



(51) International Patent Classification:

C07D 405/14 (2006.01) C07D 495/10 (2006.01)

C07D 413/14 (2006.01) A61P 31/04 (2006.01)

C07D 491/107 (2006.01) A61K 31/422 (2006.01)

(21) International Application Number:

PCT/IB2019/056322

(22) International Filing Date:

24 July 2019 (24.07.2019)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

201821027940 25 July 2018 (25.07.2018) IN

(71) Applicant: CADILA HEALTHCARE LIMITED

[IN/IN]; Zydus Tower, Satellite Cross Roads, Ahmedabad, Gujarat 380015 (IN).

(72) Inventors: DESAI, Ranjit; Cadila Healthcare Limited, Zy-

ydus Tower, Satellite Cross Roads, Ahmedabad, Gujarat 380015 (IN). PANDYA, Vrajesh; Cadila Healthcare Limited, Zydus Tower, Satellite Cross Roads, Ahmedabad, Gujarat 380015 (IN). PUJARA, Mehul; Cadila Healthcare Limited, Zydus Tower, Satellite Cross Roads, Ahmedabad, Gujarat 380015 (IN). ARGADE, Anil; Cadila Healthcare Limited, Zydus Tower, Satellite Cross Roads, Ahmedabad, Gujarat 380015 (IN). JOSHI, Jignesh; Cadila Healthcare Limited, Zydus Tower, Satellite Cross Roads, Ahmedabad, Gujarat 380015 (IN). SATYANAND, Anshul; Cadila Healthcare Limited, Zydus Tower, Satellite Cross Roads, Ahmedabad, Gujarat 380015 (IN).

(74) Agent: ELANGBAM, Nanda et al.; Subramaniam & As-

sociates, 7th Floor, M3M Cosmopolitan, Golf Course Extension Road, Sector 66, Gurugram, National Capital Region 122001 (IN).

(81) Designated States (unless otherwise indicated, for every

kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ,

OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every

kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

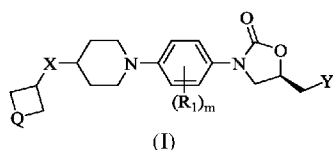
— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))

Published:

— with international search report (Art. 21(3))
— in black and white; the international application as filed contained color or greyscale and is available for download from PATENTSCOPE

(54) Title: SUBSTITUTED OXAZOLIDINONES FOR THE TREATMENT OF MAMMALIAN INFECTIONS

(57) Abstract: Present invention relates to novel compound of formula (I), their enantiomers, their diastereomers, their pharmaceutically accepted salts, or pro-drugs thereof, which are useful for the treatment of bacterial infection.

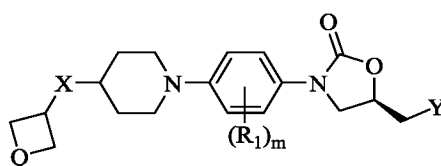


(I)

SUBSTITUTED OXAZOLIDINONES FOR THE TREATMENT OF MAMMALIAN INFECTIONS

FIELD OF INVENTION

The present invention relates to novel compounds of the formula (I), their tautomeric forms, their stereoisomers, their pharmaceutically acceptable salts, pharmaceutical compositions containing them, methods for their preparation. These compounds show activity against *Mycobacterium tuberculosis* infection.



Formula (I)

BACKGROUND OF THE INVENTION

Tuberculosis (TB) is one of the leading cause of human death from infectious disease in the world. About 33% of world's population is thought to be infected with *Mycobacterium tuberculosis* (Mtb), the pathogen that causes TB disease (WHO "Global Tuberculosis Report 2016", World Health Organization, 2017). Current treatment has a potential to cure drug-sensitive TB, however treatment of drug-resistant or multi drug-resistant TB (MDR-TB) is challenging and needs a two years of combination chemotherapy (WHO "Multidrug-Resistant Tuberculosis (MDR-TB) 2016 Update", World Health Organization, 2016). Resistance to current treatment for MDR-TB and extensively resistant TB (XDR-TB) highlights the need of new drugs with novel mechanism of actions.

Linezolid is approved antibiotic for gram positive bacterial infections. It has also shown anti-bacterial activity against *mycobacterium tuberculosis* pathogens. Linezolid and other oxazolidinone class of agents inhibit bacterial protein synthesis by binding to the peptidyl transferase center of the 50S ribosomal subunit and interfering with the placement of the aminoacyl-tRNA. They do not bind to mammalian cytoplasmic ribosomes, but do bind to mitochondrial ribosomes which are responsible for bone marrow toxicity associated with Linezolid and other oxazolidinones. Treatment of TB is lengthy which makes Linezolid not

suitable for its treatment. Hence, novel oxazolidinones with improves safety profile is required which can be utilized for the treatment of TB. WO 2017015106 describes substituted phenyl oxazolidinones for the treatment of tuberculosis. KR 101271224 describes oxazolidinone derivatives containing bicyclic group having antibacterial activity against gram positive bacteria including various resistant strains. WO 2005054234 describes novel substituted piperidino phenyloxazolidinone derivatives as active ingredients and methods of treating bacterial infection. The other documents that describe oxazolidone class of inhibitors including, WO 9323384, WO 2002080841, WO 2001042242, WO 2003064415, WO 2009020616, WO 2017070024, WO 2005054234, WO 2002051819, WO 2017156519, WO 2013044865, and WO 2006059221 are also disclosed.

SUMMARY OF THE INVENTION

The present invention discloses novel compounds of the formula (I). The compounds of the present invention are useful in the treatment of the human or animal body, by regulation of bacterial protein synthesis. The compounds of this invention are therefore suitable for the treatment of tuberculosis or *Mycobacterium* infection.

EMBODIMENTS OF THE INVENTION

The main objective of the present invention is to provide novel compounds of formula (I), their tautomeric forms, novel intermediates involved in their synthesis, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and pharmaceutical compositions containing them or their mixtures suitable for the treatment of tuberculosis or *Mycobacterium* infection.

In another embodiment is provided pharmaceutical compositions containing compounds of general formula (I), their tautomeric forms, their pharmaceutically acceptable salts, solvates and their mixtures having pharmaceutically acceptable carriers, solvents, diluents, excipients and other media normally employed in their manufacture.

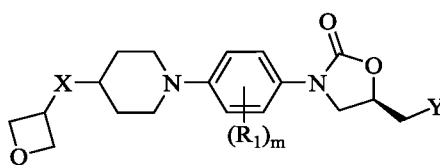
In a further another embodiment is provided the use of the novel compounds of the present invention for the treatment of mammalian infections such as tuberculosis, by administering a therapeutically effective & non-toxic amount of the compound of formula (I), or their pharmaceutically acceptable compositions to the mammals.

In yet another embodiment is provided a method of treatment of the mammalian infection such as tuberculosis using compound of formula (I) or their pharmaceutically acceptable compositions to the mammals.

In final embodiment is provided a pharmaceutical composition comprising the compound of formula (I) and second therapeutic agent for the treatment of mammalian infections such as tuberculosis.

DESCRIPTION OF THE INVENTION

Accordingly, the present invention relates to compounds of the formula (I),



Formula (I)

Wherein,

X is either absent or a bond; whenever X is absent, four membered ring is directly attached to the 6-membered piperidine ring forming spirocyclic system;

Q is either O or S(O)_p; p = 0-2 integer;

Y represents OH, NR₂R₃, NHC(O)R₄;

R₁ is selected from H, F, Cl, CH₃, CN and OCH₃; m = 1-4 integer;

R₂ and R₃ is independently selected from H, (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, aryl, heterocyclyl and heteroaryl each of which may be further optionally substituted; R₂ and R₃ taken together with the nitrogen to which they are attached may form a 4- to 8- membered heterocyclyl or heteroaryl with 1 to 3 additional heteroatoms selected from O, S, or N and may be further be optionally substituted;

R₄ is independently selected from (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, aryl, heteroaryl and (C₁-C₆)alkoxy each of which may be further optionally substituted;

In an embodiment, when any of the (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, aryl, heterocyclyl and heteroaryl groups are optionally substituted, the groups are selected from halo, hydroxyl, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, (C₁-C₆)acyloxy, haloalkyl, NO₂, CN and NH₂;

In a further embodiment the groups, radicals described above may be selected from:

- the “alkyl” group used either alone or in combination with other radicals, denotes a linear or branched radical containing one to six carbons, selected from methyl, ethyl, *n*-propyl, *iso*-propyl, *n*-butyl, *sec*-butyl, *tert*-butyl, amyl, *t*-amyl, *n*-pentyl, *n*-hexyl, and the like;

- the “alkoxy” group used either alone or in combination with other radicals, denotes a linear or branched radical containing one to six carbon attached to oxygen atom, selected from Methoxy, ethoxy, *n*-propoxy, *iso*-propoxy, *n*-butoxy, *sec*-butoxy, *iso*-butoxy, pentyloxy, hexyloxy and the like;

- the “cycloalkyl”, or “alicyclic” group used either alone or in combination with other radicals, is selected from a cyclic radical containing three to six carbons, more preferably cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and the like;

- the “haloalkyl” group is selected from an alkyl radical, as defined above, suitably substituted with one or more halogens; such as fluoromethyl, difluoromethyl, trifluoromethyl, fluoroethyl, difluoroethyl, trifluoroethyl, mono or polyhalo substituted methyl, ethyl, propyl, butyl, pentyl or hexyl groups;

- the “aryl” or “aromatic” group used either alone or in combination with other radicals, is selected from a suitable aromatic system containing one, two or three rings wherein such rings may be attached together in a pendant manner or may be fused, more preferably the groups are selected from phenyl, naphthyl, tetrahydronaphthyl, indane, biphenyl, and the like;

- the “heterocyclyl” or “heterocyclic” group used either alone or in combination with other radicals, is selected from suitable saturated, partially saturated or unsaturated aromatic or non-aromatic mono, bi or tricyclic radicals, containing one or more heteroatoms selected from nitrogen, sulfur and oxygen, more preferably selected from aziridinyl, azetidiny, pyrrolidinyl, imidazolidinyl, piperidinyl, piperazinyl, 2-oxopiperidinyl, 4-oxopiperidinyl, 2-oxopiperazinyl, 3-oxopiperazinyl, morpholinyl, thiomorpholinyl, 2-oxomorpholinyl, azepinyl, diazepinyl, oxapinyl, thiazepinyl, oxazolidinyl, thiazolidinyl, dihydrothiophene, dihydropyran, dihydrofuran, dihydrothiazole, benzopyranyl, benzopyranonyl, benzodihydrofuranly, benzodihydrothienyl, pyrazolopyrimidonyl, azaquinazolinoyl, thienopyrimidonyl,

quinazolonyl, pyrimidonyl, benzoxazinyl, benzoxazinonyl, benzothiazinyl, benzothiazinonyl, thieno piperidiny, and the like; In one embodiment, the heterocycle group, wherever applicable, may consists of appropriate number of carbon atoms and include from 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p, p =

5 0-2;

- the “heteroaryl” or “heteroaromatic” group used either alone or in combination with other radicals, is selected from suitable single or fused mono, bi or tricyclic aromatic heterocyclic radicals containing one or more hetero atoms selected from O, N or S, more preferably the groups are selected from pyridyl, thienyl, furyl, pyrrolyl, oxazolyl, thiazolyl, isothiazolyl, imidazolyl, isoxazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, benzofuranyl, benzothienyl, indoliny, indolyl, azaindolyl, azaindoliny, pyrazolopyrimidinyl, azaquinazoliny, pyridofuranyl, pyridothienyl, thienopyrimidinyl, quinoliny, pyrimidinyl, pyrazolyl, quinazoliny, pyridazinyl, triazinyl, benzimidazolyl, benzotriazolyl, phthalazynyl, naphthylidiny, puriny, carbazolyl, phenothiazinyl, phenoxazinyl, benzoxazolyl, benzothiazolyl and the like;

- the “aralkyl” group used either alone or in combination with other radicals, is selected from groups containing an aryl radical, as defined above, attached directly to an alkyl radical, as define above, more preferably groups selected from benzyl, phenethyl, and the like;

- the “heterocyclylalkyl” group used either alone or in combination with other radicals, is selected from groups containing an heterocyclyl radical, as defined above, attached directly to an alkyl radical, as define above;

- the “spirocyclic system” is a group wherein one cyclic ring is attached to another cyclic ring via one carbon atom that is common carbon atom to both cyclic ring.

Further preferred embodiments are those disclosed below.

Preferred “(C₁-C₆)alkyl” group of R₂, R₃ and R₄ is selected from methyl, ethyl, n-propyl, iso-propyl;

Preferred “(C₁-C₆)alkoxy” group of R₂, R₃ and R₄ is selected from methoxy and ethoxy;

Preferred “(C₃-C₆)cycloalkyl” group of R₂, R₃ and R₄ is selected from cyclopropyl and cyclobutyl;

Preferred “heteroaryl” group of R₂ and R₃ is selected from triazolyl, isoxazolyl, thienyl, furyl.

Suitable groups and substituents on the groups may be selected from those described anywhere in the specification.

- 5 Preferred compounds according to the present invention include but are not limited to:
- (R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)oxazolidin-2-one;
- (S)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-5-((isoxazol-3-ylamino)methyl)oxazolidin-2-one;
- 10 (S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)acetamide;
- (S)-methyl ((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate;
- (S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-2-
- 15 oxooxazolidin-5-yl)methyl)acetamide;
- (S)-N-((3-(3,5-difluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)acetamide;
- (S)-N-((3-(3-fluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)acetamide;
- 20 (S)-N-((3-(3,5-difluoro-4-(4-(oxetan-3-yl)piperidin-1-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)acetamide;
- (S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)acetamide;
- (S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)-2-oxooxazolidin-5-
- 25 yl)methyl)acetamide;
- methyl (S)-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate;
- (S)-5-(aminomethyl)-3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)oxazolidin-2-one;
- 30 (R)-3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-5-(hydroxymethyl)oxazolidin-2-one;

- (S)-5-(aminomethyl)-3-(3,5-difluoro-4-(4-(oxetan-3-yl)piperidin-1-yl)phenyl)oxazolidin-2-one;
- (S)-5-(aminomethyl)-3-(3,5-difluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)oxazolidin-2-one;
- 5 (S)-5-(aminomethyl)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)oxazolidin-2-one;
- (R)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-5-(hydroxymethyl)oxazolidin-2-one;
- (S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)thiophene-2-carboxamide;
- 10 (S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)thiophene-2-carboxamide;
- (S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)furan-2-carboxamide;
- 15 (S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)furan-2-carboxamide;
- (S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)thiophene-2-carboxamide;
- (S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)thiophene-2-carboxamide;
- 20 (S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)furan-2-carboxamide;
- (S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)furan-2-carboxamide;
- 25 (S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)butyramide;
- (S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)butyramide;
- (S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)butyramide;
- 30 (S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)butyramide;

- (S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)butyramide;
- ethyl (S)-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate;
- 5 ethyl (S)-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate;
- ethyl (S)-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate;
- ethyl (S)-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate;
- 10 (S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)cyclopropanecarboxamide;
- (S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)cyclopropanecarboxamide;
- 15 (S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)cyclopropanecarboxamide;
- (S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)cyclopropanecarboxamide;
- (S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)cyclobutanecarboxamide;
- 20 (S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)cyclobutanecarboxamide;
- (S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)cyclobutanecarboxamide;
- 25 (S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)cyclobutanecarboxamide;
- (R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)oxazolidin-2-one;
- (R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)oxazolidin-2-one;
- 30

(R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)oxazolidin-2-one;

(R)-5-((1H-1,2,4-triazol-1-yl)methyl)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)oxazolidin-2-one;

5 (R)-5-((1H-1,2,4-triazol-1-yl)methyl)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)oxazolidin-2-one;

(S)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-5-((isoxazol-3-ylamino)methyl)oxazolidin-2-one;

10 (S)-3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-5-((isoxazol-3-ylamino)methyl)oxazolidin-2-one;

methyl (S)-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate;

methyl (S)-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate;

15 methyl (S)-((3-(3-fluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)carbamate;

(R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(3-fluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)oxazolidin-2-one;

20 methyl (S)-((3-(3,5-difluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)carbamate;

(R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(3,5-difluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)oxazolidin-2-one;

(R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(3,5-difluoro-4-(4-(oxetan-3-yl)piperidin-1-yl)phenyl)oxazolidin-2-one.

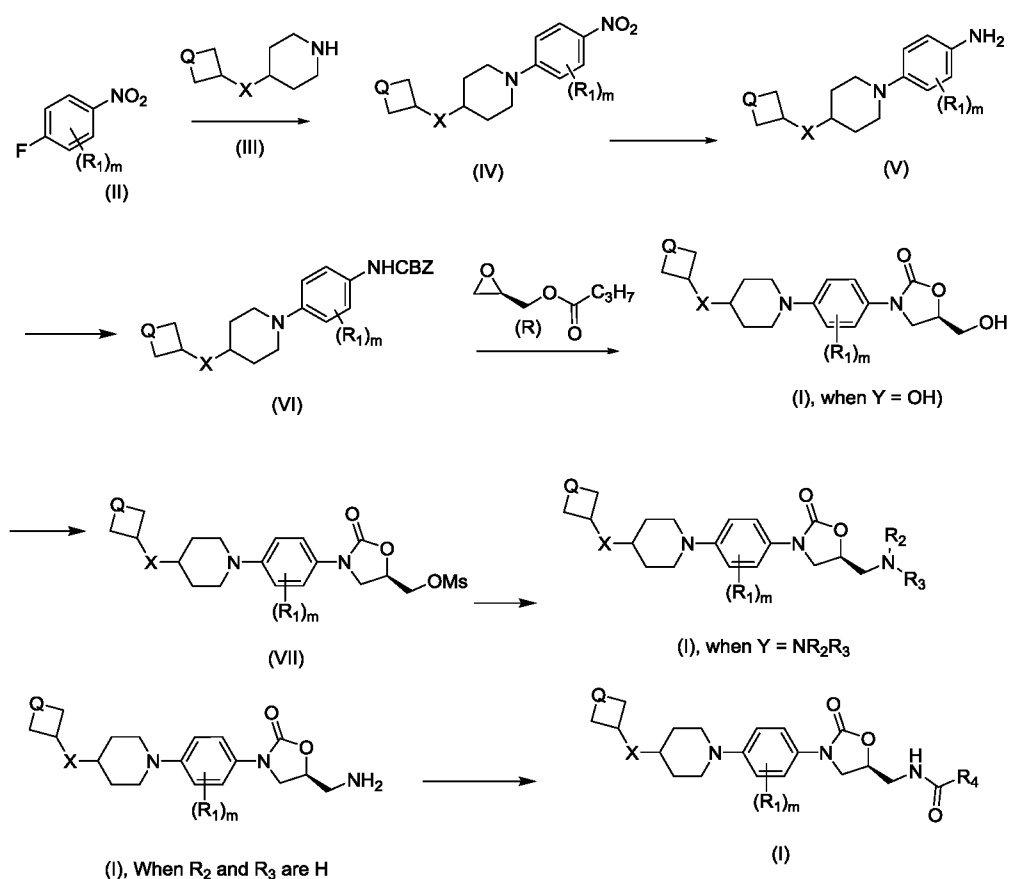
25

The novel compounds of this invention may be prepared using the reactions and techniques as shown in scheme below and described in this section. The reactions are performed in solvents appropriate to the reagents and materials employed and are suitable for the transformations being affected. It is understood by those skilled in the art that the nature and order of the synthetic steps presented may be varied for the purpose of optimizing the formation of the compounds of the present invention. It will also be well appreciated that one

30

or more of the reactants may be protected and de-protected for facile synthesis by techniques known to persons skilled in the art. It will also be appreciated that one or more of the compounds of the present invention may exist in stereoisomeric and/or diastereomeric forms. Such stereoisomers and/or diastereoisomers as well as their optical antipodes are to be construed to be within the scope of the present invention. It will also be well appreciated that one or more of these compounds may be converted to their salts and other derivatives based on the specific groups present on the compounds, which can be well comprehended by persons skilled in the art. Such salts and/or other derivatives, as the case may be should also be construed to be within the scope of the present invention.

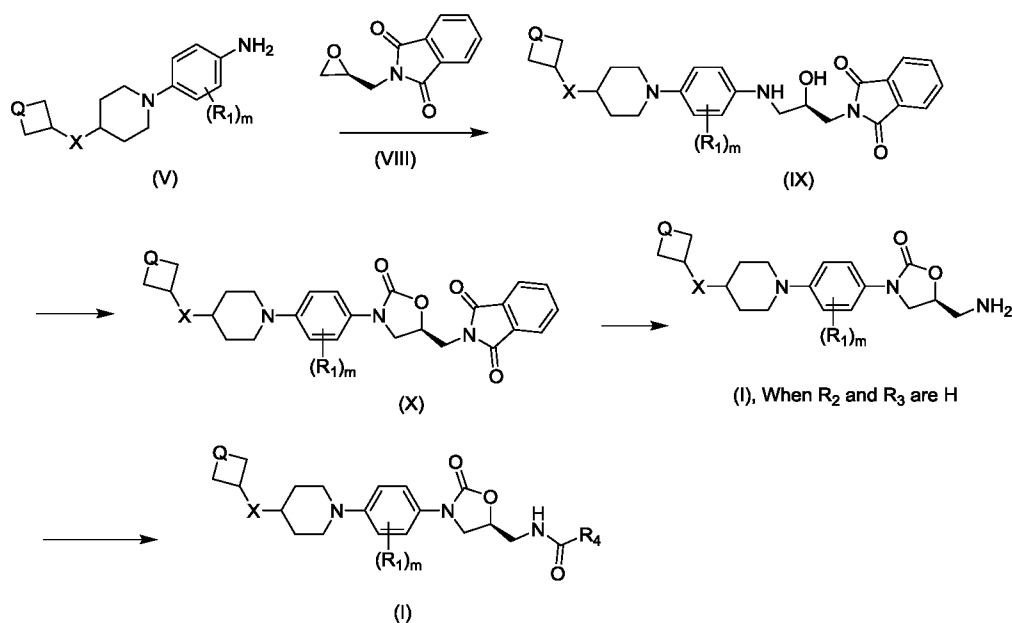
Scheme 1: Synthesis of compounds of general formula (I)



The compound (IV) can be obtained by reacting compounds of the formula (II) with (III) in the presence of base such as sodium carbonate, K₂CO₃, sodium hydride etc. in

solvents such as THF, DMF, MeOH etc. The compounds of general formula (V) can be obtained by reduction using stannous chloride dihydrate in ethyl acetate. The compounds of the general formula (VI) can be obtained by reacting (V) with benzyl oxy carbonyl chloride using sodium carbonate as a base in solvents such as water ethyl acetate, acetonitrile or mixture thereof. Compounds of the formula (I, when Y = OH) can be obtained by treating it with n-butyl lithium and R-glycidyl butyrate in THF. It was then converted into mesylate derivatives (VII) using methane sulfonyl chloride and TEA in solvents such as THF, ACN etc., which was then reacted with appropriately substituted amines to get desired compounds (I, when Y = NR₂R₃). Compounds (I, when Y = NH₂) are further reacted with appropriate acid chloride or anhydride in presence of base such as TEA or pyridine to get compounds of the formula (I) with amide or carbamate linkage.

Scheme 2: Synthesis of compounds of general formula (I)



Alternatively compound of the general formula (V) can be reacted with compounds of the formula (VIII) (prepared according to the procedure described in Tetrahedron: Asymmetry, 7(6), 1641-1648; 1996) in solvents such as MeOH, EtOH etc. to get compounds (IX). The compounds of general formula (X) can be obtained by cyclisation of (IX) with CDI in solvent such as DCM, CHCl₃ etc. The compounds (I) (when Y = NH₂) are obtained by

deprotection of phthalimide group using aq. Methyl amine in protic solvents such as MeOH, EtOH etc. Compounds (**I**, when **Y** = **NH₂**) are further reacted with appropriate acid chloride or anhydride in presence of base such as TEA or pyridine to get compounds of the formula (**I**) with amide or carbamate linkage.

5 **List of Abbreviations**

ACN: Acetonitrile

CDI: 1,1'-Carbonyldiimidazole

CHCl₃: Chloroform

DCM: Dichloromethane

10 DMAP: 4-dimethylaminopyridine

DMF: Dimethylformamide

DMSO: Dimethyl sulfoxide

EtOAc: Ethyl acetate

EtOH: Ethanol

15 K₂CO₃: Potassium Carbonate

LiAlH₄: Lithium Aluminium hydride

MeOH: Methanol

NaHCO₃: Sodium bicarbonate

Na₂SO₄: Sodium sulfate

20 NaOH: Sodium hydroxide

Pd-C: Palladium Charcoal

TEA: Triethylamine

TFA: Trifluoroacetic acid

THF: Tetrahydrofuran

25 ¹H NMR: Proton Nuclear Magnetic Resonance

h: Hour(s)

min: Minute(s)

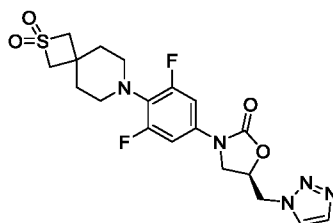
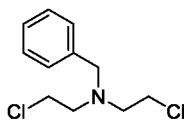
J: Coupling constant in units of Hz

Hz: Hertz

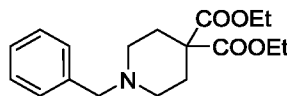
30 MABA: Microplate Alamar Blue Assay

Preparation of compounds**EXAMPLE 1**

Preparation of (R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)oxazolidin-2-one

**Step 1: N-benzyl-2-chloro-N-(2-chloroethyl)ethan-1-amine**

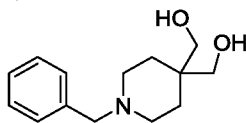
Bis(2-chloroethyl)amine (208 g, 1462 mmol) was added to DCM (200 ml) followed by 2M NaOH solution and stirred for 30 min. at 25-30°C. Separate DCM layer dry over Na₂SO₄ and evaporate to get oil (free amine). To this was added ACN (500 mL) followed by benzyl bromide (69.5 ml, 585 mmol) and K₂CO₃ (242 g, 1754 mmol) at 25-30°C and stirred for 16 h at 80°C. Reaction mixture was filtered and filtrate was evaporated to get crude oil which was purified by column chromatography using Hexane/EtOAc. ESI-MS (m/z): 232.05 [M+H]⁺.

Step 2: diethyl 1-benzylpiperidine-4,4-dicarboxylate

To a stirring solution of product of step 1 (17 g, 73.2 mmol) in DMF was added K₂CO₃ (30.4 g, 220 mmol), diethyl malonate (11.17 ml, 73.2 mmol) and tetrabutylammonium bromide (2.361 g, 7.32 mmol) at 25-30°C. Reaction mixture was stirred for 16 h at 90°C. After completion of reaction, it was diluted with EtOAc and washed with

water. EtOAc layer was dried over Na_2SO_4 and evaporated to get crude product which was purified by column chromatography using Hexane/EtOAc. ESI-MS (m/z): 320.22 $[\text{M}+\text{H}]^+$.

Step 3: (1-benzylpiperidine-4,4-diyl)dimethanol

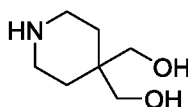


5

To a stirring solution of product of step 2 (26 g, 81 mmol) in THF was added LiAlH_4 (9.27 g, 244 mmol) at 0°C and stirred it for 16 h at $25-30^\circ\text{C}$. After completion of reaction, it was cooled to 0°C and diluted with 10 ml of water followed by 10 ml of 10% aq. NaOH solution and filtered over Hyflow bed. Residue was washed with 10% MeOH in EtOAc.

10 Filtrate was evaporated to get the title product. ESI-MS (m/z): 236.15 $[\text{M}+\text{H}]^+$.

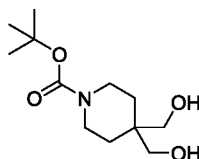
Step 4: piperidine-4,4-diyl dimethanol



To a stirring solution of product of step 3 (4.50 g, 19.12 mmol) in MeOH was added Pd-C (0.407 g, 3.82 mmol) followed by ammonium formate (3.62 g, 57.4 mmol). Reaction mixture was refluxed for 6 h. After completion of reaction, mixture was passed through hyflow bed and washed with 20% MeOH in EtOAc. Organic layer was distilled out to get the title product. ESI-MS (m/z): 146.10 $[\text{M}+\text{H}]^+$.

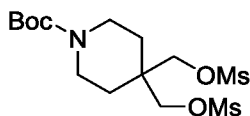
15

Step 5: tert-butyl 4,4-bis(hydroxymethyl)piperidine-1-carboxylate

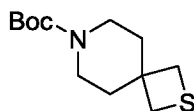


To a stirring solution of product of step 4 (9.4 g, 64.7 mmol) in DMF was added TEA (13.54 ml, 97 mmol) and Di-tert-butyl dicarbonate (15.03 ml, 64.7 mmol). Reaction mixture was stirred for 3 h at $25-30^\circ\text{C}$. After completion of reaction, reaction mixture was diluted with EtOAc (150 ml) and washed with water (30 ml). Organic layer was distilled out to get the title product.

25

Step 6: tert-butyl 4,4-bis(((methanesulfonyl)oxy)methyl)piperidine-1-carboxylate

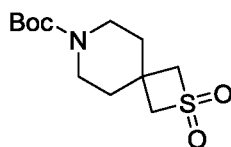
To a stirring solution of product of step 5 (10 g, 40.8 mmol) in DCM was added TEA (22.92 ml, 163 mmol) followed by methanesulfonyl chloride (9.46 ml, 122 mmol) at 0-5°C and reaction mixture was stirred for 2 h at 25-30°C. After completion of reaction it was diluted with DCM (50 ml) and water (25 ml). Organic layer was separated, dried over Na₂SO₄, and concentrated under reduced pressure to get the title product.

Step 7: tert-butyl 2-thia-7-azaspiro[3.5]nonane-7-carboxylate

10

To a stirring solution of product of step 6 (4.90 g, 12.20 mmol) in EtOH was added Sodium sulfide nonahydrate (3.52 g, 14.65 mmol) and reaction mixture was refluxed for 16 h. After completion of reaction it was diluted with EtOAc (100 mL). Organic layer was separated, dried over Na₂SO₄ and evaporated to get crude product which was purified by column chromatography using Hexane/EtOAc to get the title product.

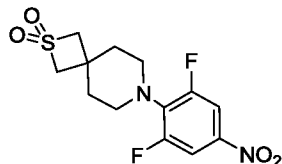
15

Step 8: tert-butyl 2-thia-7-azaspiro[3.5]nonane-7-carboxylate 2,2-dioxide

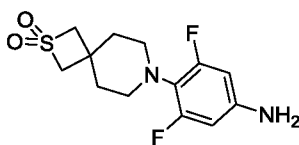
20

In a round-bottomed flask oxone (9.60 g, 15.61 mmol) in water (45 mL) was added at 0-5°C. To this was added product of step 7 (1.90 g, 7.81 mmol) dissolved in MeOH dropwise at 0-5°C. The reaction mixture was stirred at 15-20°C for 4 h. The reaction mixture was filtered and washed with MeOH (30 ml). MeOH was evaporated and residue was extracted with DCM. Organic layer was dried over Na₂SO₄ and evaporated under reduced pressure to get title product as solid.

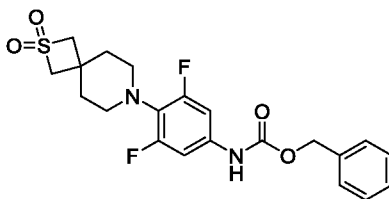
25

Step 9: 7-(2,6-difluoro-4-nitrophenyl)-2-thia-7-azaspiro[3.5]nonane 2,2-dioxide

To a stirring solution of product of step 8 (0.650 g, 2.361 mmol) in DCM was added
5 TFA (0.903 ml, 11.80 mmol) at 0-5°C and stirred for 3 h at 25-30°C. After completion of
reaction, DCM was evaporated under reduced pressure to get the crude product which was
diluted with DMF (10 mL). To this was added K₂CO₃ (0.946 g, 6.85 mmol) and 1,2,3-
trifluoro-5-nitrobenzene (0.404 g, 2.283 mmol) and stirred for 4 h at 80°C. Reaction mixture
was then diluted with water solid obtained was filtered to get the title product. ESI-MS
10 (m/z): 333.14 [M+H]⁺.

Step 10: 7-(4-amino-2,6-difluorophenyl)-2-thia-7-azaspiro[3.5]nonane 2,2-dioxide

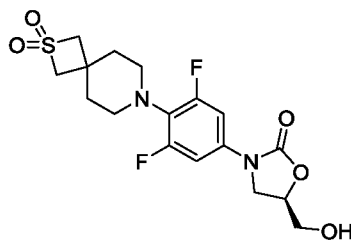
To a stirring solution of product of step 9 (0.690 g, 2.076 mmol) in EtOAc was added
15 Tin(II) chloride dihydrate (2.342 g, 10.38 mmol) and stirred for 1.5 h at 80°C. After
completion of reaction it was cooled to 25°C and basified by aq. ammonia solution. EtOAc
was decanted and residue was again extracted with EtOAc. Combined EtOAc layer was
20 dried over Na₂SO₄ and concentrated to get the titled product. ESI-MS (m/z): 303.15 [M+H]⁺.

Step 11: benzyl (4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)carbamate

To a stirring solution of product of step 10 (0.535 g, 1.770 mmol) in THF was added
25 NaHCO₃ (0.223 g, 2.65 mmol) and benzyl chloroformate (0.785 g, 2.300 mmol) at 0-5°C.
The reaction mixture was stirred at 25-30°C for 7 h. After completion of reaction it was

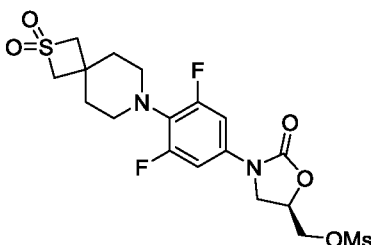
diluted with EtOAc and water. Organic layer was separated, dried and evaporated under reduced pressure to get the crude product which was purified by column chromatography using Hexane/EtOAc to get the pure product. ESI-MS (m/z) : 437.16 [M+H]⁺.

5 **Step 12 : (R)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-5-(hydroxymethyl)oxazolidin-2-one**



To a stirring solution of product of step 11 (830 mg, 1.902 mmol) in dry THF was
10 added n-butyl lithium (2.282 ml (2.5 M), 5.70 mmol) at -78°C. The resultant light yellow solution was stirred at -78 °C for 1 h and then (R)-glycidyl butyrate (685 mg, 4.75 mmol) was added at -70-75°C dropwise. The reaction mixture was stirred for an additional 1 h at -78°C. The reaction mixture was allowed to warm to room temperature and stirred for 16 h. The reaction mixture was diluted with water and EtOAc. Organic layer was separated, dried
15 over Na₂SO₄, and concentrated to get crude product as oil. The crude product was purified by column chromatography to get the title product. ESI-MS (m/z): 403.14 [M+H]⁺.

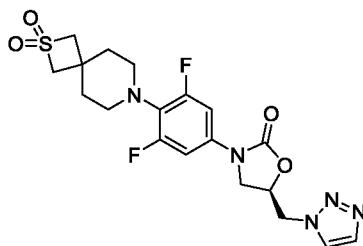
Step 13 : (R)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl methanesulfonate



20

To a stirring solution of product of step 12 (220 mg, 0.547 mmol) in DCM was added TEA (0.133 ml, 0.957 mmol) and methanesulfonyl chloride (0.047 ml, 0.601 mmol) at 0-5°C. Reaction mixture was stirred for 2 h at 25-30°C. After completion of reaction it was
25 diluted with DCM and washed with water. DCM layer was separated, dried over Na₂SO₄, and evaporated to get the title product. ESI-MS (m/z): 481.16 [M+H]⁺.

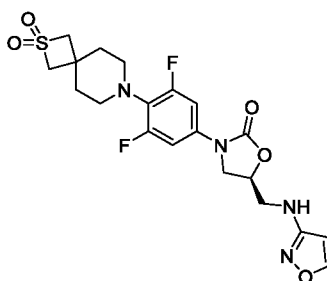
Step 14 : (R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)oxazolidin-2-one



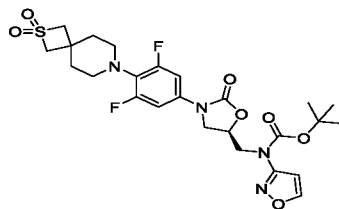
- 5 To a stirring solution of product of step 13 (100 mg, 0.208 mmol) in DMF was added 1H-1,2,3-triazole (0.024 ml, 0.416 mmol) and K₂CO₃ (57.5 mg, 0.416 mmol). Reaction mixture was heated to 80°C. After completion of reaction it was diluted with EtOAc and water. EtOAc layer was separated, washed with water, dried over Na₂SO₄, and concentrated to get crude product. The crude product was purified by column chromatography to get the
- 10 title product. ¹H NMR (DMSO-*d*₆): 8.16 (s, 1H), 7.77 (s, 1H), 7.22 (d, *J* = 8.4 Hz, 2H), 5.23 (m, 1H), 5.17-5.11 (m, 2H), 4.83-4.81 (m, 1H), 4.21-4.17 (m, 1H), 4.03 (s, 4H), 3.87-3.84 (m, 1H), 3.01 (s, 4H), 1.95 (s, 4H). ESI-MS (*m/z*): 454.12 [M+H]⁺.

EXAMPLE 2

- Preparation of (S)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-5-((isoxazol-3-ylamino)methyl)oxazolidin-2-one
- 15

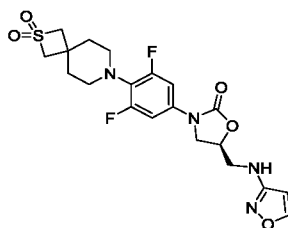


Step 1: (R)-tert-butyl ((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)(isoxazol-3-yl)carbamate



To a stirring solution of (R)-(3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl methanesulfonate (100 mg, 0.208 mmol) in DMF was added tert-butyl isoxazol-3-ylcarbamate (57.5 mg, 0.312 mmol) and K₂CO₃ (57.5 mg, 0.416 mmol). Reaction mixture was stirred at 80°C for 3 h. After completion of reaction it was diluted with EtOAc and water. EtOAc layer was separated, dried over Na₂SO₄ and concentrated to get crude product which was purified by column chromatography using EtOAc:Hexane to get the title product. ESI-MS (m/z): 569.16 [M+H]⁺.

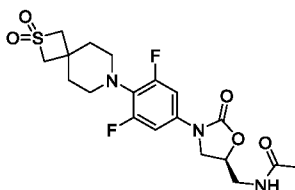
Step 2: (S)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-5-((isoxazol-3-ylamino)methyl)oxazolidin-2-one



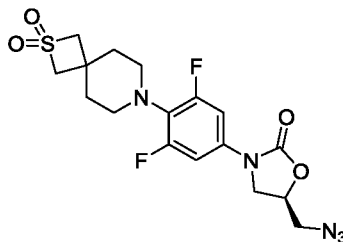
To a stirring solution of step 1 (70 mg, 0.123 mmol) in DCM (10 ml) was added TFA (0.047 ml, 0.616 mmol) at 0-5°C and stirred for 2 h. After completion of reaction it was diluted with EtOAc and washed with saturated solution of NaHCO₃. Organic layer was separated, dried over Na₂SO₄, and concentrated to get crude product. The crude product was purified by column chromatography using EtOAc:Hexane to get the title product. ¹H NMR (DMSO): 8.39 (d, *J* = 1.6 Hz, 1H), 7.25 (d, *J* = 11.6 Hz, 2H), 6.52 (t, 1H), 5.99 (d, *J* = 2.0 Hz, 1H), 5.89 (m, 1H), 4.11 (m, 1H), 4.02 (s, 4H), 3.79-3.77 (s, 1H), 3.44-3.41 (m, 2H), 3.03-3.00 (m, 4H), 1.90-1.88 (m, 4H). ESI-MS (m/z): 469.12 [M+H]⁺.

EXAMPLE 3

Preparation of (S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)acetamide

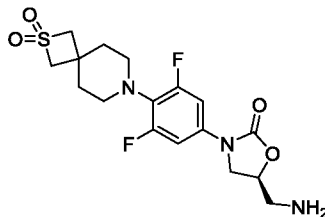


Step 1: (R)-5-(azidomethyl)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)oxazolidin-2-one



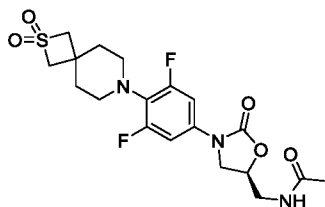
To a stirring solution of (R)-(3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl methanesulfonate (380 mg, 0.791 mmol) in DMF was added sodium azide (257 mg, 3.95 mmol) and stirred for 16 h at 60-65°C. After completion of reaction it was diluted with EtOAc and water. Organic layer was separated, dried over Na₂SO₄, and concentrated to get the title product. ESI-MS (m/z): 428.05 [M+H]⁺.

Step 2 : (S)-5-(aminomethyl)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)oxazolidin-2-one



To a stirring solution of product of step 1 (0.330 g, 0.772 mmol) in MeOH (5 ml) was added Pd-C (0.016 g, 0.154 mmol) at 0°C. To this was added sodium borohydride (0.088 g, 2.316 mmol) portion wise and stirred for 3 h at 25-30°C. After completion of reaction it was passed through hyflow bed and washed with EtOAc (50 ml). Organic layer was dried over Na₂SO₄ and concentrated to get the title product. ESI-MS (m/z): 402.09 [M+H]⁺.

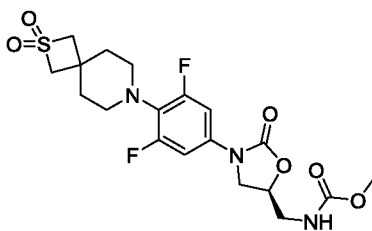
Step 3: (S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)acetamide



To a stirring solution of product of step 2 (150 mg, 0.374 mmol) in DCM was added pyridine (0.030 ml, 0.374 mmol) and acetic anhydride (0.035 ml, 0.374 mmol) and stirred for 3 h at 25-30°C. After completion of reaction it was diluted with water and product was extracted with DCM. Organic layer was dried over Na₂SO₄ and concentrated to get the crude product which was purified by column chromatography to get the title product. ¹H NMR (DMSO-*d*₆): 8.24 (t, *J* = 5.8 Hz, 1H), 7.23 (dd, *J* = 5.2 and 16.8 Hz, 2H), 4.74-4.70 (m, 1H), 4.10-4.05 (m, 1H), 4.03 (s, 4H), 3.70-3.68 (m, 1H), 3.41-3.38 (m, 2H), 3.01-3.00 (m, 4H), 1.91-1.87 (m, 4H), 1.83 (s, 4H). ESI-MS (*m/z*): 444.20 [M+H]⁺.

EXAMPLE 4

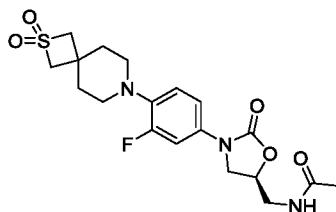
Preparation of (S)-methyl ((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate



To a stirring solution of (S)-5-(aminomethyl)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)oxazolidin-2-one (100 mg, 0.249 mmol) in DCM was added pyridine (0.030 ml, 0.374 mmol) followed by methyl chloroformate (0.023 ml, 0.299 mmol) and stirred for 3 h at 25-30°C. After completion of reaction it was diluted with water and product was extracted with DCM (20 ml). Organic layer was dried over Na₂SO₄ and concentrated to get the crude product which was purified by column chromatography to get the title product. ¹H NMR (DMSO-*d*₆): 7.53 (bs, 1H), 7.24 (d, *J* = 12 Hz, 2H), 4.73 (s, 1H), 4.10-4.06 (m, 2H), 4.02 (s, 4H), 3.741-3.61 (m, 2H), 3.40 (s, 3H), 3.19-3.13 (m, 4H), 1.89 (m, 4H). ESI-MS (*m/z*): 460.17 (M+H)⁺.

EXAMPLE 5

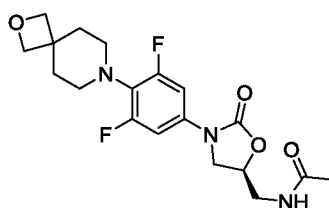
Preparation of (S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)acetamide



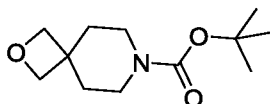
Prepared using similar process as described for example 3. ^1H NMR ($\text{DMSO}-d_6$): 8.24 (t, 1H), 7.49-7.45 (m, 1H), 7.18-7.16 (m, 1H), 7.07-7.03 (m, 1H), 4.72 (m, 1H), 4.10-4.05 (m, 1H), 4.02 (s, 4H), 2.94-2.91 (m, 4H), 1.95-1.92 (m, 4H), 1.24 (s, 3H). ESI-MS (m/z) : 426.14 $[\text{M}+\text{H}]^+$.

EXAMPLE 6

Preparation of (S)-N-((3-(3,5-difluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)acetamide

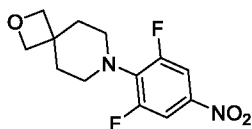


Step 1: tert-butyl 2-oxa-7-azaspiro[3.5]nonane-7-carboxylate



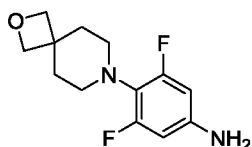
To a stirring solution of tert-butyl 4,4-bis(hydroxymethyl)piperidine-1-carboxylate (880 mg, 3.59 mmol) in THF was added n-butyllithium (1.435 ml, 3.59 mmol) dropwise at 0-5°C. The reaction mixture was stirred at 0-5°C for 30 min. To this was added a solution of p-toluene sulfonylchloride (684 mg, 3.59 mmol) in THF dropwise at 0-5°C. The reaction mixture was stirred at 0-5°C for 30 min. To this was added n-butyllithium (1.435 ml, 3.59 mmol) at 0-5°C. Reaction mixture was heated at 60°C for 2 h. RM was poured into water and product was extracted with EtOAc. Organic layer was distilled out to get crude product which was purified by column chromatography using Hexane/EtOAc to get the pure product.

Step 2: 7-(2,6-difluoro-4-nitrophenyl)-2-oxa-7-azaspiro[3.5]nonane



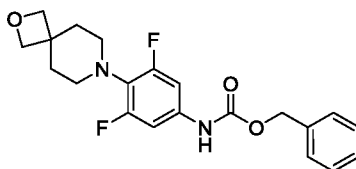
To a stirring solution of product of step 1 (840 mg, 3.70 mmol) in DCM was added TFA (1.4 ml, 18.48 mmol) at 0-5°C and stirred for 3 h at 25-30°C. After completion of reaction, DCM was evaporated under reduced pressure to get the crude product which was diluted with DMF. To this was added K₂CO₃ (1.17 g, 8.47 mmol) and 1,2,3-trifluoro-5-nitrobenzene (600 mg, 3.39mmol) and stirred for 4 h at 80°C. Reaction mixture was diluted with water to get solid product. ESI-MS (m/z): 285.08 [M+H]⁺.

Step 3: 3,5-difluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)aniline



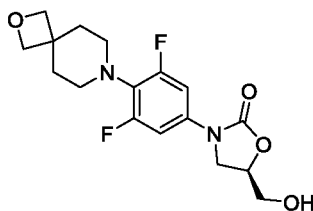
To a stirring solution of product of step 2 (720 mg, 2.53 mmol) in THF (10 ml) was added Pd-C (27 mg) and stirred under hydrogen pressure for 16 h at 25°C. After completion of reaction it was passed through hyflow bed and solvent was evaporated to get the title product. ESI-MS (m/z): 255.10 [M+H]⁺.

Step 4: benzyl (3,5-difluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)carbamate



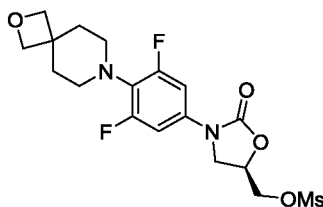
To a stirring solution of product of step 3 (700 mg, 2.75 mmol) in THF (10 ml) was added NaHCO₃ (925 mg, 11.01 mmol) and benzyl chloroformate (0.865 ml, 3.03 mmol) at 0°C. The reaction mixture was stirred at 25-30°C for 16 h. After completion of reaction it was diluted with EtOAc and water. Organic layer was evaporated under reduced pressure to get the crude product. The crude product was purified by column chromatography using Hexane/EtOAc to get the title product. ESI-MS (m/z): 389.16 [M+H]⁺.

Step 5: (R)-3-(3,5-difluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)-5-(hydroxymethyl)oxazolidin-2-one



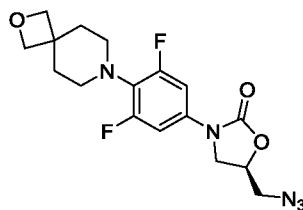
5 To a stirring solution of product of step 4 (540 mg, 1.390 mmol) in dry THF was added n-butyllithium (0.612 ml, 1.529 mmol) at -78°C. The resultant light yellow solution was stirred at -78 °C for 1 h and then (R)-glycidyl butyrate (220 mg, 1.529 mmol) was added at -70°C dropwise. The reaction mixture was stirred for an additional 1 h at -78 °C. The reaction mixture was allowed to warm to room temperature and stirred for 16 h. After
10 completion of reaction it was poured into aq. ammonium chloride solution and crude product was extracted with EtOAc which was purified by column chromatography to get the title product. ESI-MS (m/z): 355.14 [M+H]⁺.

Step 6: (R)-(3-(3,5-difluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)-2-oxooxazolidin-5-yl)methyl methanesulfonate



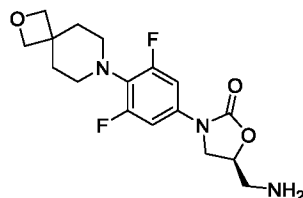
To a stirring solution of product of step 5 (316 mg, 0.892 mmol) in DCM was added TEA (0.162 ml, 1.159 mmol) and methanesulfonyl chloride (0.07 ml, 0.936 mmol) at 0°C. Reaction mixture was stirred for 2 h at 25-30°C. After completion of reaction it was diluted
20 with DCM (10 ml) and washed with water. DCM layer was dried over Na₂SO₄ and distilled out to get the title product. ESI-MS (m/z): 433.12 [M+H]⁺.

Step 7: (R)-5-(azidomethyl)-3-(3,5-difluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)oxazolidin-2-one



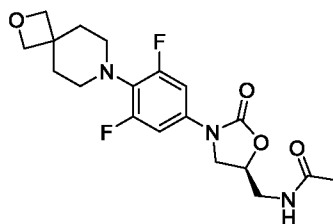
To a stirring solution of product of step 6 (397 mg, 0.918 mmol) in DMF was added sodium azide (298 mg, 4.59 mmol) and stirred for 3 h at 60-65°C. After completion of reaction it was diluted with water and filtered to get the title product. ESI-MS (m/z): 380.14 [M+H]⁺.

Step 8: (S)-5-(aminomethyl)-3-(3,5-difluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)oxazolidin-2-one



To a stirring solution of product of step 7 (242 mg, 0.638 mmol) in MeOH was added Pd-C at 0-5°C. To this was added sodium borohydride (72.4 mg, 1.914 mmol) portion wise and stirred for 3 h at 25-30°C. After completion of reaction it was passed through hyflow bed and washed with EtOAc (20 ml). Organic layer was dried over Na₂SO₄ and concentrated to get the title product. ESI-MS (m/z): 354.15 [M+H]⁺.

Step 9: (S)-N-((3-(3,5-difluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)acetamide



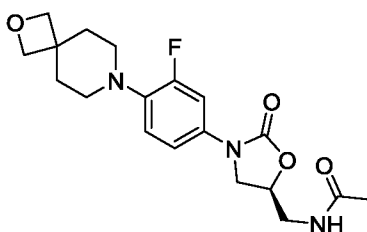
To a stirring solution of product of step 8 (100 mg, 0.283 mmol) in DCM was added pyridine (0.034 ml, 0.424 mmol) and acetic anhydride (0.037 ml, 0.396 mmol). Reaction mixture stirred for 1 h at 25-30°C. After completion of reaction it was diluted with DCM and

washed with water. Organic layer was dried over Na_2SO_4 and concentrated to get the title product. ^1H NMR ($\text{DMSO}-d_6$): 8.22 (t, $J = 5.8$ Hz, 1H), 7.23 (d, $J = 11.6$ Hz, 2H), 4.73-4.70 (m, 1H), 4.34 (s, 4H), 4.09-4.05 (m, 1H), 3.70-3.66 (m, 1H), 3.40-3.37 (m, 2H), 2.96-2.93 (m, 4H), 1.99-1.86 (m, 4H), 1.83 (s, 3H). ESI-MS (m/z): 396.16 ($\text{M}+\text{H}$) $^+$.

5

EXAMPLE 7

Preparation of (S)-N-((3-(3-fluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)acetamide

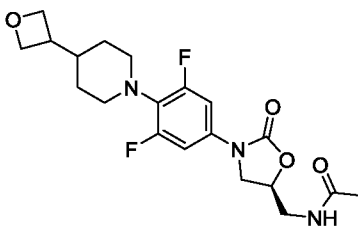


10 Prepared by following similar procedure as described for example 6 using appropriate modifications. ^1H NMR (CDCl_3): 7.41 (dd, $J = 2.4$ and 14.0 Hz, 1H), 7.08-7.06 (m, 1H), 6.95-6.90 (m, 1H), 5.99 (m, 1H), 4.78-4.77 (m, 1H), 4.50 (s, 4H), 4.05-4.01 (m, 1H), 3.77-3.75 (m, 2H), 3.73-3.70 (m, 1H), 2.96-2.93 (m, 4H), 2.07-2.04 (m, 7H). ESI-MS (m/z): 378.15 ($\text{M}+\text{H}$) $^+$

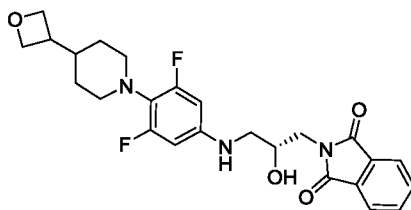
15

EXAMPLE 8

Preparation of (S)-N-((3-(3,5-difluoro-4-(4-(oxetan-3-yl)piperidin-1-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)acetamide

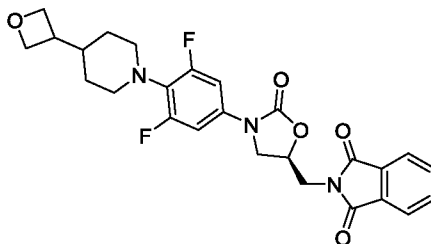


20 **Step 1: (R)-2-(3-((3,5-difluoro-4-(4-(oxetan-3-yl)piperidin-1-yl)phenyl)amino)-2-hydroxypropyl)isoindoline-1,3-dione**



A stirring solution of (S)-2-(oxiran-2-ylmethyl)isoindoline-1,3-dione (1.988 g, 9.78 mmol) and 3,5-difluoro-4-(4-(oxetan-3-yl)piperidin-1-yl)aniline (1.50 g, 5.59 mmol) in aq. EtOH was heated at 100°C for 4 h. Another (S)-2-(oxiran-2-ylmethyl)isoindoline-1,3-dione (1.988 g, 9.78 mmol) was added at 80°C and stirring continued for 16 h. Reaction mixture was filtered to get the title product. ESI-MS (m/z): 472.16 [M+H]⁺.

Step 2: (S)-2-((3-(3,5-difluoro-4-(4-(oxetan-3-yl)piperidin-1-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)isoindoline-1,3-dione

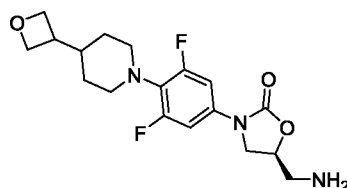


10

To a stirring solution of product of step 1 (2.0 g, 4.24 mmol) in CHCl₃ was added CDI (2.75 g, 16.97 mmol) at 25-30°C. The reaction mixture was stirred at 70°C for 5 h. Solvent was distilled out and reaction mixture was acidified by 35 % hydrochloric acid to get pH = 2. Product was extracted with DCM. Organic layer was separated, dried over Na₂SO₄ and distilled out to get the title product. ESI-MS (m/z): 498.14 [M+H]⁺.

15

Step 3 : (S)-5-(aminomethyl)-3-(3,5-difluoro-4-(4-(oxetan-3-yl)piperidin-1-yl)phenyl)oxazolidin-2-one

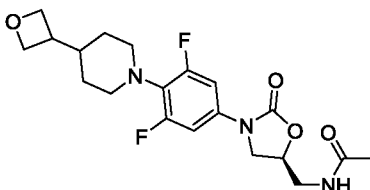


20

To a stirring solution of product of step 2 (1.90 g, 3.82 mmol) in EtOH was added aq. Methyl amine (2.97 g, 38.2 mmol) at 25-30°C. Reaction mixture was stirred at 80°C for 3 h.

After complete conversion of starting material, reaction mixture was diluted with DCM (100 ml) and washed with cold water. Organic layer was dried over Na₂SO₄ and distilled out to get the title product as solid. ESI-MS (m/z): 368.15 [M+H]⁺.

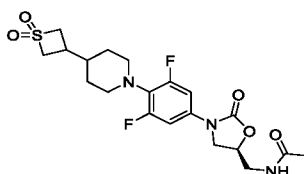
5 **Step 4 : (S)-N-((3-(3,5-difluoro-4-(4-(oxetan-3-yl)piperidin-1-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)acetamide**



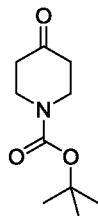
To a stirring solution of product of step 3 (1.00 g, 2.72 mmol) in DCM was added
 10 pyridine (0.330 ml, 4.08 mmol) and acetic anhydride (0.360 ml, 3.81 mmol) and stirred for 2
 h at 25-30°C. After complete conversion of starting material reaction mixture was diluted
 with water and extracted with DCM. Organic layer was separated, dried over Na₂SO₄ and
 distilled out to get crude product which was purified by preparative HPLC to get title product
 as white solid. ¹H NMR (DMSO): 8.23 (t, 1H), 7.28-7.21 (m, 2H), 4.75-4.69 (m, 1H), 4.63-
 15 4.60 (m, 2H), 4.38-4.35 (m, 2H), 4.10-4.05 (m, 1H), 3.70-3.66 (m, 1H), 3.43-3.38 (m, 1H),
 3.11-2.97 (m, 4H), 2.78-2.72 (m, 1H), 1.83 (s, 3H), 1.76-1.71 (m, 1H), 1.68-1.60 (m, 2H),
 1.19-1.06 (m, 2H). ESI-MS (m/z): 410.16 [M+H]⁺.

EXAMPLE 9

20 **Preparation of (S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)acetamide**



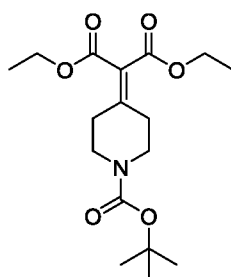
Step 1: tert-butyl 4-oxopiperidine-1-carboxylate



To a stirring suspension of piperidin-4-one hydrochloride (30 g, 221 mmol) in dry DCM was added TEA (83 ml, 597 mmol) followed by Di-tert-butyl dicarbonate (64.2 ml, 277 mmol) drop wise over a period of 15 min. at 10-15°C. The resulting mixture was stirred at 25-30°C for 16 h. The reaction mixture was diluted with DCM and washed with water.

5 The organic layer was dried over Na₂SO₄ and evaporated under reduced pressure to get the title product.

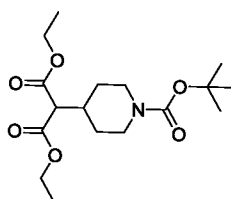
Step 2: diethyl 2-(1-(tert-butoxycarbonyl)piperidin-4-ylidene)malonate



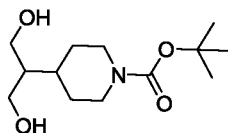
10 A stirring solution of TiCl₄ (52.0 ml, 472 mmol) in carbon tetrachloride (40 ml) was added to THF (150 mL) at 0°C. To this was added a solution of product of step 1 (37.3 g, 187 mmol) and diethyl malonate (25.7 ml, 168 mmol) in THF (150 mL) at 0°C and stirred for 15 min. To this was added pyridine (98 ml, 1217 mmol) and stirred for 16 h at 25-30°C. Reaction mixture poured into 10% citric acid solution and product was extracted with

15 EtOAc. Organic layer was separated, dried over Na₂SO₄ and evaporated under reduced pressure to get the title product.

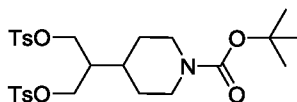
Step 3: diethyl 2-(1-(tert-butoxycarbonyl)piperidin-4-yl)malonate



20 To a stirring solution of product of step 2 (63 g, 185 mmol) in EtOH was added sodium borohydride (6.98 g, 185 mmol) and stirred for 2 h at 25-30°C. After complete conversion of starting material, reaction mixture was poured into ice water and extracted with DCM. Organic layer was separated, dried over Na₂SO₄ and evaporated under reduced pressure to get the title product.

Step 4: tert-butyl 4-(1,3-dihydroxypropan-2-yl)piperidine-1-carboxylate

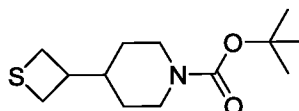
To a stirring solution of product of step 3 (63 g, 183 mmol) in EtOH (315 ml) was added sodium borohydride (69.4 g, 1834 mmol) at 25-30°C and the resulting mixture was stirred at 70°C for 3 h. After complete conversion of starting material, reaction mixture was diluted with cold water and extracted with EtOAc. Organic layer was separated, dried over Na₂SO₄ and evaporated under reduced pressure to get the title product.

Step 5: tert-butyl 4-(1,3-bis(tosyloxy)propan-2-yl)piperidine-1-carboxylate

10

To a stirring solution of product of step 4 (10 g, 38.6 mmol) in DCM was added TEA (21.50 ml, 154 mmol) and DMAP (9.42 g, 77 mmol). To this was added portion wise p-toluene sulfonylchloride (22.05 g, 116 mmol) at 0-5°C. The reaction mixture was stirred at 25-30°C for 3 h. After completion of reaction, reaction mixture was diluted with DCM and washed with water and brine, dried over Na₂SO₄ and evaporated under reduced pressure to get the title product.

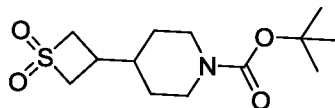
15

Step 6: tert-butyl 4-(thietan-3-yl)piperidine-1-carboxylate

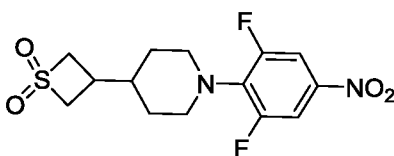
20

To a stirring solution of product of step 5 (12.1 g, 21.31 mmol) in DMF was added sodium sulfide nonahydrate (6.14 g, 25.6 mmol) and reaction mixture was heated at 80-85°C for 16 h. After completion of reaction, it was diluted with EtOAc and water. Organic layer was separated, dried over Na₂SO₄ and concentrated to get oily product. The crude product was purified by column chromatography using Hexane/EtOAc to get the title product.

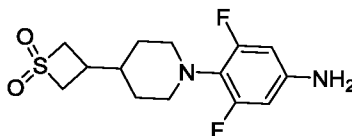
25

Step 7: tert-butyl 4-(1,1-dioxidothietan-3-yl)piperidine-1-carboxylate

To a stirring solution of product of step 6 (5.5 g, 21.371 mmol) in DCM was added meta-chloroperbenzoic acid (18.44 g, 107 mmol) and stirred for 4 h at 25-30°C. After completion of reaction, it was diluted with DCM and washed with aq. NaHCO₃. DCM layer was separated, dried over Na₂SO₄ and concentrated to get the title product. ¹H NMR (CDCl₃): 4.19-3.99 (m, 4H), 3.88-3.85 (m, 2H), 2.70-2.60 (m, 2H), 2.45-2.41 (m, 1H), 2.35-2.22 (m, 1H), 1.87-1.86 (m, 2H), 1.55 (s, 9H), 1.21-1.1 (m, 2H).

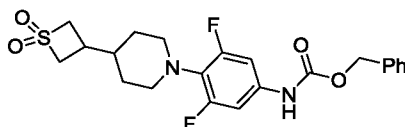
Step 8: 3-(1-(2,6-difluoro-4-nitrophenyl)piperidin-4-yl)thietane 1,1-dioxide

To a stirring solution of product of step 7 (5.5 g, 19.01 mmol) in DCM was added TFA (2.93 ml, 38.0 mmol) at 0°C and stirred for 3 h 25-30°C. After completion of reaction, DCM was evaporated to get crude product which was diluted with DMF. To this was added K₂CO₃ (5.39 g, 39.0 mmol) and 1,2,3-trifluoro-5-nitrobenzene (2.3 g, 12.99 mmol) and stirred for 4 h at 80°C. Reaction mixture was diluted with water to get product as solid. ESI-MS (m/z): 347.07 [M+H]⁺.

Step 9: 3-(1-(4-amino-2,6-difluorophenyl)piperidin-4-yl)thietane 1,1-dioxide

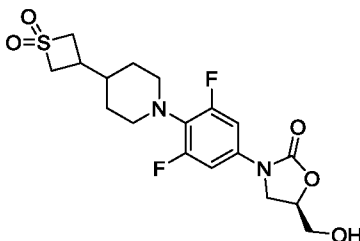
To a stirring solution of product of step 8 (2.3 g, 6.64 mmol) in THF was added Pd-C (71 mg) and stirred under hydrogen pressure for 3 h at 25-30°C. After completion of reaction, it was passed through hyflow bed and solvent was evaporated to get the title product. ESI-MS (m/z): 317.10 [M+H]⁺.

Step 10: benzyl (4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)carbamate



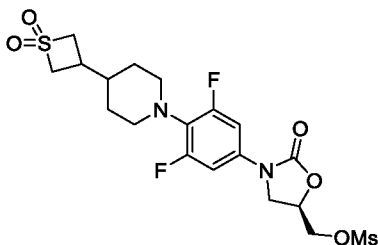
To a stirring solution of product of step 9 (2.14 g, 6.76 mmol) in THF was added
 5 NaHCO_3 (2.27 g, 27.1 mmol) and benzyl chloroformate (2.124 ml, 7.44 mmol) at 0-5°C. The reaction mixture was stirred at 25-30°C for 7 h. After completion of reaction it was diluted with EtOAc and water. Organic layer was separated and evaporated under reduced pressure to get the crude product. The crude product was purified by column chromatography using Hexane/EtOAc to get the title product. ESI-MS (m/z): 451.10 $[\text{M}+\text{H}]^+$.

Step 11: (R)-3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-5-(hydroxymethyl)oxazolidin-2-one



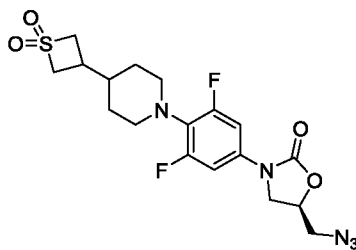
To a stirring solution of product of step 10 (2.47 g, 5.48 mmol) in dry THF was
 15 added n-butyllithium (2.41 ml, 6.03 mmol) at -78°C. The resultant light yellow solution was stirred at -78 °C for 1 h and then (R)-glycidyl butyrate (0.869 g, 6.03 mmol) was added at -70°C dropwise. The reaction mixture was stirred for an additional 1 h at -78 °C. The reaction mixture was allowed to warm to room temperature and stirred for 16 h. After completion of reaction it was poured into aq. ammonium chloride solution and crude product was extracted
 20 with EtOAc which was purified by column chromatography to get the title product. ESI-MS (m/z): 439.10 $[\text{M}+\text{Na}]^+$.

Step 12: (R)-(3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl methanesulfonate



To a stirring solution of product of step 11 (590 mg, 1.417 mmol) in DCM was added TEA (0.257 ml, 1.842 mmol) and methanesulfonyl chloride (0.116 ml, 1.488 mmol) at 0-5°C. Reaction mixture was stirred for 2 h at 25-30°C. After completion of reaction it was
5 diluted with DCM and washed with water. DCM layer was dried over Na₂SO₄ and distilled out to get the title product. ESI-MS (m/z): 495.10 [M+H]⁺.

Step 13: (R)-5-(azidomethyl)-3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)oxazolidin-2-one

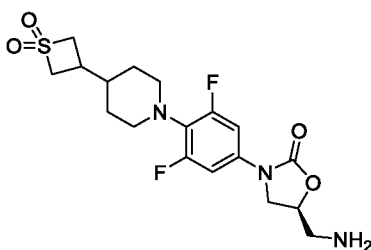


10

To a stirring solution of product of step 12 (650 mg, 1.314 mmol) in DMF was added sodium azide (427 mg, 6.57 mmol) and stirred for 3 h at 60-65°C. After completion of reaction it was diluted with water and filtered to get the title product. ESI-MS (m/z): 442.17 [M+H]⁺.

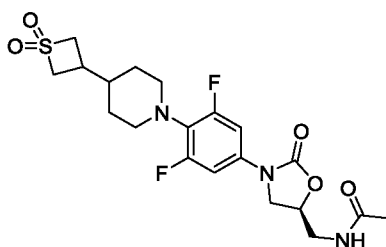
15

Step 14: (S)-5-(aminomethyl)-3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)oxazolidin-2-one



To a stirring solution of product of step 13 (500 mg, 1.133 mmol) in MeOH was added Pd-C (12 mg) at 0-5°C. To this was added sodium borohydride (129 mg, 3.40 mmol) portion wise and stirred for 3 h at 25-30°C. After completion of reaction it was passed through hyflow bed and washed with EtOAc (50ml). Organic layer was dried over Na₂SO₄ and concentrated to get the title product. ESI-MS (m/z): 416.15 [M+H]⁺.

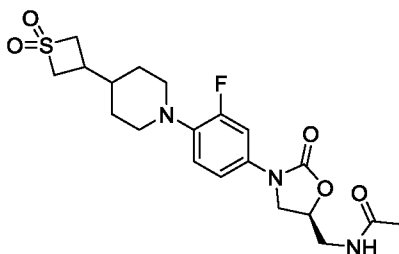
Step 15: (S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)acetamide



To a stirring solution of product of step 14 (200 mg, 0.481 mmol) in DCM (5 ml) was added pyridine (0.058 ml, 0.722 mmol), and acetic anhydride (0.064 ml, 0.674 mmol). Reaction mixture was stirred for 1 h at 25-30°C. After completion of reaction, it was diluted with DCM and washed with water. Organic layer was dried over Na₂SO₄ and concentrated to get the title product. ¹H NMR (DMSO-*d*₆): 8.23 (t, *J* = 5.8 Hz, 1H), 7.28-7.23 (m, 2H), 4.74-4.70 (m, 1H), 4.19-4.15 (m, 2H), 4.13-1.05 (m, 1H), 4.01-3.96 (m, 2H), 3.70-3.66 (m, 1H), 3.41-3.39 (m, 2H), 3.12-3.10 (m, 2H), 2.99-2.94 (m, 2H), 2.30-2.27 (m, 1H), 1.83 (s, 3H), 1.71-1.68 (m, 2H), 1.57-1.54 (m, 1H), 1.27-1.21 (m, 2H). ESI-MS (m/z): 458.18 (M+H)⁺

EXAMPLE 10

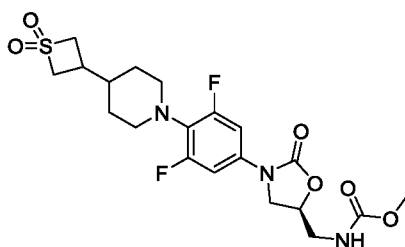
Preparation of (S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)acetamide



Prepared by following similar procedure as described for example 9 using appropriate modifications. ¹H NMR (DMSO-*d*₆): 8.24 (t, 1H), 7.44 (dd, *J* = 2.4 and 14.8 Hz, 1H), 7.16-7.14 (m, 1H), 7.09-7.06 (m, 1H), 4.72 (m, 1H), 4.20-4.10 (m, 2H), 4.07-4.02 (m, 1H), 4.01-3.97 (m, 2H), 3.71-3.67 (m, 1H), 3.40 (t, 2H), 3.29 (bs, 2H), 2.62-2.59 (m, 2H), 2.35-2.28 (m, 1H), 1.83 (s, 3H), 1.70-1.82 (m, 2H), 1.51-1.62 (m, 1H), 1.23-1.34 (m, 2H). ESI-MS (*m/z*): 440.12 (M+H)⁺.

EXAMPLE 11

Preparation of methyl (S)-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate



To a stirring solution of (S)-5-(aminomethyl)-3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)oxazolidin-2-one (100 mg, 0.241 mmol) in DCM was added pyridine (0.029 ml, 0.361 mmol) and methyl chloroformate (0.026 ml, 0.337 mmol). Reaction mixture was stirred for 1 h at 25-30°C. After completion of reaction, it was diluted with DCM. Organic layer was separated, dried over Na₂SO₄ and concentrated to get the title product. ¹H NMR (CDCl₃): 7.53 (t, 1H), 7.50 (d, *J* = 5.6 Hz, 2H), 4.73-4.70 (m, 1H), 4.19-4.15 (m, 2H), 4.13-4.10 (m, 1H), 4.08-3.96 (m, 2H), 3.74-3.70 (m, 1H), 3.54 (s, 3H), 3.12-3.00 (m, 2H), 2.97-2.94 (m, 2H), 2.30-2.26 (m, 1H), 1.71-1.68 (m, 2H), 1.57-1.55 (m, 1H), 1.24-1.21 (m, 4H). ESI-MS (*m/z*): 474.151 (M+H)⁺.

Using appropriate starting materials and suitable modifications of the process described in above examples, including suitable addition and/or deletion of steps as may be necessary, well within the scope of a person skilled in the art the following compounds were prepared in an analogues manner.

Table 1:

EX. No.	IUPAC Name	ESI-MS (m/z) (M+H) ⁺
12	(S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)thiophene-2-carboxamide	512.17
13	(S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)thiophene-2-carboxamide	494.15
14	(S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)furan-2-carboxamide	496.12
15	(S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)furan-2-carboxamide	478.15
16	(S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)thiophene-2-carboxamide	526.13
17	(S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)thiophene-2-carboxamide	508.16
18	(S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)furan-2-carboxamide	510.17
19	(S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)furan-2-carboxamide	492.11
20	(S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)butyramide	472.14
21	(S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)butyramide	544.2
22	(S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)butyramide	486.14
23	(S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)butyramide	468.16
24	ethyl (S)-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate	474.15

25	ethyl (S)-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate	456.13
26	ethyl (S)-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate	488.14
27	ethyl (S)-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate	470.16
28	(S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)cyclopropanecarboxamide	470.12
29	(S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)cyclopropanecarboxamide	452.14
30	(S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)cyclopropanecarboxamide	484.18
31	(S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)cyclopropanecarboxamide	466.15
32	(S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)cyclobutanecarboxamide	484.18
33	(S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)cyclobutanecarboxamide	466.15
34	(S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)cyclobutanecarboxamide	498.16
35	(S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)cyclobutanecarboxamide	480.2
36	(R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)oxazolidin-2-one	436.12
37	(R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)oxazolidin-2-one	468.13
38	(R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)oxazolidin-2-one	450.14
39	(R)-5-((1H-1,2,4-triazol-1-yl)methyl)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)oxazolidin-2-one	454.12

40	(R)-5-((1H-1,2,4-triazol-1-yl)methyl)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)oxazolidin-2-one	436.12
41	(S)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-5-((isoxazol-3-ylamino)methyl)oxazolidin-2-one	451.12
42	(S)-3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-5-((isoxazol-3-ylamino)methyl)oxazolidin-2-one	483.16
43	methyl (S)-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate	456.18
44	methyl (S)-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate	442.15
45	methyl (S)-((3-(3-fluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)carbamate	394.11
46	(R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(3-fluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)oxazolidin-2-one	388.18
47	methyl (S)-((3-(3,5-difluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)carbamate	412.14
48	(R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(3,5-difluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)oxazolidin-2-one	406.15
49	(R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(3,5-difluoro-4-(4-(oxetan-3-yl)piperidin-1-yl)phenyl)oxazolidin-2-one	420.17

Biological evaluation:

Minimum inhibitory concentration (MIC) determination

To assess the bacterial growth inhibitory effect of the compounds of the invention, MABA assay was performed with log phase culture of *Mycobacterium tuberculosis* H37Rv. Bacterial culture of optical density 0.6-0.8 was diluted to final density of 0.02 in 7H9 medium. 100µl of diluted *Mycobacterium tuberculosis* H37Rv was incubated with the test compounds in microtiter plate. A drug free control containing DMSO also was also prepared. Following incubation of the compound with culture for 7 days at 37°C, 20µl of 0.02% alamar blue (freshly prepared) was added in each well. The color was allowed to develop for 16 h at 37°C. Blue color in the well indicated no growth whereas pink color signifies growth

in the well. MIC value is defined as the lowest concentration that prevents the color change from blue to pink. Fluorescence was measured at excitation at 530 nm and emission at 590 nm. MIC values of the selected compounds are shown in **Table 2**.

5 **Table 2:**

Example	Mtb MIC (μ M)
1	1.25
2	1.25
3	1.25
4	1.25
5	1.25
6	1.25-2.5
7	2.5
8	2.5
9	1.25
10	2.5

The novel compounds of the present invention can be formulated into suitable pharmaceutically acceptable compositions by combining with suitable excipients by techniques and processes and concentrations as are well known. Pharmaceutical composition comprising the compounds of the present invention may comprise a suitable binder, suitable bulking agent &/or diluent and any other suitable agents as may be necessary.

Novel compounds of the present invention can be used for the treatment of mammalian infections such as tuberculosis by administering therapeutically active and non-toxic amount of compounds of formula (I) or pharmaceutically acceptable compositions thereof.

A method of treating anti-tuberculosis infection in a subject that comprising administering to a patient in need thereof an effective amount of a compound of formula (I) or its suitable pharmaceutical composition.

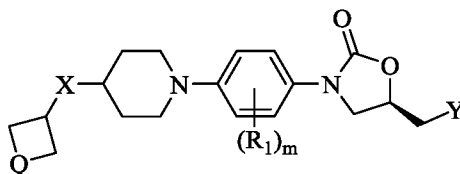
The pharmaceutical compositions according to this invention can exist in various forms. In some embodiments, the pharmaceutical composition is in the topical, oral or parenteral administration.

One or more additional pharmaceutical agents or treatment methods can be used in combination with the compounds of the present invention for treatment or prevention of mammalian infection. The therapeutic agents can be combined with the present compounds in a single dosage form, or the agents can be administered simultaneously or sequentially in separate dosage forms. The compound of formula (I) can be administered in combination with other therapeutic agents such as isoniazide, rifampin, rifapentine, rifabutin, ethambutol, pyrazinamide, streptomycin, amikacin, levofloxacin, ofloxacin, p-aminosalicylic acid.

While the present invention has been described in terms of its specific embodiments, certain modifications and equivalents will be apparent to those skilled in the art and are intended to be included within the scope of the present invention.

We claim:

1. Compounds of the general formula (I),



Formula (I)

Wherein,

X is either absent or a bond; whenever X is absent, four membered ring is directly attached to the 6-membered piperidine ring forming spirocyclic system;

Q is either O or S(O)_p; p = 0-2 integer;

Y is selected from OH, NR₂R₃, NHC(O)R₄;

R₁ is selected from H, F, Cl, CH₃, CN and OCH₃; m = 1-4 integer;

R₂ and R₃ is independently selected from H, (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, aryl, heterocyclyl and heteroaryl each of which may be further optionally substituted; R₂ and R₃ taken together with the nitrogen to which they are attached may form a 4- to 8-membered heterocyclyl or heteroaryl with 1 to 3 additional heteroatoms selected from O, S, or N and may be further be optionally substituted;

R₄ is independently selected from (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, aryl, heteroaryl and (C₁-C₆)alkoxy each of which may be further optionally substituted; substitutions are selected from halo, hydroxyl, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, (C₁-C₆)acyloxy, haloalkyl, NO₂, CN and NH₂.

2. Compounds of formula (I) as claimed in claim 1 wherein (C₁-C₆)alkyl group of R₂, R₃ and R₄ is selected from selected from methyl, ethyl, n-propyl, iso-propyl; (C₁-C₆)alkoxy group of R₂, R₃ and R₄ is selected from methoxy and ethoxy; (C₃-C₆)cycloalkyl group of R₂, R₃ and R₄ is selected from cyclopropyl and cyclobutyl.
3. Compounds of formula (I) as claimed in claim 1 wherein heteroaryl group of R₄ is selected from thienyl, furyl, isoxazolyl, triazolyl.

4. Compound of formula (I) as claimed in claim 1 is selected from

(R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)oxazolidin-2-one;

(S)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-5-

((isoxazol-3-ylamino)methyl)oxazolidin-2-one;

(S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)acetamide;

(S)-methyl ((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate;

(S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)acetamide;

(S)-N-((3-(3,5-difluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)acetamide;

(S)-N-((3-(3-fluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)acetamide;

(S)-N-((3-(3,5-difluoro-4-(4-(oxetan-3-yl)piperidin-1-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)acetamide;

(S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)acetamide;

(S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)acetamide;

methyl (S)-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate;

(S)-5-(aminomethyl)-3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)oxazolidin-2-one;

(R)-3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-5-(hydroxymethyl)oxazolidin-2-one;

(S)-5-(aminomethyl)-3-(3,5-difluoro-4-(4-(oxetan-3-yl)piperidin-1-yl)phenyl)oxazolidin-2-one;

(S)-5-(aminomethyl)-3-(3,5-difluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)oxazolidin-2-one;

(S)-5-(aminomethyl)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)oxazolidin-2-one;

(R)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-5-(hydroxymethyl)oxazolidin-2-one;

(S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)thiophene-2-carboxamide;

5 (S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)thiophene-2-carboxamide;

(S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)furan-2-carboxamide;

10 (S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)furan-2-carboxamide;

(S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)thiophene-2-carboxamide;

(S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)thiophene-2-carboxamide;

15 (S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)furan-2-carboxamide;

(S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)furan-2-carboxamide;

20 (S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)butyramide;

(S)-N-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)butyramide;

(S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)butyramide;

25 (S)-N-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)butyramide;

ethyl (S)-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate;

30 ethyl (S)-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate;

ethyl (S)-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate;

ethyl (S)-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate;

(xazolidin-5-yl)methyl)cyclobutanecarboxamide;

(R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)oxazolidin-2-one;

(R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)oxazolidin-2-one;

(R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)oxazolidin-2-one;

(R)-5-((1H-1,2,4-triazol-1-yl)methyl)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3,5-difluorophenyl)oxazolidin-2-one;

(R)-5-((1H-1,2,4-triazol-1-yl)methyl)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)oxazolidin-2-one;

(S)-3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-5-((isoxazol-3-ylamino)methyl)oxazolidin-2-one;

(S)-3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3,5-difluorophenyl)-5-((isoxazol-3-ylamino)methyl)oxazolidin-2-one;

methyl (S)-((3-(4-(4-(1,1-dioxidothietan-3-yl)piperidin-1-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate;

methyl (S)-((3-(4-(2,2-dioxido-2-thia-7-azaspiro[3.5]nonan-7-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)carbamate;

methyl (S)-((3-(3-fluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)carbamate;

(R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(3-fluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)oxazolidin-2-one;

methyl (S)-((3-(3,5-difluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)carbamate;

(R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(3,5-difluoro-4-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)oxazolidin-2-one;

(R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(3,5-difluoro-4-(4-(oxetan-3-yl)piperidin-1-yl)phenyl)oxazolidin-2-one.

5. A pharmaceutical composition comprising a therapeutically effective amount of a compound of formula (I) as claimed in claim 1 and optionally one or more pharmaceutically acceptable carriers, diluents or excipients.

6. Use of a compound of formula (I) as claimed in claim 1 in the preparation of a medicament for the prevention or treatment of anti-tuberculosis infection.
- 5 7. A method of treating anti-tuberculosis infection comprising administering to a patient in need thereof an effective amount of a compound of formula (I) as claimed in claim 1 or its suitable pharmaceutical composition.
- 10 8. Compound of formula (I) or its pharmaceutical composition as claimed in claim 1 in combination with one or more suitable pharmaceutically active agents selected from group of isoniazide, rifampin, rifapentine, rifabutin, ethambutol, pyrazinamide, streptomycin, amikacin, levofloxacin, ofloxacin, p-aminosalicylic acid .

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2019/056322

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07D405/14 C07D413/14 C07D491/107 C07D495/10 A61P31/04
A61K31/422

ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07D A61P A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2007/023507 A2 (SINDKHEDKAR MILIND D [IN]; BHAVSAR SATISH B [IN] ET AL.) 1 March 2007 (2007-03-01) examples page 1 page 72 example 1 claims	1-8
X	WO 95/25106 A1 (UPJOHN CO [US]; YAMADA HIROYOSHI [JP] ET AL.) 21 September 1995 (1995-09-21) page 1 examples compounds 30,39,48 claims ----- -/-	1-8



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

21 October 2019

Date of mailing of the international search report

29/10/2019

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Stix-Malaun, Elke

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2019/056322

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2017/015106 A1 (THE GLOBAL ALLIANCE FOR TB DRUG DEV INC [US]) 26 January 2017 (2017-01-26) abstract page 1 examples claims -----	1-8

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IB2019/056322

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2007023507	A2	01-03-2007	EP 1912980 A2 23-04-2008
		US 2009018123 A1 15-01-2009	
		WO 2007023507 A2 01-03-2007	

WO 9525106	A1	21-09-1995	AT 232862 T 15-03-2003
		AU 681953 B2 11-09-1997	
		CA 2183972 A1 21-09-1995	
		CN 1143961 A 26-02-1997	
		DE 69529670 D1 27-03-2003	
		DE 69529670 T2 18-09-2003	
		DK 0750618 T3 10-06-2003	
		EP 0750618 A1 02-01-1997	
		ES 2191048 T3 01-09-2003	
		JP 3628329 B2 09-03-2005	
		JP H0873455 A 19-03-1996	
		JP H09512785 A 22-12-1997	
		LV 13155 B 20-06-2004	
		NZ 283011 A 22-09-1997	
		PT 750618 E 30-06-2003	
		WO 9525106 A1 21-09-1995	

WO 2017015106	A1	26-01-2017	AU 2016295165 A1 25-01-2018
		BR 112018000991 A2 04-12-2018	
		CA 2990260 A1 26-01-2017	
		CN 108348507 A 31-07-2018	
		EA 201792566 A1 31-10-2018	
		EP 3307268 A1 18-04-2018	
		JP 2018524406 A 30-08-2018	
		KR 20180026491 A 12-03-2018	
		US 2018179168 A1 28-06-2018	
		WO 2017015106 A1 26-01-2017	
		ZA 201800189 B 26-06-2019	
