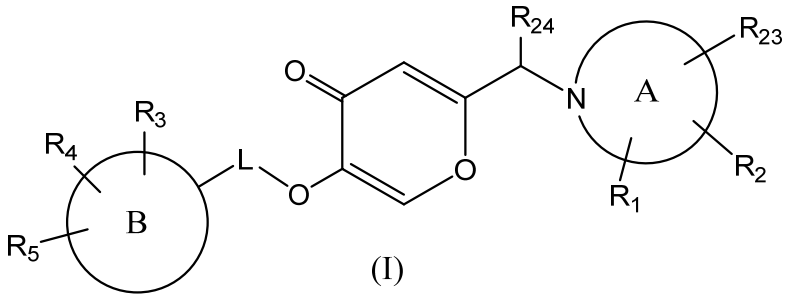
Claims

1. A compound of formula (I)

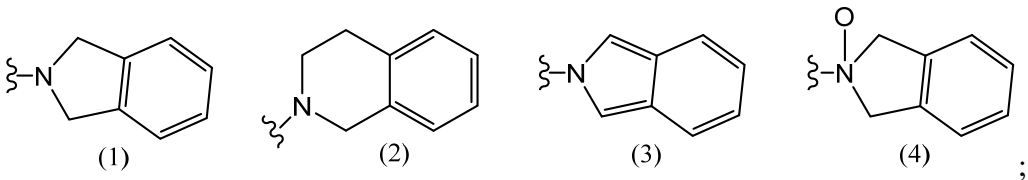


(I)

wherein

ring B is a 4-10 membered monocyclic or bicyclic ring containing 0-4 hetero-atoms independently selected from N, O or S

ring A is any of the following groups



(1) (2) (3) (4) ;

L is absent, $-CH_2-$, $-CH_2-CH_2-$ or $-CH_2-CH_2-CH_2-$, or in case ring A is (1), L can also be $-C(O)-CH_2-$;

R_1 is hydrogen, C_{1-7} alkyl, C_{1-7} alkoxy, halogen, cyano, nitro, halo C_{1-7} alkyl, halo C_{1-7} alkoxy or C_{1-7} alkylthio;

R_2 is hydrogen, C_{1-7} alkyl, halogen, hydroxy, halo C_{1-7} alkyl, nitro, halo C_{1-7} alkoxy or thiol;

or R_1 and R_2 together with the carbon atoms to which they are attached form a fused 1,3 dioxole ring;

R_3 is hydrogen, halogen, nitro, cyano, oxo, C_{1-7} alkyl, C_{2-7} alkenyl, C_{3-7} cyclo-alkyl, hydroxy C_{3-7} cycloalkyl, C_{1-7} alkoxy, hydroxy C_{1-7} alkyl, halo C_{1-7} alkyl, cyano C_{1-7} alkyl, C_{1-7} alkoxy C_{1-7} alkyl, C_{1-7} alkylthio, aminocarbonyl C_{2-7} alkenyl, halo C_{1-7} alkylthio, C_{1-7} alkoxycarbonyl C_{1-7} alkyl, C_{1-7} alkoxycarbonyl C_{2-7} alkenyl, $=NSO_2R_{20}$,$-S(O)-C_{1-7}$ alkyl, $-S(O)(NR_{14})(R_{22})$, $-S(NR_{15})(C_{1-7}$ alkyl), $-C(S)NR_{18}R_{19}$, -D-$C(O)-NR_6R_7$,

$-C(O)R_8$, -D-NR_9R_{10}, $-SO_2R_{11}$, optionally substituted 3-10 membered carbocyclyl, optionally substituted 3-10 membered carbocyclyl C_{1-7} alkyl, optionally substituted

4-10 membered heterocyclyl or optionally substituted 4-10 membered heterocyclyl C_{1-7} alkyl;

R_4 is hydrogen, halogen, hydroxy, C_{1-7} alkyl, halo C_{1-7} alkyl or oxo;

R_5 is hydrogen, halogen or C_{1-7} alkyl;

R_6 is hydrogen, C_{1-7} alkyl, C_{2-7} alkenyl, C_{3-7} cycloalkyl, hydroxy C_{1-7} alkyl, cyano C_{1-7} alkyl, -C_{1-7} alkyl-O-C(O)C_{1-7} alkyl or optionally substituted 4-10 membered heterocyclyl;

R_8 is hydrogen, C_{1-7} alkyl, C_{2-7} alkenyl, C_{3-7} cycloalkyl, C_{1-7} alkoxy, halo C_{1-7} alkyl, C_{1-7} alkoxy C_{1-7} alkyl, C_{1-7} alkylcarbonyl, C_{1-7} alkoxycarbonyl, -C_{1-7} alkyl-O-C(O)-C_{1-7} alkyl, -C_{1-7} alkyl-SO_2(C_{1-7} alkyl), -N=S(O)(C_{1-7} alkyl)(C_{1-7} alkyl) or optionally substituted 4-10 membered heterocyclyl;

R_9 is hydrogen, C_{1-7} alkyl, C_{3-7} cycloalkyl, C_{1-7} alkylcarbonyl, -SO_2(C_{1-7} alkyl) or -SO_2(C_{3-7} cycloalkyl);

R_{11} is C_{1-7} alkyl, C_{2-7} alkenyl, C_{3-7} cycloalkyl, halo C_{1-7} alkyl, cyano C_{1-7} alkyl, C_{1-7} alkoxy C_{1-7} alkyl, -$NR_{12}R_{13}$, optionally substituted 3-10 membered carbocyclyl or optionally substituted 4-10 membered heterocyclyl;

R_{12} is hydrogen, C_{1-7} alkyl, hydroxy C_{1-7} alkyl, cyano C_{1-7} alkyl, C_{1-7} alkoxy, C_{1-7} alkoxy C_{1-7} alkyl or C_{1-7} alkylcarbonyl;

R_7, R_{10}, R_{13}, R_{18}, and R_{19} are, independently, hydrogen, C_{1-7} alkyl or C_{3-7} cycloalkyl;

R_{14} is hydrogen, C_{1-7} alkyl, C_{1-7} alkylcarbonyl or -SO_2R_{21};

R_{15} is hydrogen, C_{1-7} alkyl, C_{3-7} cycloalkyl, C_{1-7} alkylcarbonyl, -SO_2R_{17};

R_{17} is C_{1-7} alkyl or an optionally substituted 3-10 membered carbocyclyl;

R_{20} and R_{21} are, independently, C_{1-7} alkyl, C_{3-7} cycloalkyl or optionally substituted 3-10 membered carbocyclyl;

R_{22} is C_{1-7} alkyl or C_{3-7} cycloalkyl;

R_{23} is hydrogen or oxo;

R_{24} is hydrogen or C_{1-7} alkyl;

D is absent, C_{1-7} alkyl or C_{2-7} alkenyl;

wherein the optional substitution in each occurrence is selected from 1-3 substituents independently selected from C_{1-7} alkyl, halogen, hydroxy, C_{1-7} alkoxy, C_{1-7} alkoxy C_{1-7} alkyl, C_{1-7} alkoxycarbonyl or oxo; and

wherein the heterocyclyl group in each occurrence has 1-4 heteroatoms independently selected from N, O and S;

or a pharmaceutically acceptable salt thereof;

with the proviso that the compound is not

2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[(2,5-dimethylphenyl) methoxy]-4*H*-pyran-4-one;

5-[(2,4-Dichlorophenyl)methoxy]-2-[(3,4-dihydro-2(1*H*)-isoquinolinyl) methyl]-4*H*-pyran-4-one;

5-[(3-Chlorophenyl)methoxy]-2-[(3,4-dihydro-2(1*H*)-isoquinolinyl)methyl]-4*H*-pyran-4-one;

2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[(4-methylphenyl)methoxy]-4*H*-pyran-4-one;

5-[(3,4-Dichlorophenyl)methoxy]-2-[(3,4-dihydro-2(1*H*)-isoquinolinyl) methyl]-4*H*-pyran-4-one;

2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[(3-fluorophenyl)methoxy]-4*H*-pyran-4-one;

2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-(1-naphthalenylmethoxy)-4*H*-pyran-4-one;

2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[[3-(trifluoromethyl)phenyl] methoxy]-4*H*-pyran-4-one;

5-[(2-Chlorophenyl)methoxy]-2-[(3,4-dihydro-2(1*H*)-isoquinolinyl)methyl]-4*H*-pyran-4-one;

5-[(2-Chloro-6-fluorophenyl)methoxy]-2-[(3,4-dihydro-2(1*H*)-isoquinolinyl) methyl]-4*H*-pyran-4-one;

5-[(4-Chlorophenyl)methoxy]-2-[(3,4-dihydro-2(1*H*)-isoquinolinyl)methyl]-4*H*-pyran-4-one;

5-[(4-Bromophenyl)methoxy]-2-[(3,4-dihydro-2(1*H*)-isoquinolinyl)methyl]-4*H*-pyran-4-one;

2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[(2-fluorophenyl)methoxy]-4*H*-pyran-4-one;

2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[(2-methylphenyl)methoxy]-4*H*-pyran-4-one;

2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-(phenylmethoxy)-4*H*-pyran-4-one;

2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[[4-(trifluoromethyl)phenyl]methoxy]-4*H*-pyran-4-one;

Methyl 4-(((6-((3,4-dihydroisoquinolin-2(1H)-yl)methyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)benzoate;

2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[(4-fluorophenyl)methoxy]-4*H*-pyran-4-one;

2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[(3,5-dimethoxyphenyl)methoxy]-4*H*-pyran-4-one;

2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[(3-nitrophenyl)methoxy]-4*H*-pyran-4-one;

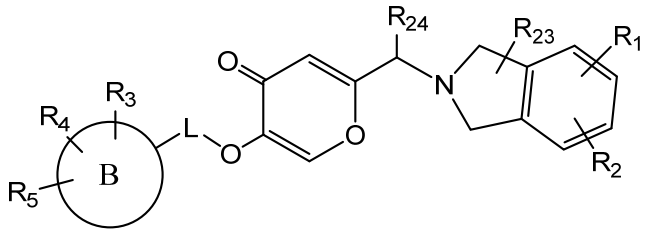
Methyl 5-(((6-((3,4-dihydroisoquinolin-2(1H)-yl)methyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)furan-2-carboxylate;

2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-(2-phenylethoxy)-4*H*-pyran-4-one;

2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[(3-methylphenyl)methoxy]-4*H*-pyran-4-one; or

2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[(4-nitrophenyl)methoxy]-4*H*-pyran-4-one.

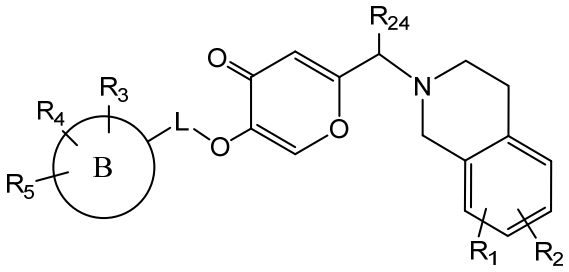
2. A compound according to claim 1, wherein the compound is represented by formula (IA):



(IA),

wherein R_1, R_2, R_3, R_4, R_5, R_{23}, R_{24}, L and B are as defined in claim 1, or a pharmaceutically acceptable salt thereof.

3. A compound according to claim 1, wherein the compound is represented by formula (IB):

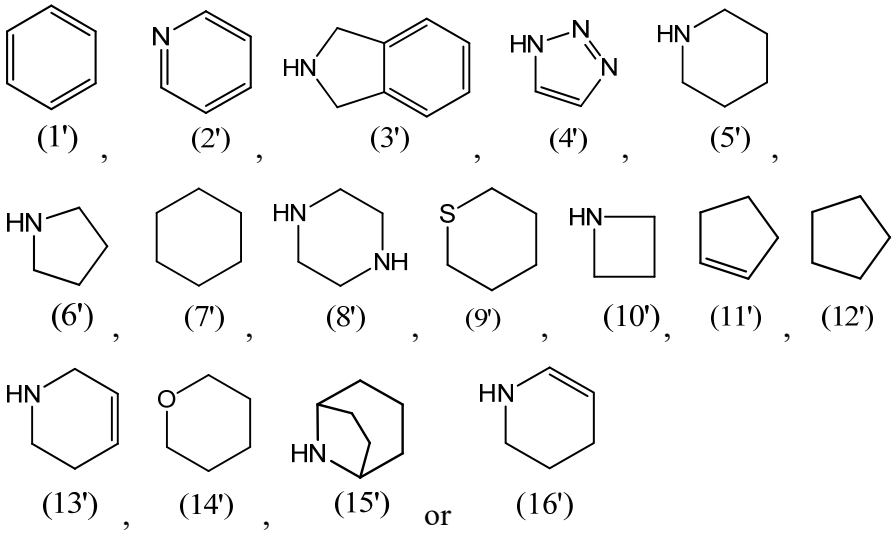


(IB),

wherein R_1, R_2, R_3, R_4, R_5, R_{24}, L and B are as defined in claim 1, or a pharmaceutically acceptable salt thereof.

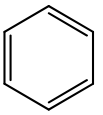
4. A compound according to any of claims 1 to 3, wherein L is $-CH_2-$ or $-CH_2-CH_2-$.

5. A compound according to any of the preceding claims, wherein ring B is any one of the following groups



R_3, R_4 and R_5 being attached to the above B-rings, optionally wherein ring B is:

a) any one of the following groups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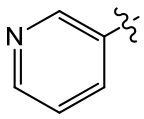
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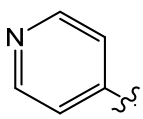
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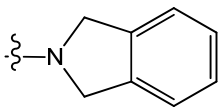
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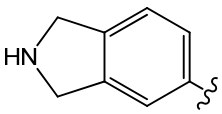
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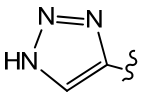
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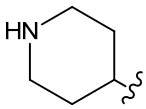
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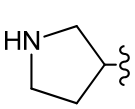
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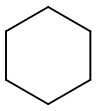
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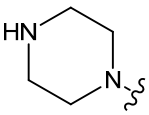
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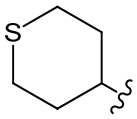
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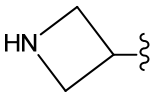
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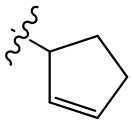
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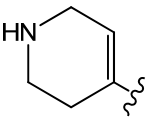
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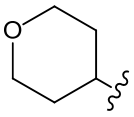
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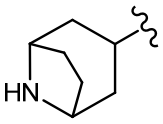
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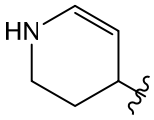
or

(16a')

R_3, R_4 and R_5 being attached to the above B-rings and the wavy line denoting the site of attachment to L;

b) (1'), (5'), (7'), (9'), (13') or (14'); or

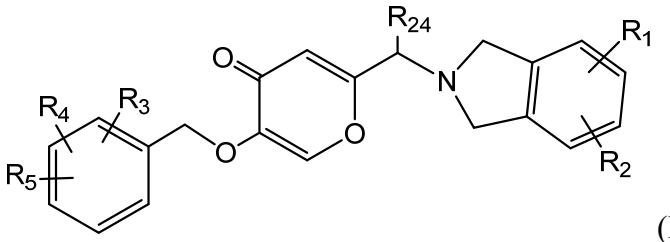
c) (1'), (5a'), (7'), (9a'), (13a') or (14a').

6. A compound according to any of the preceding claims, wherein

a) R_3 is hydrogen, C_{1-7} alkyl, C_{2-7} alkenyl, hydroxy C_{1-7} alkyl, cyano, C_{1-7} alkylthio, C_{1-7} alkoxycarbonyl C_{2-7} alkenyl, -D-C(O)-NR_6R_7, -$C(O)R_8$, -SO_2R_{11}, -D-NR_9R_{10}, -S(O)(NR_{14})(R_{22}), -S(NR_{15})(C_{1-7} alkyl), -C(S)$NR_{18}R_{19}$, an optionally substituted 3-10 membered carbocyclyl, an optionally substituted 4-10 membered heterocyclyl, or an optionally substituted 4-10 membered heterocyclyl C_{1-7} alkyl; wherein the optional substitution in each occurrence is selected from 1-3 substituents independently selected from C_{1-7} alkyl, halogen, hydroxy, C_{1-7} alkoxy, C_{1-7} alkoxy C_{1-7} alkyl, C_{1-7} alkoxycarbonyl or oxo, and wherein the heterocyclyl group in each occurrence has 1-3 heteroatoms independently selected from N, O and S and/or

b) R_4 and R_5 are hydrogen.

7. A compound according to claim 1 or 2, wherein the compound is represented by formula (IC):



(IC)

wherein R_1, R_2, R_3, R_4, R_5 and R_{24} are as defined in claim 1, or a pharmaceutically acceptable salt thereof, optionally wherein

i) R_1 is hydrogen, C_{1-7} alkoxy, halogen, nitro, halo C_{1-7} alkyl, halo C_{1-7} alkoxy or C_{1-7} alkylthio;

R_2 is hydrogen or halogen;

R_3 is C_{2-7} alkenyl, hydroxy C_{1-7} alkyl, cyano, C_{1-7} alkoxycarbonyl C_{2-7} alkenyl, -D-C(O)-NR_6R_7, -C(O)R_8, -SO_2R_{11}, -D-NR_9R_{10}, -S(O)(NR_{14})(R_{22}), -S(NR_{15})(C_{1-7} alkyl), a 3-6 membered carbocyclyl which is optionally substituted with 1-2 hydroxyl substituents, or a 4-6 membered heterocyclyl which is optionally substituted with 1-2 substituents selected from halogen or hydroxyl;

R_4 is hydrogen, hydroxy or halogen;

R_5 is hydrogen or halogen;

R_6 is C_{1-7} alkyl, hydroxy C_{1-7} alkyl or -C_{1-7} alkyl-O-C(O)C_{1-7} alkyl;

R_7 is hydrogen or C_{1-7} alkyl;

R_8 is C_{1-7} alkyl, halo C_{1-7} alkyl, -N=S(O)(C_{1-7} alkyl)(C_{1-7} alkyl) or a 4-6 membered heterocyclyl which is optionally substituted with 1-2 halogen substituents;

R_9 is C_{1-7} alkylcarbonyl or -SO_2(C_{1-7} alkyl);

R_{10} is hydrogen or C_{1-7} alkyl;

R_{11} is C_{1-7} alkyl, C_{3-7} cycloalkyl, halo C_{1-7} alkyl, C_{1-7} alkoxy C_{1-7} alkyl, -$NR_{12}R_{13}$ or a 4-6 membered heterocyclyl;

R_{12} is C_{1-7} alkyl, hydroxy C_{1-7} alkyl, cyano C_{1-7} alkyl, C_{1-7} alkoxy C_{1-7} alkyl or C_{1-7} alkylcarbonyl;

R_{13} is hydrogen or C_{1-7} alkyl;

R_{14} is hydrogen, C_{1-7} alkyl or C_{1-7} alkylcarbonyl;

R_{15} is hydrogen or -SO_2R_{17};

R_{17} is a 3-6 membered carbocyclyl which is optionally substituted by 1-2 C_{1-7} alkyl substituents;

R_{22} is C_{1-7} alkyl or C_{3-7} cycloalkyl;

R_{24} is hydrogen or C_{1-7} alkyl;

D is absent, C_{1-7} alkyl or C_{2-7} alkenyl;

wherein the heterocyclyl group in each occurrence has 1-3 heteroatoms independently selected from N, O and S; or

ii) R_1 is hydrogen, C_{1-7} alkoxy, halogen, nitro, halo C_{1-7} alkyl or halo C_{1-7} alkoxy;

R_2 and R_{10} are hydrogen;

R_3 is C_{2-7} alkenyl, hydroxy C_{1-7} alkyl, cyano, C_{1-7} alkoxycarbonyl C_{2-7} alkenyl, -D-C(O)-NR_6R_7, -C(O)R_8, -SO_2R_{11}, -D-NR_9R_{10}, -S(O)(NR_{14})(R_{22}), -S(NR_{15})(C_{1-7} alkyl), oxazolyl, cyclobutyl optionally substituted with a hydroxy substituent, or oxetanyl optionally substituted with a hydroxy substituent;

R_4 and R_5 are hydrogen or halogen;

R_6 is C_{1-7} alkyl or hydroxy C_{1-7} alkyl;

R_7, R_{13}, R_{14} and R_{24} are hydrogen or C_{1-7} alkyl;

R_8 is C_{1-7} alkyl, pyrrolidinyl, oxetanyl, or azetidinyl optionally substituted with 1-2 halogen substituents,-N=S(O)(C_{1-7} alkyl)(C_{1-7} alkyl);

R_9 is -SO_2(C_{1-7} alkyl);

R_{11} is C_{1-7} alkyl, C_{3-7} cycloalkyl, halo C_{1-7} alkyl, C_{1-7} alkoxy C_{1-7} alkyl, -$NR_{12}R_{13}$, pyrrolidinyl, piperidinyl, azetidinyl or morpholinyl;

R_{12} is C_{1-7} alkyl, hydroxy C_{1-7} alkyl, cyano C_{1-7} alkyl, C_{1-7} alkoxy C_{1-7} alkyl or C_{1-7} alkylcarbonyl;

R_{15} is hydrogen or -SO_2R_{17};

R_{17} is phenyl optionally substituted by a C_{1-7} alkyl substituent;

R_{22} is C_{1-7} alkyl or C_{3-7} cycloalkyl;

D is absent, C_{1-7} alkyl or C_{2-7} alkenyl; or

iii) R_1 is hydrogen, C_{1-7} alkoxy, halogen, halo C_{1-7} alkyl or halo C_{1-7} alkoxy;

R_2 and R_{10} are hydrogen;

R_3 is hydroxy C_{1-7} alkyl, cyano, C_{1-7} alkoxycarbonyl C_{2-7} alkenyl, -D-C(O)-NR_6R_7, -C(O)R_8, -SO_2R_{11}, -D-NR_9R_{10}, -S(O)(NR_{14})(R_{22}), -S(NR_{15})(C_{1-7} alkyl), oxazolyl, cyclobutyl optionally substituted with a hydroxy substituent, or oxetanyl optionally substituted with a hydroxy substituent;

R_4 and R_5 are hydrogen or halogen;

R_6 is C_{1-7} alkyl;

R_7, R_{13}, R_{14} and R_{24} are hydrogen or C_{1-7} alkyl;

R_8 is pyrrolidinyl, azetidinyl or -N=S(O)(C_{1-7} alkyl)(C_{1-7} alkyl);

R_9 is -SO_2(C_{1-7} alkyl);

R_{11} is C_{1-7} alkyl, halo C_{1-7} alkyl, -$NR_{12}R_{13}$ or pyrrolidinyl;

R_{12} is C_{1-7} alkyl, hydroxy C_{1-7} alkyl, cyano C_{1-7} alkyl, C_{1-7} alkoxy C_{1-7} alkyl or C_{1-7} alkylcarbonyl;

R_{15} is -SO_2R_{17};

R_{17} is phenyl optionally substituted by a C_{1-7} alkyl substituent;

R_{22} is C_{1-7} alkyl or C_{3-7} cycloalkyl;

D is absent, C_{1-7} alkyl or C_{2-7} alkenyl; or

iv) R_1 is hydrogen, halogen, halo C_{1-7} alkyl or halo C_{1-7} alkoxy;

R_2, R_4, R_5 and R_{10} are hydrogen;

R_3 is hydroxy C_{1-7} alkyl, -D-C(O)-NR_6R_7, -C(O)R_8, -SO_2R_{11}, -D-NR_9R_{10}, -S(O)(NR_{14})(R_{22}) or oxetanyl optionally substituted with a hydroxy substituent;

R_6 and R_7 is C_{1-7} alkyl;

R_8 is pyrrolidinyl, or -N=S(O)(C_{1-7} alkyl)(C_{1-7} alkyl);

R_9 is -SO_2(C_{1-7} alkyl);

R_{11} is C_{1-7} alkyl, -$NR_{12}R_{13}$ or pyrrolidinyl;

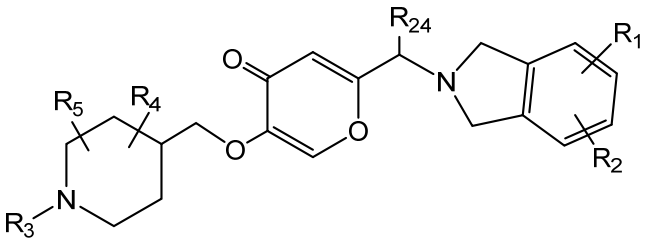
R_{12} is C_{1-7} alkyl, hydroxy C_{1-7} alkyl, or C_{1-7} alkoxy C_{1-7} alkyl;

R_{13} and R_{14} is hydrogen or C_{1-7} alkyl;

R_{22} is C_{1-7} alkyl or C_{3-7} cycloalkyl;

D is C_{1-7} alkyl or C_{2-7} alkenyl.

8. A compound according to claim 1 or 2, wherein the compound is represented by formula (ID):



(ID)

wherein R_1, R_2, R_3, R_4, R_5 and R_{24} are as defined in claim 1, or a pharmaceutically acceptable salt thereof, optionally wherein

i) R_1 is hydrogen, C_{1-7} alkyl, cyano, halogen, nitro, halo C_{1-7} alkyl, halo C_{1-7} alkoxy or C_{1-7} alkylthio;

R_2 is hydrogen or halogen;

R_3 is -D-C(O)-NR_6R_7, -C(O)R_8 , -SO_2R_{11}, or -C(S)$NR_{18}R_{19}$;

R_4 is hydrogen, C_{1-7} alkyl, hydroxy or halogen;

R_5 is hydrogen;

R_6 is C_{1-7} alkyl or C_{3-7} cycloalkyl;

R_7 and R_{24} are hydrogen or C_{1-7} alkyl;

R_8 is hydrogen, C_{1-7} alkyl, C_{2-7} alkenyl, C_{3-7} cycloalkyl, halo C_{1-7} alkyl, C_{1-7} alkylcarbonyl, C_{1-7} alkoxycarbonyl, C_{1-7} alkoxy C_{1-7} alkyl, -C_{1-7} alkyl-O-C(O)-C_{1-7} alkyl, -C_{1-7} alkyl-SO_2(C_{1-7} alkyl) or a 4-10 membered heterocyclyl;

R_{11} is C_{1-7} alkyl, C_{3-7} cycloalkyl, halo C_{1-7} alkyl, cyano C_{1-7} alkyl, C_{1-7} alkoxy C_{1-7} alkyl, -$NR_{12}R_{13}$, a 3-6 membered carbocyclyl which is optionally substituted with 1-2 halogen substituents, or a 4-6 membered heterocyclyl which is optionally substituted with 1-2 substituents selected from halogen or C_{1-7} alkyl;

R_{12} and R_{13} are C_{1-7} alkyl;

R_{18}, and R_{19} are, independently, hydrogen or C_{1-7} alkyl;

D is absent;

wherein the heterocyclyl group in each occurrence has 1-3 heteroatoms independently selected from N, O and S; or

ii) R_1 is hydrogen, C_{1-7} alkyl, halogen, halo C_{1-7} alkyl or halo C_{1-7} alkoxy;

R_2 and R_5 are hydrogen;

R_3 is -D-C(O)-NR_6R_7, -C(O)R_8 , -SO_2R_{11}, or -C(S)$NR_{18}R_{19}$, or oxetanyl optionally substituted by a hydroxy substituent;

R_4 is hydrogen, C_{1-7} alkyl or halogen;

R_6 is C_{1-7} alkyl;

R_7 is hydrogen or C_{1-7} alkyl;

R_8 is C_{1-7} alkyl, C_{2-7} alkenyl, C_{3-7} cycloalkyl, halo C_{1-7} alkyl, C_{1-7} alkylcarbonyl, C_{1-7} alkoxycarbonyl, C_{1-7} alkoxy C_{1-7} alkyl, -C_{1-7} alkyl-O-C(O)-C_{1-7} alkyl, -C_{1-7} alkyl-SO_2(C_{1-7} alkyl), azetidinyl, morpholinyl, furanyl or pyrrolidinyl;

R_{11} is C_{1-7} alkyl, C_{3-7} cycloalkyl, halo C_{1-7} alkyl, cyano C_{1-7} alkyl, C_{1-7} alkoxy C_{1-7} alkyl, -$NR_{12}R_{13}$, pyrrolidinyl, phenyl optionally substituted with a halogen substituent, oxetanyl, or pyrazolyl optionally substituted with a C_{1-7} alkyl substituent;

R_{12} and R_{13} are C_{1-7} alkyl;

R_{18}, and R_{19} are, independently, hydrogen or C_{1-7} alkyl;

R_{24} is hydrogen or C_{1-7} alkyl;

D is absent; or

iii) R_1 is hydrogen, C_{1-7} alkyl, halogen, halo C_{1-7} alkyl or halo C_{1-7} alkoxy;

R_2, R_5 and R_7 are hydrogen;

R_3 is -D-C(O)-NR_6R_7, -C(O)R_8 or -SO_2R_{11};

R_4 is hydrogen or C_{1-7} alkyl;

R_6 is C_{1-7} alkyl;

R_8 is C_{1-7} alkyl, C_{3-7} cycloalkyl, halo C_{1-7} alkyl, C_{1-7} alkylcarbonyl, -C_{1-7} alkyl-O-C(O)-C_{1-7} alkyl, -C_{1-7} alkyl-SO_2(C_{1-7} alkyl), morpholinyl or pyrrolidinyl;

R_{11} is C_{1-7} alkyl, C_{3-7} cycloalkyl, cyano C_{1-7} alkyl, C_{1-7} alkoxy C_{1-7} alkyl, -$NR_{12}R_{13}$, oxetanyl, or pyrazolyl optionally substituted with a C_{1-7} alkyl substituent;

R_{12} and R_{13} are C_{1-7} alkyl;

R_{24} is hydrogen or C_{1-7} alkyl;

D is absent; or

iv) R_1 is hydrogen, halogen, halo C_{1-7} alkyl or halo C_{1-7} alkoxy;

R_2, R_4, R_5 and R_7 are hydrogen;

R_3 is -D-C(O)-NR_6R_7, -C(O)R_8 or -SO_2R_{11};

R_6 , R_{12} and R_{13} are C_{1-7} alkyl;

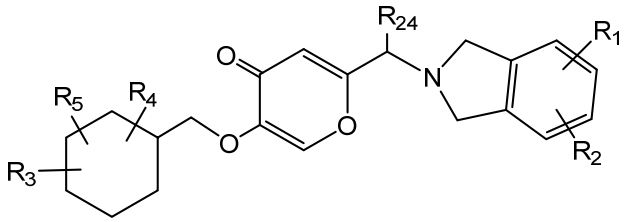
R_8 is C_{1-7} alkyl or halo C_{1-7} alkyl;

R_{11} is C_{1-7} alkyl, C_{3-7} cycloalkyl, C_{1-7} alkoxy C_{1-7} alkyl, -$NR_{12}R_{13}$ or oxetanyl;

R_{24} is hydrogen;

D is absent.

9. A compound according to claim 1 or 2, wherein the compound is represented by formula (IE):



(IE)

wherein R_1, R_2, R_3, R_4, R_5 and R_{24} are as defined in claim 1, or a pharmaceutically acceptable salt thereof, optionally wherein

i) R_1, R_2, R_4, R_5 and R_{24} are hydrogen;

R_3 is hydrogen, -D-C(O)-NR_6R_7, -C(O)R_8 , -SO_2R_{11}, -D-NR_9R_{10}, -S(O)(NR_{14})(R_{22}), a 4-6 membered heterocyclyl which is optionally substituted with 1-2 oxo substituents, or a 4-6 membered heterocyclyl C_{1-7} alkyl optionally substituted with 1-2 oxo substituents;

R_6, R_{11} and R_{22} are C_{1-7} alkyl;

R_7 is hydrogen or C_{1-7} alkyl;

R_8 is C_{1-7} alkyl, C_{1-7} alkoxy, or a 4-6 membered heterocyclyl;

R_9 is -SO_2(C_{1-7} alkyl);

R_{10} is hydrogen, C_{1-7} alkyl or C_{3-7} cycloalkyl;

R_{14} is hydrogen or -SO_2R_{21};

R_{21} is 3-6 membered carbocyclyl optionally substituted with 1-2 C_{1-7} alkyl;

D is absent or C_{1-7} alkyl;

wherein the heterocyclyl group in each occurrence has 1-3 heteroatoms independently selected from N, O and S; or

ii) R_1, R_2, R_4, R_5 and R_{24} are hydrogen;

R_3 is -D-C(O)-NR_6R_7, -C(O)R_8 , -SO_2R_{11}, -D-NR_9R_{10}, -S(O)(NR_{14})(R_{22}), 1,1-dioxidoisothiazolidinyl or 1,1-dioxidoisothiazolidinyl C_{1-7} alkyl;

R_6, R_{11} and R_{22} are C_{1-7} alkyl;

R_7 is C_{1-7} alkyl;

R_8 is C_{1-7} alkyl or azetidinyl;

R_9 is -SO_2(C_{1-7} alkyl);

R_{10} is hydrogen, C_{1-7} alkyl or C_{3-7} cycloalkyl;

R_{14} is $-SO_2R_{21}$;

R_{21} is phenyl optionally substituted with a C_{1-7} alkyl substituent;

D is absent or C_{1-7} alkyl.

10. A compound according to any of claims 7-9, wherein

R_1 is hydrogen, C_{1-7} alkyl, C_{1-7} alkoxy, halogen, cyano, nitro, halo C_{1-7} alkyl, halo C_{1-7} alkoxy or C_{1-7} alkylthio;

R_2 is hydrogen or halogen;

R_3 is hydrogen, C_{1-7} alkyl, C_{2-7} alkenyl, hydroxy C_{1-7} alkyl, cyano, C_{1-7} alkylthio, C_{1-7} alkoxycarbonyl C_{2-7} alkenyl, -D-C(O)-NR_6R_7, -C(O)R_8 , $-SO_2R_{11}$, -D-NR_9R_{10}, -S(O)(NR_{14})(R_{22}), -S(NR_{15})(C_{1-7} alkyl), -C(S)$NR_{18}R_{19}$, 4-6 membered carbocyclyl which is optionally substituted with 1-2 hydroxyl substituents, 4-6 membered heterocyclyl which is optionally substituted with 1-2 substituents selected from halogen, hydroxyl, C_{1-7} alkoxycarbonyl or oxo, or 4-6 membered heterocyclyl C_{1-7} alkyl optionally substituted with 1-2 oxo substituents;

R_4 is hydrogen, C_{1-7} alkyl, hydroxy or halogen;

R_5 is hydrogen or halogen;

R_6 is C_{1-7} alkyl, C_{3-7} cycloalkyl, hydroxy C_{1-7} alkyl, -C_{1-7} alkyl-O-C(O)C_{1-7} alkyl;

R_7 is hydrogen or C_{1-7} alkyl;

R_8 is hydrogen, C_{1-7} alkyl, C_{2-7} alkenyl, C_{3-7} cycloalkyl, C_{1-7} alkoxy, halo C_{1-7} alkyl, C_{1-7} alkoxy C_{1-7} alkyl, C_{1-7} alkylcarbonyl, C_{1-7} alkoxycarbonyl, -C_{1-7} alkyl-O-C(O)-C_{1-7} alkyl, -C_{1-7} alkyl-SO_2(C_{1-7} alkyl), -N=S(O)(C_{1-7} alkyl)(C_{1-7} alkyl) or a 4-6 membered heterocyclyl which is optionally substituted with 1-2 halogen substituents;

R_9 is C_{1-7} alkylcarbonyl, $-SO_2$(C_{1-7} alkyl) or $-SO_2$(C_{3-7} cycloalkyl);

R_{10} is hydrogen, C_{1-7} alkyl or C_{3-7} cycloalkyl;

R_{11} is C_{1-7} alkyl, C_{3-7} cycloalkyl, halo C_{1-7} alkyl, cyano C_{1-7} alkyl, C_{1-7} alkoxy C_{1-7} alkyl, -$NR_{12}R_{13}$, 3-6 membered carbocyclyl which is optionally substituted with 1-2 substituents selected from halogen or C_{1-7} alkyl, or 4-6

membered heterocyclyl which is optionally substituted with 1-2 substituents selected from halogen or C_{1-7} alkyl;

R_{12} is C_{1-7} alkyl, hydroxy C_{1-7} alkyl, cyano C_{1-7} alkyl, C_{1-7} alkoxy C_{1-7} alkyl or C_{1-7} alkylcarbonyl;

R_{13} is hydrogen or C_{1-7} alkyl;

R_{14} is hydrogen, C_{1-7} alkyl, C_{1-7} alkylcarbonyl or $-SO_2R_{21}$;

R_{15} is hydrogen, C_{1-7} alkyl, $-SO_2R_{17}$;

R_{17} is C_{1-7} alkyl or 3-6 membered carbocyclyl which is optionally substituted by 1-2 C_{1-7} alkyl substituent;

R_{18}, and R_{19} are, independently, hydrogen or C_{1-7} alkyl;

R_{21} is 3-6 membered carbocyclyl optionally substituted with 1-2 C_{1-7} alkyl;

R_{22} is C_{1-7} alkyl or C_{3-7} cycloalkyl;

R_{24} is hydrogen or C_{1-7} alkyl;

wherein the heterocyclyl group in each occurrence has 1-3 heteroatoms independently selected from N, O and S;

or a pharmaceutically acceptable salt thereof.

11. A compound according to claim 1, which is

Methyl (E)-3-(4-(((6-(isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)-methyl)phenyl)acrylate (Compound 2);

2-(Isoindolin-2-ylmethyl)-5-((4-(pyrrolidin-1-ylsulfonyl)benzyl)oxy)-4H-pyran-4-one (Compound 5);

4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)-N-methyl-benzenesulfonamide (Compound 8);

4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)-N,N-di-methylbenzenesulfonamide (Compound 10);

4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)-N-(2-methoxyethyl)benzenesulfonamide (Compound 11);

N-(2-Hydroxyethyl)-4-(((6-(isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)-oxy)methyl)-N-methylbenzenesulfonamide (Compound 12);

N-(2-Hydroxyethyl)-4-(((6-(isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)-oxy)methyl)benzenesulfonamide (Compound 15);

N-Ethyl-N-(2-hydroxyethyl)-4-(((6-(isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)benzenesulfonamide (Compound 21);

5-((4-((Difluoromethyl)sulfonyl)benzyl)oxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 22);

N-(2-Cyanoethyl)-4-(((6-(isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)-methyl)-N-methylbenzenesulfonamide (Compound 23);

2-(Isoindolin-2-ylmethyl)-5-((1-(oxetan-3-ylsulfonyl)piperidin-4-yl)methoxy)-4H-pyran-4-one (Compound 36);

5-((4-(Methylsulfonyl)benzyl)oxy)-2-((5-(trifluoromethoxy)isoindolin-2-yl)-methyl)-4H-pyran-4-one (Compound 37);

2-((3,4-dihydroisoquinolin-2(1H)-yl)methyl)-5-((4-(2-hydroxypropan-2-yl)-benzyl)oxy)-4H-pyran-4-one (Compound 44);

2-Isoindolin-2-ylmethyl)-5-((4-(prop-1-en-2-yl)benzyl)oxy)-4H-pyran-4-one (Compound 47);

5-((4-(2-Hydroxypropan-2-yl)benzyl)oxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 49);

5-(Cyclohexylmethoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 65);

5-((1-(Oxetan-3-ylsulfonyl)piperidin-4-yl)methoxy)-2-((5-(trifluoromethyl)-isoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 69a);

N-((4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)phenyl)-sulfonyl)-N-methylacetamide (Compound 70);

5-((4-(Cyclobutanesulfonimidoyl)benzyl)oxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 71);

5-((4-(Cyclopropylsulfonyl)benzyl)oxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 72);

5-((4-(Isobutylsulfonyl)benzyl)oxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 73);

5-((4-(S-methylsulfinimidoyl)benzyl)oxy)-2-((5-(trifluoromethyl)isoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 74);

4-({[6-(1,3-Dihydro-2*H*-isoindol-2-ylmethyl)-4-oxo-4*H*-pyran-3-yl]oxy}-methyl)-*N*-[dimethyl(oxido)-λ^6-sulfanylidene]benzamide (Compound 83);

N-[Dimethyl(oxido)- λ^6-sulfanylidene]-4-[({6-[(5-fluoro-1,3-dihydro-2*H*-isoindol-2-yl)methyl]-4-oxo-4*H*-pyran-3-yl}oxy)methyl]benzamide (Compound 84);

5-((4-(S-Methylsulfonimidoyl)benzyl)oxy)-2-((5-(trifluoromethyl)isoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 89);

5-((4-(S-Methylsulfonimidoyl)benzyl)oxy)-2-((5-(trifluoromethoxy)isoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 90);

2-(1-(Isoindolin-2-yl)ethyl)-5-((4-(S-methylsulfonimidoyl)benzyl)oxy)-4H-pyran-4-one (Compound 91);

5-((4-(N,S-Dimethylsulfonimidoyl)benzyl)oxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 92);

N-{[4-({[6-(1,3-dihydro-2*H*-isoindol-2-ylmethyl)-4-oxo-4*H*-pyran-3-yl]oxy}-methyl)phenyl](methyl)-λ^4-sulfanylidene}-4-methylbenzenesulfonamide (Compound 93);

5-((4-(Azetidine-1-carbonyl)-2-fluorobenzyl)oxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 95);

2-(Isoindolin-2-ylmethyl)-5-((4-(propan-2-ylsulfonimidoyl)benzyl)oxy)-4H-pyran-4-one (Compound 103);

5-((5-Fluoro-1-(methylsulfonyl)-1,2,3,6-tetrahydropyridin-4-yl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 104);

2-(Isoindolin-2-ylmethyl)-5-((4-(oxazol-2-yl)benzyl)oxy)-4*H*-pyran-4-one (Compound 109);

5-((4-(1-Hydroxycyclobutyl)benzyl)oxy)-2-(isoindolin-2-ylmethyl)-4*H*-pyran-4-one (Compound 111);

N-(4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4*H*-pyran-3-yl)oxy)methyl)benzyl)-methanesulfonamide (Compound 113);

5-((4-(3-Hydroxyoxetan-3-yl)benzyl)oxy)-2-(isoindolin-2-ylmethyl)-4*H*-pyran-4-one (Compound 114);

2-((5-Fluoroisoindolin-2-yl)methyl)-5-((4-(3-hydroxyoxetan-3-yl)benzyl)-oxy)-4*H*-pyran-4-one (Compound 115);

5-((4-(3-Hydroxyoxetan-3-yl)benzyl)oxy)-2-((5-(trifluoromethyl)isoindolin-2-yl)methyl)-4*H*-pyran-4-one (Compound 116);

2-(Isoindolin-2-ylmethyl)-5-((4-(pyrrolidine-1-carbonyl)benzyl)oxy)-4H-pyran-4-one (Compound 122);

5-((4-(Azetidine-1-carbonyl)benzyl)oxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 129);

2-((5-Bromoisoindolin-2-yl)methyl)-5-((4-(pyrrolidine-1-carbonyl)benzyl)-oxy)-4H-pyran-4-one (Compound 130);

N-(tert-Butyl)-4-(((6-(isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)-methyl)benzamide (Compound 131);

4-(((6-Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)-N,N-diiso-propylbenzamide (Compound 134);

4-(((6-((5-Chloroisoindolin-2-yl)methyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)-N,N-dimethylbenzamide (Compound 137);

4-(((6-((5-Methoxyisoindolin-2-yl)methyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)-N,N-dimethylbenzamide (Compound 138);

N,N-Dimethyl-4-(((4-oxo-6-((5-(trifluoromethyl)isoindolin-2-yl)methyl)-4H-pyran-3-yl)oxy)methyl)benzamide (Compound 139);

(E)-3-(4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)-phenyl)-N,N-dimethylacrylamide (Compound 146);

5-((4-(3,3-Difluoroazetidine-1-carbonyl)benzyl)oxy)-2-((5-methoxyisoindo-lin-2-yl)methyl)-4H-pyran-4-one (Compound 162);

3,5-Difluoro-4-(((6-(isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)-methyl)-N,N-dimethylbenzamide (Compound 172);

N-((4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)cyclo-hexyl)methyl)methanesulfonamide (Compound 173);

5-((4-((1,1-Dioxidoisothiazolidin-2-yl)methyl)cyclohexyl)methoxy)-2-(iso-indolin-2-ylmethyl)-4H-pyran-4-one (Compound 176);

5-((1-(Methylsulfonyl)piperidin-4-yl)methoxy)-2-((5-(trifluoromethyl)iso-indolin-2-yl)methyl)-4*H*-pyran-4-one (Compound 184);

2-(Isoindolin-2-ylmethyl)-5-((1-(methylsulfonyl)piperidin-4-yl)methoxy)-4H-pyran-4-one (Compound 185);

2-((5-Fluoroisoindolin-2-yl)methyl)-5-((1-(methylsulfonyl)piperidin-4-yl)-methoxy)-4H-pyran-4-one (Compound 186);

5-((1-(Cyclopropylsulfonyl)piperidin-4-yl)methoxy)-2-(isoindolin-2-yl-methyl)-4H-pyran-4-one (Compound 187);

5-((1-(Ethylsulfonyl)piperidin-4-yl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 188);

5-((1-(Ethylsulfonyl)piperidin-4-yl)methoxy)-2-((5-fluoroisoindolin-2-yl)-methyl)-4H-pyran-4-one (Compound 189);

5-((1-(Cyclopropylsulfonyl)piperidin-4-yl)methoxy)-2-((5-fluoroisoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 190);

5-((1-(Ethylsulfonyl)-4-methylpiperidin-4-yl)methoxy)-2-(isoindolin-2-yl-methyl)-4H-pyran-4-one (Compound 192);

2-(1-Isoindolin-2-yl)ethyl)-5-((1-(methylsulfonyl)piperidin-4-yl)methoxy)-4H-pyran-4-one (Compound 195);

2-(Isoindolin-2-ylmethyl)-5-((tetrahydro-2H-thiopyran-4-yl)methoxy)-4H-pyran-4-one (Compound 196);

5-((1-(Methylsulfonyl)piperidin-4-yl)methoxy)-2-((5-(trifluoromethoxy)-isoindolin-2-yl)methyl)-4*H*-pyran-4-one (Compound 205);

2-((5-Methylisoindolin-2-yl)methyl)-5-((1-(methylsulfonyl)piperidin-4-yl)-methoxy)-4H-pyran-4-one (Compound 211);

2-(Isoindolin-2-ylmethyl)-5-(3-(1-(methylsulfonyl)piperidin-4-yl)propoxy)-4H-pyran-4-one (Compound 213);

2-(Isoindolin-2-ylmethyl)-5-((1-(pyrrolidine-1-carbonyl)piperidin-4-yl)-methoxy)-4H-pyran-4-one (Compound 215);

5-(((1r,4r)-4-(1,1-Dioxidoisothiazolidin-2-yl)cyclohexyl)methoxy)-2-(iso-indolin-2-ylmethyl)-4H-pyran-4-one (Compound 216);

4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)-N,N-dimethylcyclohexane-1-carboxamide (Compound 217);

N-Cyclopropyl-N-(4-(((6-(isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)-methyl)cyclohexyl)methanesulfonamide (Compound 219);

5-((1-Butyrylpiperidin-4-yl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 221);

5-((1-(2,2-Difluoropropanoyl)piperidin-4-yl)methoxy)-2-(isoindolin-2-yl-methyl)-4H-pyran-4-one (Compound 222);

2-((5-Fluoroisoindolin-2-yl)methyl)-5-((1-propionylpiperidin-4-yl)methoxy)-4H-pyran-4-one (Compound 224);

4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4*H*-pyran-3-yl)oxy)methyl)-*N*,*N*-dimethylpiperidine-1-sulfonamide (Compound 225);

5-((1-(Cyclopropanecarbonyl)piperidin-4-yl)methoxy)-2-(isoindolin-2-ylmethyl)-4*H*-pyran-4-one (Compound 226);

4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4*H*-pyran-3-yl)oxy)methyl)-*N*-isopropylpiperidine-1-carboxamide (Compound 229);

4-(((6-((5-Fluoroisoindolin-2-yl)methyl)-4-oxo-4*H*-pyran-3-yl)oxy)methyl)-*N*,*N*-dimethylpiperidine-1-sulfonamide (Compound 230);

2-(Isoindolin-2-ylmethyl)-5-((1-(morpholine-4-carbonyl)piperidin-4-yl)-methoxy)-4*H*-pyran-4-one (Compound 232);

5-((4-(Azetidine-1-carbonyl)cyclohexyl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 234);

2-(Isoindolin-2-ylmethyl)-5-((1-(2-(methylsulfonyl)acetyl)piperidin-4-yl)-methoxy)-4H-pyran-4-one (Compound 238);

5-(((1r,4r)-4-Acetylcyclohexyl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 244);

5-((1-Propionylpiperidin-4-yl)methoxy)-2-((5-(trifluoromethyl)isoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 244a);

2-((5-((1-(methylsulfonyl)piperidin-4-yl)methoxy)-4-oxo-4H-pyran-2-yl)methyl)isoindoline-5-carbonitrile (Compound 245a);

1-(4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)piperidin-1-yl)-4-methylpentane-1,2-dione (Compound 249);

2-(Isoindolin-2-ylmethyl)-5-((1-pivaloylpiperidin-4-yl)methoxy)-4H-pyran-4-one (Compound 251);

2-((4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)piperidin-1-yl)sulfonyl)acetonitrile (Compound 254);

2-(Isoindolin-2-ylmethyl)-5-((1-((1-methyl-1H-pyrazol-5-yl)sulfonyl)piperidin-4-yl)methoxy)-4H-pyran-4-one (Compound 255);

2-(4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)piperidin-1-yl)-2-oxoethyl acetate (Compound 257);

2-(Isoindolin-2-ylmethyl)-5-((1-propionylpiperidin-4-yl)methoxy)-4H-pyran-4-one (Compound 261);

2-(Isoindolin-2-ylmethyl)-5-((1-((2-methoxyethyl)sulfonyl)piperidin-4-yl)-methoxy)-4H-pyran-4-one (Compound 262);

5-((1-(Isobutylsulfonyl)piperidin-4-yl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 271);

5-((1-Isobutyrylpiperidin-4-yl)methoxy)-2-(isoindolin-2-ylmethyl)-4*H*-pyran-4-one (Compound 272);

4-((6-((5-Bromoisoindolin-2-yl)methyl)-4-oxo-4H-pyran-3-yloxy)methyl)-benzonitrile (Compound 278);

5-((4-(S-Methylsulfonimidoyl)benzyl)oxy)-2-((5-(trifluoromethyl)isoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 285);

5-((4-(R-Methylsulfonimidoyl)benzyl)oxy)-2-((5-(trifluoromethyl)isoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 286);

and tautomers and pharmaceutically acceptable salts thereof.

12. A compound according to claim 11, which is

N-Ethyl-N-(2-hydroxyethyl)-4-(((6-(isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)benzenesulfonamide (Compound 21);

5-((4-(2-Hydroxypropan-2-yl)benzyl)oxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 49);

4-({[6-(1,3-Dihydro-2*H*-isoindol-2-ylmethyl)-4-oxo-4*H*-pyran-3-yl]oxy}-methyl)-*N*-[dimethyl(oxido)-λ^6-sulfanylidene]benzamide (Compound 83);

5-((4-(S-Methylsulfonimidoyl)benzyl)oxy)-2-((5-(trifluoromethoxy)isoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 90);

2-(1-(Isoindolin-2-yl)ethyl)-5-((4-(S-methylsulfonimidoyl)benzyl)oxy)-4H-pyran-4-one (Compound 91);

2-(Isoindolin-2-ylmethyl)-5-((4-(pyrrolidine-1-carbonyl)benzyl)oxy)-4H-pyran-4-one (Compound 122);

5-((4-((1,1-Dioxidoisothiazolidin-2-yl)methyl)cyclohexyl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 176);

5-((1-(Methylsulfonyl)piperidin-4-yl)methoxy)-2-((5-(trifluoromethyl)isoindolin-2-yl)methyl)-4*H*-pyran-4-one (Compound 184);

2-(Isoindolin-2-ylmethyl)-5-((1-(methylsulfonyl)piperidin-4-yl)methoxy)-4H-pyran-4-one (Compound 185);

5-((1-(Cyclopropylsulfonyl)piperidin-4-yl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 187);

5-((1-(Ethylsulfonyl)piperidin-4-yl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 188);

5-((1-(Ethylsulfonyl)piperidin-4-yl)methoxy)-2-((5-fluoroisoindolin-2-yl)-methyl)-4H-pyran-4-one (Compound 189);

2-(1-Isoindolin-2-yl)ethyl)-5-((1-(methylsulfonyl)piperidin-4-yl)methoxy)-4H-pyran-4-one (Compound 195);

2-(Isoindolin-2-ylmethyl)-5-(3-(1-(methylsulfonyl)piperidin-4-yl)propoxy)-4H-pyran-4-one (Compound 213);

5-(((1r,4r)-4-(1,1-Dioxidoisothiazolidin-2-yl)cyclohexyl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 216);

4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)-N,N-dimethylcyclohexane-1-carboxamide (Compound 217);

4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4*H*-pyran-3-yl)oxy)methyl)-*N*,*N*-dimethylpiperidine-1-sulfonamide (Compound 225);

5-(((1r,4r)-4-Acetylcyclohexyl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 244);

5-((1-Propionylpiperidin-4-yl)methoxy)-2-((5-(trifluoromethyl)isoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 244a);

2-(Isoindolin-2-ylmethyl)-5-((1-propionylpiperidin-4-yl)methoxy)-4H-pyran-4-one (Compound 261);

4-((6-((5-Bromoisoindolin-2-yl)methyl)-4-oxo-4H-pyran-3-yloxy)methyl)-benzonitrile (Compound 278);

and tautomers and pharmaceutically acceptable salts thereof.

13. A pharmaceutical composition comprising a compound according to any one of claims 1-12 together with a pharmaceutically acceptable carrier.

14. Pharmaceutical combination comprising a compound according to any one of claims 1-12 and at least one additional active ingredient selected from the list consisting of

- glucocorticoids;
- mineralocorticoids;
- non-steroidal androgen receptor antagonists;
- steroidogenesis inhibitors;
- chemotherapeutic agents;
- antiestrogens;
- epigenetic modulators;
- mTOR inhibitors (e.g. everolimus);
- AKT inhibitors (e.g. AZ5363);
- radiopharmaceuticals (e.g. alpharadin);
- GnRH/LHRH analogues (such as leuprorelin);
- PI3K inhibitors; and
- CDK4/6 inhibitors;

for simultaneous, separate or sequential administration.