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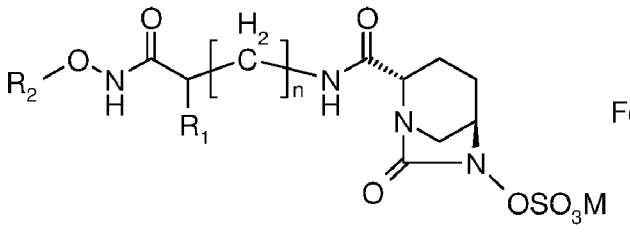
(54) **Title**: NITROGEN CONTAINING BICYCLIC COMPOUNDS AND THEIR USE IN TREATMENT OF BACTERIAL INFECTIONS



Formula (I)

(57) **Abstract**: Compounds of Formula (I), their preparation, and use in preventing or treating a bacterial infection are disclosed.

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NITROGEN CONTAINING BICYCLIC COMPOUNDS AND THEIR USE IN TREATMENT OF BACTERIAL INFECTIONS

PRIORITY APPLICATION(S)

This application claims priority to Indian Patent Application No. 2544/MUM/2015 filed on July 02, 2015, the disclosures of which is incorporated herein by reference in its entirety as if fully rewritten herein.

FIELD OF THE INVENTION

The invention relates to nitrogen containing bicyclic compounds, their preparation and their use in preventing or treating infections.

BACKGROUND OF THE INVENTION

Emergence of bacterial resistance to known antibacterial agents is becoming a major challenge in treating bacterial infections. One way forward to treat bacterial infections, and especially those caused by resistant bacteria, is to develop newer antibacterial agents that can overcome the bacterial resistant. Coates *et al.* (*Br. J. Pharmacol.* **2007**; 152(8), 1147-1154.) have reviewed novel approaches to developing new antibiotics. However, the development of new antibacterial agents is a challenging task. For example, Gwynn *et al.* (*Annals of the New York Academy of Sciences*, **2010**, 1213: 5-19) have reviewed the challenges in discovery of antibacterial agents.

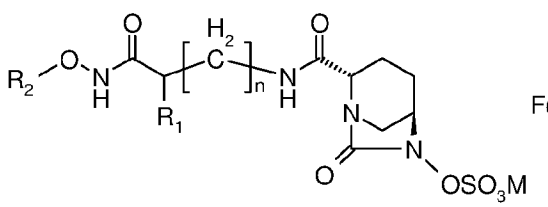
Several antibacterial agents have been described in the prior art (for example, see PCT International Application Nos. PCT/US2010/060923, PCT/EP2010/067647, PCT/US2010/052109, PCT/US2010/048109, PCT/GB2009/050609, PCT/FR01/02418, PCT/EP2009/056178, PCT/US2009/041200, PCT/IB2012/054290, PCT/IB2013/053092, PCT/IB2012/054296 and PCT/IB2012/054706, PCT/JP2013/064971, PCT/IB2012/002675, PCT/US2013/034562 and PCT/US2013/034589). However, there remains a need for development of potent antibacterial agents for preventing and/or treating bacterial infections, including those caused by bacteria that are resistant to known antibacterial agents.

The inventors have now surprisingly discovered novel nitrogen containing bicyclic compounds having antibacterial activity.

SUMMARY OF THE INVENTION

Accordingly, there are provided nitrogen containing bicyclic compounds, methods for preparation of these compounds, pharmaceutical compositions comprising these compounds, and methods for preventing or treating bacterial infection in a subject using these compounds.

In one general aspect, there are provided compounds of Formula (I):



Formula (I)

or a stereoisomer or a pharmaceutically acceptable derivative thereof;

wherein:

R_1 is:

(a) hydrogen,
(b) C_1-C_6 alkyl optionally substituted with one or more substituents independently selected from OR_3, NR_3R_4, SR_3, SOR_3, SO_2R_3, CN, halogen, $COOR_3$, $CONR_3R_4$, NR_3COR_4, or $NR_3CONR_4R_5$,
(c) NR_3R_4,
(d) CN,
(e) SOR_3,
(f) SO_2R_3 or
(g) OR_3;

R_2 is:

(a) hydrogen,
(b) C_1-C_6 alkyl optionally substituted with one or more substituents independently selected from OR_3, NR_3R_4, SR_3, SOR_3, SO_2R_3, CN, halogen, $COOR_3$, $CONR_3R_4$, NR_3COR_4, $NR_3CONR_4R_5$, $=NOCH_3$, cycloalkyl, heterocycloalkyl, aryl or heteroaryl,
(c) cycloalkyl optionally substituted with one or more substituents independently selected from OR_3, NR_3R_4, SR_3, SOR_3, SO_2R_3, CN, $(CH_2)_nNR_3R_4$, halogen, $COOR_3$, $CONR_3R_4$, NR_3COR_4 or $NR_3CONR_4R_5$,
(d) heterocycloalkyl optionally substituted with one or more substituents independently selected from OR_3, NR_3R_4, SR_3, SOR_3, SO_2R_3, CN, $(CH_2)_nNR_3R_4$, halogen, $COOR_3$, $CONR_3R_4$, NR_3COR_4 or $NR_3CONR_4R_5$,
(e) aryl optionally substituted with one or more substituents independently selected from OR_3, NR_3R_4, SR_3, SOR_3, SO_2R_3, CN, $(CH_2)_nNR_3R_4$, halogen, $COOR_3$, $CONR_3R_4$, NR_3COR_4 or $NR_3CONR_4R_5$ or
(f) heteroaryl optionally substituted with one or more substituents independently selected from OR_3, NR_3R_4, SR_3, SOR_3, SO_2R_3, CN, $(CH_2)_nNR_3R_4$, halogen, $COOR_3$, $CONR_3R_4$, NR_3COR_4 or $NR_3CONR_4R_5$;

R_3, R_4 and R_5 are each independently:

(a) hydrogen or
(b) C_1-C_6 alkyl;

n is 0,1,2 or 3;

M is hydrogen or a cation.

In one general aspect, there are provided pharmaceutical compositions comprising a compound of Formula (I), or a stereoisomer or a pharmaceutically acceptable derivative thereof.

In another general aspect, there is provided a method for preventing or treating a bacterial infection in a subject, said method comprising administering to said subject a pharmaceutically effective amount of a compound of Formula (I), or a stereoisomer or a pharmaceutically acceptable derivative thereof.

In another general aspect, there is provided a method for preventing or treating a bacterial infection in a subject, said method comprising administering to said subject a pharmaceutically

effective amount of a pharmaceutical composition comprising a compound of Formula (I), or a stereoisomer, or a pharmaceutically acceptable derivative thereof.

In yet another general aspect, there are provided pharmaceutical compositions comprising: (a) a compound of Formula (I), or a stereoisomer or a pharmaceutically acceptable derivative thereof, and (b) at least one antibacterial agent or a pharmaceutically acceptable derivative thereof.

In another general aspect, there is provided a method for preventing or treating a bacterial infection in a subject, said method comprising administering to said subject a pharmaceutically effective amount of a pharmaceutical composition comprising: (a) a compound of Formula (I), or a stereoisomer or a pharmaceutically acceptable derivative thereof, and (b) at least one antibacterial agent or a pharmaceutically acceptable derivative thereof.

In another general aspect, there is provided a method for preventing or treating a bacterial infection in a subject, said method comprising administering to said subject a pharmaceutically effective amount of: (a) a compound of Formula (I), or a stereoisomer or a pharmaceutically acceptable derivative thereof, and (b) at least one antibacterial agent or a pharmaceutically acceptable derivative thereof.

In one general aspect, there is provided a method of inhibiting beta-lactamase enzymes, wherein said method comprises administering a pharmaceutically effective amount of a compound of Formula (I), or a stereoisomer or a pharmaceutically acceptable derivative thereof.

In another general aspect, there is provided a method of inhibiting beta-lactamase enzymes, wherein said method comprises administering a pharmaceutically effective amount of a pharmaceutical composition comprising a compound of Formula (I), or a stereoisomer or a pharmaceutically acceptable derivative thereof.

In yet another general aspect, there is provided a method for increasing antibacterial effectiveness of an antibacterial agent in a subject, said method comprising co-administering said antibacterial agent or a pharmaceutically acceptable derivative thereof with a compound of Formula (I), or a stereoisomer or a pharmaceutically acceptable derivative thereof.

The details of one or more embodiments of the invention are set forth in the description below. Other features, objects and advantages of the invention will be apparent from the following description including claims.

DETAILED DESCRIPTION OF THE INVENTION

Reference will now be made to the exemplary embodiments, and specific language will be used herein to describe the same. It should nevertheless be understood that no limitation of the scope of the invention is thereby intended. Alterations and further modifications of the inventive features illustrated herein, which would occur to one skilled in the relevant art and having possession of this disclosure, are to be considered within the scope of the invention. It must be noted that, as used in this specification and the appended claims, the singular forms "a", "an", and "the" include plural referents unless the content clearly dictates otherwise. All references including patents, patent applications, and literature cited in the specification are expressly incorporated herein by reference in their entirety.

The inventors have surprisingly discovered novel bicyclic nitrogen containing compounds having antibacterial properties.

The term "C_1-C_6 alkyl" as used herein refers to branched or unbranched acyclic hydrocarbon radical with 1 to 6 carbon atoms. Typical non-limiting examples of "C_1-C_6 alkyl" include methyl,

ethyl, n-propyl, iso-propyl, *n*-butyl, *sec*-butyl, *iso*-butyl, *tert*-butyl, *n*-pentyl, *iso*-pentyl, *tert*-pentyl, neopentyl, *sec*-pentyl, 3-pentyl, n-hexyl, 2-methylpentyl, 3-methylpentyl, 2,2-dimethylbutyl, 2,3-dimethylbutyl and the like. The "C_1-C_6 alkyl" may be unsubstituted, or substituted with one or more substituents. Typical, non-limiting examples of such substituents include halogen, alkoxy, CN, SH, COOH, $COOC_1$-C_6alkyl, $CONH_2$, OH, NH_2, $NHCOCH_3$, cycloalkyl, heterocycloalkyl, heteroaryl, aryl and the like.

The term "cycloalkyl" as used herein refers to three to seven member cyclic hydrocarbon radicals. The cycloalkyl group optionally incorporates one or more double or triple bonds, or a combination of double or triple bonds, but which is not aromatic. Typical, non-limiting examples of cycloalkyl groups include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl. The cycloalkyl may be unsubstituted, or substituted with one or more substituents. Typical, non-limiting examples of such substituents include C_1-C_6 alkyl, halogen, alkoxy, CN, SH, COOH, $COOC_1$-C_6alkyl, $CONH_2$, OH, NH_2, $NHCOCH_3$, heterocycloalkyl, heteroaryl, aryl, SO_2-alkyl, SO_2-aryl, OSO_2-alkyl, OSO_2-aryl and the like.

The term "aryl" as used herein refers to a monocyclic or polycyclic aromatic hydrocarbon. Typical, non-limiting examples of aryl groups include phenyl, naphthyl, anthracenyl, flourenyl, phenanthrenyl, indenyl and the like. The aryl group may be unsubstituted, or substituted with one or more substituents. Typical, non-limiting examples of such substituents include C1-C6 alkyl, halogen, alkoxy, CN, COOH, $CONH_2$, OH, NH_2, $NHCOCH_3$, heterocycloalkyl, heteroaryl, aryl, SO_2-alkyl, SO_2-aryl, OSO_2-alkyl, OSO_2-aryl and the like. In some embodiments, the term "aryl" refers to a monocyclic or polycyclic aromatic hydrocarbon radical containing up to 14 ring atoms. In some embodiments, the term "aryl" refers to six to fourteen membered monocyclic or polycyclic aromatic hydrocarbon radical.

The term "heteroaryl" as used herein refers to a monocyclic or polycyclic aromatic hydrocarbon group wherein one or more carbon atoms have been replaced with heteroatoms selected from nitrogen, oxygen, and sulfur. If the heteroaryl group contains more than one heteroatom, the heteroatoms may be the same or different. Typical, non-limiting example of heteroaryl groups include pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazinyl, furanyl, pyrrolyl, thienyl, oxadiazolyl, thiadiazolyl, tetrazolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, triazonyl, isoxazolyl, oxadiazolyl, oxatriazolyl, isothiazolyl, thiatriazolyl, thiazinyl, oxazinyl, thiadiazinyl, oxadiazinyl, dithiazinyl, dioxazinyl, oxathiazinyl, tetrazinyl, thiatriazinyl, oxatriazinyl, dithiadiazinyl, imidazolinyl, dihydropyrimidyl, tetrahydropyrimidyl, tetrazolo-pyridazinyl, purinyl, benzofuranyl, isobenzofuranyl, benzothienyl, benzothiophenyl, carbazolyl, benzimidazolyl, benzoxazolyl, benzoisoxazolyl, benzothiazolyl, benzotriazolyl, indolyl, isoindolyl, quinolinyl, isoquinolinyl, acridinyl, naphthothienyl, thianthrenyl, chromenyl, xanthenyl, phenoxathienyl, indolizinyl,indazolyl, phthalazinyl, naphthyridinyl, qinoxalinyl, quinazolinyl, cinnolinyl, pteridinyl, beta-carbolinyl, phenanthridinyl, phenanthrolinyl, phenazinyl, phenothiazinyl, phenoxazinyl and the like. The heteroaryl group may be unsubstituted, or substituted with one or more substituents. Typical, non-limiting examples of such substituents include C_1-C_6 alkyl, halogen, alkoxy, CN, COOH, $CONH_2$, OH, SH, SCH_3, NH_2, $NHCOCH_3$, heterocycloalkyl, heteroaryl, aryl, SO_2-alkyl, SO_2-aryl, OSO_2-alkyl, OSO_2-aryl and the like. In some embodiments, the term "heteroaryl" refers to a monocyclic or polycyclic aromatic hydrocarbon radical containing up to 14 ring atoms. In some embodiments, the term "heteroaryl" refers to five to fourteen membered monocyclic or polycyclic aromatic hydrocarbon radical.

The term "heterocycloalkyl" as used herein refers to three to seven member cycloalkyl group containing one or more heteroatoms selected from nitrogen, oxygen or sulfur. The heterocycloalkyl group optionally incorporates one or more double or triple bonds, or a combination of double bonds and triple bonds, but which is not aromatic. Typical, non-limiting example of heterocycloalkyl groups include aziridinyl, azetidinyl, pyrrolidinyl, 2-oxo-pyrrolidinyl, imidazolidin-2-one-yl, piperidinyl, oxazinyl, thiazinyl, piperazinyl, piperazin-2,3-dione-yl, morpholinyl, thiomorpholinyl, azepanyl, and

the like. The heterocycloalkyl may be unsubstituted, or substituted with one or more substituents. Typical, non-limiting examples of such substituents include C_1-C_6 alkyl, halogen, alkoxy, CN, COOH, $CONH_2$, OH, NH_2, $NHCOCH_3$, heteroaryl, aryl, SO_2-alkyl, SO_2-aryl, OSO_2-aryl and the like.

The term "halogen" or halo as used herein refers to chlorine, bromine, fluorine or iodine.

The term "stereoisomers" as used herein refers to compounds that have identical chemical constitution, but differ with regard to the arrangement of their atoms or groups in space. The compounds of Formula (I) may contain asymmetric or chiral centers and, therefore, exist in different stereoisomeric forms. It is intended, unless specified otherwise, that all stereoisomeric forms of the compounds of Formula (I) as well as mixtures thereof, including racemic mixtures, form part of the present invention. In addition, the present invention embraces all geometric and positional isomers (including *cis* and *trans*-forms), as well as mixtures thereof, are embraced within the scope of the invention. In general, a reference to a compound is intended to cover its stereoisomers and mixture of various stereoisomers.

The term "optionally substituted" as used herein means that substitution is optional and therefore includes both unsubstituted and substituted atoms and moieties. A "substituted" atom or moiety indicates that any hydrogen on the designated atom or moiety can be replaced with a selection from the indicated substituent group, provided that the normal valency of the designated atom or moiety is not exceeded, and that the substitution results in a stable compound.

The term "pharmaceutically acceptable derivative" as used herein refers to and includes any pharmaceutically acceptable salt, pro-drug, metabolite, ester, ether, hydrate, polymorph, solvate, complex, and adduct of a compound described herein which, upon administration to a subject, is capable of providing (directly or indirectly) the parent compound. For example, the term "antibacterial agent or a pharmaceutically acceptable derivative thereof" includes all derivatives of the antibacterial agent (such as salts, pro-drugs, metabolites, esters, ethers, hydrates, polymorphs, solvates, complexes, and adducts) which, upon administration to a subject, are capable of providing (directly or indirectly) the antibacterial agent.

The term "pharmaceutically acceptable salt" as used herein refers to one or more salts of a given compound which possesses the desired pharmacological activity of the free compound and which are neither biologically nor otherwise undesirable. In general, the "pharmaceutically acceptable salts" refer to salts that are suitable for use in contact with the tissues of human and animals without undue toxicity, irrigation, allergic response and the like, and are commensurate with a reasonable benefit/risk ratio. Pharmaceutically acceptable salts are well known in the art. For example, S. M. Berge, et al. (*J. Pharmaceutical Sciences*, 66; 1-19, **1977**), incorporated herein by reference in its entirety, describes various pharmaceutical acceptable salts in details.

In general, the compounds according to the invention contain basic (e.g. nitrogen atoms) as well as acid moieties (e.g. compounds of Formula (I) wherein **M** is hydrogen). A person of skills in the art would appreciate that such compounds, therefore, can form acidic salts (formed with inorganic and/or organic acids), as well as basic salts (formed with inorganic and/or organic bases). Such salts can be prepared using procedures described in the art. For example, the basic moiety can be converted to its salt by treating a compound with a suitable amount of acid. Typical, non-limiting examples of such suitable acids include hydrochloric acid, trifluoroacetic acid, methanesulphonic acid or the like. Alternatively, the acid moiety may be converted into its salt by treating with a suitable base. Typical non-limiting examples of such bases include sodium carbonate, sodium bicarbonate, potassium carbonate, potassium bicarbonate, sodium ethylhexanoate, potassium ethylhexanoate or the like. In case of compounds containing more than one functional group capable of being converted into salt, each such functional group may be converted to salt independently. For example, in case of compounds containing two basic nitrogen atoms, one of the basic nitrogen can form salt with one acid

while the other basic nitrogen can form salt with another acid. Some compounds according to the invention contain both acidic as well as basic moieties, and thus can form inner salts or corresponding zwitterions. In general, all pharmaceutically acceptable salt forms of compound of Formula (I) according to invention including acid addition salts, base addition salts, zwitterions or the like are contemplated to be within the scope of the present invention and are generically referred to as pharmaceutically acceptable salts.

The term "infection" or "bacterial infection" as used herein includes presence of bacteria, in or on a subject, which, if its growth were inhibited, would result in a benefit to the subject. As such, the term "infection" in addition to referring to the presence of bacteria also refers to presence of other floras, which are not desirable. The term "infection" includes infection caused by bacteria.

The term "treat", "treating" or "treatment" as used herein refers to administration of a medicament, including a pharmaceutical composition, or one or more pharmaceutically active ingredients, for prophylactic and/or therapeutic purposes. The term "prophylactic treatment" refers to treating a subject who is not yet infected, but who is susceptible to, or otherwise at a risk of infection (preventing the bacterial infection). The term "therapeutic treatment" refers to administering treatment to a subject already suffering from infection. The terms "treat", "treating" or "treatment" as used herein also refer to administering compositions, or one or more of pharmaceutically active ingredients discussed herein, with or without additional pharmaceutically active or inert ingredients, in order to: (i) reduce or eliminate either a bacterial infection, or one or more symptoms of a bacterial infection, or (ii) retard progression of a bacterial infection, or one or more symptoms of a bacterial infection, or (iii) reduce severity of a bacterial infection, or one or more symptoms of a bacterial infection, or (iv) suppress clinical manifestation of a bacterial infection, or (v) suppress manifestation of adverse symptoms of a bacterial infection.

The terms "pharmaceutically effective amount" or "therapeutically effective amount" or "effective amount" as used herein refer to an amount, which has a therapeutic effect or is the amount required to produce a therapeutic effect in a subject. For example, a "therapeutically effective amount" or "pharmaceutically effective amount" or "effective amount" of an antibacterial agent or a pharmaceutical composition is the amount of the antibacterial agent or the pharmaceutical composition required to produce a desired therapeutic effect as may be judged by clinical trial results, model animal infection studies, and/or in vitro studies (e.g. in agar or broth media). Such effective amount depends on several factors, including but not limited to, the microorganism (e.g. bacteria) involved, characteristics of the subject (for example height, weight, sex, age and medical history), severity of infection and particular type of the antibacterial agent used. For prophylactic treatments, a prophylactically effective amount is that amount which would be effective in preventing the bacterial infection.

The term "administration" or "administering" refers to and includes delivery of a composition, or one or more pharmaceutically active ingredients to a subject, including for example, by any appropriate method, which serves to deliver the composition or its active ingredients or other pharmaceutically active ingredients to the site of infection. The method of administration may vary depending on various factors, such as for example, the components of the pharmaceutical composition or type/nature of the pharmaceutically active or inert ingredients, site of the potential or actual infection, the microorganism involved, severity of the infection, age and physical condition of the subject and a like. Some non-limiting examples of ways to administer a composition or a pharmaceutically active ingredient to a subject according to this invention include oral, intravenous, topical, intrarespiratory, intraperitoneal, intramuscular, parenteral, sublingual, transdermal, intranasal, aerosol, intraocular, intratracheal, intrarectal, vaginal, gene gun, dermal patch, eye drop and mouthwash. In case of a pharmaceutical composition comprising more than one ingredients (active or inert), one of the ways of administering such composition is by admixing the ingredients (e.g. in the form of a suitable unit dosage form such as tablet, capsule, solution, powder or a like) and then

administering the dosage form. Alternatively, the ingredients may also be administered separately (simultaneously or one after the other) as long as these ingredients reach beneficial therapeutic levels such that the composition as a whole provides a synergistic and/or desired effect.

The term "growth" as used herein refers to a growth of one or more microorganisms and includes reproduction or population expansion of the microorganism (e.g. bacteria). The term "growth" also includes maintenance of on-going metabolic processes of the microorganism, including the processes that keep the microorganism alive.

The term, "effectiveness" as used herein refers to ability of a treatment, or a composition, or one or more pharmaceutically active ingredients to produce a desired biological effect in a subject. For example, the term "antibacterial effectiveness" of a composition or of an antibacterial agent refers to the ability of the composition or the antibacterial agent to prevent or treat bacterial infection in a subject.

The term "antibacterial agent" as used herein refers to any substance, compound, a combination of substances, or a combination of compounds capable of: (i) inhibiting, reducing or preventing growth of bacteria; (ii) inhibiting or reducing ability of a bacteria to produce infection in a subject; or (iii) inhibiting or reducing ability of bacteria to multiply or remain infective in the environment. The term "antibacterial agent" also refers to compounds capable of decreasing infectivity or virulence of bacteria.

The term "beta-lactamase" or "beta-lactamase enzyme" as used herein refers to any enzyme or protein or any other substance that breaks down a beta-lactam ring. The term "beta-lactamase" includes enzymes that are produced by bacteria and have the ability to hydrolyze the beta-lactam ring in a beta-lactam compound, either partially or completely.

The term "beta-lactamase inhibitor" as used herein refers to a compound capable of inhibiting activity of one or more beta-lactamase enzymes, either partially or completely.

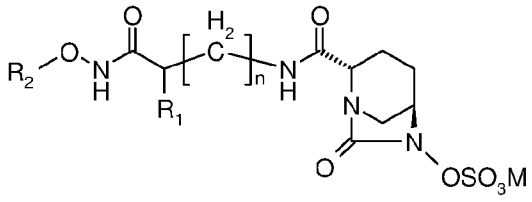
The term "pharmaceutically inert ingredient" or "carrier" or "excipient" refers to and includes compounds or materials used to facilitate administration of a compound, for example, to increase the solubility of the compound. Typical, non-limiting examples of solid carriers include starch, lactose, dicalcium phosphate, sucrose, and kaolin. Typical, non-limiting examples of liquid carriers include sterile water, saline, buffers, non-ionic surfactants, and edible oils. In addition, various adjuvants commonly used in the art may also be included. These and other such compounds are described in literature, e.g., in the Merck Index (Merck & Company, Rahway, N.J.). Considerations for inclusion of various components in pharmaceutical compositions are described, e.g., in Gilman et al. (Goodman and Gilman's: The Pharmacological Basis of Therapeutics, 8th Ed., Pergamon Press., 1990), which is incorporated herein by reference in its entirety.

The term "subject" as used herein refers to vertebrate or invertebrate, including a mammal. The term "subject" includes human, animal, a bird, a fish, or an amphibian. Typical, non-limiting examples of a "subject" include humans, cats, dogs, horses, sheep, bovine cows, pigs, lambs, rats, mice and guinea pigs.

The term "EDC" as used herein refers to 1-ethyl-3-(3-dimethylamino propyl)carbodiimide.
The term "HOBt" as used herein refers to 1-hydroxybenzotriazole.
The term "Boc anhydride" as used herein refers to di-*tert*-butyl dicarbonate.
The term "TBAHS" as used herein refers to tetrabutylammonium hydrogen sulfate.

In general, the term cation includes Na, K, Mg, Ca, NH_4^+, $(CH_3CH_2)_3N$ and the like.

In one general aspect there are provided compounds of Formula (I):



Formula (I)

or a stereoisomer or a pharmaceutically acceptable derivative thereof;

wherein:

R_1 is:

(a) hydrogen,
(b) C_1-C_6 alkyl optionally substituted with one or more substituents independently selected from OR_3, NR_3R_4, SR_3, SOR_3, SO_2R_3, CN, halogen, $COOR_3$, $CONR_3R_4$, NR_3COR_4, or $NR_3CONR_4R_5$,
(c) NR_3R_4,
(d) CN,
(e) SOR_3,
(f) SO_2R_3 or
(g) OR_3;

R_2 is:

(a) hydrogen,
(b) C_1-C_6 alkyl optionally substituted with one or more substituents independently selected from OR_3, NR_3R_4, SR_3, SOR_3, SO_2R_3, CN, halogen, $COOR_3$, $CONR_3R_4$, NR_3COR_4, $NR_3CONR_4R_5$, $=NOCH_3$, cycloalkyl, heterocycloalkyl, aryl or heteroaryl,
(c) cycloalkyl optionally substituted with one or more substituents independently selected from OR_3, NR_3R_4, SR_3, SOR_3, SO_2R_3, CN, $(CH_2)_nNR_3R_4$, halogen, $COOR_3$, $CONR_3R_4$, NR_3COR_4 or $NR_3CONR_4R_5$,
(d) heterocycloalkyl optionally substituted with one or more substituents independently selected from OR_3, NR_3R_4, SR_3, SOR_3, SO_2R_3, CN, $(CH_2)_nNR_3R_4$, halogen, $COOR_3$, $CONR_3R_4$, NR_3COR_4 or $NR_3CONR_4R_5$,
(e) aryl optionally substituted with one or more substituents independently selected from OR_3, NR_3R_4, SR_3, SOR_3, SO_2R_3, CN, $(CH_2)_nNR_3R_4$, halogen, $COOR_3$, $CONR_3R_4$, NR_3COR_4 or $NR_3CONR_4R_5$ or
(f) heteroaryl optionally substituted with one or more substituents independently selected from OR_3, NR_3R_4, SR_3, SOR_3, SO_2R_3, CN, $(CH_2)_nNR_3R_4$, halogen, $COOR_3$, $CONR_3R_4$, NR_3COR_4 or $NR_3CONR_4R_5$;

R_3, R_4 and R_5 are each independently:

(a) hydrogen or
(b) C_1-C_6 alkyl;

n is 0,1,2 or 3;

M is hydrogen or a cation.

Typical, non-limiting examples of compounds according to the invention include:

(2*S*,5*R*)-*N*-[(2*S*)-1-oxo-1-{[(2*S*)-pyrrolidin-2-ylmethoxy]amino}propan-2-yl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-[(2*S*)-1-oxo-1-{[(2*R*)- piperidine-2-ylmethoxy]amino}propan-2-yl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-{(2*S*)-1-[(2-aminoethoxy)amino]-1-oxopropan-2-yl}-7-oxo-6-(sulfooxy-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-[(2*S*)-1-oxo-1-{[(3*S*)-pyrrolidin-3-yloxy]amino}propan-2-yl]-7-oxo-6-(sulfooxy 1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*)-pyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-oxo-2-{[(3*S*)-pyrrolidin-3-yloxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo [3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-{2-[(2-aminoethoxy)amino]-2-oxoethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo [3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-[(2*S*)-3-amino-1-oxo-{[(3*S*)-pyrrolidin-3-yloxy]amino}propan-2yl]-7-oxo-6-(sulfooxy)-1,6diazabicyclo [3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-[(2*S*)-3-amino-1- oxo-1-{[(2*S*)-pyrolidin-2-yl-methoxy]amino}propan-2yl]-7-oxo-6-(sulfooxy)-1,6diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-[(2*S*)-2-amino-1-oxo-1-{[(2*S*)-pyrolidin-2-yl-methoxy]amino}propan-2yl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-3-carboxamide;

(2*S*,5*R*) -*N*-(2-oxo-2-{[(3*R*)-pyrrolidin-3-yloxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-[(2*S*)-3-({[(2*S*)-pyrrolidin-2-ylmethoxy]amino}-2-hydroxy-3-oxopropyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-[(2*S*)-3-[(2-amino)-2-hydroxy-3-oxopropyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo [3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-[(2*S*)-3-({[(3*S*)-pyrrolidin-3-yloxy]amino}-2-hydroxy-3-oxopropyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-[(2*S*)-3-({[(3*S*)-pyrrolidin-3-yloxy]amino}-2-cyano-3-oxopropyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-[2-(hydroxyamino)-2-oxoethyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-[(2*S*)-3-({[N-[2-2H-tetrazole-2-yl)-ethoxy]amino}-3-oxopropyl]-6-(sulfooxy)-7-oxo-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-[(2*S*)-3-({[N-[2-1H-tetrazole-1-yl)-ethoxy]amino}-3-oxopropyl]-6-(sulfooxy)-7-oxo-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-[2-{[{[4-(aminomethyl)phenyl]methyl}oxy]amino}-2-oxoethyl]-6-sulfooxy-7-oxo-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-[2-{[{[2-aminophenyl]methyl}oxy]amino}-2-oxoethyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-[2-{[{[3-aminophenyl]methyl}oxy]amino}-2-oxoethyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-[2-{[{[4-aminophenyl]methyl}oxy]amino}-2-oxoethyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5) -*N*-(2-oxo-2-{[2-(2*H*-1,2,3-triazol-2-yl)ethoxy]amino}ethyl))-7-oxo -6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*) -*N*-(2-oxo-2-{[2-(1*H*-1,2,3-triazol-1-yl)ethoxy]amino}ethyl) -7-oxo -6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*) -*N*-(2-oxo-2-{[2-(1*H*-1,2,4-triazol-1-yl)ethoxy]amino}ethyl)- 7-oxo 6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*, 5*R*) -*N*-(2-oxo-2-{[2-(2-(1*H*-pyrazol-1-yl)ethoxy]amino}ethyl)- 7-oxo 6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*R*)-4-hydroxypyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*S*)-4-hydroxypyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*R*)-4-aminopyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*S*)-4-aminopyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*R*)-4-cyanopyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*S*)-4-cyanopyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide.

or a stereoisomer or a pharmaceutically acceptable derivative thereof.

In some other embodiments, non-limiting examples of compounds according to the invention include:

Sodium salt of (2*S*,5*R*)-*N*-[(2*S*)-1-oxo-1-{[(2*S*)-pyrrolidin-2-ylmethoxy]amino}propan-2-yl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[(2*S*)-1-oxo-1-{[(2*R*)- piperidine-2-ylmethoxy]amino}propan-2-yl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-{(2*S*)-1-[(2-aminoethoxy)amino]-1-oxopropan-2-yl}-7-oxo-6-(sulfooxy-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[(2*S*)-1-oxo-1-{[(3*S*)-pyrrolidin-3-yloxy]amino}propan-2-yl]-7-oxo-6-(sulfooxy 1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*)-pyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-(2-oxo-2-{[(3*S*)-pyrrolidin-3-yloxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo [3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-{2-[(2-aminoethoxy)amino]-2-oxoethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo [3.2.1]octane-2-carboxamide;

Trifluoroacetate salt of (2*S*,5*R*)-*N*-[(2*S*)-3-amino-1-oxo-{[(3*S*)-pyrrolidin-3-yloxy] amino}propan-2yl]-7-oxo-6-(sulfooxy)-1,6diazabicyclo [3.2.1]octane-2-carboxamide;

Trifluoroacetate salt of (2*S*,5*R*)-*N*-[(2*S*)-3-amino-1- oxo-1-{[(2*S*)-pyrolidin-2-yl-methoxy]amino}propan-2yl]-7-oxo-6-(sulfooxy)-1,6diazabicyclo[3.2.1]octane-2-carboxamide;

Trifluoroacetate salt of (2*S*,5*R*)-*N*-[(2*S*)-2-amino-1-oxo-1-{[(2*S*)-pyrolidin-2-yl-methoxy]amino}propan-2yl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-3-carboxamide;

Sodium salt of (2*S*,5*R*) -*N*-(2-oxo-2-{[(3*R*)-pyrrolidin-3-yloxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[(2*S*)-3-({[(2*S*)-pyrrolidin-2-ylmethoxy]amino}-2-hydroxy-3-oxopropyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[(2*S*)-3-[(2-amino)-2-hydroxy-3-oxopropyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo [3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[(2*S*)-3-({[(3*S*)-pyrrolidin-3-yloxy]amino}-2-hydroxy-3-oxopropyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[(2*S*)-3-({[(3*S*)-pyrrolidin-3-yloxy]amino}-2-cyano-3-oxopropyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[2-(hydroxyamino)-2-oxoethyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[(2*S*)-3-({[N-[2-2H-tetrazole-2-yl)-ethoxy]amino}-3-oxopropyl]-6-(sulfooxy)-7-oxo-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[(2*S*)-3-({[N-[2-1H-tetrazole-1-yl)-ethoxy]amino}-3-oxopropyl]-6-(sulfooxy)-7-oxo-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[2-{[{[4-(aminomethyl)phenyl]methyl}oxy]amino}-2-oxoethyl]-6-sulfooxy-7-oxo-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[2-{[{[2-aminophenyl]methyl}oxy]amino}-2-oxoethyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[2-{[{[3-aminophenyl]methyl}oxy]amino}-2-oxoethyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[2-{[{[4-aminophenyl]methyl}oxy]amino}-2-oxoethyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5) -*N*-(2-oxo-2-{[2-(2*H*-1,2,3-triazol-2-yl)ethoxy]amino}ethyl))-7-oxo -6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*) -*N*-(2-oxo-2-{[2-(1*H*-1,2,3-triazol-1-yl)ethoxy]amino}ethyl) -7-oxo -6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*) -*N*-(2-oxo-2-{[2-(1*H*-1,2,4-triazol-1-yl)ethoxy]amino}ethyl)- 7-oxo 6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*, 5*R*) -*N*-(2-oxo-2-{[2-(2-(1*H*-pyrazol-1-yl)ethoxy]amino}ethyl)- 7-oxo 6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide.

Sodium salt of (2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*R*)-4-hydroxypyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*S*)-4-hydroxypyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*R*)-4-aminopyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*S*)-4-aminopyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*R*)-4-cyanopyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*S*)-4-cyanopyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide.

or a stereoisomer thereof.

In general, the compounds of the invention can be prepared according to the general procedure given in Scheme 1. A person of skills in the art would appreciate that the described method can be varied or optimized further to provide the desired and related compounds. In the following procedures all variables are as defined above.

In one general aspect, a compound of Formula (I) can be prepared by the general procedure as described in Scheme 1. A compound of Formula (II) is first treated with a suitable carboxyl group activating reagent, followed by treatment with esterifying agent to obtain a compound of Formula (III). Typical, non-limiting examples of carboxyl group activating compounds include thionyl chloride, oxalyl chloride, phosphorous trichloride, phosphorous oxychloride, phosphorous pentachloride, α-bromoacetyl bromide, pivaloyl chloride, diphenylphosphonic azide dicyclohexylcarbodiimide, diisopropylcarbodiimide, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC.HCl), 1,1'-carbonyldiimidazole, di-*tert*-butyldicarbonate, acetic anhydride, ethyl chloroformate, 2-ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline (EDDQ), 1-hydroxybenzotriazole (HOBt), N-hydroxysuccinimide, 1-hydroxy-7-aza-1*H*-benzotriazole, 4-(*N*,*N*-dimethylamino)pyridine, 2-propanephosphonic acid anhydride, 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium salts, bis-trichloromethylcarbonate or triphosgene, p-nitrophenol (PNP) and the pentafluorophenol (PFP), 4-

trifluoromethyl benzoic anhydride, 2-methyl-6-nitrobenzoic anhydride and the like. Typical non-limiting examples of esterifying agent include methanol, ethanol and the like.

A compound of Formula (III) is coupled with a compound of Formula (IV) [(2*S*,5*R*)-6-benzyloxy-7-oxo-1,6-diazabicyclo[3.2.1]octane-2-carboxylic acid sodium salt (prepared as per the procedure disclosed in WO2014135929)] in presence of a base, coupling agent and a solvent at a temperature of about 15°C to about 35°C for about 10 hours to about 24 hours to obtain a coupled compound of Formula (V). Typical, non-limiting examples of base are *N*-methyl morpholine, *N*-methyl pyrrolidine, *N*-ethyl diisopropylamine and the like. Typical, non-limiting examples of coupling reagent are EDC.HCl, HOBt, 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU), 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate (HATU) or a mixture thereof. Typical, non-limiting examples of solvent include dimethylformamide, dimethylacetamide and the like.

The compound of Formula (V) is hydrolyzed to obtain a compound of Formula (VI). In some embodiments, compound of Formula (V) is hydrolyzed with a suitable reagent such as lithium hydroxide in presence of a suitable solvent such as water, tetrahydrofuran, and the like, or a mixture thereof at a temperature of about -15°C to about 35°C for about 1 hour to about 24 hours to obtain a compound of Formula (VI).

The compound of Formula (VI) is reacted with a hydroxyl amine compound of Formula (VII) to obtain a compound of Formula (VIII). The compound of Formula (VI) is reacted with a compound of Formula (VII) in presence of a coupling agent and a solvent at temperature of about 15°C to about 35°C for about 10 hours to about 24 hours to obtain a compound of Formula (VIII). Typical, non-limiting examples of coupling reagent are EDC.HCl, HOBt, 2-(1*H*-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU), (1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate) (HATU) or a mixture thereof. Typical, non-limiting examples of solvent include water, dimethylformamide, dimethylacetamide and the like. In some embodiments, the compound of Formula (VI) is reacted with a compound of Formula (VII) in presence of EDC.HCl and HOBt at temperature of about 25°C for about 16 hours to obtain a compound of Formula (VIII).

The compound of Formula (VIII) is debenzylated by subjecting it for hydrogenolysis by using hydrogen source in presence of transition metal catalyst in a suitable solvent such as methanol, ethanol, methanol dichloromethane mixture, dimethylformamide dichloromethane mixture, ethyl acetate, tetrahydrofuran, or ethyl acetate and tetrahydrofuran mixture at a temperature ranging from about 10 °C to about 60°C for about 1 hour to about 14 hour to provide a compound of Formula (IX). Typical, non-limiting examples of hydrogen source include hydrogen gas, ammonium formate, cyclohexene, lithium –liquid ammonia, ammonia – *tert*-butanol, sodium – liquid ammonia – *tert*-butanol, triethyl silyl hydride and the like. Typical, non-limiting examples of transition metal catalyst include 5% palladium on carbon, 10% palladium on carbon, 20% palladium hydroxide on carbon, Raney-Nickel and the like. In some embodiments, compound of Formula (VIII) is treated with 10% palladium on carbon in presence of hydrogen gas and suitable solvent and at temperature of about 25°C for about 3 to 5 hours to provide a compound of Formula (IX). In some embodiments, the solvent used in conversion of a compound of Formula (VIII) to a compound of Formula (IX) is methanol.

The compound of Formula (IX) is sulfonated by reacting with suitable sulfonating reagent in a suitable solvent such as pyridine, dichloromethane or *N,N*-dimethylformamide, at a temperature ranging from about 0°C to about 80°C for about 1 hour to about 48 hours. Typical non-limiting examples of sulfonating reagent include sulfur trioxide pyridine complex, sulfur trioxide trimethylamine complex, sulfur trioxide triethylamine complex, sulfur trioxide *N,N*-dimethylaniline complex, sulfur trioxide 2-methylpyridine complex, sulfur trioxide dioxane complex, sulfur trioxide

thioxane complex, sulfur trioxide dimethyl sulfide complex, sulfur trioxide dimethylsulfoxide complex, sulfur trioxide *N,N*-dimethylformamide complex and the like. In some embodiments, compound of Formula (IX) is reacted with sulfur trioxide pyridine complex in presence of pyridine at a temperature of about 25°C to provide the sulfonated compound.

The obtained sulfonated compound is converted into corresponding tetrabutylammonium salt of Formula (X). In some embodiments, the sulfonated compound is treated with tetrabutylammonium hydrogen sulfate (TBAHS), wherein obtained sulfonic acid compound is converted to corresponding tetrabutylammonium salt of Formula (X). The compound according to the invention is then isolated as zwitterions, by removing the protecting groups of compound of Formula (X). The compound of Formula (X) is treated with suitable deprotecting agent such as trifluoroacetic acid in presence of a suitable solvent such as dichloromethane, chloroform or acetonitrile, at a temperature ranging from about -15°C to about 40°C for about 0.5 hour to about 14 hours. In some embodiments, compound of Formula (X) is treated with trifluoroacetic acid in presence of dichloromethane at temperature of about 0°C to about -10°C for about 1 hour to provide a compound of Formula (I).

In some embodiments, compounds according to invention are isolated as pharmaceutically acceptable salts. In some embodiments, compounds according to invention are isolated as sodium salts, wherein a compound of Formula (X) is dissolved in suitable solvent and passed through cation exchange resin. In some other embodiments, compound of Formula (X) is dissolved in 10% tetrahydrofuran: water mixture and then passed through the column packed with cation exchange resin such as Dowex 50WX8 200 Sodium resin, Indion 225 Sodium resin and the like. In some embodiments, compound of Formula (X) is dissolved in suitable solvent such as acetone, tetrahydrofuran, ethanol, isopropanol, acetonitrile, and the like, or a mixture thereof; and treated with sodium ethylhexanoate or potassium ethylhexanoate to provide corresponding sodium or potassium salt of a compound of Formula (I).

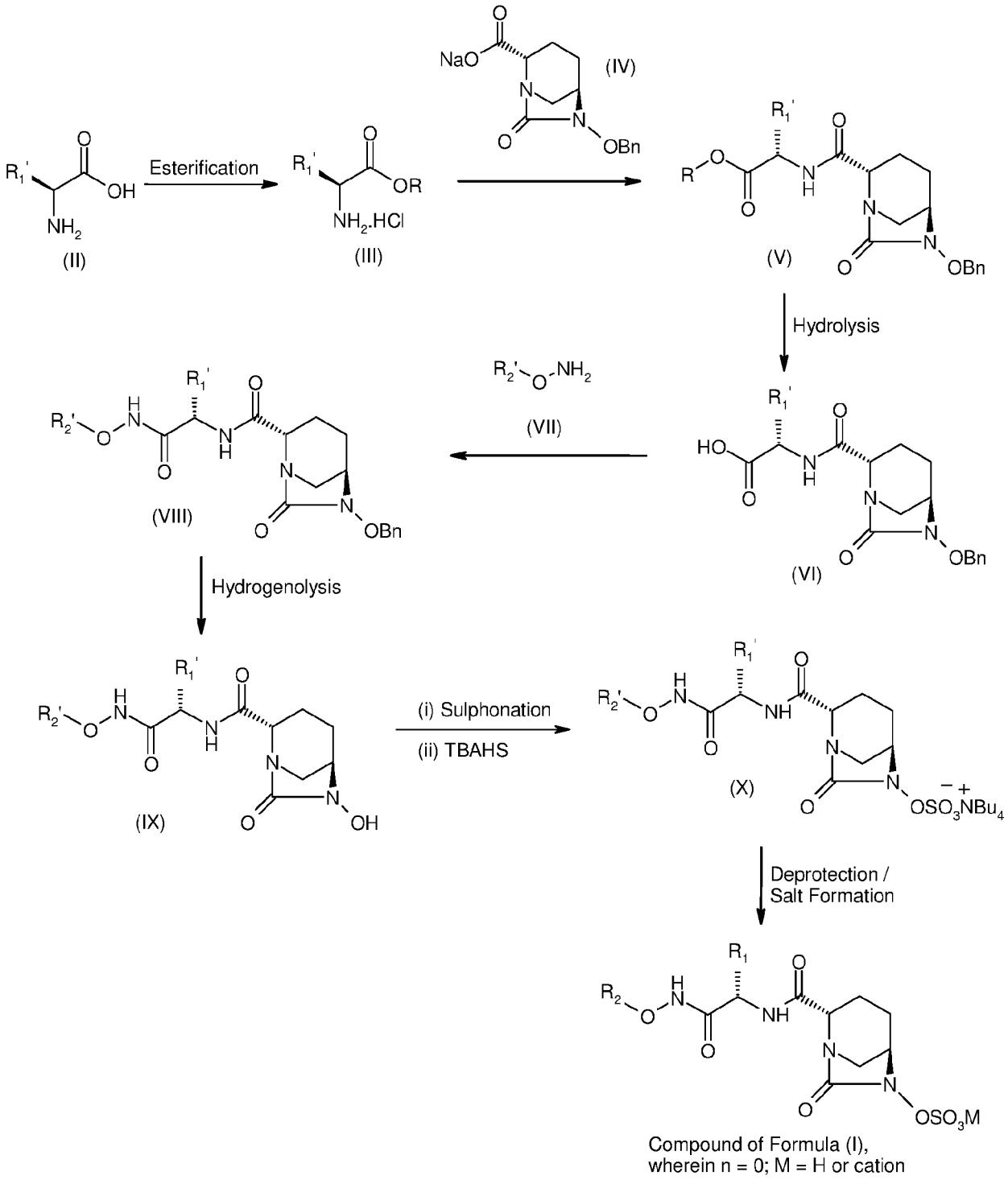
In some embodiments, there are provided pharmaceutical compositions comprising a compound of Formula (I) or a stereoisomer or a pharmaceutically acceptable derivative thereof.

In some other embodiments, there are provided pharmaceutical compositions comprising: (a) a compound of Formula (I) or a stereoisomer or a pharmaceutically acceptable derivative thereof, and (b) at least one beta-lactamase inhibitor or a pharmaceutically acceptable derivative thereof.

In some other embodiments, there are provided pharmaceutical compositions comprising: (a) a compound of Formula (I) or a stereoisomer or a pharmaceutically acceptable derivative thereof, and (b) at least one beta-lactamase inhibitor selected from sulbactam, tazobactam, clavulanic acid, avibactam or a pharmaceutically acceptable derivative thereof.

In some other embodiments, there are provided pharmaceutical compositions comprising: (a) a compound of Formula (I) or a stereoisomer or a pharmaceutically acceptable derivative thereof, and (b) at least one antibacterial agent or a pharmaceutically acceptable derivative thereof.

In some other embodiments, there are provided pharmaceutical compositions comprising: (a) a compound of Formula (I) or a stereoisomer or a pharmaceutically acceptable derivative thereof, and (b) at least one antibacterial agent selected from cefepime, cefpirome, ceftaroline, ceftazidime, ceftolozane or a pharmaceutically acceptable derivative thereof.



Scheme 1

In some other embodiments, there are provided pharmaceutical compositions comprising: (a) a compound of Formula (I) or a stereoisomer or a pharmaceutically acceptable derivative thereof, (b) at least one beta-lacatamse inhibitor or a pharmaceutically acceptable derivative thereof, and (c) at least one antibacterial agent, or a pharmaceutically acceptable derivative thereof.

In some other embodiments, there are provided methods for preventing or treating a bacterial infection in a subject, said methods comprising administering to said subject a pharmaceutical composition comprising a compound of Formula (I) or a stereoisomer or a pharmaceutically acceptable derivative thereof.

In some other embodiments, there are provided methods for preventing or treating a bacterial infection in a subject, said methods comprising administering to said subject a pharmaceutical composition comprising: (a) a compound of Formula (I), or a stereoisomer or a pharmaceutically acceptable derivative thereof and (b) at least one beta-lactamase inhibitor or pharmaceutically acceptable derivative thereof.

In some other embodiments, there are provided methods for preventing or treating a bacterial infection in a subject, said methods comprising administering to said subject a pharmaceutical composition comprising: (a) a compound of Formula (I), or a stereoisomer or a pharmaceutically acceptable derivative thereof and (b) at least one beta-lactamase inhibitor selected from sulbactam, tazobactam, clavulanic acid, avibactam, or pharmaceutically acceptable derivative thereof.

In some other embodiments, there are provided methods for preventing or treating a bacterial infection in a subject, said methods comprising administering to said subject a pharmaceutical composition comprising: (a) a compound of Formula (I) or a stereoisomer or a pharmaceutically acceptable derivative thereof, and (b) at least one antibacterial agent or a pharmaceutically acceptable derivative thereof.

In some other embodiments, there are provided methods for preventing or treating a bacterial infection in a subject, said methods comprising administering to said subject a pharmaceutical composition comprising: (a) a compound of Formula (I) or a stereoisomer or a pharmaceutically acceptable derivative thereof, and (b) at least one antibacterial agent selected from selected from cefepime, cefpirome, ceftaroline, ceftazidime, ceftolozane or a pharmaceutically acceptable derivative thereof.

In some other embodiments, there are provided methods for preventing or treating a bacterial infection in a subject, said methods comprising administering to said subject a pharmaceutical composition comprising: (a) a compound of Formula (I) or a stereoisomer or a pharmaceutically acceptable derivative thereof, (b) at least one beta-lactamase inhibitor or pharmaceutically acceptable derivative thereof and (c) at least one antibacterial agent or a pharmaceutically acceptable derivative thereof.

In some other embodiments, there are provided methods for preventing or treating a bacterial infection in a subject, said method comprising administering to said subject a compound of Formula (I) or a stereoisomer or a pharmaceutically acceptable derivative thereof.

In some other embodiments, there are provided methods for preventing or treating a bacterial infection in a subject, said methods comprising administering to said subject: (a) a compound of Formula (I) or a stereoisomer or a pharmaceutically acceptable derivative thereof, (b) at least one beta-lactamase inhibitor or pharmaceutically acceptable derivative thereof.

In some other embodiments, there are provided methods for preventing or treating a bacterial infection in a subject, said methods comprising administering to said subject: (a) a compound of Formula (I) or a stereoisomer or a pharmaceutically acceptable derivative thereof, (b) at least one beta-lactamase inhibitor selected from sulbactam, tazobactam, clavulanic acid, avibactam, or pharmaceutically acceptable derivative thereof.

In some other embodiments, there are provided methods for preventing or treating a bacterial infection in a subject, said methods comprising administering to said subject: (a) a compound of Formula (I) or a stereoisomer or a pharmaceutically acceptable derivative thereof, (b) at least one antibacterial agent or pharmaceutically acceptable derivative thereof.

In some other embodiments, there are provided methods for preventing or treating a bacterial infection in a subject, said methods comprising administering to said subject: (a) a compound of Formula (I) or a stereoisomer or a pharmaceutically acceptable derivative thereof, (b) at least one antibacterial agent selected from selected from cefepime, cefpirome, ceftaroline, ceftazidime, ceftolozane or pharmaceutically acceptable derivative thereof.

In some other embodiments, there are provided methods for preventing or treating a bacterial infection in a subject, said methods comprising administering to said subject: (a) a compound of Formula (I) or a stereoisomer or a pharmaceutically acceptable derivative thereof, (b) at least one beta-lactamase inhibitor or pharmaceutically acceptable derivative thereof, and (c) at least one antibacterial agent or pharmaceutically acceptable derivative thereof.

In some embodiments, the compositions and methods according to the invention use compounds of Formula (I), or a stereoisomer or a pharmaceutically acceptable derivative thereof in combination with at least one antibacterial agent or a pharmaceutically acceptable derivative thereof. A wide variety of antibacterial agents can be used. Typical, non-limiting examples of antibacterial agents include one or more of antibacterial compounds generally classified as aminoglycosides, ansamycins, carbacephems, cephalosporins, cephamycins, lincosamides, lipopeptides, macrolides, monobactams, nitrofurans, penicillins, polypeptides, quinolones, penems, carbapenems, sulfonamides, tetracyclines, oxazolidinone and the like. Typical, non-limiting examples of aminoglycoside antibacterial agents include amikacin, gentamicin, kanamycin, neomycin, netilmicin, tobramycin, paromomycin, arbekacin, streptomycin, apramycin and the like. Typical, non-limiting examples of ansamycin antibacterial agents include geldanamycin, herbimycin and the like. Typical, non-limiting examples of carbacephem antibacterial agents include loracarbef and the like. Typical, non-limiting examples of carbapenem antibacterial agents include ertapenem, doripenem, imipenem, meropenem and the like.

Typical, non-limiting examples of cephalosporin and cephamycin antibacterial agents include cefazolin, cefacetrile, cefadroxil, cefalexin, cefaloglycin, cefalonium, cefaloridine, cefalotin, cefapirin, cefatrizine, cefazedone, cefazaflur, cefradine, cefroxadine, ceftezole, cefaclor, cefamandole, cefminox, cefonicid, ceforanide, cefotiam, cefprozil, cefbuperazone, cefuroxime, cefuzonam, cephamycin, cefoxitin, cefotetan, cefmetazole, carbacephem, cefixime, ceftazidime, ceftriaxone, cefcapene, cefdaloxime, cefdinir, cefditoren, cefetamet, cefmenoxime, cefodizime, cefoperazone, cefotaxime, cefpimizole, cefpiramide, cefpodoxime, cefsulodin, cefteram, ceftibuten, ceftiolene, ceftizoxime, oxacephem, cefepime, cefozopran, ceftamet, cefpirome, cefquinome, ceftobiprole, ceftiofur, cefquinome, cefovecin, ceftolozane, ceftaroline, ceftobiprole and the like

Typical, non-limiting examples of lincosamide antibacterial agents include clindamycin, lincomycin and the like. Typical, non-limiting examples of macrolide antibacterial agents include azithromycin, clarithromycin, dirithromycin, erythromycin, roxithromycin, troleandomycin, telithromycin, spectinomycin, solithromycin and the like. Typical, non-limiting examples of monobactam antibacterial agents include aztreonam and the like. Typical, non-limiting examples of nitrofuran antibacterial agents include furazolidone, nitrofurantoin and the like. Typical, non-limiting examples of penicillin antibacterial agents include amoxicillin, ampicillin, azlocillin, carbenicillin, cloxacillin, dicloxacillin, flucloxacillin, mezlocillin, methicillin, nafcillin, oxacillin, penicillin G, penicillin V, piperacillin, temocillin, ticarcillin and the like. Typical, non-limiting examples of polypeptide antibacterial agents include bacitracin, colistin, polymyxin B and the like.

Typical, non-limiting examples of quinolone antibacterial agents include ciprofloxacin, enoxacin, gatifloxacin, levofloxacin, lomefloxacin, moxifloxacin, nalidixic acid, levonadifloxacin, norfloxacin, ofloxacin, trovafloxacin, grepafloxacin, sparfloxacin, temafloxacin and the like. Typical, non-limiting examples of sulfonamide antibacterial agents include mafenide, sulfonamidochrysoidine, sulfacetamide, sulfadiazine, sulfamethizole, sulfamethoxazole, sulfasalazine, sulfisoxazole, trimethoprim and the like. Typical, non-limiting examples of tetracycline antibacterial agents include

demeclocycline, doxycycline, minocycline, oxytetracycline, tetracycline, tigecycline and the like. Typical, non-limiting examples of oxazolidinone antibacterial agents include tedizolid, linezolid, ranbezolid, torezolid, radezolid and the like.

The pharmaceutical compositions according to the invention may include one or more pharmaceutically acceptable carriers or excipients or the like, Typical, non-limiting examples of such carriers or excipient include mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, sodium crosscarmellose, glucose, gelatin, sucrose, magnesium carbonate, wetting agents, emulsifying agents, solubilizing agents, pH buffering agents, lubricants, stabilizing agents, binding agents etc.

In some embodiments, pharmaceutical compositions according to the present invention are administered orally or parenterally.

The pharmaceutical compositions according to this invention can exist in various forms. In some embodiments, the pharmaceutical composition is in the form of a powder or a solution. In some other embodiments, the pharmaceutical compositions according to the invention are in the form of a powder that can be reconstituted by addition of a compatible reconstitution diluent prior to parenteral administration. Non-limiting example of such a compatible reconstitution diluent includes water. In some other embodiments, the pharmaceutical compositions according to the invention are in the form of a frozen composition that can be diluted with a compatible diluent prior to parenteral administration. In some other embodiments, the pharmaceutical compositions according to the invention are in the form ready to use for oral or parenteral administration.

In the methods according to the invention, the pharmaceutical composition and/or other pharmaceutically active ingredients disclosed herein may be administered by any appropriate method, which serves to deliver the composition or its constituents or the active ingredients to the desired site. The method of administration can vary depending on various factors, such as for example, the components of the pharmaceutical composition and nature of the active ingredients, the site of the potential or actual infection, the microorganism (e.g. bacteria) involved, severity of infection, age and physical condition of the subject. Some non-limiting examples of administering the composition to a subject according to this invention include oral, intravenous, topical, intrarespiratory, intraperitoneal, intramuscular, parenteral, sublingual, transdermal, intranasal, aerosol, intraocular, intratracheal, intrarectal, vaginal, gene gun, dermal patch, eye drop, ear drop or mouthwash.

The compositions according to the invention can be formulated into various dosage forms wherein the active ingredients and/or excipients may be present either together (e.g. as an admixture) or as separate components. When the various ingredients in the composition are formulated as a mixture, such composition can be delivered by administering such a mixture to a subject using any suitable route of administration. Alternatively, pharmaceutical compositions according to the invention may also be formulated into a dosage form wherein one or more ingredients (active or inactive ingredients) are present as separate components. The composition or dosage form wherein the ingredients do not come as a mixture, but come as separate components, such composition/dosage form may be administered in several ways. In one possible way, the ingredients may be mixed in the desired proportions and the mixture is then administered as required. Alternatively, the components or the ingredients (active or inert) may be separately administered (simultaneously or one after the other) in appropriate proportion so as to achieve the same or equivalent therapeutic level or effect as would have been achieved by administration of the equivalent mixture.

In some embodiments, pharmaceutical compositions according to the invention are formulated into a dosage form such that the compound of Formula (I) or a stereoisomer or a pharmaceutically acceptable derivative thereof, and the antibacterial agent or a pharmaceutically acceptable derivative thereof, are present in the composition as admixture or as a separate components. In some other

embodiments, pharmaceutical compositions according to the invention are formulated into a dosage form such that the compound of Formula (I) or a stereoisomer or a pharmaceutically acceptable derivative thereof, and the antibacterial agent or a pharmaceutically acceptable derivative thereof, are present in the composition as separate components.

Similarly, in the methods according to the invention, the active ingredients disclosed herein may be administered to a subject in several ways depending on the requirements. In some embodiments, the active ingredients are admixed in appropriate amounts and then the admixture is administered to a subject. In some other embodiments, the active ingredients are administered separately. Since the invention contemplates that the active ingredients agents may be administered separately, the invention further provides for combining separate pharmaceutical compositions in kit form. The kit may comprise one or more separate pharmaceutical compositions, each comprising one or more active ingredients. Each of such separate compositions may be present in a separate container such as a bottle, vial, syringes, boxes, bags, and the like. Typically, the kit comprises directions for the administration of the separate components. The kit form is particularly advantageous when the separate components are preferably administered in different dosage forms (e.g., oral and parenteral) ore are administered at different dosage intervals. When the active ingredients are administered separately, they may be administered simultaneously or sequentially.

The pharmaceutical composition or the active ingredients according to the present invention may be formulated into a variety of dosage forms. Typical, non-limiting examples of dosage forms include solid, semi-solid, liquid and aerosol dosage forms; such as tablets, capsules, powders, solutions, suspensions, suppositories, aerosols, granules, emulsions, syrups, elixirs and a like.

In general, the pharmaceutical compositions and method disclosed herein are useful in preventing or treating bacterial infections. Advantageously, the compositions and methods disclosed herein are also effective in preventing or treating infections caused by bacteria that are considered be less or not susceptible to one or more of known antibacterial agents or their known compositions. Some non-limiting examples of such bacteria known to have developed resistance to various antibacterial agents include *Acinetobacter, E. coli, Pseudomonas aeruginosa, Staphylococcus aureus, Enterobacter, Klebsiella, Citrobacter* and a like. Other non-limiting examples of infections that may be prevented or treated using the compositions and/or methods of the invention include: skin and soft tissue infections, febrile neutropenia, urinary tract infection, intraabdominal infections, respiratory tract infections, pneumonia (nosocomial), bacteremia meningitis, surgical, infections etc.

Surprisingly, the compounds, compositions and methods according to the invention are also effective in preventing or treating bacterial infections that are caused by bacteria producing one or more beta-lactamase enzymes. The ability of compositions and methods according to the present invention to treat such resistant bacteria with typical beta-lactam antibiotics represents a significant improvement in the art.

In some embodiments, there is provided a method of inhibiting beta-lactamase enzymes, wherein said method comprises administering a pharmaceutically effective amount of a compound of Formula (I), or a stereoisomer or a pharmaceutically acceptable derivative thereof.

In some embodiments, there is provided a method of inhibiting beta-lactamase enzymes, wherein said method comprises administering a pharmaceutically effective amount of a pharmaceutical composition comprising a compound of Formula (I), or a stereoisomer or a pharmaceutically acceptable derivative thereof.

In some embodiments, there is provided a method for preventing or treating a bacterial infection in a subject, said infection being caused by one or more beta-lactamase enzymes, wherein the

method comprises administering to said subject a pharmaceutically effective amount of a compound of Formula (I), or a stereoisomer or a pharmaceutically acceptable derivative thereof.

In general, the compounds of Formula (I), or a stereoisomer or pharmaceutically acceptable salt thereof according to invention are also useful in increasing antibacterial effectiveness of antibacterial agent in a subject. The antibacterial effectiveness of one or more antibacterial agents may increased, for example, by co-administering said antibacterial agent or a pharmaceutically acceptable derivative thereof with a pharmaceutically effective amount of a compound of Formula (I), or a stereoisomer or a pharmaceutically acceptable salt thereof according to the invention. In some embodiments, there is provided a method for increasing antibacterial effectiveness of the antibacterial agent in a subject, said method comprising co-administering said antibacterial agent or a pharmaceutically acceptable derivative thereof with a of a compound of Formula (I), or a stereoisomer or a pharmaceutically acceptable derivative thereof.

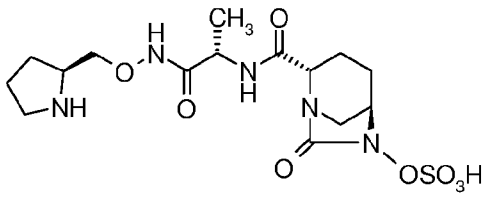
It will be readily apparent to one skilled in the art that varying substitutions and modifications may be made to the invention disclosed herein without departing from the scope and spirit of the invention. For example, those skilled in the art will recognize that the invention may be practiced using a variety of different compounds within the described generic descriptions.

EXAMPLES

The following examples illustrate the embodiments of the invention that are presently best known. However, it is to be understood that the following are only exemplary or illustrative of the application of the principles of the present invention. Numerous modifications and alternative compositions, methods and systems may be devised by those skilled in the art without departing from the spirit and scope of the present invention. The appended claims are intended to cover such modifications and arrangements. Thus, while the present invention has been described above with particularity, the following examples provide further detail in connection with what are presently deemed to be the most practical and preferred embodiments of the invention.

Example 1

Synthesis of (2S, 5R)-6-(sulfooxy)-7-oxo-N-[(2S)-1-oxo-1-{[(2S)-pyrrolidin-2-ylmethoxy]amino}propan-2-yl]-1,6-diazabicyclo[3.2.1]octane-2-carboxamide:



Step 1: **Preparation of (*S*)-methyl 2-aminopropanoate hydrochloride:**

Thionyl chloride (66.76 g, 0.56 mol) was added drop-wise to the solution of *L*-alanine (20 g, 0.22 mol) in methanol (200 ml), under stirring at 0°C. The resulting mixture was allowed to warm to room temperature and stirring continued further for 16 hours. The reaction mixture was concentrated under reduced pressure (2 mm Hg). The residual mass was diluted with diethyl ether (100 ml) and the mixture was stirred for 15 minutes. The separated solid was filtered and washed with additional diethyl ether (40 ml). The solid was dried under reduced pressure to obtain 18 g of the titled product as white solid in 78% yield.

Analysis:

Mass: 104 (M+1) as free base; for Molecular Formula of $C_4H_{10}ClNO_2$ and Molecular Weight of 139.58.

Step 2: Synthesis of methyl (2*S*)-2-({[(2*S*,5*R*)-6-(benzyloxy)-7-oxo-1,6-diazabicyclo [3.2.1]oct-2-yl]carbonyl}amino)propanoate:

To a stirred solution of sodium (2*S*, 5*R*)-7-oxo-6-benzyloxy-1,6-diazabicyclo[3.2.1]octane-2-carboxylate (prepared according to the process disclosed in PCT/IB2013/059264) (38 g, 0.12 mol) in dimethylformamide (380 ml), EDC.HCl (36.50 g, 0.19 mol), 4-methylmorpholine (38 g, 0.38 mol) and HOBT (17.19 g, 0.12 mol) under nitrogen were added successively at 25°C. After 15 minutes solid (*S*)-methyl 2-aminopropanoate hydrochloride (20g, 0.224 mol) was added and the reaction mixture was stirred for 16 hours. The resulting mixture was slowly poured into 1.5 liters of water and stirred for 1 hour. The separated solid was filtered under suction and washed with water (100 ml). The solid was dried under reduced pressure (2 mm Hg) to obtain 31 g of the titled product as white solid in 67% yield.

Analysis:

Mass: 362.2 (M+1); for Molecular Formula of $C_{18}H_{23}N_3O_5$ and Molecular Weight of 361.39.

Step 3: Synthesis of lithium (2*S*)-2-({[(2*S*,5*R*)-6-(benzyloxy)-7-oxo-1,6-diazabicyclo[3.2.1]oct-2-yl]carbonyl} amino)propanoate:

To the solution of above obtained ester compound (8.48 g, 23 mmol) in tetrahydrofuran (84 ml), was added drop-wise a solution lithium hydroxide (0.98 g, 23 mmol) in 16 ml of water at 0°C under stirring. Stirring was continued further for 2 hour at 0°C. The resulting solution was diluted with a mixture of ethyl acetate (84 ml) and water (68 ml) and stirred for 5 minutes. The organic layer was separated and the aqueous layer was taken for next step as such

Analysis:

Mass: 346.1 (M-1) as free acid; for Molecular Formula of $C_{17}H_{20}LiN_3O_5$ and Molecular Weight of 353.29.

Step 4: Synthesis of (2*S*,5*R*)-6-(benzyloxy)-7-oxo-*N*-[(2*S*)-1-oxo-1-{[*tert*-butyl (2*S*)-pyrrolidin-2-ylmethoxy]amino}propan-2-yl-1-carboxylate]-1,6-diazabicyclo[3.2.1]octane-2-carboxamide:

The EDC.HCl (9.70 g, 50 mmol), and HOBT (3.11 g, 23 mmol) were added successively to the solution of lithium salt compound (water layer from step-3) (8.16 g, 23 mmol) at room temperature, the solution was stirred and *tert*-butyl (2*S*)-2-[(aminooxy)methyl]pyrolidine-1-carboxylate (4.99 g; 23 mmol) was added in one portion. Stirring was continued further for 16 hours. The reaction mixture was extracted with ethyl acetate (2 × 20 ml). The combined organic extracts were dried over sodium sulphate and the solvent evaporated under reduced pressure to yield crude product. The crude product was purified by column chromatography using silica gel (60-120 mesh size) and by carrying elution with a mixture of ethyl acetate: hexane (20:80) and evaporation of the combined fractions gave 3.5 g of the titled product as white solid 3.5 g in 29% yield.

Analysis:

Mass: 546.1 (M+1); for Molecular Formula of $C_{27}H_{39}N_5O_7$ and Molecular Weight of 545.62.

Step 5: Synthesis of (2*S*,5*R*)-6-hydroxy-7-oxo-*N*-[(2*S*)-1-oxo-1-{[*tert*-butyl (2*S*)-pyrrolidin-2-ylmethoxy]amino}propan-2-yl-1-carboxylate]-1,6-diazabicyclo[3.2.1]octane-2-carboxamide:

To a solution of above obtained benzyl compound (3.4 g, 6 mmol) in methanol was added 10% Pd-C (340 mg; 50% wet) under stirring and was hydrogenated at atmospheric pressure for 3 hour at 25°C. The resulting mixture was filtered through celite bed and the residual catalyst washed with 5 ml of methanol. The filtrate was concentrated under reduced pressure to obtain 2.7 g of the titled product as white solid in 95% yield.

Analysis:

Mass: 456 (M+1); for Molecular Formula of $C_{20}H_{33}N_5O_7$ and Molecular Weight of 455.50.

Step 6: Synthesis of tetrabutylammonium salt of (2*S*,5*R*)-6-(sulfooxy)-7-oxo-*N*-[(2*S*)-1-oxo-1-{[*tert*-butyl (2*S*)-pyrrolidin-2-ylmethoxy]amino}propan-2-yl-1-carboxylate]-1,6-diazabicyclo [3.2.1]octane-2-carboxamide:

To a stirred solution of above obtained hydroxy compound (2.7 g, 5 mmol) in pyridine (14 ml), sulphur trioxide pyridine complex (4.71 g, 29 mmol) was added under argon atmosphere at 25°C. The stirring was continued further for 46 hours at same temperature. The resulting suspension was filtered through paper and the residue was washed with dichloromethane (5 ml). The filtrate was concentrated under reduced pressure to obtain oil. This oil was dissolved in 270 ml of 0.5M potassium dihydrogen phosphate solution and stirred for 0.5 hour at 25°C. The resulting mixture was washed with ethyl acetate (50 ml). The aqueous layer was separated and to it was added tetrabutylammonium hydrogen sulphate (2.01 g, 5 mmol) and this mixture was stirred for 3 hours at 25°C. The resulting mixture was extracted with dichloromethane (2 × 30 ml). The organic layer was dried over anhydrous sodium sulphate and the solvent was evaporated under reduced pressure to obtain the crude product as oil. The obtained product was purified by column chromatography using silica gel (60-120 mesh size) and eluting with a mixture of dichloromethane: methanol (5: 95). The combined fractions of eluent were evaporated to provide 1.5 g of the title product as white solid in 33% yield.

Analysis:

Mass: 536.3 (M+1) as free acid; for Molecular Formula of $C_{36}H_{68}N_6O_{10}S$ and Molecular Weight of 777.

Step 7: Synthesis of (2*S*,5*R*)-6-(sulfooxy)-7-oxo-*N*-[(2*S*)-1-oxo-1-{[(2*S*)-pyrrolidin-2-ylmethoxy] amino}propan-2-yl-1-carboxylate]-1,6-diazabicyclo[3.2.1]octane-2-carboxamide

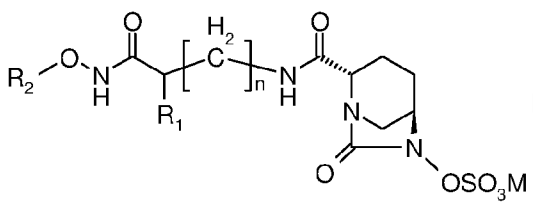
To a stirred solution of above obtained tetrabutylammonium salt (1.5 g, 2 mmol) in dichloromethane (7.5 ml) trifluro acetic acid (3.75 ml) was added drop-wise, under argon atmosphere at 0°C. Stirring was continued further for 1 hour at 0°C. The progress of reaction was monitored by mass spectra and after 1 hour the complete consumption of starting material was observed. The resulting reaction mixture was diluted with diethyl ether (6 ml), well triturated and stirred for 10 minutes. The separated solid was filtered. The solid was then stirred with acetonitrile (6 ml) filtered and re-washed with acetonitrile (6 ml). The obtained solid was dried under reduced pressure (2mmHg) to provide 490 mg of the titled product as white solid in 66% yield.

Analysis:

Mass: 436.3 (M+1); for Molecular Formula of $C_{15}H_{25}N_5O_8S$ and Molecular Weight of 435.45.

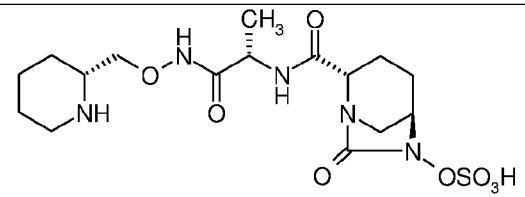
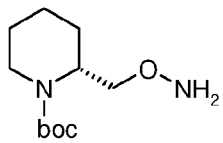
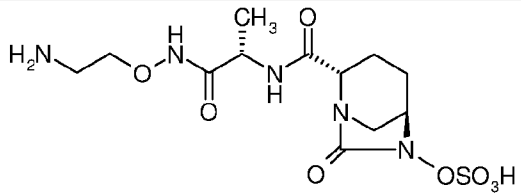
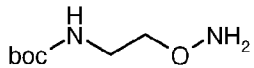
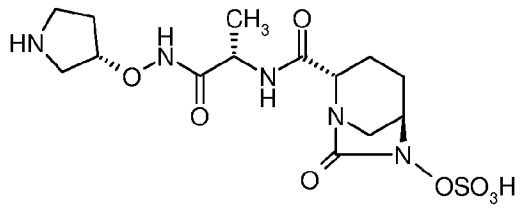
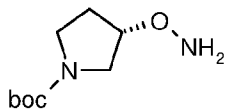
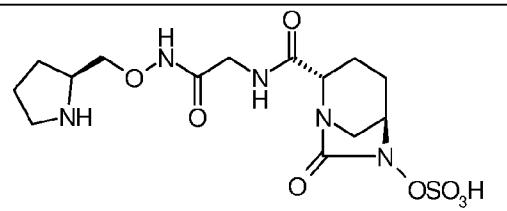
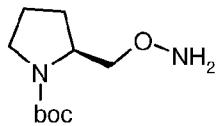
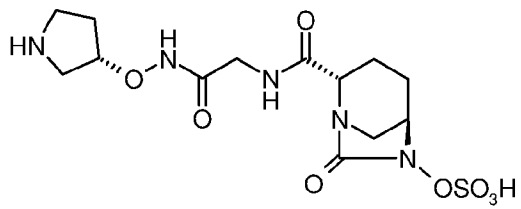
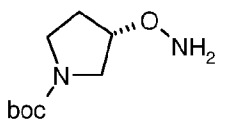
General procedure for synthesis of sodium salt: The tetra-butylammonium salt intermediate compound (10 mmol) was dissolved in 10% tetrahydrofuran in water (2 ml), poured onto a column packed with INDION 225 Na (sodium ion exchange resin; 20g) and eluted with 10% tetrahydrofuran in water. The combined fractions were evaporated under reduced pressure (4mm Hg) to obtain the corresponding sodium salt.

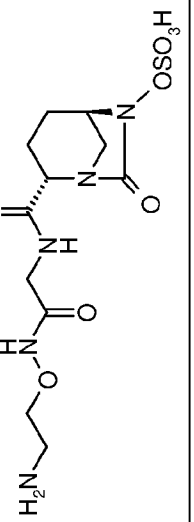
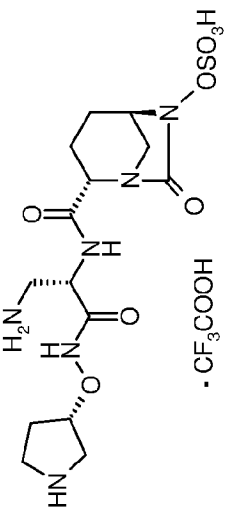
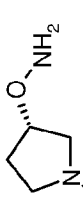
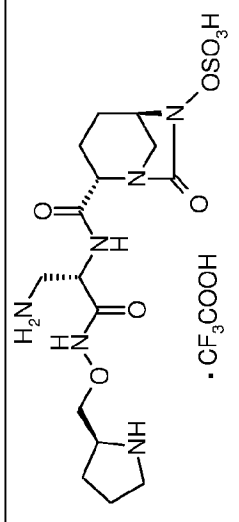
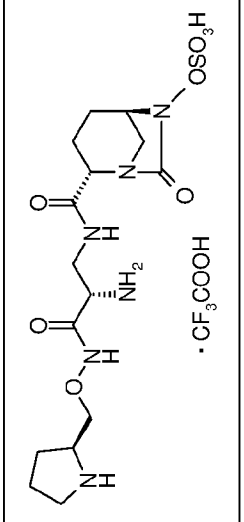
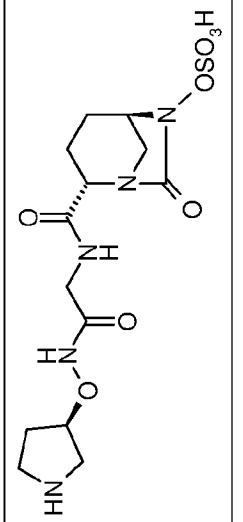
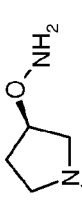
Compounds 2 to 32 (Table 1) were prepared by using the procedure described in Example 1 and using corresponding hydroxylamine compound of Formula (VII) in place of *tert*-butyl (2*S*)-2-[(aminooxy)methyl]pyrolidine-1-carboxylate. For preparation of compounds 16 to 18, the intermediate tetrabutylammonium salts were converted to their sodium salts; followed by deprotection step.

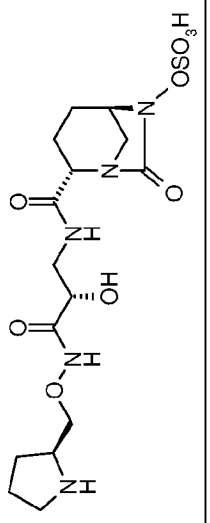
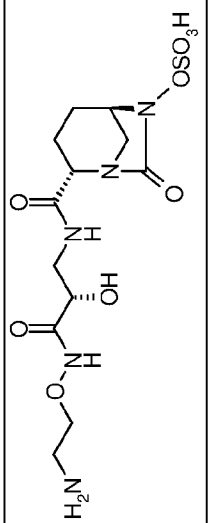
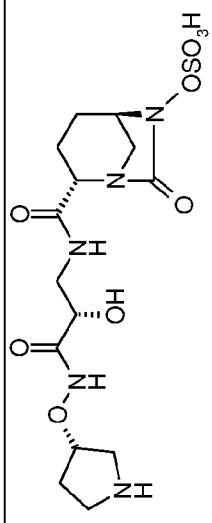
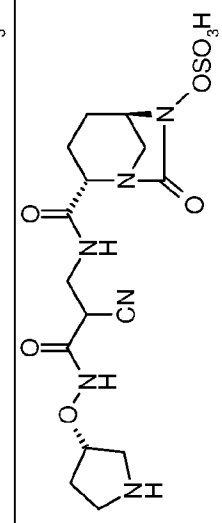
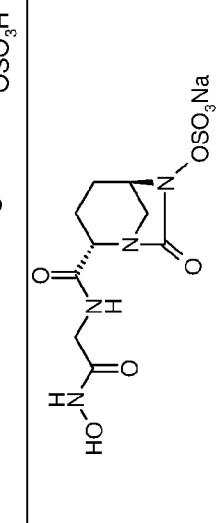


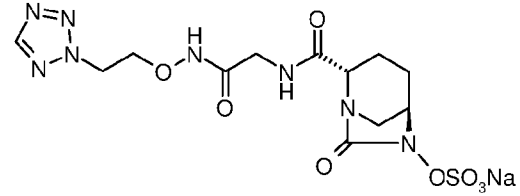
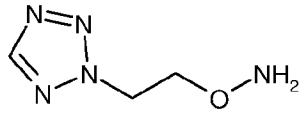
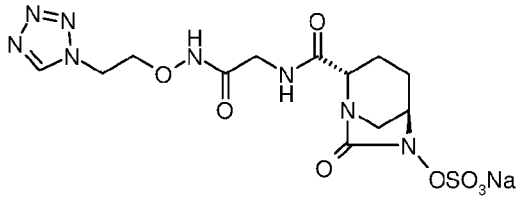
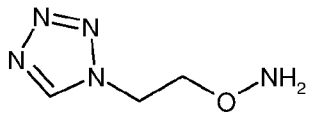
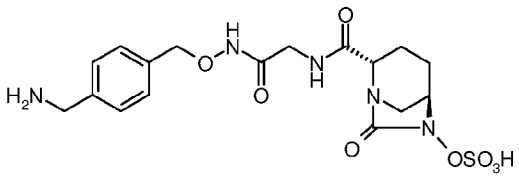
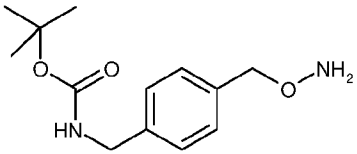
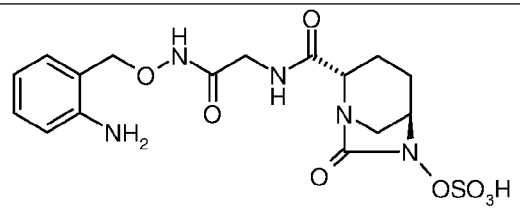
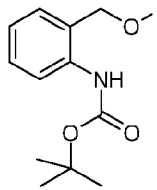
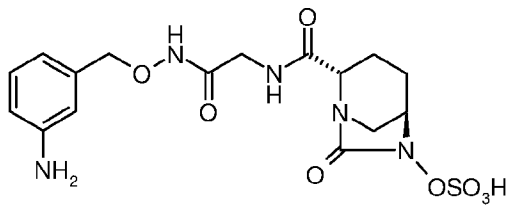
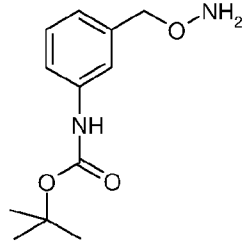
Formula (I)

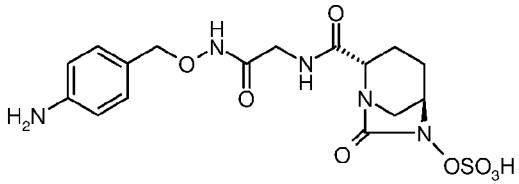
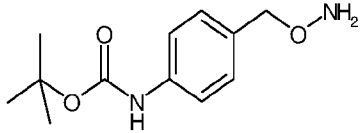
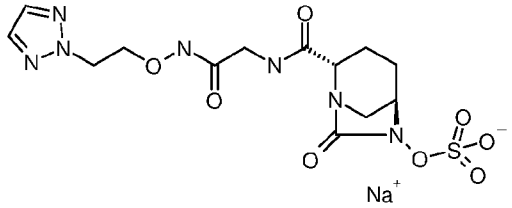
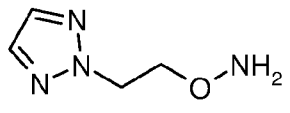
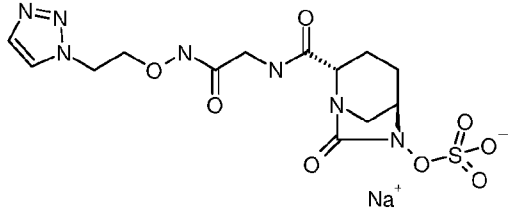
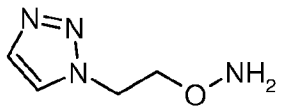
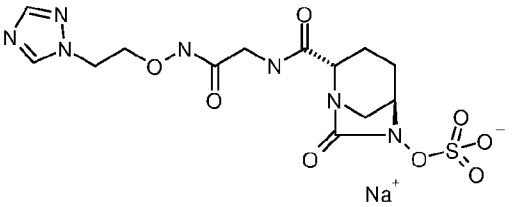
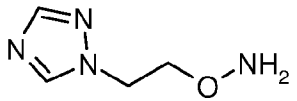
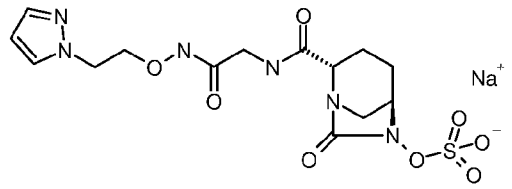
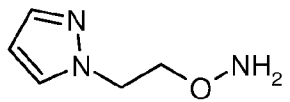
Table-1

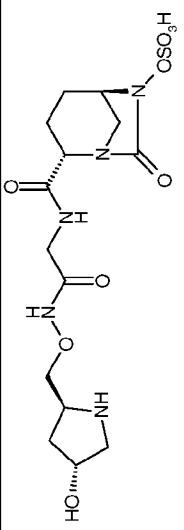
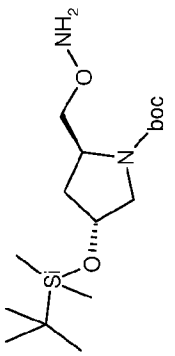
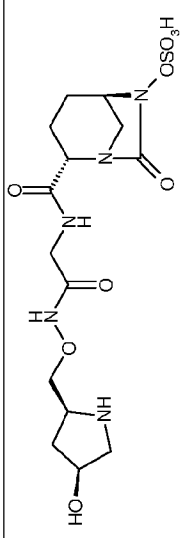
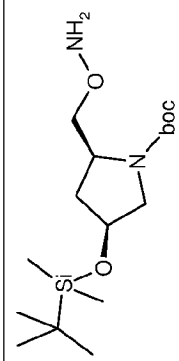
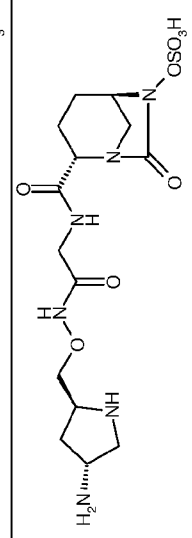
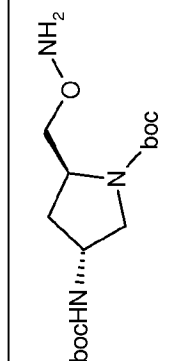
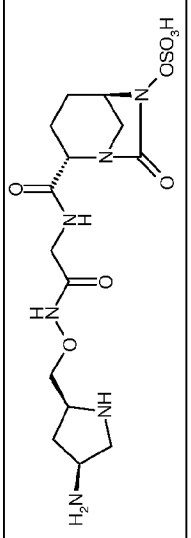
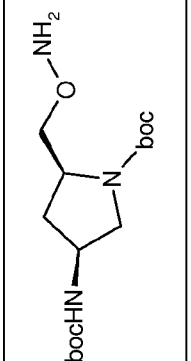
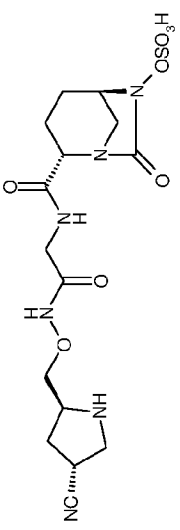
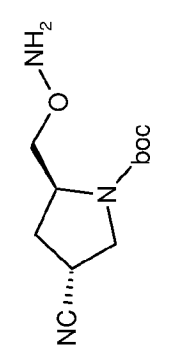
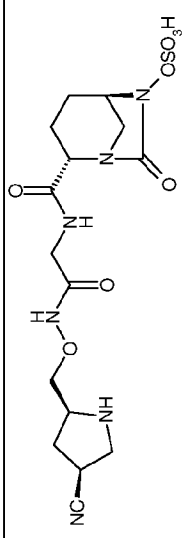
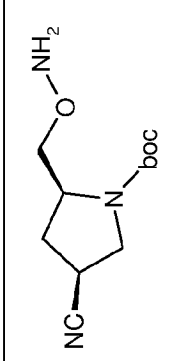
Example No.	Structure	Hydroxylamine compounds	H^1 NMR (DMSO-d_6)	Mass (as free acid) Molecular Formula
2.			δ 11.70 (1H, s), 8.6 (1H, s), 4.16-4.20 (1H, m), 4.00 (1H, s), 3.82-3.91 (3H, m), 2.93-3.03 (2H, m), 2.69-2.75 (1H, m), 1.86-2.02 (2H, m), 1.52-1.88 (5H, m), 1.33-1.43 (1H, m), 1.28 (3H, d, J=8 Hz)	450.3 (M+1) $C_{16}H_{27}N_5O_8S$
3.			δ 8.20 (1H, d, J=7.2 Hz), 7.8-8.0 (1H, s), 4.21 (1H, t, J=6.8 Hz), 3.93-3.95 (3H, m), 3.82 (1H, d, J=6.4 Hz), 2.91-3.02 (3H, m), 2.92 (1H, d, J=12 Hz), 1.87-2.03 (1H, m), 1.86-1.87 (1H, s), 1.62-1.69 (2H, m), 1.28 (3H, d, J=7.2)	396.3 (M+1) $C_{12}H_{21}N_5O_8S$
4.			δ 11.6 (1H, s), 9.0 (1H, s), 8.3 (1H, s), 4.59 (1H, s), 4.18-4.21 (1H, m), 3.99 (1H, s), 3.80 (1H, d, J=7.2), 3.21-3.37 (7H, m), 2.92-3.21 (2H, m), 1.87-2.13 (4H, m), 1.65-1.85 (2H, m), 1.27 (2H, d, J=6.8 Hz)	422.4 (M+1) $C_{14}H_{23}N_5O_8S$
5.			δ 11.5 (1H, s), 8.6-9.0 (2H, m), 8.3 (1H, s), 3.89-4.00 (2H, m), 3.7-3.82 (3H, m), 1.14-1.18 (2H, m), 3.00 (1H, s), 1.91-2.13 (1H, m), 1.70-1.88 (2H, m), 1.56-1.70 (2H, m)	422.3 (M+1) $C_{14}H_{23}N_5O_8S$
6.			δ 10.8-11.4 (1H, s), 8.3 (1H, s), 4.59 (1H, s), 4.35 (1H, s), 4.0 (1H, s), 3.66-3.82 (3H, m), 3.24-3.37 (3H, m), 3.0 (1H, s), 1.84-2.15 (4H, m), 1.55-1.68 (2H, m)	408.3 (M+1) $C_{13}H_{21}N_5O_8S$

7.			δ 11.2-11.8 (1H, s), 8.3 (1H, s), 7.8 (1H, s), 4.00 (1H, s), 3.94 (2H, s), 3.69-3.82 (3H, m), 3.36-3.40 (1H, m), 3.15-3.18 (1H, m), 2.96-3.01 (4H, s), 2.07-2.13 (1H, m), 1.84 (1H, s), 1.56-1.69 (3H, m)	382.3 (M+1) $C_{11}H_{19}N_5O_8S$
8.			δ 4.63 (m, 1H), 4.54 (m, 1H), 4.02 (m, 1H), 3.93 (d, 1H, J = 8 Hz), 3.40-2.93 (m, 8H), 2.15(m, 2H) 2.03-1.56 (m, 4H)	437.4 (M+1), 435.3(M-1) $C_{14}H_{24}N_6O_8S.C_2HO_2F_3$
9.			δ 4.57 (m, 1H), 4.03-3.91 (m, 4H), 3.77 (m, 1H), 3.40-2.97 (m, 6H), 2.13 (m, 2H) 2.01-1.60 (m, 6H)	451.3 (M+1), 449.3(M-1) $C_{15}H_{26}N_6O_8S.C_2HO_2F_3$
10.			δ 4.03-3.96 (m, 2H), 3.82-3.70 (m, 2H), 3.53-3.44 (m, 2H), 3.22-3.13 (m, 4H), 3.07(m, 1H), 2.90 (d,1H, J=10.8Hz), 2.13 (m, 2H) 1.94-1.87 (m, 2H), 1.72-1.56 (m, 3H), 1.34(m, 1H)	449.4(M-1) $C_{15}H_{26}N_6O_8S.C_2HO_2F_3$
11.			δ 11.23 (s, 1H), 8.83 (s, 2H), 8.25 (s, 1H), 4.59 (s, 1H), 4.0 (s, 1H), 3.81-3.80 (d, 1H), 3.68 (s, 2H), 3.27 (s, 4H), 3.0 (s, 2H), 2.11-1.85 (m, 4H), 1.69-1.56 (m, 2H).	408.2 (M+1) $C_{13}H_{21}N_5O_8S$

12.		-	452.46 (M+1) $C_{15}H_{25}N_5O_9S$
13.		-	412.39 (M+1) $C_{12}H_{21}N_5O_9S$
14.		-	438.43 (M+1) $C_{14}H_{23}N_5O_9S$
15.		-	447.44 (M+1) $C_{15}H_{22}N_6O_8S$
16.		-	337.30 (M-1) $C_9H_{13}N_4O_8S.Na$

17.			δ 11.19 (s, 1H), 8.99 (s, 1H), 8.13 (s, 1H), 4.95 (s, 2H), 4.30 (t, 2H, J=4.4 Hz), 3.99 (s, 1H), 3.78 (d, 1H, J=6.4 Hz), 3.57-3.63 (m, 2H), 3.00 (s, 2H), 2.07-2.12 (m, 1H), 1.56-1.83 (m, 3H).	433.3 (M-1) $C_{12}H_{17}N_8O_8S.Na$
18.			δ 11.19 (s, 1H), 9.47 (d, 1H, J=13.6 Hz), 8.02-8.09 (m, 2H), 4.70 (t, 2H, J=4.8 Hz), 3.99-4.35 (m, 2H), 3.63-3.79 (m, 2H), 3.16 (d, 1H, J=12.0 Hz), 3.00 (s, 2H), 2.08-2.13 (m, 2H), 1.56-1.84 (m, 3H).	433.3 (M-1) $C_{12}H_{17}N_8O_8S.Na$
19.			δ 11.18 (1H, s), 8.00-8.15 (4H, m), 4.95 (1H, s), 4.80 (2H, s), 3.99-4.03 (3H, m), 3.64-3.80 (3H, m), 2.99 (2H, m), 2.08-2.11 (2H, m), 1.57-1.84 (4H, m).	458.3 (M+1). $C_{17}H_{23}N_5O_8S$
20.			δ 11.60 (1H, s), 8.25 (1H, t, J=9.2 Hz), 7.23 (2H, d, J=6.4 Hz), 6.82-6.96 (2H, m), 7.76 (2H, s), 3.98 (2H, s), 3.70-3.82 (4H, m), 2.93-3.01 (2H, m), 2.05-2.10 (1H, m), 1.33-1.66 (4H, m).	444.3 (M+1) $C_{16}H_{21}N_5O_8S$
21.			-	444.3 (M+1) $C_{16}H_{21}N_5O_8S$

22.			δ 11.10 (1H, s), 8.13 (1H, s), 7.45 (2H, d, J=7.6 Hz), 7.23 (2H, s), 4.76 (2H, s), 3.98 (2H, s), 3.77 (2H, d, J=6.4 Hz), 3.61 (2H, d, J=5.2 Hz), 2.98 (2H, s), 2.06-2.07 (1H, m), 1.82 (1H, s),1.55-1.66 (2H, m).	444.3 (M+1) $C_{16}H_{21}N_5O_8S$
23			δ 11.1 (s, 1H), 8.07 (s, 1H), 7.78 (s, 1H), 4.63 (m, 2H), 4.21-4.20 (m, 2H), 3.96 (s, 1H), 3.77-3.75 (d, 1H, J=6.4 Hz), 3.62-3.55 (m, 3H), 2.99 (s, 2H), 2.11-2.05 (m, 1H), 1.83-1.54 (m, 3H).	432.3 (M-H, Free Acid). $C_{13}H_{18}N_7O_8SNa$
24			δ 11.2 (s, 1H), 8.30 (s, 1H), 8.20 (s, 1H), 7.71 (s, 1H), 4.59 (m, 2H), 4.11 (m, 2H), 3.96 (s, 1H), 3.77-3.76 (d, 1H, J=6.8 Hz), 3.63-3.58 (m, 2H), 2.98 (s, 2H), 2.10-1.80 (m, 1H), 1.67 (m, 1H), 1.65-1.55 (m, 2H).	432.3 (M-1). $C_{13}H_{18}N_7O_8SNa$
25			δ 11.12 (s, 1H), 8.57 (s, 1H), 8.12 (s, 1H), 7.95 (s, 1H), 4.39 (m, 2H), 4.09 (m, 3H), 3.78-3.76 (d, 1H, J=7.2), 3.72-3.58 (m, 2H), 2.99 (m, 2H), 2.11-2.06 (m, 1H), 1.81-1.51 (m, 3H).	432.3 (M-1). $C_{13}H_{18}N_7O_8SNa$
26			δ 11.13 (1H, bs), 8.15 (1H, bs), 7.83 (1H, s), 7.43 (1H, s), 6.23 (1H, s), 4.26-4.33 (2H, m), 3.99-4.08 (2H, m), 3.79-3.81 (1H, m), 3.58-3.75 (3H, m), 2.98-3.01 (2H, m), 2.08-2.13 (1H, m), 1.68-1.83 (3H, m)	431.2 (M-1). $C_{14}H_{19}N_6O_8SNa$

27.			-	436.4 (M-1) $C_{14}H_{23}N_5O_9S$
28.			-	436.4 (M-1) $C_{14}H_{23}N_5O_9S$
29.			-	437.4 (M+1) $C_{14}H_{24}N_6O_8S$
30.			-	437.4 (M+1) $C_{14}H_{24}N_6O_8S$
31.			-	447.4 (M+1) $C_{15}H_{22}N_6O_8S$
32.			-	447.4(M+1) $C_{14}H_{22}N_7O_8S$

BIOLOGICAL ACTIVITY DATA

The biological activity of representative compounds according to the invention in combination with antibacterial agent was investigated against various bacterial strains.

Method for the determination of MIC: The Minimum Inhibitory Concentration (MIC) determination for the combinations was carried out in Muller Hinton Agar (MHA) (BD, USA) according to Clinical and Laboratory Standards Institute (CLSI) recommendations, (Clinical and Laboratory Standards Institute (CLSI), Performance Standards for Antimicrobial Susceptibility Testing, 20th Informational Supplement, M 100-S20, Volume 30, No. 1, 2010). In short, the test strains were adjusted to deliver about 10^4 CFU per spot with a multipoint inoculator (Applied Quality Services, UK). The plates were poured with MHA containing doubling concentration range of representative compounds according to present invention. The plates were inoculated and were incubated at 35°C for 18 hour. MICs were read as the lowest concentration of drug that completely inhibited bacterial growth. The Table 2 depicts the antibacterial activity profile of compounds according to present invention against various bacterial strains. These compounds when tested alone exhibited higher MIC values.

Table 2. Antibacterial activity of representative compounds according to the invention (MIC expressed in mcg/ml)

Sr.	Compounds	Bacterial Strains						
		K. pneumoniae ATCC 700603	*E. coli* NCTC 13352	*E. coli* NCTC 13353	*E. coli* M50	*E. coli* 7MP	*K. pneumoniae* H521	*K. pneumoniae* H525
1.	Example 1	> 32	32	32	> 32	> 32	32	32
2.	Example 2	> 32	> 32	> 32	> 32	> 32	> 32	> 32
3.	Example 3	> 32	32	32	> 32	> 32	32	32
4.	Example 4	> 32	32	32	> 32	> 32	32	32
5.	Example 5	> 32	> 32	> 32	> 32	> 32	> 32	> 32
6.	Example 6	> 32	> 32	> 32	16	> 32	> 32	> 32
7.	Example 7	> 32	> 32	> 32	16	> 32	> 32	> 32
8.	Example 8	> 32	> 32	> 32	> 32	> 32	> 32	> 32
9.	Example 9	> 32	> 32	> 32	> 32	> 32	> 32	> 32
10.	Example 10	> 32	> 32	> 32	> 32	> 32	> 32	> 32
11.	Example 11	> 32	> 32	> 32	> 32	> 32	> 32	> 32
12.	Example 17	> 32	> 32	> 32	> 32	> 32	> 32	> 32
13.	Example 18	> 32	> 32	> 32	> 32	> 32	> 32	> 32
14.	Example 19	> 32	> 32	> 32	> 32	> 32	> 32	> 32
15.	Example 20	> 32	> 32	> 32	> 32	> 32	> 32	> 32
16.	Example 22	> 32	> 32	> 32	32	> 32	> 32	> 32
17.	Ceftazidime	32	> 32	32	> 32	> 32	> 32	> 32

Method for the Determination of Combination MIC: The Minimum Inhibitory Concentration (MIC) determination for the combinations was carried out in Muller Hinton Agar (MHA) (BD, USA) according to Clinical and Laboratory Standards Institute (CLSI) recommendations,

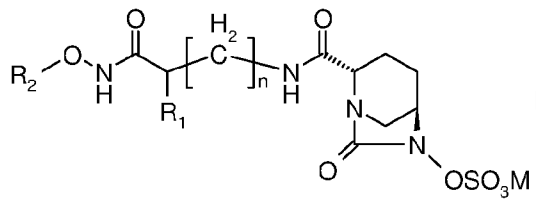
(Clinical and Laboratory Standards Institute (CLSI), Performance Standards for Antimicrobial Susceptibility Testing, 20th Informational Supplement, M 100-S20, Volume 30, No. 1, 2010). In short, the test strains were adjusted to deliver about 10^4 CFU per spot with a multipoint inoculator (Applied Quality Services, UK). The plates were poured with MHA containing doubling concentration range of Ceftazidime in combination with constant concentration (4µg/ml) of representative compounds of Formula (I). The Table 3 shows the MIC values of Ceftazidime in presence of compounds according to the invention (at 4 µg/ml) against various bacterial strains. As shown in Table 3, the MIC value of Ceftazidime was significantly lowered in presence of compounds according to the invention.

Table 3. Antibacterial activity of representative compounds according to the invention in combination with Ceftazidime

Sr.	Compounds	Ceftazidime MIC (expressed in mcg/ml)						
		K. pneumoniae ATCC 700603	*E. coli* NCTC 13352	*E. coli* NCTC 13353	*E. coli* M50	*E. coli* 7MP	*K. pneumoniae* H521	*K. pneumoniae* H525
	Ceftazidime alone	32	> 32	32	> 32	> 32	> 32	> 32
1.	Ceftazimime + Example 1 (4mcg/ml)	2	4	0.5	2	8	16	16
2.	Ceftazidime + Example 2 (4mcg/ml)	2	8	0.5	1	16	32	32
3.	Ceftazidime + Example 3 (4mcg/ml)	1	4	0.5	0.5	8	16	16
4.	Ceftazidime + Example 4 (4mcg/ml)	1	4	0.5	1	4	16	16
5.	Ceftazidime + Example 5 (4mcg/ml)	0.5	2	0.5	1	4	4	4
6.	Ceftazidime + Example 6 (4mcg/ml)	0.5	4	0.5	1	-	> 32	> 32
7.	Ceftazidime + Example 7 (4mcg/ml)	0.5	2	0.5	1	-	16	8
8.	Ceftazidime + Example 11 (4mcg/ml)	0.5	2	0.12	0.25	-	0.5	0.12
9.	Ceftazidime + Example 17 (4mcg/ml)	1	4	0.5	2	4	16	8
10.	Ceftazidime + Example 18 (4mcg/ml)	1	4	1	1	4	16	8
11.	Ceftazidime + Example 19 (4mcg/ml)	1	4	0.5	2	8	16	8
12	Ceftazidime + Example 20 (4mcg/ml)	1	8	0.5	1	8	16	16
13	Ceftazidime + Example 23 (4mcg/ml)	1	8	0.5	1	8	8	8
14	Ceftazidime + Example 24(4mcg/ml)	0.5	2	0.25	1	2	4	4
15	Ceftazidime + Example 25(4mcg/ml)	0.5	4	0.5	2	8	8	8
16	Ceftazidime + Example 26(4mcg/ml)	1	8	0.5	2	4	16	8

CLAIMS

1. A compound of Formula (I):



Formula (I)

or a stereoisomer or a pharmaceutically acceptable derivative thereof;

wherein:

R_1 is:

(a) hydrogen,
(b) C_1-C_6 alkyl optionally substituted with one or more substituents independently selected from OR_3, NR_3R_4, SR_3, SOR_3, SO_2R_3, CN, halogen, $COOR_3$, $CONR_3R_4$, NR_3COR_4, or $NR_3CONR_4R_5$,
(c) NR_3R_4,
(d) CN,
(e) SOR_3,
(f) SO_2R_3 or
(g) OR_3;

R_2 is:

(a) hydrogen,
(b) C_1-C_6 alkyl optionally substituted with one or more substituents independently selected from OR_3, NR_3R_4, SR_3, SOR_3, SO_2R_3, CN, halogen, $COOR_3$, $CONR_3R_4$, NR_3COR_4, $NR_3CONR_4R_5$, $=NOCH_3$, cycloalkyl, heterocycloalkyl, aryl or heteroaryl,
(c) cycloalkyl optionally substituted with one or more substituents independently selected from OR_3, NR_3R_4, SR_3, SOR_3, SO_2R_3, CN, $(CH_2)_nNR_3R_4$, halogen, $COOR_3$, $CONR_3R_4$, NR_3COR_4 or $NR_3CONR_4R_5$,
(d) heterocycloalkyl optionally substituted with one or more substituents independently selected from OR_3, NR_3R_4, SR_3, SOR_3, SO_2R_3, CN, $(CH_2)_nNR_3R_4$, halogen, $COOR_3$, $CONR_3R_4$, NR_3COR_4 or $NR_3CONR_4R_5$,
(e) aryl optionally substituted with one or more substituents independently selected from OR_3, NR_3R_4, SR_3, SOR_3, SO_2R_3, CN, $(CH_2)_nNR_3R_4$, halogen, $COOR_3$, $CONR_3R_4$, NR_3COR_4 or $NR_3CONR_4R_5$ or
(f) heteroaryl optionally substituted with one or more substituents independently selected from OR_3, NR_3R_4, SR_3, SOR_3, SO_2R_3, CN, $(CH_2)_nNR_3R_4$, halogen, $COOR_3$, $CONR_3R_4$, NR_3COR_4 or $NR_3CONR_4R_5$;

R_3, R_4 and R_5 are each independently:

(a) hydrogen or
(b) C_1-C_6 alkyl;

n is 0,1,2 or 3;

M is hydrogen or a cation.

2. A compound according to Claim 1, selected from:
(2*S*,5*R*)-*N*-[(2*S*)-1-oxo-1-{[(2*S*)-pyrrolidin-2-ylmethoxy]amino}propan-2-yl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-[(2*S*)-1-oxo-1-{[(2*R*)- piperidine-2-ylmethoxy]amino}propan-2-yl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-{(2*S*)-1-[(2-aminoethoxy)amino]-1-oxopropan-2-yl}-7-oxo-6-(sulfooxy-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-[(2*S*)-1-oxo-1-{[(3*S*)-pyrrolidin-3-yloxy]amino}propan-2-yl]-7-oxo-6-(sulfooxy 1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*)-pyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-(2-oxo-2-{[(3*S*)-pyrrolidin-3-yloxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo [3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-{2-[(2-aminoethoxy)amino]-2-oxoethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo [3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-[(2*S*)-3-amino-1-oxo-{[(3*S*)-pyrrolidin-3-yloxy]amino}propan-2yl]-7-oxo-6-(sulfooxy)-1,6diazabicyclo [3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-[(2*S*)-3-amino-1- oxo-1-{[(2*S*)-pyrolidin-2-yl-methoxy]amino}propan-2yl]-7-oxo-6-(sulfooxy)-1,6diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-[(2*S*)-2-amino-1-oxo-1-{[(2*S*)-pyrolidin-2-yl-methoxy]amino}propan-2yl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-3-carboxamide;
(2*S*,5*R*) -*N*-(2-oxo-2-{[(3*R*)-pyrrolidin-3-yloxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-[(2*S*)-3-({[(2*S*)-pyrrolidin-2-ylmethoxy]amino}-2-hydroxy-3-oxopropyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-[(2*S*)-3-[(2-amino)-2-hydroxy-3-oxopropyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo [3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-[(2*S*)-3-({[(3*S*)-pyrrolidin-3-yloxy]amino}-2-hydroxy-3-oxopropyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-[(2*S*)-3-({[(3*S*)-pyrrolidin-3-yloxy]amino}-2-cyano-3-oxopropyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-[2-(hydroxyamino)-2-oxoethyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-[(2*S*)-3-({[N-[2-2H-tetrazole-2-yl)-ethoxy]amino}-3-oxopropyl]-6-(sulfooxy)-7-oxo-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-[(2*S*)-3-({[N-[2-1H-tetrazole-1-yl)-ethoxy]amino}-3-oxopropyl]-6-(sulfooxy)-7-oxo-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-[2-{[{[4-(aminomethyl)phenyl]methyl}oxy]amino}-2-oxoethyl]-6-sulfooxy-7-oxo-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-[2-{[{[2-aminophenyl]methyl}oxy]amino}-2-oxoethyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-[2-{[{[3-aminophenyl]methyl}oxy]amino}-2-oxoethyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-[2-{[{[4-aminophenyl]methyl}oxy]amino}-2-oxoethyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5) -*N*-(2-oxo-2-{[2-(2*H*-1,2,3-triazol-2-yl)ethoxy]amino}ethyl))-7-oxo -6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*) -*N*-(2-oxo-2-{[2-(1*H*-1,2,3-triazol-1-yl)ethoxy]amino}ethyl) -7-oxo -6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*) -*N*-(2-oxo-2-{[2-(1*H*-1,2,4-triazol-1-yl)ethoxy]amino}ethyl)- 7-oxo 6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*, 5*R*) -*N*-(2-oxo-2-{[2-(2-(1*H*-pyrazol-1-yl)ethoxy]amino}ethyl)- 7-oxo 6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*R*)-4-hydroxypyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*S*)-4-hydroxypyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*R*)-4-aminopyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*S*)-4-aminopyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*R*)-4-cyanopyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*S*)-4-cyanopyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide.

or a stereoisomer or a pharmaceutically acceptable derivative thereof.

3. A compound according to Claim 1, selected from:

Sodium salt of (2*S*,5*R*)-*N*-[(2*S*)-1-oxo-1-{[(2*S*)-pyrrolidin-2-ylmethoxy]amino}propan-2-yl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[(2*S*)-1-oxo-1-{[(2*R*)- piperidine-2-ylmethoxy]amino}propan-2-yl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-{(2*S*)-1-[(2-aminoethoxy)amino]-1-oxopropan-2-yl}-7-oxo-6-(sulfooxy-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[(2*S*)-1-oxo-1-{[(3*S*)-pyrrolidin-3-yloxy]amino}propan-2-yl]-7-oxo-6-(sulfooxy 1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*)-pyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-(2-oxo-2-{[(3*S*)-pyrrolidin-3-yloxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo [3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-{2-[(2-aminoethoxy)amino]-2-oxoethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo [3.2.1]octane-2-carboxamide;

Trifluoroacetate salt of (2*S*,5*R*)-*N*-[(2*S*)-3-amino-1-oxo-{[(3*S*)-pyrrolidin-3-yloxy] amino}propan-2yl]-7-oxo-6-(sulfooxy)-1,6diazabicyclo [3.2.1]octane-2-carboxamide;

Trifluoroacetate salt of (2*S*,5*R*)-*N*-[(2*S*)-3-amino-1- oxo-1-{[(2*S*)-pyrolidin-2-yl-methoxy]amino}propan-2yl]-7-oxo-6-(sulfooxy)-1,6diazabicyclo[3.2.1]octane-2-carboxamide;

Trifluoroacetate salt of (2*S*,5*R*)-*N*-[(2*S*)-2-amino-1-oxo-1-{[(2*S*)-pyrolidin-2-yl-methoxy]amino}propan-2yl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-3-carboxamide;

Sodium salt of (2*S*,5*R*) -*N*-(2-oxo-2-{[(3*R*)-pyrrolidin-3-yloxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[(2*S*)-3-({[(2*S*)-pyrrolidin-2-ylmethoxy]amino}-2-hydroxy-3-oxopropyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[(2*S*)-3-[(2-amino)-2-hydroxy-3-oxopropyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo [3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[(2*S*)-3-({[(3*S*)-pyrrolidin-3-yloxy]amino}-2-hydroxy-3-oxopropyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[(2*S*)-3-({[(3*S*)-pyrrolidin-3-yloxy]amino}-2-cyano-3-oxopropyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[2-(hydroxyamino)-2-oxoethyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[(2*S*)-3-({[N-[2-2H-tetrazole-2-yl)-ethoxy]amino}-3-oxopropyl]-6-(sulfooxy)-7-oxo-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[(2*S*)-3-({[N-[2-1H-tetrazole-1-yl)-ethoxy]amino}-3-oxopropyl]-6-(sulfooxy)-7-oxo-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[2-{[{[4-(aminomethyl)phenyl]methyl}oxy]amino}-2-oxoethyl]-6-sulfooxy-7-oxo-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[2-{[{[2-aminophenyl]methyl}oxy]amino}-2-oxoethyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[2-{[{[3-aminophenyl]methyl}oxy]amino}-2-oxoethyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[2-{[{[4-aminophenyl]methyl}oxy]amino}-2-oxoethyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5) -*N*-(2-oxo-2-{[2-(2*H*-1,2,3-triazol-2-yl)ethoxy]amino}ethyl))-7-oxo -6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*) -*N*-(2-oxo-2-{[2-(1*H*-1,2,3-triazol-1-yl)ethoxy]amino}ethyl) -7-oxo -6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*) -*N*-(2-oxo-2-{[2-(1*H*-1,2,4-triazol-1-yl)ethoxy]amino}ethyl)- 7-oxo 6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*, 5*R*) -*N*-(2-oxo-2-{[2-(2-(1*H*-pyrazol-1-yl)ethoxy]amino}ethyl)- 7-oxo 6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*R*)-4-hydroxypyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*S*)-4-hydroxypyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*R*)-4-aminopyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*S*)-4-aminopyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*R*)-4-cyanopyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*) -*N*-(2-oxo-2-{[(2*S*, 4*S*)-4-cyanopyrrolidin-2-ylmethoxy]amino}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide.

or a stereoisomer thereof.

4. A pharmaceutical composition comprising a compound according to any one of Claims 1 to 3.

5. The pharmaceutical composition according to Claim 4, further comprising at least one antibacterial agent or a pharmaceutically acceptable derivative thereof.

6. The pharmaceutical composition according to Claim 5, wherein the antibacterial agent is selected from a group consisting of aminoglycosides, ansamycins, carbacephems, cephalosporins, cephamycins, lincosamides, lipopeptides, macrolides, penems, carbapenems, monobactams, nitrofurans, penicillins, polypeptides, quinolones, sulfonamides, tetracyclines, or oxazolidinone antibacterial agents.

7. The pharmaceutical composition according to Claim 5, wherein the antibacterial agent is a beta-lactam antibacterial agent.

8. The pharmaceutical composition according to Claim 5, wherein the antibacterial agent is a cephalosporin antibiotic selected from a group consisting of cephalothin, cephaloridine, cefaclor, cefadroxil, cefamandole, cefazolin, cephalexin, cephradine, ceftizoxime, cefoxitin, cephacetrile, cefotiam, cefotaxime, cefsulodin, cefoperazone, ceftizoxime, cefmenoxime, cefmetazole, cephaloglycin, cefonicid, cefodizime, cefpirome, ceftazidime, ceftriaxone, cefpiramide, cefbuperazone, cefozopran, cefepime, cefoselis, cefluprenam, cefuzonam, cefpimizole, cefclidin, cefixime, ceftibuten, cefdinir, cefpodoxime, cefteram, cefetamet, cefcapene, cefditoren, cefuroxime, ceftaroline and ceftolozane.

9. A method for preventing or treating a bacterial infection in a subject, said method comprising administering to said subject a pharmaceutically effective amount of a compound according to any one of Claims 1 to 3.

10. A method for preventing or treating a bacterial infection in a subject, said method comprising administering to said subject a pharmaceutically effective amount of a pharmaceutical composition according to any one of Claims 4 to 8.

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2016/053969

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D471/08 A61K31/439 A61P31/04
ADD.

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2013/030733 A1 (WOCKHARDT LTD [IN]; PATEL MAHESH VITHALBHAI [IN]; DESHPANDE PRASAD KES) 7 March 2013 (2013-03-07) page 1 table 1 claim 1 -----	1-10
A	WO 2014/033560 A1 (WOCKHARDT LTD [IN]) 6 March 2014 (2014-03-06) page 1 tables 1-3 claim 1 -----	1-10

☐ 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

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

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"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

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
15 September 2016	24/10/2016

Name and mailing address of the ISA/	Authorized officer
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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2016/053969

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