁₋₆)alkylaminocarbonyl, (C₁₋₆)-alkylpiperidinylaminocarbonyl, *N*-[(C₁₋₆)alkyl]-*N*-[(C₁₋₆)alkylpiperidinyl]aminocarbonyl, piperidinyl(C₁₋₆)alkylaminocarbonyl, heteroarylaminocarbonyl, heteroaryl(C₁₋₆)alkyl-aminocarbonyl, azetidinylcarbonyl, hydroxyazetidinylcarbonyl, aminoazetidinylcarbonyl, C₂₋₆ alkoxycarbonylamozazetidinylcarbonyl, pyrrolidinylcarbonyl, (C₁₋₆)alkyl-pyrrolidinylcarbonyl, C₁₋₆ alkoxy(C₁₋₆)alkylpyrrolidinylcarbonyl, di(C₁₋₆)alkylamino-pyrrolidinylcarbonyl, thiazolidinylcarbonyl, oxothiazolidinylcarbonyl, piperidinyl-

carbonyl, (C₁₋₆)alkylpiperazinylcarbonyl, morpholinylcarbonyl, C₁₋₆ alkylthio, C₁₋₆ alkylsulphanyl, C₁₋₆ alkylsulphonyl, C₁₋₆ alkylsulphonylmethyl, aminosulphonyl, C₁₋₆ alkylaminosulphonyl, di(C₁₋₆)alkylaminosulphonyl, C₂₋₆ alkoxy carbonyloxy, trimethylsilyl and tetra(C₁₋₆)alkyldioxaborolanyl.

5 Particular examples of typical substituents on R¹³ include C₁₋₆ alkyl and di(C₁₋₆)alkylaminocarbonyl.

Selected examples of specific substituents on R¹³ include fluoro, chloro, bromo, cyano, nitro, methyl, *n*-propyl, isopropyl, trifluoromethyl, allyl, cyclopropyl, methylphenyl, dimethylphenyl, piperidinylmethylphenyl, piperazinylmethylphenyl, 10 methylpiperazinylmethylphenyl, morpholinylmethylphenyl, methoxyphenyl, cyanomethoxyphenyl, dimethylaminomethylphenyl, methylaminocarbonylphenyl, benzyl, oxazolinyl, azetidinyl, pyrrolidinyl, chlorophenylpyrrolidinyl, dioxopyrrolidinyl, aminopyrrolidinyl, dimethylaminopyrrolidinyl, indolinyl, oxoindolinyl, phenylpiperidinyl, benzoylpiperidinyl, diethylaminocarbonylpiperidinyl, piperazinyl, 15 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, 20 (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, (dihydroxypropyl)pyrazolyl, [(hydroxy)- 25 (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, 30 piperidinylpyrazolyl, tetrahydropyranylmethylpyrazolyl, (dimethyl)(tetrahydropyranyl-methyl)pyrazolyl, pyrrolidinylethylpyrazolyl, piperidinylethylpyrazolyl, methyl-piperidinylethylpyrazolyl, morpholinylethylpyrazolyl, pyridinylmethylpyrazolyl, oxypridinylmethylpyrazolyl, (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,
5 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*-
10 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,
15 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,
20 (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-
25 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-
30 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,
5 methylenedioxyphenylamino, morpholinylmethylphenylamino, oxazolinylphenylamino,
(methyl)(oxo)pyrazolylphenylamino, oxazolylphenylamino, isoxazolylphenylamino,
triazolylphenylamino, methyltriazolylphenylamino, methylpyrimidinylphenylamino,
pyrazolylmethylphenylamino, triazolylmethylphenylamino, methylsulphonylphenylamino-
phenylamino, morpholinylcarbonylphenylamino, methylsulphonylphenylamino,
10 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,
15 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*-(acetyl)piperidinyl)-*N*-(methyl)amino,
dihydroquinolinonylamino, benzoxazinonylamino, pyrrolidinylethylamino,
20 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,
25 imidazolylamino, (ethoxycarbonyl)(methyl)imidazolylamino, methylbenzimidazolyl-
amino, benzimidazolonylamino, dimethylbenzimidazolonylamino, methyloxadiazolyl-
amino, furyloxadiazolylamino, methylthiadiazolylamino, pyridinylamino, chloropyridinyl-
amino, bromopyridinylamino, methylpyridinylamino, dimethylpyridinylamino,
trifluoromethylpyridinylamino, hydroxypyridinylamino, hydroxyethylpyridinylamino,
30 dihydroxyethylpyridinylamino, methoxypyridinylamino, dihydroxypropoxypyridinyl-
amino, dimethyldioxolanymethoxypyridinylamino, methoxyethylpyridinylamino,
methoxyvinylpyridinylamino, dihydroxypropylaminopyridinylamino, dimethylamino-
pyridinylamino, methylaminomethylpyridinylamino, dimethylaminomethylpyridinyl-

amino, 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, dimethyl-5
pyridazinylamino, phenylpyridazinylamino, piperidinylpyridazinylamino, methoxypyridazinylamino, (chloro)(methoxy)pyridazinylamino, dimethylamino-pyridazinylamino, bis(methylpyridazinyl)amino, methylcinnolinylamino, oxopyrimidinyl-amino, thioxopyrimidinylamino, quinoxalinylamino, methylchromenylamino, benzofurylmethylamino, thienylmethylamino, indolylmethylamino, methylpyrazolyl-methylamino, (chloro)(dimethyl)pyrazolylmethylamino, dimethylisoxazolylmethylamino, thiazolylmethylamino, imidazolylmethylamino, methylimidazolylmethylamino, pyridinylmethylamino, methylpyridinylmethylamino, *N*-(methyl)-*N*-(pyridinylethyl)-amino, *N*-(dihydroxypropyl)-*N*-(pyridinylmethyl)amino, *N*-(dihydroxypropyl)-*N*-10
(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, 15
aminocarbonyl, methylaminocarbonyl, (hydroxyethyl)aminocarbonyl, (dimethyl-aminoethyl)aminocarbonyl, (1-hydroxyprop-2-yl)aminocarbonyl, dimethylamino-carbonyl, *N*-(cyanomethyl)-*N*-methylaminocarbonyl, *N*-(cyanoethyl)-*N*-methylaminocarbonyl, *N*-(hydroxyethyl)-*N*-methylaminocarbonyl, *N*-(methoxyethyl)-*N*-methyl-aminocarbonyl, *N*-(dimethylaminoethyl)-*N*-methylaminocarbonyl, *N*-isopropyl-*N*-methyl-20
aminocarbonyl, diethylaminocarbonyl, cyclopropylmethylaminocarbonyl, benzylamino-carbonyl, methylpiperidinylaminocarbonyl, *N*-(methyl)-*N*-(methylpiperidinyl)amino-carbonyl, piperidinylethylaminocarbonyl, pyrazolylaminocarbonyl, pyridinylmethylaminocarbonyl, azetidinylcarbonyl, hydroxyazetidinylcarbonyl, aminoazetidinylcarbonyl, *tert*-butoxycarbonylaminozetidinylcarbonyl, pyrrolidinylcarbonyl, methylpyrrolidinyl-carbonyl, methoxymethylpyrrolidinylcarbonyl, dimethylaminopyrrolidinylcarbonyl, thiazolidinylcarbonyl, oxothiazolidinylcarbonyl, piperidinylcarbonyl, methylpiperazinyl-carbonyl, morpholinylcarbonyl, isopropylthio, isopropylsulphanyl, methylsulphonyl, isopropylsulphonyl, methylsulphonylmethyl, aminosulphonyl, methylaminosulphonyl, 25
30

dimethylaminosulphonyl, *tert*-butoxycarbonyloxy, trimethylsilyl and tetramethyl-dioxaborolanyl.

Particular examples of specific substituents on R¹³ include methyl and dimethylaminocarbonyl.

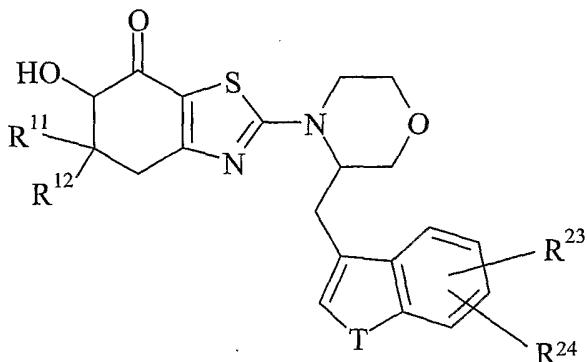
- 5 Typical values of R¹³ include hydrogen, methyl, phenoxy methyl, phenylthiomethyl, aminomethyl, phenylaminomethyl, N-methyl-N-phenylaminomethyl, pyridinylaminomethyl, benzofurylcarbonylaminomethyl, phenylsulphonylaminomethyl, benzothienylmethylaminocarbonylmethyl, propynyl, trimethylsilylpropynyl, benzyl, chlorobenzyl, bromobenzyl, methylenedioxyphenylaminobenzyl,
- 10 morpholinylmethylphenylaminobenzyl, oxazolinylphenylaminobenzyl, (methyl)(oxo)pyrazolylphenylaminobenzyl, oxazolylphenylaminobenzyl, isoxazolylphenylaminobenzyl, triazolylphenylaminobenzyl, methyltriazolylphenylaminobenzyl, methylpyrimidinylphenylaminobenzyl, pyrazolylmethylphenylaminobenzyl, triazolylmethylphenylaminobenzyl,
- 15 methylsulphonylaminophenylaminobenzyl, morpholinylcarbonylphenylaminobenzyl, methylsulphonylphenylaminobenzyl, morpholinylsulphonylphenylaminobenzyl, dihydrobenzofuranylaminobenzyl, methylsulphonylindolinylaminobenzyl, chromanylaminobenzyl, dihydroquinolinonylaminobenzyl, benzoxazinonyl-aminobenzyl, benzothienylaminobenzyl, indolylaminobenzyl, dioxoindolylaminobenzyl,
- 20 (bromo)(methyl)pyrazolylaminobenzyl, trimethylpyrazolylaminobenzyl, methylindazolyl-aminobenzyl, benzoxazolylaminobenzyl, benzoxazolonylaminobenzyl, dimethyl-isoxazolylaminobenzyl, benzothiazolylaminobenzyl, methylisothiazolylaminobenzyl, methylbenzimidazolylaminobenzyl, benzimidazolonylaminobenzyl, dimethyl-benzimidazolonylaminobenzyl, methyloxadiazolylaminobenzyl, furyloxadiazolyl-aminobenzyl, pyridinylaminobenzyl, chloropyridinylaminobenzyl, methylpyridinylamino-benzyl, dimethylpyridinylaminobenzyl, methoxypyridinylaminobenzyl, oxypyridinyl-aminobenzyl, oxypyrimidinylaminobenzyl, thioxopyrimidinylaminobenzyl, (chloro)-(methoxy)pyridazinylaminobenzyl, methylcinnolinylaminobenzyl, quinoxalinylamino-benzyl, methylchromenylaminobenzyl, benzofurylmethyl, cyanobenzofurylmethyl,
- 25 methoxycarbonylbenzofurylmethyl, dimethylaminocarbonylbenzofurylmethyl, azetidinylcarbonylbenzofurylmethyl, indolymethyl, fluoroindolymethyl, cyanoindolymethyl, (cyano)(methyl)indolymethyl, nitroindolymethyl, methylindolymethyl, oxazolinylindolymethyl, triazolylindolymethyl,
- 30 methoxycarbonylbenzofurylmethyl, dimethylaminocarbonylbenzofurylmethyl, azetidinylcarbonylbenzofurylmethyl, indolymethyl, fluoroindolymethyl, cyanoindolymethyl, (cyano)(methyl)indolymethyl, nitroindolymethyl, methylindolymethyl, oxazolinylindolymethyl, triazolylindolymethyl,

methoxyindolylmethyl, (chloro)(methoxy)indolylmethyl, di(methoxy)indolylmethyl,
difluoromethoxyindolylmethyl, trifluoromethoxyindolylmethyl, (chloro)(trifluoro-
methoxy)indolylmethyl, cyclobutyloxyindolylmethyl, cyclopropylmethoxyindolylmethyl,
morpholinylethoxyindolylmethyl, methylenedioxyindolylmethyl, difluoromethylenedioxy-
5 indolylmethyl, azetidinylindolylmethyl, morpholinylindolylmethyl, acetylamino-
indolylmethyl, acetylaminomethylindolylmethyl, methoxycarbonylaminoindolylmethyl,
N-methoxycarbonyl-N-methylaminoindolylmethyl, methylsulphonylaminoindolylmethyl,
acetylindolylmethyl, [acetyl oxime]indolylmethyl, [acetyl O-(methyl)oxime]-
indolylmethyl, trifluoromethylcarbonylindolylmethyl, carboxyindolylmethyl, (carboxy)-
10 (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-
15 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-
20 indolylmethyl, N-(methoxyethyl)-N-methylaminocarbonylindolylmethyl, [N-(methoxy-
ethyl)-N-methylaminocarbonyl](methyl)indolylmethyl, N-(dimethylaminoethyl)-N-
methylaminocarbonylindolylmethyl, N-isopropyl-N-methylaminocarbonylindolylmethyl,
diethylaminocarbonylindolylmethyl, cyclopropylmethylenaminocarbonylindolylmethyl,
benzylaminocarbonylindolylmethyl, pyrazolylaminocarbonylindolylmethyl,
25 pyridinylmethylenaminocarbonylindolylmethyl, azetidinylcarbonylindolylmethyl,
(azetidinylcarbonyl)(methyl)indolylmethyl, hydroxyazetidinylcarbonylindolylmethyl,
aminoazetidinylcarbonylindolylmethyl, *tert*-butoxycarbonylaminoazetidinylcarbonyl-
indolylmethyl, pyrrolidinylcarbonylindolylmethyl, methylpyrrolidinylcarbonyl-
indolylmethyl, methoxymethylpyrrolidinylcarbonylindolylmethyl, dimethylamino-
30 pyrrolidinylcarbonylindolylmethyl, thiazolidinylcarbonylindolylmethyl, oxothiazolidinyl-
carbonylindolylmethyl, piperidinylcarbonylindolylmethyl, methylpiperazinylcarbonyl-
indolylmethyl, morpholinylcarbonylindolylmethyl, methylsulphonylindolylmethyl,

methylsulphonylmethylindolylmethyl, dimethylaminosulphonylindolylmethyl, trimethylsilylindolylmethyl and pyrrolo[3,2-*c*]pyridinylmethyl.

A particular value of R¹³ is (dimethylaminocarbonyl)(methyl)indolylmethyl.

One particular sub-group of the compounds of formula (IIA) is represented by the 5 compounds of formula (IIB), and pharmaceutically acceptable salts and solvates thereof:



(IIB)

wherein

- 10 R¹¹ and R¹² are as defined above;
T represents oxygen or N-R²⁵;
R²³ represents hydrogen, halogen, cyano, nitro, C₁₋₆ alkyl, hydroxy(C₁₋₆)alkyl, trifluoromethyl, aryl(C₁₋₆)alkyl, oxazolinyl, triazolyl, hydroxy, C₁₋₆ alkoxy, difluoromethoxy, trifluoromethoxy, C₃₋₇ cycloalkoxy, C₃₋₇ cycloalkyl(C₁₋₆)alkoxy,
15 morpholinyl(C₁₋₆)alkoxy, aryloxy, aryl(C₁₋₆)alkoxy, C₁₋₆ alkylthio, C₁₋₆ alkylsulphanyl, arylsulphanyl, arylsulphonyl, C₁₋₆ alkylsulphonyloxy, amino, azetidinyl, morpholinyl, C₂₋₆ alkylcarbonylamino, C₂₋₆ alkylcarbonylaminomethyl, C₂₋₆ alkoxycarbonylamino, [(C₂₋₆)aloxycarbonyl][(C₁₋₆)alkyl]amino, C₁₋₆ alkylsulphonylamino, C₂₋₆ alkylcarbonyl, C₂₋₆ alkylcarbonyl oxime, C₂₋₆ alkylcarbonyl O-(methyl)oxime, trifluoromethylcarbonyl, 20 carboxy, C₂₋₆ aloxycarbonyl, aminocarbonyl, C₁₋₆ alkylaminocarbonyl, [hydroxy(C₁₋₆)-alkyl]aminocarbonyl, [di(C₁₋₆)alkylamino(C₁₋₆)alkyl]aminocarbonyl, di(C₁₋₆)alkyl-aminocarbonyl, [(C₁₋₆)alkyl][cyano(C₁₋₆)alkyl]aminocarbonyl, [(C₁₋₆)alkyl][hydroxy(C₁₋₆)-alkyl]aminocarbonyl, [(C₁₋₆)alkoxy(C₁₋₆)alkyl][(C₁₋₆)alkyl]aminocarbonyl, [di(C₁₋₆)alkyl-amino(C₁₋₆)alkyl][(C₁₋₆)alkyl]aminocarbonyl, C₃₋₇ cycloalkyl(C₁₋₆)alkylaminocarbonyl, 25 aryl(C₁₋₆)alkylaminocarbonyl, heteroarylaminocarbonyl, heteroaryl(C₁₋₆)alkylamino-

carbonyl, azetidinylcarbonyl, hydroxyazetidinylcarbonyl, aminoazetidinylcarbonyl, C₂₋₆ alkoxycarbonylaminoazetidinylcarbonyl, pyrrolidinylcarbonyl, (C₁₋₆)alkylpyrrolidinylcarbonyl, C₁₋₆ alkoxy(C₁₋₆)alkylpyrrolidinylcarbonyl, di(C₁₋₆)alkylaminopyrrolidinylcarbonyl, thiazolidinylcarbonyl, oxothiazolidinylcarbonyl, piperidinylcarbonyl, (C₁₋₆)-

- 5 alkylpiperazinylcarbonyl, morpholinylcarbonyl, C₁₋₆ alkylsulphonyl, C₁₋₆ alkylsulphonylmethyl or di(C₁₋₆)alkylaminosulphonyl; and

R²⁴ represents hydrogen, halogen, C₁₋₆ alkoxy or di(C₁₋₆)alkylaminocarbonyl; or

R²³ and R²⁴, when situated on adjacent carbon atoms, together represent methylenedioxy or difluoromethylenedioxy; and

- 10 R²⁵ represents hydrogen or C₁₋₆ alkyl.

In a preferred embodiment, T is N-R²⁵. In another embodiment, T is oxygen.

A suitable value of R²³ is di(C₁₋₆)alkylaminocarbonyl.

Illustrative values of R²³ include hydrogen, fluoro, chloro, cyano, nitro, oxazolinyl, triazolyl, methoxy, difluoromethoxy, trifluoromethoxy, cyclobutyloxy, cyclopropyl-

- 15 methoxy, morpholinylethoxy, azetidinyl, morpholinyl, acetylarnino, acetylaminomethyl, methoxycarbonylamino, N-methoxycarbonyl-N-methylarnino, methylsulphonylamino, acetyl, acetyl oxime, acetyl O-(methyl)oxime, trifluoromethylcarbonyl, carboxy, methoxycarbonyl, aminocarbonyl, methylaminocarbonyl, (hydroxyethyl)aminocarbonyl, (dimethylaminoethyl)aminocarbonyl, (1-hydroxyprop-2-yl)aminocarbonyl, dimethyl-

- 20 aminocarbonyl, N-(cyanomethyl)-N-methylaminocarbonyl, N-(cyanoethyl)-N-methyl-aminocarbonyl, N-(hydroxyethyl)-N-methylaminocarbonyl, N-(methoxyethyl)-N-methyl-aminocarbonyl, N-(dimethylaminoethyl)-N-methylaminocarbonyl, N-isopropyl-N-methyl-aminocarbonyl, diethylaminocarbonyl, cyclopropylmethylaminocarbonyl, benzylaminocarbonyl, pyrazolylaminocarbonyl, pyridinylmethylaminocarbonyl, azetidinylcarbonyl,

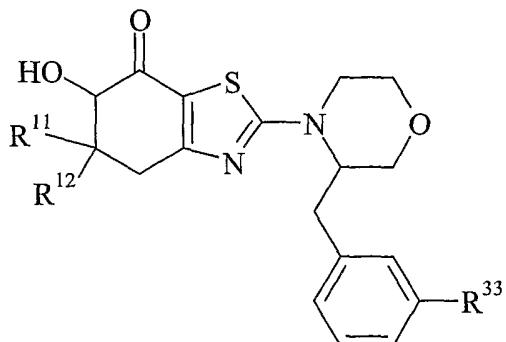
- 25 hydroxyazetidinylcarbonyl, aminoazetidinylcarbonyl, *tert*-butoxycarbonylamino-azetidinylcarbonyl, pyrrolidinylcarbonyl, methylpyrrolidinylcarbonyl, methoxymethyl-pyrrolidinylcarbonyl, dimethylaminopyrrolidinylcarbonyl, thiazolidinylcarbonyl, oxothiazolidinylcarbonyl, piperidinylcarbonyl, methylpiperazinylcarbonyl, morpholinylcarbonyl, methylsulphonyl, methylsulphonylmethyl and dimethylamino-sulphonyl.

A particular value of R²³ is dimethylaminocarbonyl.

Definitive values of R²⁴ include hydrogen, chloro, methoxy and dimethylamino-carbonyl. A particular value of R²⁴ is hydrogen.

In one embodiment, R²⁵ is hydrogen. In another embodiment, R²⁵ is C₁₋₆ alkyl, especially methyl.

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



(IIC)

wherein

- 10 R¹¹ and R¹² are as defined above;
- R³³ represents halogen or -NHR³⁴; or aryl or heteroaryl, either of which groups may be optionally substituted by one or more substituents; and
- 15 R³⁴ represents methylenedioxyphenyl, morpholinyl(C₁₋₆)alkylphenyl, oxazolinyl-phenyl, [(C₁₋₆)alkyl](oxo)pyrazolylphenyl, oxazolylphenyl, isoxazolylphenyl, triazolyl-phenyl, (C₁₋₆)alkyltriazolylphenyl, (C₁₋₆)alkylpyrimidinylphenyl, pyrazolyl(C₁₋₆)alkyl-phenyl, triazolyl(C₁₋₆)alkylphenyl, C₁₋₆ alkylsulphonylaminophenyl, morpholinylcarbonyl-phenyl, C₁₋₆ alkylsulphonylphenyl, morpholinylsulphonylphenyl, dihydrobenzofuranyl, C₁₋₆ alkylsulphonylindolinyl, chromanonyl, dihydroquinolinonyl, benzoxazinonyl, benzothienyl, indolyl, dioxoindolyl, [(C₁₋₆)alkyl](halo)pyrazolyl, tri(C₁₋₆)alkylpyrazolyl,
- 20 (C₁₋₆)alkylindazolyl, benzoxazolyl, benzoxazolonyl, di(C₁₋₆)alkylisoxazolyl, benzothiazolyl, (C₁₋₆)alkylisothiazolyl, (C₁₋₆)alkylbenzimidazolyl, benzimidazolonyl, di(C₁₋₆)alkylbenzimidazolonyl, (C₁₋₆)alkyloxadiazolyl, furyloxadiazolyl, pyridinyl, halopyridinyl, (C₁₋₆)alkylpyridinyl, di(C₁₋₆)alkylpyridinyl, (C₁₋₆)alkoxypyridinyl, oxypyridinyl, oxopyrimidinyl, thioxopyrimidinyl, [(C₁₋₆)alkoxy](halo)pyridazinyl,
- 25 (C₁₋₆)alkylcinnolinyl, quinoxalinyl or (C₁₋₆)alkylchromenyl.

Suitably, R³³ represents halogen or -NHR³⁴, in which R³⁴ is as defined above. In one embodiment, R³³ represents halogen, especially bromo. In another embodiment, R³³ represents -NHR³⁴, in which R³⁴ is as defined above.

5 In one embodiment, R³³ represents unsubstituted or substituted aryl. In another embodiment, R³³ represents unsubstituted or substituted heteroaryl.

Typical values of R³⁴ include pyridinyl, halopyridinyl, (C₁₋₆)alkylpyridinyl, di(C₁₋₆)alkylpyridinyl and (C₁₋₆)alkoxypyridinyl.

Particular values of R³⁴ include methylenedioxypyhenyl, 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, 15 methylindazolyl, benzoxazolyl, benzoxazolonyl, dimethylisoxazolyl, benzothiazolyl, methylisothiazolyl, methylbenzimidazolyl, benzimidazolonyl, dimethylbenzimidazolonyl, methyloxadiazolyl, furyloxadiazolyl, pyridinyl, chloropyridinyl, methylpyridinyl, dimethylpyridinyl, methoxypyridinyl, oxypyridinyl, oxopyrimidinyl, thioxopyrimidinyl, (chloro)(methoxy)pyridazinyl, methylcinnolinyl, quinoxalinyl and methylchromenyl.

20 Suitable values of R³⁴ include pyridinyl, chloropyridinyl, methylpyridinyl, dimethylpyridinyl and methoxypyridinyl.

Illustratively, R³³ represents halogen or -NHR³⁴, in which R³⁴ is as defined above. Additionally, R³³ 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.

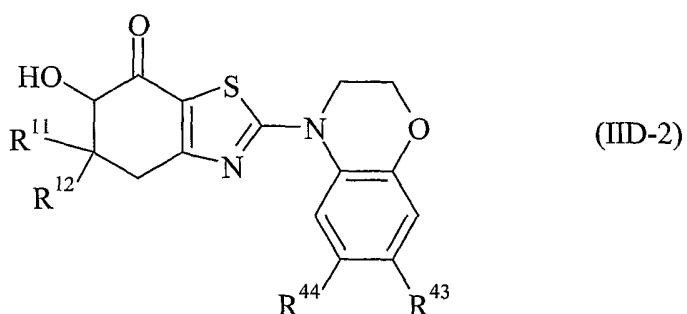
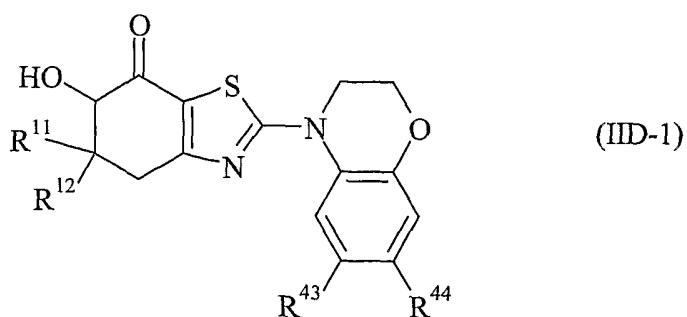
Selected examples of suitable substituents on R³³ include halogen, cyano, C₁₋₆ alkyl, hydroxy(C₁₋₆)alkyl, trifluoromethyl, C₁₋₆ alkoxy, trifluoromethoxy, aryloxy, methylenedioxy, C₁₋₆ alkylthio, arylsulphonyl, amino, C₂₋₆ alkylcarbonylamino, C₁₋₆ alkylsulphonylamino, C₂₋₆ alkylcarbonyl and aminocarbonyl.

30 Selected examples of representative substituents on R³³ include fluoro, chloro, bromo, cyano, methyl, hydroxymethyl, trifluoromethyl, methoxy, ethoxy, trifluoromethoxy, phenoxy, methylenedioxy, methylthio, phenylsulphonyl, amino, acetylamino, methylsulphonylamino, acetyl and aminocarbonyl.

Specific values of R³³ include bromo, methylenedioxypyrenylamino, morpholinylmethylphenylamino, oxazolinylphenylamino, (methyl)(oxo)pyrazolylphenylamino, oxazolylphenylamino, isoxazolylphenylamino, triazolylphenylamino, methyltriazolylphenylamino, methylpyrimidinylphenylamino, pyrazolylmethylphenylamino, triazolylmethylphenylamino, methylsulphonylaminophenylamino, morpholinylcarbonylphenylamino, methylsulphonylphenylamino, morpholinylsulphonylphenylamino, dihydrobenzofuranylarnino, methylsulphonylindolylamino, 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, oxypyridinylamino, oxypyrimidinylamino, thioxypyrimidinylamino, (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, 20 methylenedioxypyrenyl, trifluoromethoxyphenyl, phenoxyphenyl, methylthiophenyl, aminophenyl, acetylaminophenyl, methylsulphonylaminophenyl, acetylphenyl, aminocarbonylphenyl, naphthyl, benzofuryl, thienyl, methylthienyl, acetylthienyl, benzothienyl, phenylsulphonylindolyl, dimethylisoxazolyl, methylpyrazolyl, benzylpyrazolyl, pyridinyl, fluoropyridinyl, chloropyridinyl, methoxypyridinyl and 25 pyrimidinylbenzyl.

A particular value of R³³ is bromo.

Other 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:



wherein

- R^{11} and R^{12} are as defined above;
- 5 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, haloaryl-piperazinyl, 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})alkyl-pyrazolyl, (difluoromethyl)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})alkyl-pyrazolyl, [hydroxy(C_{1-6})alkyl][$di(C_{1-6})$ alkyl]pyrazolyl, methoxy(C_{1-6})alkylpyrazolyl, [$dihydroxy(C_{1-6})$ alkyl]pyrazolyl, [(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, $di(C_{1-6})$ alkoxypyrophosphono(C_{1-6})alkyl-pyrazolyl, (C_{2-6})alkenylpyrazolyl, (C_{3-7})cycloalkyl(C_{1-6})alkylpyrazolyl, [(C_{3-7})cycloalkyl-
- 10 20

(C₁₋₆)alkyl][di(C₁₋₆)alkyl]pyrazolyl, [(C₁₋₆)alkyl](aryl)pyrazolyl, (aryl)(trifluoromethyl)-pyrazolyl, aryl(C₁₋₆)alkylpyrazolyl, aminoaryl(C₁₋₆)alkylpyrazolyl, piperidinylpyrazolyl, tetrahydropyran(C₁₋₆)alkylpyrazolyl, [di(C₁₋₆)alkyl][tetrahydropyran(C₁₋₆)alkyl]-pyrazolyl, pyrrolidinyl(C₁₋₆)alkylpyrazolyl, piperidinyl(C₁₋₆)alkylpyrazolyl, (C₁₋₆)alkyl-5-piperidinyl(C₁₋₆)alkylpyrazolyl, morpholinyl(C₁₋₆)alkylpyrazolyl, pyridinyl(C₁₋₆)alkyl-pyrazolyl, oxypyridinyl(C₁₋₆)alkylpyrazolyl, [arylcarbonyl(C₁₋₆)alkyl][di(C₁₋₆)alkyl]-pyrazolyl, [(C₁₋₆)alkyl](piperazinylcarbonyl)pyrazolyl, [(C₁₋₆)alkylaminocarbonyl][(C₁₋₆)-alkylaryl]pyrazolyl, [(C₁₋₆)alkyl][amino(C₁₋₆)alkylaminocarbonyl]pyrazolyl, aminocarbonyl(C₁₋₆)alkylpyrazolyl, [aminocarbonyl(C₁₋₆)alkyl][di(C₁₋₆)alkyl]pyrazolyl, 10 di(C₁₋₆)alkylaminocarbonyl(C₁₋₆)alkylpyrazolyl, pyrazolo[1,5-*a*]pyridinyl, di(C₁₋₆)alkyl-isoxazolyl, (amino)[(C₁₋₆)alkyl]isoxazolyl, thiazolyl, di(C₁₋₆)alkylthiazolyl, imidazolyl, (C₁₋₆)alkylimidazolyl, di(C₁₋₆)alkylimidazolyl, imidazo[1,2-*a*]pyridinyl, (C₁₋₆)alkyl-imidazo[1,2-*a*]pyridinyl, (C₁₋₆)alkylimidazo[4,5-*b*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyrazinyl, (C₁₋₆)alkylthiadiazolyl, pyridinyl, halopyridinyl, (C₁₋₆)alkyl-pyridinyl, [(C₁₋₆)alkyl](halo)pyridinyl, di(C₁₋₆)alkylpyridinyl, (C₂₋₆)alkenylpyridinyl, 15 (C₁₋₆)alkylpiperazinylpyridinyl, [(C₁₋₆)alkyl](piperazinyl)pyridinyl, [(C₁₋₆)alkoxycarbonyl-piperazinyl][(C₁₋₆)alkyl]pyridinyl, piperidinyl(C₁₋₆)alkylpyridinyl, [(C₁₋₆)alkyl]-oxy)pyridinyl, hydroxypyridinyl, hydroxy(C₁₋₆)alkylpyridinyl, (C₁₋₆)alkoxypyridinyl, [(C₁₋₆)alkoxy][(C₁₋₆)alkyl]pyridinyl, [(C₁₋₆)alkoxy][di(C₁₋₆)alkyl]pyridinyl, 20 (C₁₋₆)alkoxy(C₁₋₆)alkylpyridinyl, aminopyridinyl, carboxy(C₁₋₆)alkylpyridinyl, (C₁₋₆)alkoxycarbonyl(C₁₋₆)alkylpyridinyl, pyridazinyl, (C₁₋₆)alkylpyridazinyl, piperidinylpyridazinyl, oxypyridazinyl, (C₁₋₆)alkoxypyridazinyl, aminopyridazinyl, hydroxy(C₁₋₆)alkylaminopyridazinyl, di(C₁₋₆)alkylaminopyridazinyl, pyrimidinyl, (C₁₋₆)alkylpyrimidinyl, [(C₁₋₆)alkyl](halo)pyrimidinyl, di(C₁₋₆)alkylpyrimidinyl, 25 pyrrolidinylpyrimidinyl, (C₁₋₆)alkylpiperazinylpyrimidinyl, [(C₁₋₆)alkyl](piperazinyl)-pyrimidinyl, [(C₁₋₆)alkoxycarbonyl][(C₁₋₆)alkyl]piperazinylpyrimidinyl, hydroxypyrimidinyl, [(C₁₋₆)alkyl](hydroxy)pyrimidinyl, [(C₁₋₆)alkyl][hydroxy(C₁₋₆)alkyl]-pyrimidinyl, [(C₁₋₆)alkyl][hydroxy(C₂₋₆)alkynyl]pyrimidinyl, (C₁₋₆)alkoxypyrimidinyl, aminopyrimidinyl, di(C₁₋₆)alkylaminopyrimidinyl, [di(C₁₋₆)alkylamino](halo)pyrimidinyl, 30 carboxypyrimidinyl, [(C₁₋₆)alkoxycarbonyl(C₁₋₆)alkyl][(C₁₋₆)alkyl]pyrimidinyl, aminocarbonylpyrimidinyl, pyrazinyl, (C₁₋₆)alkoxypyrazinyl, aminopyrazinyl, hydroxy, (C₁₋₆)alkoxy, aryl(C₁₋₆)alkoxycarbonylpiperidinyloxy, morpholinyl(C₁₋₆)alkoxy, aryloxy, haloaryloxy, di(C₁₋₆)alkylpyrazoloyloxy, halopyridinyloxy, pyrrolidinylpyridinyloxy,

(C₁₋₆)alkylpiperazinylpyridinyloxy, (C₁₋₆)alkylpyrazolylpyridinyloxy,
(C₁₋₆)alkylaminopyridinyloxy, carboxypyridinyloxy, aminocarbonylpyridinyloxy,
pyridazinyloxy, (C₁₋₆)alkylpyridazinyloxy, pyrimidinyloxy, (C₁₋₆)alkylpyrimidinyloxy,
[(C₁₋₆)alkyl](halo)pyrimidinyloxy, hydroxy(C₁₋₆)alkyl, dihydroxy(C₁₋₆)alkyl,
5 pyridinyloxy(C₁₋₆)alkyl, amino, (C₁₋₆)alkylamino, dihydroxy(C₁₋₆)alkylamino, (C₁₋₆)-
alkoxy(C₁₋₆)alkylamino, N-[(C₁₋₆)alkoxy(C₁₋₆)alkyl]-N-[(C₁₋₆)alkyl]amino, di(C₁₋₆)-
alkylamino(C₁₋₆)alkylamino, N-[(C₁₋₆)alkyl]-N-[di(C₁₋₆)alkylamino(C₁₋₆)alkyl]amino, N-
[(C₁₋₆)alkyl]-N-[(C₃₋₇)cycloalkyl]amino, haloarylarnino, N-[(C₁₋₆)alkyl]-N-(haloaryl)arnino,
N-[(C₁₋₆)alkyl]-N-[aryl(C₁₋₆)alkyl]amino, N-[di(C₁₋₆)alkylamino(C₁₋₆)alkyl]-N-[aryl(C₁₋₆)-
10 alkyl]amino, cyanoaryl(C₁₋₆)alkylamino, (cyano)(halo)aryl(C₁₋₆)alkylamino, methylene-
dioxyaryl(C₁₋₆)alkylamino, N-[(C₁₋₆)alkyl]-N-[(C₁₋₆)alkylpyrrolidinyl]amino, piperidinyl-
amino, N-[(C₁₋₆)alkyl]-N-(piperidinyl)amino, N-[(C₃₋₇)cycloalkyl(C₁₋₆)alkyl]-N-
(piperidinyl)amino, (C₁₋₆)alkylpiperidinylamino, N-[(C₁₋₆)alkyl]-N-[(C₁₋₆)alkyl-
15 piperidinyl]amino, N-[(C₁₋₆)alkyl]-N-[(C₃₋₇)cycloalkylpiperidinyl]amino, N-[(C₁₋₆)alkyl]-
N-[(C₂₋₆)alkylcarbonylpiperidinyl]amino, pyrrolidinyl(C₁₋₆)alkylamino, N-[(C₁₋₆)alkyl]-N-
[pyrrolidinyl(C₁₋₆)alkyl]amino, N-[(C₁₋₆)alkyl]-N-[piperidinyl(C₁₋₆)alkyl]amino, (C₁₋₆)-
alkylpyrazolylamino, di(C₁₋₆)alkylpyrazolylamino, tri(C₁₋₆)alkylpyrazolylamino, N-[(C₁₋₆)-
alkyl]-N-[(C₁₋₆)alkylpyrazolyl]amino, thiazolylamino, imidazolylamino, [(C₁₋₆)alkoxy-
carbonyl][(C₁₋₆)alkyl]imidazolylamino, (C₁₋₆)alkylthiadiazolylamino, pyridinylamino,
20 halopyridinylamino, (C₁₋₆)alkylpyridinylamino, di(C₁₋₆)alkylpyridinylamino, trifluoro-
methylpyridinylamino, hydroxypyridinylamino, hydroxy(C₁₋₆)alkylpyridinylamino,
dihydroxy(C₁₋₆)alkylpyridinylamino, (C₁₋₆)alkoxypyridinylamino, dihydroxy(C₁₋₆)alkoxy-
pyridinylamino, di(C₁₋₆)alkyldioxolanyl(C₁₋₆)alkoxypyridinylamino, (C₁₋₆)alkoxy(C₁₋₆)-
alkylpyridinylamino, (C₁₋₆)alkoxy(C₂₋₆)alkenylpyridinylamino, dihydroxy(C₁₋₆)alkyl-
25 aminopyridinylamino, di(C₁₋₆)alkylaminopyridinylamino, (C₁₋₆)alkylamino(C₁₋₆)alkyl-
pyridinylamino, di(C₁₋₆)alkylamino(C₁₋₆)alkylpyridinylamino, carboxypyridinylamino, N-
[(C₁₋₆)alkyl]-N-[(C₁₋₆)alkylpyridinyl]amino, bis[(C₁₋₆)alkylpyridinyl]amino, bis(trifluoro-
methylpyridinyl)amino, isoquinolinylamino, (C₁₋₆)alkylpyridazinylamino, N-[(C₁₋₆)alkyl]-
N-[(C₁₋₆)alkylpyridazinyl]amino, N-[aryl(C₁₋₆)alkyl]-N-[(C₁₋₆)alkylpyridazinyl]amino,
30 di(C₁₋₆)alkylpyridazinylamino, arylpyridazinylamino, piperidinylpyridazinylamino, (C₁₋₆)-
alkoxypyridazinylamino, di(C₁₋₆)alkylaminopyridazinylamino, bis[(C₁₋₆)alkylpyridazinyl]-
amino, benzofuryl(C₁₋₆)alkylamino, thienyl(C₁₋₆)alkylamino, indolyl(C₁₋₆)alkylamino,
(C₁₋₆)alkylpyrazolyl(C₁₋₆)alkylamino, [di(C₁₋₆)alkyl](halo)pyrazolyl(C₁₋₆)alkylamino,

di(C₁₋₆)alkylisoxazolyl(C₁₋₆)alkylamino, thiazolyl(C₁₋₆)alkylamino, imidazolyl(C₁₋₆)alkylamino, (C₁₋₆)alkylimidazolyl(C₁₋₆)alkylamino, pyridinyl(C₁₋₆)alkylamino, (C₁₋₆)alkylpyridinyl(C₁₋₆)alkylamino, N-[(C₁₋₆)alkyl]-N-[pyridinyl(C₁₋₆)alkyl]amino, N-[dihydroxy(C₁₋₆)alkyl]-N-[pyridinyl(C₁₋₆)alkyl]amino, N-[(C₁₋₆)alkylpyridinyl(C₁₋₆)alkyl]-N-

- 5 [dihydroxy(C₁₋₆)alkyl]amino, amino(C₁₋₆)alkyl, (C₁₋₆)alkylamino(C₁₋₆)alkyl, di(C₁₋₆)alkylamino(C₁₋₆)alkyl, pyridinylamino(C₁₋₆)alkyl, N-[(C₂₋₆)alkylcarbonyl]-N-[(C₁₋₆)alkylpyridinyl(C₁₋₆)alkyl]amino, di(C₁₋₆)alkylamino(C₁₋₆)alkylcarbonylamino, (C₃₋₇)cycloalkylcarbonylamino, (C₁₋₆)alkylpiperidinylcarbonylamino, (C₁₋₆)alkylimidazolylcarbonylamino, formyl, C₂₋₆ alkylcarbonyl, (C₁₋₆)alkylpiperidinylaminocarbonyl, N-[(C₁₋₆)alkyl]-N-[(C₁₋₆)alkylpiperidinyl]aminocarbonyl, piperidinyl(C₁₋₆)alkylaminocarbonyl, (C₁₋₆)alkylpiperazinylcarbonyl, C₁₋₆ alkylthio, C₁₋₆ alkylsulphanyl, C₁₋₆ alkylsulphonyl, C₂₋₆ alkoxy carbonyloxy and tetra(C₁₋₆)alkyldioxaborolanyl; and

R⁴⁴ represents hydrogen, halogen, C₁₋₆ alkyl or C₁₋₆ alkoxy.

Suitable values of R⁴³ include halogen, hydroxy(C₁₋₆)alkylpyrazolyl and

- 15 [dihydroxy(C₁₋₆)alkyl]pyrazolyl.

Specific values of R⁴³ include fluoro, chloro, bromo, nitro, methyl, n-propyl, isopropyl, allyl, cyclopropyl, methylphenyl, dimethylphenyl, piperidinylmethylphenyl, piperazinylmethylphenyl, methylpiperazinylmethylphenyl, morpholinylmethylphenyl, methoxyphenyl, cyanomethoxyphenyl, dimethylaminomethylphenyl, 20 methylaminocarbonylphenyl, benzyl, chlorophenylpyrrolidinyl, dioxopyrrolidinyl, aminopyrrolidinyl, dimethylaminopyrrolidinyl, indolinyl, oxoindolinyl, phenylpiperidinyl, benzoylpiperidinyl, diethylaminocarbonylpiperidinyl, piperazinyl, methylpiperazinyl, chlorophenylpiperazinyl, pyridinylpiperazinyl, furoylpiperazinyl, homopiperazinyl, methylhomopiperazinyl, methylpiperazinylmethyl, methylpiperazinylethyl, 25 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, (difluoromethyl)pyrazolyl, (dimethyl)(trifluoromethyl)pyrazolyl, cyanomethylpyrazolyl, 30 (cyanomethyl)(dimethyl)pyrazolyl, hydroxyethylpyrazolyl, hydroxypropylpyrazolyl, 2-hydroxy-2-methylpropylpyrazolyl, (hydroxymethyl)(isopropyl)(methyl)pyrazolyl, (hydroxyethyl)(dimethyl)pyrazolyl, (hydroxypropyl)(dimethyl)pyrazolyl, methoxypropylpyrazolyl, (dihydroxypropyl)pyrazolyl, [(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, tetrahydropyranyl methylpyrazolyl, (dimethyl)(tetrahydropyranyl-methyl)pyrazolyl, pyrrolidinylethylpyrazolyl, piperidinylethylpyrazolyl, methyl-piperidinylethylpyrazolyl, morpholinylethylpyrazolyl, pyridinylmethylpyrazolyl, oxypyridinylmethylpyrazolyl, (dimethyl)(phenylcarbonylmethyl)pyrazolyl, 10 (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, 20 hydroxymethylpyridinyl, hydroxyethylpyridinyl, (1-hydroxy-1-methylethyl)pyridinyl, methoxypyridinyl, (methoxy)(methyl)pyridinyl, (dimethyl)(methoxy)pyridinyl, methoxymethylpyridinyl, aminopyridinyl, carboxymethylpyridinyl, ethoxycarbonylmethylpyridinyl, pyridazinyl, methylpyridazinyl, piperidinylpyridazinyl, oxypyridazinyl, methoxypyridazinyl, aminopyridazinyl, hydroxyethylaminopyridazinyl, 25 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, 30 methoxypyrimidinyl, aminopyrimidinyl, dimethylaminopyrimidinyl, (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, pyridazinyloxy, methylpyridazinyloxy, pyrimidinyloxy, methylpyrimidinyloxy,

5 (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*-

10 (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*-

15 (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*-(acetyl)piperidinyl)-*N*-(methyl)amino, pyrrolidinylethylamino,

20 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,

25 bromopyridinylamino, methylpyridinylamino, dimethylpyridinylamino, trifluoromethylpyridinylamino, hydroxypyridinylamino, hydroxyethylpyridinylamino, dihydroxyethylpyridinylamino, methoxypyridinylamino, dihydroxypropoxypyridinyl-amino, dimethyldioxolanylmethoxypyridinylamino, methoxyethylpyridinylamino, methoxyvinylpyridinylamino, dihydroxypropylaminopyridinylamino, dimethylamino-

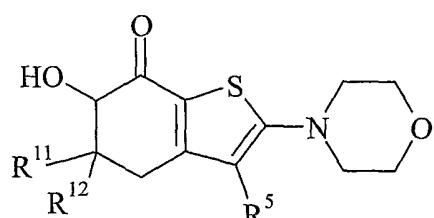
30 pyridinylamino, methylaminomethylpyridinylamino, dimethylaminomethylpyridinyl-amino, carboxypyridinylamino, *N*-(methyl)-*N*-(methylpyridinyl)amino, *N*-(ethyl)-*N*-(methylpyridinyl)amino, bis(methylpyridinyl)amino, bis(trifluoromethylpyridinyl)amino, isoquinolinylamino, methylpyridazinylamino, *N*-(methyl)-*N*-(methylpyridazinyl)amino, *N*-

(benzyl)-*N*-(methylpyridazinyl)amino, dimethylpyridazinylamino, phenylpyridazinyl-amino, piperidinylpyridazinylamino, methoxypyridazinylamino, dimethylamino-pyridazinylamino, bis(methylpyridazinyl)amino, benzofurylmethylamino, thienylmethyl-amino, indolylmethylamino, methylpyrazolylmethylamino, (chloro)(dimethyl)pyrazolyl-methylamino, dimethylisoxazolylmethylamino, thiazolylmethylamino, imidazolylmethyl-amino, methylimidazolylmethylamino, pyridinylmethylamino, methylpyridinylmethyl-amino, *N*-(methyl)-*N*-(pyridinylethyl)amino, *N*-(dihydroxypropyl)-*N*-(pyridinylmethyl)-amino, *N*-(dihydroxypropyl)-*N*-(methylpyridinylmethyl)amino, aminomethyl, methylaminomethyl, dimethylaminomethyl, pyridinylaminomethyl, *N*-(acetyl)-*N*-(methyl-pyridinyl)amino, dimethylaminoethylcarbonylamino, cyclohexylcarbonylamino, methylpiperidinylcarbonylamino, methylimidazolylcarbonylamino, formyl, acetyl, methylpiperidinylaminocarbonyl, *N*-(methyl)-*N*-(methylpiperidinyl)aminocarbonyl, piperidinylethylaminocarbonyl, methylpiperazinylcarbonyl, isopropylthio, isopropyl-sulphanyl, isopropylsulphonyl, *tert*-butoxycarbonyloxy and tetramethyldioxaborolanyl.

15 Particular values of R⁴³ include bromo, hydroxyethylpyrazolyl and (dihydroxypropyl)pyrazolyl.

In one embodiment, R⁴⁴ represents hydrogen. In another embodiment, R⁴⁴ represents halogen, especially fluoro, chloro or bromo. In a further embodiment, R⁴⁴ represents C₁₋₆ alkyl, especially methyl. In an additional embodiment, R⁴⁴ represents C₁₋₆ alkoxy, especially methoxy.

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



(IIE)

25

wherein

R⁵, R¹¹ and R¹² are as defined above.

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 5 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 10 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, 15 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 20 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.

25 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 30 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 5 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. 10 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.

15 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 20 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.

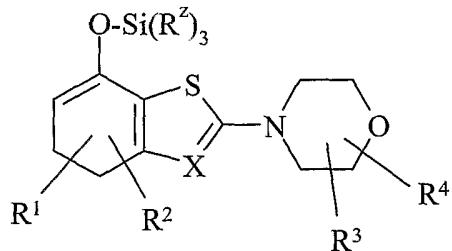
25 For ophthalmic administration the compounds according to the present invention may be conveniently formulated as micronized suspensions in isotonic, pH-adjusted sterile saline, either with or without a preservative such as a bactericidal or fungicidal agent, for example phenylmercuric nitrate, benzylalkonium chloride or chlorhexidine acetate. Alternatively, for ophthalmic administration compounds may be formulated in an ointment 30 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 10 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):



(III)

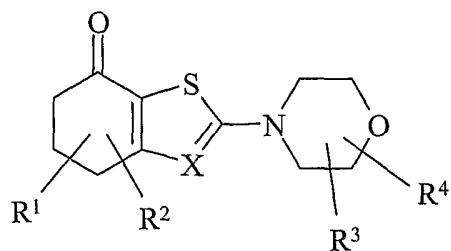
15

wherein X, R¹, R², R³ and R⁴ are as defined above, and R^z represents C₁₋₆ alkyl; with an oxidising agent.

Suitably, R^z represents methyl.

The oxidising agent of use in the reaction with compound (III) is suitably a peroxyacid, e.g. *m*-chloroperbenzoic acid, in which case the reaction is conveniently effected in a suitable solvent, e.g. a chlorinated solvent such as dichloromethane.

The compounds of formula (III) above may be prepared by treating a compound of formula (IV):



(IV)

wherein X, R¹, R², R³ and R⁴ are as defined above; with a strong base; followed by reaction with a compound of formula L¹-Si(R^z)₃, wherein R^z is as defined above, and L¹ represents a halogen atom.

The halogen atom L¹ is suitably chloro.

The strong base of use in the reaction with compound (IV) is suitably a hexa(C₁₋₆)-alkyldisilazide reagent, e.g. sodium bis(trimethylsilyl)amide, in which case the reaction is conveniently effected in an inert solvent, e.g. a cyclic ether such as tetrahydrofuran.

10 The intermediates of formula (IV) above may be prepared by the methods described in WO 2006/114606, WO 2007/141504, WO 2008/001076, and copending international patent application no. PCT/GB2007/003853, which was published on 17 April 2008 as WO 2008/044022; or by procedures analogous thereto.

15 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, e.g. by methods analogous to those described in WO 2006/114606, WO 2007/141504, WO 2008/001076, and copending international patent application no. PCT/GB2007/003853, which was published on 17 April 2008 as WO 2008/044022.

20 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.

25 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

- 5 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
10 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
15 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

- 20 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.

- 25 The compounds in accordance with this invention potently inhibit the activity of human PI3K α and/or PI3K β and/or PI3K γ and/or PI3K δ .

Enzyme Inhibition Assays

- Measurement of the ability of compounds to inhibit the lipid kinase activity of the
30 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 μ M 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 IC₅₀.

5 When tested in the above assay, the compounds of the accompanying Examples were all found to possess IC₅₀ values for inhibition of activity of human PI3K α and/or PI3K β and/or PI3K γ and/or PI3K δ of 50 μ M or better.

EXAMPLES

10 **Abbreviations**

	EtOAc:	ethyl acetate		DCM:	dichloromethane
	MeOH:	methanol		THF:	tetrahydrofuran
	MeCN:	acetonitrile		Et ₂ O:	diethyl ether
15	DMF:	<i>N,N</i> -dimethylformamide		DIPEA:	<i>N,N</i> -diisopropylethylamine
	SiO ₂ :	silica			
	brine:	sat. aqueous sodium chloride solution		sat.:	saturated
	r.t.:	room temperature		RT:	retention time
	h:	hour		br:	broad
20	M:	mass			
	HPLC:	High Performance Liquid Chromatography			
	LCMS:	Liquid Chromatography Mass Spectrometry			
	ES+:	Electrospray Positive Ionisation			

25 **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.

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

Preparative HPLC methods

Method 1: Phenomenex Luna C18(2) 250 × 21.2 mm, 5 µm column. Mobile phase A: 99.92% water, 0.08% formic acid. Mobile phase B: 99.92% MeCN, 0.08% formic acid. Gradient program (flow rate 25.0 mL/min), column temperature: ambient, variable

5 gradient.

Method 2: Phenomenex Luna C18(2) 250 × 21.2 mm, 5 µm column. Mobile phase A: 10 mM ammonium acetate in water. Mobile phase B: 10 mM ammonium acetate in MeCN. Gradient program (flow rate 25.0 mL/min), column temperature: ambient, variable

10 gradient.

Analytical LCMS method

Method 3: Phenomenex Luna C18(2) 100 × 4.6 mm, 5 µm column. Mobile phase A: 99.92% water, 0.08% formic acid. Mobile phase B: 99.92% MeCN, 0.08% formic acid.

15 Gradient program (flow rate 3.0 mL/min, column temperature 35°C):

Time	A %	B %
0.00	95.0	5.0
4.40	5.0	95.0
5.30	5.0	95.0
20	5.32	95.0
	6.50	5.0

INTERMEDIATE 1

25 2-(6-Bromo-2,3-dihydrobenzo[1,4]oxazin-4-yl)-5,5-dimethyl-5,6-dihydro-4H-benzothiazol-7-one

6-Bromo-3,3-dihydro-2H-benzo[1,4]oxazine (WO 2008/001076, Intermediate 62) (2.0 g, 9.4 mmol) and 1,1'-thiocarbonyldiimidazole (3.3 g, 18.8 mmol) were combined in THF (16 mL) and heated to 125°C under microwave irradiation for 15 minutes. The mixture was cooled to r.t., reduced *in vacuo*, and ammonia (50 mL of a 7N solution in methanol, 0.35 mol) was added. It was stirred for 2 h, then concentrated *in vacuo*. The residue was partitioned between EtOAc (100 mL) and 2N HCl (100 mL). The combined organic phases were washed with brine (100 mL), dried ($MgSO_4$), filtered and

concentrated *in vacuo*. The residue was triturated with Et₂O and heptane to give a yellow solid. Of this material, 0.5 g (1.8 mmol) was combined with 2-bromo-5,5-dimethylcyclohexane-1,3-dione (0.69 g, 3.1 mmol) and DIPEA (0.6 mL, 3.4 mmol) in THF (18 mL) and heated to 140°C under microwave irradiation for 30 minutes. After cooling to r.t. the mixture was partitioned between EtOAc (130 mL) and water (130 mL). The combined organic phases were washed with water (150 mL) and brine (100 mL), dried (MgSO₄), filtered and concentrated *in vacuo*. The resulting crude material was purified by preparative HPLC (*Method 1*) to yield the *title compound* (166 mg, 23%) as an off-white solid. δ_H (CDCl₃) 8.22 (d, *J* 2.3 Hz, 1H), 7.17 (dd, *J* 8.7, 2.3 Hz, 1H), 6.84 (d, *J* 8.7 Hz, 1H), 4.27-4.38 (m, 2H), 4.07-4.17 (m, 2H), 2.79 (s, 2H), 2.44 (s, 2H), 1.16 (s, 6H). LCMS (ES+) 393 (M+H)⁺, RT 4.4 minutes (*Method 1*).

INTERMEDIATE 2

15 2-[4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)pyrazol-1-yl]ethanol

4-Pyrazoleboronic acid pinacol ester (250 mg, 1.29 mmol), ethylene carbonate (125 mg, 1.42 mmol) and sodium hydroxide (5 mg, 0.13 mmol) were dissolved in DMF (1 mL) and the reaction mixture was heated to reflux for 2.5 h. It was cooled to r.t. before addition of activated charcoal (25 mg). The resulting suspension was stirred at r.t. for 1 h and then filtered through celite, washed with DMF (6 mL) and concentrated *in vacuo* to give the *title compound* (0.26g, 85%) as a yellow oil. LCMS (ES+) 239.18 (M+H)⁺.

INTERMEDIATE 3

25 2-{6-[1-(2-Hydroxyethyl)-1*H*-pyrazol-4-yl]-2,3-dihydro-4*H*-1,4-benzoxazin-4-yl}-5,5-dimethyl-5,6-dihydro-1,3-benzothiazol-7(4*H*)-one

A mixture of *Intermediate 1* (275 mg, 0.70 mmol), *Intermediate 2* (0.25 g, 1.05 mmol), potassium acetate (82 mg, 0.84 mmol) and bis(*tri-tert*-butylphosphino)palladium(0) (32 mg, 0.063 mmol) in DMF (2 mL) was heated to 140°C under microwave irradiation for 1 h. After cooling to r.t. activated charcoal (25 mg) was added and the resulting suspension stirred for 2 h. It was filtered through celite, washed with DMF (3 mL) and concentrated *in vacuo*. The residue was purified by preparative HPLC (*Method 3*) then dissolved in DCM (15 mL), washed with aqueous potassium carbonate solution

(0.7M, 15 mL) and the organic fraction was concentrated *in vacuo* to give the *title compound* (113 mg, 38%) as a pale yellow solid. δ_H ($CDCl_3$) 7.99 (d, J 1.9 Hz, 1H), 7.74 (d, J 0.6 Hz, 1H), 7.64 (s, 1H), 7.19 (dd, J 8.5, 2.1 Hz, 1H), 6.96 (d, J 8.3 Hz, 1H), 4.22-4.36 (m, 6H), 4.02-4.08 (m, 2H), 3.06 (t, J 6.0 Hz, 1H), 2.77 (s, 2H), 2.43 (s, 2H), 1.16 (s, 6H). LCMS (ES+) 425.17 ($M+H$)⁺, RT 3.1 minutes (*Method 1*).

INTERMEDIATE 4

2-[6-(1-Allyl-1*H*-pyrazol-4-yl)-2,3-dihydrobenzo[1,4]oxazin-4-yl]-5,5-dimethyl-5,6-

10 dihydro-4*H*-benzothiazol-7-one

A mixture of *Intermediate 1* (1.1 g, 2.76 mmol), 1-allyl-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-1*H*-pyrazole (WO 2008/001076, Intermediate 130) (1.29 g, 5.53 mmol), tetrakis(triphenylphosphine)palladium(0) (661 mg, 0.55 mmol), potassium phosphate (1.76 g, 8.3 mmol) and tetra-*n*-butylammonium bromide (894 mg, 2.76 mmol) in THF (10 mL) and water (5 mL) was heated to 140°C under microwave irradiation for 20 minutes. After cooling to r.t. the reaction mixture was concentrated *in vacuo*. Purification by column chromatography (SiO_2 , gradient elution 10-100% EtOAc in heptane) gave the *title compound* (400 mg, 34%) as a yellow oil. δ_H ($CDCl_3$) 7.99 (d, J 1.9 Hz, 1H), 7.73 (s, 1H), 7.60 (s, 1H), 7.20 (dd, J 8.5, 2.1 Hz, 1H), 6.96 (d, J 8.5 Hz, 1H), 5.98-6.16 (m, 1H), 5.23-5.36 (m, 2H), 4.74-4.82 (m, 2H), 4.31-4.38 (m, 2H), 4.21-4.27 (m, 2H), 2.77 (s, 2H), 2.43 (s, 2H), 1.16 (s, 6H).

INTERMEDIATE 5

25 2-[6-[1-(2,3-Dihydroxypropyl)-1*H*-pyrazol-4-yl]-2,3-dihydro-4*H*-1,4-benzoxazin-4-yl]-5,5-dimethyl-5,6-dihydro-1,3-benzothiazol-7(4*H*)-one

A mixture of *Intermediate 4* (0.40 g, 0.95 mmol), osmium tetroxide (12 mg, 0.05 mmol), 4-methylmorpholine *N*-oxide (134 mg, 1.14 mmol), acetone (10 mg, 0.2 mmol), *tert*-butanol (0.035 mL, 0.4 mmol) and water (1 mL) was stirred at r.t. overnight. Purification by preparative HPLC (*Method 2*) gave the *title compound* (116 mg, 22%) as a beige foam. δ_H ($CDCl_3$) 8.00 (d, J 2.1 Hz, 1H), 7.75 (s, 1H), 7.65 (s, 1H), 7.19 (dd, J 8.5, 2.1 Hz, 1H), 6.97 (d, J 8.5 Hz, 1H), 4.09-4.39 (m, 7H), 3.64-3.70 (m, 2H), 2.77 (s, 2H), 2.44 (s, 2H), 1.16 (s, 6H). LCMS (ES+) 455.3 ($M+H$)⁺, RT 2.96 minutes (*Method 3*).

EXAMPLE 1**6-Hydroxy-5,5-dimethyl-2-(morpholin-4-yl)-5,6-dihydro-1,3-benzothiazol-7(4H)-one**

5 A solution of 5,5-dimethyl-2-(morpholin-4-yl)-5,6-dihydro-1,3-benzothiazol-
7(4H)-one (WO 2006/114606, Example 48) (578 mg, 2.17 mmol) in THF (25 mL) was
cooled to -70°C. A solution of sodium bis(trimethylsilyl)amide in THF (1N, 2.40 mL,
2.40 mmol) was added gradually and the reaction mixture was allowed to warm to 0°C.
The mixture was recooled to -70°C before the addition of chlorotrimethylsilane (0.28 mL,
10 2.21 mmol), then allowed to warm to r.t. The solvent was removed *in vacuo*, then
redissolved in DCM (15 mL). *m*-Chloroperbenzoic acid (535 mg, 2.39 mmol) was added
and the reaction mixture was stirred at r.t. for 2 h. The mixture was partitioned between
sat. aqueous NaHCO₃ solution (50 mL) and DCM (50 mL), and the aqueous phase
reextracted with DCM (75 mL). The organic phase was washed with sat. aqueous
15 NaHCO₃ solution (150 mL), dried (MgSO₄) and the solvent removed *in vacuo*. A sample
of the crude product was purified by preparative HPLC (*Method 1*) to give the *title
compound* (30 mg, 11%) as a white solid. δ_H (DMSO-d₆) 5.24 (d, *J* 4.3 Hz, 1H), 3.91 (d,
J 4.3 Hz, 1H), 3.67-3.74 (m, 4H), 3.52-3.58 (m, 4H), 2.64-2.79 (m, 2H), 1.09 (s, 3H),
0.85 (s, 3H). LCMS (ES+) 283.2 (M+H)⁺, RT 2.29 minutes (*Method 3*).
20

EXAMPLE 2**2-(6-Bromo-2,3-dihydro-4H-1,4-benzoxazin-4-yl)-6-hydroxy-5,5-dimethyl-5,6-dihydro-
1,3-benzothiazol-7(4H)-one**

25 The *title compound* was prepared in a similar manner to *Example 1*, using
Intermediate 1, and was obtained as a solid (15%) after purification by preparative HPLC
(*Method 1*). δ_H (DMSO-d₆) 8.47 (d, *J* 2.3 Hz, 1H), 7.16 (dd, *J* 8.7, 2.3 Hz, 1H), 6.86 (d, *J*
8.9 Hz, 1H), 5.35 (d, *J* 4.5 Hz, 1H), 4.23-4.30 (m, 2H), 3.93-4.00 (m, 2H), 3.88-3.92 (m,
1H), 2.69-2.85 (m, 2H), 1.04 (s, 3H), 0.81 (s, 3H). LCMS (ES+) 411.0, 409.0 (M+H)⁺,
30 RT 4.10 minutes (*Method 3*).

EXAMPLE 3**6-Hydroxy-2-{6-[1-(2-hydroxyethyl)-1*H*-pyrazol-4-yl]-2,3-dihydro-4*H*-1,4-benzoxazin-4-yl}-5,5-dimethyl-5,6-dihydro-1,3-benzothiazol-7(4*H*)-one**

5 The *title compound* was prepared in a similar manner to *Example 1*, using *Intermediate 3*, and was obtained as a solid (31%) after stirring the crude product in a mixture of THF/aqueous HCl at 70°C for 1 h, evaporation to dryness *in vacuo* and purification by preparative HPLC (*Method 1*). δ_{H} (CDCl₃) 7.96 (d, *J* 2.1 Hz, 1H), 7.74 (d, *J* 0.8 Hz, 1H), 7.65 (d, *J* 0.6 Hz, 1H), 7.27 (s, 1H), 7.21 (dd, *J* 8.5, 2.1 Hz, 1H), 6.97 (d, *J* 8.5 Hz, 1H), 4.26-4.42 (m, 5H), 4.18-4.24 (m, 1H), 4.16 (s, 1H), 4.01-4.08 (m, 2H), 2.87 (s, 2H), 1.32 (s, 3H), 0.94 (s, 3H). LCMS (ES+) 441.2 (M+H)⁺, RT 2.82 minutes (*Method 3*).

EXAMPLE 4

15 **2-{6-[1-(2,3-Dihydroxypropyl)-1*H*-pyrazol-4-yl]-2,3-dihydro-4*H*-1,4-benzoxazin-4-yl}-6-hydroxy-5,5-dimethyl-5,6-dihydro-1,3-benzothiazol-7(4*H*)-one**

A mixture of *Intermediate 5* (75 mg, 0.17 mmol) and 4-toluenesulfonic acid monohydrate (5 mg, 0.03 mmol) in acetone (3.0 mL) was heated at 120°C under microwave irradiation for 50 minutes. The reaction mixture was partitioned between DCM and aqueous NaHCO₃ solution and the organic phase was evaporated to dryness *in vacuo* to give 2-{6-[1-(2,2-dimethyl-[1,3]dioxolan-4-ylmethyl)-1*H*-pyrazol-4-yl]-2,3-dihydro-4*H*-1,4-benzoxazin-4-yl}-5,5-dimethyl-5,6-dihydro-1,3-benzothiazol-7(4*H*)-one. The *title compound* was then prepared in a similar manner to *Example 1*, using 2-{6-[1-(2,2-dimethyl-[1,3]dioxolan-4-ylmethyl)-1*H*-pyrazol-4-yl]-2,3-dihydro-4*H*-1,4-benzoxazin-4-yl}-5,5-dimethyl-5,6-dihydro-1,3-benzothiazol-7(4*H*)-one, and was obtained as a solid (34%) after stirring the crude product in a mixture of THF/aqueous HCl at 60°C for 17 h, evaporation to dryness *in vacuo* and purification by preparative HPLC (*Method 1*). δ_{H} (CDCl₃) 7.97 (d, *J* 1.9 Hz, 1H), 7.74 (s, 1H), 7.65 (s, 1H), 7.26 (s, 2H), 7.21 (dd, *J* 8.5, 2.1 Hz, 1H), 6.97 (d, *J* 8.5 Hz, 1H), 4.26-4.42 (m, 5H), 4.11-4.24 (m, 3H), 3.64-3.70 (m, 2H), 2.87 (s, 2H), 1.32 (s, 3H), 0.94 (s, 3H). LCMS (ES+) 471.1 (M+H)⁺, RT 2.63 minutes (*Method 3*).

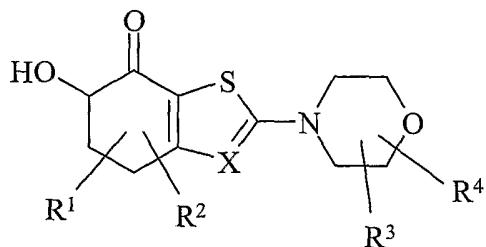
EXAMPLE 5**6-Hydroxy-5,5-dimethyl-2-(morpholin-4-yl)-5,6-dihydro-1-benzothiophen-7(4H)-one**

A solution of 5,5-dimethyl-2-(morpholin-4-yl)-5,6-dihydro-1-benzothiophen-7(4H)-one (WO 2007/141504, Example 13) (1.0 g, 3.77 mmol) in THF (20 mL) was cooled to -60°C. A solution of sodium bis(trimethylsilyl)amide in THF (1N, 4.1 mL, 4.1 mmol) was added gradually and the reaction mixture was allowed to warm to 0°C. The mixture was recooled to -60°C before the addition of chlorotrimethylsilane (0.48 mL, 3.78 mmol), then allowed to warm to r.t. and stirred for 1.5 h. The solvent was removed *in vacuo*, then redissolved in DCM (20 mL). *m*-Chloroperbenzoic acid (840 mg, 3.75 mmol) was added and the reaction mixture was stirred at r.t. for 1.5 h. The mixture was partitioned between sat. aqueous NaHCO₃ solution (75 mL) and DCM (75 mL). The organic phase was washed with sat. aqueous NaHCO₃ solution (2 x 75 mL), dried (MgSO₄) and the solvent removed *in vacuo*. The residue was purified by column chromatography (SiO₂, 2% MeOH in DCM) and a sample of this product was then further purified by preparative HPLC (*Method 1*) to give the *title compound* (27 mg, 13%) as a white solid. δ_H (DMSO-d₆) 6.14 (s, 1H), 5.03 (d, *J* 4.0 Hz, 1H), 3.89 (d, *J* 4.0 Hz, 1H), 3.68-3.75 (m, 4H), 3.23-3.29 (m, 4H), 2.58-2.72 (m, 2H), 1.08 (s, 3H), 0.81 (s, 3H). LCMS (ES+) 282.1 (M+H)⁺, RT 2.71 minutes (*Method 3*).

Claims:

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

5



(I)

wherein

X represents N or C-R⁵;

10 R¹ and R² independently represent hydrogen; or C₁₋₆ alkyl, C₃₋₇ cycloalkyl, C₃₋₇ cycloalkyl(C₁₋₆)alkyl, aryl, aryl(C₁₋₆)alkyl, C₃₋₇ heterocycloalkyl, C₃₋₇ heterocycloalkyl-(C₁₋₆)alkyl, heteroaryl or heteroaryl(C₁₋₆)alkyl, any of which groups may be optionally substituted by one or more substituents; or

15 R¹ and R², when both are attached to the same carbon atom, represent, when taken together with the carbon atom to which they are both attached, C₃₋₇ cycloalkyl or C₃₋₇ heterocycloalkyl, either of which groups may be optionally substituted by one or more substituents; or

20 R¹ and R², when attached to adjacent carbon atoms, represent, when taken together with the carbon atoms to which they are attached, C₅₋₇ cycloalkyl, phenyl or heteroaryl, any of which groups may be optionally benzo-fused and/or substituted by one or more substituents;

25 R³ and R⁴ independently represent hydrogen; or C₁₋₆ alkyl, C₂₋₆ alkynyl, C₃₋₇ cycloalkyl, C₃₋₇ cycloalkyl(C₁₋₆)alkyl, aryl, aryl(C₁₋₆)alkyl, aryl(C₂₋₆)alkenyl, aryl(C₂₋₆)-alkynyl, biaryl(C₁₋₆)alkyl, C₃₋₇ heterocycloalkyl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkyl, C₃₋₇ heterocycloalkylcarbonyl, heteroaryl, heteroaryl(C₁₋₆)alkyl, heteroaryl-aryl(C₁₋₆)alkyl or aryl-heteroaryl(C₁₋₆)alkyl, any of which groups may be optionally substituted by one or more substituents; or

R³ and R⁴, when both are attached to the same carbon atom, represent, when taken together with the carbon atom to which they are both attached, C₃₋₇ cycloalkyl or C₃₋₇ heterocycloalkyl, either of which groups may be optionally substituted by one or more substituents; or

5 R³ and R⁴, when attached to adjacent carbon atoms, represent, when taken together with the carbon atoms to which they are attached, C₅₋₇ cycloalkyl, phenyl or heteroaryl, any of which groups may be optionally benzo-fused and/or substituted by one or more substituents;

R⁵ represents hydrogen, halogen, cyano, -SR^a, -COR^e, -CO₂R^b, -CONR^cR^d or
10 -C(=N-OR^f)R^e; or R⁵ represents C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkenylcarbonyl, C₂₋₆ alkynyl, C₃₋₇ cycloalkyl, C₃₋₇ cycloalkyl(C₁₋₆)alkyl, C₃₋₇ cycloalkyl(C₂₋₆)alkenyl, C₃₋₇ cycloalkyl-(C₂₋₆)alkynyl, aryl, aryl(C₁₋₆)alkyl, aryl(C₂₋₆)alkenyl, aryl(C₂₋₆)alkynyl, biaryl, C₃₋₇ heterocycloalkyl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkyl, C₃₋₇ heterocycloalkyl(C₂₋₆)alkenyl, C₃₋₇ heterocycloalkyl(C₂₋₆)alkynyl, C₃₋₇ heterocycloalkylcarbonyl(C₂₋₆)alkynyl, C₅₋₉
15 heterobicycloalkyl(C₂₋₆)alkynyl, C₃₋₇ heterocycloalkyl-aryl, C₃₋₇ heterocycloalkyl(C₁₋₆)-alkyl-aryl, C₃₋₇ heterocycloalkyl-biaryl, heteroaryl, heteroaryl(C₁₋₆)alkyl, heteroaryl(C₁₋₆)-alkylcarbonyl, heteroaryl(C₂₋₆)alkenyl, heteroaryl(C₂₋₆)alkynyl, heteroaroylcarbonyl, C₃₋₇ heterocycloalkyl-heteroaryl, C₃₋₇ heterocycloalkyl-heteroaryl(C₂₋₆)alkynyl, heteroaryl-aryl, heteroaryl-aryl(C₁₋₆)alkyl, aryl-heteroaryl, aryl-heteroaryl(C₁₋₆)alkyl, C₃₋₇
20 heterocycloalkyl-aryl-heteroaryl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkyl-aryl-heteroaryl, C₅₋₉ heterobicycloalkyl(C₁₋₆)alkyl-aryl-heteroaryl, heteroaryl-aryl-heteroaryl, bi(heteroaryl), C₃₋₇ heterocycloalkylcarbonyl-bi(heteroaryl), aryloxyaryl, aryl(C₁₋₆)alkoxyaryl, heteroaryl(C₁₋₆)alkoxyaryl, aryl(C₁₋₆)alkylaminoaryl, heteroaryl(C₁₋₆)alkylaminoaryl, C₃₋₇ cycloalkylcarbonylaminoaryl, arylcarbonylaminoaryl, aryl(C₁₋₆)alkylcarbonylaminoaryl,
25 C₃₋₇ heterocycloalkylcarbonylaminoaryl, heteroarylcarbonylaminoaryl, aryl-(C₃₋₇)heterocycloalkylcarbonylaminoaryl, arylsulphonylaminoaryl, aryl(C₁₋₆)alkyl-sulphonylaminoaryl, heteroaryl(C₁₋₆)alkylsulphonylaminoaryl, C₃₋₇ cycloalkylamino-carbonylaminoaryl, arylaminocarbonylaminoaryl, C₃₋₇ heterocycloalkylaminocarbonyl-aminoaryl, C₃₋₇ heterocycloalkylaminocarbonylaminoaryl, heteroaryl(C₁₋₆)alkyl-aminocarbonylaminoaryl, C₃₋₇ heterocycloalkylaminocarbonylaminoaryl, C₃₋₇
30 aminocarbonylaminoaryl, C₃₋₇ heterocycloalkylcarbonylcarbonylaminoaryl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkylaminocarbonylcarbonylaminoaryl, arylcarbonylaryl, C₃₋₇ heterocycloalkylcarbonylaryl, C₃₋₇ heterocycloalkylcarbonyl(C₁₋₆)alkylaryl, aryl(C₁₋₆)-alkylaminocarbonylaryl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkylaminocarbonylaryl, heteroaryl-

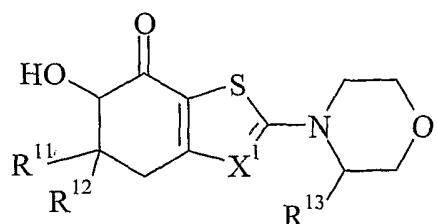
aminocarbonylaryl, heteroaryl(C₁₋₆)alkylaminocarbonylaryl, C₃₋₇ heterocycloalkylamino-carbonyl(C₁₋₆)alkylaryl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkylaminocarbonyl(C₁₋₆)alkylaryl, heteroarylaminocarbonyl(C₁₋₆)alkylaryl, heteroaryl(C₁₋₆)alkylaminocarbonyl(C₁₋₆)alkyl-aryl, arylaminoheteroaryl, C₃₋₇ heterocycloalkylamino-aryl-heteroaryl, C₃₋₇

- 5 heterocycloalkylcarbonylamino-aryl-heteroaryl, C₃₋₇ heterocycloalkylaminocarbonyl-amino-aryl-heteroaryl, C₃₋₇ cycloalkylcarbonyl-aryl-heteroaryl, C₃₋₇ heterocycloalkyl-carbonyl-aryl-heteroaryl, C₃₋₇ heterocycloalkyl(C₁₋₆)alkylcarbonyl-aryl-heteroaryl, C₅₋₉ heterobicycloalkylcarbonyl-aryl-heteroaryl, C₃₋₇ heterocycloalkylcarbonyl(C₁₋₆)alkyl-aryl-heteroaryl, C₃₋₇ heterocycloalkyl-aminocarbonyl-aryl-heteroaryl, C₃₋₇ heterocycloalkyl-
- 10 (C₁₋₆)alkylaminocarbonyl-aryl-heteroaryl or C₃₋₇ heterocycloalkylaminocarbonyl(C₁₋₆)-alkyl-aryl-heteroaryl, any of which groups may be optionally substituted by one or more substituents;

R^a represents C₁₋₆ alkyl, aryl or heteroaryl, any of which groups may be optionally substituted by one or more substituents;

- 15 R^b represents hydrogen; or optionally substituted C₁₋₆ alkyl;
R^c represents hydrogen; or C₁₋₆ alkyl, aryl, aryl(C₁₋₆)alkyl, heteroaryl, heteroaryl(C₁₋₆)alkyl or (aryl)(heteroaryl)(C₁₋₆)alkyl, any of which groups may be optionally substituted by one or more substituents;
R^d represents hydrogen or C₁₋₆ alkyl;
20 R^e represents C₁₋₆ alkyl; and
R^f represents C₁₋₆ alkyl, aryl, aryl(C₁₋₆)alkyl, heteroaryl or heteroaryl(C₁₋₆)alkyl, any of which groups may be optionally substituted by one or more substituents.

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



(IIA)

wherein

X^1 represents N or CH;

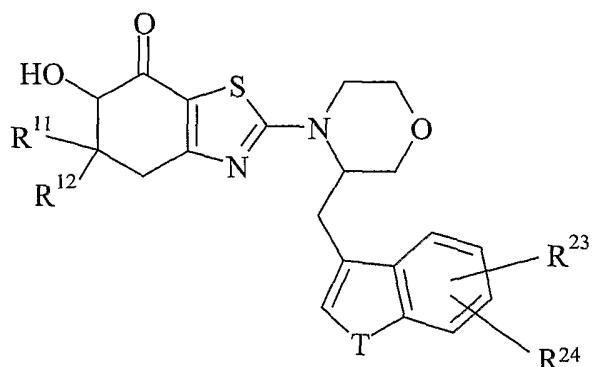
R^{11} represents hydrogen or C_{1-6} alkyl; and

5 R^{12} 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, 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

10 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 15 optionally substituted by one or more substituents; and

15 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.

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



20

(IIB)

wherein

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

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

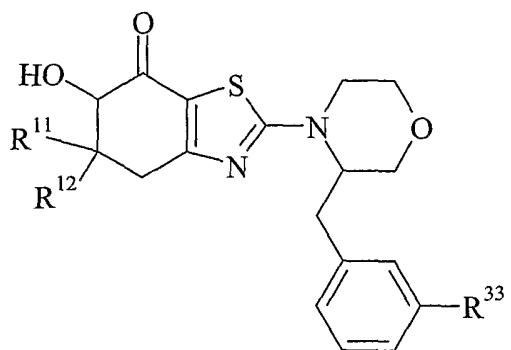
R²³ represents hydrogen, halogen, cyano, nitro, C₁₋₆ alkyl, hydroxy(C₁₋₆)alkyl, trifluoromethyl, aryl(C₁₋₆)alkyl, oxazolinyl, triazolyl, hydroxy, C₁₋₆ alkoxy, difluoromethoxy, trifluoromethoxy, C₃₋₇ cycloalkoxy, C₃₋₇ cycloalkyl(C₁₋₆)alkoxy, morpholinyl(C₁₋₆)alkoxy, aryloxy, aryl(C₁₋₆)alkoxy, C₁₋₆ alkylthio, C₁₋₆ alkylsulphiny, 5 arylsulphiny, arylsulphonyl, C₁₋₆ alkylsulphonyloxy, amino, azetidinyl, morpholinyl, C₂₋₆ alkylcarbonylamino, C₂₋₆ alkylcarbonylaminomethyl, C₂₋₆ alkoxycarbonylamino, [(C₂₋₆)aloxycarbonyl][(C₁₋₆)alkyl]amino, C₁₋₆ alkylsulphonylamino, C₂₋₆ alkylcarbonyl, C₂₋₆ alkylcarbonyl oxime, C₂₋₆ alkylcarbonyl O-(methyl)oxime, trifluoromethylcarbonyl, carboxy, C₂₋₆ alkoxycarbonyl, aminocarbonyl, C₁₋₆ alkylaminocarbonyl, [hydroxy(C₁₋₆)-10 alkyl]aminocarbonyl, [di(C₁₋₆)alkylamino(C₁₋₆)alkyl]aminocarbonyl, di(C₁₋₆)alkyl-aminocarbonyl, [(C₁₋₆)alkyl][cyano(C₁₋₆)alkyl]aminocarbonyl, [(C₁₋₆)alkyl][hydroxy(C₁₋₆)-alkyl]aminocarbonyl, [(C₁₋₆)alkoxy(C₁₋₆)alkyl][(C₁₋₆)alkyl]aminocarbonyl, [di(C₁₋₆)alkyl-amino(C₁₋₆)alkyl][(C₁₋₆)alkyl]aminocarbonyl, C₃₋₇ cycloalkyl(C₁₋₆)alkylaminocarbonyl, 15 aryl(C₁₋₆)alkylaminocarbonyl, heteroarylaminoacarbonyl, heteroaryl(C₁₋₆)alkylamino-carbonyl, azetidinylcarbonyl, hydroxyazetidinylcarbonyl, aminoazetidinylcarbonyl, C₂₋₆ alkoxycarbonylaminoazetidinylcarbonyl, pyrrolidinylcarbonyl, (C₁₋₆)alkylpyrrolidinyl-carbonyl, C₁₋₆ alkoxy(C₁₋₆)alkylpyrrolidinylcarbonyl, di(C₁₋₆)alkylaminopyrrolidinyl-carbonyl, thiazolidinylcarbonyl, oxothiazolidinylcarbonyl, piperidinylcarbonyl, (C₁₋₆)-20 alkylpiperazinylcarbonyl, morpholinylcarbonyl, C₁₋₆ alkylsulphonyl, C₁₋₆ alkylsulphonyl-methyl or di(C₁₋₆)alkylaminosulphonyl; and

R²⁴ represents hydrogen, halogen, C₁₋₆ alkoxy or di(C₁₋₆)alkylaminocarbonyl; or R²³ and R²⁴, when situated on adjacent carbon atoms, together represent methylenedioxy or difluoromethylenedioxy; and

R²⁵ represents hydrogen or C₁₋₆ alkyl.

25

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



(IIc)

wherein

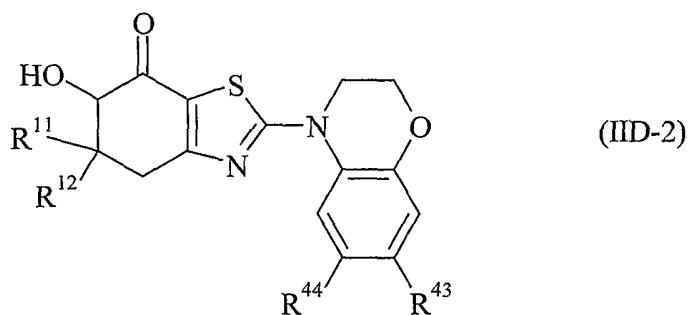
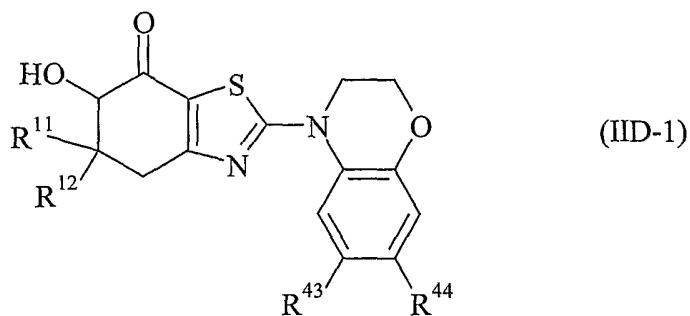
R¹¹ and R¹² are as defined in claim 2;

5 R³³ represents halogen or -NHR³⁴; or aryl or heteroaryl, either of which groups may be optionally substituted by one or more substituents; and

R³⁴ represents methylenedioxypyhenyl, morpholinyl(C₁₋₆)alkylphenyl, oxazolinyl-phenyl, [(C₁₋₆)alkyl](oxo)pyrazolylphenyl, oxazolylphenyl, isoxazolylphenyl, triazolyl-phenyl, (C₁₋₆)alkyltriazolylphenyl, (C₁₋₆)alkylpyrimidinylphenyl, pyrazolyl(C₁₋₆)alkyl-phenyl, triazolyl(C₁₋₆)alkylphenyl, C₁₋₆ alkylsulphonylaminophenyl, morpholinylcarbonyl-phenyl, C₁₋₆ alkylsulphonylphenyl, morpholinylsulphonylphenyl, dihydrobenzofuranyl, C₁₋₆ alkylsulphonylindolinyl, chromanonyl, dihydroquinolinonyl, benzoxazinonyl, benzothienyl, indolyl, dioxoindolyl, [(C₁₋₆)alkyl](halo)pyrazolyl, tri(C₁₋₆)alkylpyrazolyl, (C₁₋₆)alkylindazolyl, benzoxazolyl, benzoxazolonyl, di(C₁₋₆)alkylisoxazolyl, 10 benzothiazolyl, (C₁₋₆)alkylisothiazolyl, (C₁₋₆)alkylbenzimidazolyl, benzimidazolonyl, di(C₁₋₆)alkylbenzimidazolonyl, (C₁₋₆)alkyloxadiazolyl, furyloxadiazolyl, pyridinyl, halopyridinyl, (C₁₋₆)alkylpyridinyl, di(C₁₋₆)alkylpyridinyl, (C₁₋₆)alkoxypyridinyl, oxopyridinyl, oxopyrimidinyl, thioxopyrimidinyl, [(C₁₋₆)alkoxy](halo)pyridazinyl, (C₁₋₆)alkylcinnolinyl, quinoxalinyl or (C₁₋₆)alkylchromenyl.

20

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



wherein

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

- 5 R^{43} represents hydrogen, halogen, nitro, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₃₋₇ cycloalkyl, (C₁₋₆)alkylaryl, di(C₁₋₆)alkylaryl, piperidinyl(C₁₋₆)alkylaryl, piperazinyl(C₁₋₆)alkylaryl, (C₁₋₆)alkylpiperazinyl(C₁₋₆)alkylaryl, morpholinyl(C₁₋₆)alkylaryl, (C₁₋₆)alkoxyaryl, cyano(C₁₋₆)alkoxyaryl, di(C₁₋₆)alkylamino(C₁₋₆)alkylaryl, (C₁₋₆)alkylaminocarbonylaryl, aryl(C₁₋₆)alkyl, haloarylpyrrolidinyl, dioxopyrrolidinyl, aminopyrrolidinyl, di(C₁₋₆)alkyl-10 aminopyrrolidinyl, indolinyl, oxoindolinyl, arylpiperidinyl, arylcarbonylpiperidinyl, di(C₁₋₆)alkylaminocarbonylpiperidinyl, piperazinyl, (C₁₋₆)alkylpiperazinyl, haloaryl-piperazinyl, pyridinylpiperazinyl, furoylpiperazinyl, homopiperazinyl, (C₁₋₆)alkyl-homopiperazinyl, (C₁₋₆)alkylpiperazinyl(C₁₋₆)alkyl, morpholinyl(C₁₋₆)alkyl, benzofuryl, benzothienyl, pyrazolyl, (C₁₋₆)alkylpyrazolyl, di(C₁₋₆)alkylpyrazolyl, tri(C₁₋₆)alkyl-15 pyrazolyl, (difluoromethyl)pyrazolyl, [di(C₁₋₆)alkyl](trifluoromethyl)pyrazolyl, cyano(C₁₋₆)alkylpyrazolyl, [cyano(C₁₋₆)alkyl][di(C₁₋₆)alkyl]pyrazolyl, hydroxy(C₁₋₆)alkyl-pyrazolyl, [hydroxy(C₁₋₆)alkyl][di(C₁₋₆)alkyl]pyrazolyl, methoxy(C₁₋₆)alkylpyrazolyl, [dihydroxy(C₁₋₆)alkyl]pyrazolyl, [(hydroxy)(methoxy)(C₁₋₆)alkyl]pyrazolyl, amino(C₁₋₆)-alkylpyrazolyl, [(C₁₋₆)alkyl][amino(C₁₋₆)alkyl]pyrazolyl, [amino(C₁₋₆)alkyl][di(C₁₋₆)alkyl]-20 pyrazolyl, di(C₁₋₆)alkylamino(C₁₋₆)alkylpyrazolyl, di(C₁₋₆)alkoxyphosphono(C₁₋₆)alkyl-pyrazolyl, (C₂₋₆)alkenylpyrazolyl, (C₃₋₇)cycloalkyl(C₁₋₆)alkylpyrazolyl, [(C₃₋₇)cycloalkyl-

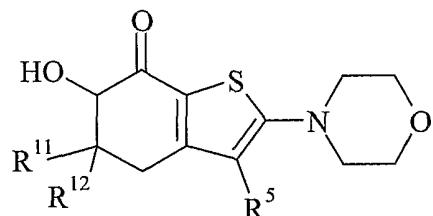
(C₁₋₆)alkyl][di(C₁₋₆)alkyl]pyrazolyl, [(C₁₋₆)alkyl](aryl)pyrazolyl, (aryl)(trifluoromethyl)-pyrazolyl, aryl(C₁₋₆)alkylpyrazolyl, aminoaryl(C₁₋₆)alkylpyrazolyl, piperidinylpyrazolyl, tetrahydropyranyl(C₁₋₆)alkylpyrazolyl, [di(C₁₋₆)alkyl][tetrahydropyranyl(C₁₋₆)alkyl]-pyrazolyl, pyrrolidinyl(C₁₋₆)alkylpyrazolyl, piperidinyl(C₁₋₆)alkylpyrazolyl, (C₁₋₆)alkyl-5-piperidinyl(C₁₋₆)alkylpyrazolyl, morpholinyl(C₁₋₆)alkylpyrazolyl, pyridinyl(C₁₋₆)alkyl-pyrazolyl, oxypyridinyl(C₁₋₆)alkylpyrazolyl, [arylcarbonyl(C₁₋₆)alkyl][di(C₁₋₆)alkyl]-pyrazolyl, [(C₁₋₆)alkyl](piperazinylcarbonyl)pyrazolyl, [(C₁₋₆)alkylaminocarbonyl][(C₁₋₆)-alkylaryl]pyrazolyl, [(C₁₋₆)alkyl][amino(C₁₋₆)alkylaminocarbonyl]pyrazolyl, aminocarbonyl(C₁₋₆)alkylpyrazolyl, [aminocarbonyl(C₁₋₆)alkyl][di(C₁₋₆)alkyl]pyrazolyl, di(C₁₋₆)alkylaminocarbonyl(C₁₋₆)alkylpyrazolyl, pyrazolo[1,5-*a*]pyridinyl, di(C₁₋₆)alkyl-isoxazolyl, (amino)[(C₁₋₆)alkyl]isoxazolyl, thiazolyl, di(C₁₋₆)alkylthiazolyl, imidazolyl, (C₁₋₆)alkylimidazolyl, di(C₁₋₆)alkylimidazolyl, imidazo[1,2-*a*]pyridinyl, (C₁₋₆)alkyl-imidazo[1,2-*a*]pyridinyl, (C₁₋₆)alkylimidazo[4,5-*b*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyrazinyl, (C₁₋₆)alkylthiadiazolyl, pyridinyl, halopyridinyl, (C₁₋₆)alkyl-15-pyridinyl, [(C₁₋₆)alkyl](halo)pyridinyl, di(C₁₋₆)alkylpyridinyl, (C₂₋₆)alkenylpyridinyl, (C₁₋₆)alkylpiperazinylpyridinyl, [(C₁₋₆)alkyl](piperazinyl)pyridinyl, [(C₁₋₆)alkoxycarbonyl-piperazinyl][(C₁₋₆)alkyl]pyridinyl, piperidinyl(C₁₋₆)alkylpyridinyl, [(C₁₋₆)alkyl]-oxy)pyridinyl, hydroxypyridinyl, hydroxy(C₁₋₆)alkylpyridinyl, (C₁₋₆)alkoxypyridinyl, [(C₁₋₆)alkoxy][(C₁₋₆)alkyl]pyridinyl, [(C₁₋₆)alkoxy][di(C₁₋₆)alkyl]pyridinyl, 20(C₁₋₆)alkoxy(C₁₋₆)alkylpyridinyl, aminopyridinyl, carboxy(C₁₋₆)alkylpyridinyl, (C₁₋₆)alkoxycarbonyl(C₁₋₆)alkylpyridinyl, pyridazinyl, (C₁₋₆)alkylpyridazinyl, piperidinylpyridazinyl, oxypyridazinyl, (C₁₋₆)alkoxypyridazinyl, aminopyridazinyl, hydroxy(C₁₋₆)alkylaminopyridazinyl, di(C₁₋₆)alkylaminopyridazinyl, pyrimidinyl, (C₁₋₆)alkylpyrimidinyl, [(C₁₋₆)alkyl](halo)pyrimidinyl, di(C₁₋₆)alkylpyrimidinyl, 25pyrrolidinylpyrimidinyl, (C₁₋₆)alkylpiperazinylpyrimidinyl, [(C₁₋₆)alkyl](piperazinyl)-pyrimidinyl, [(C₁₋₆)alkoxycarbonyl][(C₁₋₆)alkyl]piperazinylpyrimidinyl, hydroxypyrimidinyl, [(C₁₋₆)alkyl](hydroxy)pyrimidinyl, [(C₁₋₆)alkyl][hydroxy(C₁₋₆)alkyl]-pyrimidinyl, [(C₁₋₆)alkyl][hydroxy(C₂₋₆)alkynyl]pyrimidinyl, (C₁₋₆)alkoxypyrimidinyl, aminopyrimidinyl, di(C₁₋₆)alkylaminopyrimidinyl, [di(C₁₋₆)alkylamino](halo)pyrimidinyl, 30carboxypyrimidinyl, [(C₁₋₆)alkoxycarbonyl(C₁₋₆)alkyl][(C₁₋₆)alkyl]pyrimidinyl, aminocarbonylpyrimidinyl, pyrazinyl, (C₁₋₆)alkoxypyrazinyl, aminopyrazinyl, hydroxy, (C₁₋₆)alkoxy, aryl(C₁₋₆)alkoxycarbonylpiperidinyloxy, morpholinyl(C₁₋₆)alkoxy, aryloxy, haloaryloxy, di(C₁₋₆)alkylpyrazolyloxy, halopyridinyloxy, pyrrolidinylpyridinyloxy,

(C₁₋₆)alkylpiperazinylpyridinyloxy, (C₁₋₆)alkylpyrazolylpyridinyloxy,
(C₁₋₆)alkylaminopyridinyloxy, carboxypyridinyloxy, aminocarbonylpyridinyloxy,
pyridazinyloxy, (C₁₋₆)alkylpyridazinyloxy, pyrimidinyloxy, (C₁₋₆)alkylpyrimidinyloxy,
[(C₁₋₆)alkyl](halo)pyrimidinyloxy, hydroxy(C₁₋₆)alkyl, dihydroxy(C₁₋₆)alkyl,
5 pyridinyloxy(C₁₋₆)alkyl, amino, (C₁₋₆)alkylamino, dihydroxy(C₁₋₆)alkylamino, (C₁₋₆)-
alkoxy(C₁₋₆)alkylamino, N-[(C₁₋₆)alkoxy(C₁₋₆)alkyl]-N-[(C₁₋₆)alkyl]amino, di(C₁₋₆)-
alkylamino(C₁₋₆)alkylamino, N-[(C₁₋₆)alkyl]-N-[di(C₁₋₆)alkylamino(C₁₋₆)alkyl]amino, N-
[(C₁₋₆)alkyl]-N-[(C₃₋₇)cycloalkyl]amino, haloarylarnino, N-[(C₁₋₆)alkyl]-N-(haloaryl)amino,
N-[(C₁₋₆)alkyl]-N-[aryl(C₁₋₆)alkyl]amino, N-[di(C₁₋₆)alkylamino(C₁₋₆)alkyl]-N-[aryl(C₁₋₆)-
10 alkyl]amino, cyanoaryl(C₁₋₆)alkylamino, (cyano)(halo)aryl(C₁₋₆)alkylamino, methylene-
dioxyaryl(C₁₋₆)alkylamino, N-[(C₁₋₆)alkyl]-N-[(C₁₋₆)alkylpyrrolidinyl]amino, piperidinyl-
amino, N-[(C₁₋₆)alkyl]-N-(piperidinyl)amino, N-[(C₃₋₇)cycloalkyl(C₁₋₆)alkyl]-N-
(piperidinyl)amino, (C₁₋₆)alkylpiperidinylamino, N-[(C₁₋₆)alkyl]-N-[(C₁₋₆)alkyl-
15 piperidinyl]amino, N-[(C₁₋₆)alkyl]-N-[(C₃₋₇)cycloalkylpiperidinyl]amino, N-[(C₁₋₆)alkyl]-
N-[(C₂₋₆)alkylcarbonylpiperidinyl]amino, pyrrolidinyl(C₁₋₆)alkylamino, N-[(C₁₋₆)alkyl]-N-
[pyrrolidinyl(C₁₋₆)alkyl]amino, N-[(C₁₋₆)alkyl]-N-[piperidinyl(C₁₋₆)alkyl]amino, (C₁₋₆)-
alkylpyrazolylamino, di(C₁₋₆)alkylpyrazolylamino, tri(C₁₋₆)alkylpyrazolylamino, N-[(C₁₋₆)-
alkyl]-N-[(C₁₋₆)alkylpyrazolyl]amino, thiazolylamino, imidazolylamino, [(C₁₋₆)alkoxy-
carbonyl][(C₁₋₆)alkyl]imidazolylamino, (C₁₋₆)alkylthiadiazolylamino, pyridinylamino,
20 halopyridinylamino, (C₁₋₆)alkylpyridinylamino, di(C₁₋₆)alkylpyridinylamino, trifluoro-
methylpyridinylamino, hydroxypyridinylamino, hydroxy(C₁₋₆)alkylpyridinylamino,
dihydroxy(C₁₋₆)alkylpyridinylamino, (C₁₋₆)alkoxypyridinylamino, dihydroxy(C₁₋₆)alkoxy-
pyridinylamino, di(C₁₋₆)alkyldioxolanyl(C₁₋₆)alkoxypyridinylamino, (C₁₋₆)alkoxy(C₁₋₆)-
alkylpyridinylamino, (C₁₋₆)alkoxy(C₂₋₆)alkenylpyridinylamino, dihydroxy(C₁₋₆)alkyl-
25 aminopyridinylamino, di(C₁₋₆)alkylaminopyridinylamino, (C₁₋₆)alkylamino(C₁₋₆)alkyl-
pyridinylamino, di(C₁₋₆)alkylamino(C₁₋₆)alkylpyridinylamino, carboxypyridinylamino, N-
[(C₁₋₆)alkyl]-N-[(C₁₋₆)alkylpyridinyl]amino, bis[(C₁₋₆)alkylpyridinyl]amino, bis(trifluoro-
methylpyridinyl)amino, isoquinolinylamino, (C₁₋₆)alkylpyridazinylamino, N-[(C₁₋₆)alkyl]-
N-[(C₁₋₆)alkylpyridazinyl]amino, N-[aryl(C₁₋₆)alkyl]-N-[(C₁₋₆)alkylpyridazinyl]amino,
30 di(C₁₋₆)alkylpyridazinylamino, arylpyridazinylamino, piperidinylpyridazinylamino, (C₁₋₆)-
alkoxypyridazinylamino, di(C₁₋₆)alkylaminopyridazinylamino, bis[(C₁₋₆)alkylpyridazinyl]-
amino, benzofuryl(C₁₋₆)alkylamino, thienyl(C₁₋₆)alkylamino, indolyl(C₁₋₆)alkylamino,
(C₁₋₆)alkylpyrazolyl(C₁₋₆)alkylamino, [di(C₁₋₆)alkyl](halo)pyrazolyl(C₁₋₆)alkylamino,

di(C₁₋₆)alkylisoxazolyl(C₁₋₆)alkylamino, thiazolyl(C₁₋₆)alkylamino, imidazolyl(C₁₋₆)alkylamino, (C₁₋₆)alkylimidazolyl(C₁₋₆)alkylamino, pyridinyl(C₁₋₆)alkylamino, (C₁₋₆)alkylpyridinyl(C₁₋₆)alkylamino, N-[(C₁₋₆)alkyl]-N-[pyridinyl(C₁₋₆)alkyl]amino, N-[dihydroxy-(C₁₋₆)alkyl]-N-[pyridinyl(C₁₋₆)alkyl]amino, N-[(C₁₋₆)alkylpyridinyl(C₁₋₆)alkyl]-N-[dihydroxy(C₁₋₆)alkyl]amino, amino(C₁₋₆)alkyl, (C₁₋₆)alkylamino(C₁₋₆)alkyl, di(C₁₋₆)alkylamino(C₁₋₆)alkyl, pyridinylamino(C₁₋₆)alkyl, N-[(C₂₋₆)alkylcarbonyl]-N-[(C₁₋₆)alkylpyridinyl(C₁₋₆)alkyl]amino, di(C₁₋₆)alkylamino(C₁₋₆)alkylcarbonylamino, (C₃₋₇)cycloalkylcarbonylamino, (C₁₋₆)alkylpiperidinylcarbonylamino, (C₁₋₆)alkylimidazolylcarbonylamino, formyl, C₂₋₆ alkylcarbonyl, (C₁₋₆)alkylpiperidinylaminocarbonyl, N-[(C₁₋₆)alkyl]-N-[(C₁₋₆)alkylpiperidinyl]aminocarbonyl, piperidinyl(C₁₋₆)alkylaminocarbonyl, (C₁₋₆)alkylpiperazinylcarbonyl, C₁₋₆ alkylthio, C₁₋₆ alkylsulphanyl, C₁₋₆ alkylsulphonyl, C₂₋₆ alkoxy carbonyloxy and tetra(C₁₋₆)alkyldioxaborolanyl; and

R⁴⁴ represents hydrogen, halogen, C₁₋₆ alkyl or C₁₋₆ alkoxy.

15 6. A compound as claimed in claim 1 represented by formula (II E), or a pharmaceutically acceptable salt or solvate thereof:



(II E)

20 wherein

R⁵ is as defined in claim 1; and

R¹¹ and R¹² are as defined in claim 2.

25 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.

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

10 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 10 for which the administration of a selective PI3K inhibitor is indicated.

15 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 15 selective PI3K inhibitor is indicated.

20 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/GB2009/000818

A. CLASSIFICATION OF SUBJECT MATTER				
INV.	C07D277/82	C07D333/66	C07D417/04	C07D417/14
	A61K31/538	A61P9/00	A61P25/00	A61P27/02
	A61P35/00	A61P37/00		A61K31/5377
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, WPI Data, BEILSTEIN Data				
C. DOCUMENTS CONSIDERED TO BE RELEVANT				
Category*	Citation of document, with indication, where appropriate, of the relevant passages			Relevant to claim No.
P,A	ALEXANDER R ET AL: "4-(1,3-Thiazol-2-yl)morpholine derivatives as inhibitors of phosphoinositide 3-kinase" <i>BIOORGANIC & MEDICINAL CHEMISTRY LETTERS</i> , <i>PERGAMON, ELSEVIER SCIENCE, GB</i> , <i>vol. 18, no. 15, 1 August 2008 (2008-08-01)</i> , pages 4316-4320, XP023180546 <i>ISSN: 0960-894X [retrieved on 2008-06-28]</i> tables 1,2 ----- -/--			1-12
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C.		<input checked="" type="checkbox"/> 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 *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. *&* document member of the same patent family				
Date of the actual completion of the international search		Date of mailing of the international search report		
4 June 2009		15/06/2009		
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer Gettins, Marc		

INTERNATIONAL SEARCH REPORT

International application No PCT/GB2009/000818

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,A	PERRY B ET AL: "Achieving multi-isoform PI3K inhibition in a series of substituted 3,4-dihydro-2H-benzo[1,4]oxazines" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, PERGAMON, ELSEVIER SCIENCE, GB, vol. 18, no. 16, 15 August 2008 (2008-08-15), pages 4700-4704, XP023613453 ISSN: 0960-894X [retrieved on 2008-07-05] examples 1,3; table 1 -----	1-12
A	STEPANOV D E ET AL: "New derivatives of 4,5,6,7-tetrahydrobenzothiazol-7-one and 5,6,7,8-tetrahydro-4H-thiazolo[5,4-c]azepin-8-one" RUSSIAN JOURNAL OF GENERAL CHEMISTRY, PLEIADES PUBLISHING / SPRINGER, MELVILLE, NY, US, vol. 70, no. 5, 1 January 2000 (2000-01-01), pages 784-787, XP009069169 ISSN: 1070-3632 cited in the application examples VIIa,VIIe -----	1-7
A	WO 2006/114606 A (UCB SA [BE]; ALEXANDER RIKKI PETER [GB]; AUJLA PAVANDEEP [GB]; BATCHEL) 2 November 2006 (2006-11-02) cited in the application claim 1 -----	1-12
A	WO 2007/141504 A (UCB PHARMA SA [BE]; ALEXANDER RIKKI PETER [GB]; BAILEY STUART [GB]; BR) 13 December 2007 (2007-12-13) cited in the application Compounds (IB) claims 2,8 -----	1-12
P,A	WO 2008/044022 A (UCB PHARMA SA [BE]; BUCKLEY GEORGE MARTIN [GB]; MORGAN TREVOR [GB]; SA) 17 April 2008 (2008-04-17) cited in the application claims 1,10 -----	1-12

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB2009/000818

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 2006114606 A	02-11-2006	AU 2006239018 A1		02-11-2006
		CA 2607426 A1		02-11-2006
		EP 1881827 A1		30-01-2008
		JP 2008539215 T		13-11-2008
		US 2008306060 A1		11-12-2008
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WO 2007141504 A	13-12-2007	EP 2029570 A1		04-03-2009
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WO 2008044022 A	17-04-2008	NONE		
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