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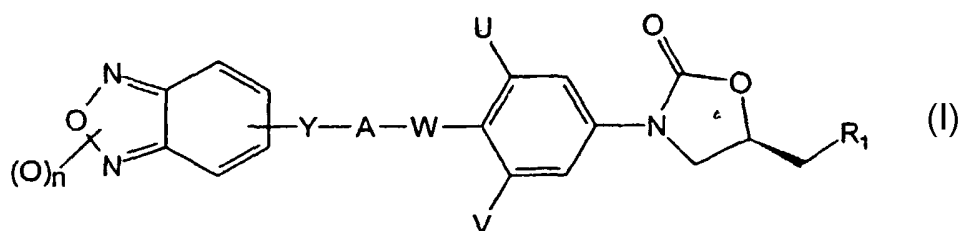
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(54) Title: OXAZOLIDINONE DERIVATIVES AS ANTIMICROBIALS



(57) Abstract: The present invention relates to substituted phenyl oxazolidinones and processes for preparing thereof. This invention also relates to pharmaceutical compositions comprising compounds of the present invention. Such compounds can be useful antimicrobial agents that can be particularly effective against a number of human and veterinary pathogens, including gram-positive aerobic bacteria (e.g., multiple-resistant staphylococci, streptococci and enterococci), anaerobic organisms (e.g., *Bacterioides* spp. and *Clostridia* spp. species), and acid-fast organisms (e.g., *Mycobacterium tuberculosis*, *Mycobacterium avium* and *Mycobacterium* spp.). Formula (I).

OXAZOLIDINONE DERIVATIVES AS ANTIMICROBIALS

Filed of the Invention

The present invention relates to substituted phenyl oxazolidinones and processes for preparing thereof. This invention also relates to pharmaceutical compositions comprising compounds of the present invention. Such compounds can be useful antimicrobial agents that can be particularly effective against a number of human and veterinary pathogens, including gram-positive aerobic bacteria (e.g., multiple-resistant staphylococci, streptococci and enterococci), anaerobic organisms (e.g., *Bacterioides spp.* and *Clostridia spp.* species), and acid-fast organisms (e.g., *Mycobacterium tuberculosis*, *Mycobacterium avium* and *Mycobacterium spp.*).

Background of the Invention

Increasing antibacterial resistance in Gram-positive bacteria has presented a formidable treatment problem. The *Enterococci*, although traditionally no virulent pathogens, have been shown, when associated with Vancomycin resistance, to have an attributable mortality of approximately 40 %. *Staphylococcus aureus*, the traditional pathogen of postoperative wounds, was reportedly resistant to Penicillin due to production of penicillinases. This resistance was overcome by the development of various penicillinase stable β lactams. However, the pathogen responded by synthesizing modified target penicillin binding protein- 2' leading to less affinity for β -lactam antibiotics and a phenotype known as Methicillin Resistant *S. aureus* (MRSA). Until recently, these strains were susceptible to Vancomycin, which in spite of its various drawbacks has become the drug of choice for MRSA infections. *Streptococcus pneumoniae* is a major pathogen causing pneumonia, sinusitis and meningitis. Until recently, *Streptococcus pneumoniae* was highly susceptible to penicillin, however different PBP 2' strains with different susceptibility to penicillin have been reported from across the globe.

Oxazolidinones are a new class of synthetic antimicrobial agents, which kill gram-positive pathogens by inhibiting a very early stage of protein synthesis. In particular, oxazolidinones inhibit the formation of ribosomal initiation complex involving 30S and

50S ribosomes leading to prevention of initiation complex formation. These compounds are generally active against pathogens resistant to other clinically useful antibiotics.

J. Med. Chem., (1998), 41, 3727-3735 discloses pyridine, diazine, triazine, heteroaromatic rings directly attached to the piperazinyl oxazolidinone core. *J. Org. Chem.*, (1999), 64, 6019-6022 and *J. Org. Chem.*, (2000), 65, 1144-1157. *Bioorg. Med. Chem. Lett.*, (2001), 11, 1829-1832 discloses oxazolidinone derivatives, which are active against gram positive strains including the resistant strains of *Staphylococcus* and *Enterococcus*. *J. Med. Chem.*, (1968), 11, 305-311 discloses the synthesis of various benzo-2,1,3-oxadiazoles and their N-oxides. *Org. Proc. Res. Dev.*, (2003), 7, 436-445 describes the synthesis of 5-bromobenzofurazan. *J. Cardiovasc. Pharmacol.*, (1982), 4, 344 discloses a new benzoxadiazolyl dihydropyridine derivative.

WO 04/056817 discloses substituted biaryl-oxazolidinyl derivatives said to be effective against Gram-positive and Gram-negative pathogens. WO 04/056818 discloses substituted biaryl-oxazolidinyl derivatives described as effective against Gram-positive and Gram-negative pathogens. WO 04/014392 discloses piperazinyl oxazolidinyl acetamide derivatives as antimicrobials. WO 03/008389 discloses substituted phenyl oxazolidinones, which are apparently useful antimicrobial agents, effective against a number of human and veterinary pathogens, including Gram-positive aerobic bacteria, for example, multiple-resistant *Staphylococci*, *Streptococci* and *Enterococci* as well as anaerobic organisms, for example, *Bactericides spp.* *Clostridium spp.* and acid-fast organisms, for example, *Mycobacterium tuberculosis*, *Mycobacterium avium* and *Mycobacterium spp.*

WO 03/007870 discloses oxazolidinone derivatives, which are reportedly useful antimicrobial agents, effective against human and veterinary pathogens. WO 03/072575 discloses 3-cyclyl-5-(nitrogen containing 5-membered ring) methyl oxazolidinones and their putative use as antimicrobials. WO 03/022824 discloses oxazolidinone and/or isoxazoline as antibacterial agents. WO 03/072553 discloses N-aryl-2-oxazolidinone-5-carboxamides and their derivatives and their use as antibacterial agents. WO 03/006447 discloses oxazolidinone compounds having thiocarbonyl functionality as antibacterial agents. WO 03/022824 discloses oxazolidinone and/or isoxazoline as antibacterial agents. WO 02/06278 discloses phenyl oxazolidinone derivatives as antimicrobial agents.

WO 01/94342 and U.S. Patent No. 6,689,779 disclose oxazolidinone derivatives having pyridine or pyrimidine moiety and a process for the preparation thereof. WO 01/80841 discloses use of thioamide oxazolidinones for the treatment of bone resorption and osteoporosis. WO 00/29396 discloses substituted phenyloxazolidinone derivatives for
5 producing antibacterial medicament for treating human beings and animals. WO 00/32599 discloses oxazolidinone compounds having thiocarbonyl functionality as antibacterial agents. WO 99/64416 discloses substituted oxazolidinyl derivatives as antimicrobials. WO 99/64417 discloses substituted oxazolidinyl derivatives as antimicrobials.

10 WO 98/01446 discloses 6-membered heteroaryl ring containing 2 or 3 ring nitrogen atoms, attached to the piperazinyl oxazolidinyl derivatives as antimicrobial agents. WO 98/01447 discloses pyridyl-piperazinyl oxazolidinyl derivatives as antimicrobial agents. WO 98/54161 and U.S. Patent No. 6,255,304 disclose oxazolidinone antibacterial agents having a thiocarbonyl functionality. WO 93/23384 discloses
15 substituted aryl and heterocyclylphenyl oxazolidinones that are reportedly useful antibacterial agents. WO 93/09103 discloses substituted aryl and heteroarylphenyl oxazolidinones that are reportedly useful antibacterial agents. EP 352 781 discloses phenyl-methyl and pyridinyl-methyl substituted oxazolidinones. U.S. Patent Nos. 5,547,950 and 5,700,799 disclose substituted aryl and heterocyclylphenyl oxazolidinones
20 that are reportedly useful antibacterial agents.

U.S. Patent No. 5,719,154 describes substituted or unsubstituted 2-pyrimidinyl, 4-pyrimidinyl, or 3-pyridazinyl rings directly attached to the piperazinyl oxazolidinyl core. U.S. Patent No. 5,736,545 discloses substituted piperazinyl oxazolidinyl derivatives as antimicrobial agents. U.S. Patent Nos. 5,565,571, 5,801,246, 5,756,732, 5,654,435, and
25 5,654,428 disclose substituted aryl and heteroaryl phenyloxazolidinones which are reportedly useful antibacterial agents.

Other references disclosing various phenyloxazolidinones include U.S. Patent Nos. 4,801,600 and 4,921,869; Gregory W.A., *et al.*, *J. Med. Chem.*, (1989); 32: 1673-81; Gregory W.A., *et al.*, *J. Med. Chem.*, (1990); 33: 2569-78; Wang C., *et al.*, *Tetrahedron*,
30 (1989); 45: 1323-26; Brittelli, *et al.*, *J. Med. Chem.*, (1992); 35: 1156; *Ann. Rep. Med. Chem.*, Vol 35, pp 135-144; *Bioorg. Med. Chem. Lett.*, (1999); 9: 2679-84; Antibacterial

& Antifungal Drug Discovery & Development Summit, Strategic Research Institute, June 28-29, 2001, Amsterdam, The Netherlands; Posters No. 1822, 1823, 1824, 1825, 1826, 1827, 1828, 1829, 1830, 1831, 1832, 1833 and 1834, 40th Interscience Conference on Antimicrobial Agents and Chemotherapy, Sept 17-20, (2000), Toronto, Canada; and
 5 Posters No 1023, 1040, 1041, 1042, 1043, 1044, 1045, 1046, 1047, 1048, 1049, 1050, and 1051, 41st Interscience Conference on Antimicrobial Agents and Chemotherapy, December 16-19, (2001), Chicago, USA.

However, in view of the above, there remains a need for novel oxazolidinones and particular, novel oxazolidinones that can be effective antimicrobials.

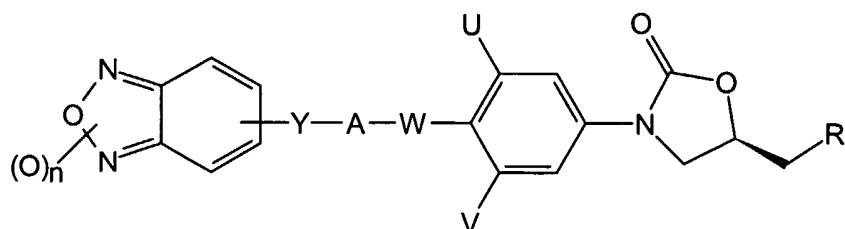
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Summary of the Invention

Oxazolidinone derivatives have good activity against multiple resistant gram-positive pathogens, for example, methicilline resistant *Staphylococcus aureus* (MRSA), Vancomycin-resistant *Enterococci* (VRE) and *Streptococcus pneumonia*. Such
 15 oxazolidinone derivatives have activity against multiple drug resistant tuberculosis (MDR-TB) strain, while others have significant activity against important anaerobic bacteria.

Provided are benzoxadiazole phenyloxazolidinones derivatives exhibiting antibacterial activity against Gram-positive pathogens, for example, MRSA, VRE and PRSP; against MDR-TB and MAI strains, Gram-negative pathogens, for example,
 20 *Moraxella catarrhalis* and *Haemophilus influenza*. Such derivatives provide safe and effective treatment of bacterial infections.

Thus in one aspect, provided are compounds of Formula I,



Formula I

or its pharmaceutically acceptable salts, pharmaceutically acceptable solvates, enantiomers, diastereomers or polymorphs, wherein

R_1 can be OR_j , SR_j , NHY_1R_f , NR_fR_q , heterocyclyl or heteroaryl; wherein

R_j can be hydrogen, alkyl, alkenyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, heteroarylalkyl or heterocyclylalkyl;

Y_1 can be $(C=O)$, $(C=S)$ or SO_2

R_f can be hydrogen, alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl or heterocyclylalkyl; and

R_q can be hydrogen, alkyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl or heterocyclyl;

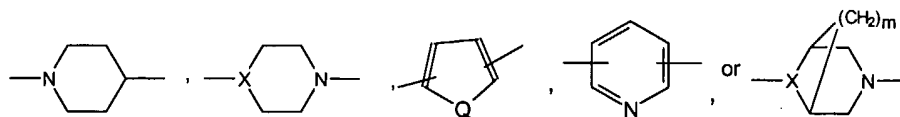
U and V each can independently be hydrogen, lower (C_{1-6}) alkyl or halogen;

Y and W each can independently be no atom, O, CH_2 , CO, CH_2NH , $-NHCH_2$, $-CH_2NHCH_2$, $-CH_2-N(R_{11})CH_2-$, $CH_2(R_e)N-$, $CH(R_{11})$, S, $CH_2(CO)$, NH, NR_e , $(CO)CH_2$, $N(R_e)CON(R_e)$, $N(R_e)C(=S)N(R_e)$, SO_2 or SO, wherein

R_{11} can be optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl or heteroaryl; and

R_e can be hydrogen, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl or heteroaryl; and

A can be no group or can be selected from;



wherein

X can be CH, CH-S, CH-O or N;

Q can be O, N or S;

n can be an integer 0-1; and

m can be an integer from 0-2.

In another aspect, provided are compounds selected from:

- N*-({(5*S*)-3-[4-(2,1,3-benzoxadiazol-5-yl)-3-fluorophenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl}acetamide (Compound No.1);
- 5 *N*-({(5*S*)-3-[4-(2,1,3-benzoxadiazol-5-yl)-3,5-difluorophenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl}acetamide (Compound No. 2);
- (5*R*)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-fluorophenyl}-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one (Compound No. 3);
- (5*R*)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-fluorophenyl}-5-(2*H*-1,2,3-triazol-2-ylmethyl)-1,3-oxazolidin-2-one (Compound No. 4);
- 10 (5*R*)-3-(4-{[1-(2,1,3-benzoxadiazol-5-yl)piperidin-4-yl]oxy}-3-fluorophenyl)-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one (Compound No. 5);
- (5*S*)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-fluorophenyl}-5-[(isoxazol-3-ylamino)methyl]-1,3-oxazolidin-2-one (Compound No. 6);
- 15 (5*S*)-3-(4-{[1-(2,1,3-benzoxadiazol-5-yl)piperidin-4-yl]oxy}-3-fluorophenyl)-5-[(isoxazol-3-ylamino)methyl]-1,3-oxazolidin-2-one (Compound No. 7);
- (5*S*)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-fluorophenyl}-5-(isoxazol-3-ylmethyl)-1,3-oxazolidin-2-one (Compound No. 8);
- (5*R*)-3-(4-{[1-(2,1,3-benzoxadiazol-5-yl)piperidin-4-yl]oxy}-3-fluorophenyl)-5-[(isoxazol-3-yloxy)methyl]-1,3-oxazolidin-2-one (Compound No. 9);
- 20 *N*-{[(5*S*)-3-(3-fluoro-4-{4-[(oxido-2,1,3-benzoxadiazol-5-yl)methyl] piperazin-1-yl}phenyl)-2-oxo-1,3-oxazolidin-5-yl)methyl}acetamide (Compound No. 10);
- N*-[[(5*S*)-3-{4-[4-(2,1,3-benzoxadiazol-5-ylmethyl)piperazin-1-yl]-3-fluorophenyl}-2-oxo-1,3-oxazolidin-5-yl)methyl]acetamide (Compound No. 11);
- 25 *N*-{[(5*S*)-3-(4-{[1-(2,1,3-benzoxadiazol-5-yl)piperidin-4-yl]oxy}-3-fluorophenyl)-2-oxo-1,3-oxazolidin-5-yl)methyl}acetamide (Compound No. 12);
- N*-[[(5*S*)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-fluorophenyl}-2-oxo-1,3-oxazolidin-5-yl)methyl]acetamide (Compound No. 13);

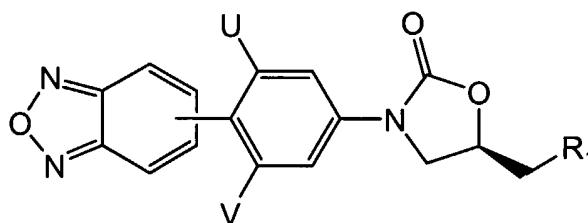
N-[(((5*S*)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3,5-difluorophenyl}-2-oxo-1,3-oxazolidin-5-yl)methyl]acetamide (Compound No. 14),

or pharmaceutically acceptable salts and solvates thereof.

In another aspect, provided are pharmaceutical compositions comprising a
 5 pharmaceutically effective amount of one or more compounds described herein or their pharmaceutically acceptable salts thereof and one or more pharmaceutical acceptable carriers.

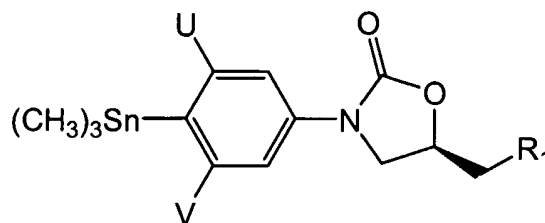
In yet another aspect, provided herein are methods of treating or preventing
 microbial infections in a mammal comprising administering to the mammal one or more
 10 compounds described herein. Such methods may include one or more of the following embodiments. For example, the microbial infections can be caused by Gram-positive or Gram-negative bacteria. Gram-positive bacteria can be *Staphylococcus spp.*, *Streptococcus spp.*, *Bacillus spp.*, *Corynebacterium spp.*, *Clostridia spp.*, *Peptostreptococcus spp.*, *Listeria spp.* or *Legionella spp.* The microbial infections can be
 15 aerobic or anaerobic bacterial infections.

In another aspect, provided are processes for preparing a compound of Formula IV



Formula IV

or its pharmaceutically acceptable salts, pharmaceutically acceptable solvates, enantiomers, diastereomers or polymorphs, comprising reacting a compound of Formula II

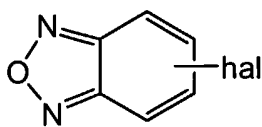


Formula II

20

with a compound of Formula III

8



Formula III

to form a compound of Formula IV,

wherein,

U and V each can independently be hydrogen, lower (C₁₋₆)alkyl or halogen;

5 **R₁** can be OR_j, SR_j, NHY₁R_f, NR_fR_q, heterocyclyl or heteroaryl; wherein

R_j can be hydrogen, alkyl, alkenyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, heteroarylalkyl or heterocyclalkyl;

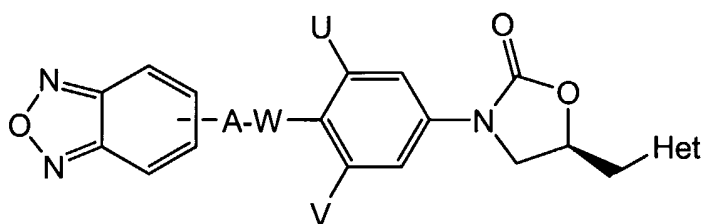
Y₁ can be (C=O), (C=S) or SO₂;

10 **R_f** can be hydrogen, alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl or heterocyclalkyl;

R_q can be hydrogen, alkyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl or heterocyclalkyl.

Such processes can include one or more of the following embodiments. For example, the compound of Formula II can be reacted with the compound of Formula III in the presence of one or more bases, for example, triethylamine, 4-dimethylamino pyridine, N-methyl morpholine or mixtures thereof. The compound of Formula II can also be reacted with the compound of Formula III in the presence of one or more catalysts, for example, palladium catalysts selected from dichlorobis(triphenylphosphine) palladium (II), tetrakis(triphenylphosphine) palladium (0) or mixtures thereof.

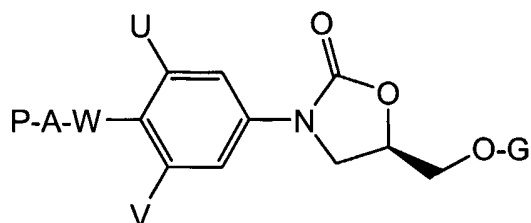
20 In another aspect, also provided are processes for preparing a compound of Formula IX



Formula IX

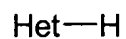
or its pharmaceutically acceptable salts, pharmaceutically acceptable solvates, enantiomers, diastereomers or polymorphs, comprising the steps of:

- a) reacting a compound of Formula V



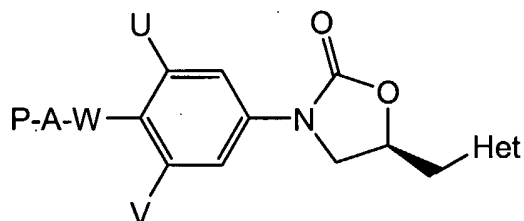
Formula V

- 5 with a compound of Formula VI



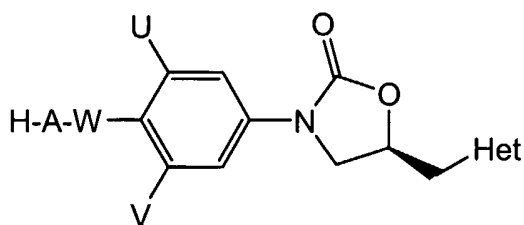
Formula VI

to form a compound of Formula VII;



Formula VII

- 10 b) deprotecting the compound of Formula VII to form a compound of Formula VIII;

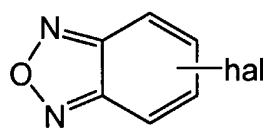


Formula VIII

and

- c) reacting the compound of Formula VIII with compound of Formula III

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Formula III

to form a compound of Formula IX,

wherein,

U and **V** each can independently be hydrogen, lower (C₁₋₆)alkyl or halogen;

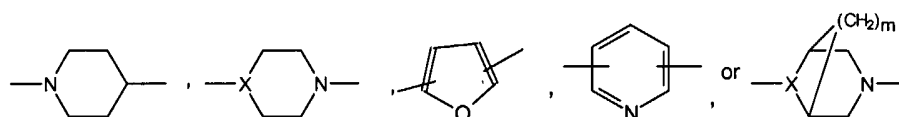
5 **W** can be no atom or can be selected from O, CH₂, CO, CH₂NH, -NHCH₂, -CH₂NHCH₂, -CH₂-N(R₁₁)CH₂-, CH₂(R_e)N-, CH(R₁₁), S, CH₂(CO), NH, NR_e, (CO)CH₂, N(R_e)CON(R_e), N(R_e)C(=S)N(R_e), SO₂ or SO, wherein

R₁₁ can be optionally substituted C₁₋₁₂ alkyl, C₃₋₁₂ cycloalkyl, C₁₋₆ alkoxy, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, C₁₋₆ alkylcarboxy, aryl or heteroaryl, and

10 **R**_e can be hydrogen, optionally substituted C₁₋₁₂ alkyl, C₃₋₁₂ cycloalkyl, C₁₋₆ alkoxy, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, C₁₋₆ alkylcarboxy, aryl or heteroaryl;

Het can be a heterocyclyl or heteroaryl;

A can be no group or can be selected from;



15 wherein

X can be CH, CH-S, CH-O or N;

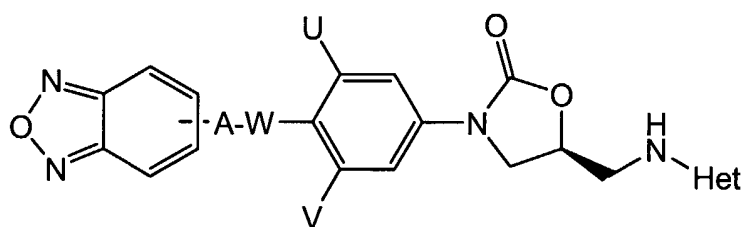
Q can be O, N or S;

and **m** can be an integer from 0-2;

20 Such processes can include one or more of the following embodiments. For example, the reaction of compound of Formula V with a compound of Formula VI to form a compound of Formula VII can be carried out in the presence of one or more bases, for example, Group I hydrides selected from sodium hydride, potassium hydride, lithium

hydride or mixtures thereof. The compound of Formula VII can be deprotected to form the compound of Formula VIII in the presence of one or more deprotection agents, for example, trifluoroacetic acid in dichloromethane or hydrochloric acid in ethanol. The reaction of the compound of Formula VIII with the compound of Formula III to form the compound of Formula IX can be carried out in the presence of one or more bases, for example, sodium carbonate, potassium carbonate, cesium carbonate, sodium tertiary butoxide, potassium tertiary butoxide or mixtures thereof. The reaction of the compound of Formula VIII with the compound of Formula III to form the compound of Formula IX can be carried out in the presence of one or more catalysts and one or more ligands. The one or more catalysts can be selected from *tris*-(dibenzylideneacetone) dipalladium(0), palladium diacetate, palladium dichloride or mixtures thereof; and the one or more ligands can be selected from 1,1'-binaphthalene-2,2'-diylbis(diphenylphosphine), tri-*tert*-butylphosphine, di-1-adamantyl(butyl)phosphine, biphenyl-2-yl(di-*tert*-butyl)phosphine or mixtures thereof.

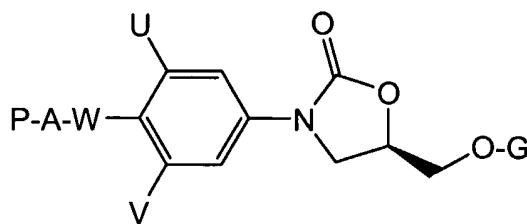
In another aspect, provided are processes for preparing a compound of Formula XIII



Formula XIII

or its pharmaceutically acceptable salts, pharmaceutically acceptable solvates, enantiomers, diastereomers or polymorphs, comprising the steps of:

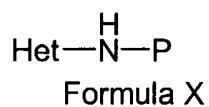
a) reacting a compound of Formula V



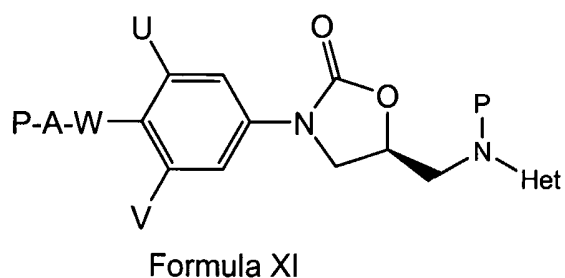
Formula V

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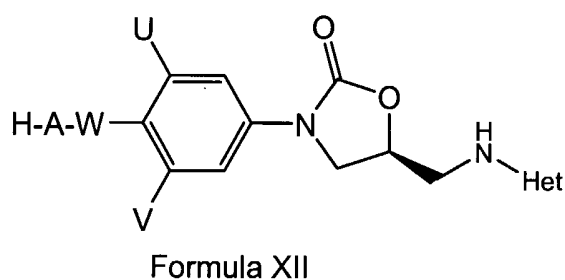
with a compound of Formula X



to form a compound of Formula XI,

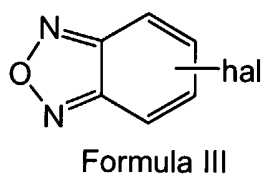


- 5 b) deprotecting the compound of Formula XI to form a compound of Formula XII,



and

- c) reacting the compound of Formula XII with a compound of Formula III



10

to form a compound of Formula XIII,

wherein,

U and V each can independently be hydrogen, lower (C₁₋₆)alkyl or halogen;

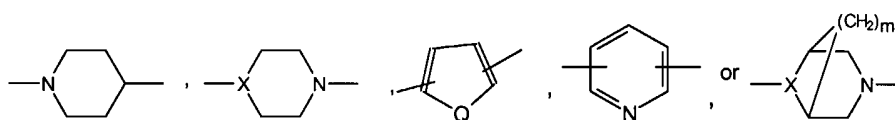
W can be no atom or can be selected from O, CH₂, CO, CH₂NH, -NHCH₂, -CH₂NHCH₂, -CH₂-N(R₁₁)CH₂-, CH₂(R_e)N-, CH(R₁₁), S, CH₂(CO), NH, NR_e, (CO)CH₂, N(R_e)CON(R_e), N(R_e)C(=S)N(R_e), SO₂ or SO, wherein

R₁₁ can be optionally substituted C₁₋₁₂ alkyl, C₃₋₁₂ cycloalkyl, C₁₋₆ alkoxy, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, C₁₋₆ alkylcarboxy, aryl or heteroaryl,

R_e can be hydrogen, optionally substituted C₁₋₁₂ alkyl, C₃₋₁₂ cycloalkyl, C₁₋₆ alkoxy, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, C₁₋₆ alkylcarboxy, aryl or heteroaryl;

Het can be a heterocyclyl or heteroaryl; and

A can be no group or can be selected from,



wherein

X can be CH, CH-S, CH-O or N;

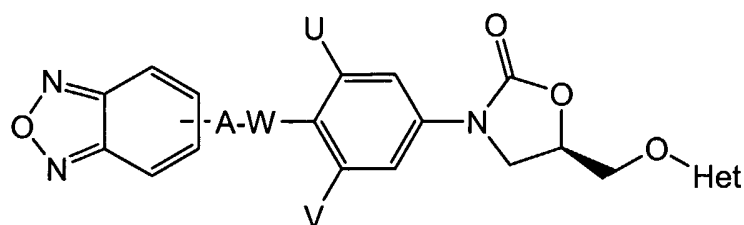
Q can be O, N or S;

m can be an integer from 0-2.

Such processes can include one or more of the following embodiments. For example, the reaction of the compound of Formula V with the compound of Formula XIV to form the compound of Formula XI can be carried out in the presence of one or more bases, for example, Group I hydrides selected from sodium hydride, potassium hydride, lithium hydride or mixtures thereof. The deprotection of the compound of Formula XI to form the compound of Formula XII can be carried out in the presence of one or more deprotection agents, for example, trifluoroacetic acid in dichloromethane or hydrochloric acid in ethanol. The reaction of the compound of Formula XII with the compound of Formula III to form the compound of Formula XIII can be carried out in the presence of one or more bases, for example, sodium carbonate, potassium carbonate, cesium carbonate, sodium tertiary butoxide, potassium tertiary butoxide or mixtures thereof. The reaction the compound of Formula XII with the compound of Formula III to form the

compound of Formula XIII can be carried out in the presence of one or more catalysts and one or more ligands. The one or more catalysts can be selected from *tris*-(dibenzylideneacetone) dipalladium(0), Pd₂(dba)₃, palladium diacetate, palladium dichloride, or mixtures thereof; and the one or more suitable ligands can be selected from 1,1'-binaphthalene-2,2'-diylbis(diphenylphosphine), tri-*tert*-butylphosphine, di-1-adamantyl(butyl)phosphine, biphenyl-2-yl(di-*tert*-butyl)phosphine or mixtures thereof.

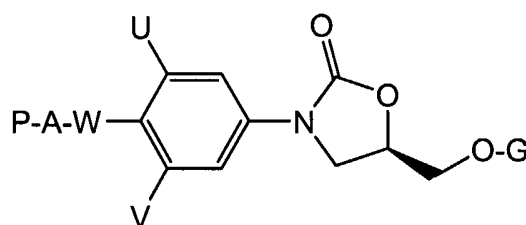
In another aspect, provided are processes for preparing a compound of Formula XVII



Formula XVII

or its pharmaceutically acceptable salts, pharmaceutically acceptable solvates, enantiomers, diastereomers or polymorphs, comprising the steps of:

a) reacting a compound of Formula V



Formula V

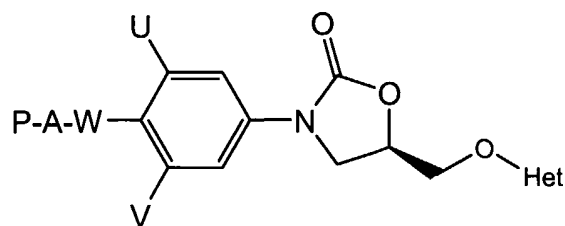
with a compound of XIV



Formula XIV

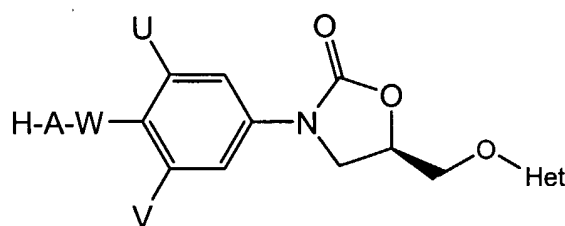
to form a compound of Formula XV,

15



Formula XV

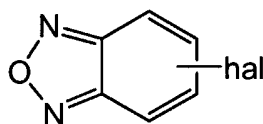
b) deprotecting the compound of Formula XV to form a compound of Formula XVI,



Formula XVI

5 and

c) reacting the compound of Formula XVI with a compound of Formula III



Formula III

to form a compound of Formula XVII,

wherein,

10 U and V each can independently be hydrogen, lower (C₁₋₆)alkyl or halogen;

W can be no atom or can be selected from O, CH₂, CO, CH₂NH, -NHCH₂, -CH₂NHCH₂, -CH₂-N(R₁₁)CH₂-, CH₂(R_e)N-, CH(R₁₁), S, CH₂(CO), NH, NR_e, (CO)CH₂, N(R_e)CON(R_e), N(R_e)C(=S)N(R_e), SO₂ or SO, wherein

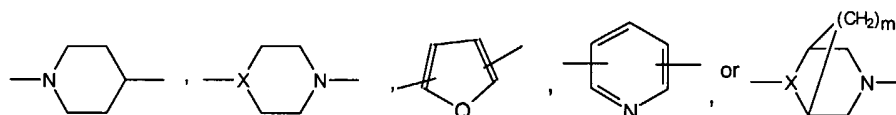
R₁₁ can be optionally substituted C₁₋₁₂ alkyl, C₃₋₁₂ cycloalkyl, C₁₋₆ alkoxy,

15 C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, C₁₋₆ alkylcarboxy, aryl or heteroaryl, and

R_e can be hydrogen, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl or heteroaryl;

Het can be a heterocyclyl or heteroaryl;

A can be no group or can be selected from,



wherein

X can be CH, CH-S, CH-O or N;

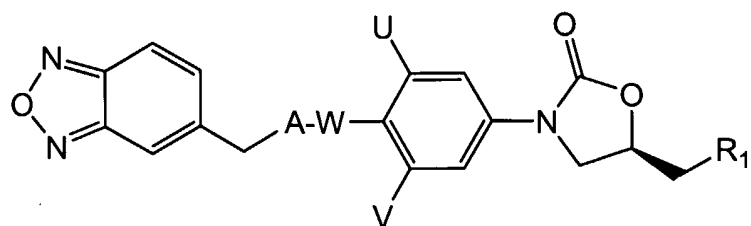
Q can be O, N or S;

m can be an integer from 0-2.

- 10 Such processes can include one or more of the following embodiments. For example, the reaction of the compound of Formula V with a compound of Formula XIV to form a compound of Formula XV can be carried out in the presence of one or more coupling agents, for example, diethyl diazocarboxylate, diisopropyl diazocarboxylate or mixtures thereof. The reaction of the compound of Formula V with a compound of
- 15 Formula XIV to form a compound of Formula XV can be carried out in the presence of one or more catalysts, for example, triphenyl phosphine, trioctyl phosphine, tributyl phosphine or mixtures thereof. The compound of Formula XV can be deprotected to form the compound of Formula XVI in the presence of one or more deprotection agents, for example, trifluoroacetic acid in dichloromethane or hydrochloric acid in ethanol. The
- 20 reaction of the compound of Formula XVI with the compound of Formula III to form the compound of Formula XVII can be carried out in the presence of one or more bases, for example, sodium carbonate, potassium carbonate, cesium carbonate, sodium tertiary butoxide, potassium tertiary butoxide or mixtures thereof. The reaction of the compound of Formula XVI with the compound of Formula III to form the compound of Formula
- 25 XVII can be carried out in the presence of one or more catalysts and one or more ligands. The one or more catalysts can be selected from *Tris*-(dibenzylideneacetone) dipalladium(0), $Pd_2(dba)_3$, palladium diacetate, palladium dichloride or mixtures thereof;

and the one or more ligands can be selected from 1,1'-binaphthalene-2,2'-diylbis(diphenylphosphine), tri-*tert*-butylphosphine, di-1-adamantyl(butyl)phosphine, biphenyl-2-yl(di-*tert*-butyl)phosphine or mixtures thereof.

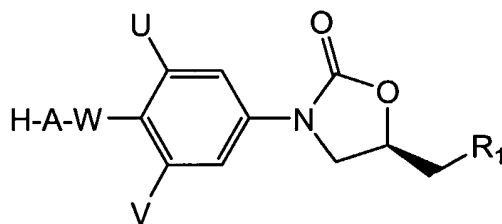
In yet another aspect, provided can be processes for preparing a compound of
5 Formula XX



Formula XX

or its pharmaceutically acceptable salts, pharmaceutically acceptable solvates, enantiomers, diastereomers or polymorphs, comprising the steps of:

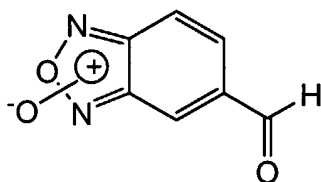
a) reacting a compound of Formula XVIII



Formula XVIII

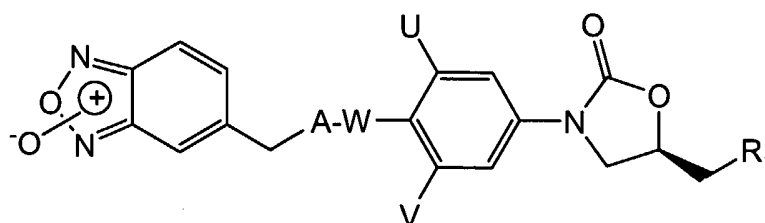
10

with 5-formylbenzofuroxan



to form a compound of Formula XIX,

18



Formula XIX

and

b) deoxygenating the compound of Formula XIX to form a compound of Formula XX,

5 wherein,

R_1 can be OR_j , SR_j , NHY_1R_f , NR_fR_q , heterocyclyl or heteroaryl, wherein

R_j can be hydrogen, alkyl, alkenyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, heteroarylalkyl or heterocyclalkyl;

10 Y_1 can be $(C=O)$, $(C=S)$ or SO_2 and R_f can be hydrogen, alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl or heterocyclalkyl; and

R_q can be hydrogen, alkyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl or heterocyclalkyl;

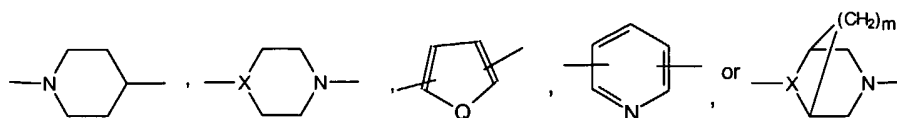
U and V each can independently be hydrogen, lower (C_{1-6}) alkyl or halogen;

15 Y and W can be no atom or selected from O , CH_2 , CO , CH_2NH , $-NHCH_2$, $-CH_2NHCH_2$, $-CH_2-N(R_{11})CH_2-$, $CH_2(R_e)N-$, $CH(R_{11})$, S , $CH_2(CO)$, NH , NR_e , $(CO)CH_2$, $N(R_e)CON(R_e)$, $N(R_e)C(=S)N(R_e)$, SO_2 or SO , wherein

R_{11} can be optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl or heteroaryl, and

20 R_e can be hydrogen, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl or heteroaryl;

A can be no group or selected from group consisting of;



wherein

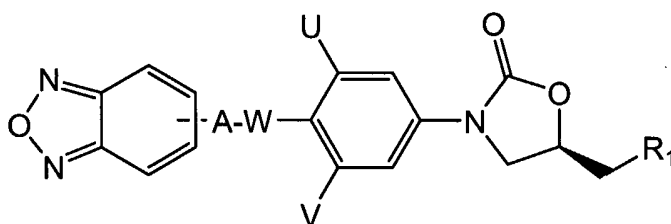
X can be CH, CH-S, CH-O or N;

Q can be O, N or S; and

m can be an integer from 0-2.

Such processes can include one or more of the following embodiments. For example, the reaction of compound of Formula XVIII with 5-formylbenzoxofuroxan to form the compound of Formula XIX can be carried out in the presence of one or more reducing agents, for example, sodium triacetoxy borohydride, sodium borohydride, sodium cyano borohydride, or mixtures thereof. The deoxygenation of compound of Formula XIX to form the compound of Formula XX can be carried out in presence of one or more catalysts, for example, triphenyl phosphine, trioctyl phosphine, tributyl phosphine or mixtures thereof.

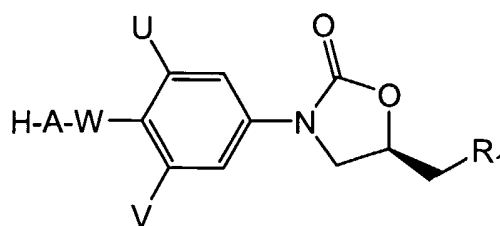
In another aspect, provided are processes for preparing a compound of Formula XXII



Formula XXII

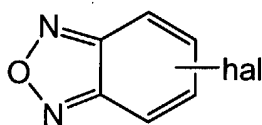
or its pharmaceutically acceptable salts, pharmaceutically acceptable solvates, enantiomers, diastereomers or polymorphs, comprising reacting a compound of Formula XXI

20



Formula XXI

with a compound of Formula III



Formula III

to form a compound of Formula XXII,

5 wherein,

R_1 can be OR_j , SR_j , NHY_1R_f , NR_fR_q , heterocyclyl or heteroaryl; wherein

R_j can be hydrogen, alkyl, alkenyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, heteroarylalkyl or heterocyclalkyl;

10 Y_1 can be $(C=O)$, $(C=S)$ or SO_2 and R_f can be hydrogen, alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl or heterocyclalkyl; and

R_q can be hydrogen, alkyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl or heterocyclalkyl;

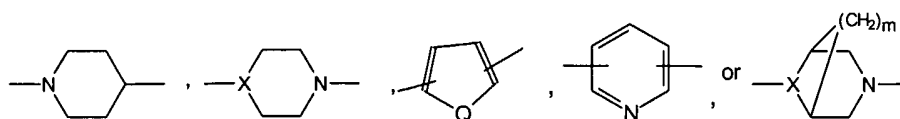
U and V each can independently be hydrogen, lower (C_{1-6}) alkyl or halogen;

15 Y and W can be no atom or selected from O, CH_2 , CO, CH_2NH , $-NHCH_2$, $-CH_2NHCH_2$, $-CH_2-N(R_{11})CH_2-$, $CH_2(R_e)N-$, $CH(R_{11})$, S, $CH_2(CO)$, NH, NR_e , $(CO)CH_2$, $N(R_e)CON(R_e)$, $N(R_e)C(=S)N(R_e)$, SO_2 or SO, wherein

R_{11} can be optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl or heteroaryl, and

R_e can be hydrogen, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl or heteroaryl;

A can be no group or can be selected from,



5 wherein

X can be CH, CH-S, CH-O or N;

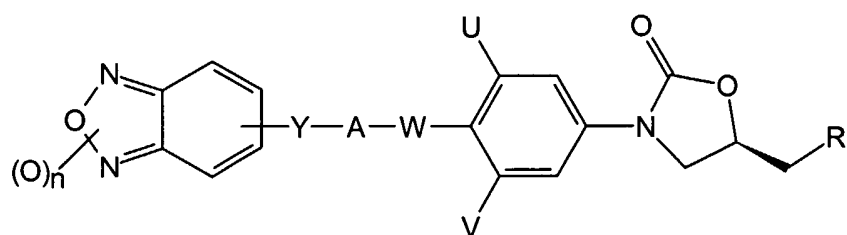
Q can be O, N or S;

m can be an integer from 0-2.

Such processes can include one or more of the following embodiments. For example, the
 10 reaction of the compound of Formula XXI with the compound of Formula III to form the
 compound of Formula XXII can be carried out in the presence of one or more bases, for
 example, sodium carbonate, potassium carbonate, diisopropyl ethylamine, triethylamine,
 N-methyl morpholine or mixtures thereof. The reaction of the compound of Formula XXI
 with the compound of Formula III to form the compound of Formula XXII can be carried
 15 out in the presence of one or more catalysts and one or more ligands. The one or more
 catalysts can be selected from *tris*-(dibenzylideneacetone) dipalladium(0), $Pd_2(dba)_3$,
 palladium diacetate, palladium dichloride, or mixtures thereof; and the one or more
 suitable ligands can be selected from 1,1'-binaphthalene-2,2'-diylbis(diphenylphosphine),
 tri-*tert*-butylphosphine, di-1-adamantyl(butyl)phosphine, biphenyl-2-yl(di-*tert*-
 20 butyl)phosphine or mixtures thereof.

Detailed Description of the Invention

Provided are processes for synthesizing benzoxadiazole phenyloxazolidinones
 derivatives represented by Formula I,



Formula I

and its pharmaceutically acceptable salts, pharmaceutically acceptable solvates, stereoisomers, prodrugs or polymorphs, wherein,

R_1 can be OR_j , SR_j , NHY_1R_f , NR_fR_q , heterocyclyl or heteroaryl, wherein

5 R_j can be hydrogen, alkyl, alkenyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, heteroarylalkyl or heterocyclylalkyl,

Y_1 can be $(C=O)$, $(C=S)$ or SO_2 ,

R_f can be hydrogen, alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl or heterocyclylalkyl, and

10 R_q can be hydrogen, alkyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl or heterocyclyl;

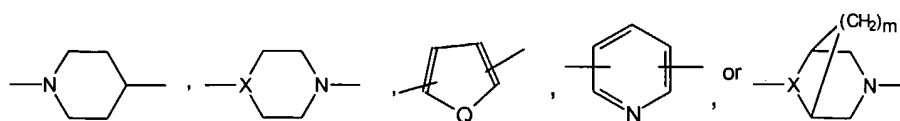
U and V can be independently hydrogen, lower C_{1-6} alkyl or halogen (e.g., Cl, F or Br);

Y and W can be no atom or selected from O, CH_2 , CO, CH_2NH , $NHCH_2$,
15 CH_2NHCH_2 , $CH_2-N(R_{11})CH_2$, $CH_2(R_e)N$, $CH(R_{11})$, S, $CH_2(CO)$, NH, NR_e ,
(CO) CH_2 , $N(R_e)CON(R_e)$, $N(R_e)C(=S)N(R_e)$, SO_2 or SO, wherein

R_{11} can be optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl or heteroaryl, and

R_e can be hydrogen, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl or heteroaryl;
20

A can be no group or selected from



wherein, X can be CH, CH-S, CH-O or N;

Q can be O, N or S;

n is an integer 0-1; and

10 m is an integer from 0-2.

Compounds disclosed herein can be useful antimicrobial agents that are effective against a number of human and veterinary pathogens, particularly aerobic and Gram-positive bacteria (*e.g.*, multiply-antibiotic resistant *Staphylococci* and *Streptococci*) and anaerobic organisms (*e.g.*, *Mycobacterium tuberculosis* and other *Mycobacterium* species).

Also provided are pharmaceutical compositions comprising compounds described herein, their enantiomers, diastereomers, polymorphs, pharmaceutically acceptable salts, pharmaceutically acceptable solvates, N-oxides or metabolites in combination with one or more pharmaceutically acceptable carriers and optionally included excipients.

For preparing pharmaceutical compositions comprising compounds described herein, pharmaceutically acceptable carriers can be either solid or liquid. Solid form preparations include powders, tablets, dispersible granules, capsules, cachets, suppositories and ointments. Solid carriers can comprise one or more substances, which may also act as diluents, flavoring agents, solubilizers, lubricants, suspending agents, binders, or disintegrating agents. Solid carriers can also be finely divided solids in admixture with the finely divided active compound. For preparing tablets, active compounds can be mixed with one or more carriers having necessary binding properties in suitable proportions and compacted into desired shapes and sizes. Powders and tablets preferably comprise from about 5 to about 70 percent of one or more compounds described herein. Suitable solid carriers include, for example, lactose, pectin, dextrin, starch, gelatin, tragacanth, low melting wax, cocoa butter and the like. The term "preparation," unless otherwise specified, refers to a formulation comprising one or more

active compounds (*i.e.*, compounds described herein) with encapsulating material as carrier and providing a capsule in which the active component (with or without other carriers) is surrounded by carrier, which is thus in association with it. Similarly, capsules can be used, as solid dosage forms suitable for oral administration.

5 Liquid form preparations include solutions, suspensions and emulsions. One example includes water or water-propylene glycol solutions for parenteral injection. Such solutions can be prepared to be acceptable to/compatible with biological systems (particularly in terms of isotonicity, pH, etc.). Liquid preparations can also be formulated in solution in aqueous polyethylene glycol solution. Aqueous solutions suitable for oral
10 use can be prepared by dissolving one or more active components (*i.e.*, compounds described herein) in water and adding one or more suitable colorants, flavors, stabilizing, or thickening agents as desired. Aqueous suspensions suitable for oral use can be made by dispersing finely divided active components (*i.e.*, compounds described herein) in water with viscous material, *i.e.*, natural or synthetic gums, resins, methyl cellulose, sodium
15 carboxymethyl cellulose or other well-known suspending agents.

Ointment preparations can comprise compounds described herein with one or more physiologically acceptable carriers. Carriers can be conventional water-dispersible hydrophilic or oil-in-water carriers, particularly conventional semi-soft or cream-like water-dispersible or water soluble, oil-in-water emulsions. Suitable compositions may be
20 prepared by incorporating or homogeneously admixing finely divided compounds described herein with one or more hydrophilic carriers or bases or ointments.

Pharmaceutical preparations can be in unit dosage form. In such forms, preparations can be subdivided into unit doses comprising appropriate quantities of one or more active components (*i.e.*, compounds described herein). Unit dosage forms can be
25 packaged preparations, the package containing discrete capsules, powders in vials or ampoules and ointments, cachets, tablets, gels, or creams itself, or it can be the appropriate number of any of these packaged forms.

Quantities of active ingredients, *i.e.*, compounds described herein, in a unit dose of preparation may be varied or adjusted from less than 1 mg to several grams according to
30 the particular application and the potency of the active ingredient.

Compounds described herein can be administered at initial dosages of about 3 mg to about 40 mg per kilogram daily to a patient in need of treating bacterial infections. The dosages, however, may be varied depending upon the requirements of the patient and the compound(s) being employed. Proper dosages can be determined for a particular situation and utilize small dosages that are less than optimum doses. Small increments until the optimum effect under the daily dosage may be divided and administered in portions during the day if desired.

In another aspect, processes for synthesizing compounds of Formula I are provided. Pharmaceutically acceptable acid addition salts of the compounds of Formula I may be formed with one or more inorganic or organic acids and by methods known to one of ordinary skill in the art.

In general, prodrugs of compounds described herein can be functional derivatives of such compounds, which can readily be converted *in vivo* into defined compounds. Conventional procedures for the selection and preparation of suitable prodrugs are known to one of ordinary skill in the art.

The following definitions apply to terms as used herein;

The term "alkyl," unless otherwise specified, refers to a monoradical branched or unbranched saturated hydrocarbon chain having from 1 to 20 carbon atoms. This term can be exemplified by groups, for example, methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, *sec*-butyl, *tert*-butyl, n-pentyl, isopentyl, neopentyl, n-hexyl, n-decyl, tetradecyl, and the like. Alkyl groups may be substituted further with one or more substituents selected from alkenyl, alkynyl, alkoxy, cycloalkyl, cycloalkenyl, acyl, acylamino, acyloxy, alkoxycarbonylamino, azido, cyano, halogen, hydroxy, oxo, thiocarbonyl, carboxy, carboxyalkyl, aryl, heterocyclyl, heteroaryl, arylthio, thiol, alkylthio, aryloxy, nitro, aminosulfonyl, aminocarbonylamino, -NHC(=O)R_m , $\text{-NR}_m\text{R}_n$, $\text{-C(=O)NR}_m\text{R}_n$, $\text{-NHC(=O)NR}_m\text{R}_n$, -C(=O)heteroaryl , C(=O)heterocyclyl , $\text{-O-C(=O)NR}_m\text{R}_n$ {wherein R_m and R_n are independently selected from alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, aralkyl, heterocyclyl, heteroaryl, heterocyclylalkyl, heteroarylalkyl}, nitro, or $\text{-SO}_2\text{R}_6$ (wherein R_6 is alkyl, alkenyl, alkynyl, cycloalkyl, aralkyl, aryl, heterocyclyl, heteroaryl, heteroarylalkyl or heterocyclylalkyl). Unless otherwise constrained by the definition, alkyl substituents may be further substituted by 1-3 substituents selected from alkyl,

carboxy, $-NR_mR_n$, $-C(=O)NR_mR_n$, $-OC(=O)NR_mR_n$, $-NHC(=O)NR_mR_n$ (wherein R_m and R_n are the same as defined earlier), hydroxy, alkoxy, halogen, CF_3 , cyano, and $-SO_2R_6$, (wherein R_6 are the same as defined earlier); or an alkyl group also may be interrupted by 1-5 atoms of groups independently selected from oxygen, sulfur or $-NR_a$ - {wherein R_a is selected from hydrogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, acyl, aralkyl, $-C(=O)OR_m$ (wherein R_m is the same as defined earlier), SO_2R_6 (wherein R_6 is as defined earlier), or $-C(=O)NR_mR_n$ (wherein R_m and R_n are as defined earlier)}. Unless otherwise constrained by the definition, all substituents may be substituted further by 1-3 substituents selected from alkyl, carboxy, $-NR_mR_n$, $-C(=O)NR_mR_n$, $-O-C(=O)NR_mR_n$ (wherein R_m and R_n are the same as defined earlier) hydroxy, alkoxy, halogen, CF_3 , cyano, and $-SO_2R_6$ (wherein R_6 is same as defined earlier); or an alkyl group as defined above that has both substituents as defined above and is also interrupted by 1-5 atoms or groups as defined above.

The term "alkenyl," unless otherwise specified, refers to a monoradical of a branched or unbranched unsaturated hydrocarbon group having from 2 to 20 carbon atoms with cis, trans, or geminal geometry. In the event that alkenyl is attached to a heteroatom, the double bond cannot be alpha to the heteroatom. Alkenyl groups may be substituted further with one or more substituents selected from alkyl, alkynyl, alkoxy, cycloalkyl, cycloalkenyl, acyl, acylamino, acyloxy, $-NHC(=O)R_m$, $-NR_mR_n$, $-C(=O)NR_mR_n$, $-NHC(=O)NR_mR_n$, $-O-C(=O)NR_mR_n$ (wherein R_m and R_n are the same as defined earlier), alkoxycarbonylamino, azido, cyano, halogen, hydroxy, oxo, thiocarbonyl, carboxy, arylthio, thiol, alkylthio, aryl, aralkyl, aryloxy, heterocyclyl, heteroaryl, heterocyclyl alkyl, heteroaryl alkyl, aminosulfonyl, aminocarbonylamino, alkoxyamino, nitro, or SO_2R_6 (wherein R_6 are is same as defined earlier). Unless otherwise constrained by the definition, alkenyl substituents optionally may be substituted further by 1-3 substituents selected from alkyl, carboxy, hydroxy, alkoxy, halogen, $-CF_3$, cyano, $-NR_mR_n$, $-C(=O)NR_mR_n$, $-O-C(=O)NR_mR_n$ (wherein R_m and R_n are the same as defined earlier) and $-SO_2R_6$ (wherein R_6 is same as defined earlier).

The term "alkynyl," unless otherwise specified, refers to a monoradical of an unsaturated hydrocarbon, having from 2 to 20 carbon atoms. In the event that alkynyl is attached to a heteroatom, the triple bond cannot be alpha to the heteroatom. Alkynyl

groups may be substituted further with one or more substituents selected from alkyl, alkenyl, alkoxy, cycloalkyl, cycloalkenyl, acyl, acylamino, acyloxy, alkoxycarbonylamino, azido, cyano, halogen, hydroxy, oxo, thiocarbonyl, carboxy, arylthio, thiol, alkylthio, aryl, aralkyl, aryloxy, aminosulfonyl, aminocarbonylamino, nitro, heterocyclyl, heteroaryl, heterocyclylalkyl, heteroarylalkyl, -NHC(=O)R_m, -NR_mR_n, -NHC(=O)NR_mR_n, -C(=O)NR_mR_n, -O-C(=O)NR_mR_n (wherein R_m and R_n are the same as defined earlier), or -SO₂R₆ (wherein R₆ is as defined earlier). Unless otherwise constrained by the definition, alkynyl substituents optionally may be substituted further by 1-3 substituents selected from alkyl, carboxy, carboxyalkyl, hydroxy, alkoxy, halogen, CF₃, -NR_mR_n, -C(=O)NR_mR_n, -NHC(=O)NR_mR_n, -C(=O)NR_mR_n (wherein R_m and R_n are the same as defined earlier), cyano, or -SO₂R₆ (wherein R₆ is same as defined earlier).

The term "cycloalkyl," unless otherwise specified, refers to cyclic alkyl groups of from 3 to 20 carbon atoms having a single cyclic ring or multiple condensed rings, which may optionally contain one or more olefinic bonds, unless otherwise constrained by the definition. Such cycloalkyl groups can include, for example, single ring structures, including cyclopropyl, cyclobutyl, cyclooctyl, cyclopentenyl, and the like, or multiple ring structures, including adamantanyl, and bicyclo[2.2.1]heptane, or cyclic alkyl groups to which is fused an aryl group, for example, indane, and the like. Spiro and fused ring structures can also be included. Cycloalkyl groups may be substituted further with one or more substituents selected from alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, cycloalkenyl, acyl, acylamino, acyloxy, alkoxycarbonylamino, azido, cyano, halogen, hydroxy, oxo, thiocarbonyl, carboxy, carboxyalkyl, arylthio, thiol, alkylthio, aryl, aralkyl, aryloxy, aminosulfonyl, aminocarbonylamino, -NR_mR_n, -NHC(=O)NR_mR_n, -NHC(=O)R_m, -C(=O)NR_mR_n, -O-C(=O)NR_mR_n (wherein R_m and R_n are the same as defined earlier), nitro, heterocyclyl, heteroaryl, heterocyclylalkyl, heteroarylalkyl, or SO₂R₆ (wherein R₆ is same as defined earlier). Unless otherwise constrained by the definition, cycloalkyl substituents optionally may be substituted further by 1-3 substituents selected from alkyl, carboxy, hydroxy, alkoxy, halogen, CF₃, -NR_mR_n, -C(=O)NR_mR_n, -NHC(=O)NR_mR_n, -OC(=O)NR_mR_n (wherein R_m and R_n are the same as defined earlier), cyano or -SO₂R₆ (wherein R₆ is same as defined earlier). "Cycloalkylalkyl" refers to alkyl-cycloalkyl group linked through alkyl portion, wherein the alkyl and cycloalkyl are the same as defined earlier.

The term "alkoxy" denotes the group O-alkyl, wherein alkyl is the same as defined above.

The term "aryl," unless otherwise specified, refers to carbocyclic aromatic groups, for example, phenyl, biphenyl or naphthyl ring and the like, optionally substituted with 1 to 3 substituents selected from halogen (*e.g.*, F, Cl, Br, I), hydroxy, alkyl, alkenyl, alkynyl, cycloalkyl, alkoxy, acyl, aryloxy, CF₃, cyano, nitro, COOR_p (wherein R_p is hydrogen, alkyl, alkenyl, cycloalkyl, aralkyl, heterocyclalkyl, heteroarylalkyl), NHC(=O)R_m, -NR_mR_n, -C(=O)NR_mR_n, -NHC(=O)NR_mR_n, -O-C(=O)NR_mR_n (wherein R_m and R_n are the same as defined earlier), -SO₂R₆ (wherein R₆ is same as defined earlier), carboxy, heterocycl, heteroaryl, heterocyclalkyl, heteroarylalkyl or amino carbonyl amino. The aryl group optionally may be fused with a cycloalkyl group, wherein the cycloalkyl group may optionally contain heteroatoms selected from O, N or S.

The term "aralkyl," unless otherwise specified, refers to alkyl-aryl linked through an alkyl portion (wherein alkyl is as defined above) and the alkyl portion contains 1-6 carbon atoms and aryl is as defined below. Examples of aralkyl groups include benzyl, ethylphenyl and the like.

The term "heteroaryl," unless otherwise specified, refers to an aromatic ring structure containing 5 or 6 ring atoms, or a bicyclic aromatic group having from 8 to 10 ring atoms, with one or more heteroatom(s) independently selected from N, O or S optionally substituted with 1 to 4 substituent(s) selected from halogen (*e.g.*, F, Cl, Br, I), hydroxy, alkyl, alkenyl, alkynyl, cycloalkyl, acyl, carboxy, aryl, alkoxy, aralkyl, cyano, nitro, heterocycl, heteroaryl, -NR_mR_n, CH=NOH, -(CH₂)_wC(=O)R_g {wherein w is an integer from 0-4 and R_g is hydrogen, hydroxy, OR_m, NR_mR_n, -NHOR_z or -NHOH}, -C(=O)NR_mR_n and -NHC(=O)NR_mR_n, -SO₂R₆, -O-C(=O)NR_mR_n, -O-C(=O)R_m, -O-C(=O)OR_m (wherein R₆, R_m and R_n are as defined earlier, and R_z is alkyl, cycloalkyl, aryl, heteroaryl, heterocycl, heteroarylalkyl or heterocyclalkyl). Unless otherwise constrained by the definition, the substituents are attached to a ring atom, *i.e.*, carbon or heteroatom in the ring. Examples of heteroaryl groups include oxazolyl, imidazolyl, pyrrolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, tetrazolyl, thiazolyl, oxadiazolyl, benzoimidazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, thienyl, isoxazolyl, triazinyl, furanyl, benzofuranyl, indolyl, benzothiazolyl, or benzoxazolyl, and the like.

The term "heterocyclyl," unless otherwise specified, refers to a non-aromatic monocyclic or bicyclic cycloalkyl group having 5 to 10 atoms wherein 1 to 4 carbon atoms in a ring are replaced by heteroatoms selected from O, S or N, and optionally are benzofused or fused heteroaryl having 5-6 ring members and/or optionally are substituted, wherein the substituents are selected from halogen (*e.g.*, F, Cl, Br, I), hydroxy, alkyl, alkenyl, alkynyl, cycloalkyl, acyl, aryl, alkoxy, alkaryl, cyano, nitro, oxo, carboxy, heterocyclyl, heteroaryl, $-O-C(=O)R_m$, $-O-C(=O)OR_m$, $-C(=O)NR_mR_n$, SO_2R_6 , $-O-C(=O)NR_mR_n$, $-NHC(=O)NR_mR_n$, $-NR_mR_n$ (wherein R_6 , R_m and R_n are as defined earlier) or guanidine. Heterocyclyl can optionally include rings having one or more double bonds. Unless otherwise constrained by the definition, the substituents are attached to the ring atom, *i.e.*, carbon or heteroatom in the ring. Also, unless otherwise constrained by the definition, the heterocyclyl ring optionally may contain one or more olefinic bond(s). Examples of heterocyclyl groups include oxazolidinyl, tetrahydrofuranyl, dihydrofuranyl, dihydropyridinyl, dihydroisoxazolyl, dihydrobenzofuryl, azabicyclohexyl, dihydroindolyl, pyridinyl, isoindole 1,3-dione, piperidinyl or piperazinyl.

The term "acyl" refers to $-C(=O)R''$ wherein R'' is selected from hydrogen, alkyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl or heterocyclylalkyl.

"Substituted amino" unless and otherwise specified refers to a group $-N(R_k)_2$ wherein each R_k is independently selected from the group hydrogen (provided that both R_k groups are not hydrogen (defined as "amino")), alkyl, alkenyl, alkynyl, aralkyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, heterocyclylalkyl, heteroarylalkyl, acyl, SO_2R_6 (wherein R_6 is the same as defined above), $-C(=T)NR_mR_n$ or $NHC(=T)NR_mR_n$ (wherein T, R_m and R_n are the same as defined earlier).

The term "leaving group" refers to groups that exhibit or potentially exhibit the properties of being labile under the synthetic conditions and also, of being readily separated from synthetic products under defined conditions. Examples of leaving groups include, but are not limited to, halogen (*e.g.*, F, Cl, Br, I), triflates, tosylate, mesylates, alkoxy, thioalkoxy, or hydroxy radicals and the like.

The term "protecting groups" refers to moieties that prevent chemical reaction at a location of a molecule intended to be left unaffected during chemical modification of such

molecule. Unless otherwise specified, protecting groups may be used on groups, such as hydroxy, amino, or carboxy. Examples of protecting groups are found in T.W. Greene and P.G.M. Wuts, "Protective Groups in Organic Synthesis", 2nd Ed., John Wiley and Sons, New York, N.Y., which is incorporated herein by reference. The species of the carboxylic protecting groups, amino protecting groups or hydroxy protecting groups employed are not critical, as long as the derivatized moieties/moiety is/are stable to conditions of subsequent reactions and can be removed without disrupting the remainder of the molecule.

The term "pharmaceutically acceptable salts" refers to derivatives of compounds that can be modified by forming their corresponding acid or base salts. Examples of pharmaceutically acceptable salts include, but are not limited to, mineral or organic acids salts of basic residues (such as amines), or alkali or organic salts of acidic residues (such as carboxylic acids), and the like.

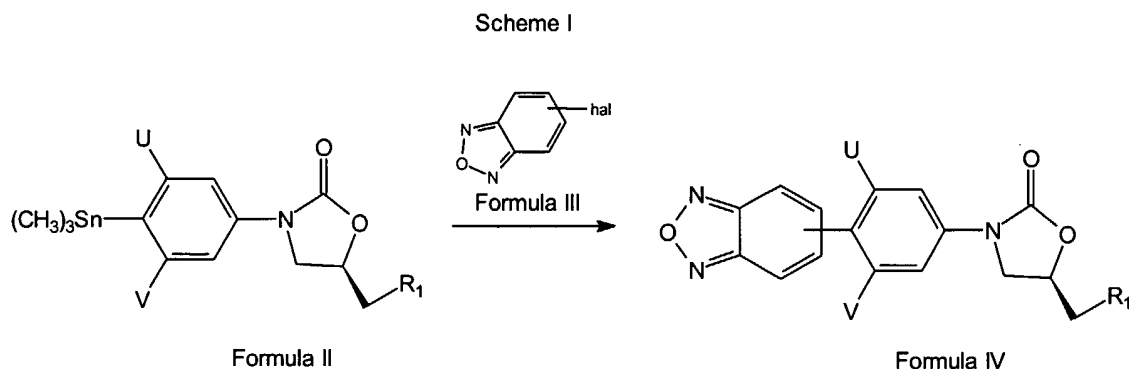
The present invention includes all isotopes of atoms occurring in the compounds described herein. Isotopes include those atoms having the same atomic number but different mass numbers. By way of general example and without limitation, isotopes of hydrogen include tritium and deuterium. Isotopes of carbon include ¹³C and ¹⁴C.

The compounds of this invention contain one or more asymmetric carbon atoms and thus occur as racemates and racemic mixtures, single enantiomers, diastereomeric mixtures and individual diastereomers. All such isomeric forms of these compounds are expressly encompassed by the present invention. Each stereogenic carbon may have the R or S configuration. Although specific compounds described herein may be depicted in a particular stereochemical configuration, such compounds having either the opposite stereochemistry at any given chiral center or mixtures thereof are envisioned as part of the invention. Although amino acids and amino acid side chains may be depicted in a particular configuration, both natural and unnatural forms are encompassed herein.

The compounds described herein can be represented by general Formula I and may be prepared by techniques well known to one of ordinary skill in the art. In addition, the compounds of the present invention may be prepared by the following reaction sequence as depicted in Schemes I, II, III, IV and V.

Scheme I

Compounds of Formula IV can be prepared by following Scheme I.



Thus, compounds of Formula II (wherein U, V and R₁ are same as defined earlier) can be reacted with compounds of Formula III (wherein hal can be chlorine, bromine or fluorine) to yield compounds of Formula IV. This reaction can be carried out in one or more organic solvents, for example, dimethyl formamide, 1,4-dioxane, tetrahydrofuran or mixture thereof. This reaction can also be carried out in the presence of one or more bases, for example, triethylamine, 4-dimethylamino pyridine, N-methyl morpholine or mixtures thereof. This reaction can also be carried out in the presence of one or more palladium catalysts, for example, dichlorobis(triphenylphosphine) palladium (II), tetrakis(triphenylphosphine) palladium (0) or mixture thereof.

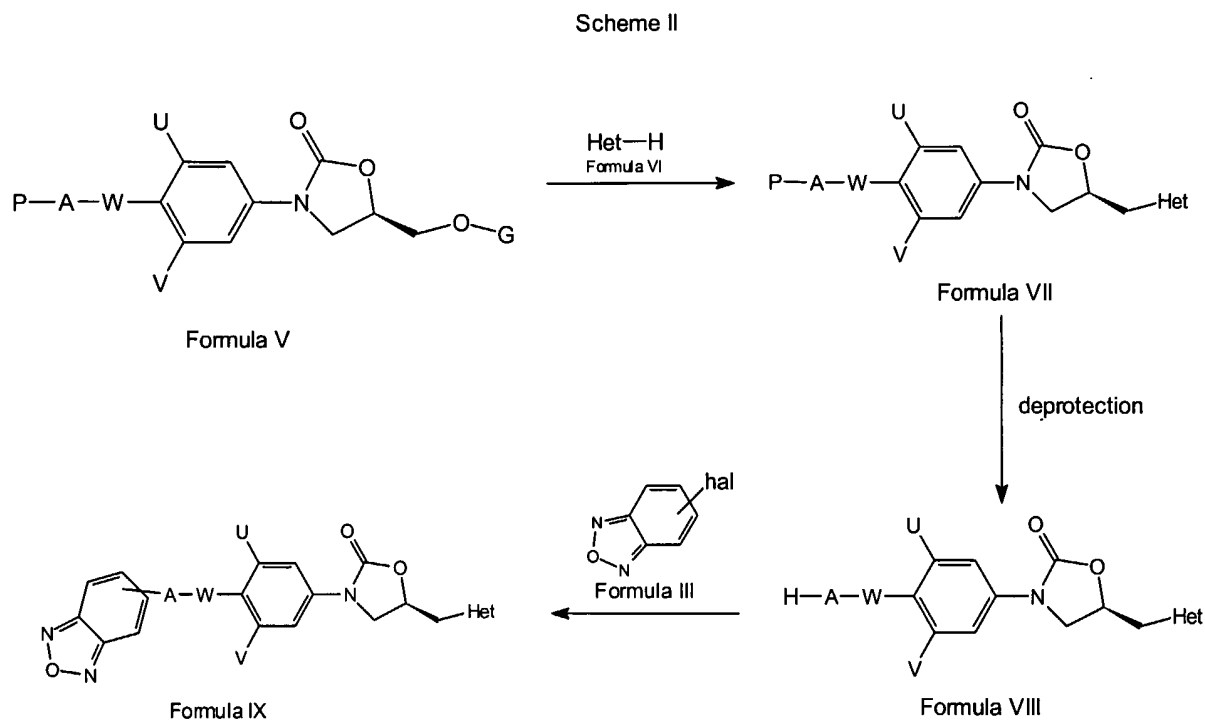
Compounds which may be prepared following Scheme I include, for example:

N-({(5*S*)-3-[4-(2,1,3-benzoxadiazol-5-yl)-3-fluorophenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl}acetamide (Compound No. 1)

N-((5*S*)-3-[4-(2,1,3-benzoxadiazol-5-yl)-3,5-difluorophenyl]-2-oxo-1,3-oxazolidin-5-yl)methylacetamide (Compound No. 2)

Scheme II

Compounds of Formula IX can be prepared by following Scheme II.



Thus, compounds of Formula V (wherein U, V, W and A are as defined earlier, P can be a protecting group and G can be H or a leaving group, *e.g.*, mesyl, tosyl or triflyl) can be reacted with compounds of Formula VI (wherein Het can be a heterocyclyl or heteroaryl) to form compounds of Formula VII. Compounds of Formula VII can be deprotected to form compounds of Formula VIII. Compounds of Formula VIII can be reacted with compounds of Formula III to form compounds of Formula IX.

Compounds of Formula V can be reacted with compounds of Formula VI to form compounds of Formula VII in one or more organic solvents, for example, dimethyl formamide, 1,4-dioxane, tetrahydrofuran or mixtures thereof. This reaction can also be carried out in the presence of one or more bases, for example, Group I hydrides, *e.g.*, sodium hydride, potassium hydride, lithium hydride or mixtures thereof.

Compounds of Formula VII can be deprotected to form compounds of Formula VIII in the presence of one or more deprotection agents, for example, one or more strong

protic acids in suitable solvents, *e.g.*, trifluoroacetic acid in dichloromethane or hydrochloric acid in ethanol.

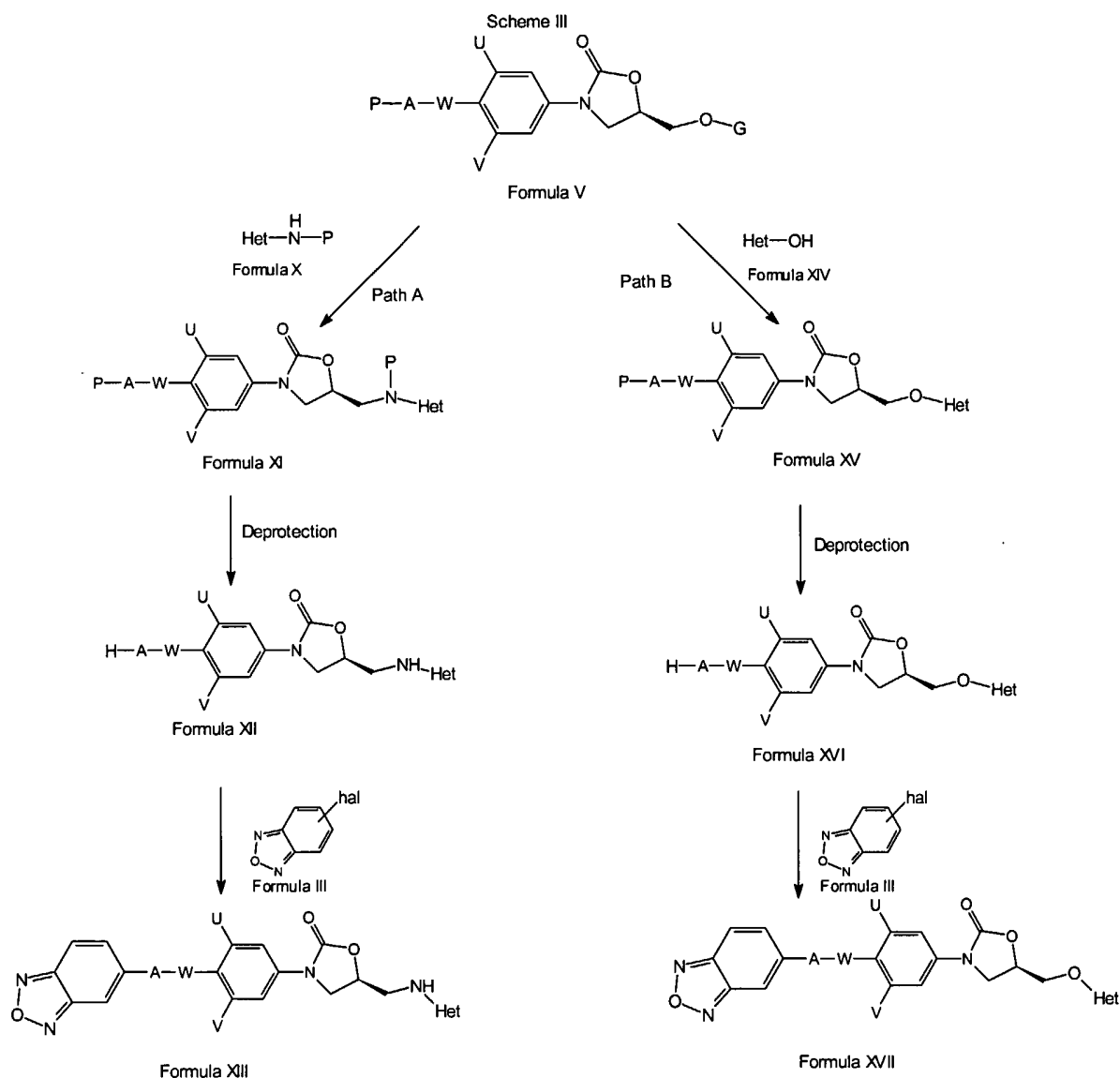
Compounds of Formula VIII can be reacted with compounds of Formula III to form compounds of Formula IX in one or more organic solvents, for example, 5 tetrahydrofuran, benzene, dimethylformamide, carbon tetrachloride or mixtures thereof. This reaction can also be carried out in the presence of one or more bases, for example, sodium carbonate, potassium carbonate, cesium carbonate, sodium tertiary butoxide, potassium tertiary butoxide or mixtures thereof. This reaction can also be carried out in the presence of one or more catalysts, for example, *Tris*-(dibenzylideneacetone) 10 dipalladium(0), palladium diacetate, palladium dichloride or mixtures thereof; and one or more suitable ligands, for example, 1,1'-binaphthalene-2,2'-diylbis(diphenylphosphine), tri-*tert*-butylphosphine, di-1-adamantyl(butyl)phosphine, biphenyl-2-yl(di-*tert*-butyl)phosphine or mixtures thereof.

Compounds which may be prepared following Scheme II include, for example:

- 15 (5*R*)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-fluorophenyl}-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one (Compound No. 3);
- (5*R*)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-fluorophenyl}-5-(2*H*-1,2,3-triazol-2-ylmethyl)-1,3-oxazolidin-2-one (Compound No. 4);
- (5*R*)-3-(4-{[1-(2,1,3-benzoxadiazol-5-yl)piperidin-4-yl]oxy}-3-fluorophenyl)-5-(1*H*-1,2,3- 20 triazol-1-ylmethyl)-1,3-oxazolidin-2-one (Compound No. 5).

Scheme III

Compounds of Formulae XIII and XVII can be prepared following Scheme III.



5 Path A: Compounds of Formula V (wherein U, V, W, A, P and G are as defined earlier) can be reacted with compounds of Formula X (Het and P are same as defined earlier) to form compounds of Formula XI. Compounds of Formula XI can be deprotected to form compounds of Formula XII. Compounds of Formula XII can be reacted with compounds of Formula III to form compounds of Formula XIII.

10 Path B: Compounds of Formula V (wherein U, V, W, A, P and G are as defined earlier) can be reacted with compounds of Formula XIV (wherein Het is same as defined

earlier) to form compounds of Formula XV. Compounds of Formula XV can be deprotected to form compounds of Formula XVI. Compounds of Formula XVI can be reacted with compounds of Formula III to form compounds of Formula XVII.

Compounds of Formula V can be reacted with compounds of Formula X (Path A) to form compounds of Formula XI in one or more organic solvents, for example, dimethylformamide, 1,4-dioxane, tetrahydrofuran or mixtures thereof. This reaction can also be carried out in the presence of one or more bases, for example, Group I hydrides, *e.g.*, sodium hydride, potassium hydride, lithium hydride or mixtures thereof.

Compounds of Formula XI can also be deprotected to form compounds of Formula XII in the presence of one or more deprotection agents, for example, one or more strong protic acids in suitable solvents, *e.g.*, trifluoroacetic acid in dichloromethane or hydrochloric acid in ethanol.

Compounds of Formula XII can be reacted with compounds of Formula III to form compounds of Formula XIII in one or more organic solvents, for example, tetrahydrofuran, benzene, dimethylformamide, carbon tetrachloride or mixtures thereof. This reaction can be carried out in the presence of one or more bases, for example, sodium carbonate, potassium carbonate, cesium carbonate, sodium tertiary butoxide, potassium tertiary butoxide or mixtures thereof. This reaction can also be carried out in the presences of one or more catalysts, for example, *Tris*-(dibenzylideneacetone) dipalladium(0), Pd₂(dba)₃, palladium diacetate; palladium dichloride or mixtures thereof; and one or more suitable ligands, for example, 1,1'-binaphthalene-2,2'-diylbis(diphenylphosphine), tri-*tert*-butylphosphine, di-1-adamantyl(butyl)phosphine, biphenyl-2-yl(di-*tert*-butyl)phosphine or mixtures thereof.

Compounds of Formula V can be reacted with compounds of Formula XIV (Path B) to form compounds of Formula XV in one or more organic solvents, for example, tetrahydrofuran, benzene, dimethylformamide, carbon tetrachloride or mixtures thereof. This reaction can also be carried out in the presence of one or more suitable coupling agents, for example, diethyl diazocarbonylate, diisopropyl diazocarbonylate or mixtures thereof. This reaction can also be carried out in the presence of one or more catalysts, for example, triphenyl phosphine, trioctyl phosphine, tributyl phosphine or mixtures thereof.

Compounds of Formula XV can be deprotected to form compounds of Formula XVI in the presence of one or more deprotection agents, for example, one or more strong protic acids in suitable solvents, *e.g.*, trifluoroacetic acid in dichloromethane or hydrochloric acid in ethanol.

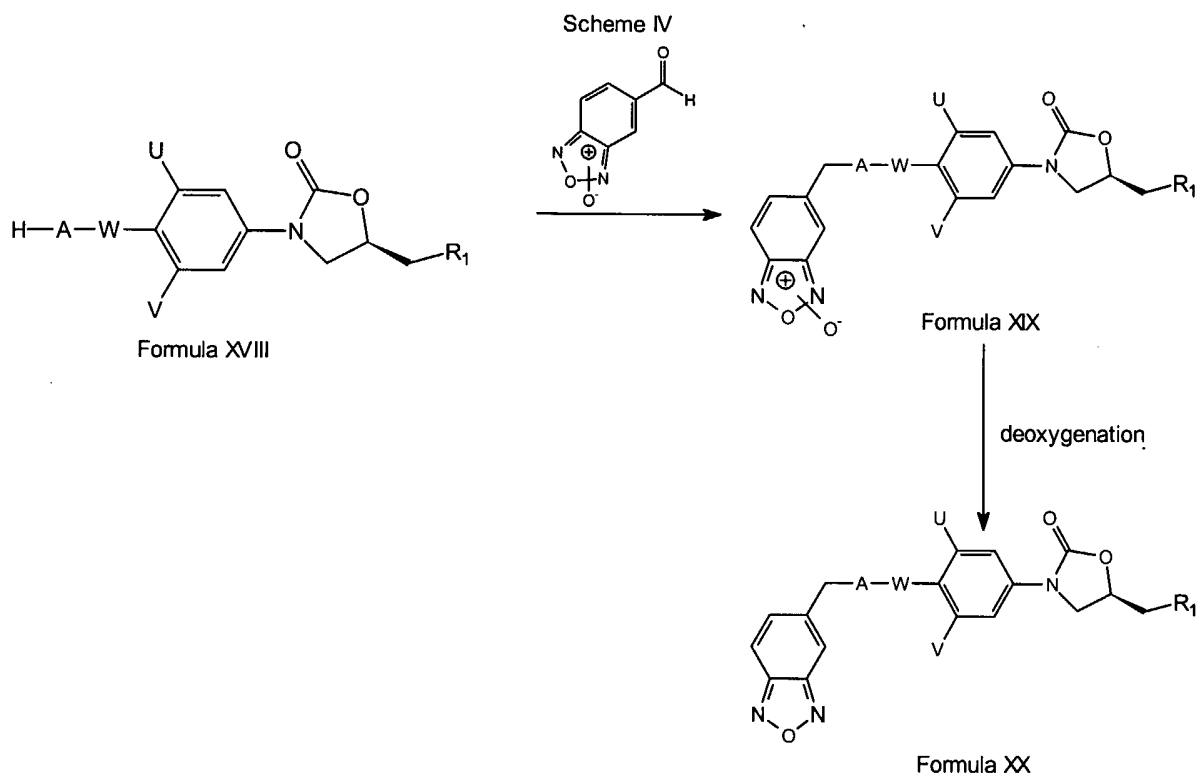
- 5 Compounds of Formula XVI can be reacted with compounds of Formula III to form compounds of Formula XVII in one or more organic solvents, for example, tetrahydrofuran, benzene, dimethylformamide, carbon tetrachloride or mixtures thereof. This reaction can also be carried out in the presence of one or more bases, for example, sodium carbonate, potassium carbonate, cesium carbonate, sodium tertiary butoxide,
- 10 potassium tertiary butoxide or mixtures thereof. This reaction can also be carried out in the presence of one or more catalysts, for example, *Tris*-(dibenzylideneacetone) dipalladium(0), Pd₂(dba)₃, palladium diacetate, palladium dichloride or mixtures thereof; and one or more suitable ligands, for example, 1,1'-binaphthalene-2,2'-diylbis(diphenylphosphine), tri-*tert*-butylphosphine, di-1-adamantyl(butyl)phosphine,
- 15 biphenyl-2-yl(di-*tert*-butyl)phosphine or mixtures thereof.

Compounds which may be prepared following Scheme III include, for example:

- (5*S*)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-fluorophenyl}-5-[(isoxazol-3-ylamino)methyl]-1,3-oxazolidin-2-one (Compound No. 6);
- (5*S*)-3-(4-{[1-(2,1,3-benzoxadiazol-5-yl)piperidin-4-yl]oxy}-3-fluorophenyl)-5-[(isoxazol-3-ylamino)methyl]-1,3-oxazolidin-2-one (Compound No. 7);
- 20 (5*R*)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-fluorophenyl}-5-(isoxazol-3-ylmethyl)-1,3-oxazolidin-2-one (Compound No. 8);
- (5*R*)-3-(4-{[1-(2,1,3-benzoxadiazol-5-yl)piperidin-4-yl]oxy}-3-fluorophenyl)-5-[(isoxazol-3-yloxy)methyl]-1,3-oxazolidin-2-one (Compound No. 9).

Scheme IV

Compounds of Formulae XIX and XX can be prepared following Scheme IV.



Thus, compounds of Formula XVIII can be coupled with 5-formylbenzofuroxan to form compounds of Formula XIX. Compounds of Formula XIX can be deoxygenated to form compounds of Formula XX.

Compounds of Formula XVIII can be reacted with 5-formylbenzofuroxan to form compounds of Formula XIX in one or more organic solvents, for example, tetrahydrofuran, dimethyl formamide, 1,4-dioxane or mixtures thereof. This reaction can also be carried out in the presence of one or more reducing agents, for example, sodium triacetoxy borohydride, sodium borohydride, sodium cyano borohydride, or mixtures thereof.

Compounds of Formula XIX can be deoxygenated to form compounds of Formula XX in one or more organic solvents, for example, alcohols, *e.g.*, ethanol, methanol or mixtures thereof. This reaction can also be carried out in the presence of one or more

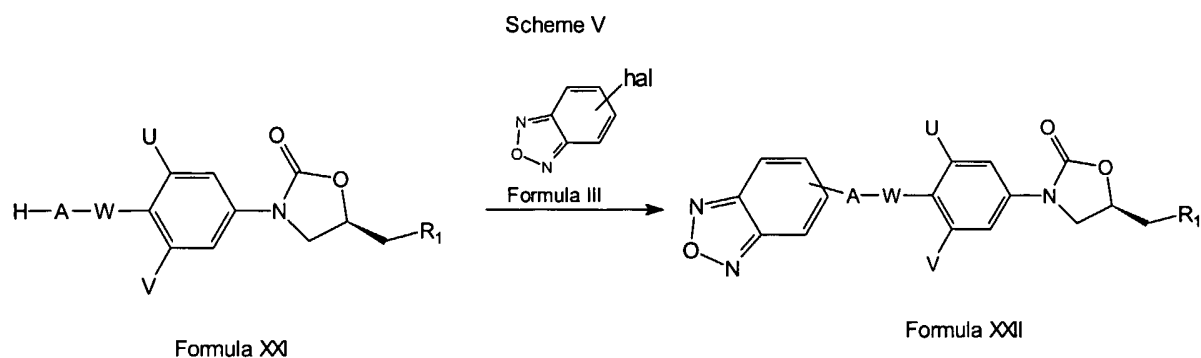
catalysts, for example, phosphines, *e.g.*, triphenyl phosphine, trioctyl phosphine, tributyl phosphine or mixtures thereof.

Compounds which may be prepared following Scheme IV include, for example:

- 5 *N*-{[(*5S*)-3-(3-fluoro-4-{4-[(oxido-2,1,3-benzoxadiazol-5-yl)methyl]piperazin-1-yl}phenyl)-2-oxo-1,3-oxazolidin-5-yl]methyl}acetamide (Compound No. 10);
- N*-{[(*5S*)-3-{4-[4-(2,1,3-benzoxadiazol-5-ylmethyl)piperazin-1-yl]-3-fluorophenyl}-2-oxo-1,3-oxazolidin-5-yl]methyl}acetamide (Compound No. 11).

Scheme V

Compounds of Formula XXII can be prepared according to Scheme V.



Thus, compounds of Formula XXI can be coupled with compounds of Formula III to form compounds of Formula XXII.

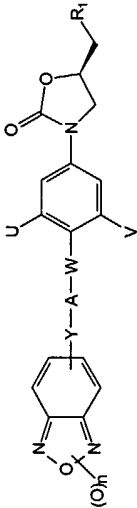
Compounds of Formula XXI can be reacted with compounds of Formula III to form compounds of Formula XXII in one or more solvents, for example, acetonitrile, chloroform, carbon tetrachloride or mixtures thereof; and in presence of one or more bases, for example, sodium carbonate, potassium carbonate, diisopropyl ethylamine, triethylamine, *N*-methyl morpholine or mixtures thereof. Alternatively, this reaction can also be carried out in one or more organic solvents, for example, acetonitrile, tetrahydrofuran, benzene, dimethylformamide, carbon tetrachloride or mixtures thereof; one or more bases, for example, sodium carbonate, potassium carbonate, cesium carbonate, sodium tertiary butoxide, potassium tertiary butoxide or mixtures thereof, and in the presence of one or more catalysts, for example, *Tris*-(dibenzylideneacetone) dipalladium(0), Pd₂(dba)₃, palladium diacetate, palladium dichloride or mixtures thereof;

and one or more suitable ligands, for example, 1,1'-binaphthalene-2,2'-diylbis(diphenylphosphine), tri-*tert*-butylphosphine, di-1-adamantyl(butyl)phosphine, biphenyl-2-yl(di-*tert*-butyl)phosphine or mixtures thereof.

Compounds which may be prepared following Scheme V include, for example:

- 5 *N*-{[(5*S*)-3-(4-{[1-(2,1,3-benzoxadiazol-5-yl)piperidin-4-yl]oxy})-3-fluorophenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl}acetamide (Compound No. 12);
- N*-[[(5*S*)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-fluorophenyl}-2-oxo-1,3-oxazolidin-5-yl)methyl]acetamide (Compound No. 13);
- N*-[[(5*S*)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3,5-difluorophenyl}-2-oxo-
- 10 1,3-oxazolidin-5-yl)methyl]acetamide (Compound No. 14).

TABLE I – Compound Moieties of Formula I

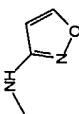
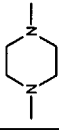
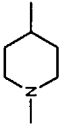
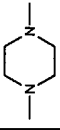
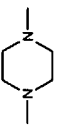
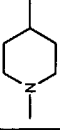
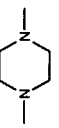
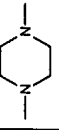


Formula I

wherein U is F and the following groups being:

Compound No.	W	A	n	Y	V	R ₁	Compound No.	W	A	n	Y	V	R ₁
1	-	-	0	-	H	-NHCOCH ₃	2	-	-	0	-	F	-NHCOCH ₃
3	-		0	-	H		4	-		0	-	H	
5	-		0	-O-	H		6	-		0	-	H	

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7	-		0	-O-	H		8	-		0	-	H	
9	-		0	-O-	H		10	-CH ₂ -		1	-	H	-NHCOCH ₃
11	-CH ₂ -		0	-	H	-NHCOCH ₃	12	-		0	-O-	H	-NHCOCH ₃
13	-		0	-	H	-NHCOCH ₃	14	-		0	-	F	-NHCOCH ₃

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 included within the scope of the present invention. The examples are provided to illustrate particular aspects of the disclosure and do not limit the scope of the present invention as defined by the claims.

Examples

Example 1: Synthesis of *N*-({(5*S*)-3-[4-(2,1,3-benzoxadiazol-5-yl)-3-fluorophenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)acetamide

5-bromo-2,1,3-benzoxadiazole (0.17 g) (which can be prepared according to *Org. Proc. Res. Dev.*, (2003), 7, 436-445 at page 437), triethylamine (0.11 g) and dichlorobis(triphenyl)phosphine palladium (II) (0.12 g) were added to a solution of *N*-({(5*S*)-3-[3-fluoro-4-(trimethylstannyl)phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)acetamide (0.18 g) (which can be prepared according to Example 8 of WO 01/94342, page 52) in dry dimethyl formamide (15 mL) and the reaction mixture was heated at 100 °C for about 3 hours, cooled and diluted with ethyl acetate. The organic layer was washed with water, dried over sodium sulfate and concentrated. The crude product was purified by column chromatography using 2 % methanol in dichloromethane as eluent to yield the title compound (0.14 g).

Melting point: 156-165 °C; EIMS (m/z): 388 (M+H);

¹HNMR(CDCl₃): δ 7.91 (m, 2H), 7.62 (m, 2H), 7.52 (t, 1H), 7.35 (dd, 1H), 6.10 (t, 1H), 4.84 (m, 1H), 4.12 (t, 1H), 3.87 (t, 1H), 3.71 (m, 2H), 2.02 (s, 3H).

Example 2: Synthesis of *N*-({(5*S*)-3-[4-(2,1,3-benzoxadiazol-5-yl)-3,5-difluorophenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)acetamide

Triethylamine (0.12 g), 5-bromo-2,1,3-benzoxadiazole (0.19 g) and dichlorobis(triphenyl)phosphine palladium(II) (0.13 g) were added to a solution of *N*-({(5*S*)-3-[3,5-difluoro-4-(trimethylstannyl)phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)acetamide (0.21 g) (which can be prepared according to Example 8 of WO 01/94342, at page 52) in dry dimethyl formamide (15 mL) and the reaction mixture was heated at 100 °C for about 3 hours. The reaction mixture was filtered and diluted with ethyl acetate. The organic layer was washed with water, dried over sodium sulfate and concentrated. The crude

product was purified by column chromatography using 2 % methanol in dichloromethane as eluent to yield the title compound (0.035 g).

Melting point: 165-168 °C; EIMS (m/z): 388;

¹HNMR(CDCl₃): δ 7.92 (m, 2H), 7.48 (dd, 1H), 7.32 (dd, 2H), 5.98 (t, 1H), 4.85 (m, 1H),
5 4.09 (t, 1H), 3.84 (m, 1H), 3.72 (m, 2H), 2.03 (s, 3H).

Example 3: Synthesis of (5R)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-fluorophenyl}-5-(1H-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one

Step a: Synthesis of tert-butyl 4-{2-fluoro-4-[(5R)-2-oxo-5-(1H-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-3-yl]phenyl}piperazine-1-carboxylate.

10 Sodium hydride (0.61 g) and 1H-1,2,3-triazole (0.7 mL) were added to a solution of *tert*-butyl 4-[2-fluoro-4-((5R)-5-{[(methylsulfonyl)oxy]methyl}-2-oxo-1,3-oxazolidin-3-yl)phenyl]piperazine-1-carboxylate (4 g) (which can be prepared according to Example 1(h) of WO93/23384, page 13) in dry dimethylformamide (15 mL) and the reaction
15 mixture was stirred at 80 °C for about 17 hours and extracted with ethyl acetate. The organic layer was washed with water, dried over sodium sulfate and concentrated. The crude product was purified by column chromatography using (4 %) methanol in dichloromethane as eluent to yield the title compound (1.45 g).

Step b: Synthesis of (5R)-3-(3-fluoro-4-piperazin-1-ylphenyl)-5-(1H-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one.

20 Trifluoroacetic acid (5 mL) was added to a solution of *tert*-butyl-4-{2-fluoro-4-[(5R)-2-oxo-5-(1H-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-3-yl]phenyl}piperazine-1-carboxylate (0.7 g) (obtained from Step a) in dichloromethane (15 mL) and the reaction mixture was stirred for about 2 hours. The reaction mixture was concentrated and to the residue thus obtained was added ethyl acetate (20 mL) followed by 10 % sodium
25 hydroxide (10 mL) until the pH was about 12-14. The organic layer was separated and washed with water, dried over sodium sulfate and concentrated to yield the title compound (0.98 g).

Step c: Synthesis of (5R)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-fluorophenyl}-5-(1H-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one.

5-bromo-2,1,3-benzoxadiazol (0.56 g), cesium carbonate (1.1 g), 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl(0.14 g) and *Tris*-(dibenzylideneacetone) dipalladium(0) (0.1 g) were added to a solution of (5*R*)-3-(3-fluoro-4-piperazin-1-ylphenyl)-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one(0.98 g) (obtained from
5 Step b) in dry dimethylformamide (15 mL) and the reaction mixture was heated at 100 °C for about 17 hours. The reaction mixture was filtered, the solvent was removed by evaporation and the crude product thus obtained was purified by column chromatography using 2 % methanol in dichloromethane to yield the title product (0.17 g).

Melting point: 153-173 °C; EIMS (*m/z*): 465.17;

10 ¹HNMR(DMSO): δ 8.17 (s, 1H), 7.90-7.87 (d, 1H), 7.74 (t, 2H), 7.44 (dd, 1H), 7.13 (m, 2H), 6.89 (s, 1H), 5.15-5.10 (m, 1H), 4.83 (d, 2H), 4.21 (t, 1H), 3.89-3.84 (t, 1H), 3.48 (m, 4H), 3.14 (m, 4H).

Example 4: Synthesis (5*R*)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-fluorophenyl}-5-(2*H*-1,2,3-triazol-2-ylmethyl)-1,3-oxazolidin-2-one

15 **Step a: Synthesis of *tert*-butyl 4-{2-fluoro-4-[(5*R*)-2-oxo-5-(2*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-3-yl]phenyl}piperazine-1-carboxylate**

Sodium hydride (0.61 g) and 2*H*-1,2,3-triazole (0.7 mL) were added to a solution of *tert*-butyl 4-[2-fluoro-4-((5*R*)-5-{[(methylsulfonyl)oxy]methyl}-2-oxo-1,3-oxazolidin-3-yl)phenyl]piperazine-1-carboxylate (4 g) (which can be prepared according to Example
20 1(h) of WO93/23384, page 13) in dry dimethylformamide (15 mL) and the reaction mixture was stirred at 80 °C for about 17 hours. The reaction mixture was extracted with ethyl acetate and the organic layer was washed with water, dried over sodium sulfate and concentrated. The crude product thus obtained was purified by column chromatography using (3 %) methanol in dichloromethane as eluent to yield the title compound (0.9 g).

25 **Step b: Synthesis of (5*R*)-3-(3-fluoro-4-piperazin-1-ylphenyl)-5-(2*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one.**

Trifluoroacetic acid (5 mL) was added to a solution of *tert*-butyl 4-{2-fluoro-4-[(5*R*)-2-oxo-5-(2*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-3-yl]phenyl}piperazine-1-carboxylate (0.7 g) (obtained from Step a) in dichloromethane (15 mL) and the reaction
30 mixture was stirred for about 2 hours. The reaction mixture was concentrated and to the

residue thus obtained was added ethyl acetate (20 mL) followed by 10 % sodium hydroxide (10 mL) until the pH was about 12-14. The organic layer separated out and was washed with water, dried over sodium sulfate and concentrated to yield the title compound (0.7 g).

5 Step c: Synthesis of (5R)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-fluorophenyl}-5-(2H-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one.

5-bromo-2,1,3-benzoxadiazole (0.4 g), cesium carbonate (0.79 g), 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (0.1 g) and *tris*-(dibenzylideneacetone)dipalladium(0) (0.74 g) were added to (5R)-3-(3-fluoro-4-piperazin-1-ylphenyl)-5-(2H-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one (0.7 g) (obtained from Step b) in dry dimethylformamide (15 mL) and the reaction mixture was heated at 100 °C for about 17 hours. The reaction mixture was filtered, the solvent was evaporated and the crude product thus obtained was purified by column chromatography using 2 % methanol in dichloromethane to yield the title product (0.2g). Melting point: 215-220 °C; EIMS (m/z): 465.21;

¹HNMR(DMSO): δ 7.91-7.83 (m, 3H), 7.73 (d, 1H), 7.43 (dd, 1H), 7.13 (d, 2H), 6.89 (s, 1H), 5.18 (m, 1H), 4.86 (d, 2H), 4.22 (t, 1H), 3.91-3.86 (m, 1H), 3.48 (m, 4H), 3.14 (m, 4H).

20 Example 5: Synthesis of (5R)-3-(4-{[1-(2,1,3-benzoxadiazol-5-yl)piperidin-4-yl]oxy}-3-fluorophenyl)-5-(1H-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one

Step a: *Tert*-butyl 4-{4-[(5R)-2-oxo-5-(1H-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-3-yl]phenoxy}piperidine-1-carboxylate.

Sodium hydride (0.3 g) and 1H-1,2,3-triazole (0.3 mL) were added to a solution of *tert*-butyl 4-[2-fluoro-4-((5R)-5-[[[(methylsulfonyl)oxy]methyl]-2-oxo-1,3-oxazolidin-3-yl]phenoxy]piperidine-1-carboxylate (2 g) (which can be prepared according to Example 6, after the first step in the conversion of compound 6 to 7, in *Biorg. Med. Chem. Lett.*, 11 (2001), 1829-1832, at page 1830) in dry dimethylformamide (15 mL) and the reaction mixture was stirred at 80 °C for about 17 hours. The reaction mixture was extracted with ethyl acetate, washed with water, dried over sodium sulfate and concentrated. The crude

thus obtained was purified by column chromatography using (2 %) methanol in dichloromethane as eluent to yield the title compound (0.68 g).

Step b: Synthesis of (5R)-3-[3-fluoro-4-(piperidin-4-yloxy)phenyl]-5-(1H-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one.

5 Trifluoroacetic acid (4 mL) was added to a solution of *tert*-butyl 4-{4-[(5R)-2-oxo-5-(1H-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-3-yl]phenoxy}piperidine-1-carboxylate (0.68 g) (obtained from Step a) in dichloromethane (10 mL) and the reaction mixture was stirred for about 2 hours. The reaction mixture was concentrated and to the residue thus obtained was added ethyl acetate (20 mL) followed by 10 % sodium hydroxide (10 mL)
10 until the pH was about 12-14. The organic layer, which separated out, was washed with water, dried over sodium sulfate and concentrated to yield the title compound (1 g).

Step c: Synthesis of (5R)-3-(4-{[1-(2,1,3-benzoxadiazol-5-yl)piperidin-4-yl]oxy}-3-fluorophenyl)-5-(1H-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one.

5-bromo-2,1,3-benzoxadiazole (0.61 g), cesium carbonate (1.2 g), 2,2'-
15 bis(diphenylphosphino)-1,1'-binaphthyl (0.51 g) and *Tris*-(dibenzylideneacetone)dipalladium(0) (0.11 g) were added to a solution (5R)-3-[3-fluoro-4-(piperidin-4-yloxy)phenyl]-5-(1H-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one (1 g) (obtained from Step b) in dry dimethylformamide (10 mL) and the reaction mixture was heated at 100 °C for about 17 hours. The reaction mixture was filtered and the solvent was evaporated.
20 The crude product thus obtained was purified by column chromatography using 1 % methanol in dichloromethane to yield the title product (0.15g).

Melting point: 148-150 °C; EIMS (m/z): 480.02;

¹HNMR(DMSO): δ 7.85 (d, 3H), 7.68 (d, 1H), 7.46 (dd, 1H), 7.28 (t, 1H), 7.15 (d, 1H), 6.85 (s, 1H), 5.2 (m, 1H), 4.86-4.85 (d, 2H), 4.6 (m, 1H), 4.22 (t, 1H), 3.9 (m, 1H), 3.72-
25 3.68 (m, 2H), 3.47-3.46 (d, 1H), 2.04 (m, 2H), 1.76 (m, 2H).

Example 6: Synthesis of (5S)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-fluorophenyl}-5-[(isoxazol-3-ylamino)methyl]-1,3-oxazolidin-2-one (Path A)

Step a: Synthesis of *tert*-butyl 4-(2-fluoro-4-{(5S)-5-[(isoxazol-3-ylamino)methyl]-2-oxo-1,3-oxazolidin-3-yl}phenyl)piperazine-1-carboxylate.

Sodium hydride (0.23 g) and *tert*-butyl isoxazol-3-ylcarbamate (0.88 g) were added to a solution of *tert*-butyl 4-[2-fluoro-4-((5*R*)-5-[[[(methylsulfonyl)oxy]methyl]-2-oxo-1,3-oxazolidin-3-yl]phenyl]piperazine-1-carboxylate (1 g) (which can be prepared according to Example 1(h) given in WO93/23384, at page 13) in dry dimethylformamide (10 mL) and the reaction mixture was stirred at 80 °C for about 17 hours. The reaction mixture was extracted with ethyl acetate and the organic layer was washed with water, dried over sodium sulfate and concentrated. The crude product thus obtained was purified by column chromatography using 2 % methanol in dichloromethane as eluent to yield the title compound (1 g).

Step b: Synthesis of (5*S*)-3-(3-fluoro-4-piperazin-1-ylphenyl)-5-[(isoxazol-3-ylamino)methyl]-1,3-oxazolidin-2-one.

Trifluoroacetic acid (4 mL) was added to a solution of *tert*-butyl 4-(2-fluoro-4-[(5*S*)-5-[(isoxazol-3-ylamino)methyl]-2-oxo-1,3-oxazolidin-3-yl]phenyl)piperazine-1-carboxylate (1 g) (obtained from Step a in) dichloromethane (10 mL) and the reaction mixture was stirred for about 2 hours. The reaction mixture was concentrated and to the residue thus obtained was added ethyl acetate (15 mL) followed by 10 % sodium hydroxide (10 mL) until the pH was about 12-14. The organic layer, which separated out, was washed with water, dried over sodium sulfate and concentrated to yield the title compound (1.36 g crude weight)

Step c: Synthesis of (5*S*)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-fluorophenyl}-5-[(isoxazol-3-ylamino)methyl]-1,3-oxazolidin-2-one.

5-bromo-2,1,3-benzoxadiazol (0.75 g), cesium carbonate (1.47 g), 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (0.18 g) and *Tris*-(dibenzylideneacetone) dipalladium(0) (0.13 g) were added to a solution of (5*S*)-3-(3-fluoro-4-piperazin-1-ylphenyl)-5-[(isoxazol-3-ylamino)methyl]-1,3-oxazolidin-2-one (1.36 g) (obtained from Step b) in dry dimethylformamide (10 mL) and the reaction mixture was heated at 100 °C for about 17 hours. The reaction mixture was filtered and the solvent was evaporated. The crude product thus obtained was purified by column chromatography using 1 % methanol in dichloromethane to yield the title product (0.1 g).

Melting point: 213-215 °C; EIMS (*m/z*): 480.26, *M*+Na 502.22;

¹HNMR(DMSO): δ 8.38 (s, 1H), 7.88 (d, 1H), 7.72 (d, 1H), 7.53 (dd, 1H), 7.15 (m, 2H), 6.89 (s, 1H), 6.54 (t, 1H), 6.0 (s, 1H), 4.86 (m, 1H), 4.13 (t, 1H), 3.79 (t, 1H), 3.53 (m, 4H), 3.15 (m, 4H).

Example 7: Synthesis of (5S)-3-(4-{[1-(2,1,3-benzoxadiazol-5-yl)piperidin-4-yl]oxy}-3-fluorophenyl)-5-[(isoxazol-3-ylamino)methyl]-1,3-oxazolidin-2-one (Path A)

Step a: Synthesis of *tert*-butyl 4-[4-((5R)-5-[[*tert*-butoxycarbonyl](isoxazol-3-yl)amino)methyl]-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenoxy]piperidine-1-carboxylate.

Sodium hydride (0.15 g) and *tert*-butyl isoxazol-3-ylcarbamate (0.87 g) were added to a solution of *tert*-butyl 4-[2-fluoro-4-((5R)-5-[[*tert*-butoxycarbonyl](isoxazol-3-yl)amino)methyl]-2-oxo-1,3-oxazolidin-3-yl)phenoxy]piperidine-1-carboxylate (1.5 g) (which can be prepared according to Example 6, after the first step in the conversion of the compound 6 to 7, in *Biorg. Med. Chem. Lett.*, 11 (2001), 1829-1832, at page 1830) in dry dimethylformamide (10 mL). The reaction mixture was stirred at 80 °C for about 17 hours. The reaction mixture was extracted with ethyl acetate and the organic layer was washed with water, dried over sodium sulfate and concentrated. The crude product thus obtained was purified by column chromatography using 2 % methanol in dichloromethane as eluent to yield the title compound (2 g).

Step b: Synthesis of (5S)-3-[3-fluoro-4-(piperidin-4-yloxy)phenyl]-5-[(isoxazol-3-ylamino)methyl]-1,3-oxazolidin-2-one.

Trifluoroacetic acid (10 mL) was added to a solution of *tert*-butyl 4-[4-((5R)-5-[[*tert*-butoxycarbonyl](isoxazol-3-yl)amino)methyl]-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenoxy]piperidine-1-carboxylate (2 g) obtained from Step a in dichloromethane (15 mL) and stirred for about 2 hours. The reaction mixture was concentrated and to the residue thus obtained was added ethyl acetate (20 mL) followed by 10 % sodium hydroxide (10 mL) until the pH was about 12-14. The organic layer, which separated out, was washed with water, dried over sodium sulfate and concentrated to yield the title compound (5 g).

Step c: Synthesis of (5S)-3-[3-fluoro-4-(piperidin-4-yloxy)phenyl]-5-[(isoxazol-3-ylamino)methyl]-1,3-oxazolidin-2-one.

5-bromo-2,1,3-benzoxadiazol (2.74 g) (which can be prepared according to *Org. Proc. Res. Dev.*, (2003), 7, 436-445), cesium carbonate (5.38 g), 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (0.68 g) and *tris*-(dibenzylideneacetone)dipalladium(0) (0.5 g) were added to a solution of (5S)-3-[3-fluoro-4-(piperidin-4-yloxy)phenyl]-5-[(isoxazol-3-ylamino)methyl]-1,3-oxazolidin-2-one (5 g) (obtained from Step b) in dry dimethylformamide (15 mL) and the reaction mixture was heated at 100 °C for about 17 hours. The reaction mixture was filtered and the solvent was evaporated. The crude product thus obtained was purified by column chromatography using 1 % methanol in dichloromethane to yield the title product (0.4g). Melting point: 134-140 °C; EIMS (m/z): 495.25; ¹HNMR(DMSO): δ 8.41 (s, 1H), 7.88 (d, 1H), (d, 1H), 7.6 (dd, 1H), 7.32 (t, 1H), 7.25 (d, 1H), 6.88 (s, 1H), 6.56 (t, 1H), 6.03 (s, 1H), 4.8 (m, 1H), 4.63-4.62 (m, 1H), 4.17 (t, 1H), 3.81 (m, 4H), 3.49-3.43 (m, 3H), 2.07 (m, 2H), 1.8 (m, 2H).

Example 8: Synthesis of (5R)-3-(4-{[1-(2,1,3-benzoxadiazol-5-yl)piperidin-4-yl]oxy}-3-fluorophenyl)-5-[(isoxazol-3-yloxy)methyl]-1,3-oxazolidin-2-one (Path B)

Step a: Synthesis of *tert*-butyl 4-(2-fluoro-4-[(5R)-5-[(isoxazol-3-yloxy)methyl]-2-oxo-1,3-oxazolidin-3-yl]phenoxy)piperidine-1-carboxylate

Triphenyl phosphine(0.99 g) and 3-hydroxy-isoxazole (0.25 g) and diethylazodicarboxylate (0.75 mL) were added under nitrogen atmosphere to a solution of *tert*-butyl 4-{2-fluoro-4-[(5R)-5-(hydroxymethyl)-2-oxo-1,3-oxazolidin-3-yl]phenoxy}piperidine-1-carboxylate (1 g) (which can be prepared according to Example 6, after the first step in the conversion of the compound 6 to 7, in *Biorg. Med. Chem. Lett.*, 11 (2001), 1829-1832, at page 1830) in dry tetrahydrofuran (10 mL) and the reaction mixture was stirred at room temperature for about 17 hours. The reaction mixture was extracted with ethyl acetate, washed with water, dried over sodium sulfate and concentrated. The crude product thus obtained was purified by column chromatography using 0.5 % methanol in dichloromethane as eluent to yield the title compound (0.81 g).

Step b: Synthesis of (5S)-3-[3-fluoro-4-(piperidin-4-yloxy)phenyl]-5-[(isoxazol-3-ylamino)methyl]-1,3-oxazolidin-2-one.

Trifluoroacetic acid (4 mL) was added to a solution of *tert*-butyl 4-(2-fluoro-4-
{(5*R*)-5-[(isoxazol-3-yloxy)methyl]-2-oxo-1,3-oxazolidin-3-yl}phenoxy)piperidine-1-
carboxylate (0.81 g) (obtained from Step a) in dichloromethane (20 mL) and the reaction
mixture was stirred for about 2 hours. The reaction mixture was concentrated and to the
5 residue thus obtained was added ethyl acetate (20 mL) followed by 10 % sodium
hydroxide (10 mL) until the pH was about 12-14. The organic layer, which separated out,
was and washed with water, dried over sodium sulfate and concentrated to yield the title
compound (1.3 g).

**Step c: Synthesis of (5*S*)-3-[3-fluoro-4-(piperidin-4-yloxy)phenyl]-5-[(isoxazol-3-
10 ylamino)methyl]-1,3-oxazolidin-2-one.**

5-bromo-2,1,3-benzoxadiazole (0.71 g), cesium carbonate (1.4 g), 2,2'-
bis(diphenylphosphino)-1,1'-binaphthyl (0.17 g) and *Tris*-(dibenzylideneacetone)
dipalladium(0) (0.13g) were added to a solution of (5*S*)-3-[3-fluoro-4-(piperidin-4-
yloxy)phenyl]-5-[(isoxazol-3-ylamino)methyl]-1,3-oxazolidin-2-one (1.3 g) (obtained
15 from Step b) in dry dimethylformamide (15 mL) and the reaction mixture was heated at
100 °C for about 17 hours. The reaction mixture was filtered and the solvent was
evaporated. The crude product thus obtained was purified by column chromatography
using 1 % methanol in dichloromethane to yield the title product (0.07g).

Melting point: 75-100 °C; EIMS (*m/z*): 534.21;

20 ¹HNMR(DMSO): δ 8.16 (s, 1H), 7.66 (d, 1H), 7.48 (dd, 1H), 7.3 (m, 2H), 7.17 (d, 1H),
7.08-7.05 (t, 1H), 6.75 (s, 1H), 4.99 (m, 1H), 4.53 (m, 3H), 4.14-4.11 (t, 1H), 3.95 (t, 1H),
3.61 (m, 2H), 3.3 (m, 2H), 2.04 (m, 4H).

Example 9: Synthesis (5*R*)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-
fluorophenyl}-5-(isoxazol-3-ylmethyl)-1,3-oxazolidin-2-one (Path B)

**25 Step a: Synthesis of *tert*-butyl 4-(2-fluoro-4-{(5*R*)-5-[(isoxazol-3-yloxy)methyl]-2-oxo-
1,3-oxazolidin-3-yl}phenyl)piperazine-1-carboxylate**

Triphenyl phosphine (1.49 g) and 3-hydroxy-isoxazole (0.38 g) and
diethylazodicarboxylate (1.12 mL) were added under nitrogen atmosphere to a solution of
tert-butyl 4-{2-fluoro-4-[(5*R*)-5-(hydroxymethyl)-2-oxo-1,3-oxazolidin-3-
30 yl]phenyl}piperazine-1-carboxylate (1.5 g) (which can be prepared according to Example

1(g) given in WO93/23384, at page 13) in dry tetrahydrofuran (10 mL) and the reaction mixture was stirred at room temperature for about 17 hours. The reaction mixture was extracted with ethyl acetate and the organic layer was washed with water, dried over sodium sulfate and concentrated. The crude product thus obtained was purified by column chromatography using 1 % methanol in dichloromethane as eluent to yield the title compound (1.4 g).

Step b: Synthesis of (5R)-3-(3-fluoro-4-piperazin-1-ylphenyl)-5-[(isoxazol-3-yloxy)methyl]-1,3-oxazolidin-2-one.

Trifluoroacetic acid (4 mL) was added to a solution of *tert*-butyl 4-(2-fluoro-4-((5R)-5-[(isoxazol-3-yloxy)methyl]-2-oxo-1,3-oxazolidin-3-yl)phenyl)piperazine-1-carboxylate (1.4 g) (obtained from Step a) in dichloromethane (15 mL). The organic layer, which separated out, was washed with water, dried over sodium sulfate and concentrated to yield the title compound (0.91 g).

Step c: Synthesis of (5R)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-fluorophenyl}-5-[(isoxazol-3-yloxy)methyl]-1,3-oxazolidin-2-one.

5-bromo-2,1,3-benzoxadiazole (0.52 g), cesium carbonate (1.01 g), 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (0.13 g) and *tris*-(dibenzylideneacetone)dipalladium(0) (0.09 g) were added to a solution of (5R)-3-(3-fluoro-4-piperazin-1-ylphenyl)-5-[(isoxazol-3-yloxy)methyl]-1,3-oxazolidin-2-one (0.91 g) (obtained from Step b) in dry dimethylformamide (15 mL) and heated at 100 °C for about 17 hours. The reaction mixture was filtered and the solvent was evaporated. The crude product thus obtained was purified by column chromatography using 80 % ethyl acetate in hexane to yield the title product (0.03g).

Melting point: 125-143 °C; EIMS (m/z): 481.25;

¹HNMR(DMSO): δ 8.69 (s, 1H), 7.88 (d, 1H), 7.73 (d, 1H), 7.53 (dd, 1H), 7.24 (d, 1H), 7.15 (t, 1H), 6.89 (s, 1H), 6.39 (s, 1H), 4.99 (m, 1H), 4.47 (m, 2H), 4.18 (t, 1H), 3.91 (t, 1H), 3.53 (m, 4H), 3.15 (m, 4H).

Example 10: Synthesis of N-{[(5S)-3-(3-fluoro-4-{4-[(oxido-2,1,3-benzoxadiazol-5-yl)methyl]piperazin-1-yl}phenyl)-2-oxo-1,3-oxazolidin-5-yl]methyl}acetamide

5-formyl benzofuroxan (0.34 g) and molecular sieves were added to a solution of N-{[(5S)-3-(3-fluoro-4-piperazin-1-ylphenyl)-2-oxo-1,3-oxazolidin-5-yl]methyl}acetamide trifluoroacetate (1.72mmoles) (which can be prepared according to Example 1(k) in WO93/23384 at page 14) in tetrahydrofuran (20 mL) and the reaction mixture was stirred for 5 minutes. Sodium triacetoxy borohydride (1.45 g) was then added and the reaction mixture was stirred for 3 hours and filtered. The crude product thus obtained was purified by column chromatography using 4 % methanol in dichloromethane as eluent to yield the title compound (0.41 g).

Melting point: 66-70 °C; EIMS (m/z): 388;

¹HNMR(CDCl₃): δ 8.24 (t, 1H), 7.83 (br m, 2H), 7.5 (d, 2H), 7.15 (m, 2H), 4.69 (m, 1H), 4.33 (m, 2H), 4.08 (t, 1H), 3.69 (t, 1H), 3.23 (m, 8H), 1.83 (s, 3H)

Example 11: Synthesis of N-[(5S)-3-{4-[4-(2,1,3-benzoxadiazol-5-ylmethyl)piperazin-1-yl]-3-fluorophenyl}-2-oxo-1,3-oxazolidin-5-yl)methyl]acetamide

Triphenylphosphine (0.15 g) was added to a solution of N-{[(5S)-3-(3-fluoro-4-{4-[(oxido-2,1,3-benzoxadiazol-5-yl)methyl]piperazin-1-yl}phenyl)-2-oxo-1,3-oxazolidin-5-yl]methyl}acetamide (obtained in Example 10) in absolute ethanol (10 mL) and the reaction was refluxed for about 3 hours at 85 °C. The reaction mixture was concentrated and the crude product thus obtained was purified by column chromatography using 3 % methanol in dichloromethane to yield the title compound (0.08 g).

Melting point: 165-168 °C; EIMS (m/z): 469;

¹HNMR(DMSO): δ 8.22 (t, 1H), 8.01 (dd, 1H), 7.91 (s, 1H), 7.61 (d, 1H), 7.46 (dd, 1H), 7.15 (d, 1H), 7.07 (t, 1H), 4.69 (m, 1H), 4.06 (t, 1H), 3.69 (m, 4H), 3.39 (m, 2H), 3.01 (m, 4H), 2.61 (m, 4H), 1.83 (s, 3H).

Example 12: Synthesis of N-{[(5S)-3-(4-{[1-(2,1,3-benzoxadiazol-5-yl)piperidin-4-yl]oxy}-3-fluorophenyl)-2-oxo-1,3-oxazolidin-5-yl]methyl}acetamide (Path A)

5-bromo-2,1,3-benzoxadiazole (0.14 g) and diisopropyl ethylamine (1.16 mL) were added to a solution of *tert*-butyl 4-(4-{(5S)-5-[(acetyl amino)methyl]-2-oxo-1,3-

oxazolidin-3-yl}-2-fluorophenoxy)piperidine-1-carboxylate (0.3 g) (which can be prepared according to Example 7 in *Biorg. Med. Chem. Lett.*, 11 (2001), 1829-1832 at page 1830) in acetonitrile and the reaction mixture was heated at 80 °C for about 48 hours. The reaction mixture was filtered and the solvent was evaporated. The crude product thus obtained was purified by preparative thin layer chromatography using 5 % methanol in dichloromethane to yield the title product (0.03 g).

Melting point: 96-100 °C; EIMS (m/z): 470.13;

¹HNMR(CDCl₃): δ 7.6 (dd, 1H), 7.47 (dd, 1H), 7.30 (d, 1H), 7.06 (m, 2H), 6.73 (dd, 1H), 5.94 (6s, 1H), 4.76 (m, 1H), 4.49 (m, 1H), 4.03 (t, 1H), 3.76-3.44 (m, 6H), 3.28 (m, 1H), 2.03 (m, 7H).

Example 13: Synthesis of N-[(5S)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-fluorophenyl}-2-oxo-1,3-oxazolidin-5-yl)methyl]acetamide (Path B)

Cesium carbonate (0.46 g), 5-bromo-2,1,3-benzoxadiazole (0.23 g), 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (0.074 g) and *tris*-(dibenzylideneacetone) dipalladium(0) (0.054 g) were added to a solution of *N*-{[(5S)-3-(3-fluoro-4-piperazin-1-ylphenyl)-2-oxo-1,3-oxazolidin-5-yl]methyl}acetamide (0.4 g) (which can be prepared according to Example 1(k) in WO 93/23384, at page 14) in dry dimethyl formamide (15 mL) and the reaction mixture was heated at 100 °C for 17 hours. The reaction mixture was filtered and the solvent was evaporated. The crude product thus obtained was purified by column chromatography using 2 % methanol in dichloromethane and sonicated in ether to yield the title compound (0.12 g).

Melting point: 201-222 °C; EIMS (m/z): 455;

¹HNMR(CDCl₃): δ 7.71 (d, 1H), 7.48 (dd, 1H), 7.33 (dd, 1H), 7.12 (dd, 1H), 6.98 (t, 1H), 6.79 (s, 1H), 5.99 (t, 1H), 4.76 (m, 1H), 4.02 (t, 1H), 3.85-3.55 (m, 3H), 3.47 (m, 4H), 3.24 (m, 4H), 2.03 (s, 3H).

Example 14: Synthesis of N-[(5S)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3,5-difluorophenyl}-2-oxo-1,3-oxazolidin-5-yl)methyl]acetamide(Path B)

Cesium carbonate (0.23 g), 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (0.06 g), 5-bromo-2,1,3-benzoxadiazole (0.12 g) and *Tris*-(dibenzylideneacetone) dipalladium(0) (0.1

g) were added to a solution of *N*-{[(5*S*)-3-(3,5-difluoro-4-piperazin-1-ylphenyl)-2-oxo-1,3-oxazolidin-5-yl]methyl}acetamide (0.21 g) (which can be prepared according to Example 32(i) in U.S. Patent No. 5,547,950 at page 25) in dry dimethyl formamide (10 mL) and the reaction mixture was heated at 100 °C for 17 hours. The reaction mixture
5 was filtered and the solvent was evaporated. The crude product thus obtained was purified by column chromatography using 2 % methanol in dichloromethane as eluent to yield the title compound (0.025 g).

Melting point: 207-213 °C; EIMS (m/z): 388;

¹HNMR(CDCl₃): δ 7.91 (m, 2H), 7.62 (m, 2H), 7.52 (t, 1H), 7.35 (dd, 1H), 6.10 (t, 1H),
10 4.84 (m, 1H), 4.12 (t, 1H), 3.87 (t, 1H), 3.71 (m, 2H), 2.02 (s, 3H).

Example 15: Assay for in vitro Antibacterial Activity

Compounds described herein displayed antibacterial activity when tested by the agar incorporation method. The following minimum inhibitory concentrations (μg/mL) were obtained for representative compounds of the invention, which are given below.

15 In vitro (μg/mL) activity data:

S. aureus ATCC 25923 --*Staphylococcus aureus* ATCC 25923; MIC was about 0.5-16 μg/mL with Linezolid 2 μg/mL; about 0.5 to 8 μg/mL with Linezolid 2 μg/mL; and even about 0.5 to 4 μg/mL with Linezolid 2 μg/mL.

S. aureus ATCC 15187 --*Staphylococcus aureus* ATCC 15187; MIC was about 0.25-16 μg/mL with Linezolid 2 μg/mL; about 0.25 to 8 μg/mL with Linezolid 2 μg/mL; and even
20 about 0.25 to 4 μg/mL with Linezolid 2 μg/mL.

S. aureus MRSA ATCC562 --*Methicilline Resistant Staphylococcus aureus* ATCC562; MIC was about 0.25-16 μg/mL with Linezolid 2 μg/mL; about 0.25 to 4 μg/mL with Linezolid 2 μg/mL; and even about 0.25 to 2 μg/mL with Linezolid 2 μg/mL.

25 *S. aureus* MRSA ATCC33 --*Methicilline Resistant Staphylococcus aureus* ATCC33; MIC was about 0.25-16 μg/mL with Linezolid 2 μg/mL; about 0.25 to 8 μg/mL with Linezolid 2 μg/mL; and even about 0.25 to 4 μg/mL with Linezolid 2 μg/mL.

Ent. faecalis ATCC 29212 --*Enterococcus faecalis* ATCC 29212; MIC was about 0.25-16 $\mu\text{g/mL}$ with Linezolid 2 $\mu\text{g/mL}$; about 0.25 to 8 $\mu\text{g/mL}$ with Linezolid 2 $\mu\text{g/mL}$; and even about 0.25 to 4 $\mu\text{g/mL}$ with Linezolid 2 $\mu\text{g/mL}$.

5 *VRE* --- *Vancomycin-resistant Enterococci* ATCC 6A; MIC was about 0.25-16 $\mu\text{g/mL}$ with Linezolid 2 $\mu\text{g/mL}$; about 0.25 to 8 $\mu\text{g/mL}$ with Linezolid 2 $\mu\text{g/mL}$; and even about 0.25 to 4 $\mu\text{g/mL}$ with Linezolid 2 $\mu\text{g/mL}$.

Strep. pyog. ATCC 19615 --*Streptococcus pyogenes* ATCC 19615; MIC was about 0.125-8 $\mu\text{g/mL}$ with Linezolid 2 $\mu\text{g/mL}$; about 0.125 to 2 $\mu\text{g/mL}$ with Linezolid 2 $\mu\text{g/mL}$; and even about 0.125 to 1 $\mu\text{g/mL}$ with Linezolid 2 $\mu\text{g/mL}$.

10 *Strep. pneum.* AB34 DRSP --*Streptococcus pneumoniae* AB34 DRSP; MIC was about 0.25-8 $\mu\text{g/mL}$ with Linezolid 2 $\mu\text{g/mL}$; about 0.25 to 4 $\mu\text{g/mL}$ with Linezolid 2 $\mu\text{g/mL}$; and even about 0.25 to 1 $\mu\text{g/mL}$ with Linezolid 2 $\mu\text{g/mL}$.

Strep. pneum. ATCC6303 --*Streptococcus pneumoniae* ATCC 6303; MIC was about 0.125-8 $\mu\text{g/mL}$ with Linezolid 1 $\mu\text{g/mL}$; about 0.125 to 4 $\mu\text{g/mL}$ with Linezolid 1 $\mu\text{g/mL}$; and
15 even about 0.125 to 2 $\mu\text{g/mL}$ with Linezolid 1 $\mu\text{g/mL}$.

M.catt.----*Moraxella catarrhalis* ATCC 8176; MIC was about 2-8 $\mu\text{g/mL}$ with Linezolid 2 $\mu\text{g/mL}$.

H. influ.---*Haemophilus influenzae* ATCC 49247; MIC was about 8-32 $\mu\text{g/mL}$ with Linezolid 8 $\mu\text{g/mL}$; even about 8-16 $\mu\text{g/mL}$ with Linezolid 8 $\mu\text{g/mL}$.

20 *B. fragillus*---*Bacillus fragillus* ATCC 25285; MIC was about 0.5-16 $\mu\text{g/mL}$ with Linezolid 4 $\mu\text{g/mL}$; about 0.5 to 8 $\mu\text{g/mL}$ with Linezolid 4 $\mu\text{g/mL}$; and even about 0.5 to 1 $\mu\text{g/mL}$ with Linezolid 4 $\mu\text{g/mL}$.

For Linezolid resistant strains.

S. aureus MRSA 32---Methicilline Resistant *Staphylococcus aureus* 32; MIC was 4-16
25 $\mu\text{g/mL}$ with Linezolid 32 $\mu\text{g/mL}$

Ent. faecalis 303 --*Enterococcus faecalis* 303; MIC was 0.125-4 $\mu\text{g/mL}$ with Linezolid 16 $\mu\text{g/mL}$

Strep. pneum. ATCC6303 --*Streptococcus pneumoniae* ATCC 6303; with Linezolid >16 $\mu\text{g/mL}$.

The *in vitro* antibacterial activity of the compounds was demonstrated by the agar dilution method (NCCLS M 7-A5 and M 100-S8 documents). In general, the compounds were dissolved in dimethylsulfoxide and doubling dilution of the compounds was incorporated into Muller Hilton agar before solidification. Inoculum was prepared by direct colony suspension in normal saline solution and adjusting the turbidity to 0.5 Macfarland turbidity and subsequently diluting as per NCCLS guidelines in order to obtain 10^4 CFU/spot. CFU/mL of few randomly selected cultures was performed. The cultures were replicated on agar plate using Denley's multipoint replicator. The agar plates were incubated for 18 hours-24 hours (24 hours for MRSA studies) at $35 \pm 2^\circ\text{C}$. Q.C. strains were also included in each run of the study.

The *in vitro* activity for Haemophilus MICs were performed by using a Micro broth dilution method as follows:

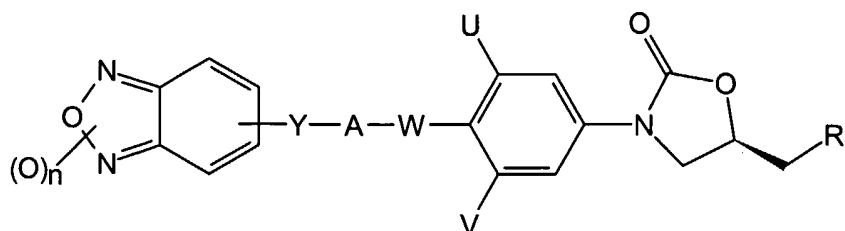
Media used: Mueller Hinton Broth (MHB-Difco) - Cation adjusted + 5 grams per liter Yeast extract + supplements

Preparation of drug concentrations in 96 well microtitre plates was done as per the NCCLS method. Inoculum was prepared by direct colony suspensions in normal saline and adjusted to 1 McFarland turbidity and subsequently diluted in broth 100 times as per NCCLS guidelines in order to obtain 10^5 CFU/spot.

The concentration showing no growth of the inoculated culture was recorded as the MIC. Appropriate ATCC standard strains were simultaneously tested and result recorded only when the MIC's against standard antibiotics were within an acceptable range. 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 included within the scope of the present invention.

WE CLAIM:

1. A compound of Formula I,



Formula I

2

- 3 or its pharmaceutically acceptable salts, pharmaceutically acceptable solvates,
4 enantiomers, diastereomers or polymorphs, wherein

5 R_1 is OR_j , SR_j , NHY_1R_f , NR_fR_q , heterocyclyl or heteroaryl; wherein

6 R_j is hydrogen, alkyl, alkenyl, cycloalkyl, aryl, aralkyl, heterocyclyl,
7 heteroaryl, heteroarylalkyl or heterocyclylalkyl;

8 Y_1 is $(C=O)$, $(C=S)$ or SO_2

9 R_f is hydrogen, alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, aryl, aralkyl,
10 heteroaryl, heterocyclyl, heteroarylalkyl or heterocyclylalkyl; and

11 R_q is hydrogen, alkyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl,
12 heteroarylalkyl or heterocyclyl;

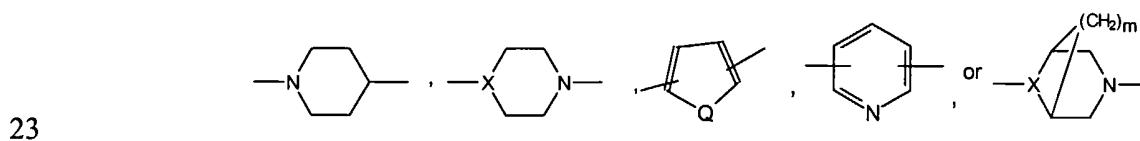
13 U and V are each independently hydrogen, lower (C_{1-6}) alkyl or halogen;

14 Y and W are each independently no atom, O , CH_2 , CO , CH_2NH , $-NHCH_2$, $-$
15 CH_2NHCH_2 , $-CH_2-N(R_{11})CH_2-$, $CH_2(R_e)N-$, $CH(R_{11})$, S , $CH_2(CO)$, NH , NR_e ,
16 $(CO)CH_2$, $N(R_e)CON(R_e)$, $N(R_e)C(=S)N(R_e)$, SO_2 or SO , wherein

17 R_{11} is optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6}
18 alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl or heteroaryl; and

19 R_e is hydrogen, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6}
20 alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl or heteroaryl;
21 and

22 A is no group or is selected from;



24 wherein

25 X is CH, CH-S, CH-O or N;

26 Q is O, N or S;

27 n is an integer 0-1; and

28 m is an integer from 0-2.

1 2. A compound selected from:

2 N-({(5S)-3-[4-(2,1,3-benzoxadiazol-5-yl)-3-fluorophenyl]-2-oxo-1,3-oxazolidin-5-
3 yl}methyl)acetamide (Compound No.1);

4 N-({(5S)-3-[4-(2,1,3-benzoxadiazol-5-yl)-3,5-difluorophenyl]-2-oxo-1,3-
5 oxazolidin-5-yl}methyl)acetamide (Compound No. 2);

6 (5R)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-fluorophenyl}-5-(1H-
7 1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one (Compound No. 3);

8 (5R)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-fluorophenyl}-5-(2H-
9 1,2,3-triazol-2-ylmethyl)-1,3-oxazolidin-2-one (Compound No. 4);

10 (5R)-3-(4-{[1-(2,1,3-benzoxadiazol-5-yl)piperidin-4-yl]oxy}-3-fluorophenyl)-5-
11 (1H-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one (Compound No. 5);

12 (5S)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-fluorophenyl}-5-
13 [(isoxazol-3-ylamino)methyl]-1,3-oxazolidin-2-one (Compound No. 6);

14 (5S)-3-(4-{[1-(2,1,3-benzoxadiazol-5-yl)piperidin-4-yl]oxy}-3-fluorophenyl)-5-
15 [(isoxazol-3-ylamino)methyl]-1,3-oxazolidin-2-one (Compound No. 7);

16 (5S)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-fluorophenyl}-5-
17 (isoxazol-3-ylmethyl)-1,3-oxazolidin-2-one (Compound No. 8);

18 (5*R*)-3-(4-{[1-(2,1,3-benzoxadiazol-5-yl)piperidin-4-yl]oxy}-3-fluorophenyl)-5-
19 [(isoxazol-3-yloxy)methyl]-1,3-oxazolidin-2-one (Compound No. 9);
20 *N*-{[(5*S*)-3-(3-fluoro-4-{4-[(oxido-2,1,3-benzoxadiazol-5-yl)methyl] piperazin-1-
21 yl}phenyl)-2-oxo-1,3-oxazolidin-5-yl]methyl}acetamide (Compound No. 10);
22 *N*-[[(5*S*)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)methyl]piperazin-1-yl]-3-
23 fluorophenyl]-2-oxo-1,3-oxazolidin-5-yl]methyl]acetamide (Compound No. 11);
24 *N*-{[(5*S*)-3-(4-{[1-(2,1,3-benzoxadiazol-5-yl)piperidin-4-yl]oxy}-3-fluorophenyl)-
25 2-oxo-1,3-oxazolidin-5-yl]methyl}acetamide (Compound No. 12);
26 *N*-[[(5*S*)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3-fluorophenyl]-2-
27 oxo-1,3-oxazolidin-5-yl]methyl]acetamide (Compound No. 13);
28 *N*-[[(5*S*)-3-{4-[4-(2,1,3-benzoxadiazol-5-yl)piperazin-1-yl]-3,5-difluorophenyl]-2-
29 oxo-1,3-oxazolidin-5-yl]methyl]acetamide (Compound No. 14),
30 or pharmaceutically acceptable salts and solvates thereof.

1 3. A pharmaceutical composition comprising a pharmaceutically effective amount of
2 one or more compounds of claim 1 or their pharmaceutically acceptable salts thereof and
3 one or more pharmaceutical acceptable carriers.

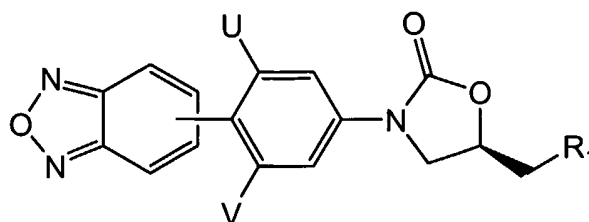
1 4. A method of treating or preventing microbial infections in a mammal comprising
2 administering to the mammal one or more compounds of claim 1.

1 5. The method of claim 4, wherein the microbial infections are caused by Gram-
2 positive or Gram-negative bacteria.

1 6. The method of claim 4, wherein the Gram-positive bacteria is *Staphylococcus spp.*,
2 *Streptococcus spp.*, *Bacillus spp.*, *Corynebacterium spp.*, *Clostridia spp.*,
3 *Peptostreptococcus spp.*, *Listeria spp.* or *Legionella spp.*

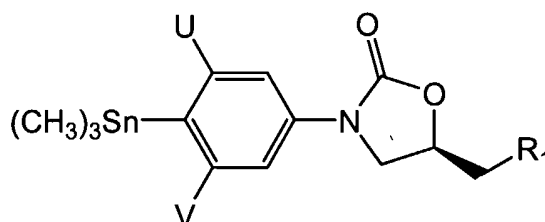
1 7. The method of claim 4, wherein the microbial infections are aerobic or anaerobic
2 bacterial infections.

- 1 8. A process for preparing a compound of Formula IV



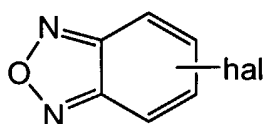
2 Formula IV

- 3 or its pharmaceutically acceptable salts, pharmaceutically acceptable solvates,
4 enantiomers, diastereomers or polymorphs, comprising reacting a compound of Formula II



5 Formula II

- 6 with a compound of Formula III



7 Formula III

- 8 to form a compound of Formula IV,
9 wherein,

10 U and V are each independently hydrogen, lower (C₁₋₆)alkyl or halogen;

11 R₁ is OR_j, SR_j, NHY₁R_f, NR_fR_q, heterocyclyl or heteroaryl; wherein

12 R_j is hydrogen, alkyl, alkenyl, cycloalkyl, aryl, aralkyl, heterocyclyl,
13 heteroaryl, heteroarylalkyl or heterocyclylalkyl;

14 Y₁ is (C=O), (C=S) or SO₂;

15 R_f is hydrogen, alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, aryl, aralkyl,
16 heteroaryl, heterocyclyl, heteroarylalkyl or heterocyclylalkyl;

17 R_q is hydrogen, alkyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl,
18 heteroarylalkyl or heterocyclyl.

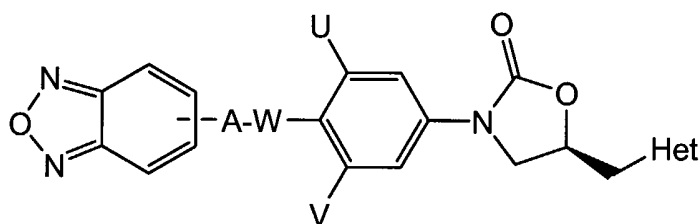
1 9. The process of claim 8, wherein the compound of Formula II is reacted with the
2 compound of Formula III in the presence of one or more bases.

1 10. The process of claim 9, wherein the one or more bases are selected from
2 triethylamine, 4-dimethylamino pyridine, N-methyl morpholine or mixtures thereof.

1 11. The process of claim 8, wherein the compound of Formula II is reacted with the
2 compound of Formula III in the presence of one or more catalysts.

1 12. The process of claim 11, wherein the one or more catalysts are palladium catalysts
2 selected from dichlorobis(triphenylphosphine) palladium (II), tetrakis(triphenylphosphine)
3 palladium (0) or mixtures thereof.

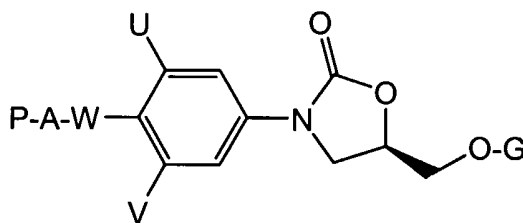
1 13. A process for preparing a compound of Formula IX



2 Formula IX

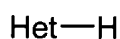
3 or its pharmaceutically acceptable salts, pharmaceutically acceptable solvates,
4 enantiomers, diastereomers or polymorphs, comprising the steps of:

5 b) reacting a compound of Formula V



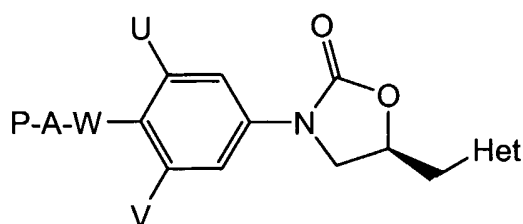
6 Formula V

7 with a compound of Formula VI



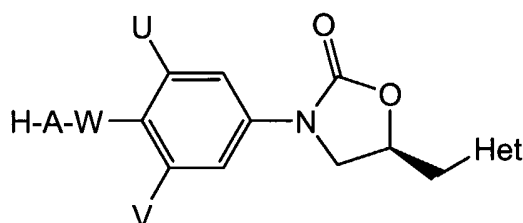
8 Formula VI

9 to form a compound of Formula VII;



10 Formula VII

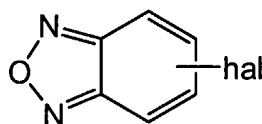
11 b) deprotecting the compound of Formula VII to form a compound of Formula
12 VIII;



13 Formula VIII

14 and

15 c) reacting the compound of Formula VIII with a compound of Formula III



16 Formula III

17 to form a compound of Formula IX,

18 wherein,

19 U and V are each independently hydrogen, lower (C₁₋₆)alkyl or halogen;

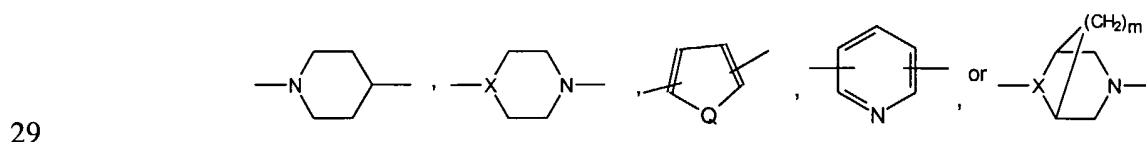
20 W is no atom or is selected from O, CH₂, CO, CH₂NH, -NHCH₂, -CH₂NHCH₂, -
21 CH₂-N(R₁₁)CH₂-, CH₂(R_e)N-, CH(R₁₁), S, CH₂(CO), NH, NR_e, (CO)CH₂,
22 N(R_e)CON(R_e), N(R_e)C(=S)N(R_e), SO₂ or SO, wherein

23 R₁₁ is optionally substituted C₁₋₁₂ alkyl, C₃₋₁₂ cycloalkyl, C₁₋₆ alkoxy, C₁₋₆
24 alkyl, C₁₋₆ alkylcarbonyl, C₁₋₆ alkylcarboxy, aryl or heteroaryl, and

25 R_e is hydrogen, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6}
 26 alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl or heteroaryl;

27 **Het** is a heterocyclyl or heteroaryl;

28 **A** is no group or is selected from;



30 wherein

31 **X** is CH, CH-S, CH-O or N;

32 **Q** is O, N or S;

33 and **m** is an integer from 0-2;

1 14. The process of claim 13, wherein the reaction of compound of Formula V with a
 2 compound of Formula VI to form a compound of Formula VII is carried out in the
 3 presence of one or more bases.

1 15. The process of claim 14, wherein the one or more bases are Group I hydrides
 2 selected from sodium hydride, potassium hydride, lithium hydride or mixtures thereof

1 16. The process of claim 13, wherein the compound of Formula VII is deprotected to
 2 form the compound of Formula VIII in the presence of one or more deprotection agents.

1 17. The process of claim 16, wherein the one or more deprotection agents is selected
 2 from trifluoroacetic acid in dichloromethane or hydrochloric acid in ethanol.

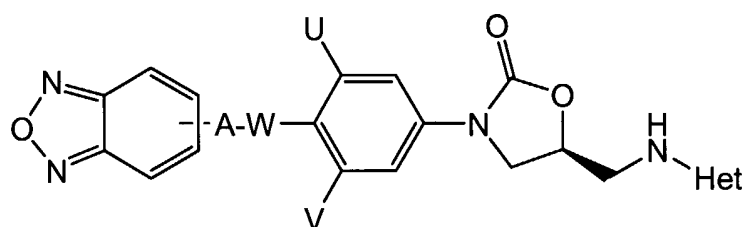
1 18. The process of claim 13, wherein the reaction of the compound of Formula VIII
 2 with the compound of Formula III to form the compound of Formula IX is carried out in
 3 the presence of one or more bases.

1 19. The process of claim 18, wherein the one or more bases are selected from sodium
 2 carbonate, potassium carbonate, cesium carbonate, sodium tertiary butoxide, potassium
 3 tertiary butoxide or mixtures thereof.

1 20. The process claim 12, wherein the reaction of the compound of Formula VIII with
 2 the compound of Formula III to form the compound of Formula IX is carried out in the
 3 presence of one or more catalysts and one or more ligands.

1 21. The process of claim 20, wherein the one or more catalysts is selected from *tris*-
 2 (dibenzylideneacetone) dipalladium(0), palladium diacetate, palladium dichloride or
 3 mixtures thereof; and the one or more ligands are selected from 1,1'-binaphthalene-2,2'-
 4 diylbis(diphenylphosphine), tri-*tert*-butylphosphine, di-1-adamantyl(butyl)phosphine,
 5 biphenyl-2-yl(di-*tert*-butyl)phosphine or mixtures thereof.

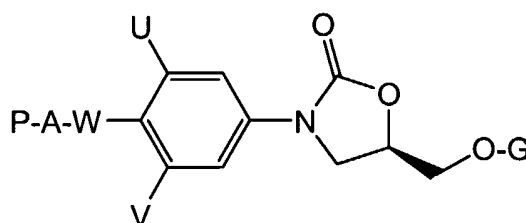
1 22. A process for preparing a compound of Formula XIII



2 Formula XIII

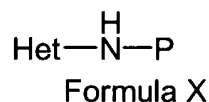
3 or its pharmaceutically acceptable salts, pharmaceutically acceptable solvates,
 4 enantiomers, diastereomers or polymorphs, comprising the steps of:

5 a) reacting a compound of Formula V



6 Formula V

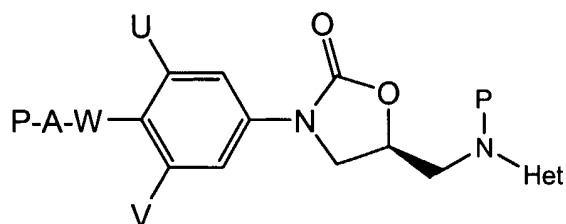
7 with a compound of Formula X



8 Formula X

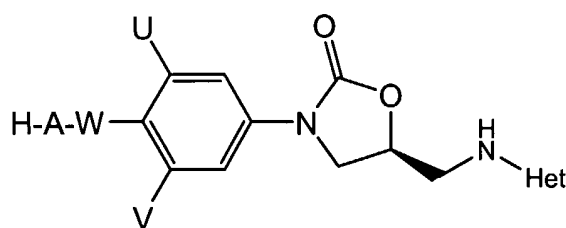
9 to form a compound of Formula XI,

65



Formula XI

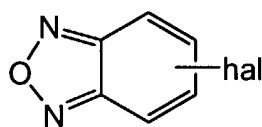
b) deprotecting the compound of Formula XI to form a compound of Formula XII,



Formula XII

and

c) reacting the compound of Formula XII with a compound of Formula III



Formula III

to form a compound of Formula XIII,

wherein,

U and V are each independently hydrogen, lower (C₁₋₆)alkyl or halogen;

W is no atom or is selected from O, CH₂, CO, CH₂NH, -NHCH₂, -CH₂NHCH₂, -

CH₂-N(R₁₁)CH₂-, CH₂(R_e)N-, CH(R₁₁), S, CH₂(CO), NH, NR_e, (CO)CH₂,

N(R_e)CON(R_e), N(R_e)C(=S)N(R_e), SO₂ or SO, wherein

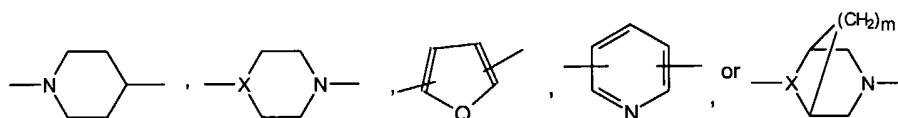
R₁₁ is optionally substituted C₁₋₁₂ alkyl, C₃₋₁₂ cycloalkyl, C₁₋₆ alkoxy, C₁₋₆

alkyl, C₁₋₆ alkylcarbonyl, C₁₋₆ alkylcarboxy, aryl or heteroaryl,

25 **R_e** is hydrogen, optionally substituted C₁₋₁₂ alkyl, C₃₋₁₂ cycloalkyl, C₁₋₆
 26 alkoxy, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, C₁₋₆ alkylcarboxy, aryl or heteroaryl;

27 **Het** is a heterocyclyl or heteroaryl; and

28 **A** is no group or is selected from,



30 wherein

31 **X** is CH, CH-S, CH-O or N;

32 **Q** is O, N or S;

33 **m** is an integer from 0-2.

1 23. The process of claim 22, wherein the reaction of the compound of Formula V with
 2 the compound of Formula XIV to form the compound of Formula XI is carried out in the
 3 presence of one or more bases.

1 24. The process of claim 23, wherein the one or more bases are Group I hydrides
 2 selected from sodium hydride, potassium hydride, lithium hydride or mixtures thereof.

1 25. The process of claim 22, wherein the deprotection of the compound of Formula XI
 2 to form the compound of Formula XII is carried out in the presence of one or more
 3 deprotection agents.

1 26. The process of claim 25, wherein the one or more deprotection agents is selected
 2 from trifluoroacetic acid in dichloromethane or hydrochloric acid in ethanol.

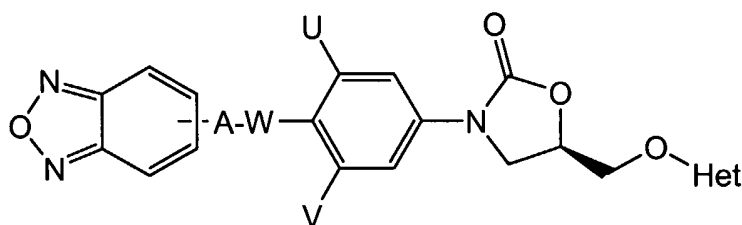
1 27. The process of claim 22, wherein the reaction of the compound of Formula XII
 2 with the compound of Formula III to form the compound of Formula XIII is carried out in
 3 the presence of one or more bases.

1 28. The process of claim 27, wherein the one or more bases are selected from sodium
 2 carbonate, potassium carbonate, cesium carbonate, sodium tertiary butoxide, potassium
 3 tertiary butoxide or mixtures thereof.

1 29. The process of claim 22, wherein the reaction the compound of Formula XII with
 2 the compound of Formula III to form the compound of Formula XIII is carried out in the
 3 presence of one or more catalysts and one or more ligands.

1 30. The process of claim 29, wherein the one or more catalysts are selected from *tris*-
 2 (dibenzylideneacetone) dipalladium(0), Pd₂(dba)₃, palladium diacetate, palladium
 3 dichloride, or mixtures thereof; and the one or more suitable ligands are selected from 1,1'-
 4 binaphthalene-2,2'-diylbis(diphenylphosphine), tri-*tert*-butylphosphine, di-1-
 5 adamantyl(butyl)phosphine, biphenyl-2-yl(di-*tert*-butyl)phosphine or mixtures thereof.

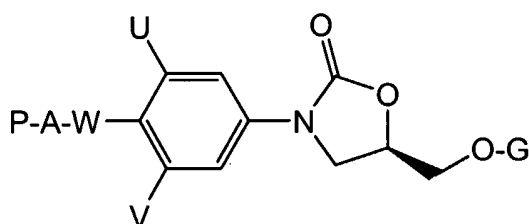
1 31. A process for preparing a compound of Formula XVII



2 Formula XVII

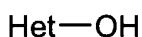
3 or its pharmaceutically acceptable salts, pharmaceutically acceptable solvates,
 4 enantiomers, diastereomers or polymorphs, comprising the steps of:

5 a) reacting a compound of Formula V



6 Formula V

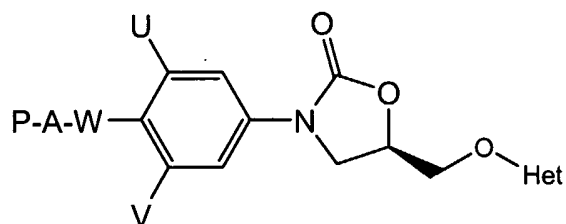
7 with a compound of XIV



8 Formula XIV

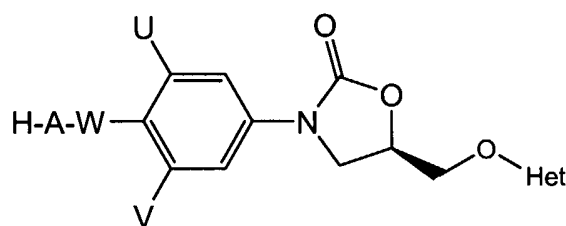
9 to form a compound of Formula XV,

68



Formula XV

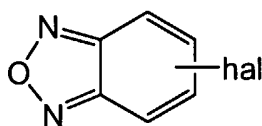
b) deprotecting the compound of Formula XV to form a compound of Formula XVI,



Formula XVI

and

c) reacting the compound of Formula XVI with a compound of Formula III



Formula III

to form a compound of Formula XVII,

wherein,

U and **V** are each independently hydrogen, lower (C₁₋₆)alkyl or halogen;

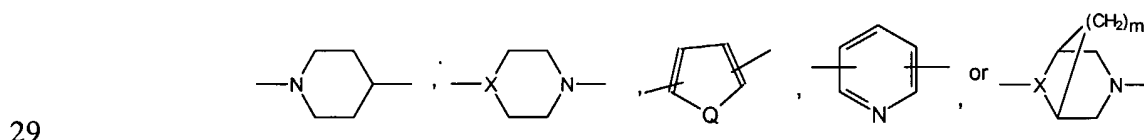
W is no atom or is selected from O, CH₂, CO, CH₂NH, -NHCH₂, -CH₂NHCH₂, -CH₂-N(R₁₁)CH₂-, CH₂(R_e)N-, CH(R₁₁), S, CH₂(CO), NH, NR_e, (CO)CH₂, N(R_e)CON(R_e), N(R_e)C(=S)N(R_e), SO₂ or SO, wherein

R₁₁ is optionally substituted C₁₋₁₂ alkyl, C₃₋₁₂ cycloalkyl, C₁₋₆ alkoxy, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, C₁₋₆ alkylcarboxy, aryl or heteroaryl, and

25 R_e is hydrogen, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6}
 26 alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl or heteroaryl;

27 **Het** is a heterocyclyl or heteroaryl;

28 **A** is no group or is selected from,



30 wherein

31 **X** is CH, CH-S, CH-O or N;

32 **Q** is O, N or S;

33 **m** is an integer from 0-2.

1 32. The process of claim 31, wherein the reaction of the compound of Formula V with
 2 a compound of Formula XIV to form a compound of Formula XV is carried out in the
 3 presence of one or more coupling agents.

1 33. The process of claim 32, wherein the one or more coupling agents are selected
 2 from diethyl diazocarboxylate, diisopropyl diazocarboxylate or mixtures thereof.

1 34. The process of claim 31, wherein the reaction of the compound of Formula V with
 2 a compound of Formula XIV to form a compound of Formula XV is carried out in the
 3 presence of one or more catalysts.

1 35. The process of claim 34, wherein the one or more catalysts are selected from
 2 triphenyl phosphine, trioctyl phosphine, tributyl phosphine or mixtures thereof.

1 36. The process of claim 31, wherein the compound of Formula XV is deprotected to
 2 form the compound of Formula XVI in the presence of one or more deprotection agents.

1 37. The process of claim 36, wherein the one or more deprotection agents are selected
 2 from trifluoroacetic acid in dichloromethane or hydrochloric acid in ethanol.

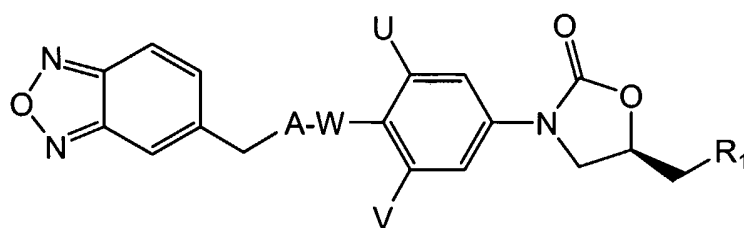
1 38. The process of claim 31, wherein the reaction of the compound of Formula XVI
 2 with the compound of Formula III to form the compound of Formula XVII is carried out
 3 in the presence of one or more bases.

1 39. The process of claim 38, wherein the one or more bases are selected from sodium
2 carbonate, potassium carbonate, cesium carbonate, sodium tertiary butoxide, potassium
3 tertiary butoxide or mixtures thereof.

1 40. The process of claim 31, wherein the reaction of the compound of Formula XVI
2 with the compound of Formula III to form the compound of Formula XVII is carried out
3 in the presence of one or more catalysts and one or more ligands.

1 41. The process of claim 40, wherein the one or more catalysts are selected from *Tris*-
2 (dibenzylideneacetone) dipalladium(0), Pd₂(dba)₃, palladium diacetate, palladium
3 dichloride or mixtures thereof; and the one or more ligands is selected from 1,1'-
4 binaphthalene-2,2'-diylbis(diphenylphosphine), tri-*tert*-butylphosphine, di-1-
5 adamantyl(butyl)phosphine, biphenyl-2-yl(di-*tert*-butyl)phosphine or mixtures thereof.

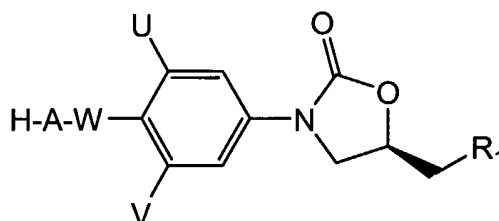
1 42. A process for preparing a compound of Formula XX



2 Formula XX

3 or its pharmaceutically acceptable salts, pharmaceutically acceptable solvates,
4 enantiomers, diastereomers or polymorphs, comprising the steps of:

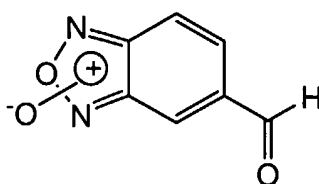
5 a) reacting a compound of Formula XVIII



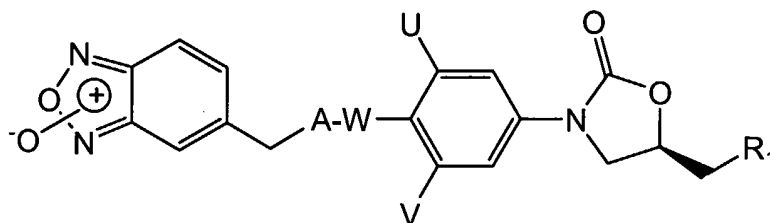
6 Formula XVIII

7 with 5-formylbenzofuroxan

71



to form a compound of Formula XIX,



Formula XIX

and

b) deoxygenating the compound of Formula XIX to form a compound of Formula XX,

wherein,

R_1 is OR_j , SR_j , NHY_1R_f , NR_fR_q , heterocyclyl or heteroaryl, wherein

R_j is hydrogen, alkyl, alkenyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, heteroarylalkyl or heterocyclylalkyl;

Y_1 is (C=O), (C=S) or SO_2 and R_f is hydrogen, alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl or heterocyclylalkyl; and

R_q is hydrogen, alkyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl or heterocyclyl;

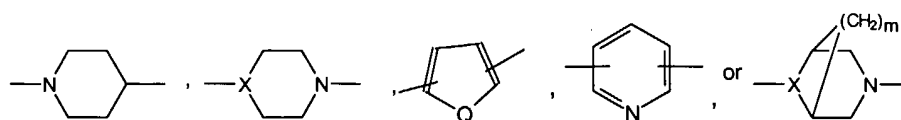
U and V are each independently hydrogen, lower (C_{1-6})alkyl or halogen;

Y and W are each independently no atom or selected from O, CH_2 , CO, CH_2NH , $-NHCH_2$, $-CH_2NHCH_2$, $-CH_2-N(R_{11})CH_2-$, $CH_2(R_e)N-$, $CH(R_{11})$, S, $CH_2(CO)$, NH, NR_e , $(CO)CH_2$, $N(R_e)CON(R_e)$, $N(R_e)C(=S)N(R_e)$, SO_2 or SO, wherein

R_{11} is optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl or heteroaryl, and

29 R_e is hydrogen, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6}
 30 alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl or heteroaryl;

31 A is no group or selected from group consisting of;



32

33 wherein

34 X is CH, CH-S, CH-O or N;

35 Q is O, N or S; and

36 m is an integer from 0-2.

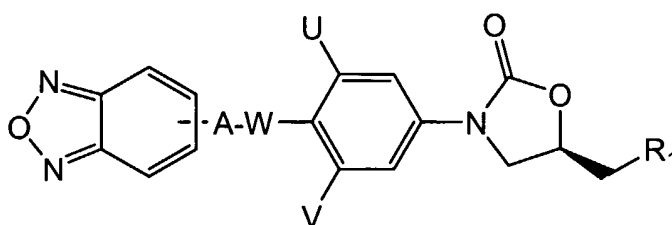
1 43. The process of claim 42, wherein the reaction of compound of Formula XVIII with
 2 5-formylbenzoxofuroxan to form the compound of Formula XIX is carried out in the
 3 presence of one or more reducing agents.

1 44. The process of claim 43, wherein the one or more reducing agents are selected
 2 from sodium triacetoxo borohydride, sodium borohydride, sodium cyano borohydride, or
 3 mixtures thereof.

1 45. The process of claim 42, wherein the deoxygenation of compound of Formula XIX
 2 to form the compound of Formula XX is carried out in presence of one or more catalysts.

1 46. The process of claim 45, wherein the one or more catalysts are selected from
 2 triphenyl phosphine, trioctyl phosphine, tributyl phosphine or mixtures thereof.

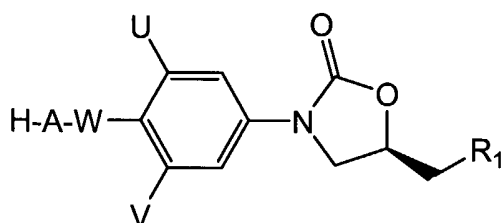
1 47. A process for preparing a compound of Formula XXII



Formula XXII

2

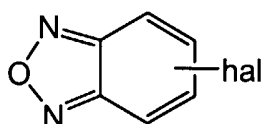
3 or its pharmaceutically acceptable salts, pharmaceutically acceptable solvates,
 4 enantiomers, diastereomers or polymorphs, comprising reacting a compound of Formula
 5 XXI



Formula XXI

6

7 with a compound of Formula III



Formula III

8

9 to form a compound of Formula XXII,

10 wherein,

11 **R₁** is OR_j, SR_j, NHY₁R_f, NR_fR_q, heterocyclyl or heteroaryl; wherein

12 **R_j** is hydrogen, alkyl, alkenyl, cycloalkyl, aryl, aralkyl, heterocyclyl,
 13 heteroaryl, heteroarylalkyl or heterocyclylalkyl;

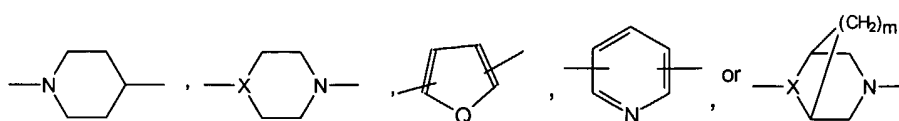
14 **Y₁** is (C=O), (C=S) or SO₂ and **R_f** is hydrogen, alkyl, alkenyl, alkynyl,
 15 alkoxy, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl or
 16 heterocyclylalkyl; and

17 **R_q** is hydrogen, alkyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl,
 18 heteroarylalkyl or heterocyclyl;

19 **U** and **V** are each independently hydrogen, lower (C₁₋₆)alkyl or halogen;

20 **Y** and **W** are each independently no atom or selected from O, CH₂, CO, CH₂NH, -
 21 NHCH₂, -CH₂NHCH₂, -CH₂-N(R₁₁)CH₂-, CH₂(R_e)N-, CH(R₁₁), S, CH₂(CO), NH,
 22 NR_e, (CO)CH₂, N(R_e)CON(R_e), N(R_e)C(=S)N(R_e), SO₂ or SO, wherein

- 23 R_{11} is optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6}
 24 alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl or heteroaryl, and
 25 R_e is hydrogen, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6}
 26 alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl or heteroaryl;
 27 A is no group or is selected from,



28

29 wherein

30 X is CH, CH-S, CH-O or N;

31 Q is O, N or S;

32 m is an integer from 0-2.

1 48. The process of claim 47, wherein the reaction of the compound of Formula XXI
 2 with the compound of Formula III to form the compound of Formula XXII is carried out
 3 in the presence of one or more bases.

1 49. The process of claim 48, wherein the one or more bases are selected from sodium
 2 carbonate, potassium carbonate, diisopropyl ethylamine, triethylamine, N-methyl
 3 morpholine or mixtures thereof.

1 50. The process of claim 47, wherein the reaction of the compound of Formula XXI
 2 with the compound of Formula III to form the compound of Formula XXII is carried out
 3 in the presence of one or more catalysts and one or more ligands.

1 51. The process of claim 50, wherein the one or more catalysts are selected from *tris*-
 2 (dibenzylideneacetone) dipalladium(0), $Pd_2(dba)_3$, palladium diacetate, palladium
 3 dichloride, or mixtures thereof; and the one or more suitable ligands are selected from 1,1'-
 4 binaphthalene-2,2'-diylbis(diphenylphosphine), *tri-tert*-butylphosphine, di-1-
 5 adamantyl(butyl)phosphine, biphenyl-2-yl(di-*tert*-butyl)phosphine or mixtures thereof.

INTERNATIONAL SEARCH REPORT

International application No
/IB2005/002840

A. CLASSIFICATION OF SUBJECT MATTER C07D413/10 C07D413/12 C07D413/14 A61K31/4245 A61P31/04		
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 A61K A61P		
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 practical, search terms used) EPO-Internal, CHEM ABS Data, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 883 611 A (PHARMACIA & UPJOHN COMPANY) 16 December 1998 (1998-12-16) page 29 - page 35; examples 1-10 -----	1,3,4,8, 13,22, 31,42,47
A	TUCKER J A ET AL: "PIPERAZINYL OXAZOLIDINONE ANTIBACTERIAL AGENTS CONTAINING A PYRIDINE, DIAZENE, OR TRIAZENE HETEROAROMATIC RING" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, US, vol. 41, no. 19, 1998, pages 3727-3735, XP001203467 ISSN: 0022-2623 the whole document ----- -/--	1,3,4,8, 13,22, 31,42,47
☒ 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 document 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 27 January 2006		Date of mailing of the international search report 16/02/2006
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer Megido, B

INTERNATIONAL SEARCH REPORT

International application No

.../IB2005/002840

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	YEONG WOO JO, WEON BIN IM, JAE KEOL RHEE, MI JA SHIM, WON BAE KIM, EUNG CHIL CHOI: "Synthesis and antibacterial activity of oxazolidinones containing pyridine substituted with heteroaromatic ring" BIOORGANIC & MEDICINAL CHEMISTRY, vol. 12, 11 September 2004 (2004-09-11), pages 5909-5915, XP002364530 the whole document -----	1,3,4,8, 13,22, 31,42,47
A	PHILILIPS O A ET AL: "Synthesis and antibacterial activity of 5-substituted oxazolidinones" BIOORGANIC & MEDICINAL CHEMISTRY, ELSEVIER SCIENCE LTD, GB, vol. 11, no. 1, 2 January 2003 (2003-01-02), pages 35-41, XP002283683 ISSN: 0968-0896 the whole document -----	1,3,4,8, 13,22, 31,42,47

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2005/002840

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 4-7
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 4-7 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

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