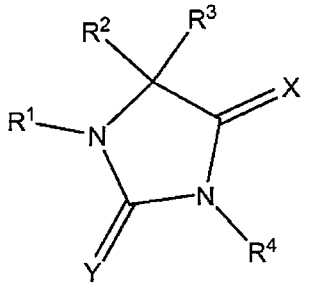
Claims

1. A compound of formula (I):



(I)

or a pharmaceutically acceptable salt, solvate or polymorph thereof, including all tautomers and stereoisomers thereof wherein:

R^1 represents -C_{3-8}carbocyclyl-heteroaryl, -C_{2-6}alkenylheteroaryl, -C_{1-6}alkylheteroaryl, or $(CH_2)_aCR^5R^6(CH_2)_b$heteroaryl wherein a and b independently represent integers 0-5 provided that a + b = 0-5 and R^5 and R^6 are alkylene which, together with the carbon to which they are attached, form a C_3-C_5 cycloalkyl group, or a bicyclic heteroaryl group;

in which any of aforesaid heteroaryl groups may optionally be substituted by one or more groups selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, -C_{1-6}thioalkyl, -SOC_{1-4}alkyl, -SO_2C_{1-4}alkyl, C_{1-6}alkoxy-, -O-C_{3-8}cycloalkyl, C_{3-8}cycloalkyl, -SO_2C_{3-8}cycloalkyl, -SOC_{3-6}cycloalkyl, C_{3-6}alkenyloxy-, C_{3-6}alkynyloxy-, -$C(O)C_{1-6}$alkyl, -$C(O)OC_{1-6}$alkyl, C_{1-6}alkoxy-C_{1-6}alkyl-, nitro, halogen, cyano, hydroxyl, -C(O)OH, -NH_2, -NHC_{1-4}alkyl, -$N(C_{1-4}alkyl)(C_{1-4}alkyl)$, -$C(O)N(C_{1-4}alkyl)(C_{1-4}alkyl)$, -$C(O)NH_2$, -$C(O)NH(C_{1-4}alkyl)$ and -$C(O)NH(C_{3-10}cycloalkyl)$;

and in which any of aforesaid carbocyclyl groups may optionally be substituted by one or more groups selected from C_{1-4}alkyl, oxo, halogen and C_{1-4}alkoxy;

R^2 represents C_{1-8}alkyl, aryl, heteroaryl, carbocyclyl, heterocyclyl, -C_{1-4}alkylaryl, -C_{1-4}alkylheteroaryl, -C_{1-4}alkylcarbocyclyl or -C_{1-4}alkylheterocyclyl;

in which any of aforesaid aryl and heteroaryl groups may optionally be substituted by one or more groups selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, -C_{1-6}thioalkyl, -SOC_{1-4}alkyl, -SO_2C_{1-4}alkyl, C_{1-6}alkoxy-, -O-C_{3-8}cycloalkyl, C_{3-8}cycloalkyl, -SO_2C_{3-8}cycloalkyl, -SOC_{3-6}cycloalkyl, C_{3-6}alkenyloxy-, C_{3-6}alkynyloxy-, -$C(O)C_{1-6}$alkyl, -$C(O)OC_{1-6}$alkyl, C_{1-6}alkoxy-C_{1-6}alkyl-, nitro, halogen, cyano, hydroxyl, -C(O)OH, -NH_2, -NHC_{1-4}alkyl, -$N(C_{1-4}alkyl)(C_{1-4}alkyl)$, -$C(O)N(C_{1-4}alkyl)(C_{1-4}alkyl)$, -$C(O)NH_2$, -$C(O)NH(C_{1-4}alkyl)$ and -$C(O)NH(C_{3-10}cycloalkyl)$;

and in which any of aforesaid carbocyclyl and heterocyclyl groups may optionally be substituted by one or more groups selected from C_{1-4}alkyl, oxo, halogen and C_{1-4}alkoxy;

or R^2 represents phenyl substituted by phenyl, phenyl substituted by a monocyclic heteroaryl group, phenyl substituted by benzyloxy, phenyl fused to carbocyclyl, phenyl fused to heterocyclyl, -C_{1-4}alkyl(phenyl substituted by phenyl), -C_{1-4}alkyl(phenyl substituted by a monocyclic heteroaryl group), -C_{1-4}alkyl(phenyl substituted by benzyloxy), -C_{1-4}alkyl(optionally substituted phenyl fused to optionally substituted carbocyclyl or -C_{1-4}alkyl(optionally substituted phenyl fused to optionally substituted heterocyclyl);
in which any of aforesaid phenyl, benzyloxy and heteroaryl groups may optionally be substituted by one or more groups selected from C_{1-4}alkyl, halogen and C_{1-4}alkoxy, and in which any of aforesaid carbocyclyl and heterocyclyl groups may optionally be substituted by one or more groups selected from C_{1-4}alkyl, oxo, halogen and C_{1-4}alkoxy;

R^3 represents H, -C_{1-4}alkyl or aryl;
in which aforesaid aryl may optionally be substituted by one or more groups selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, -C_{1-6}thioalkyl, -SOC_{1-4}alkyl, -SO_2C_{1-4}alkyl, C_{1-6}alkoxy-, -O-C_{3-8}cycloalkyl, C_{3-8}cycloalkyl, -SO_2C_{3-8}cycloalkyl, -SOC_{3-6}cycloalkyl, C_{3-6}alkenyloxy-, C_{3-6}alkynyloxy-, -C(O)C_{1-6}alkyl, -C(O)OC_{1-6}alkyl, C_{1-6}alkoxy-C_{1-6}alkyl-, nitro, halogen, cyano, hydroxyl, -C(O)OH, -NH_2, -NHC_{1-4}alkyl, -N(C_{1-4}alkyl)(C_{1-4}alkyl), -C(O)N(C_{1-4}alkyl)(C_{1-4}alkyl), -C(O)NH_2, -C(O)NH(C_{1-4}alkyl) and, -C(O)NH(C_{3-10}cycloalkyl);

or R^2 and R^3 are joined to form a carbocyclyl ring which is optionally substituted by one or more C_{1-2}alkyl groups;

or R^2 and R^3 are joined to form a carbocyclyl ring which is fused to phenyl, wherein aforesaid carbocyclyl and/or phenyl may optionally be substituted by one or more groups selected from C_{1-4}alkyl, halogen and C_{1-4}alkoxy;

or R^2 and R^3 are joined to form a carbocyclyl ring which is fused to monocyclic heteroaryl, wherein aforesaid carbocyclyl and/or heteroaryl may optionally be substituted by one or more groups selected from C_{1-4}alkyl, halogen and C_{1-4}alkoxy;

R^4 represents H, -C_{1-8}alkyl, -C(O)C_{1-6}alkyl or –NH_2;

X represents O or S; and

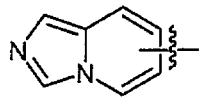
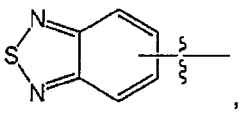
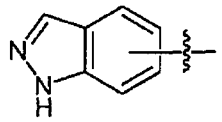
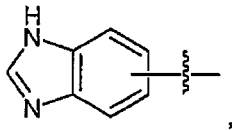
Y represents O or S.

2. A compound according to claim 1, wherein R^1 represents a bicyclic heteroaryl group.

3. A compound according to claim 2, wherein R^1 represents a benzene or pyridine ring fused to a 5-membered ring containing one or two nitrogen atoms.

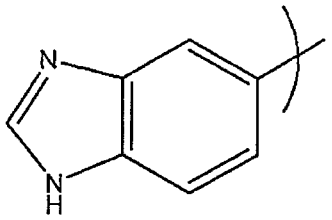
4. A compound according to claim 3, wherein the point of attachment is through the benzene or pyridine ring.

5. A compound according to claim 4, wherein R^1 is:


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,

,

,

imidazo[1,2-a]pyridine or benzo[c][1,25]thiadiazolyl.

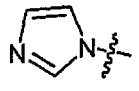
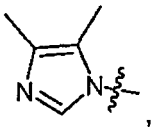
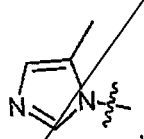
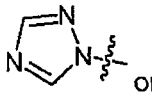
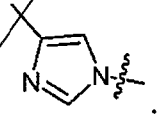
6. A compound according to claim 5, wherein R^1 represents:


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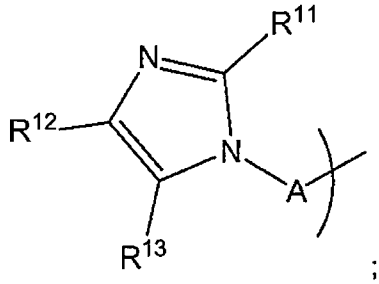
7. A compound according to claim 1, wherein R^1 represents -C_{1-6}alkylheteroaryl.

8. A compound according to claim 7, wherein the heteroaryl group of R^1 is a 5-membered ring containing 1 to 3 nitrogen atoms optionally substituted by one or more substituents selected from C_{1-4} alkyl, C_{1-4} alkoxy- and halogen.

9. A compound according to claim 8, wherein the heteroaryl group is:


,

,

,

or

.

10. A compound according to claim 1, wherein R^1 represents:

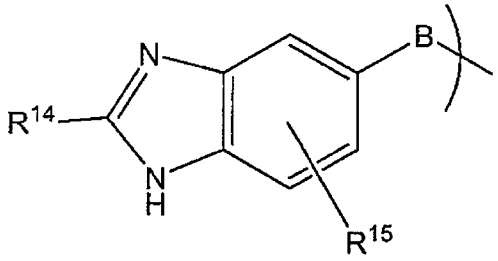


;

wherein A represents an unbranched or branched C_{1-6}alkylene chain or A represents a branched C_{1-6}alkylene chain or A represents $(CH_2)_aCR^5R^6(CH_2)_b$ and

R^{11}, R^{12} and R^{13} independently represent H or C_{1-2}alkyl.

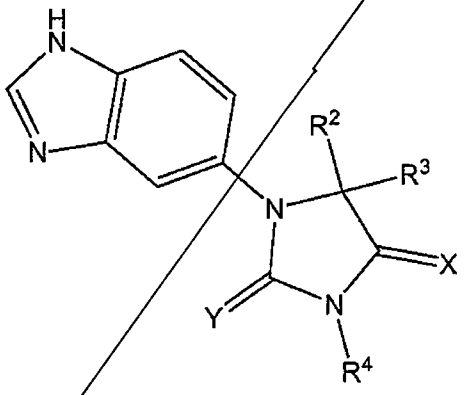
11. A compound according to claim 2 or claim 7, wherein R^1 represents



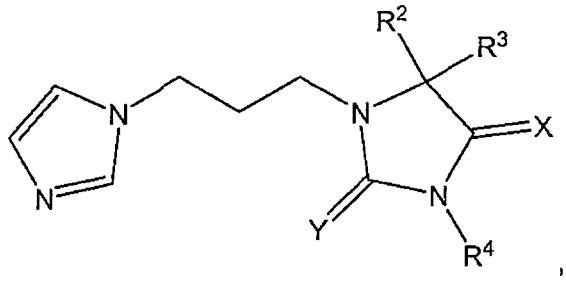
wherein B represents a bond, $-CH_2-$, $-CH_2-CH_2-$, -CH(Me)-, -CH(Me)-CH_2- or $-CH_2$-CH(Me)- and

R^{14} and R^{15} independently represent H or C_{1-2}alkyl.

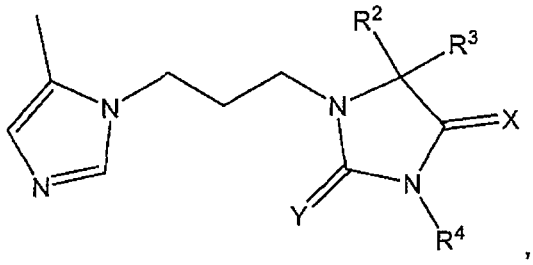
12. A compound according to any one of claims 1 to 11 represented by the formula:



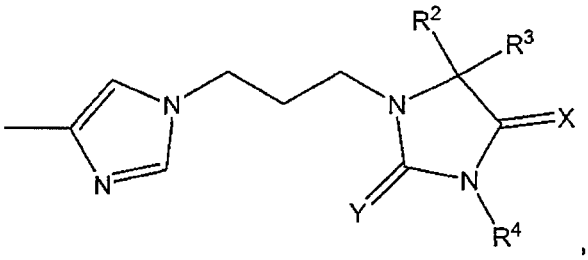
, or



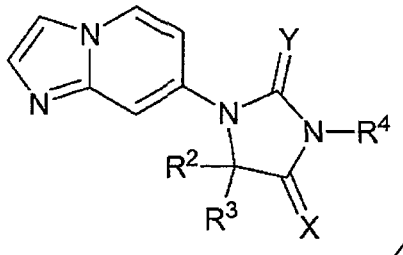
, or



, or



, or



.

Wherein R^2, R^3, R^4, X and Y are as defined in claim 1.

13. A compound according to any one of claims 1 to 12, wherein R^2 represents aryl, heteroaryl, phenyl substituted by phenyl, phenyl fused to heterocyclyl or R^2 and R^3 are joined to form a carbocyclyl ring which is fused to phenyl; the aforesaid aryl, heteroaryl, phenyl, heterocyclyl and carbocyclyl optionally being substituted.

14. A compound according to claim 13, wherein R^2 represents phenyl substituted by phenyl, the aforesaid phenyl groups optionally being substituted by one or more substitutents which may be the same or different and are chosen from halo, OH, C_{1-3}alkyl, C_{1-3} haloalkyl, C_{1-3} alkoxy, C_{1-3} haloalkoxy.

15. A compound according to claim 14, wherein R^2 is -biphenyl-4-yl.

16. A compound according to claim 13, wherein R^2 represents phenyl optionally substituted by one, two or three substituents, which may be the same or different and are chosen from halo, OH, C_{1-3}alkyl, C_{1-3} haloalkyl, C_{1-3} alkoxy, C_{1-3} haloalkoxy.

17. A compound according to claim 16, wherein R^2 is phenyl substituted by n-propyloxy.

18. A compound according to any one of claims 1 to 17 wherein R^3 represents H.

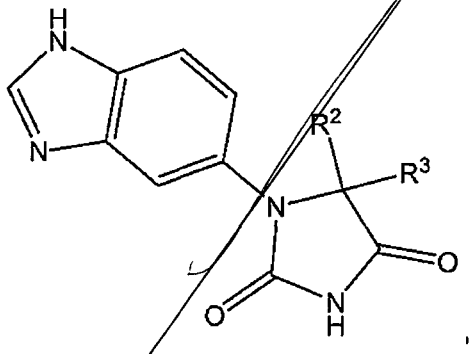
19. A compound according to any one of claims 1 to 13 wherein R^2 and R^3 are joined to form a carbocyclyl ring which is fused to phenyl.

20. A compound according to any one of claims 1 to 19, wherein R^4 represents H.

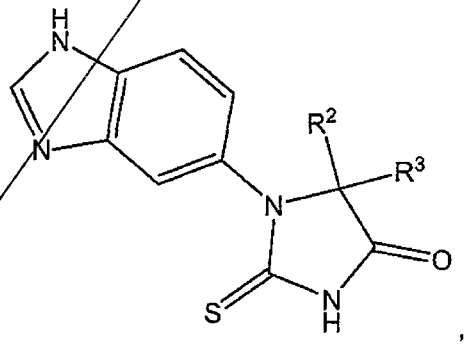
21. A compound according to any one of claims 1 to 20, wherein X represents O.

22. A compound according to any one of claims 1 to 21, wherein Y represents O.

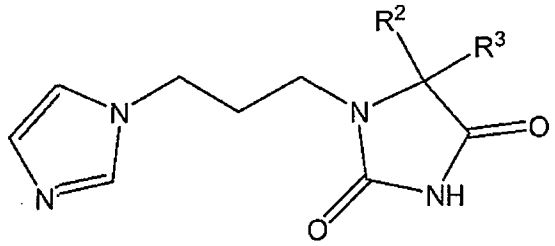
23. A compound according to any preceding claim wherein the compound of formula (I) is represented by



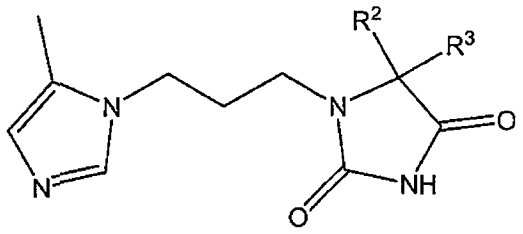
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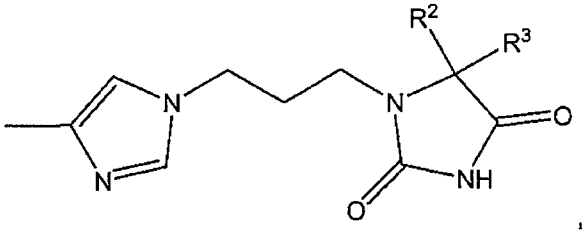
, or



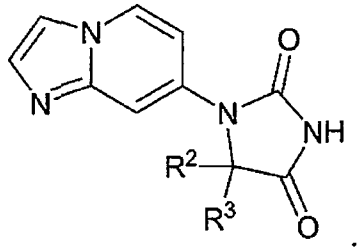
, or



, or



, or



;

wherein R^2 and R^3 are as defined in claim 1.

24. A compound of formula (I) selected from:

5-(benzo[c][1,2,5]thiadiazol-6-yl)-1-(1H-benzo[d]imidazol-5-yl)imidazolidine-2,4-dione;

1-(1H-benzo[d]imidazol-5-yl)-5-phenylimidazolidine-2,4-dione;

1-(1H-benzo[d]imidazol-5-yl)-5-(2-hydroxy-5-methylphenyl)imidazolidine-2,4-dione;

1-(1H-benzo[d]imidazol-5-yl)-5-(2-fluoro-5-trifluoromethyl)phenyl)imidazolidine-2,4-dione;

1-(1H-benzo[d]imidazol-5-yl)-5-(2-bromo-5-fluorophenyl)imidazolidine-2,4-dione;

1-(1H-benzo[d]imidazol-5-yl)-5-(4-propoxyphenyl)imidazolidine-2,4-dione;

1-(1H-benzo[d]imidazol-5-yl)-5-(4-chloro-3-trifluoromethyl)phenyl)imidazolidine-2,4-dione;

1-(1H-benzo[d]imidazol-5-yl)-5-(3-fluoro-4(trifluoromethyl)phenyl)imidazolidine-2,4-dione;

1-(1H-benzo[d]imidazol-5-yl)-5-(3-hydroxy-4-methoxyphenyl)imidazolidine-2,4-dione;

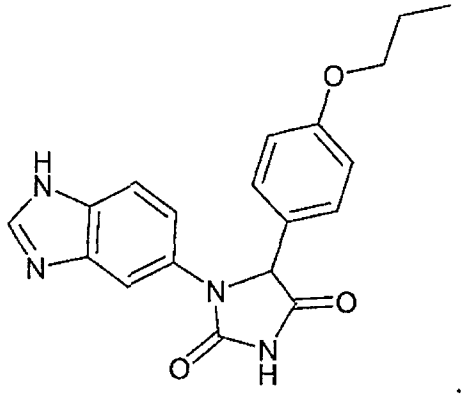
1-(1H-benzo[d]imidazol-5-yl)-5-(2-hydroxy-3-methoxyphenyl)imidazolidine-2,4-dione;

1-(1H-benzimidazol-5-yl)-5-(1,1'-biphenyl-4-yl)imidazolidine-2,4-dione;

1-(1H-benzo[d]imidazol-5-yl)-5-(3-chlorophenyl)imidazolidine-2,4-dione;
1-(1H-benzo[d]imidazol-5-yl)-5-(4-chlorophenyl)imidazolidine-2,4-dione;
1-(1H-benzo[d]imidazol-5-yl)-5-(2-chlorophenyl)imidazolidine-2,4-dione;
1-(1H-benzo[d]imidazol-5-yl)-5-(4-fluorophenyl)imidazolidine-2,4-dione;
1-(1H-benzo[d]imidazol-5-yl)-5-(2,3-dihydrobenzo[b][1,4]dioxin-7-yl)imidazolidine-2,4-dione;
1-(3-(1H-imidazol-1-yl)propyl)-5-phenylimidazolidine-2,4-dione;
1-(3-(1H-imidazol-1-yl)propyl)-5-(2-bromo-4-fluorophenyl)imidazolidine-2,4-dione;
1-(3-(1H-imidazol-1-yl)propyl)-5-(4-propoxyphenyl)imidazolidine-2,4-dione;
1-(3-(1H-imidazol-1-yl)propyl)-5-(3-fluoro-4-(trifluoromethyl)phenyl) imidazolidine-2,4-dione;
1-[3-(1H-imidazol-1-yl)propyl]-5-(4-biphenyl)imidazolidine-2,4-dione;
1-(3-(1H-imidazol-1-yl)propyl)-5-(3-chlorophenyl)imidazolidine-2,4-dione;
1-(3-(1H-imidazol-1-yl)propyl)-5-(2-chlorophenyl)imidazolidine-2,4-dione;
1-(3-(5-methyl-1H-imidazol-1-yl)propyl)-5-phenylimidazolidine-2,4-dione;
5-(2-bromo-5-fluorophenyl)-1-(3-(5-methyl-1H-imidazol-1-yl)propyl)imidazolidine-2,4-dione;
1-(3-(5-methyl-1H-imidazol-1-yl)propyl)-5-(4-propoxyphenyl)imidazolidine-2,4-dione;
1-[3-(5-methyl-1H-imidazol-1-yl)propyl]-5-(4-phenylphenyl)imidazolidine-2,4-dione;
5-(3-chlorophenyl)-1-(3-(5-methyl-1H-imidazol-1-yl)propyl)imidazolidine-2,4-dione;
1-(3-(4-methyl-1H-imidazol-1-yl)propyl)-5-phenylimidazolidine-2,4-dione;
1-[3-(4-methyl-1H-imidazol-1-yl)propyl]-5-(4-biphenyl)imidazolidine-2,4-dione;
5-(3-chlorophenyl)-1-(3-(4-methyl-1H-imidazol-1-yl)propyl)imidazolidine-2,4-dione;
3-(1H-benzimidazol-5-yl)-1',3'-dihydro-2H,5H-spiro[imidazolidine-4,2'-indene]-2,5-dione;
5-(benzo[c][1,2,5]thiadiazol-6-yl)-1-(1H-benzo[d]imidazol-5-yl)-2-thioxoimidazolidin-4-one;
1-(1H-benzo[d]imidazol-5-yl)-5-phenyl-2-thioxoimidazolidin-4-one;
1-(1H-benzimidazol-5-yl)-5-(1,1'-biphenyl-4-yl)-2-thioxoimidazolidin-4-one;
1-(1H-benzo[d]imidazol-5-yl)-5-(3-hydroxy-4-methoxyphenyl)-2-thioxoimidazolidin-4-one;
1-(1H-benzo[d]imidazol-5-yl)-5-phenyl-4-thioxoimidazolidin-2-one;
1-(1H-benzimidazol-5-yl)-5-(1,1'-biphenyl-4-yl)-4-thioxoimidazolidin-2-one;
3-(1H-benzimidazol-5-yl)-5-thioxo-1',3'-dihydro-2H-spiro[imidazolidine-4,2'-inden]-2-one;
1-(1H-benzo[d]imidazol-5-yl)-5-(4-chlorophenyl)-4-thioxoimidazolidin-2-one;
1-(1H-benzo[d]imidazol-5-yl)-5-(2,3,4-trifluorophenyl)-4-thioxoimidazolidin-2-one;
1-(1H-benzo[d]imidazol-6-yl)-5-(4-bromo-2-fluorophenyl)-4-thioxoimidazolidin-2-one;
1-(1H-benzo[d]imidazol-5-yl)-5-(2,3-difluoro-4-methylphenyl)-4-thioxoimidazolidin-2-one;
1-(1H-benzo[d]imidazol-5-yl)-5-(4-chloro-3-methylphenyl)-4-thioxoimidazolidin-2-one;
1-(1H-benzo[d]imidazol-5-yl)-3-methyl-5-phenylimida4zolidine-2,4-dione;
1-(H-imidazo[1,2-a]pyridin-7-yl)-5-phenylimidazolidine-2,4-dione;

or a pharmaceutically acceptable salt, solvate or polymorph thereof, including all tautomers and stereoisomers thereof.

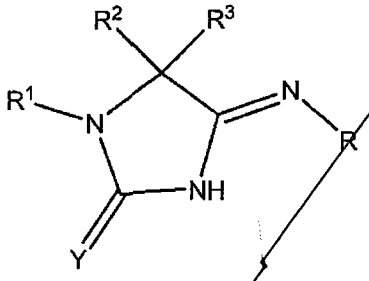
25. A compound which is the compound of Example 6, 1-(1H-benzo[d]imidazol-5-yl)-5-(4-propoxyphenyl)imidazolidine-2,4-dione, which has the structure:



or a pharmaceutically acceptable salt, solvate or polymorph thereof, including all tautomers and stereoisomers thereof.

26. A process for the preparation of a compound of formula (I) as claimed in any one of claims 1 to 25, the process comprising either:

a) reacting a compound of formula (II)

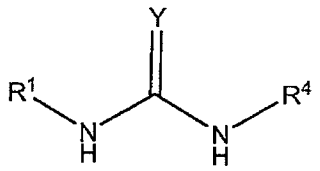


(II)

wherein R^1, R^2, R^3 and Y are as defined in claim 1 and R represents alkyl (e.g. butyl) by converting the imine to a carbonyl under aqueous conditions (e.g. aqueous trifluoroacetic acid) to give a compound of formula (I) wherein X is O and R^4 is H; or

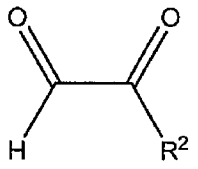
b) reacting a compound of formula (II) as defined above with a source of sulfide ions e.g. sodium sulfide to give a compound of formula (I) wherein X is S and R^4 is H; or

c) reacting a compound of formula (VIII)



(VIII)

wherein R^1 and R^4 are as defined in claim 1; with a compound of formula (IX):

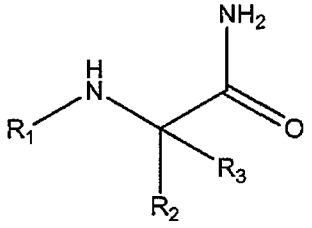


(IX)

wherein R^2 is as defined in claim 1;

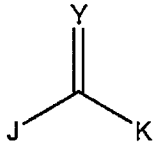
to give a compound of formula (I) wherein R^1, R^2 and Y are as defined in claim 1, R^3 represents H, R^4 represents H, -C_{1-8}alkyl or -C(O)C_{1-6}alkyl and X represents O; or

d) Reacting a compound of formula (XIII)



(XIII)

wherein R^1, R^2 and R^3 are as defined in claim 1; with a compound of formula (XIV)



(XIV)

wherein either J and K both represent H or J and K both represent leaving groups (e.g. J and K both represent imidazolyl or J represents alkoxy (such as ethoxy) and K represents halogen (e.g. chloro);

to give a compound of formula (I) wherein R^1, R^2 R^3, R^4 and Y are as defined above and X represents O; or

e) reacting a compound of formula (I) wherein R^4 represents H with a nitrite ion source (e.g. sodium nitrite). followed by reduction (e.g. using zinc dust to give a compound of formula (I) wherein R^1, R^2, R^3, X and Y are as defined above, and R^4 represents $-NH_2$.

27. A compound according to any one of claims 1 to 25 for use as a medicament.

28. A pharmaceutical composition comprising a compound according to any one of claims 1 to 25 in combination with one or more pharmaceutically acceptable diluents or carriers.

29. A pharmaceutical composition according to claim 28 which comprises additionally at least one compound, selected from the group consisting of neuroprotectants, antiparkinsonian drugs, amyloid protein deposition inhibitors, beta amyloid synthesis inhibitors, antidepressants, anxiolytic drugs, antipsychotic drugs and anti-multiple sclerosis drugs.

30. A pharmaceutical composition according to claim 28 or claim 29, which comprises additionally at least one compound, selected from the group consisting of PEP-inhibitors, LiCl, inhibitors of inhibitors of DP IV or DP IV-like enzymes, acetylcholinesterase (ACE) inhibitors, PIMT enhancers, inhibitors of beta secretases, inhibitors of gamma secretases, inhibitors of neutral endopeptidase, inhibitors of Phosphodiesterase-4 (PDE-4), TNFalpha inhibitors, muscarinic M1 receptor antagonists, NMDA receptor antagonists, sigma-1 receptor inhibitors, histamine H3 antagonists, immunomodulatory agents, immunosuppressive agents or an agent selected from the group consisting of antegren (natalizumab), Neurelan (fampridine-SR), campath (alemtuzumab), IR 208, NBI 5788/MSP 771 (tiplimotide), paclitaxel, Anergix.MS (AG 284), SH636, Differin (CD 271, adapalene), BAY 361677 (interleukin-4), matrix-metalloproteinase-inhibitors, interferon-tau (trophoblastin) and SAIK-MS.

31. A compound according to any one of claims 1 to 25 or a pharmaceutical composition according to any one of claims 28 to 30 for use in the treatment of a disease selected from the group consisting of mild cognitive impairment, Alzheimer's disease, Familial British Dementia, Familial Danish Dementia, neurodegeneration in Down Syndrome and Huntington's disease.

32. A compound according to any one of claims 1 to 25 or a pharmaceutical composition according to any one of claims 28 to 30 for use in the treatment of a disease selected from the group consisting of rheumatoid arthritis, atherosclerosis, pancreatitis and restenosis.

33. A method for the treatment or prevention of a disease selected from the group consisting of Kennedy's disease, duodenal cancer with or without *Helicobacter pylori* infections, colorectal cancer, Zolliger-Ellison syndrome, gastric cancer with or without *Helicobacter pylori* infections, pathogenic psychotic conditions, schizophrenia, infertility, neoplasia, inflammatory host responses, cancer, malign metastasis, melanoma, psoriasis, impaired humoral and cell-mediated immune responses, leukocyte adhesion and migration processes in the endothelium, impaired food intake, impaired sleep-wakefulness, impaired homeostatic regulation of energy metabolism, impaired autonomic function, impaired hormonal balance or impaired regulation of body fluids, multiple sclerosis, the Guillain-Barré syndrome and chronic inflammatory demyelinizing polyradiculoneuropathy, the method comprising administering to a patient in need of such treatment an effective amount of a compound according to any one of claims 1 to 25 or a pharmaceutical composition according to any one of claims 28 to 30.

34. A method for the treatment or prevention of a disease selected from the group consisting of mild cognitive impairment, Alzheimer's disease, Familial British Dementia, Familial Danish Dementia, neurodegeneration in Down Syndrome and Huntington's disease, the method comprising administering to a patient in need of such treatment an effective amount of a compound according to any one of claims 1 to 25 or a pharmaceutical composition according to any one of claims 28 to 30.

35. A method for the treatment or prevention of a disease selected from the group consisting of rheumatoid arthritis, atherosclerosis, pancreatitis and restenosis, the method comprising administering to a patient in need of such treatment an effective amount of a compound according to any one of claims 1 to 25 or a pharmaceutical composition according to any one of claims 28 to 30.

36. The use of a compound according to any one of claims 1 to 25 or a pharmaceutical composition according to any one of claims 28 to 30 in the manufacture of a medicament for the treatment of a disease selected from the group consisting of Kennedy's disease, duodenal cancer with or without *Helicobacter pylori* infections, colorectal cancer, Zolliger-Ellison syndrome, gastric cancer with or without *Helicobacter pylori* infections, pathogenic

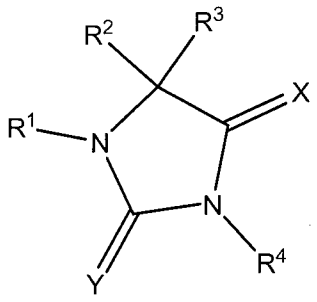
psychotic conditions, schizophrenia, infertility, neoplasia, inflammatory host responses, cancer, malign metastasis, melanoma, psoriasis, impaired humoral and cell-mediated immune responses, leukocyte adhesion and migration processes in the endothelium, impaired food intake, impaired sleep-wakefulness, impaired homeostatic regulation of energy metabolism, impaired autonomic function, impaired hormonal balance or impaired regulation of body fluids, multiple sclerosis, the Guillain-Barré syndrome and chronic inflammatory demyelinizing polyradiculoneuropathy.

37. The use of a compound according to any one of claims 1 to 25 or a pharmaceutical composition according to any one of claims 28 to 30 in the manufacture of a medicament for the treatment of a disease selected from the group consisting of mild cognitive impairment, Alzheimer's disease, Familial British Dementia, Familial Danish Dementia, neurodegeneration in Down Syndrome and Huntington's disease.

38. The use of a compound according to any one of claims 1 to 25 or a pharmaceutical composition according to any one of claims 28 to 30 in the manufacture of a medicament for the treatment of a disease selected from the group consisting of rheumatoid arthritis, atherosclerosis, pancreatitis and restenosis.

Claims

1. A compound of formula (I):

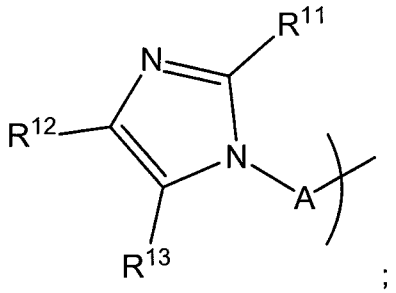


(I)

or a pharmaceutically acceptable salt, solvate or polymorph thereof, including all tautomers and stereoisomers thereof wherein:

R^1 represents 1H-benzimidazolyl

or



;

wherein A represents an unbranched or branched C_{1-6}alkylene chain; and

R^{11}, R^{12} and R^{13} independently represent H or C_{1-2}alkyl;

R^2 represents aryl, heteroaryl, phenyl substituted by phenyl, phenyl fused to heterocyclyl or R_2 and R_3 are joined to form a carbocyclyl ring which is fused to phenyl; the aforesaid aryl, heteroaryl, phenyl, heterocyclyl and carbocyclyl optionally being substituted by one or more groups selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, -C_{1-6}thioalkyl, -SOC_{1-4}alkyl, -SO_2C_{1-4}alkyl, C_{1-6}alkoxy-, -O-C_{3-8}cycloalkyl, C_{3-8}cycloalkyl, -SO_2C_{3-8}cycloalkyl, -SOC_{3-6}cycloalkyl, C_{3-6}alkenyloxy-, C_{3-6}alkynyloxy-, -$C(O)C_{1-6}$alkyl, -$C(O)OC_{1-6}$alkyl, C_{1-6}alkoxy-C_{1-6}alkyl-, nitro, halogen, cyano, hydroxyl, -C(O)OH, $-NH_2$, -NHC_{1-4}alkyl, -$N(C_{1-4}alkyl)(C_{1-4}alkyl)$, -$C(O)N(C_{1-4}alkyl)(C_{1-4}alkyl)$, $-C(O)NH_2$, -$C(O)NH(C_{1-4}alkyl)$ and -$C(O)NH(C_{3-10}cycloalkyl)$;

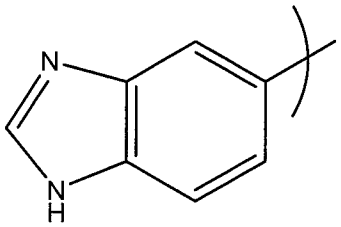
R^3 represents H or R^2 and R_3 are joined to form a carbocyclyl ring which is fused to phenyl;

R^4 represents H;

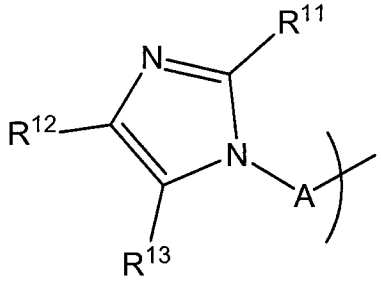
X represents O or S; and

Y represents O or S.

2. A compound according to claim 1, wherein R^1 represents:



3. A compound according to claim 1, wherein R^1 represents:

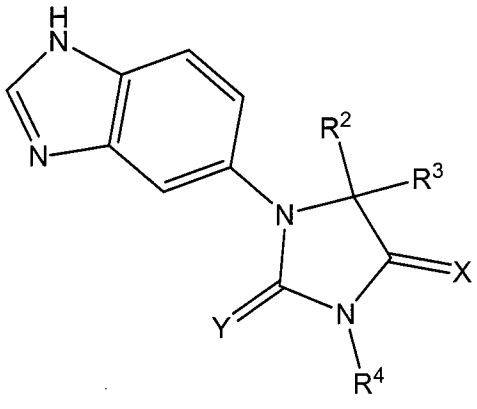


;

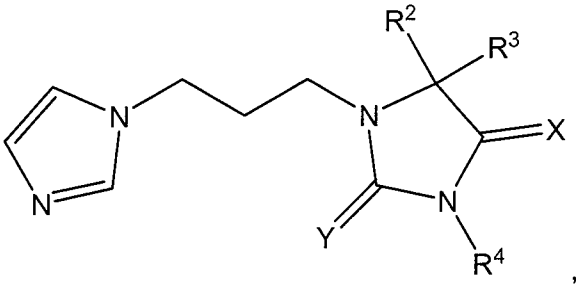
wherein A represents an unbranched or branched C_{1-6}alkylene chain and

R^{11}, R^{12} and R^{13} independently represent H or C_{1-2}alkyl.

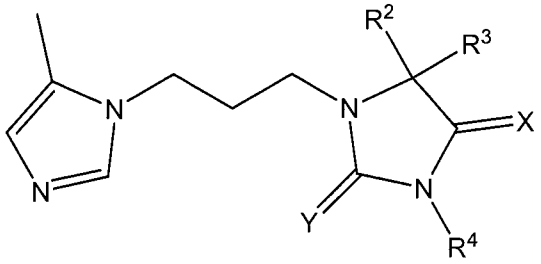
4. A compound according to any one of claims 1 to 3 represented by the formula:



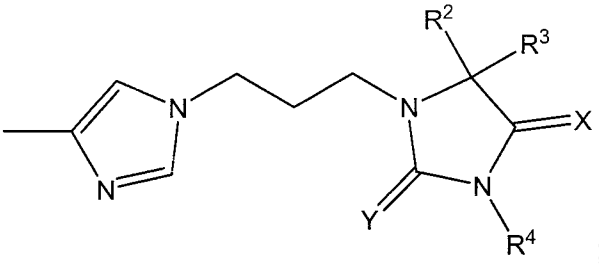
, or



, or



, or



;

wherein R^2, R^3, R^4, X and Y are as defined in claim 1.

5. A compound according to any one of claims 1 to 4, wherein R^2 represents phenyl substituted by phenyl, the aforesaid phenyl groups optionally being substituted by one or more substitutents which may be the same or different and are chosen from halo, OH, C_{1-3}alkyl, C_{1-3} haloalkyl, C_{1-3} alkoxy, C_{1-3} haloalkoxy;

or

wherein R^2 is -biphenyl-4-yl;

or

wherein R^2 represents phenyl optionally substituted by one, two or three substituents, which may be the same or different and are chosen from halo, OH, C_{1-3}alkyl, C_{1-3} haloalkyl, C_{1-3} alkoxy, C_{1-3} haloalkoxy;

or

wherein R^2 is phenyl substituted by n-propyloxy.

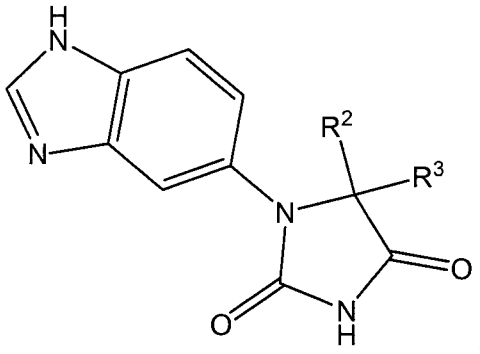
6. A compound according to any one of claims 1 to 5 wherein R^3 represents H.

7. A compound according to any one of claims 1 to 4 wherein R^2 and R^3 are joined to form a carbocyclyl ring which is fused to phenyl.

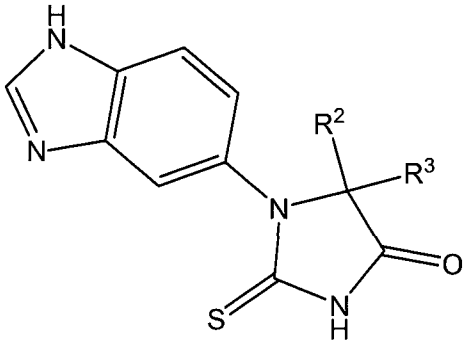
8. A compound according to any one of claims 1 to 7, wherein X represents O.

9. A compound according to any one of claims 1 to 8, wherein Y represents O.

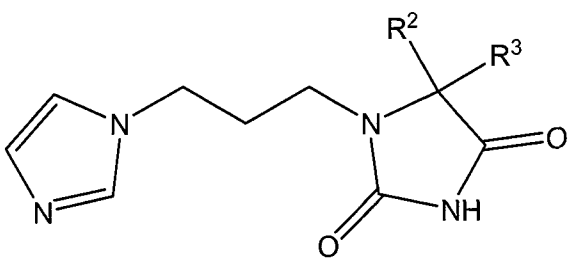
10. A compound according to any preceding claim wherein the compound of formula (I) is represented by



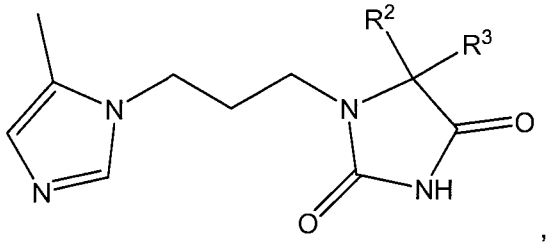
, or



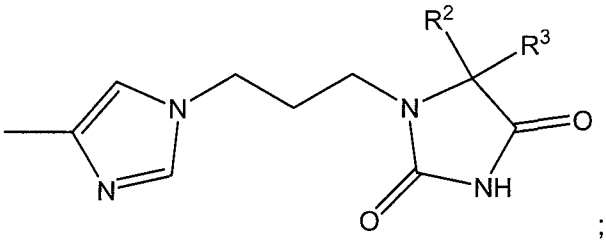
, or



, or



, or



;

wherein R^2 and R^3 are as defined in claim 1.

11. A compound of formula (I) selected from:

1-(1H-benzo[d]imidazol-5-yl)-5-phenylimidazolidine-2,4-dione;

1-(1H-benzo[d]imidazol-5-yl)-5-(2-hydroxy-5-methylphenyl)imidazolidine-2,4-dione;

1-(1H-benzo[d]imidazol-5-yl)-5-(2-fluoro-5-trifluoromethyl)phenyl)imidazolidine-2,4-dione;

1-(1H-benzo[d]imidazol-5-yl)-5-(2-bromo-5-fluorophenyl)imidazolidine-2,4-dione;

1-(1H-benzo[d]imidazol-5-yl)-5-(4-propoxyphenyl)imidazolidine-2,4-dione;

1-(1H-benzo[d]imidazol-5-yl)-5-(4-chloro-3-trifluoromethyl)phenyl)imidazolidine-2,4-dione;

1-(1H-benzo[d]imidazol-5-yl)-5-(3-fluoro-4(trifluoromethyl)phenyl)imidazolidine-2,4-dione;

1-(1H-benzo[d]imidazol-5-yl)-5-(3-hydroxy-4-methoxyphenyl)imidazolidine-2,4-dione;

1-(1H-benzo[d]imidazol-5-yl)-5-(2-hydroxy-3-methoxyphenyl)imidazolidine-2,4-dione;

1-(1H-benzimidazol-5-yl)-5-(1,1'-biphenyl-4-yl)imidazolidine-2,4-dione;

1-(1H-benzo[d]imidazol-5-yl)-5-(3-chlorophenyl)imidazolidine-2,4-dione;

1-(1H-benzo[d]imidazol-5-yl)-5-(4-chlorophenyl)imidazolidine-2,4-dione;

1-(1H-benzo[d]imidazol-5-yl)-5-(2-chlorophenyl)imidazolidine-2,4-dione;

1-(1H-benzo[d]imidazol-5-yl)-5-(4-fluorophenyl)imidazolidine-2,4-dione;

1-(1H-benzo[d]imidazol-5-yl)-5-(2,3-dihydrobenzo[b][1,4]dioxin-7-yl)imidazolidine-2,4-dione;

1-(3-(1H-imidazol-1-yl)propyl)-5-phenylimidazolidine-2,4-dione;

1-(3-(1H-imidazol-1-yl)propyl)-5-(2-bromo-4-fluorophenyl)imidazolidine-2,4-dione;

1-(3-(1H-imidazol-1-yl)propyl)-5-(4-propoxyphenyl)imidazolidine-2,4-dione;

1-(3-(1H-imidazol-1-yl)propyl)-5-(3-fluoro-4-(trifluoromethyl)phenyl) imidazolidine-2,4-dione;

1-[3-(1H-imidazol-1-yl)propyl]-5-(4-biphenyl)imidazolidine-2,4-dione;

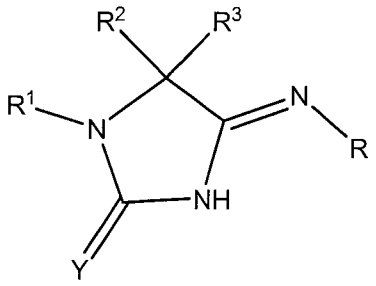
1-(3-(1H-imidazol-1-yl)propyl)-5-(3-chlorophenyl)imidazolidine-2,4-dione;

1-(3-(1H-imidazol-1-yl)propyl)-5-(2-chlorophenyl)imidazolidine-2,4-dione;
1-(3-(5-methyl-1H-imidazol-1-yl)propyl)-5-phenylimidazolidine-2,4-dione;
5-(2-bromo-5-fluorophenyl)-1-(3-(5-methyl-1H-imidazol-1-yl)propyl)imidazolidine-2,4-dione;
1-(3-(5-methyl-1H-imidazol-1-yl)propyl)-5-(4-propoxyphenyl)imidazolidine-2,4-dione;
1-[3-(5-methyl-1H-imidazol-1-yl)propyl]-5-(4-phenylphenyl)imidazolidine-2,4-dione;
5-(3-chlorophenyl)-1-(3-(5-methyl-1H-imidazol-1-yl)propyl)imidazolidine-2,4-dione;
1-(3-(4-methyl-1H-imidazol-1-yl)propyl)-5-phenylimidazolidine-2,4-dione;
1-[3-(4-methyl-1H-imidazol-1-yl)propyl]-5-(4-biphenyl)imidazolidine-2,4-dione;
5-(3-chlorophenyl)-1-(3-(4-methyl-1H-imidazol-1-yl)propyl)imidazolidine-2,4-dione;
3-(1H-benzimidazol-5-yl)-1',3'-dihydro-2H,5H-spiro[imidazolidine-4,2'-indene]-2,5-dione;
5-(benzo[c][1,2,5]thiadiazol-6-yl)-1-(1H-benzo[d]imidazol-5-yl)-2-thioxoimidazolidin-4-one;
1-(1H-benzo[d]imidazol-5-yl)-5-phenyl-2-thioxoimidazolidin-4-one;
1-(1H-benzimidazol-5-yl)-5-(1,1'-biphenyl-4-yl)-2-thioxoimidazolidin-4-one;
1-(1H-benzo[d]imidazol-5-yl)-5-(3-hydroxy-4-methoxyphenyl)-2-thioxoimidazolidin-4-one;
1-(1H-benzo[d]imidazol-5-yl)-5-phenyl-4-thioxoimidazolidin-2-one;
1-(1H-benzimidazol-5-yl)-5-(1,1'-biphenyl-4-yl)-4-thioxoimidazolidin-2-one;
3-(1H-benzimidazol-5-yl)-5-thioxo-1',3'-dihydro-2H-spiro[imidazolidine-4,2'-inden]-2-one;
1-(1H-benzo[d]imidazol-5-yl)-5-(4-chlorophenyl)-4-thioxoimidazolidin-2-one;
1-(1H-benzo[d]imidazol-5-yl)-5-(2,3,4-trifluorophenyl)-4-thioxoimidazolidin-2-one;
1-(1H-benzo[d]imidazol-6-yl)-5-(4-bromo-2-fluorophenyl)-4-thioxoimidazolidin-2-one;
1-(1H-benzo[d]imidazol-5-yl)-5-(2,3-difluoro-4-methylphenyl)-4-thioxoimidazolidin-2-one;
1-(1H-benzo[d]imidazol-5-yl)-5-(4-chloro-3-methylphenyl)-4-thioxoimidazolidin-2-one; and
1-(1H-benzo[d]imidazol-5-yl)-3-methyl-5-phenylimida4zolidine-2,4-dione;

or a pharmaceutically acceptable salt, solvate or polymorph thereof, including all tautomers and stereoisomers thereof.

12. A process for the preparation of a compound of formula (I) as claimed in any one of claims 1 to 11, the process comprising either:

a) reacting a compound of formula (II)

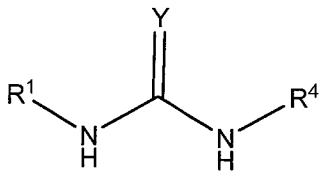


(II)

wherein R^1, R^2, R^3 and Y are as defined in claim 1 and R represents alkyl (e.g. butyl) by converting the imine to a carbonyl under aqueous conditions (e.g. aqueous trifluoroacetic acid) to give a compound of formula (I) wherein X is O and R^4 is H; or

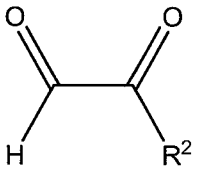
b) reacting a compound of formula (II) as defined above with a source of sulfide ions e.g. sodium sulfide to give a compound of formula (I) wherein X is S and R^4 is H; or

c) reacting a compound of formula (VIII)



(VIII)

wherein R^1 and R^4 are as defined in claim 1; with a compound of formula (IX):

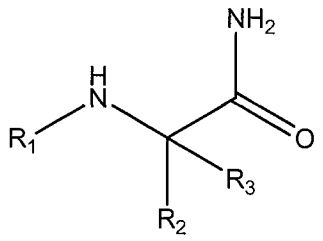


(IX)

wherein R^2 is as defined in claim 1;

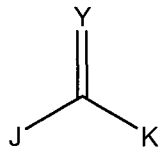
to give a compound of formula (I) wherein R^1, R^2 and Y are as defined in claim 1, R^3 represents H, R^4 represents H, and X represents O; or

d) Reacting a compound of formula (XIII)



(XIII)

wherein R^1, R^2 and R^3 are as defined in claim 1; with a compound of formula (XIV)



(XIV)

wherein either J and K both represent H or J and K both represent leaving groups (e.g. J and K both represent imidazolyl or J represents alkoxy (such as ethoxy) and K represents halogen (e.g. chloro);
to give a compound of formula (I) wherein R^1, R^2 R^3, R^4 and Y are as defined above and X represents O.

13. A compound according to any one of claims 1 to 11 for use as a medicament.

14. A pharmaceutical composition comprising a compound according to any one of claims 1 to 11 in combination with one or more pharmaceutically acceptable diluents or carriers.

15. A pharmaceutical composition according to claim 14 which comprises additionally at least one compound, selected from the group consisting of neuroprotectants, antiparkinsonian drugs, amyloid protein deposition inhibitors, beta amyloid synthesis inhibitors, antidepressants, anxiolytic drugs, antipsychotic drugs and anti-multiple sclerosis drugs.

16. A pharmaceutical composition according to claim 14 or claim 15, which comprises additionally at least one compound, selected from the group consisting of PEP-inhibitors, LiCl, inhibitors of inhibitors of DP IV or DP IV-like enzymes, acetylcholinesterase (ACE) inhibitors, PIMT enhancers, inhibitors of beta secretases, inhibitors of gamma secretases, inhibitors of neutral endopeptidase, inhibitors of Phosphodiesterase-4 (PDE-4), TNFalpha

inhibitors, muscarinic M1 receptor antagonists, NMDA receptor antagonists, sigma-1 receptor inhibitors, histamine H3 antagonists, immunomodulatory agents, immunosuppressive agents or an agent selected from the group consisting of antegren (natalizumab), Neurelan (fampridine-SR), campath (alemtuzumab), IR 208, NBI 5788/MSP 771 (tiplimotide), paclitaxel, Anergix.MS (AG 284), SH636, Differin (CD 271, adapalene), BAY 361677 (interleukin-4), matrix-metalloproteinase-inhibitors, interferon-tau (trophoblastin) and SAIK-MS.