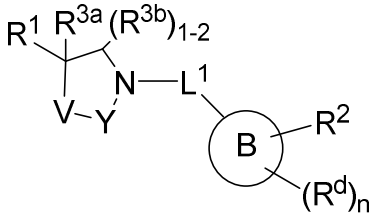
CLAIMS

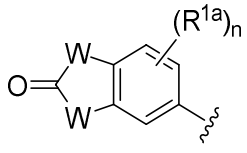
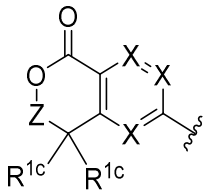
What is claimed is:

1. A compound having the structure of Formula (I)



(I)

or a salt thereof, wherein:

R^1 is:  or  ;

each W is independently NR^{1b} or O;

Z is a bond or CHR^{1d};

X is independently N or CR^{1a}, wherein X is N at only 0, 1, or 2 positions;

each R^{1a} is independently H, F, Cl, -OH, -CN, C_{1-3} alkyl, C_{1-3} fluoroalkyl, C_{3-6} cycloalkyl, C_{1-3} alkoxy, or C_{1-3} fluoroalkoxy;

each R^{1b} is independently H, C_{1-3} alkyl, C_{2-3} fluoroalkyl, C_{3-6} cycloalkyl

R^{1c} is independently H, deuterium, C_{1-4} alkyl, C_{1-4} fluoroalkyl, or C_{3-6} cycloalkyl;

R^{1d} is H, C_{1-3} alkyl, C_{1-4} fluoroalkyl, or C_{3-6} cycloalkyl;

Y is $-C(R^6)_2-$, $-C(R^6)_2-C(R^6)_2-$, -C(O)-, $-C(O)-C(R^6)_2-$, $-C(R^6)_2-C(O)-$, or $–SO_2-$;

V is –O-, $-NR^4-$, $-CR^5R^5-$, -S-, -S(O)-, $-SO_2-$, or -C(O)-; wherein if V is –O-, -S-, -S(O)-, $-SO_2-$, or –C(O)-, then Y is not $–SO_2-$, and wherein if V is –O-, -S-, or NR^4, then Y is not $C(R^6)_2$, and wherein if V is –S(O)-, $-SO_2-$, or C(=O)-, then Y is not –C(=O)-, $–C(=O)-C(R^6)_2-$;

L^1 is $–C(R)_2-$, -C(O)-, or $-C(R)_2–C(R)_2-$; wherein R is independently H, F, OH, C_{1-3} alkyl, C_{1-3} hydroxyalkyl, C_{1-3} alkoxyalkyl, or C_{1-3} fluoroalkyl; wherein R is not –OH or F if it is attached to a carbon atom that is adjacent to a nitrogen atom:

Ring B is phenyl, pyridinyl, pyrimidinyl, pyrrazolyl, thiazolyl, imidazolyl, triazolyl,

tetrazolyl, oxadiazolyl, thiadiazolyl, isoxazolyl, isothiazolyl, pyrrolyl, pyrazinyl, oxazolyl, pyridazinyl, pyrrolidinyl, or imidazolidinyl;

R^2 is a C_{6-10} aryl, or a 5 to 10 membered heterocycle ring containing 1 to 4 heteroatoms selected from N, O, and S, the heterocycle ring optionally containing an oxo substitution, the aryl or heterocycle ring are substituted with 0-3 R^{2a};

R^{2a} is independently OH, =O, CN, halo, C_{1-4} alkyl, C_{1-4} deuteroalkyl, C_{1-4} fluoroalkyl, C_{1-4} alkoxy, C_{1-4} deuteroalkoxy, C_{1-4} fluoroalkoxy, C_{3-6} cycloalkyl, C_{3-6} cycloalkoxy, $C(=O)NR^{4b}R^{4b}$, $C(=O)C_{1-4}$ alkyl, SO_2R^e, $NR^{4b}SO_2R^{4b}$, or a 4 to 6 membered heterocycle having 1, 2, 3, or 4 heteroatoms selected from O, S, and N, the heterocycle optionally containing an oxo substitution and is substituted with 0-3 R^{2b};

R^{2b} is independently C_{1-3} alkyl, C_{1-3} fluoralkyl, C_{1-3} hydroxyalkyl, C_{3-6} cycloalkyl, or C_{3-6} fluorocycloalkyl ;

R^{3a} is H, halo, OH, CN, C_{1-3} alkyl, C_{1-3} hydroxyalkyl, C_{1-3} fluoroalkyl, C_{1-3} alkoxy, or C_{3-6} cycloalkyl, wherein if V is –O-, -NR^4-, -S-, -S(O)-, -SO_2-, or –C(=O)-, then R^{3a} is not halo, and wherein if V is –O-, -NR^4-, -S-, then R^{3a} is not OH, CN;

R^{3b} is H, =O, C_{1-3} alkyl, C_{1-3} hydroxyalkyl, C_{1-3} fluoroalkyl, C_{1-3} alkoxy, or C_{3-6} cycloalkyl;

R^4 is H, C_{1-3} alkyl, C_{2-3} fluoroalkyl, C_{2-3} hydroxyalkyl, CO_2R^{4a}, $C(O)R^{4a}$, SO_2R^{4a}, $C(O)N(R^{4b}R^{4b})$, $SO_2N(R^{4b}R^{4b})$, or OH;

R^{4a} is C_{1-3} alkyl, C_{1-3} fluoroalkyl, C_{3-6} cycloalkyl, C_{3-6} fluorocycloalkyl, C_{6-10} aryl or a 4 to10 membered heterocycle having 1, 2, 3 or 4 heteroatoms selected from O, S, and N, the aryl or heterocycle being substituted with 0-3 R^{4c};

R^{4b} is independently H, C_{1-3} alkyl, C_{2-3} fluoroalkyl, C_{3-6} cycloalkyl, C_{3-6} fluorocycloalkyl, C_{6-10} aryl or a 4 to10 membered heterocycle having 1, 2, 3 or 4 heteroatoms selected from O, S, and N;

alternatively, 2 R^{4b}s, along with the atom to which they are attached, join to form a 3 to 6 membered saturated ring containing an additional 0-2 heteroatoms selected from O, S, and N;

R^{4c} is independently H, F, Cl, or C_{1-3} alkyl;

R^5 is independently H, F, OH, C_{1-3} alkoxy, C_{1-3} fluoroalkoxy, C_{1-3} alkyl, C_{1-3} fluoroalkyl, C_{1-3} hydroxyalkyl, C_{3-6} cycloalkyl, C_{3-6} fluorocycloalkyl, $NR^{5b}R^{5b}$, O-R^{5c}, or 2 R^5s are =O; wherein if one R^5 is F, OH or $NR^{5b}R^{5b}$, then the other R^5 is not OH, or $NR^{5b}R^{5b}$.

R^{5b} is independently H, C_{1-3} alkyl, C_{3-6} cycloalkyl, $C(O)R^a$, SO_2R^a, or $C(O)NR^bR^b$;

alternatively, 2 R^{5b}s, along with the atom to which they are attached, join to form a 3 to 6 membered saturated ring containing 0-2 heteroatoms selected from O, S, or N;

R^{5c} is independently H, C_{1-3} alkyl, C_{3-6} cycloalkyl, or $C(O)NR^bR^b$;

R^6 is independently H, OH, F, C_{1-3} alkyl, C_{1-3} deuteroalkyl, C_{1-3} fluoroalkyl, C_{3-6} cycloalkyl, C_{3-6} fluorocycloalkyl, C_{1-3} alkoxy, C_{1-3} hydroxyalkyl, C_{1-3} hydroxydeuteroalkyl, C_{1-3} alkoxyalkyl, or C_{1-3} fluoroalkoxyalkyl, or $NR^{6b}R^{6b}$; wherein if one R^6 on one carbon atom is F, OH or $NR^{6b}R^{6b}$, then the other R^6 on the same carbon atom is not OH or $NR^{6b}R^{6b}$.

R^{6b} is independently H, C_{1-3} alkyl, C_{3-6} cycloalkyl, $C(O)R^a$, SO_2R^a, or $C(O)NR^bR^b$; alternatively, 2 R^6s along with the same atom to which they are attached can form a 3 to 6 membered saturated ring containing 0-2 heteroatoms selected from O, S, and N;

R^a is independently H, C_{1-3} alkyl, C_{2-3} fluoroalkyl, C_{3-6} cycloalkyl, C_{3-6} fluorocycloalkyl, C_{6-10} aryl or a 4 to 10 membered heterocycle having 1, 2, 3, or 4 heteroatoms selected from O, S, and N;

R^b is independently H, C_{1-3} alkyl, C_{2-3} fluoroalkyl, C_{3-6} cycloalkyl, C_{3-6} fluorocycloalkyl, C_{6-10} aryl or a 4 to10 membered heterocycle having 1, 2, 3 or 4 heteroatoms selected from O, S, and N;

alternatively, 2 R^b's along with the atom to which they are attached, join to form a 3 to 6 membered saturated ring, containing 0-2 heteroatoms selected from O, S, and N;

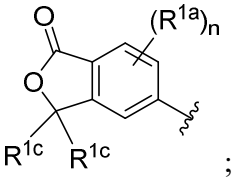
each R^d is independently H, F, C_{1-3} alkyl, C_{1-3} fluoroalkyl, C_{1-3} alkoxy, C_{1-3} fluoroalkoxy, C_{1-3} hydroxyalkyl, C_{3-6} cycloalkyl, halo, OH, =O, CN, OCF_3, $OCHF_2$, CHF_2 CF_3, or $C(O)NR^eR^e$;

each R^e is independently H, C_{1-3} alkyl, C_{2-3} fluoroalkyl, C_{3-6} cycloalkyl, C_{2-3} hydroxyalkyl, C_{2-3} alkoxyalkyl, C_{6-10} aryl, or a 5 to 10 membered heteroaryl having 1, 2, 3, or 4 heteroatoms selected from O, S, and N;

alternatively, 2 R^es along with the atom to which they are attached, join to form a 3 to 6 membered saturated ring, containing 0-2 heteroatoms selected from O, S, or N; and

n is 0, 1, or 2.

2. A compound according to claim 1, or salt thereof, wherein:

R^1 is:  ;

each R^{1a} is independently selected from F, Cl, C_{1-3} alkyl, C_{1-3} fluoroalkyl, and C_{3-6} cycloalkyl;

R^{1c} is independently H, deuterium, C_{1-2} alkyl, or C_{3-6} cycloalkyl;

n is zero, 1, or 2.

3. A compound according to any one of claims 1 to 2, or salt thereof, wherein:

R^2 is phenyl, pyridinyl, indolyl, indazolyl, benzo[d]oxazol-onyl, pyrazolo[4,3-b]pyridinyl, pyridin-2-onyl, pyrazolyl, [1,2,4]triazolo[1,5-a]pyridinyl, imidazo[1,2-b]pyridazinyl, pyrazinyl, pyrazolo[1,5-a]pyrimidinyl, thiazolyl, thiophenyl, 1,2,3-triazolyl, benzo[d][1,2,3]triazolyl, [1,2,4]triazolo[4,3-b]pyridazinyl, benzo[d]imidazolyl, imidazolyl, pyrazolo[3,4-b]pyridinyl, pyrazolo[3,4-c]pyridinyl, pyrazolo[4,3-c]pyridinyl, pyrrolyl, pyrrolo[2,3-b]pyridinyl, pyrrolo[2,3-c]pyridinyl, pyrrolo[3,2-b]pyridinyl, pyrrolo[3,2-c]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, tetrazolyl, 1,2,4-triazolyl, isothiazolyl, isoxazolyl, oxazolyl, pyridazinyl, pyrimidinyl,or benzo[d]oxazol-2-onyl, triazolyl, oxadiazolyl, or pyrrolopyridinyl, each being substituted with 0-3 R^{2a}.

4. A compound according to any one of claims 1 to 3, or salt thereof, wherein:

Ring B is pyridinyl, pyrimidinyl, pyrrazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, oxadiazolyl, thiadiazolyl, isoxazolyl, pyrazinyl, oxazolyl, or pyridazinyl.

5. A compound according to any one of claims 1 to 4, or salt thereof, wherein:

V is –O-, -NR^4-, -CR^5R^5-, or -C(=O)-;

wherein if V is –O-, or NR^4, then Y is not $C(R^6)_2$;

Y is -$C(R^6)_2$-, -$C(R^6)_2$-$C(R^6)_2$-, -C(=O)-, -C(=O)-$C(R^6)_2$-, or -$C(R^6)_2$-C(O)-;

L^1 is –$C(R)_2$-, -C(O)-, or -CH_2–$C(R)_2$-; wherein R is independently from hydrogen, F, OH, C_{1-3} alkyl, C_{1-3} hydroxyalkyl, C_{1-3} alkoxyalkyl, or C_{1-3}fluoroalkyl.

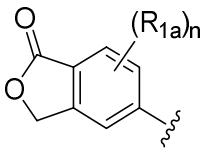
6. A compound according to any one of claims 1 to 5, or salt thereof, wherein:

R^2 is phenyl, pyridinyl, indolyl, indazolyl, benzo[d]oxazol-2(3H)-onyl, pyrazolo[4,3-b]pyridinyl, pyridin-2(1H)-onyl, pyrazolyl, pyrimidinyl, imidazolyl, pyrazolyl, triazolyl, oxadiazolyl, thiadiazolyl, [1,2,4]triazolo[1,5-a]pyridinyl, imidazo[1,2-b]pyridazinyl, pyrazinyl, pyrazolo[1,5-a]pyrimidinyl, thiophenyl, [1,2,4]triazolo[4,3-b]pyridazinyl, pyrazolo[1,5-a]pyrimidinyl, or benzo[d]oxazol-2(3H)-only, each being substituted with with 0-3 R^{2a}; and

R^{2a} is OH, =O, CN, halo, SO_2C_{1-4} alkyl, oxazolidin-2-one substituted with 0-1 R^{2b};

R^{2b} is C_{1-3}alkyl, C_{1-3} fluoroalkyl, C_{1-3} alkoxy, or C_{1-3} fluoroalkoxy.

7. A compound according to any one of claims 1 to 6, or salt thereof, wherein:

R^1 is 

R^{1a} is independently H or -CH_3.

8. The compound according to any one of claims 1 to 7, or salt thereof, wherein:

Ring B is pyridinyl, triazolyl, thiazolyl, oxadiazolyl, imidazolyl,or pyrrazolyl; and

R^2 is phenyl, pyridinyl, pyrimidinyl, benzo[d]oxazol-2(3H)-onyl, imidazolyl, pyrazolyl, triazolyl, or oxadiazolyl, each being substituted with 0-3 R^{2a}.

9. The compound according to any one of claims 1 to 8, or salt thereof, wherein:

V is –O-, -NR^4-, or -CR^5R^5-;

Y is -$C(R^6)_2$-$C(R^6)_2$- or -$C(R^6)_2$-;

L^1 is –$C(R)_2$-; wherein R is independently hydrogen, F, OH, C_{1-3} alkyl, C_{1-3} hydroxyalkyl, C_{1-3} alkoxyalkyl, or C_{1-3} fluoroalkyl; and

R^6 is independently H, C_{1-3}-alkyl, C_{1-3}-fluoroalkyl, or C_{3-6}-cycloalkyl.

10. A compound according to claim 1, or salt thereof, wherein the compound is selected from

(*R*)-4-methyl-6-(4-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)-1H-pyrazol-1-yl)nicotinonitrile;

(*R*)-4-methyl-6-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)nicotinonitrile;

(*R*)-3-methyl-5-(5-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)pyridin-2-yl)benzo[d]oxazol-2(3H)-one;

5-(4-((4,4-difluoro-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-1-yl)methyl)-1H-pyrazol-1-yl)-3-methylbenzo[d]oxazol-2(3H)-one ;

6-(4-((4,4-difluoro-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile;

(*R*)-6-(5-methoxy-4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile;

(*R*)-4-methyl-5-(4-((1-(2-methylthiazol-5-yl)-1H-pyrazol-4-yl)methyl)morpholin-2-yl)isobenzofuran-1(3H)-one;

(*R*)-4-cyclopropyl-6-(4-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)-1H-pyrazol-1-yl)nicotinonitrile;

(*R*)-4-methyl-6-(4-((5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)-2-oxooxazolidin-3-yl)methyl)-1H-pyrazol-1-yl)nicotinonitrile;

(*R*)-4-methyl-6-(4-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)-5-oxomorpholino)methyl)-1H-pyrazol-1-yl)nicotinonitrile;

(R)-4-methoxy-6-(4-(2-(2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)ethyl)-1H-pyrazol-1-yl)nicotinonitrile;

(*R*)-6-(5-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)-1,3,4-oxadiazol-2-yl)nicotinonitrile;

(*R*)-4-methyl-6-(5-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1,3,4-oxadiazol-2-yl)nicotinonitrile;

(*R*)-4-methoxy-6-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-imidazol-1-yl)nicotinonitrile;

(*R*)-4-methyl-6-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)-5-oxopiperazin-1-yl)methyl)-1H-pyrazol-1-yl)nicotinonitrile;

(*R*)-4-methyl-5-(4-((6-(4-methyl-1H-imidazol-1-yl)pyridin-3-yl)methyl)morpholin-2-

yl)isobenzofuran-1(3H)-one;

(*R*)-4-methoxy-5'-((5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)-2-oxooxazolidin-3-yl)methyl)-[2,2'-bipyridine]-5-carbonitrile;

6-(4-(1-hydroxy-2-((*R*)-2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)ethyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile (Diastereomer-I & II);

(*R*)-3-methyl-5-(5-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)thiazol-2-yl)benzo[d]oxazol-2(3H)-one;

(*R*)-3-methyl-5-(5-(2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholine-4-carbonyl)thiazol-2-yl)benzo[d]oxazol-2(3H)-one;

(*R*)-1-(5-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)thiazol-2-yl)-1H-imidazole-4-carbonitrile;

(*R*)-4-methyl-6-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2H-1,2,3-triazol-2-yl)nicotinonitrile;

(*R*)-4-methyl-6-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-1,2,3-triazol-1-yl)nicotinonitrile;

Methyl-(*R*)-4-((1-(5-cyano-4-methylpyridin-2-yl)-1H-pyrazol-4-yl)methyl)-2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazine-1-carboxylate;

(*S*)-4-methyl-6-(4-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)-1H-pyrazol-1-yl)nicotinonitrile;

(*R*)-3-methyl-5-(4-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)-1H-pyrazol-1-yl)benzo[d]oxazol-2(3H)-one;

(*R*)-6-(5-methoxy-4-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile;

(*R*)-4-methoxy-6-(4-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)-1H-imidazol-1-yl)nicotinonitrile;

(*R*)-6-(4-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)-1H-imidazol-1-yl)nicotinonitrile;

(*R*)-3-methyl-5-(4-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)-1H-imidazol-1-yl)benzo[d]oxazol-2(3H)-one;

(*R*)-4-methyl-6-(5-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)-1,3,4-oxadiazol-2-yl)nicotinonitrile;

(*R*)-4-methyl-6-(4-(2-(2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)ethyl)-1H-

pyrazol-1-yl)nicotinonitrile;

(*R*)-4-methoxy-6-(5-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)thiazol-2-yl)nicotinonitrile;

(*R*)-4-methyl-6-(5-(2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholine-4-carbonyl)thiazol-2-yl)nicotinonitrile;

(*R*)-4-methoxy-6-(5-(2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholine-4-carbonyl)thiazol-2-yl)nicotinonitrile;

(*R*)-4-methoxy-5'-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)-[2,2'-bipyridine]-5-carbonitrile;

(*R*)-4-methyl-5-(4-((2-(4-methyl-1H-imidazol-1-yl)thiazol-5-yl)methyl)morpholin-2-yl)isobenzofuran-1(3H)-one;

(*R*)-1-(5-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)pyridin-2-yl)-1H-imidazole-4-carbonitrile;

(*R*)-4-methyl-5-(4-((1-(thiophen-3-yl)-1H-pyrazol-4-yl)methyl)morpholin-2-yl)isobenzofuran-1(3H)-one;

(*R*)-4-methyl-5-(4-((1-(pyrazin-2-yl)-1H-pyrazol-4-yl)methyl)morpholin-2-yl)isobenzofuran-1(3H)-one;

(*R*)-4-(4-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)-1H-pyrazol-1-yl)benzonitrile;

(*R*)-4-methyl-5-(4-((1-(6-methylpyrazin-2-yl)-1H-pyrazol-4-yl)methyl)morpholin-2-yl)isobenzofuran-1(3H)-one;

(*R*)-5-(4-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)-1H-pyrazol-1-yl)nicotinonitrile;

(*R*)-3-(4-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)-1H-pyrazol-1-yl)benzonitrile;

(*R*)-4-methyl-5-(4-((1-(pyridin-4-yl)-1H-pyrazol-4-yl)methyl)morpholin-2-yl)isobenzofuran-1(3H)-one;

(*R*)-4-methyl-5-(4-((1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)methyl)morpholin-2-yl)isobenzofuran-1(3H)-one;

(*R*)-2-methyl-4-(4-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)-1H-pyrazol-1-yl)benzonitrile;

(*R*)-3-methyl-4-(4-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)-1H-pyrazol-1-yl)benzonitrile;

(*R*)-5-(4-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)-1H-pyrazol-1-yl)picolinonitrile;

(*R*)-2-methoxy-4-(4-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)-1H-pyrazol-1-yl)benzonitrile;

(*R*)-4-methyl-5-(4-((1-(pyrazolo[1,5-a]pyrimidin-5-yl)-1H-pyrazol-4-yl)methyl)morpholin-2-yl)isobenzofuran-1(3H)-one;

(*R*)-3-methoxy-4-(4-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)-1H-pyrazol-1-yl)benzonitrile;

(*R*)-4-methyl-6-(3-methyl-4-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)-1H-pyrazol-1-yl)nicotinonitrile;

(*R*)-4-methyl-6-(3-((2-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)-1H-pyrazol-1-yl)nicotinonitrile;

(*S*)-4-methyl-6-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)nicotinonitrile;

(*R*)-5-(5-methoxy-4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)-3-methylbenzo[d]oxazol-2(3H)-one;

(*R*)-7-fluoro-3-methyl-5-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)benzo[d]oxazol-2(3H)-one;

(*R*)-7-methoxy-3-methyl-5-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)benzo[d]oxazol-2(3H)-one;

(*R*)-3,7-dimethyl-5-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)benzo[d]oxazol-2(3H)-one;

(*R*)-3-methyl-5-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)benzo[d]oxazol-2(3H)-one;

(*R*)-4-methoxy-6-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)nicotinonitrile;

(*R*)-3-methyl-5-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-1,2,3-triazol-1-yl)benzo[d]oxazol-2(3H)-one;

(*R*)-6-(5-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1,3,4-oxadiazol-2-yl)nicotinonitrile;

(*R*)-4-methoxy-5'-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-[2,2'-bipyridine]-5-carbonitrile;

(*R*)-1-(5-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyridin-2-yl)-1H-pyrazole-4-carbonitrile;

(*R*)-1-(5-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyridin-2-yl)-1H-imidazole-4-carbonitrile;

(*R*)-4-methyl-5-(4-((6-(4-methyl-1H-imidazol-1-yl)pyridin-3-yl)methyl)piperazin-2-yl)isobenzofuran-1(3H)-one;

(*R*)-4-methyl-5-(4-((6-(3-methyl-1H-1,2,4-triazol-1-yl)pyridin-3-yl)methyl)piperazin-2-yl)isobenzofuran-1(3H)-one;

(*R*)-6-(4-((4-acetyl-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile;

(*R*)-4-methyl-6-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)-4-(methylsulfonyl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)nicotinonitrile;

(*R*)-4-methyl-6-(4-((4-methyl-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)nicotinonitrile;

(*R*)-3-methyl-5-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)-5-oxopiperazin-1-yl)methyl)-1H-pyrazol-1-yl)benzo[d]oxazol-2(3H)-one;

(*R*)-3-methyl-5-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)-5-oxopiperazin-1-yl)methyl)-1H-1,2,3-triazol-1-yl)benzo[d]oxazol-2(3H)-one;

(*R*)-1-(5-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)-5-oxopiperazin-1-yl)methyl)pyridine-2-yl)-1H-1,2,4-triazole-3-carbonitrile;

(*R*)-4-methoxy-5'-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)-5-oxopiperazin-1-yl)methyl)-[2,2'-bipyridine]-5-carbonitrile;

(*R*)-6-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)-4-((6-(3-methyl-1H-1,2,4-triazol-1-yl)pyridin-3-yl)methyl)piperazin-2-one;

(*R*)-6-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)-4-((6-(4-methyl-1H-imidazol-1-yl)pyridin-3-yl)methyl)piperazin-2-one;

(*R*)-4-methyl-6-(4-((4-methyl-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)-5-oxopiperazin-1-yl)methyl)-1H-pyrazol-1-yl)nicotinonitrile;

(*R*)-4-methoxy-6-(4-((5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)-2-oxooxazolidin-3-yl)methyl)-1H-imidazol-1-yl)nicotinonitrile;

(*R*)-6-(5-methoxy-4-((5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)-2-oxooxazolidin-3-yl)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile;

(*R*)-3-methyl-5-(4-((5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)-2-oxooxazolidin-3-yl)methyl)-1H-pyrazol-1-yl)benzo[d]oxazol-2(3H)-one;

6-(4-(((3*R*,5*R*)-3-(hydroxymethyl)-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile;

6-(4-((3,3-dimethyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2H-1,2,3-triazol-2-yl)-4-methylnicotinonitrile;

4-methyl-6-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2H-1,2,3-triazol-2-yl)nicotinonitrile;

6-(4-(((3*R*,4*R*)-4-hydroxy-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-1-yl)methyl)-1H-1,2,3-triazol-1-yl)-4-methylnicotinonitrile;

2,4-dimethyl-6-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2H-1,2,3-triazol-2-yl)nicotinonitrile;

4-methoxy-2-methyl-6-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-1,2,3-triazol-1-yl)nicotinonitrile;

6-(4-((3-(hydroxymethyl)-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile, (Enantiomer-III);

6-(4-((3-(hydroxymethyl)-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-1,2,3-triazol-1-yl)-4-methylnicotinonitrile, (Enantiomer-III);

6-(4-((3-(hydroxymethyl)-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methoxynicotinonitrile, (Enantiomer-III);

6-(4-((3-(hydroxymethyl-d2)-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile, (Enantiomer-I);

1-(5-(((3*R*,5*R*)-3-(hydroxymethyl)-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyridin-2-yl)-3-methyl-1H-pyrazole-4-carbonitrile;

6-(4-(((3*R*,4*R*)-4-hydroxy-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-1-yl)methyl)-1H-pyrazol-1-yl)-2,4-dimethylnicotinonitrile;

2-methoxy-6-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)nicotinonitrile;

5-((2*R*,6*S*)-4-((2-(4,5-dimethyl-1H-imidazol-1-yl)pyrimidin-5-yl)methyl)-6-methylpiperazin-2-yl)-4-methylisobenzofuran-1(3H)-one;

4,6-dimethyl-2-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-imidazol-1-yl)pyrimidine-5-carbonitrile;

4-methyl-2-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)pyrimidine-5-carbonitrile;

4-methoxy-6-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-imidazol-1-yl)nicotinonitrile;

4-methyl-6-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-imidazol-1-yl)nicotinonitrile;

4-methoxy-2-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)pyrimidine-5-carbonitrile;

4-methyl-2-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2H-1,2,3-triazol-2-yl)pyrimidine-5-carbonitrile;

2-methoxy-4-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-imidazol-1-yl)benzonitrile;

4-methyl-5-((2*R*,6*S*)-6-methyl-4-((1-(2-methylpyridin-4-yl)-1H-pyrazol-4-yl)methyl)piperazin-2-yl)isobenzofuran-1(3H)-one;

4-methoxy-2-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-imidazol-1-yl)pyrimidine-5-carbonitrile;

2-(4-(((3*R*,5*R*)-3-(hydroxymethyl)-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2H-1,2,3-triazol-2-yl)-4-methylpyrimidine-5-carbonitrile;

4-methyl-6-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)nicotinonitrile;

4-methyl-6-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-1,2,3-triazol-1-yl)nicotinonitrile;

4-methoxy-6-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2H-1,2,3-triazol-2-yl)nicotinonitrile;

3-methyl-1-(5-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyrimidin-2-yl)-1H-pyrazole-4-carbonitrile;

5-(4-(((3*R*,5*R*)-3-(hydroxymethyl)-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2H-1,2,3-triazol-2-yl)-3-methylbenzo[d]oxazol-2(3H)-one;

6-(4-(((3*R*,4*R*)-4-hydroxy-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile;

6-(4-(((3*R*,4*R*)-4-hydroxy-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-1-yl)methyl)-2H-1,2,3-triazol-2-yl)-4-methoxynicotinonitrile;

6-(4-(((3*R*,4*R*)-4-hydroxy-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methoxynicotinonitrile;

4,4-methyl-6-(5-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)thiazol-2-yl)nicotinonitrile;

6-(4-((4-hydroxy-4-methyl-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile;

4-methyl-6-(4-((2-methyl-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)nicotinonitrile;

6-(4-((4-hydroxy-3,3-dimethyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile;

4-methyl-6-(5-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2-oxooxazol-3(2H)-yl)nicotinonitrile;

(*R*)-4-methyl-6-(4-((4-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)-2-oxoimidazolidin-1-yl)methyl)-1*H*-pyrazol-1-yl)nicotinonitrile;

(*R*)-4-methyl-6-(4-((4-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)-1,1-dioxido-1,2,5-thiadiazolidin-2-yl)methyl)-1*H*-pyrazol-1-yl)nicotinonitrile;

2-methyl-6-(5-(((3S,5R)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyridin-2-yl)pyridazin-3(2H)-one;

4-methyl-6-(4-(1-((*R*)-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)ethyl)-2H-1,2,3-triazol-2-yl)nicotinonitrile (Dia-I:Ena-I);

4-methyl-6-(4-(1-((*R*)-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)ethyl)-2H-1,2,3-triazol-2-yl)nicotinonitrile (Dia-II:Ena-I);

4-methyl-6-(3-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-1,2,4-triazol-1-yl)nicotinonitrile;

6-(4-((2-(hydroxymethyl)-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile (Dia-I:Ena-I);

6-(4-((2-(hydroxymethyl)-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile (Dia-I:Ena-II);

6-(5-(((3*R*,4*R*)-4-hydroxy-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-1-yl)methyl)thiazol-2-yl)-4-methylnicotinonitrile;

5-((2*R*,6*S*)-4-((1-(2-methoxypyridin-4-yl)-1*H*-imidazol-4-yl)methyl)-6-methylpiperazin-2-yl)-4-methylisobenzofuran-1(3*H*)-one;

5-((2*R*,6*S*)-4-((1-(2-(difluoromethyl)pyridin-4-yl)-1*H*-pyrazol-4-yl)methyl)-6-methylpiperazin-2-yl)-4-methylisobenzofuran-1(3*H*)-one;

4-methyl-5-((2*R*,6*S*)-6-methyl-4-((1-(2-(trifluoromethyl)pyridin-4-yl)-1*H*-pyrazol-4-yl)methyl)piperazin-2-yl)isobenzofuran-1(3*H*)-one;

1-(difluoromethyl)-4-(4-(((3S,5R)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)pyridin-2(1H)-one;

1-(5-(((3*R*,5*R*)-3-(hydroxymethyl)-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyridin-2-yl)-3-methyl-1H-pyrazole-4-carbonitrile;

1-(difluoromethyl)-4-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-imidazol-1-yl)pyridin-2(1*H*)-one;

6-(4-(((3*R*,4*R*)-4-hydroxy-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-1-yl)methyl)oxazol-2-yl)-4-methylnicotinonitrile;

4-methyl-6-(5-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)oxazol-2-yl)nicotinonitrile;

5-((2*R*,6*S*)-4-((1-(6-(difluoromethyl)pyridin-3-yl)-1*H*-imidazol-4-yl)methyl)-6-methylpiperazin-2-yl)-4-methylisobenzofuran-1(3*H*)-one;

(*R*)-3,4-dimethyl-5-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1*H*-pyrazol-1-yl)benzo[d]oxazol-2(3*H*)-one;

(*R*)-1-(5-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyridin-2-yl)-1*H*-pyrazole-3-carbonitrile;

(*R*)-4-ethoxy-6-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1*H*-pyrazol-1-yl)nicotinonitrile;

(*R*)-1-(5-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyridin-2-yl)-1*H*-pyrazole-4-carboxamide;

(*R*)-5-(4-((2-(2,4-dimethyl-1*H*-imidazol-1-yl)pyrimidin-5-yl)methyl)piperazin-2-yl)-4-methylisobenzofuran-1(3*H*)-one;

(*R*)-4-isopropoxy-6-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1*H*-pyrazol-1-yl)nicotinonitrile;

(*R*)-4-methyl-5-(4-((4-methyl-6-(4-methyl-1H-imidazol-1-yl)pyridin-3-yl)methyl)piperazin-2-yl)isobenzofuran-1(3H)-one;

(*R*)-4-methyl-5-(4-((2-methyl-6-(4-methyl-1H-imidazol-1-yl)pyridin-3-yl)methyl)piperazin-2-yl)isobenzofuran-1(3H)-one;

(*R*)-4,6'-dimethoxy-5'-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-[2,2'-bipyridine]-5-carbonitrile;

(*R*)-5-(4-((5-fluoro-6-(4-methyl-1H-imidazol-1-yl)pyridin-3-yl)methyl)piperazin-2-yl)-4-methylisobenzofuran-1(3H)-one;

(*R*)-4-methyl-6-(3-methyl-4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)nicotinonitrile;

(*R*)-4-methyl-6-(5-methyl-4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)nicotinonitrile;

(*R*)-4-methyl-5-(4-((6-(4-methyl-1H-imidazol-1-yl)-4-(trifluoromethyl)pyridin-3-yl)methyl)piperazin-2-yl)isobenzofuran-1(3H)-one;

(*R*)-5-(4-((2-(4,5-dimethyl-1H-imidazol-1-yl)pyrimidin-5-yl)methyl)piperazin-2-yl)-4-methylisobenzofuran-1(3H)-one;

(*R*)-5-(4-((4-methoxy-6-(4-methyl-1H-imidazol-1-yl)pyridin-3-yl)methyl)piperazin-2-yl)-4-methylisobenzofuran-1(3H)-one;

(*R*)-5-(4-((2-(5-(difluoromethyl)-4-methyl-1H-imidazol-1-yl)pyrimidin-5-yl)methyl)piperazin-2-yl)-4-methylisobenzofuran-1(3H)-one;

4,6-dimethyl-2-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2H-1,2,3-triazol-2-yl)pyrimidine-5-carbonitrile;

3-(3-methyl-5-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)phenyl)oxazolidin-2-one;

(*R*)-4-methyl-5-(4-((6-(4-methyl-1H-imidazol-1-yl)pyridazin-3-yl)methyl)piperazin-2-yl)isobenzofuran-1(3H)-one;

4-methoxy-6-(3-(((*R*)-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyrrolidin-1-yl)nicotinonitrile (Diastereomer-I);

4-methoxy-6-(3-(((*R*)-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyrrolidin-1-yl)nicotinonitrile (Diastereomer-II);

4-methyl-6-(3-(((*R*)-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyrrolidin-1-yl)nicotinonitrile (Diastereomer-I);

4-methyl-6-(3-(((*R*)-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyrrolidin-1-yl)nicotinonitrile (Diastereomer-II);

4-methyl-6-(4-(((*R*)-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2-oxopyrrolidin-1-yl)nicotinonitrile (Diastereomer-II);

4-methoxy-6-(4-(((*R*)-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2-oxopyrrolidin-1-yl)nicotinonitrile (Diastereomer-I);

4-methyl-6-(5-(((*R*)-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2-oxooxazolidin-3-yl)nicotinonitrile (Diastereomer-II);

4-methyl-5-((2*R*,6*S*)-6-methyl-4-((1-(5-(methylsulfonyl)pyridin-2-yl)-1H-pyrazol-4-yl)methyl)piperazin-2-yl)isobenzofuran-1(3H)-one;

4-(4-(((3*R*,4*R*)-4-hydroxy-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-1-yl)methyl)-1H-imidazol-1-yl)-2-methoxybenzonitrile;

6-(4-(((3*R*,4*R*)-4-hydroxy-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-1-yl)methyl)-1H-imidazol-1-yl)-4-methylnicotinonitrile;

4-methyl-2-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-imidazol-1-yl)pyrimidine-5-carbonitrile;

4-methyl-5-((2*R*,6*S*)-6-methyl-4-((6'-(methylsulfonyl)-[2,3'-bipyridin]-5-yl)methyl)piperazin-2-yl)isobenzofuran-1(3H)-one;

4-methoxy-2-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2H-1,2,3-triazol-2-yl)pyrimidine-5-carbonitrile;

4-methoxy-2-(2-methyl-4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-imidazol-1-yl)pyrimidine-5-carbonitrile;

(*R*)-4-methoxy-6-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2H-1,2,3-triazol-2-yl)nicotinonitrile;

(*R*)-4-methyl-6-(4-methyl-5-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2H-1,2,3-triazol-2-yl)nicotinonitrile;

4-methoxy-6-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2-oxopyrrolidin-1-yl)nicotinonitrile (Diastereomer-I);

6-(4-(((3*R*,4*R*)-4-hydroxy-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-1-yl)methyl)-3-methyl-2-oxo-2,3-dihydro-1H-imidazol-1-yl)-4-methoxynicotinonitrile;

6-(3-isopropyl-4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2-oxo-2,3-dihydro-1H-imidazol-1-yl)-4-methoxynicotinonitrile;

3-methyl-4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1-(2-methylpyrimidin-4-yl)-1,3-dihydro-2H-imidazol-2-one;

3-(5-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-[2,4'-bipyridin]-2'-yl)oxazolidin-2-one;

6-(4-((3,3-dimethyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-5-methyl-2H-1,2,3-triazol-2-yl)-4-methylnicotinonitrile (Enantiomer-I);

4-methyl-6-(5-methyl-4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-1,2,3-triazol-1-yl)nicotinonitrile;

(*R*)-4-methyl-5-(4-((1-(1-methyl-1*H*-pyrrolo[2,3-b]pyridin-4-yl)-1*H*-pyrazol-4-yl)methyl)morpholin-2-yl)isobenzofuran-1(3*H*)-one;

4-methyl-5-((2*R*,6*S*)-6-methyl-4-((1-(p-tolyl)-1*H*-imidazol-4-yl)methyl)piperazin-2-yl)isobenzofuran-1(3*H*)-one;

4-methyl-5-((2*R*,6*S*)-6-methyl-4-((1-(3-methylpyridin-4-yl)-1*H*-imidazol-4-yl)methyl)piperazin-2-yl)isobenzofuran-1(3*H*)-one;

4-methyl-5-((2*R*,6*S*)-6-methyl-4-((1-(6-methylpyridin-3-yl)-1*H*-imidazol-4-yl)methyl)piperazin-2-yl)isobenzofuran-1(3*H*)-one;

5-((2*R*,6*S*)-4-((1-(2,6-dimethylpyridin-4-yl)-1*H*-imidazol-4-yl)methyl)-6-methylpiperazin-2-yl)-4-methylisobenzofuran-1(3*H*)-one;

5-((2*R*,6*S*)-4-((1-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)-1*H*-imidazol-4-yl)methyl)-6-methylpiperazin-2-yl)-4-methylisobenzofuran-1(3*H*)-one;

(*R*)-4-methyl-6-(2-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyrimidin-5-yl)nicotinonitrile;

(*R*)-2,4-dimethyl-6-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2H-1,2,3-triazol-2-yl)nicotinonitrile;

(*R*)-3-(2-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)pyridin-4-yl)oxazolidin-2-one;

(*R*)-2,4-dimethyl-6-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-1,2,3-triazol-1-yl)nicotinonitrile;

(*R*)-4-methoxy-2-methyl-6-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-1,2,3-triazol-1-yl)nicotinonitrile;

(*R*)-4-methoxy-2-methyl-6-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2H-1,2,3-triazol-2-yl)nicotinonitrile;

(*R*)-2-methoxy-4-methyl-6-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-1,2,3-triazol-1-yl)nicotinonitrile;

6-(4-((3,3-dimethyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2H-1,2,3-triazol-2-yl)-4-methoxynicotinonitrile (Enantiomer-I);

4-methyl-6-(5-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1,3,4-oxadiazol-2-yl)nicotinonitrile;

4-methoxy-6-(4-(2-((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)ethyl)-1H-pyrazol-1-yl)nicotinonitrile;

6-(5-(((3*R*,4*R*)-4-hydroxy-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-1-yl)methyl)isoxazol-3-yl)-4-methylnicotinonitrile;

5-((2*R*,6*S*)-4-((1-(4-methoxy-1,3,5-triazin-2-yl)-1H-pyrazol-4-yl)methyl)-6-methylpiperazin-2-yl)-4-methylisobenzofuran-1(3H)-one;

6-(4-(((3*R*,5*R*)-3-(hydroxymethyl)-4-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile;

6-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)-4-(trifluoromethyl)nicotinonitrile;

4-methyl-6-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-1-yl)methyl)-1H-pyrazol-1-yl)nicotinonitrile (Enantiomer-I);

(*R*)-2-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)isonicotinonitrile;

6-(4-((3-hydroxy-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile (Enantiomer-IV);

6-(4-((3-methoxy-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile (Enantiomer-II);

(*R*)-5-(4-((2-(3,5-dimethyl-4H-1,2,4-triazol-4-yl)pyrimidin-5-yl)methyl)piperazin-2-yl)-4-methylisobenzofuran-1(3H)-one;

3-methyl-2-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)isonicotinonitrile;

6-(4-((3-fluoro-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-1-yl)methyl)-1H-1,2,3-triazol-1-yl)-4-methylnicotinonitrile (Enantiomer-I);

6-(4-((3-(1-hydroxyethyl)-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methoxynicotinonitrile (Enantiomer-I);

6-(4-((3-(difluoromethyl)-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile (Enantiomer-I);

4-methyl-5-((2*R*,6*S*)-6-methyl-4-((1-(5-methylpyrazin-2-yl)-1H-pyrazol-4-yl)methyl)piperazin-2-yl)isobenzofuran-1(3H)-one;

5-((2*R*,6*S*)-4-((1-(6-methoxypyrimidin-4-yl)-1H-pyrazol-4-yl)methyl)-6-methylpiperazin-2-yl)-4-methylisobenzofuran-1(3H)-one;

5-((2*R*,6*S*)-4-((1-(2-methoxypyrimidin-5-yl)-1H-pyrazol-4-yl)methyl)-6-methylpiperazin-2-yl)-4-methylisobenzofuran-1(3H)-one;

4-methyl-5-((2*R*,6*S*)-6-methyl-4-((1-(2-methylpyrimidin-5-yl)-1H-pyrazol-4-yl)methyl)piperazin-2-yl)isobenzofuran-1(3H)-one;

4-methyl-6-(3-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)isoxazol-5-yl)nicotinonitrile;

6-(4-((3-hydroxy-4-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)pyrrolidin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile (Diastereomer-I: Enantiomer-I);

6-(4-((3-fluoro-4-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)pyrrolidin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile (Diastereomer-I: Enantiomer-II);

6-(4-((3-(2-hydroxypropan-2-yl)-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile (Enantiomer-I);

4-methyl-6-(5-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)isoxazol-3-yl)nicotinonitrile;

(*R*)-4-methyl-5-(4-((2-(4-methyl-1H-imidazol-1-yl)pyrimidin-5-yl)methyl)piperazin-2-yl)isobenzofuran-1(3H)-one;

(*R*)-1-(5-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyrimidin-2-yl)-1H-imidazole-4-carbonitrile;

(*R*)-1-(5-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyrimidin-2-yl)-1H-1,2,4-triazole-3-carbonitrile;

(*R*)-3-cyclopropyl-1-(5-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyrimidin-2-yl)-1H-pyrazole-4-carbonitrile;

(*R*)-3-(difluoromethoxy)-1-(5-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyridin-2-yl)-1H-pyrazole-4-carbonitrile;

(*R*)-6-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)-4-morpholinonicotinonitrile;

(*R*)-3-methyl-1-(5-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyrimidin-2-yl)-1H-pyrazole-4-carbonitrile;

(*R*)-4-methyl-5-(4-((6-(4-methyl-1H-1,2,3-triazol-1-yl)pyridin-3-yl)methyl)piperazin-2-yl)isobenzofuran-1(3H)-one;

(*R*)-3-methoxy-1-(5-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyridin-2-yl)-1H-pyrazole-4-carbonitrile;

(*R*)-4-methyl-5-(4-((2-(4-methyl-1H-imidazol-1-yl)pyrimidin-5-yl)methyl)morpholin-2-yl)isobenzofuran-1(3H)-one;

(*R*)-1-(5-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyridin-2-yl)-1H-1,2,3-triazole-4-carbonitrile;

(*R*)-3-ethyl-1-(5-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyridin-2-yl)-1H-pyrazole-4-carbonitrile;

(*R*)-3-methoxy-1-(5-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyrimidin-2-yl)-1H-pyrazole-4-carbonitrile;

(*R*)-3-ethyl-1-(5-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyrimidin-2-yl)-1H-pyrazole-4-carbonitrile;

(*R*)-3-(difluoromethyl)-1-(5-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyrimidin-2-yl)-1H-pyrazole-4-carbonitrile;

(*R*)-4-methyl-2-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)pyrimidine-5-carbonitrile;

(*R*)-2-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)-5-(pyrrolidin-1-yl)isonicotinonitrile;

4-methyl-6-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)-4-oxopiperidin-1-yl)methyl)-1H-pyrazol-1-yl)nicotinonitrile;

(*R*)-6-(3-(difluoromethyl)-4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile;

(*R*)-5-(4-((2-(1H-1,2,4-triazol-1-yl)pyrimidin-5-yl)methyl)piperazin-2-yl)-4-methylisobenzofuran-1(3H)-one;

(*R*)-5-(4-((6-(4 (difluoromethyl)-1H-imidazol-1-yl)pyridin-3-yl)methyl)piperazin-2-yl)-4-methylisobenzofuran-1(3H)-one;

(*R*)-4-methyl-5-(4-((2-(4-(trifluoromethyl)-1H-imidazol-1-yl)pyrimidin-5-yl)methyl)piperazin-2-yl)isobenzofuran-1(3H)-one;

(*R*)-6-(3-cyclopropyl-4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile;

1'-methyl-5-(((3*S*, 5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-[2,3'-bipyridin]-6'(1'H)-one;

(*R*)-4-methyl-6-(4-((3-(1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)nicotinonitrile;

4-methyl-6-(4-(((6*R*)-2-methyl-6-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)-1H-pyrazol-1-yl)nicotinonitrile (Diastereomer-I);

(*R*)-3-methyl-1-(6-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyridin-3-yl)-1H-pyrazole-4-carbonitrile;

(*R*)-4-methyl-1-(5-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyridin-2-yl)-1H-pyrazole-3-carbonitrile;

(*R*)-4-methyl-1-(5-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyrimidin-2-yl)-1H-pyrazole-3-carbonitrile;

4-methyl-6-(4-((2-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)nicotinonitrile (Enantiomer-II);

6-(3-(difluoromethyl)-4-(((3*R*,4*R*)-4-hydroxy-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile;

6-(4-(((3*S*,5*R*)-4-hydroxy-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2H-1,2,3-triazol-2-yl)-4-methylnicotinonitrile;

4'-methyl-4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2-oxo-2H-[1,2'-bipyridine]-5'-carbonitrile;

N-(1-((1-(5-cyano-4-methylpyridin-2-yl)-1H-pyrazol-4-yl)methyl)-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-4-yl)acetamide (Diastereomer-II Enantiomer-I);

3-(6-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)pyridin-2-yl)oxazolidin-2-one;

6-(4-(((3*R*,4*R*)-4-hydroxy-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-1-yl)methyl)-3-methyl-2-oxo-2,3-dihydro-1H-imidazol-1-yl)-4-methylnicotinonitrile;

3-(2-methyl-6-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)pyridin-4-yl)oxazolidin-2-one;

N-methyl-N-(6-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazol-1-yl)pyridin-2-yl)methanesulfonamide;

5-((2*R*,6*S*)-4-((1-(4-(1,1-dioxidoisothiazolidin-2-yl)-6-methylpyridin-2-yl)-1H-pyrazol-4-yl)methyl)-6-methylpiperazin-2-yl)-4-methylisobenzofuran-1(3H)-one;

1-(2-methoxypyridin-4-yl)-4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)pyrrolidin-2-one (Diastereomer-I);

(*R*)-4-methoxy-6-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-1,2,3-triazol-1-yl)nicotinonitrile;

6-(4-((2,2-dimethyl-6-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)morpholino)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile (Enantiomer-II);

N-(1-((1-(5-cyano-4-methylpyridin-2-yl)-1H-pyrazol-4-yl)methyl)-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-3-yl)acetamide (Enantiomer-I);

1-((1-(5-cyano-4-methylpyridin-2-yl)-1H-pyrazol-4-yl)methyl)-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-4-yl methylcarbamate (Enantiomer-I);

4-methyl-6-(3-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1,2,4-oxadiazol-5-yl)nicotinonitrile;

(*R*)-1-(5-cyano-4-methoxypyridin-2-yl)-N-methyl-4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazole-3-carboxamide;

6-(4-((3-(hydroxymethyl)-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-1-yl)methyl)-1H-pyrazol-1-yl)-4-methylnicotinonitrile (Diastereomer-II: Enantiomer-II);

(*R*)-1-(5-cyano-4-methoxypyridin-2-yl)-4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-pyrazole-3-carboxamide;

(*R*)-4-(methoxy-d3)-6-(4-((3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1H-1,2,3-triazol-1-yl)nicotinonitrile;

(*R*)-4-methyl-5-(4-((6-(3-methyl-1,2,4-oxadiazol-5-yl)pyridin-3-yl)methyl)piperazin-2-yl)isobenzofuran-1(3H)-one;

2-methyl-4-(5-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2H-tetrazol-2-yl)benzonitrile;

3-methyl-4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1-(2-methylpyridin-4-yl)-1,3-dihydro-2H-imidazol-2-one;

6-(5-((3,3-dimethyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1,3,4-oxadiazol-2-yl)-4-methylnicotinonitrile (Enantiomer-I);

6-(5-((3,3-dimethyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)isoxazol-3-yl)-4-methylnicotinonitrile (Enantiomer-I);

4-methoxy-6-(5-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)isoxazol-3-yl)nicotinonitrile;

1-(difluoromethyl)-4-(4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2*H*-1,2,3-triazol-2-yl)pyridin-2(1*H*)-one;

5-((2*R*,6*S*)-4-((1-(2-(difluoromethyl)pyrimidin-4-yl)-1H-imidazol-4-yl)methyl)-6-methylpiperazin-2-yl)-4-methylisobenzofuran-1(3H)-one;

4-(5-(((3*R*,4*R*)-4-hydroxy-3-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperidin-1-yl)methyl)-2H-tetrazol-2-yl)-2-methoxybenzonitrile;

6-(5-((3-(difluoromethyl)-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1,3,4-oxadiazol-2-yl)-4-methylnicotinonitrile (Enantiomer-I);

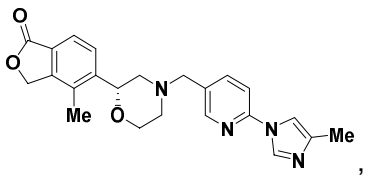
4-methoxy-6-(3-methyl-4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-2-oxoimidazolidin-1-yl)nicotinonitrile (Diastereomer-I);

1-(2-methoxypyridin-4-yl)-3-methyl-4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1,3-dihydro-2H-imidazol-2-one;

1-(2-(difluoromethyl)pyridin-4-yl)-3-methyl-4-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl)piperazin-1-yl)methyl)-1,3-dihydro-2H-imidazol-2-one; and

4-methoxy-6-(5-(((3*S*,5*R*)-3-methyl-5-(4-methyl-1-oxo-1,3-dihydroisobenzofuran-5-yl-3,3-d2)piperazin-1-yl)methyl)isoxazol-3-yl)nicotinonitrile.

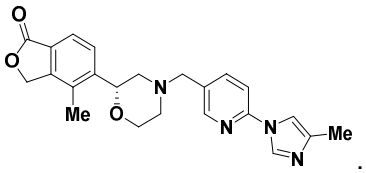
11. A compound, wherein the compound is



,

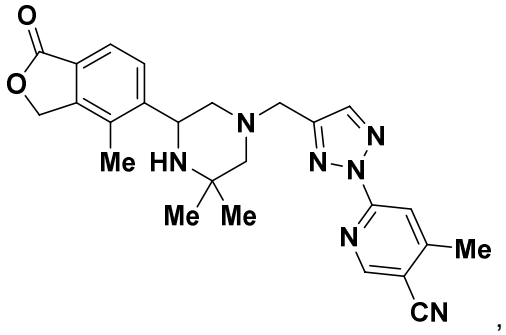
or salt thereof.

12. A compound, wherein the compound is



.

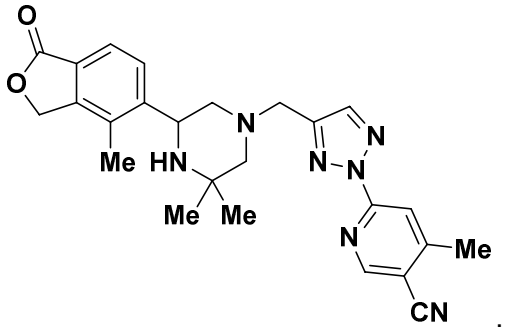
13. A compound, wherein the compound is



,

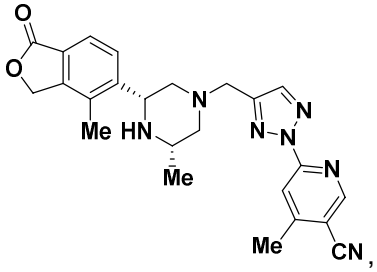
or salt thereof.

14. A compound, wherein the compound is



.

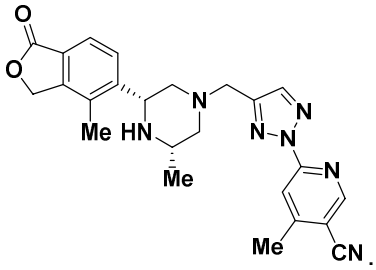
15. A compound, wherein the compound is



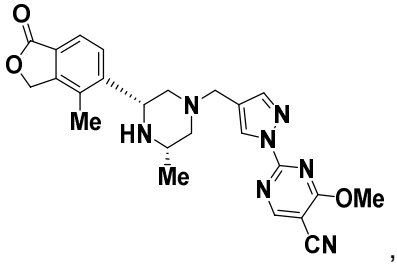
,

or salt thereof.

16. A compound, wherein the compound is

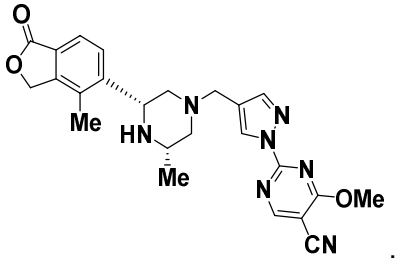


17. A compound, wherein the compound is

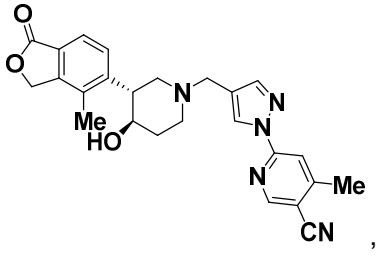


or salt thereof.

18. A compound, wherein the compound is

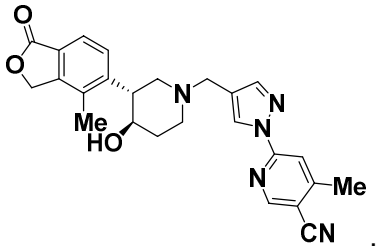


19. A compound, wherein the compound is



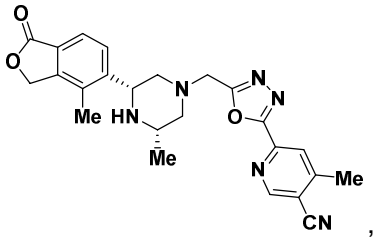
or salt thereof.

20. A compound, wherein the compound is



.

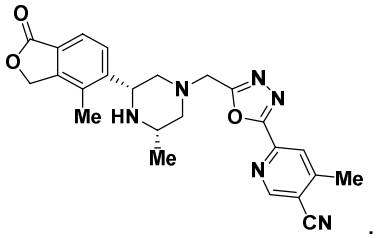
21. A compound, wherein the compound is



,

or salt thereof.

22. A compound, wherein the compound is



.

23. A pharmaceutical composition comprising one or more compounds according to any one of claims 1 to 22, or a salt thereof; and a pharmaceutically acceptable carrier or diluent.

24. A pharmaceutical composition, which comprises a pharmaceutically acceptable carrier and a compound as defined in any one of claims 1 to 22, or pharmaceutically acceptable salt, alone or in combination with another therapeutic agent.

25. A compound according to any one of claims 1 to 22 for use as a medicament.

26. A compound according to any one of claims 1 to 22 for use in therapy.

27. A compound according to any one of claims 1 to 22, or pharmaceutically acceptable salt thereof, for use in the treatment of a cardiovascular disease, wherein a therapeutically affective amount of the compound or the pharmaceutically acceptable salt is to be administered to a patient in need thereof.

28. The compound for use according to claim 27, wherein the cardiovascular disease is selected from hypertension, coronary heart disease, stroke, heart failure, systolic heart failure, diastolic heart failure, diabetic heart failure, acute-decompensated heart failure, post-operative volume overload, idiopathic edema, pulmonary hypertension, pulmonary arterial hypertension, cardiac insufficiency, nephrotic syndrome, and acute kidney insufficiency.

29. A compound of any one of claims 1 to 22, or pharmaceutically acceptable salt thereof, for use in promoting diuresis or natriuresis, wherein a therapeutically affective amount of the compound or the pharmaceutically acceptable salt is to be administered to a patient in need thereof.