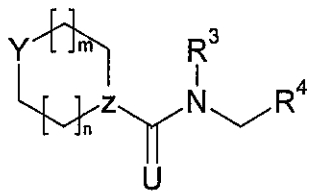
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Claims

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



(I)

Y is -N(R^{1A})- or -C(R^{1B})(R^2)-; and

R^{1A} is -X-R^5 and R^{1B} is -Q-R^5;

X is independently selected from a direct bond, -C(O)-, -(CHR^6)$_p$-, -N(R^6)- or, in either orientation, -(CH_2CHR^6)-;

Q is independently selected from a direct bond, -O-, -S-, -N(R^6)-, -C(O)-, C(H)(OH)-, -(CHR^6)$_p$- or, in either orientation, -(CH_2CHR^6)-;

p is 1 or 2;

U = O or S

R^5 is a monocyclic aromatic or non-aromatic carbocyclic or heterocyclic ring having 5 or 6 ring atoms, optionally fused to a second aromatic or non-aromatic monocyclic carbocyclic or heterocyclic ring to form a 5-5, 5-6, 6-5, or 6-6 bicyclic ring system, which monocyclic ring or bicyclic ring system is optionally substituted with one more substituents independently selected from halogen, hydroxy, cyano, nitro, CF_3, C_{1-4}-alkyl, C_{1-4}-alkoxy and -$NR^{7A}R^{7B}$, wherein

R^{7A}, R^{7B} are each independently selected from hydrogen and C_{1-4}-alkyl, wherein any alkyl residue is optionally substituted with one or more substituents independently selected from fluorine, hydroxyl and C_{1-4}-alkoxy,

or

R^{7A} and R^{7B}, together with the nitrogen atom to which they are bound, form a 4- to 7-membered saturated heterocyclic ring, optionally substituted with one or more substituents independently selected from fluorine, hydroxyl, C_{1-4}-alkyl, fluoro-C_{1-4}-alkyl and C_{1-4}-alkoxy;

R^2 is H,

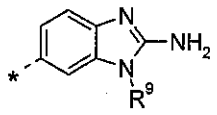
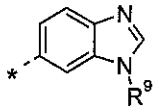
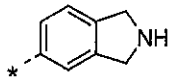
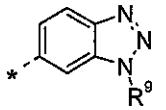
Z is N, and the ring comprising Z and Y is optionally substituted,

n = 0, 1, or 2, and m = 0 or 1, provided that m = 0 when n = 2, and provided that neither m nor n = 0 when Z and Y are each N, and

R^3 and R^6 are each independently selected from H, C_{1-4} alkyl, or cyclopropyl each of which C_{1-4} alkyl, or cyclopropyl being optionally substituted with one or more substituents independently selected from fluoro, and C_{1-4} alkoxy;

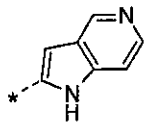
R^4 is

(i) a 6-5 bicyclic ring system selected from

optionally substituted on either ring, and wherein the bond marked * is connected to the CH_2, or

(ii) the 5-6 bicyclic ring system

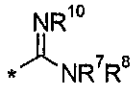
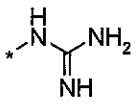
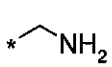
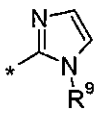
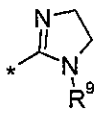


optionally substituted on either ring, and wherein the bond marked * is connected to the CH_2, or

(iii) a radical of formula $-(W)_v(CH_2)_t B$

wherein W is an optionally substituted phenyl or pyridyl ring, v is 0 or 1, and t is 0 or 3 provided that when v = 0, t = 3, and when v = 1, t = 0; and

B is selected from:

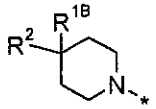
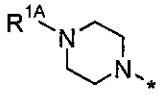
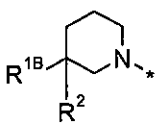
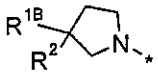






wherein R^7, R^8,R^9 and R^{10} are independently selected from H, C_{1-4} alkyl, or cyclopropyl, each of which C_{1-4} alkyl, or cyclopropyl being optionally substituted with one or more substituents independently selected from fluoro and C_{1-4} alkoxy; or

R^7 and R^8 together with the nitrogen atom to which they are attached form a 3-5 membered heterocyclic ring selected from aziridine, azetidine, and pyrrolidine each of which being optionally substituted with one or more substituents independently selected from fluoro and C_{1-4} alkoxy.

2. A compound according to claim 1 wherein R^7 and R^8 are independently selected from H, C_{1-4} alkyl, or cyclopropyl, each of which C_{1-4} alkyl, or cyclopropyl being optionally substituted with one or more substituents independently selected from fluoro and C_{1-4} alkoxy

3. A compound according to claim 1 or 2 wherein the ring comprising Z and Y is selected from:

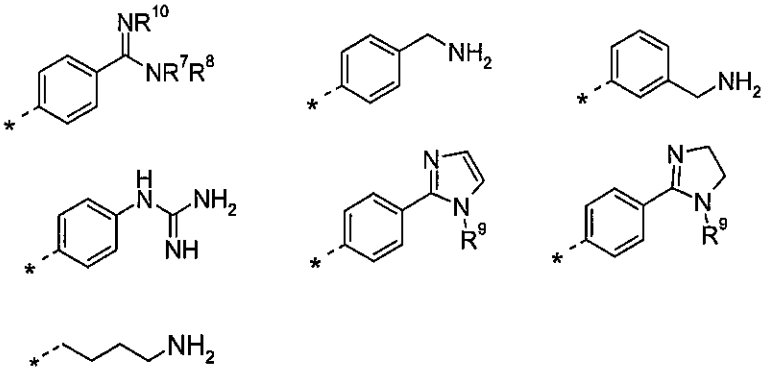





wherein the bond marked* connects to the carbon of the carbonyl group.

4. A compound according to any preceding claim wherein the ring comprising Z and Y is optionally substituted with one more substituents

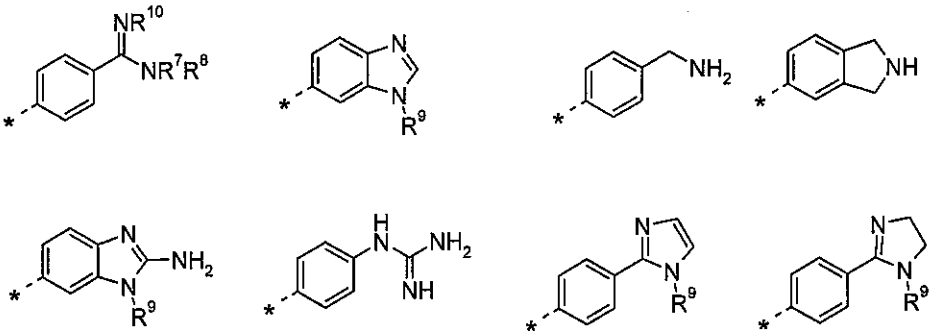
independently selected from fluoro, C_{1-4}-alkyl, C_{1-4}-alkoxy, fluoro-C_{1-4}-alkyl and fluoro-C_{1-4}-alkoxy.

5. A compound according to any preceding claim wherein the radical $-(W)_v(CH_2)_t B$ is selected from:



any of which being optionally substituted, and wherein the bond marked * is connected to the CH_2.

6. A compound according to any one of claims 1 to 4 wherein R^4 is selected from:



any of which being optionally substituted, and wherein the bond marked * is connected to the CH_2.

~~7. A compound according to any preceding claims wherein R^{10} is hydrogen.~~

~~8~~7. A compound according to any preceding claim wherein W is an optionally substituted phenyl ring.

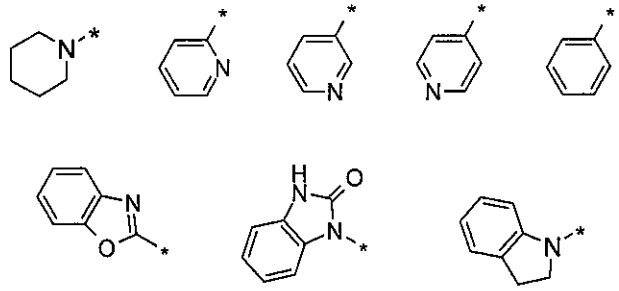
~~9. A compound according to any preceding claim wherein the the R^4 substituent is optionally substituted with one or more fluoro substituents~~

~~10. A compound according to any preceding claim wherein R^3 is H.~~

~~11. A compound according to any preceding claim wherein R^6 is H or methyl.~~

~~12. A compound according to any preceding claim wherein R^9 is H or methyl.~~

~~13~~8. A compound according to any preceding claim wherein R^5 is selected from:



wherein the bond marked * connects R^5 to the rest of the molecule, each of which being optionally substituted by the optional substituents defined in claim 1.

~~14. A compound according to any of the preceding claims wherein U = O.~~

~~15~~9. A compound according to any one of the preceding claims wherein X is independently selected from -C(O)-, -$(CHR^6)_p$-, -$N(R^6)$- or, in either orientation, -(CH_2CHR^6)-.

~~16~~10. A compound according to any one of claims 1 to 15 wherein Q is independently selected from -O-, -S-, -$N(R^6)$-, -C(O)-, C(H)(OH)-, -$(CHR^6)_p$- or, in either orientation, -(CH_2CHR^6)-.

~~17. A compound according to any one of claims 1 to 15 wherein X is independently selected from -C(O)-, -$(CHR^6)_p$-, or -$N(R^6)$-.~~

~~18. A compound according to any one of claims 1 to 15 wherein Q is independently selected from -O-, -$N(R^6)$-, -C(O)-, C(H)(OH)-, -$(CHR^6)_p$-.~~

~~19~~11. A compound as claimed in claim 1 selected from:

(4-{[(4-Benzylpiperidin-1-yl)carbonylamino]methyl}phenyl)methanaminium chloride;

2,2,2-Trifluoroacetic acid; N-{[4-(aminomethyl) phenyl]methyl}-4-[(4-methoxyphenyl)methyl] piperidine-1-carboxamide;

2,2,2-Trifluoroacetic acid; N-{[4-(aminomethyl) phenyl]methyl}-4-[(3-fluorophenyl)methyl] piperidine-1-carboxamide;

N-{[4-(Aminomethyl)phenyl]methyl}-4-[(4-fluorophenyl)methyl]piperidine-1-carboxamide hydrochloride;

2,2,2-Trifluoroacetic acid; N-{[4-(aminomethyl) phenyl]methyl}-4-[(4-chlorophenyl)methyl] piperidine-1-carboxamide;

2,2,2-Trifluoroacetic acid; N-{[4-(aminomethyl) phenyl]methyl}-4-[(4-methylphenyl)methyl] piperidine-1-carboxamide

N-{[4-(Aminomethyl)phenyl]methyl}-4-(pyridin-2-ylmethyl)piperidine-1-carboxamide;

N-{[4-(Aminomethyl)phenyl]methyl}-4-(pyridin-4-ylmethyl)piperidine-1-carboxamide;

N-{[4-(Aminomethyl)phenyl]methyl}-4-(4-fluorophenoxy)piperidine-1-carboxamide;

N-{[4-(Aminomethyl)phenyl]methyl}-4-(phenylsulfanyl)piperidine-1-carboxamide hydrochloride;

N-{[4-(Aminomethyl)phenyl]methyl}-4-[(2-chlorophenyl)amino]piperidine-1-carboxamide dihydrochloride;

2,2,2-Trifluoroacetic acid; N-{[4-(aminomethyl) phenyl]methyl}-4-[(4-fluorophenyl)carbonyl] piperidine-1-carboxamide;

N-{[4-(Aminomethyl)phenyl]methyl}-4-[(4-fluorophenyl)(hydroxy)methyl] piperidine-1-carboxamide;

N-{[4-(Aminomethyl)phenyl]methyl}-1-[(3-fluorophenyl)methyl]piperidine-4-carboxamide;

N-{[4-(Aminomethyl)phenyl]methyl}-4-benzylpiperazine-1-carboxamide;

N-{[4-(Aminomethyl)phenyl]methyl}-4-[(2-chlorophenyl)methyl]piperazine-1-carboxamide dihydrochloride;

N-{[4-(Aminomethyl)phenyl]methyl}-4-(1,3-benzoxazol-2-yl)piperidine-1-carboxamide;

N-{[4-(Aminomethyl)-3-fluorophenyl]methyl}-4-benzylpiperidine-1-carboxamide;

4-Benzyl-N-[(4-carbamimidoylphenyl)methyl]piperidine-1-carboxamide;

2,2,2-Trifluoroacetic acid; 4-benzyl-N-{[4-(N,N-dimethylcarbamimidoyl)phenyl]methyl} piperidine-1-carboxamide;

N-[(4-Carbamimidoylphenyl)methyl]-4-(pyridin-4-ylmethyl)piperidine-1-carboxamide;

N-(1H-1,3-Benzodiazol-6-ylmethyl)-4-benzylpiperidine-1-carboxamide;

2,2,2-Trifluoroacetic acid; N-(1H-1,3-benzodiazol-5-ylmethyl)-3-phenylpyrrolidine-1-carboxamide;

2,2,2-Trifluoroacetic acid; N-(1H-1,3-benzodiazol-5-ylmethyl)-3-benzylpyrrolidine-1-carboxamide;

N-[(2-Amino-1H-1,3-benzodiazol-6-yl)methyl]-4-benzylpiperidine-1-carboxamide;

2,2,2-Trifluoroacetic acid; 4-benzyl-N-[(4-carbamimidamidophenyl)methyl]piperidine-1-carboxamide;

4-Benzyl-N-(2,3-dihydro-1H-isoindol-5-ylmethyl)piperidine-1-carboxamide

~~20~~12. A pharmaceutical composition comprising a compound as claimed in any of the preceding claims, together with a pharmaceutically acceptable carrier.

~~21~~13. The use of a compound of formula (I) as claimed in any of claims 1 to 19 in the preparation of a composition for the treatment of diseases or conditions responsive to the reduction of PAR2 mediated activity.

~~22~~14. The use as claimed in claim 21 for the reduction of PAR2 mediated activity, *ex vivo* or *in vivo*.

~~23~~15. The use as claimed in claim 21 wherein the diseases or conditions are selected from inflammation, intestinal inflammation, inflammatory skin diseases including psoriasis and itch, fibrosis, arthritis, pain, cancer and pancreatitis.

~~24. A method for the treatment of diseases or conditions responsive to the reduction of PAR2 mediated activity, which comprises administering to a subject suffering such disease an effective amount of a compound of formula (I) as claimed in any of claims 1 to 19.~~

~~25. A method as claimed in claim 24 for the treatment of inflammation, intestinal inflammation, inflammatory skin diseases including psoriasis and itch, fibrosis, arthritis, pain, cancer and pancreatitis.~~