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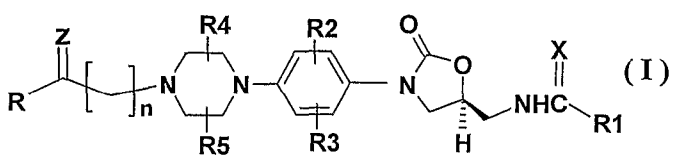
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(54) Title: NOVEL OXAZOLIDINONE DERIVATIVES



(I)

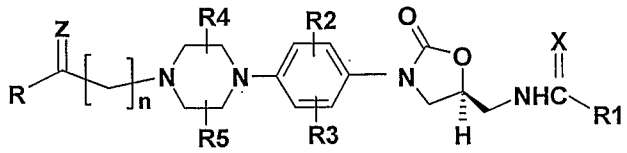
(57) Abstract: The present invention relates to novel compounds of the general formula (I), their derivatives, analogs, tautomeric forms, stereoisomers, polymorphs, hydrates, solvates, pharmaceutically acceptable salts, pharmaceutical compositions, metabolites and prodrugs thereof. The present invention more particularly provides novel Oxazolidinone derivatives of the general formula (I). The novel Oxazolidinone derivatives of the present invention may be useful as antibacterial agents, particularly for intravenous injections and are also useful in the treatment of conditions such as nosocomial pneumoniae, community acquired pneumoniae, Vancomycin resistant enterococci (VRE) caused by Methicillin resistant Staphylococcus Aureus (MRSA) and penicillin resistant Streptococcus Pneumoniae. The compounds of the present invention are effective against a number of human or animal pathogens, clinical isolates, including Vancomycin and Methicillin resistant organisms.

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NOVEL OXAZOLIDINONE DERIVATIVES

Field of the Invention

The present invention relates to novel compounds of the general formula (I), their derivatives, analogs, tautomeric forms, stereoisomers, polymorphs, hydrates, solvates, pharmaceutically acceptable salts, pharmaceutical compositions, metabolites and prodrugs thereof. The present invention more particularly provides novel Oxazolidinone derivatives of the general formula (I).



(I)

The present invention also provides a process for the preparation of the above said novel Oxazolidinones of the formula (I), their derivatives, analogs, tautomeric forms, stereoisomers, polymorphs, hydrates, solvates, pharmaceutically acceptable salts, pharmaceutical compositions, metabolites and prodrugs thereof.

The novel Oxazolidinone derivatives of the present invention are expected to be more soluble and can be easily formulated in an appropriate vehicle for the purpose of intravenous delivery. Also the present invention provides methods and exemplary compounds with enhanced solubility, which might be useful for the design of better compounds with improved therapeutic index towards second-generation Oxazolidinone antibacterials.

The novel Oxazolidinone derivatives of the present invention may be useful as antibacterial agents, particularly for intravenous injections and are also useful in the treatment of conditions such as nosocomial pneumoniae, community acquired pneumoniae, Vancomycin resistant enterococci (VRE) caused by Methicillin resistant Staphylococcus Aureus (MRSA) and penicillin resistant Streptococcus Pneumoniae.

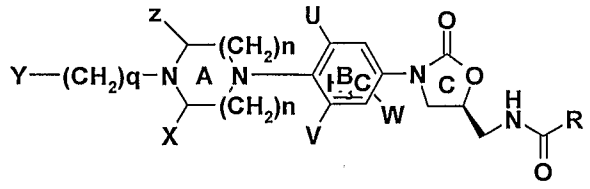
The compounds of the present invention are effective against a number of human or animal pathogens, clinical isolates, including Vancomycin and Methicillin resistant organisms.

Background of Invention

The Oxazolidinone class of compounds represents totally synthetic antibacterials endowed with a mechanism different from the mode of action of known antibacterial compounds. The Oxazolidinones interact with 50S ribosomal subunit to form an initiation complex and thus prevent the bacterial translation necessary for the replication of the bacteria. These compounds had shown antibacterial activity against gram +ve organisms and a host of opportunistic pathogens such as Methicillin resistant Staphylococcus Aureus (MRSA), penicillin resistant Streptococcus Pneumoniae (PRSP) and Vancomycin resistant Enterococci (VRE). The best-represented compounds are Linezolid and Eperezolid, Linezolid being approved by the US FDA for treatment of severe bacterial infections. A lot of work had been done however; there is still a need for research to extend the activity of Oxazolidinones to act against gram -ve pathogens. Some literature and patents are available where efforts have been made to modify the Oxazolidinone moiety to impart the gram -ve activity. In the literature there are many inventions in this class of compounds but there are problems regarding bioavailability, metabolic stability and in particular solubility. It is also mentioned in the literature that the Oxazolidinone antibacterials developed had severe problems of rapid metabolism or have poor permeability. The present compounds represented by this patent have largely alleviated solubility and represent a novel class of Oxazolidinone compounds with very good water solubility.

Several Oxazolidinone derivatives have been reported in the literature. **Few prior art reference which disclose the closest Oxazolidinone derivatives are given here:**

1. **US 5,547,950** discloses and claims compounds of formula (I),

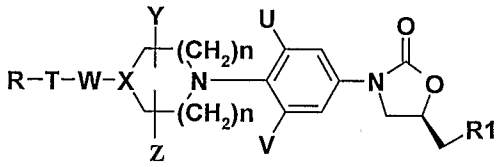


(I)

or pharmaceutically acceptable salts thereof wherein, each n is independently 1 to 3; Y is selected from a-n as defined in the patent; U, V and W are independently (C_1-C_6)alkyl, fluoro, chloro, bromo, hydrogen or a (C_1-C_6)alkyl substituted with one or more of fluoro, chloro, bromo or iodo, preferably U and V are fluoro and W is

hydrogen; R is hydrogen, (C_1-C_{12})alkyl, (C_3-C_{12})cycloalkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkyl substituted with one or more of fluoro, chloro, bromo, iodo or hydroxy and q is 0 to 4 inclusive.

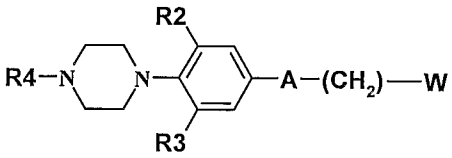
2. WO 02/06278 describes a series of Oxazolidinone derivatives useful as antimicrobial agents, of the formula (I),



(I)

wherein, T is a five to seven membered heterocyclic ring, aryl, substituted aryl; R is a substituent on T; X is CH_2, CH-S, CH-O and N; Y and Z are independently selected from hydrogen, alkyl, cycloalkyl; U and V are independently selected from alkyl, halogen; W is selected from group CH_2, CO, CH_2NH, CH_2NHCH_2, S, CH_2CO etc; R^1 is selected from $-NH(C=O)R^2$, wherein R^2 is hydrogen alkyl, cycloalkyl, alkoxy and the like.

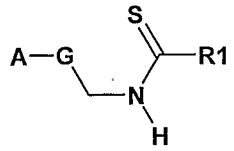
3. US 2002/0137754 describes a series of Oxazolidinone derivatives useful as antimicrobial agents of the formula (I),



(I)

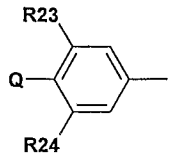
wherein, A represents a Oxazolidinone ring and the like; W is $NHC(=S)R^1$, or -Y-het; Y is NH, O, or S; R^1 is H, NH_2, NHC_{1-4}alkyl, C_{1-4}alkenyl, etc; R^2 and R^3 are independently H, F, Cl or C_{1-2}alkyl; R^4 is (a) $-C(=O)-CR^5R^6-O-R^7$, (b) $-C(=O)-CH_2S(O)n-CH_3$, (c) $-C(=O)-CH_2-S(=O)(=NR^8)CH_3$, (d) $-C(=S)-R^9$, etc; R^5 is H; R^6 is phenyl, benzyl, etc, R^7 is H, CH_3 or C_{1-4} alkanoyl; R^8 is H, C_{1-4} alkyl, C_{1-4} alkanoyl, $-C(=O)NH-C_{1-4}$ alkyl or $-CO_2C_{1-4}$ alkyl; R^9 is C_{1-4} alkyl, CH_2OR_{11}, $S-C_{1-4}$ alkyl, OC_{1-4} alkyl, or $NR^{12}R^{13}$; R^{11} is H, phenyl, benzyl, CH_3 etc; R^{12} and R^{13} are independently H or C_{1-3} alkyl; or R^{12} and R^{13} taken together form a 5- or 6- membered saturated heterocycle, wherein said saturated heterocycle may further contain one or two additional hetero-atoms selected from a group consisting of O, $S(O)_n$ or NR^7; n is 0, 1 or 2; and m is 0 or 1.

4. US 6,342,513 and **WO 00/32599** disclose compounds of the formula (I),

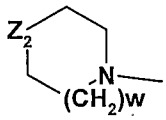


(I)

wherein, G represents Oxazolidinone ring and the like; R^1 is H, NH_2, NH alkyl, alkyl, alkoxy etc, A is

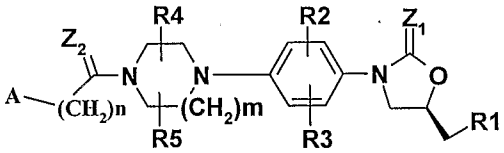


wherein R^{23} and R^{24} represent H, halogen and the like; Q is



etc., wherein Z_2 is SO_2-, -O-, -(NR^{107})-OS-, -S-, and the like; R^{107} is –R^{108}CO- etc, R^{108} is H, alkyl, aryl etc.

5. WO 04/018439 describes a series of Oxazolidinone derivatives useful as antimicrobial agents, of the formula (I),



(I)

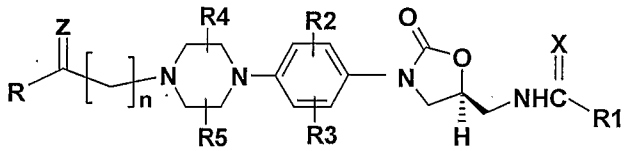
wherein, Z^1 and Z^2 may be same or different and represent O or S; suitable groups represented by R^1 may be selected from halogen atom such as fluorine, chlorine, bromine or iodine; azido, nitro, cyano, XR^6, $N(R^{7a}R^{7b})$, –$NHC(=Y)R^8$; –$NHS(O)_p(C_1$-$C_4)$alkyl, –$NHS(O)_p(C_1$-$C_4)$aryl or –$NHS(O)_p(C_1$-$C_4)$heteroaryl; R^6 represents hydrogen, formyl, $(C_1$-$C_6)$alkyl, cycloalkyl, aryl, etc; R^{7a} and R^{7b} represent hydrogen, formyl, $(C_1$-$C_6)$alkyl, aryl, aralkyl, etc; R^8 is hydrogen, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, aryl, $(C_3$-$C_6)$cycloalkyl, amino, etc; R^2 and R^3 represent hydrogen, halogen, hydroxy, alkyl, alkoxy; R^4 and R^5 represent hydrogen, cyano, nitro, amino, halogen, hydroxyl, substituted or unsubstituted groups selected from $(C_1$-$C_6)$alkyl, haloalkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkylthio, etc; n is 0, 1 or 2; A represents a NHR^9, cycloalkyl, aryl, five to seven membered heteroaryl, heterocyclyl etc.

Objective of the Invention

We have focused our research to identify novel Oxazolidinone derivatives, which are effective against resistant organisms. Our sustained efforts have resulted in novel Oxazolidinone derivatives of the formula (I) wherein functionalities such as oxoimino, hydroxy, amido, fluoro, oxo and more particularly the oxoimino could be introduced either individually or in combination with aromatic and heterocyclic moieties containing one or more nitrogen atoms, sulphur and oxygen either singly or in combination, through reaction schemes as described herein. These novel Oxazolidinone derivatives may be useful as antibacterial agents and hence are useful in the treatment of conditions such as nosocomial pneumoniae, community acquired pneumoniae, Vancomycin resistant enterococci (VRE) caused by Methicillin resistant Staphylococcus Aureus (MRSA) and penicillin resistant Streptococcus pneumoniae. The compounds of the present invention are effective against a number of human or animal pathogens, clinical isolates, including Vancomycin and Methicillin resistant organisms.

Summary of the invention

The present invention relates to novel Oxazolidinone derivatives of the formula (I),



(I)

their derivatives, analogs, tautomeric forms, stereoisomers, polymorphs, hydrates, solvates, pharmaceutically acceptable salts, pharmaceutical compositions, metabolites and prodrugs thereof, wherein, X represents O or S;

R_1 is selected from hydrogen, alkyl, haloalkyl, O-alkyl, S- alkyl, NH_2, NH-alkyl or $N(alkyl)_2$, O-het, S-het or -NH-het;

R_2 and R_3 may be same or different and independently represent hydrogen, halogen, hydroxy, haloakyl, alkyl or alkoxy;

R_4 and R_5 may be same or different and independently represent hydrogen, cyano, nitro, amino, halogen, hydroxy, haloalkyl, alkylthio, alkyl, alkoxy or benzyl;

Z represents S, O and NR_6; R_6 represents hydrogen, hydroxy, cyano, alkyl, alkoxy, –O-(C_3 – C_7) cycloalkyl, -O-aryl, -O-heteroaryl or -O-heterocyclyl ;

R represents a five to seven membered heterocyclic ring, aryl, alkyl, aralkyl, aralkylamino, aralkylthio group and is further substituted by a group selected from halogen, cyano, nitro, alkoxy, acyl, phenyl, aralkyl, heteroaryl, heterocyclyl, amino groups or substituted or unsubstituted groups selected from alkyl, -O-alkoxyalkyl, alkoxy, acyl, aralkyl, cycloalkyl groups, $-OCH_2R_7$;

R_7 represents hydrogen, halogen, hydroxy, alkyl, cycloalkyl, aryl, aralkyl, amino, arylakylamino, heteroaryl and heterocyclyl groups.

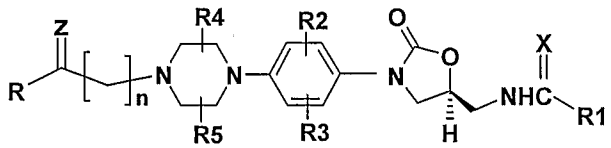
n is an integer of 0-1, with the condition that when n is 1 then Z is not S, and when n is 0 then Z is S, X represents O, R represents $–OCH_2R_7$, -O-alkoxyalkyl, $–CH_2OCH_2-R_8$, $-CH_2OH$, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl; and R_1 represents substituted or unsubstituted haloalkyl group.

When n is 0 then Z is O and X represents O, R represents $–OCH_2R_7$, -O-alkoxyalkyl, $–CH_2OCH_2-R_8$, $-CH_2OH$, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and R_1 represents substituted or unsubstituted haloalkyl group.

When n is 0 then Z is N-R_6 and X represents O, R represents $–OCH_2R_7$, -O-alkoxyalkyl, $–CH_2OCH_2-R_8$, $-CH_2OH$, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and R_1 represents substituted or unsubstituted haloalkyl group, wherein R_8 represents hydrogen, halogen, hydroxyl, alkyl, cycloalkyl, aryl, aralkyl, amino, aralkylamino, heteroaryl and heterocyclyl group.

Detailed Description of the Invention

The present invention relates to novel Oxazolidinone derivatives of the formula (I),



(I)

their derivatives, analogs, tautomeric forms, stereoisomers, polymorphs, hydrates, solvates, pharmaceutically acceptable salts, pharmaceutical compositions, metabolites and prodrugs thereof, wherein, suitable groups represented by X may be selected from O or S;

R_1 represents substituted or unsubstituted groups selected from hydrogen, (C_1-C_4) alkyl groups such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, t-butyl and the like; haloalkyl groups such as dichloromethyl, difluoromethyl, trichloromethyl, trifluoromethyl and the like; O-alkyl, S- alkyl, NH_2, NHalkyl or $N(alkyl)_2$, O-het, S-het or -NH-het, wherein het is a C-linked five or six membered saturated or unsaturated heterocyclic ring having 1, 2 or 3 hetero atoms selected from the group consisting of oxygen, sulfur and nitrogen, which is optionally fused to a benzene ring, such as pyridyl, thienyl, furyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isooxazolyl, oxadiazolyl, triazolyl, thiadiazolyl, tetrazolyl, pyrimidinyl, pyrazinyl, pyridazinyl, benzopyranyl, indolyl, indolinyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, benzopyrrolyl, benzoxadiazolyl, benzothiadiazolyl, benzodioxolyl, quinolinyl, dihydroquinolinyl, tetrahydroquinolinyl, isoquinolinyl, dihydroisoquinolinyl, tetrahydroisoquinolinyl and the like.

R_2 and R_3 represents substituted or unsubstituted groups selected from hydrogen, halogen atoms such as fluorine, chlorine, bromine or iodine; hydroxy, (C_1-C_6)alkyl groups such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, t-butyl and the like; (C_1-C_6)alkoxy groups, such as methoxy, ethoxy, n-propoxy, isopropoxy and the like; haloalkyl groups such as chloromethyl, chloroethyl, trifluoromethyl, trifluoroethyl, dichloromethyl, dichloroethyl and the like.

R_4 and R_5 represent substituted or unsubstituted groups selected from hydrogen, cyano, nitro, amino, hydroxy; halogen atoms such as fluorine, chlorine, bromine or iodine; (C_1-C_4) alkyl groups such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, t-butyl, and the like; haloalkyl groups such as chloromethyl, chloroethyl, trifluoromethyl, trifluoroethyl, dichloromethyl, dichloroethyl and the like; (C_1-C_4)alkoxy groups, such as methoxy, ethoxy, n-propoxy, isopropoxy and the like; (C_1-C_6)alkylthio groups such as methylthio, ethylthio, n-propylthio, iso-propylthio and the like; benzyl group, which may substituted with hydroxyl group.

R_6 represents substituted or unsubstituted groups selected from hydrogen, hydroxyl, cyano, linear or branched (C_1-C_4) alkyl groups; –O-alkyl groups in which the alkyl groups are such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, t-butyl and the like; –O-(C_3 – C_7) cycloalkyl groups in which the cylcoalkyl groups are such as cyclopropyl, cyclobutyl, cyclopentyl, and the like; -O-aryl groups in which the aryl groups are such as phenyl, naphthyl and the like; -O-heteroaryl groups in which

heteraoaryl groups are such as pyridyl, thienyl, furyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isooxazolyl, oxadiazolyl, triazolyl, thiadiazolyl, tetrazolyl, pyrimidinyl, pyrazinyl, pyridazinyl, benzopyranyl, indolyl, indolinyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, benzopyrrolyl, benzoxadiazolyl, benzothiadiazolyl, benzodioxolyl, quinolinyl, dihydroquinolinyl, tetrahydroquinolinyl, isoquinolinyl, dihydroisoquinolinyl, tetrahydroisoquinolinyl and the like; -O-heterocyclyl groups in which heteraocyclyl groups are such as pyrrolidinyl, thiazolidinyl, oxazolidinyl, morpholinyl, thiomorpholinyl, piperidinyl, piperazinyl and the like.

R_7 represents substituted or unsubstituted groups selected from hydrogen, halogen, hydroxy, linear or branched (C_1-C_4) alkyl groups such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, t-butyl, and the like; (C_4-C_8) cycloalkyl groups such as cyclobutyl, cyclopentyl, cyclohexyl and the like; aryl groups such as phenyl, naphthyl and the like; aralkyl groups such as phenylmethyl, phenylethyl, naphthylmethyl, naphthylethyl and the like; the amino group; aralkylamino groups such as benzylamino and the like; heteroaryl groups such as pyridyl, thienyl, furyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isooxazolyl, oxadiazolyl, triazolyl, thiadiazolyl, tetrazolyl, pyrimidinyl, pyrazinyl, pyridazinyl, benzopyranyl, indolyl, indolinyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, benzopyrrolyl, benzoxadiazolyl, benzothiadiazolyl, benzodioxolyl, quinolinyl, dihydroquinolinyl, tetrahydroquinolinyl, isoquinolinyl, dihydroisoquinolinyl, tetrahydroisoquinolinyl and the like; heterocyclyl groups such as pyrrolidinyl, thiazolidinyl, oxazolidinyl, morpholinyl, thiomorpholinyl, piperidinyl, piperazinyl, and the like.

R_8 represents substituted or unsubstituted groups selected from hydrogen, halogen, hydroxyl, linear or branched (C_1-C_4) alkyl groups such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, t-butyl, and the like; (C_3 – C_7) cycloalkyl groups such as cyclopropyl, cyclobutyl, cyclopentyl, and the like; aryl groups such as phenyl, naphthyl and the like; aralkyl groups such as phenylmethyl, phenylethyl, naphthylmethyl, naphthylethyl and the like; the amino group; aralkylamino groups such as benzylamino and the like; heteroaryl groups such as pyridyl, thienyl, furyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isooxazolyl, oxadiazolyl, triazolyl, thiadiazolyl, tetrazolyl, pyrimidinyl, pyrazinyl, pyridazinyl, benzopyranyl, indolyl, indolinyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, benzopyrrolyl, benzoxadiazolyl, benzothiadiazolyl, benzodioxolyl, quinolinyl, dihydroquinolinyl, tetrahydroquinolinyl,

isoquinolinyl, dihydroisoquinolinyl, tetrahydroisoquinolinyl and the like; heterocyclyl groups such as pyrrolidinyl, thiazolidinyl, oxazolidinyl, morpholinyl, thiomorpholinyl, piperidinyl, piperazinyl, and the like.

R represents substituted or unsubstituted groups selected from hydrogen, halogen, cyano, nitro, amino, halogen, hydroxy, $-CH_2OH$, substituted or unsubstituted linear or branched (C_1-C_4) alkyl groups such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, t-butyl, and the like; -O-alkoxyalkyl groups such as $-O-CH_2-O-CH_3$, $-O-(CH_2)_{1-3}-O-(CH_2)_{1-3}-O-CH_3$ and the like, which may be substituted; $-O-CH_2-O-CH_2-R_8$; $-O-CH_2-R_7$; acyl groups such as $-C(=O)CH_3$, $-C(=O)C_2H_5$, benzoyl and the like; alkylcarboxy groups; alkylcarboxyalkyl groups; (C_1-C_{10})alkoxy groups such as methoxy, ethoxy, n-propoxy, isopropoxy, butoxy and the like; aryl groups such as phenyl, naphthyl and the like, aralkyl groups such as phenylmethyl, phenylethyl, naphthylmethyl, naphthylethyl and the like; the amino group; aralkylamino groups such as benzylamino and the like; heteroaryl groups such as pyridyl, thienyl, furyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isooxazolyl, oxadiazolyl, triazolyl, thiadiazolyl, tetrazolyl, pyrimidinyl, pyrazinyl, pyridazinyl, benzopyranyl, indolyl, indolinyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, benzopyrrolyl, benzoxadiazolyl, benzothiadiazolyl, benzodioxolyl, quinolinyl, dihydroquinolinyl, tetrahydroquinolinyl, isoquinolinyl, dihydroisoquinolinyl, tetrahydroisoquinolinyl and the like; heterocyclyl groups such as pyrrolidinyl, thiazolidinyl, oxazolidinyl, morpholinyl, thiomorpholinyl, piperidinyl, piperazinyl, and the like.

Z is selected from O, S and NR_6;

n is an integer of 0-1, with the condition that when n is 1 then Z is not S, and when n is 0 then Z is S, X represents O, R represents $-OCH_2R_7$, -O-alkoxyalkyl, $-CH_2OCH_2-R_8$, $-CH_2OH$, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and R_1 represents substituted or unsubstituted haloalkyl. When n is 0 then Z is O, X represents O, R represents $-OCH_2R_7$, -O-alkoxyalkyl, $-CH_2OCH_2-R_8$, $-CH_2OH$, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and R_1 represents substituted or unsubstituted haloalkyl. When n is 0 then Z is $N-R_6$, X represents O, R represents $-OCH_2R_7$, -O-alkoxyalkyl, $-CH_2OCH_2-R_8$, $-CH_2OH$, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and R_1 represents substituted or unsubstituted haloalkyl.

L represents a suitable leaving group selected from fluoro, chloro, bromo, carboxylic hydroxyl groups and similar leaving groups.

The substituents on any of the groups represented by R, R_1, R_2, R_3, R_4, R_5, R_6, R_7 and R_8 are selected from halogen, hydroxy, formyl, nitro, cyano, azido, amino, alkyl, aryl, alkylamino, alkylaminocarbonyl, haloalkyl, acylamino, alkoxy, acyl and these substituents are as defined above.

The compounds of this invention may be useful in their natural form or as their salts. The salt when required for infusion may be formulated in its stable non-toxic and non-allergic acceptable form. Typically the acceptable salts are those formed with acids which form under physiological conditions as anion or conjugate base, for example tosylate, mesylate, acetate, tartarate, succinate, malonate, base of phosphate, citrate and lactate. Also suitable inorganic salts such as hydrochloride, hydroiodide, methyl iodide, sulfate, nitrate, carbonate, bicarbonate and bisulphate. The pharmacologically acceptable salts of the present invention include alkali metals like Li, Na, and K, alkaline earth metals like Ca and Mg, salts of organic bases such as diethanolamine, α-phenylethylamine, benzylamine, piperidine, morpholine, pyridine, hydroxyethylpyrrolidine, hydroxyethylpiperidine, choline and the like, ammonium or substituted ammonium salts, aluminum salts. Salts also include amino acid salts such as glycine, alanine, cystine, cysteine, lysine, arginine, phenylalanine, guanidine etc. Salts may include acid addition salts where appropriate which are, sulphates, nitrates, phosphates, perchlorates, borates, hydrohalides, acetates, tartrates, maleates, citrates, succinates, palmoates, methanesulphonates, tosylates, benzoates, salicylates, hydroxynaphthoates, benzenesulfonates, ascorbates, glycerophosphates, ketoglutarates and the like. Pharmaceutically acceptable solvates may be hydrates or comprising other solvents of crystallization such as alcohols.

Representative compounds according to the present invention include:

1. 3-{4-[4-(1-(4-Methoxyphenyl)ethanoneoxime-2-yl)piperazinyl]3-fluorophenyl} -2-oxo-1,3-oxazolidin-5(*S*)-methyl acetamide;
2. 3-{4-[4-(1-Methylethanon-2yl)piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin -5(*S*)-methyl acetamide;
3. 3-{4-[4-(1-(1-Methyl)ethanoneoxime-2-yl)piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methyl acetamide;

4. 3-{4-[4-(1-(4-Fluorophenyl)ethanon-2-yl)piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methyl acetamide;
5. 3-{4-[4-(1-(4-Fluorophenyl)ethanoneoxime-2-yl)piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methyl acetamide;
6. 3-{4-[4-(1-(3-Methoxyphenyl)ethanon-2-yl)piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methyl acetamide;
7. 3-{4-[4-(1-(3-Methoxyphenyl)ethanoneoxime-2-yl)piperazinyl]3-fluorophenyl }-2-oxo-1,3-oxazolidin-5(*S*)-methyl acetamide;
8. 3-{4-[4-(1-(4-Methylphenyl)ethanon-2-yl)piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methyl acetamide;
9. 3-{4-[4-(1-(4-Methylphenyl)-ethanoneoxime-2-yl)piperazinyl]3-fluorophenyl} -2-oxo-1,3-oxazolidin-5(*S*)-methyl acetamide;
10. 3-{4-[4-(1-(4-Methoxyphenyl)ethanoneoxime-2-yl)piperazinyl]3-fluorophenyl} -2-oxo-1,3-oxazolidin-5(*S*)-methylthioacetamide;
11. 3-{4-[4-(1-(4-Methoxyphenyl)ethanone-O-methyloxime-2-yl)piperazinyl] 3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-ethylthioacetamide;
12. O-Methyl-4-[4-(5(*S*)-{[(dichloroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin -3-yl)-2-fluorophenyl]piperazine-1-carbothioate;
13. O-Methyl-4-[4-(5(*S*)-{[(difluoroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin -3-yl)-2-fluorophenyl]piperazine-1-carbothioate;
14. O-Isopropyl-4-[4-(5(*S*)-{[(difluoroacetyl)amino]methyl}-2-oxo-1,3 -oxazolidin-3-yl)-2-fluorophenyl]piperazine-1-carbothioate;
15. O-n-Butyl-4-[4-(5(*S*)-{[(difluoroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl]piperazine-1-carbothioate;
16. O-n-Propyl-4-[4-(5(*S*)-{[(difluoroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl]piperazine-1-carbothioate;
17. O-Ethyl-4-[4-(5(*S*)-{[(dichloroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl]piperazine-1-carbothioate;
18. O-n-Butyl-4-[4-(5(*S*)-{[(dichloroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin -3-yl)-2-fluorophenyl]piperazine-1-carbothioate;
19. O-Isopropyl-4-[4-(5(*S*)-{[(dichloroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin -3-yl)-2-fluorophenyl]piperazine-1-carbothioate;
20. 2,2-Difluoro-*N*-({3-[3-fluoro-4-{(3,5-dimethyl-4-[(benzyloxy)acetyl]piperazin

-1-yl}phenyl)]-2-oxo-1,3-oxazolidin-5(*S*)-yl}methyl)acetamide;

21. 2,2-Difluoro-*N*-({3-[3-fluoro-4-{(4-[(benzyloxy)acetyl]piperazin-1-yl}phenyl)]-2-oxo-1,3-oxazolidin-5(*S*)-yl}methyl)acetamide;

22. 2,2-Difluoro-*N*-({3-[3-fluoro-4-(3,5-dimethyl-4-glycoloylpiperazin-1-yl) phenyl] -2-oxo-1,3-oxazolidin-5(*S*)-yl}methyl)acetamide;

23. 2,2-Difluoro-*N*-({3-[3-fluoro-4-(4-glycoloylpiperazin-1-yl)phenyl]-2-oxo-1,3-oxazolidin-5(*S*)-yl}methyl)acetamide;

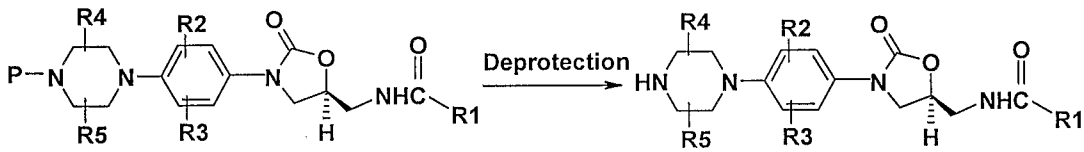
24. O-[2-(2-Methoxyethoxy)ethyl]-4-[4-(5(*S*)-{[(difluoroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl] piperazine-1-carbothioate and

25. 2,2-Dichloro-*N*-({3-[3-fluoro-4-(4-(3,4,5-trimethoxybenzoyl)piperazin-1-yl}phenyl)]-2-oxo-1,3-oxazolidin-5-(*S*)-yl}methyl)acetamide.

The compounds of general formula (I) may be prepared by one or more schemes or combinations of reactions given below.

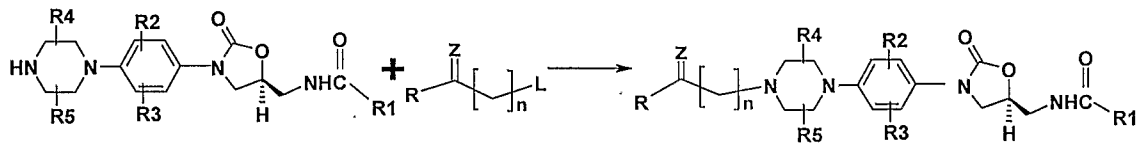
i) <u>Scheme I</u>:

a) Deprotecting the compound of formula (1a), wherein P is the protecting group and all the other groups are as defined earlier, to produce the compound of formula (1b). The compound of formula (1a) is prepared according to the procedure described in our WO 2004/018439.



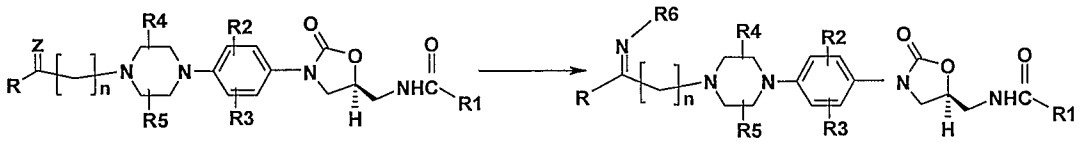
(1a) (1b)

b) Reacting the compound of the formula (1b) with a compound of formula (2a) to give the compound of formula (3a), wherein L is a leaving group and all symbols are as defined earlier.



(1b) (2a) (3a)

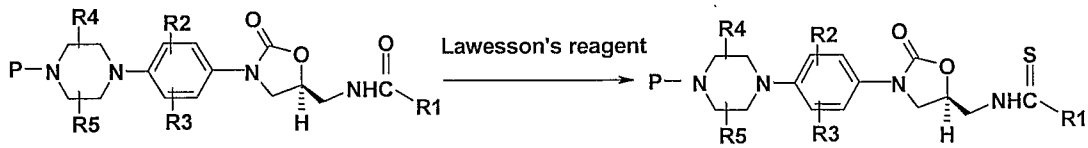
c) Optionally converting the compound of formula (3a) wherein n represents 1, and Z represents O to an Oxime of the formula (3b) wherein Z represents NR_6 and all the other symbols are as defined earlier.



(3a) (3b)

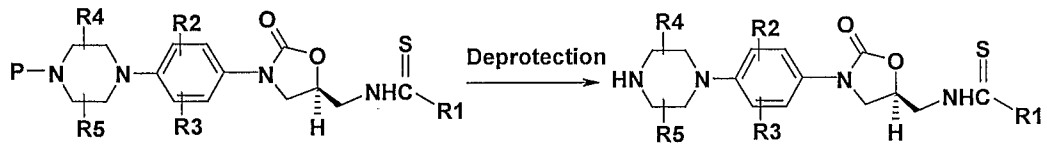
ii) Scheme II:

a) Converting the compound of the formula (1a) to produce the compound of formula (1c) with Lawesson's reagent and all the other symbols are as defined earlier.



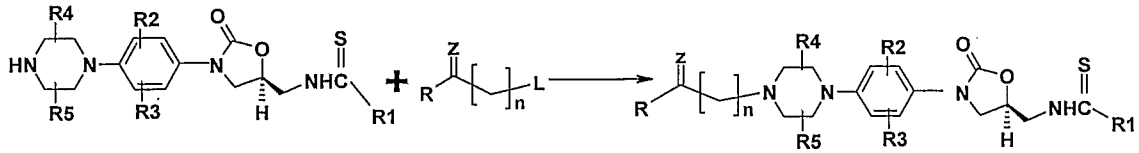
(1a) (1c)

b) Deprotecting the compound of formula (1c) where P is the protecting group and all the other groups are as defined earlier to produce the compound of formula (1d).



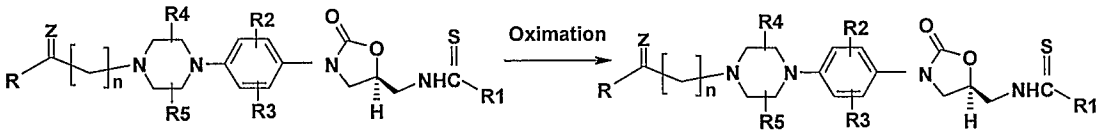
(1c) (1d)

c) Reacting the compound of the formula (1d) with a compound of formula (2a) to give the compound of formula (3a), wherein L is a leaving group and all the other symbols are as defined earlier.



(1d) (2a) (3a)
(where n= 1, Z=O)

d) Alternatively converting the compound formula (3a) wherein all the other symbols are as defined earlier to give the Oxime of formula (3b).

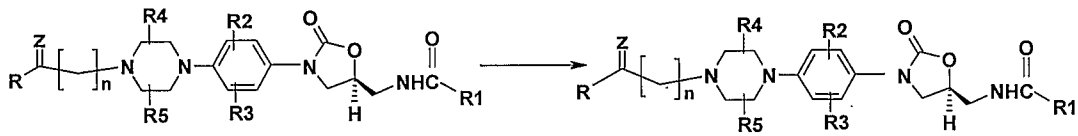


(3a)
(where n=1 and Z=O)

(3b)
(where n=1 and Z=NR$_6$)

iii) Scheme III:

Optionally converting the compound of formula (3c) wherein Z represents S, n represents 0 and R represents imidazolyl to the compound of formula (3d) wherein, R represents $-OCH_2R_7$, -O-alkoxyalkyl, and R_1 represents substituted or unsubstituted haloalkyl group and all the other symbols are as defined earlier.



(3c)

(3d)

The reactions described in the processes outlined above may be performed by using the methods described herein:

Scheme I:

Compounds of the general formula (I) may be obtained from the compound of general formula (1a) by deprotecting the compound of formula (1a) where P is the protecting group and all other groups are as defined earlier to produce the compound of formula (1b) with suitable reagents such as TFA and the like in the presence of solvents such as DCM and the like. Reacting the compound of formula (1b) with the compound of the formula (2a) (wherein L is a leaving group and all other symbols are as defined earlier) is carried out in the presence of an organic base such as triethylamine, pyridine, dimethylamine and the like or in the presence of an inorganic base such as potassium carbonate, sodium carbonate and the like and in solvents selected from toluene, trifluoroacetic acid, DMF, tetrahydrofuran, chloroform, dichloromethane, dichloroethane, ethyl acetate or a mixture thereof or by using conventional coupling procedures employed in the carboxylic acid and amine couplings . The reaction may be

carried out at a temperature in the range of 0 °C to 50 °C. The duration of the reaction may range from 4 to 24 hours, to produce the compound of the general formula (3a).

Optionally the compound of formula (3a) is converted to the respective oxime of formula (3b) by treatment with substituted or unsubstituted hydroxylamine hydrochloride in the presence of a inorganic bases such as sodium acetate, ammonium acetate, potassium carbonate, cesium carbonate and the like or in the presence of organic bases such as pyridine, diisopropylethylamine and the like, and in the presence of solvents such as methanol, ethanol and the like or the mixture thereof. The reaction may be carried out at a temperature in the range of 10 °C to 100 °C. The reaction time ranges from 1 to 12 hours.

Scheme II:

Compounds of general formula (I) may be obtained by converting the compound of formula (1a) to the thioamides by using Lawesson's reagent in the presence of a base such as triethylamine, pyridine and the like and solvents such as toluene, benzene, tetrahydrofuran, chloroform, dichloromethane, dichloroethane, ethyl acetate, o-dichlorobenzene or a mixture thereof. The reaction may be carried out at a. temperature in the range of 80 ° to 120 °C. The duration of the reaction may range from 4 to 8 hours to produce the compound of formula (1c).

The reaction of the compound of formula (1c) with suitable reagents such as TFA and the like in the presence of solvents such as DCM and the like leads to the compound of formula (1d).

The reaction of the compound of formula (1d) with the compound of the formula (2a) (wherein L is a leaving group and all the other symbols are as defined earlier) is carried out in the presence of an organic base such as triethylamine, pyridine, dimethylamine and the like or in the presence of an inorganic base such as potassium carbonate, sodium carbonate and the like and in solvents selected from toluene, trifluoroacetic acid, DMF, tetrahydrofuran, chloroform, dichloromethane, dichloroethane, ethyl acetate or a mixture thereof. The reaction may be carried out at a temperature in the range of 0 °C to 50 °C. The duration of the reaction may range from 4 to 24 hours to produce the compound of the general formula (3a).

Optionally the compound of formula (3a) is converted to the oxime of formula (3b) by treatment with substituted or unsubstituted hydroxylamine hydrochloride in the

presence of a inorganic base such as sodium acetate, ammonium acetate, potassium carbonate, cesium carbonate and the like or in the presence of organic bases such as pyridine, diisopropylethylamine and the like, in the presence of solvents such as methanol, ethanol, tetrahydrofuran, pyridine, N,N-dimethylformamide and the like or the mixture thereof. The reaction may be carried out at a temperature in the range of 10 to 100 °C. The reaction time ranges from 1 to 12 hours.

Scheme III:

Compounds of the general formula (3d) may be obtained by converting the compound of formula (3c) to the carbothioate ester by treatment with R_7CH_2OH in the presence of base such as sodium acetate, potassium carbonate, cesium carbonate and the like and in the presence or absence of a suitable solvent such as dimethylformamide, dichloromethane, toluene, acetonitrile, dioxane, methyl ethyl ketone and the like or the mixture thereof. The reaction may be carried out at a temperature in the range of 10 to 100 °C. The reaction time ranges from 1 to 36 hours.

The protecting groups P used in the invention are conventional protecting groups such as t-butoxy carbonyl (t-Boc), trityl, trifluoroacetyl, benzyloxy, benzyloxy carbonyl (Cbz) and the like.

It is appreciated that in any of the above-mentioned reactions, any reactive group in the substrate molecule may be protected according to the conventional chemical practice. Suitable protecting groups in any of the above-mentioned reactions are those used conventionally in the art. The methods of formation and removal of such protecting groups are those conventional methods appropriate to the molecule being protected.

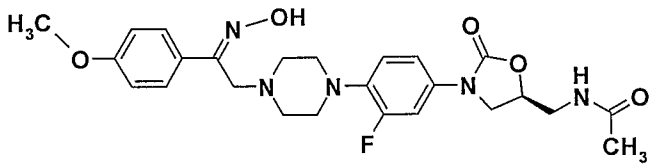
The pharmaceutical composition may be in the forms normally employed, such as tablets, capsules, powders, syrups, solutions, aerosols, suspensions and the like, may contain flavoring agents, sweeteners etc. in suitable solid or liquid carriers or diluents or in suitable sterile media to form injectable solutions or suspensions. The compositions may be prepared by processes known in the art. The amount of the active ingredient in the composition may be less than 70% by weight. Such compositions typically contain from 1 to 20 %, preferably 1 to 10 % by weight of the active compound, the remainder of the composition being the pharmaceutically acceptable carriers, diluents or solvents.

From the foregoing description, one skilled in the art can easily ascertain the essential characteristics of this invention, and without departing from the spirit and scope thereof, can make various changes and modifications of the invention to adapt it to various usages and conditions.

The present invention is provided by the examples shown below, which are provided by way of illustration only and should not be considered to limit the scope of the invention.

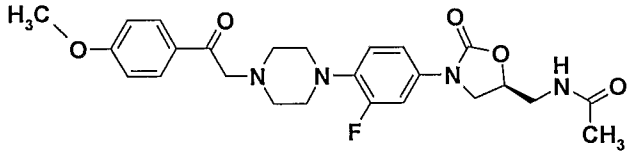
Example 1

Synthesis of 3-{4-[4-(1-(4-methoxyphenyl)ethanoneoxime-2-yl)piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methylacetamide.



Step-I

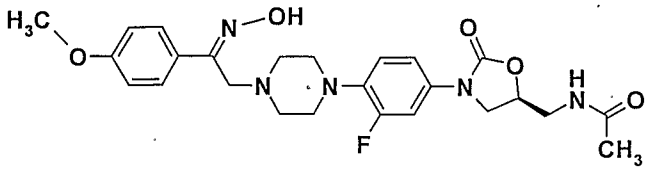
Preparation of 3-{4-[4-(4-methoxy phenacyl)piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methylacetamide.



To a cold solution of 0.77g (2.29mmol) 3-{4-[1-piperazinyl]-3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methylacetamide in 30ml of N,N-dimethyl formamide was added 4-methoxyphenacyl bromide (0.66g, 2.88mmol), potassium carbonate (0.93g, 6.9mmol) and the resulting mixture was stirred for 5 hours at ambient temperature. The reaction mixture was extracted with ethyl acetate and water, the organic phase was separated, dried over anhydrous Na_2SO_4 and evaporated under reduced pressure to afford the crude product, which was purified by column chromatography using silicagel 60-120 mesh to afford the pure product (250mg). H^1-NMR (DMSO-d_6):δ 1.82(s, 3H), 2.6 (t, 4H), 2.98 (t, 4H), 3.38 (t, 2H), 3.67(t, 1H), 3.82 (s, 2H), 3.84 (s, 3H), 4.05(t, 1H), 4.67 (m, 1H), and 7.03 - 7.99 (m, 7H). MS m/z: 485 (M^++1).

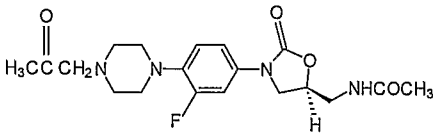
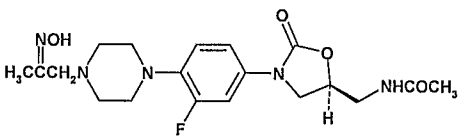
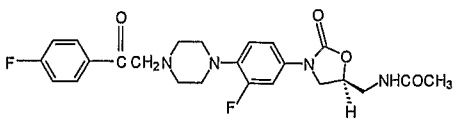
Step II

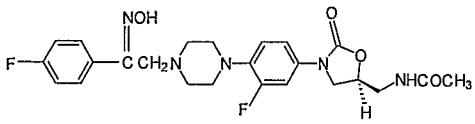
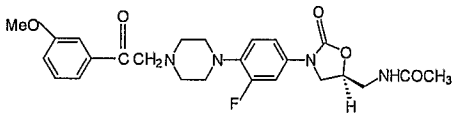
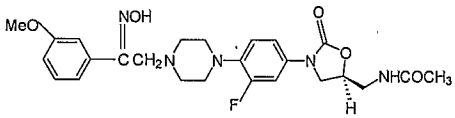
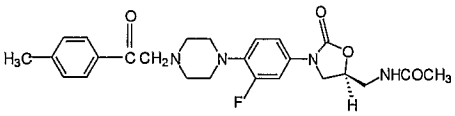
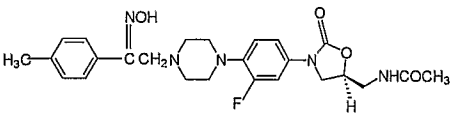
Preparation of 3-{4-[4-(1-(4-methoxyphenyl)ethanoneoxime-2-yl) piperazinyl] 3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methylacetamide



To the solution of 3-{4-[(4-(4-methoxyphenacyl) piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methylacetamide (0.15g, 0.31mmol) in ethanol (15ml) was added hydroxylamine hydrochloride (0.09g, 1.3mmol), sodium acetate (0.21g, 2.56mmol) and water (3ml) and the reaction mixture was heated for 8 hours at 90 °C, after which it was evaporated under reduced pressure to afford the crude product, which was purified by preparative chromatography using silica gel $60F_{254}$ plates to afford the pure product (50mg). H^1-NMR (DMSO-d_6): δ 2.02(s, 3H), 2.81 (t, 4H), 3.12 (t, 4H), 3.57 (m, 1H), 3.71 (m, 2H), 3.82 (s, 2H), 3.83 (s, 3H), 3.99 (t, 1H), 4.77 (m, 1H), and 6.89-7.6 (m, 7H). MS m/z: 500 (M^++1).

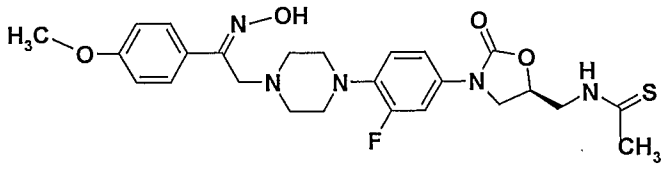
The following compounds were prepared according to the procedure given in the Example 1

Example	Structure	Analytical Data
2		^{1}H-NMR (DMSO-d_6): δ 1.9, (s, 3H), 2.1 (s, 3H), 2.8 (m, 4H), 2.9 (s, 1H), 3.1 (m, 3H), 3.4 (s, 2H), 3.5 (m, 2H), 3.8 (m, 1H), 4.1 (m, 1H), 4.9 (m, 1H), and 7.0 - 7.5 (m, 3H). MS m/z: 393 (M^++1).
3		^{1}H-NMR (DMSO-d_6): δ 1.8 (s, 3H), 1.9 (s, 3H), 2.7 (t, 4H), 3.1 (t, 4H), 3.4 (s, 2H), 3.5 (m, 2H), 3.7 (m, 1H), 4.0 (m, 1H), 4.8 (m, 1H), and 7.0 – 7.5 (m, 3H). MS m/z: 408 (M^++1).
4		^{1}H-NMR (DMSO-d_6): δ 1.82 (s, 3H), 2.67 (t, 4H), 2.98 (t, 4H), 3.38 (t, 2H), 3.67 (t, 1H), 3.89 (s, 2H), 4.07 (t, 1H), 4.7 (m, 1H), and 7.06–8.1 (m, 7H). MS

		m/z: 473 (M^++1).
5		^{1}H-NMR (DMSO-d_6): δ 1.6 (s, 2H), 1.82 (s, 3H), 2.5 (t, 4H), 2.88 (m, 5H), 3.66 (s, 2H), 4.0(t, 1H), 4.67 (m, 1H), and 6.9 - 7.81 (m, 7H). MS m/z: 488 (M^++1).
6		^{1}H-NMR (DMSO-d_6): δ 1.82 (s, 3H), 2.68 (t, 4H), 2.99 (t, 4H), 3.38 (t, 2H), 3.67 (t, 1H), 3.8 (s, 3H), 3.91 (s, 2H), 4.05 (t, 1H), 4.7 (m, 1H), and 7.06 - 7.61 (m, 7H). MS m/z: 485 (M^++1).
7		^{1}H-NMR (DMSO-d_6): δ 1.82 (s, 3H), 2.58 (t, 4H), 2.91 (t, 4H), 3.37 (m, 3H), 3.67 (s, 2H), 3.76 (s, 3H), 4.06 (t, 1H), 4.7(m, 1H), and 6.92-8.2 (m, 7H). MS m/z: 500 (M^++1).
8		^{1}H-NMR (DMSO-d_6): δ 1.8 (s, 3H), 2.35 (s, 3H), 2.65 (t, 4H), 2.96 (t, 4H), 3.36 (t, 2H), 3.7 (t, 1H), 3.85 (s, 2H), 4.05 (t, 1H), 4.7 (m, 1H), 7.04 - 7.9 (m, 7H). MS m/z: 469 (M^++1)
9		^{1}H-NMR (DMSO-d_6): δ 1.6 (s, 2H), 1.82 (s, 3H), 2.3 (s, 3H), 2.57 (s, 4H), 2.89 (s, 4H), 3.67 (s, 3H), 4.06(t, 1H), 4.7 (m, 1H), and 7.0 - 7.64 (m, 7H). MS m/z: 484 (M^++1).

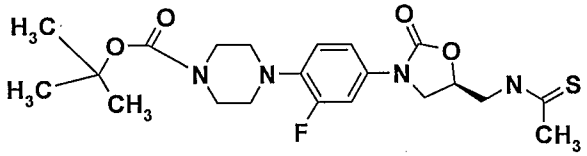
Example 10

Synthesis of 3-{4-[4-(1-(4-methoxyphenyl)ethanoneoxime-2-yl)piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methylthioacetamide.



Step I

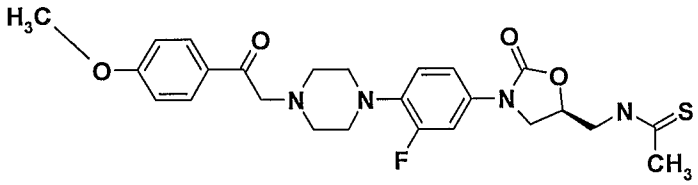
Preparation of 3-{4-[4(tert-butoxycarbonyl) piperazinyl]-3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methylthioacetamide.



To the solution of 3-{4-[(4-(tert-butoxycarbonyl)piperazinyl]3-fluoro phenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methylacetamide (3g, 6.9mmol) in toluene (40 ml), was added Lawesson's reagent (1.3g, 3.24mmol) and the reaction mixture was stirred for 6 hours at 120 °C, after which it was extracted with ethyl acetate and water. The organic phase was separated and evaporated under reduced pressure to afford crude product, which was purified by column chromatography using silica gel 60-120A° mesh to afford the pure product (2.08g). H^1-NMR (DMSO-d_6): δ 1.41 (s, 9H), 2.43 (t, 3H), 2.9 (t, 4H), 3.62 (t, 4H), 3.46 (t, 4H), 3.76 (t, 1H), 3.87 (m, 2H), 4.1(t, 1H), 4.93 (m, 1H), and 7.06 –7.71(m, 3H). MS m/z: 453 (M^++1).

Step II

Synthesis of 3-{4-[4-(1-(4-methoxyphenacyl))piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methylthioacetamide.

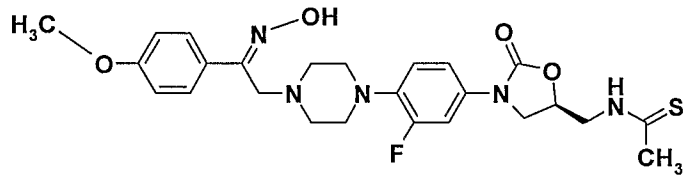


To solution of 3-{4-[4(tert-butoxycarbonyl)piperazinyl]-3-fluorophenyl}-2-oxooxazolidin-5(*S*)-methylthioacetamide (3.04g 6.73mmol, obtained according to the procedure described in the step-I) in dichloromethane (50ml) was added 8 % trifluoroacetic acid at 4 °C under stirring and continued the stirring for 4 hours. After which triethylamine (12ml, 86mmol) was added and the stirring was continued for

another 10 minutes, then it was evaporated under vacuum to afford the crude product, which was dissolved in N,N-dimethylformamide and cooled (0-4 °C). To the resulting solution was added potassium carbonate (2.72g, 20mmol) and 4-methoxyphenacyl bromide (1.96g, 8.56mmol) under stirring. The stirring was continued for 8 hours at ambient temperature, after which the reaction mixture was extracted with ethyl acetate and water, the organic phase was separated and evaporated under reduced pressure to afford the crude product. The crude product thus obtained was purified by column chromatography using silica gel 60-120A° mesh to afford the pure product (2.77g). H^1-NMR (DMSO-d_6): δ2.4 (s, 3H), 2.6 (t, 4H), 2.98 (t, 4H), 3.38 (t, 2H), 3.67 (t, 1H), 3.82 (s, 2H), 3.84 (s, 3H), 4.05 (t, 1H), 4.67 (m, 1H), and 7.03 - 7.99 (m, 7H). MS m/z: 502 (M^++1).

Step III

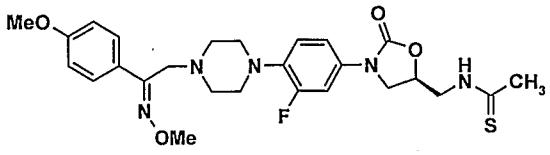
Synthesis of 3-{4-[4-(1-(4-methoxyphenyl)ethanoneoxime-2-yl)piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methylthio acetamide.



To the solution of 3-{4-[4-(1-(4-methoxyphenacyl))piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methylthio acetamide (0.205g, 0.41 mmol, obtained according to the procedure described in the step II) in ethanol (25ml) was added hydroxylamine hydrochloride (0.15g, 2.1mmol), sodium acetate (0.27g, 3.29mmol) and water (2ml) under stirring. The reaction mass was heated at 80 °C for 5 hours. After which the reaction mixture was evaporated under reduced pressure to afford crude product, which was purified by preparative chromatography using silica gel $60F_{254}$ plates to afford the pure product (38mg). H^1-NMR (DMSO-d_6): δ 2.43 (s, 3H), 2.57 (s, 4H), 2.9 (s, 4H), 3.66 (s, 2H), 3.77 (s, 4H), 3.88 (t, 2H), 4.08 (s, 3H), 4.9 (m, 1H), and 6.9-7.7 (m, 7H). MS m/z: 516 (M^++1).

Example 11

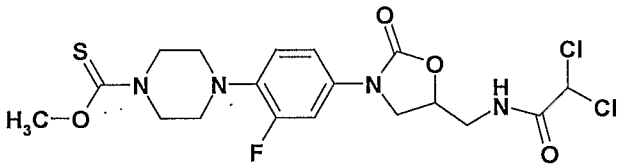
Synthesis of 3-{4-[4-(1-(4-methoxyphenyl)ethanone O-methyloxime-2-yl)piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methylthio acetamide



To the solution of 3-{4-[4-(1-(4-methoxyphenacyl))piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methylthio acetamide (0.17g, 0.3mmol), obtained according to the procedure described in the step II of example 10) in tetrahydrofuran (9ml) was added O-methylhydroxylamine hydrochloride (0.042g, 0.5mmol), pyridine (5ml) and ethanol (5ml) under stirring. The reaction mass was heated at 80 °C for 5 hours. After which the reaction mixture was evaporated under reduced pressure to afford crude product, which was purified by flash chromatography to afford the pure product (0.02g). H^1-NMR (DMSO-d_6): δ 0.82-0.87 (m, 2H), 2.43 (s, 3H), 2.55 (s, 5H), 2.89 (s, 4H), 3.65 (s, 3H), 3.75 – 3.89 (m, 5H), 4.08 - 4.13 (m, 1H), 4.9-4.93 (m, 1H), 6.93 – 6.95 (m, 2H), 6.99- 7.04 (m, 1H), 7.13 – 7.15 (m, 1H), 7.44 – 7.48 (m, 1H), 7.70- 7.73 (m, 2H), 10.36 (t, 1H, D_2O exchangeable). MS m/z: 530.1(M^++1).

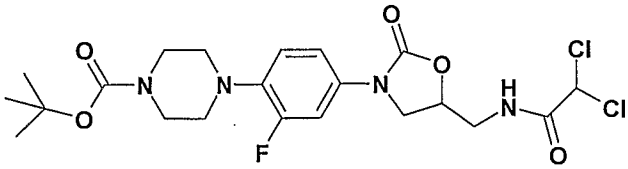
Example 12

Synthesis of O-methyl4-[4-(5(*S*)-{[(dichloroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl]piperazine-1-carbothioate.



Step I

Synthesis of *tert* butyl 4-[4-(5(S)-{[(dichloroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl]piperazine-1-carboxylate.

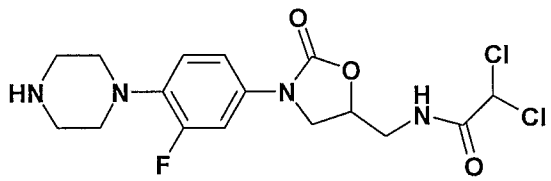


To a solution of *tert* butyl 4-{4-[5(*S*)-(aminomethyl)-2-oxo-1,3-oxazolidin-3-yl]-2-fluorophenyl}piperazine-1-carboxylate (2g, 5.3mmol, prepared according to the procedure described in our PCT IB03/03459) in N,N-dimethylformamide (70ml), was

first added potassium carbonate (1.24g, 9mmol) and then dichloroacetyl chloride (2.2g, 14.8mmol) under stirring at 0 °C. After stirring for 1 hour at 0 °C the reaction mass was further stirred at 37 °C for 24 hours. On completion of the reaction, as confirmed by TLC using ethyl acetate as the solvent system, the reaction mixture was poured on to ice-water mixture. The resulted solid was extracted with ethyl acetate (250ml) and finally the organic layer was washed with water (100ml). The resultant organic layer was collected and dried over anhydrous Na_2SO_4, then distilled under vacuum to yield the crude product (1.8g, 66% yield), which was used in the step-II without further purification.

Step II:

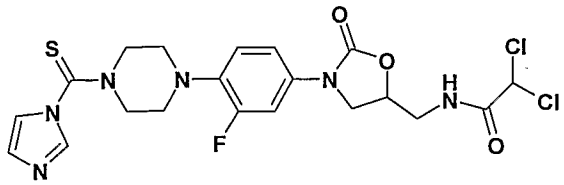
Synthesis of 2,2-dichloro-*N*-{[3-(3-fluoro-4-piperazin-1-ylphenyl)-2-oxo-1,3-oxazolidin-5(*S*)-yl]methyl}acetamide



To the solution of *tert* butyl 4-[4-(5(*S*)-{[(dichloroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl]piperazine-1-carboxylate (1.8g, 3mmol, obtained in the step-I) in dichloromethane (35ml) was added thioanisole (2.2g, 17.5mmol), trifluoroacetic acid (3.4g, 30mmol) at 0 °C under stirring. After 1 hour of stirring at this condition the reaction mixture was allowed to further stir at 37 °C. On completion of the reaction, as confirmed by TLC using ethylacetate:hexane (8:2) as solvent system, the reaction mixture was neutralized by using triethylamine at 0 °C. The reaction mixture was concentrated to dryness under vacuum to yield the crude product (0.8g, 57% yield).

Step III:

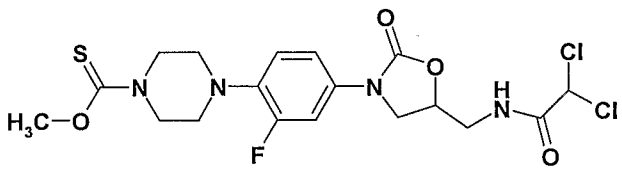
Synthesis of *N*-[(3-{4-[4-(1*H*-Imidazol-1-ylcarbonothioyl)piperazin-1-yl]-3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-yl)methyl]-2,2-dichloroacetamide.



To a solution of 2,2-dichloro-*N*-{[3-(3-fluoro-4-piperazin-1-ylphenyl)-2-oxo-1,3-oxazolidin-5(*S*)-yl]methyl}acetamide (0.8g, 1.9mmol, obtained in the step-II) in N,N-dimethylformamide (25ml) was added triethylamine (0.57g, 5.9 mmol) and 1,1-thiocarbonyldiimidazole (1.0g, 5.7mmol) under stirring at 0 °C. After 1hour of stirring, the reaction mixture was allowed to stir for another 24 hours at 37 °C. On completion of the reaction, the reaction mixture was poured on to ice-water mixture. The solid obtained was extracted with ethyl acetate (100ml) and the organic layer was washed with cold water (50ml), and dried over anhydrous Na_2SO_4. The solvent was distilled off under vacuum to yield the crude product, which was purified by column chromatography using silica gel and ethyl acetate:hexane mixture as eluent, to yield the title compound (0.2g, 19.8 % yield). ^{1}H-NMR (DMSO-d_6): δ 3.19 (s, 4H), 3.73 – 3.54 (m, 3H), 4.05 – 4.1 (m, 5H), 4.83 (s, 1H), 5.94 (s, 1H), 6.91 – 6.95 (m, 2H), 7.08 – 7.13 (m, 2H), 7.24 (s, 1H), 7.3 – 7.49 (m, 1H), 7.91 (s, 1H). MS m/z (M^++1): 516.9.

Step IV:

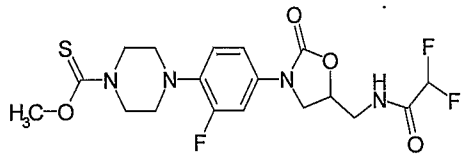
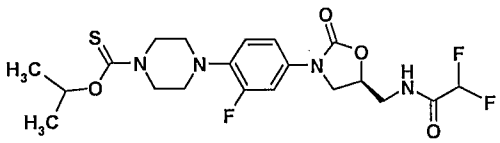
Synthesis of O-Methyl4-[4-(5(*S*)-{[(dichloroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl]piperazine-1-carbothioate

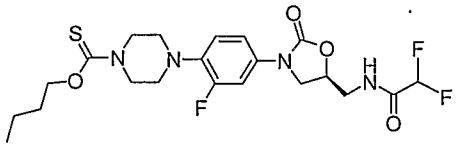
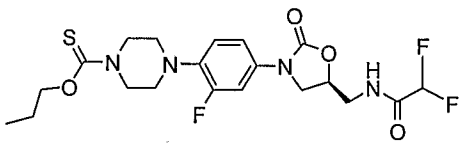
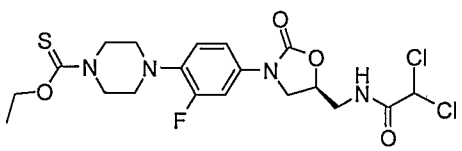


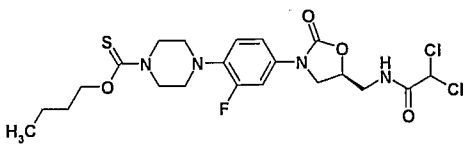
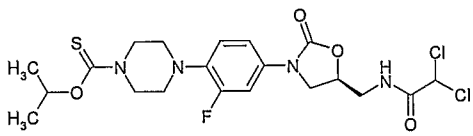
Potassium carbonate (0.06g, 4.6 mmol) was added to the solution of *N*-[(3-{4-[4-(1*H*-imidazol-1-ylcarbonothioyl)piperazin-1-yl]-3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-yl)methyl]-2,2-dichloroacetamide (0.2g, 0.38mmol, obtained in the step III) in methanol (20 ml) under stirring. The resulted reaction mixture was refluxed until completion of the reaction as confirmed by TLC using (ethyl acetate:hexane, 8:2) as the solvent system. The resultant reaction mass was allowed to cool to room temperature and filtered the solid thus obtained at suction. This solid was washed with ethyl acetate:hexane (1:1 mixture, 10ml) to yield the pure compound (0.08g, 43% yield,

purity 99.59 % by HPLC). ^{1}H-NMR (DMSO-d_6): δ 2.98 – 3.03 (m, 4H), 3.52 – 3.54 (t, 2H), 3.69 – 3.72 (m, 1H), 3.83 – 3.86 (m, 2H), 3.96 (s, 3H), 4.09 – 4.14 (m, 3H), 4.76 – 4.8 (m, 1H), 6.48 (s, 1H), 7.06 – 7.11 (m, 1H), 7.16 – 7.18 (m, 1H), 7.47 – 7.51 (d, 1H), and 8.97 (s, 1H, D_2O exchangeable). MS m/z (M^++1): 480.9

The following compound was prepared according to the procedure given in the Example 12

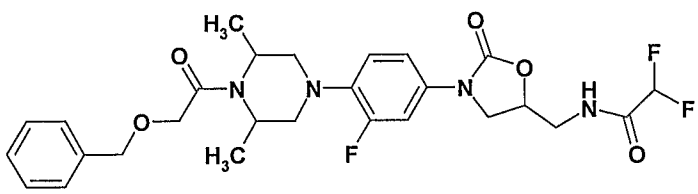
Example	Structure	Analytical Data
13		^{1}H-NMR (DMSO-d_6): δ 2.98 – 3.04 (m, 4H), 3.5 – 3.53 (t, 2H), 3.50 – 3.53 (m, 1H), 3.72 – 3.76 (m, 2H), 3.96 (s, 3H), 4.09 – 4.14 (m, 3H), 4.76 – 4.78 (m, 1H), 6.12 - 6.38 (m, 1H), 7.07 – 7.12 (m, 1H), 7.16 – 7.19 (m, 1H), 7.48 – 7.51 (d, 1H), 9.17 (s, 1H, D_2O exchangeable). MS m/z: 447.1(M^++1).
14		^{1}H-NMR (DMSO-d_6): δ 1.29 - 1.3 (m, 6H), 2.97 - 3.03 (m, 4H), 3.51 - 3.53 (m, 2H), 3.73 - 3.76 (m, 3H), 3.84 – 4.14 (m, 3H), 4.78 – 4.79 (m, 1H), 5.46 – 5.49 (m, 1H), 6.12 – 6.39 (m, 1H). 7.12 – 7.13 (m, 1H), 7.16 – 7.17 (m, 1H), 7.47 – 7.52 (m, 1H), 9.16 – 9.19 (m, 1H, D_2O exchangeable). MS m/z: 475.1(M^++1).

15		^{1}H-NMR (DMSO-d_6): δ 0.9 - 0.93 (t, 3H), 1.35 – 1.41 (m, 2H), 1.65 – 1.69 (m, 2H), 3.73 - 3.76 (m, 3H), 2.99 – 3.03 (m, 4H), 3.49 – 3.51 (m, 2H), 3.74 - 3.75 (m, 1H), 3.85 – 3.86 (m, 2H), 4.11 – 4.13 (m, 3H), 4.39 – 4.42 (m, 2H), 4.77 – 4.8 (m, 1H), 6.09 – 6.36 (t, 1H), 7.08 – 7.19 (m, 2H), 7.48 – 7.51 (m, 1H), 9.16 – 9.19 (m, 1H, D_2O exchangeable). MS m/z: 489.1(M^++1).
16		^{1}H-NMR (DMSO-d_6): δ 0.92 - 0.96 (t, 3H), 1.68 – 1.73 (m, 2H), 2.99 – 3.04 (m, 4H), 3.50 - 3.51 (m, 2H), 3.74 - 3.75 (m, 1H), 3.86 – 3.87 (m, 2H), 4.09 – 4.14 (m, 3H), 4.34 – 4.38 (m, 2H), 4.77 – 4.8 (m, 1H),
		6.09 – 6.23 (t, 1H), 7.10 – 7.12 (m, 1H), 7.16 – 7.19 (m, 1H), 7.48 – 7.52 (m, 1H), 9.16 – 9.19 (m, 1H, D_2O exchangeable). MS m/z: 475.1(M^++1).
17		^{1}H-NMR (DMSO-d_6): δ 1.27 – 1.31 (t, 3H), 2.98 – 3.03 (m, 4H), 3.52 - 3.53 (m, 2H), 3.71 – 3.73 (m, 1H), 3.86 – 3.87 (m, 2H), 4.10 – 4.14 (m, 3H), 4.43 – 4.48 (m, 2H), 4.77 – 4.81 (m, 1H), 6.49 (s, 1H), 7.07 – 7.12 (m, 1H), 7.16 – 7.18 (m, 1H), 7.48 – 7.52 (m, 1H), 8.98 - 8.99 (m, 1H, D_2O exchangeable). MS m/z: 493 (M^+).

18		^{1}H-NMR (DMSO-d_6): δ 0.90 – 0.93 (t, 3H), 1.35 – 1.41 (m, 2H), 1.65 – 1.69 (m, 2H), 2.98 – 3.03 (m, 4H), 3.51 - 3.53 (m, 2H), 3.70 – 3.71 (m, 1H), 3.85 – 3.86 (m, 2H), 4.10 – 4.14 (m, 3H), 4.39 – 4.42 (m, 2H), 4.78 – 4.79 (m, 1H), 6.49 (s, 1H), 7.07 – 7.12 (m, 1H), 7.15 – 7.18 (m, 1H), 7.48 – 7.52 (m, 1H), 8.97 - 8.99 (m, 1H, D_2O exchangeable). MS m/z: 521.1 (M^+).
19		^{1}H-NMR (DMSO-d_6): δ 1.29 – 1.30 (d, 6H), 2.97 – 3.03 (m, 4H), 3.51 - 3.53 (m, 2H), 3.69 – 3.72 (m, 1H), 3.84 – 3.85 (m, 2H), 4.10 – 4.14 (m, 3H), 4.78 – 4.79 (m, 1H), 5.46 – 5.49 (m, 1H), 6.48 (s, 1H), 7.07 – 7.12 (m, 2H), 7.47 – 7.52 (m, 1H), 8.96 - 8.99 (m, 1H, D_2O exchangeable). MS m/z: 507.1(M^+).

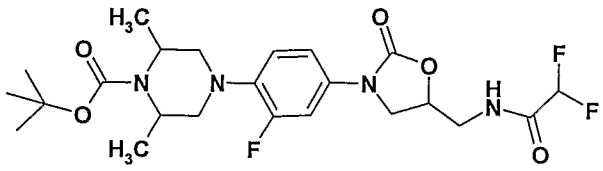
Example 20

Synthesis of 2,2-difluoro-*N*-({3-[3-fluoro-4-{(3,5-dimethyl-4-[(benzyloxy) acetyl]piperazin-1-yl}phenyl)]-2-oxo-1,3-oxazolidin-5(*S*)-yl}methyl)acetamide



Step I

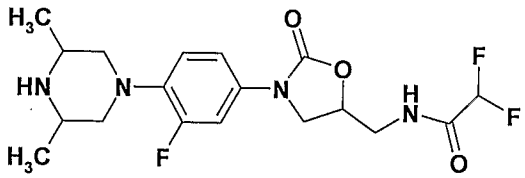
Synthesis of *tert* butyl 4-[4-(5(*S*)-{[(difluoroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl]-3,5-dimethylpiperazine-1-carboxylate



To a solution of difluoroacetic acid (0.45ml, 7.1mmol) in N,N-dimethylformamide (5ml) added 1-hydroxybenzotriazole (0.64g, 4.7mmol) and followed by 1-(3-dimethylaminopropyl)-3-ethylcarbodimide hydrochloride (3g, 15.6mmol) at 0 °C under stirring and continued for 45 minutes. Then to the resulted reaction mass added solution of *tert* butyl 4-{4-[5(*S*)-(aminomethyl)-2-oxo-1,3-oxazolidin-3-yl]-2-fluorophenyl}-3,5-dimethylpiperazine-1-carboxylate (2g, 4.7mmol) with N, N-diisopropylethyl amine (1.7ml, 9.8mmol) in dimethylformamide (5ml) at 0 °C under stirring. After 1 hour the reaction mixture was slowly raised to 37 °C and continued further until completion of the reaction confirmed by TLC using ethyl acetate:hexane (1:1) solvent system. Then the resulted reaction was poured on to the ice-water mixture (200ml) and the solid thus obtained was extracted with ethyl acetate (200ml) and finally the organic layer was washed with water (100ml). The resulted organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuo to yield the crude product (2.2 g). It was used in the step-II without further purification.

Step II:

Synthesis of 2,2-difluoro-*N*-({3-[3-fluoro-4-(3,5-dimethylpiperazin-1-yl) phenyl]-2-oxo-1,3-oxazolidin-5(*S*)-yl}methyl)acetamide

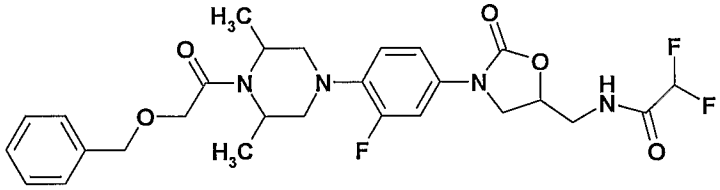


To the solution of *tert* butyl 4-[4-(5(*S*)-{[(difluoroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl]-3,5-dimethylpiperazine-1-carboxylate (0.7g, 1.3mmol, obtained in the Example 20, step-I) in dichloromethane (2ml) was added trifluoroacetic acid (0.46ml, 5.6mmol) at 0 °C under stirring. After 1hr of stirring at this condition the reaction mixture was allowed to warm to 37 °C and stirred for until

completion of the reaction, which was confirmed by performing TLC using ethyl acetate:hexane (8:2) as solvent system. Then the resulted reaction mass was concentrated to dryness under vacuo to yield the crude sticky product which was further washed with diethylether (20ml) to afford a free solid (0.5g, 90% yield).

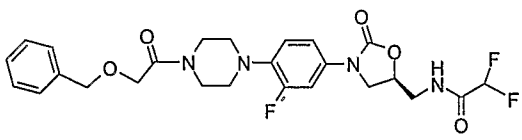
Step III:

Synthesis of 2,2-difluoro-(*S*)-*N*-({3-[3-fluoro-4-{(3,5-dimethyl-4-[(benzyloxy) acetyl]piperazin-1-yl}phenyl)]-2-oxo-1,3-oxazolidin-5(*S*)-yl} methyl)acetamide



A solution of 2,2-difluoro-*N*-({3-[3-fluoro-4-(3,5-dimethylpiperazin-1-yl)phenyl]-2-oxo-1,3-oxazolidin-5(*S*)-yl}methyl)acetamide (0.5g, 1.25mmol, obtained in the Example 20, step-II) in dichloromethane (1ml), was added triethylamine (0.5ml, 3.7mmol) and benzyloxyacetylchloride (0.27ml, 1.7mmol) under stirring at 0 °C. After 1hr the reaction was allowed warm to 37 °C and stirred for 24 hours. On completion of the reaction the resulted reaction mass was poured onto water (50ml) and extracted with dichloromethane (100ml). The organic layer was washed with brine solution (50ml) and dried over anhydrous Na_2SO_4, then concentrated under vacuo to yield the crude product. The resulted crude product was purified by flash chromatography using ethyl acetate:hexane mixture as an eluent to yield title compound (0.42g, 60 % yield, purity 92.45% by HPLC). ^{1}H-NMR (DMSO-d_6): δ 3.19 (s, 4H), 3.73 – 3.54 (m, 3H), 4.05 – 4.1 (m, 5H), 4.83 (s, 1H), 5.94 (s, 1H), 6.91 – 6.95 (m, 2H), 7.08 – 7.13 (m, 2H), 7.24 (s, 1H), 7.3 – 7.49 (m, 1H), 7.91 (s, 1H). MS m/z: 549.2 (M^++1).

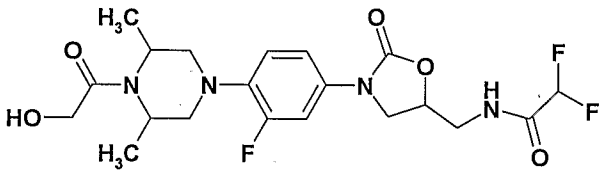
The following compound was prepared according to the procedure given in the Example 20

Example	Structure	Analytical Data
21		^{1}H-NMR (DMSO-d_6): δ 2.94 – 2.95 (s, 4H), 3.42 – 3.55 (m, 7H), 3.74 - 3.76 (m, 1H), 4.11 – 4.12 (m, 1H), 4.24 (s, 2H), 4.52 (s, 2H),

		4.78 – 4.79 (m, 1H),
		6.12 – 6.24 (t, 1H), 7.06 – 7.08 (m, 1H), 7.15 – 7.16 (m, 1H), 7.29 – 7.31 (m, 1H), 7.35 – 7.36 (m, 3H), 7.46 – 7.50 (m, 1H), 9.16 – 9.19 (m, 1H, D_2O exchangeable). MS m/z: 521.2(M^++1).

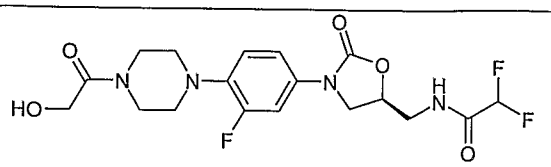
Example 22

Synthesis of 2,2-difluoro-*N*-({3-[3-fluoro-4-(3,5-dimethyl-4-glycoloylpiperazin-1-yl)phenyl]-2-oxo-1,3-oxazolidin-5(*S*)-yl} methyl) acetamide



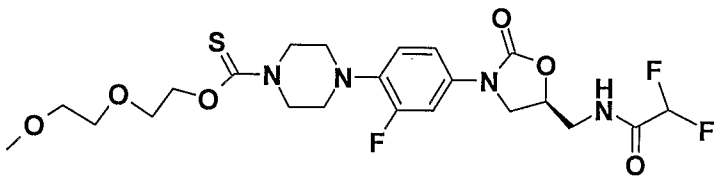
Dry palladium carbon (0.05g) was added to the solution of 2,2-difluoro-*N*-({3-[3-fluoro-4-{(3,5-dimethyl-4-[(benzyloxy)acetyl]piperazin-1-yl}phenyl)]-2-oxo-1,3-oxazolidin-5(*S*)-yl}methyl)acetamide (0.2g, 0.3mmol, obtained according to the procedure described in the example 20) in methanol:ethyl acetate (1:1 mixture, 10ml) with vigorous shaking. The resulted reaction mixture was kept in parshaker under hydrogen pressure of 80 psi and continued for 36 hours, then the completion of the reaction was confirmed by TLC using solvent system (ethyl acetate:hexane, 8:2). The resulted reaction mass was filtered using celite-545 bed and filtrate was concentrated under vacuo to yield desired compound (0.1g, 61% yield, purity 92.73% by HPLC). ^{1}H-NMR (DMSO-d_6): δ2.98 – 3.03 (m, 4H), 3.52 – 3.54 (t, 2H), 3.69 – 3.72 (m, 1H), 3.83 – 3.86 (m, 2H), 3.96 (s, 3H), 4.09 – 4.14 (m, 3H), 4.76 – 4.8 (m, 1H), 6.48 (s, 1H), 7.06 – 7.11 (m, 1H), 7.16 – 7.18 (m, 1H), 7.47 – 7.51 (d, 1H), 8.97 (s, 1H, D_2O exchangeable). MS m/z: 459.2(M^++1).

The following compound was prepared according to the procedure given in the Example 22

Example	Structure	Analytical Data
23		^{1}H-NMR (DMSO-d_6): δ 2.95 (br.s, 4H), 3.51 - 3.53 (m, 4H), 3.62 (s, 2H), 3.73 – 3. 77(m, 1H), 4.10 – 4.13 (m, 3H), 4.62 – 4.65 (m, 1H), 4.77 – 4.8 (m, 1H), 6.12 – 6.39 (t, 1H), 7.05 –7.1(m, 1H), 7.16 – 7.19 (m, 1H), 7.47 – 7.51 (m, 1H), 9.15 – 9.18 (m, 1H, D_2O exchangeable). MS m/z: 431.1(M^++1).

Example 24

Synthesis of O-[2-(2-methoxyethoxy)ethyl]-4-[4-(5*S*)-{[(difluoroacetyl) amino]methyl}-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl] piperazine-1-carbothioate

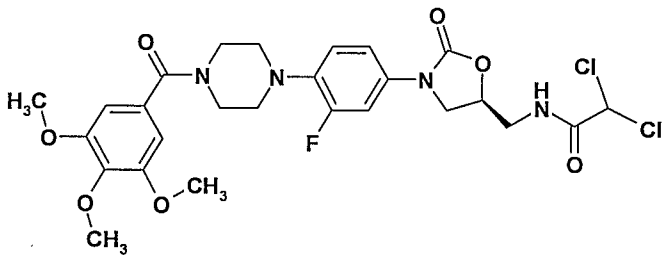


To a solution of 1, 1'-thiocarbonyl diimidazole (1.45g, 8.17mmol) in tetrahydrofuran (25ml) at 0 °C, 2-(2-methoxyethoxy)ethanol (0.96ml, 8.17mmol) was added dropwise for five minutes. This reaction mixture was allowed to stir at room temperature for 4 hours. Subsequently the resulting solution was added to a suspension of 2,2-difluoro-*N*-{[3-(3-fluoro-4-piperazin-1-ylphenyl)-2-oxo-1,3-oxazolidin-5(*S*)-yl]methyl}acetamide (0.3 g, 8.17 mmol) (prepared according to the procedure described in the example 12, step-II from *tert* butyl 4-[4-(5(*S*)-{[(difluoroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl]-piperazine-1-carboxylate) in tetrahydrofuran (25ml), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (0.82ml, 8.17mmol) and triethylamine (1.13ml, 8.17mmol) under stirring. The resulted reaction mass was stirred until completion of the reaction as confirmed by TLC after 15 hours of stirring. The reaction mass was poured on to the water and then

the product was extracted with ethyl acetate. The organic layer was separated, dried over anhydrous Na_2SO_4 and the solvent was removed under vacuum. The product was purified by column chromatography using ethyl acetate and hexane mixture (35:65) as an eluent to afford the title compound (0.055g, yield 1.25%). ^{1}H-NMR (DMSO-d_6): δ 2.99 - 3.04 (m, 4H), 3.23 - 3.24 (m, 5H), 3.43 – 3.46 (m, 2H), 3.55 – 3.57 (m, 4H), 3.71 – 3.72 (m, 3H), 3.87-3.88 (m, 2H), 4.12 – 4.14 (m, 3H), 4.5 – 4.52 (m, 2H), 4.77- 4.78 (m, 1H), 6.12 – 6.38 (t, 1H), 7.1 – 7.17 (m, 2H), 7.47 – 7.52 (d, 1H), 9.16 – 9.19 (m, 1H, D_2O exchangeable). Mass (m/z): 535.2(M^++1).

Example 25

Synthesis of 2,2-dichloro-*N*-({3-[3-fluoro-4-(4-(3,4,5-trimethoxybenzoyl) piperazin-1-yl}phenyl)]-2-oxo-1,3-oxazolidin-5-(*S*)-yl} methyl) acetamide



To a solution of 2,2-dichloro-*N*-{[3-(3-fluoro-4-piperazin-1-ylphenyl)-2-oxo-1,3-oxazolidin-5(*S*)-yl]methyl}acetamide (0.2g, 0.5mmol) (prepared according to the step II procedure described in the example 12) in N,N-dimethylformamide (15 ml), 3,4,5-trimethoxybenzoic acid (0.15g, 0.75mmol), 1-hydroxybenztriazole hydrate (HOBt) (0.027g, 0.2mmol), 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC) (0.38g, 2mmol) and triethylamine (0.3ml, 2mmol) were added under stirring. The resulted reaction mass was stirred until completion of the reaction as confirmed by TLC after 15 hours of stirring. The reaction mass was poured on to the water and then the product was extracted with ethyl acetate. The organic layer was separated, dried over anhydrous Na_2SO_4 and the solvent was removed under vacuum. The product was purified by column chromatography using methanol and dichloromethane mixture as a eluent to afford the title compound (0.14g, yield 47.8%). ^{1}H-NMR ($CDCl_3$): δ 3.07 (bs, 4H), 3.7 – 3.78 (m, 4H), 3.87 – 3.88 (m, 10H), 4.05 – 4.1(m, 1H), 4.82 – 4.84 (m, 1H), 5.94 (s, 1H), 6.66 (s, 2H), 6.9 – 6.95 (m, 1H), 7.02 – 7.1 (m, 2H), 7.42 – 7.46 (m, 1H). Mass (m/z): 599.1(M^+).

Anti-microbial Activity

The compounds of the present invention showed *in vitro* antibacterial activity when tested by the Agar Dilution Method as specified in documents published by the National Committee for Clinical Laboratory Standards (NCCLS), USA (now CLSI).

Briefly, the compounds of the invention were weighed, dissolved in dimethyl sulfoxide (DMSO), serially two fold diluted in the same solvent and then incorporated into molten Mueller Hinton Agar in a petridish before solidification, with each petridish containing a different concentration of a compound.

The bacterial inoculum was prepared by picking 3 to 5 well isolated bacterial colonies with the same morphological appearance from an 18-24 hours old culture with an inoculating loop, then transferring the growth to a tube containing 3 mL of normal saline and adjusting the turbidity of the saline suspension to 0.5 McFarland Turbidity Standard equivalent to a bacterial population of 1.5×10^8 colony forming units (CFU) per mL of the suspension. The suspension was diluted 1:10 in saline (i.e. 0.5 mL suspension + 4.5 mL saline) to get a bacterial population of 1.5×10^7.CFU/mL as inoculum.

The bacterial inoculum prepared in the above manner was inoculated onto petri dishes containing Mueller Hinton Agar which had earlier been incorporated with different dilutions of the compounds of invention by a Multipoint Inoculator with each inoculum spot containing approximately 1×10^4 colony forming units (CFU) of bacteria.

The inoculated petridishes were incubated at 35°C in an ambient atmosphere for 16-20 hours. Petridishes containing different concentrations of Vancomycin and Oxacillin and inoculated with *Staphylococcus aureus*, Coagulase Negative Staphylococci and Enterococci were incubated for 24 hours.

The petridishes after incubation were placed on a dark non-reflecting surface and the Minimum Inhibitory Concentration (MIC) was recorded as the concentration, which showed no growth of the inoculated culture.

1) *S. aureus - Staphylococus aureus*

2) *S. epidermidis - Staphylococcus epidermidis*

3) *E. faecium - Enterococcus faecium*

4) *E. faecalis - Enterococcus faecalis*

5) *M. catarrhalis - Moraxella catarrhalis*

ATCC – American Type Culture Collection

MRO - Microbial Resource Orchid

The following minimum inhibitory concentrations (μg/mL) were obtained for representative compounds of the invention which are given in the Table I and Table II:

Table I:

Minimum Inhibitory Concentration (MIC in μg/mL)

Organism	Example No.						
	Ex-1	Ex-5	Ex-7	Ex-9	Ex-10	Ex-11	Ex-12
S.aureus MRO 00013	8	8	8	4	2	8	2
S.aureus MRO 00055	8	8	8	4	2	8	2
S.epidermidis MRO 02046	4	8	2	2	2	8	0.5
S.aureus MRO 00001	4	8	4	2	1	4	1
S.aureus MRO 00003	4	8	4	4	2	8	1
S.aureus MRO 00030	4	8	4	4	1	8	1
S.aureus MRO 00048	4	8	4	2	1	4	0.5
S.aureus MRO 00059	4	8	4	4	1	8	1
E.faecium ATCC 700221	2	8	2	2	1	4	1
E.faecalis ATCC 51299	4	8	2	2	1	4	1
E.faecalis ATCC 29212	4	8	4	4	1	8	1
S.aureus ATCC 29213	4	8	4	4	2	8	1
S.aureus ATCC 43300	4	8	4	4	1	8	1
M.catarrhalis ATCC 43617	16	16	16	16	4	8	2
M.catarrhalis ATCC 43627	16	>16	16	>16	4	16	2
M.catarrhalis ATCC 43628	16	16	16	16	4	16	2

Table II:
Minimum Inhibitory Concentration (MIC in μg/mL)

Organism	Example No.					
	Ex-13	Ex-14	Ex-21	Ex-23	Ex-24	Ex-25
S.aureus MRO 00013	2	8	4	2	8	8
S.aureus MRO 00055	2	8	4	2	8	8
S.epidermidis MRO 02046	1	4	2	1	4	4
S.aureus MRO 00001	1	4	4	1	8	8
S.aureus MRO 00003	2	4	4	2	8	8
S.aureus MRO 00030	2	8	4	2	8	8
S.aureus MRO 00048	1	4	2	1	4	4
S.aureus MRO 00059	1	4	4	2	8	8
E.faecium ATCC 700221	1	4	2	1	4	4
E.faecalis ATCC 51299	1	4	2	1	4	4
E.faecalis ATCC 29212	1	4	2	1	4	4
S.aureus ATCC 29213	2	8	4	2	8	8
S.aureus ATCC 43300	2	4	4	2	8	8
M.catarrhalis ATCC 43617	4	>16	8	2	16	-
M.catarrhalis ATCC 43627	4	>16	8	8	>16	-
M.catarrhalis ATCC 43628	4	>16	8	8	>16	-

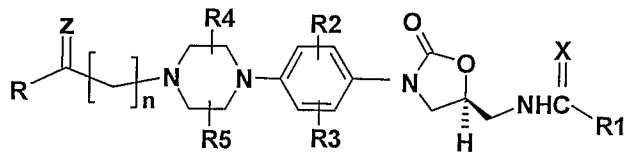
***In vivo* efficacy studies:**

Therapeutic effects were assessed in mice infected with Oxacillin resistant *S. aureus* ATCC 43300. Swiss albino mice, 20 □ 2 g, from in-house breeding facility were challenged by the intraperitoneal injection of bacterial suspensions in 0.5 ml of hog gastric mucin (usu.100 x 50% lethal dose). Four or five dose levels of the compound of invention was administered orally at 0.75 h and 4 h post infection. All the untreated control animals died within 36 to 48 h of infection. In each experiment, in-house Linezolid was used as a comparator in four doses. Median (50%) effective dose (ED_{50}) were determined by applying the Reed and Muench's method of the 7-day survival ratios.

ED_{50} of the Example 23 against ORSA is 16.31 mg/kg b.w.

We claim:

1. Novel compounds of the formula (I),



(I)

their derivatives, analogs, tautomeric forms, stereoisomers, polymorphs, solvates, pharmaceutically acceptable salts and compositions, metabolites and prodrugs thereof, wherein, X represents O or S;

R_1 represents substituted and unsubstituted groups selected from hydrogen, (C_1-C_4) alkyl groups comprising methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl and *t*-butyl; haloalkyl groups comprising dichloromethyl, difluoromethyl, trichloromethyl and trifluoromethyl; O-alkyl, S- alkyl, NH_2, NHalkyl or $N(alkyl)_2$, O-het, S-het or -NH-het, wherein het is a C-linked five or six membered saturated or unsaturated heterocyclic ring having 1, 2 or 3 hetero atoms selected from the group consisting of oxygen , sulfur and nitrogen, which is optionally fused to a benzene ring, comprising pyridyl, thienyl, furyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isooxazolyl, oxadiazolyl, triazolyl, thiadiazolyl, tetrazolyl, pyrimidinyl, pyrazinyl, pyridazinyl, benzopyranyl, indolyl, indolinyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, benzopyrrolyl, benzoxadiazolyl, benzothiadiazolyl, benzodioxolyl, quinolinyl, dihydroquinolinyl, tetrahydroquinolinyl, isoquinolinyl, dihydroisoquinolinyl and tetrahydroisoquinolinyl;

R_2 and R_3 represent substituted or unsubstituted groups selected from hydrogen, halogen atoms comprising fluorine, chlorine, bromine or iodine; hydroxy, (C_1-C_6)alkyl groups comprising methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl and t-butyl; (C_1-C_6)alkoxy groups comprising methoxy, ethoxy, n-propoxy and isopropoxy; haloalkyl groups comprising chloromethyl, chloroethyl, trifluoromethyl, trifluoroethyl, dichloromethyl and dichloroethyl;

R_4 and R_5 represent substituted or unsubstituted groups selected from hydrogen, cyano, nitro, amino, hydroxy; halogen atoms comprising fluorine, chlorine, bromine or iodine; (C_1-C_4) alkyl groups comprising methyl, ethyl, n-propyl, isopropyl, n-butyl,

isobutyl and *t*-butyl; haloalkyl groups comprising chloromethyl, chloroethyl, trifluoromethyl, trifluoroethyl, dichloromethyl and dichloroethyl; (C_1-C_4)alkoxy groups comprising methoxy, ethoxy, n-propoxy and isopropoxy; (C_1-C_6)alkylthio groups comprising methylthio, ethylthio, n-propylthio and iso-propylthio; benzyl group, which is optionally with hydroxyl group;

R_6 represents substituted or unsubstituted groups selected from hydrogen, hydroxyl, cyano, substituted or unsubstituted linear or branched (C_1-C_4) alkyl groups or –O-alkyl groups comprising methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl and *t*-butyl; substituted or unsubstituted –O-(C_3–C_7) cycloalkyl, the cylcoalkyl groups comprising cyclopropyl, cyclobutyl and cyclopentyl; -O-aryl groups, in which the aryl groups comprising phenyl and naphthyl; -O-heteroaryl groups, in which heteraoaryl groups comprising pyridyl, thienyl, furyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isooxazolyl, oxadiazolyl, triazolyl, thiadiazolyl, tetrazolyl, pyrimidinyl, pyrazinyl, pyridazinyl, benzopyranyl, indolyl, indolinyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, benzopyrrolyl, benzoxadiazolyl, benzothiadiazolyl, benzodioxolyl, quinolinyl, dihydroquinolinyl, tetrahydroquinolinyl, isoquinolinyl, dihydroisoquinolinyl and tetrahydroisoquinolinyl; -O-heterocyclyl groups, in which heteraocyclyl groups comprising pyrrolidinyl, thiazolidinyl, oxazolidinyl, morpholinyl, thiomorpholinyl, piperidinyl and piperazinyl;

R_7 represents substituted and unsubstituted groups selected from hydrogen, halogen, hydroxy, substituted or unsubstituted groups selected from linear or branched (C_1-C_4)alkyl groups comprising methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl and *t*-butyl; (C_4-C_8)cycloalkyl groups comprising cyclobutyl, cyclopentyl and cyclohexyl; aryl groups comprising phenyl and naphthyl; aralkyl groups comprising phenylmethyl, phenylethyl, naphthylmethyl and naphthylethyl; amino group; aralkylamino groups comprising benzylamino; heteroaryl groups comprising pyridyl, thienyl, furyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isooxazolyl, oxadiazolyl, triazolyl, thiadiazolyl, tetrazolyl, pyrimidinyl, pyrazinyl, pyridazinyl, benzopyranyl, indolyl, indolinyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, benzopyrrolyl, benzoxadiazolyl, benzothiadiazolyl, benzodioxolyl, quinolinyl, dihydroquinolinyl, tetrahydroquinolinyl, isoquinolinyl, dihydroisoquinolinyl and tetrahydroisoquinolinyl; heterocyclyl groups comprising pyrrolidinyl, thiazolidinyl, oxazolidinyl, morpholinyl, thiomorpholinyl, piperidinyl and piperazinyl;

R_8 represents substituted or unsubstituted groups selected from hydrogen, halogen, hydroxyl, substituted or unsubstituted groups selected from linear or branched (C_1-C_4)alkyl groups comprising methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl and *t*-butyl; substituted or unsubstituted (C_3–C_7)cycloalkyl groups comprising cyclopropyl, cyclobutyl and cyclopentyl; aryl groups comprising phenyl and naphthyl; aralkyl groups comprising phenylmethyl, phenylethyl, naphthylmethyl and naphthylethyl; aralkyl groups; amino group; aralkylamino groups comprising benzylamino; aralkylamino group; heteroaryl groups comprising pyridyl, thienyl, furyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isooxazolyl, oxadiazolyl, triazolyl, thiadiazolyl, tetrazolyl, pyrimidinyl, pyrazinyl, pyridazinyl, benzopyranyl, indolyl, indolinyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, benzopyrrolyl, benzoxadiazolyl, benzothiadiazolyl, benzodioxolyl, quinolinyl, dihydroquinolinyl, tetrahydroquinolinyl, isoquinolinyl, dihydroisoquinolinyl and tetrahydroisoquinolinyl; heterocyclyl groups comprising pyrrolidinyl, thiazolidinyl, oxazolidinyl, morpholinyl, thiomorpholinyl, piperidinyl and piperazinyl;

R represents substituted or unsubstituted groups selected from hydrogen, halogen, cyano, nitro, amino, halogen, hydroxy, $-CH_2OH$, linear or branched (C_1-C_4)alkyl groups comprising methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl and t-butyl; -O-alkoxyalkyl groups comprising $-O-CH_2-O-CH_3$, $-O-(CH_2)_{1-3}-O-(CH_2)_{1-3}-O-CH_3$; $-O-CH_2-O-CH_2-R_8$; $-O-CH_2-R_7$; acyl groups comprising $-C(=O)CH_3$, $-C(=O)C_2H_5$ and benzoyl; alkylcarboxy groups; alkylcarboxyalkyl groups; (C_1-C_{10})alkoxy groups comprising methoxy, ethoxy, n-propoxy, isopropoxy and butoxy; aryl groups comprising phenyl and naphthyl; aralkyl groups comprising phenylmethyl, phenylethyl, naphthylmethyl and naphthylethyl; the amino group; aralkylamino groups comprising benzylamino; heteroaryl groups comprising pyridyl, thienyl, furyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isooxazolyl, oxadiazolyl, triazolyl, thiadiazolyl, tetrazolyl, pyrimidinyl, pyrazinyl, pyridazinyl, benzopyranyl, indolyl, indolinyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, benzopyrrolyl, benzoxadiazolyl, benzothiadiazolyl, benzodioxolyl, quinolinyl, dihydroquinolinyl, tetrahydroquinolinyl, isoquinolinyl, dihydroisoquinolinyl and tetrahydroisoquinolinyl; heterocyclyl groups comprising pyrrolidinyl, thiazolidinyl, oxazolidinyl, morpholinyl, thiomorpholinyl, piperidinyl and piperazinyl;

Z is selected from O, S and NR_6;

n is an integer of 0-1, with the condition that when n is 1 then Z is not S, and when n is 0 then Z is S, X represents O, R represents $-OCH_2R_7$, -O-alkoxyalkyl, $-CH_2OCH_2-R_8$, $-CH_2OH$, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and R_1 represents substituted or unsubstituted haloalkyl. When n is 0 then Z is O, X represents O, R represents $-OCH_2R_7$, -O-alkoxyalkyl, $-CH_2OCH_2-R_8$, $-CH_2OH$, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and R_1 represents substituted or unsubstituted haloalkyl. When n is 0 then Z is N-R_6, X represents O, R represents $-OCH_2R_7$, -O-alkoxyalkyl, $-CH_2OCH_2-R_8$, $-CH_2OH$, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and R_1 represents substituted or unsubstituted haloalkyl;

L represents a suitable leaving group selected from fluoro, chloro, bromo, carboxylic hydroxyl groups and similar leaving groups;

Substituents on any of the groups represented by R, R_1, R_2, R_3, R_4, R_5, R_6, R_7 and R_8 are selected from halogen, hydroxy, formyl, nitro, cyano, azido, amino, alkyl, aryl, alkylamino, alkylaminocarbonyl, haloalkyl, acylamino, alkoxy, acyl and these substituents are as defined above.

2. A compound of formula (I), as claimed in claim 1, which is selected from a group consisting of:

3-{4-[4-(1-(4-Methoxyphenyl)ethanoneoxime-2-yl)piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methyl acetamide;

3-{4-[4-(1-Methylethanon-2yl)piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methyl acetamide;

3-{4-[4-(1-(1-Methyl)ethanoneoxime-2-yl)piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methyl acetamide;

3-{4-[4-(1-(4-Fluorophenyl)ethanon-2-yl)piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methyl acetamide;

3-{4-[4-(1-(4-Fluorophenyl)ethanoneoxime-2-yl)piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methyl acetamide;

3-{4-[4-(1-(3-Methoxyphenyl)ethanon-2-yl)piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methyl acetamide;

3-{4-[4-(1-(3-Methoxyphenyl)ethanoneoxime-2-yl)piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methyl acetamide;

3-{4-[4-(1-(4-Methylphenyl)ethanon-2-yl)piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methyl acetamide;

3-{4-[4-(1-(4-Methylphenyl)-ethanoneoxime-2-yl)piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-methyl acetamide;

3-{4-[4-(1-(4-Methoxyphenyl)ethanoneoxime-2-yl)piperazinyl]3-fluorophenyl} -2-oxo-1,3-oxazolidin-5(*S*)-methylthioacetamide;

3-{4-[4-(1-(4-Methoxyphenyl)ethanone-O-methyloxime-2-yl)piperazinyl]3-fluorophenyl}-2-oxo-1,3-oxazolidin-5(*S*)-ethylthioacetamide;

O-Methyl-4-[4-(5(*S*)-{[(dichloroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl]piperazine-1-carbothioate;

O-Methyl-4-[4-(5(*S*)-{[(difluoroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl]piperazine-1-carbothioate;

O-Isopropyl-4-[4-(5(*S*)-{[(difluoroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl]piperazine-1-carbothioate;

O-n-Butyl-4-[4-(5(*S*)-{[(difluoroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl]piperazine-1-carbothioate;

O-n-Propyl-4-[4-(5(*S*)-{[(difluoroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl]piperazine-1-carbothioate;

O-Ethyl-4-[4-(5(*S*)-{[(dichloroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl]piperazine-1-carbothioate;

O-n-Butyl-4-[4-(5(*S*)-{[(dichloroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl]piperazine-1-carbothioate;

O-Isopropyl-4-[4-(5(*S*)-{[(dichloroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl]piperazine-1-carbothioate;

2,2-Difluoro-*N*-({3-[3-fluoro-4-{(3,5-dimethyl-4-[(benzyloxy)acetyl]piperazin-1-yl}phenyl)]-2-oxo-1,3-oxazolidin-5(*S*)-yl}methyl)acetamide;

2,2-Difluoro-*N*-({3-[3-fluoro-4-{(4-[(benzyloxy)acetyl]piperazin-1-yl}phenyl)]-2-oxo-1,3-oxazolidin-5(*S*)-yl}methyl)acetamide;

2,2-Difluoro-*N*-({3-[3-fluoro-4-(3,5-dimethyl-4-glycoloylpiperazin-1-yl)phenyl]-2-oxo-1,3-oxazolidin-5(*S*)-yl}methyl)acetamide;

2,2-Difluoro-*N*-({3-[3-fluoro-4-(4-glycoloylpiperazin-1-yl)phenyl]-2-oxo-1,3-oxazolidin-5(*S*)-yl}methyl)acetamide;

O-[2-(2-Methoxyethoxy)ethyl]-4-[4-(5(*S*)-{[(difluoroacetyl)amino]methyl}-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl] piperazine-1-carbothioate and 2,2-Dichloro-*N*-({3-[3-fluoro-4-(4-(3,4,5-trimethoxybenzoyl)piperazin-1-yl}phenyl)]-2-oxo-1,3-oxazolidin-5-(*S*)-yl}methyl)acetamide.

3. A pharmaceutical composition comprising a compound of formula (I) as claimed in claim 1, or a pharmaceutically acceptable salt thereof as an active ingredient along with a pharmaceutically acceptable carrier, diluent, excipient or solvate.

4. A pharmaceutical composition as claimed in claim 3, wherein the amount of the compound of claim 1 in the composition is less than 70% by weight.

5. A pharmaceutical composition as claimed in claim 1, in the form of a tablet, capsule, powder, syrup, solution, aerosol or suspension.

6. A method of treating or preventing an infectious disorder in a human or animal, comprising administering an effective amount of a compound as claimed in the claim 1 or claim 2 or a composition of the claim 3, to the mammal in need thereof.

7. A method as claimed in claim 6, wherein, the infectious disorder is caused by bacteria.