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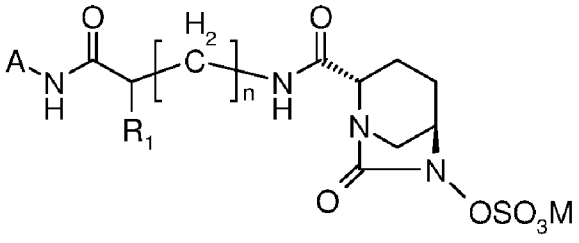

Formula (I)

(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. 2546/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.

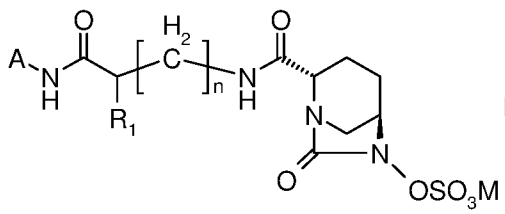
Several antibacterial agents have been described in the prior art (for example, see PCT International Application Nos. PCT/US2010/060923, PCT/EP2010/067647, PCT/US2010/052109, PCT/US2010/048109, PCT/GB2009/050609, PCT/FR01/02418, PCT/EP2009/056178, PCT/US2009/041200, PCT/IB2012/054290, PCT/IB2013/053092, 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 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:

A is $NHCOR_2$, NR_2R_3 or $N=CHR_2$;

R_1 is:

(a) hydrogen,
(b) C_1-C_6 alkyl optionally substituted with one or more substituents independently selected from OR_4, NR_4R_5, SR_4, SOR_4, SO_2R_4, CN, halogen, $COOR_4$, $CONR_4R_5$, NR_4COR_5, or $NR_4CONR_5R_6$,
(c) NR_4R_5,
(d) CN,
(e) SOR_4,
(f) SO_2R_4 or
(g) OR_4;

R_2 and R_3 are each independently:

(a) hydrogen,
(b) C_1-C_6 alkyl optionally substituted with one or more substituents independently selected from OR_4, NR_4R_5, SR_5, SOR_4, SO_2R_4, CN, halogen, $COOR_4$, $CONR_4R_5$, NR_4COR_5, $NR_4CONR_5R_6$, $=NOCH_3$, heterocyclyl, cycloalkyl, aryl or heteroaryl,
(c) cycloalkyl optionally substituted with one or more substituents independently selected from OR_4, NR_4R_5, SR_4, SOR_4, SO_2R_4, CN, $(CH_2)_mNR_4R_5$, halogen, $COOR_4$, $CONR_4R_5$, NR_4COR_5 or $NR_4CONR_5R_6$,
(d) heterocycloalkyl optionally substituted with one or more substituents independently selected from OR_4, NR_4R_5, SR_4, SOR_4, SO_2R_4, CN, $(CH_2)_mNR_4R_5$, halogen, $COOR_4$, $CONR_4R_5$, NR_4COR_5 or $NR_4CONR_5R_6$,
(e) aryl optionally substituted with one or more substituents independently selected from OR_4, NR_4R_5, SR_4, SOR_4, SO_2R_4, CN, $(CH_2)_mNR_4R_5$, halogen, $COOR_4$, $CONR_4R_5$, NR_4COR_5 or $NR_4CONR_5R_6$,
(f) heteroaryl optionally substituted with one or more substituents independently selected from OR_4, NR_4R_5, SR_4, SOR_4, SO_2R_4, CN, $(CH_2)_mNR_4R_5$, halogen, $COOR_4$, $CONR_4R_5$, NR_4COR_5 or $NR_4CONR_5R_6$ or
(g) R_2 and R_3 are joined together to form a four to seven member ring;

R_4, R_5 and R_6 are each independently:

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

n is 0,1,2 or 3;
m is 1 to 6;

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 nitrogen containing bicyclic 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 twenty 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 twenty 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 azridinyl, 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

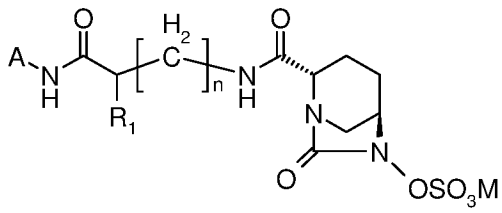
and Gilman's: The Pharmacological Basis of Therapeutics, 8th Ed., Pergamon Press., 1990), which is incorporated herein by reference in its entirety.

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 "TFA" as used herein refers to trifluoroacetic acid.
The term "TBAA" as used herein refers to tetrabutylammonium acetate.

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:

A is $NHCOR_2$, NR_2R_3 or $N{=}CHR_2$;

R_1 is:

(a) hydrogen,
(b) C_1-C_6 alkyl optionally substituted with one or more substituents independently selected from OR_4, NR_4R_5, SR_4, SOR_4, SO_2R_4, CN, halogen, $COOR_4$, $CONR_4R_5$, NR_4COR_5, or $NR_4CONR_5R_6$,
(c) NR_4R_5,
(d) CN,
(e) SOR_4,
(f) SO_2R_4 or
(g) OR_4;

R_2 and R_3 are each independently:

(a) hydrogen,
(b) C_1-C_6 alkyl optionally substituted with one or more substituents independently selected from OR_4, NR_4R_5, SR_5, SOR_4, SO_2R_4, CN, halogen, $COOR_4$,

$CONR_4R_5$, NR_4COR_5, $NR_4CONR_5R_6$, $=NOCH_3$, heterocyclyl, cycloalkyl, aryl or heteroaryl,

(c) cycloalkyl optionally substituted with one or more substituents independently selected from OR_4, NR_4R_5, SR_4, SOR_4, SO_2R_4, CN, $(CH_2)_mNR_4R_5$, halogen, $COOR_4$, $CONR_4R_5$, NR_4COR_5 or $NR_4CONR_5R_6$,

(d) heterocycloalkyl optionally substituted with one or more substituents independently selected from OR_4, NR_4R_5, SR_4, SOR_4, SO_2R_4, CN, $(CH_2)_mNR_4R_5$, halogen, $COOR_4$, $CONR_4R_5$, NR_4COR_5 or $NR_4CONR_5R_6$,

(e) aryl optionally substituted with one or more substituents independently selected from OR_4, NR_4R_5, SR_4, SOR_4, SO_2R_4, CN, $(CH_2)_mNR_4R_5$, halogen, $COOR_4$, $CONR_4R_5$, NR_4COR_5 or $NR_4CONR_5R_6$,

(f) heteroaryl optionally substituted with one or more substituents independently selected from OR_4, NR_4R_5, SR_4, SOR_4, SO_2R_4, CN, $(CH_2)_mNR_4R_5$, halogen, $COOR_4$, $CONR_4R_5$, NR_4COR_5 or $NR_4CONR_5R_6$ or

(g) R_2 and R_3 are joined together to form a four to seven member ring;

R_4, R_5 and R_6 are each independently:

(a) hydrogen or

(b) C_1-C_6 alkyl;

n is 0,1,2 or 3;
m is 1 to 6;

M is hydrogen or a cation.

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

(2*S*,5*R*)-*N*-[(2*S*)-3-Amino-1-[(3*R*)-3-(hydrazinylcarbonyl)piperidine]-1-oxopropan-2-yl] -7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-[(2*S*)-3-Hydroxy-1-[(3*R*)-3-(hydrazinylcarbonyl)piperidine]-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-{2-[(3*R*)-piperidine-3-ylcarbonyl]hydrazinyl}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*R*)-Azepan-2-yl-carbonyl]hydrazinyl}-1-oxo-propan-2-yl]-2-methyl-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*, 5*R*)-*N*-[(2*S*)-1-{(2*S*)-Azepan-2-yl-carbonyl]hydrazinyl}-1-oxo-propan-2-yl]-2-methyl-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*- (2-Oxo-2-{2-[(3*R*)-piperidin-3-ylcarbonyl]hydrazinyl}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-[(2*S*)-3-Amino-1-[(2*R*)-2-(hydrazinylcarbonyl azepane]-1-oxopropan-2-yl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

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

(2*S*,5*R*)-*N*-[(2*S*)-1-Hydrazinyl-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-[2-(thiophen-2-ylacetyl)hydrazinyl] propan-2-yl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-[(2*R*)-1-[(2*S*)-(Pyrrolidineacetyl)hydrazinyl]-4-(methylsulfonyl) -1-oxobutan-2-yl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-[(2*S*)-2-Amino-1-[(3*R*)-3-(hydrazinylcarbonyl) piperidine]-1-oxopropan-2-yl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-3-carboxamide;

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

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

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

(2*S*,5*R*)-*N*-{2-Oxo-2-[2-(pyridin-2-ylcarbonyl)hydrazinyl]ethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*- {2-Oxo-2-[2-(thiophen-2-ylacetyl)hydrazinyl]ethyl}-7-oxo -6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

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

(2*S*,5*R*)-*N*-(2-{2-[(4-Aminophenyl)carbonyl] hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(2*E*)-2-(2-Amino-1,3-thiazol-4-yl)-2-(methoxyimino) acetyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)--1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*) -*N*-{2-Oxo-2-[2-(thiophen-2-ylcarbonyl)hydrazinyl]ethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-[2-(2-{[4-(Aminomethyl)phenyl]carbonyl}hydrazinyl) -2-oxoethyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

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

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

(2*S*,5*R*)-*N*- {[2-Oxo-(2-hydroxyphen-2-ylcarbonyl)hydrazinyl]ethyl}-7-oxo-6- (sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

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

(2*S*,5*R*)-*N*- {2-Oxo-2-[2-(pyridin-3-ylcarbonyl)hydrazinyl]ethyl-7-oxo-6- (sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

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

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

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

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

(2*S*,5*R*)-*N*-{2-[(2*E*)-2-(2',4'-Dimethoxybenzylidenehydrazinyl]-2-oxoethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-2-({2-[(2*E*)-2-(3-Aminopropylidene)hydrazinyl]-2-oxoethyl}carbamoyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-{2-[(2*E*)-2-(4' Methylaminobenzylidenehydrazinyl]-2-oxoethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-{2-[2-(1*H*-1,2,4-Triazol-1-ylcarbonyl)hydrazinyl]-2-oxo-ethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-{2-[2-(2*H*-1,2,3-Triazol-2-ylcarbonyl)hydrazinyl]-2-oxo-ethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-{2-[2-(1*H*-1,2,3-Triazol-1-ylcarbonyl)hydrazinyl]-2-oxo-ethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(3-Aminophenyl)carbonyl] hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(2*E*)-2-(2-Amino-1,3-thiazol-4-yl)-2-oxoethyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)- *N*-(2-{2-[(4-(2*S*)-2-(Phenoxymethyl)pyrrolidine)acetyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)- *N*-(2-{2-[(4-(2-[(2-Phenoxyethanamine)acetyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

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

(2*S*,5*R*)-*N*-(2-{2-[(2-Chloro-3,4-dihydroxyphenyl)carbonyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(4-Cyanophenyl)carbonyl] hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(4-Amino-2-hydroxyphenyl)carbonyl] hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(2,4-Dichlorophenyl)carbonyl] hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(4-{1-[(2-Methylpropanoyl)oxy]ethoxy}carbonyl) phenyl)carbonyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1] octane-2-carboxamide1-(carbamoyloxy) ethyl 2-methylpropanoate;

(2*S*,5*R*)-*N*-(2-{2-[(4-Carboxamidophenyl)carbonyl] hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(4-Amino-2-aminoethoxyphenyl)carbonyl] hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[Piperidin-4-ylcarbonyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(3*R*)-Pyrrolidin-2-ylcarbonyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

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

(2*S*,5*R*)-*N*-(2-{2-[(2*S*,4*R*)-4-Hydroxypyrrolidin-2-ylcarbonyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(2*S*,4*S*)-4-Hydroxypyrrolidin-2-ylcarbonyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(2*S*,4*R*)-4-Cyanopyrrolidin-2-ylcarbonyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(2*S*,4*S*)-4-Cyanopyrrolidin-2-ylcarbonyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(4-Aminocylohehane-4-yl)carbonyl]hydrazinyl}-2-oxoethyl)-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:

Trifluoroacetate salt of (2*S*,5*R*)-*N*-[(2*S*)-3-amino-1-[(3*R*)-3-(hydrazinylcarbonyl)piperidine]-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*)-3-hydroxy-1-[(3*R*)-3-(hydrazinylcarbonyl)piperidine]-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-{2-[(3*R*)-piperidine-3-ylcarbonyl]hydrazinyl}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*R*)-azepan-2-yl-carbonyl]hydrazinyl}-1-oxo-propan-2-yl]-2-methyl-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*S*)-azepan-2-yl-carbonyl]hydrazinyl}-1-oxo-propan-2-yl]-2-methyl-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-[(3*R*)-piperidin-3-ylcarbonyl]hydrazinyl}ethyl)-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-[(2*R*)-2-(hydrazinylcarbonyl azepane]-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-hydrazinyl-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*)-1-hydrazinyl-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-[2-(thiophen-2-ylacetyl)hydrazinyl] 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*R*)-1-[(2*S*)-(pyrrolidineacetyl)hydrazinyl]-4-(methylsulfonyl) -1-oxobutan-2-yl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Trifluoroacetate salt of (2*S*,5*R*)-*N*-[(2*S*)-2-amino-1-[(3*R*)-3-(hydrazinylcarbonyl) piperidine]-1-oxopropan-2-yl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-3-carboxamide;

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

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

Sodium salt of (2*S*,5*R*)-*N*- {2-[2-(hydroxyacetyl)hydrazinyl]-2-oxoethyl}-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-(pyridin-2-ylcarbonyl)hydrazinyl]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-(thiophen-2-ylacetyl)hydrazinyl]ethyl}-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-[(2*R*)-2-hydroxypropanoyl]hydrazinyl}-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-{2-[(4-aminophenyl)carbonyl] hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-(2-{2-[(2*E*)-2-(2-amino-1,3-thiazol-4-yl)-2-(methoxyimino) acetyl]hydrazinyl}-2-oxoethyl)-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-(thiophen-2-ylcarbonyl)hydrazinyl]ethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[2-(2-{[4-(aminomethyl)phenyl]carbonyl}hydrazinyl) -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*)-1-[2-(cyanoacetyl)hydrazinyl]-1-oxoethyl}-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-(cyanoacetyl)hydrazinyl]-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-oxo-(2-hydroxyphen-2-ylcarbonyl)hydrazinyl]ethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*- (2-{2-[(2-aminophenyl)carbonyl]hydrazinyl}-2-oxoethyl)-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-(pyridin-3-ylcarbonyl)hydrazinyl]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-({[(3*R*)-piperidin-3-ylcarbonyl]hydrazinyl}-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-(2-methylhydrazinyl)-2-oxoethyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

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

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

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

Sodium salt of (2*S*,5*R*)-2-({2-[(2*E*)-2-(3-aminopropylidene)hydrazinyl]-2-oxoethyl}carbamoyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

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

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

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

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

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

Sodium salt of (2*S*,5*R*)-*N*-(2-{2-[(2*E*)-2-(2-amino-1,3-thiazol-4-yl)-2-oxoethyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)- *N*-(2-{2-[(4-(2*S*)-2-(phenoxymethyl)pyrrolidine)acetyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

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

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

Sodium salt of (2*S*,5*R*)-*N*-(2-{2-[(2-chloro-3,4-dihydroxyphenyl)carbonyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

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

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

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

Sodium salt of (2*S*,5*R*)-*N*-(2-{2-[(4-{1-[(2-methylpropanoyl)oxy]ethoxy}carbonyl) phenyl)carbonyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1] octane-2-carboxamide1-(carbamoyloxy) ethyl 2-methylpropanoate;

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

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

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

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

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

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

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

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

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

Sodium salt of (2*S*,5*R*)-*N*-(2-{2-[(4-aminocylohehane-4-yl)carbonyl]hydrazinyl}-2-oxoethyl)-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 Schemes 1 and 2. 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), wherein A is $NHCOR_2$, 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-1H-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] in presence of a base, coupling agent and a solvent at a temperature of about 15ºC to about 35ºC for about 10 hours to about 24 hours to obtain a coupled compound of Formula (V). Typical, non-limiting examples of base include *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 15ºC to about 35ºC for about 10 hours to about 24 hours to obtain a compound of Formula (VI).

The compound of Formula (VI) is reacted with a hydrazide 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 about -10ºC to about 40ºC for about 1 hour to about 25 hour to obtain a compound of Formula (VIII). Typical, non-limiting examples of coupling reagent include 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 (VIII) is debenzylated by carrying out hydrogenolysis in presence of hydrogen source, transition metal catalyst and a suitable solvent at a temperature ranging from about 10°C to about 60°C for about 1 hour to about 14 hours 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. Typical, non-limiting examples of solvent include methanol, ethanol, dichloromethane, dimethylformamide, ethyl acetate, tetrahydrofuran, and the like or a mixture thereof. 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 5 hour 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 at a temperature ranging from about 0°C to about 80°C for about 1 hour to about 24 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. Typical, non-limiting examples of solvent include pyridine, dichloromethane, dimethylformamide and the like. In some embodiments, compound of Formula (IX) is reacted with dimethylformamide sulfur trioxide complex in presence of pyridine and dichloromethane at a temperature of about 10°C for about 1 hour 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 acetate (TBAA) to provide tetrabutylammonium salt of sulfonic acid compound 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 reacted 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, a compound of Formula (I), wherein A is $NHCOR_2$ can be prepared by the general procedure as described in Scheme 2. The compound of Formula (VI) is obtained by adopting a reaction sequence similar to as disclosed in Scheme 1. The compound of Formula (VI) is coupled with protected hydrazine (XI) to obtain a compound of Formula (XII). The compound of Formula (XII) is debenzylated to obtain a hydroxyl containing compound of Formula (XIII). The compound of Formula (XIII) is sulphonated, followed by conversion to tetrabutylammonium salt to obtain a compound of Formula (XIV). The compound of Formula (XIV) is deprotected to obtain a compound of Formula (XV). The compound of Formula (XV) is then coupled with a carboxylic acid compound of Formula (XVI) in presence of a coupling agent at temperature of about 0°C to about 40°C to obtain a compound of Formula (X). Finally, protecting groups in a compound of Formula (XVII) are removed to obtain a compound of Formula (I).

In some embodiments, compound of Formula (I), wherein A is $N=CHR_2$, are prepared by the general procedure described in Scheme 2. The hydrazine compound of Formula (XV) is reacted with an aldehyde compound of Formula (XVIa) to obtain a hydrazone compound of Formula (XVII). The so obtained hydrazone compound is further deprotected with a suitable deprotecting agent to obtain a compound of Formula (I), wherein A is $N=CHR_2$.

The compounds according to the invention are either isolated as zwitterions or as corresponding pharmaceutically acceptable salts. The compounds according to invention are isolated as corresponding pharmaceutically acceptable salts by passing solution of a compound of Formula (X) or a compound of Formula (XVII) in suitable solvent through a cation exchange resin. In some embodiments, a compound of Formula (X)or a compound of Formula (XVII) is dissolved in suitable solvent such as 10% tetrahydrofuran: water mixture and is passed through the column packed with Dowex 50WX8 200 Na resin or through Indion 225 Na resin to provide sodium salt of a compound of Formula (I). In some embodiments, a compound of Formula (X) or a compound of Formula (XVII) is dissolved in suitable solvent such as acetone, tetrahydrofuran, ethanol, isopropanol, acetonitrile or a mixture thereof, and thereby treating with sodium ethylhexanoate or potassium ethylhexanoate to provide sodium or potassium salt of compound of Formula (I).

In some embodiments, compound of Formula (I) having azepane ring moeity are also prepared. The starting reaction compounds containing azepane ring are synthesized by a general procedure as described in Scheme 3. Azepane-2-carboxylic acid (XVIII) is treated with a suitable nitrogen protecting group such as Boc anhydride to obtain a compound of Formula (XIX). The racemic compound of Formula (XIX) is further separated to obtain a compound of Formula (XXI) and a compound of Formula (XXIV).

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

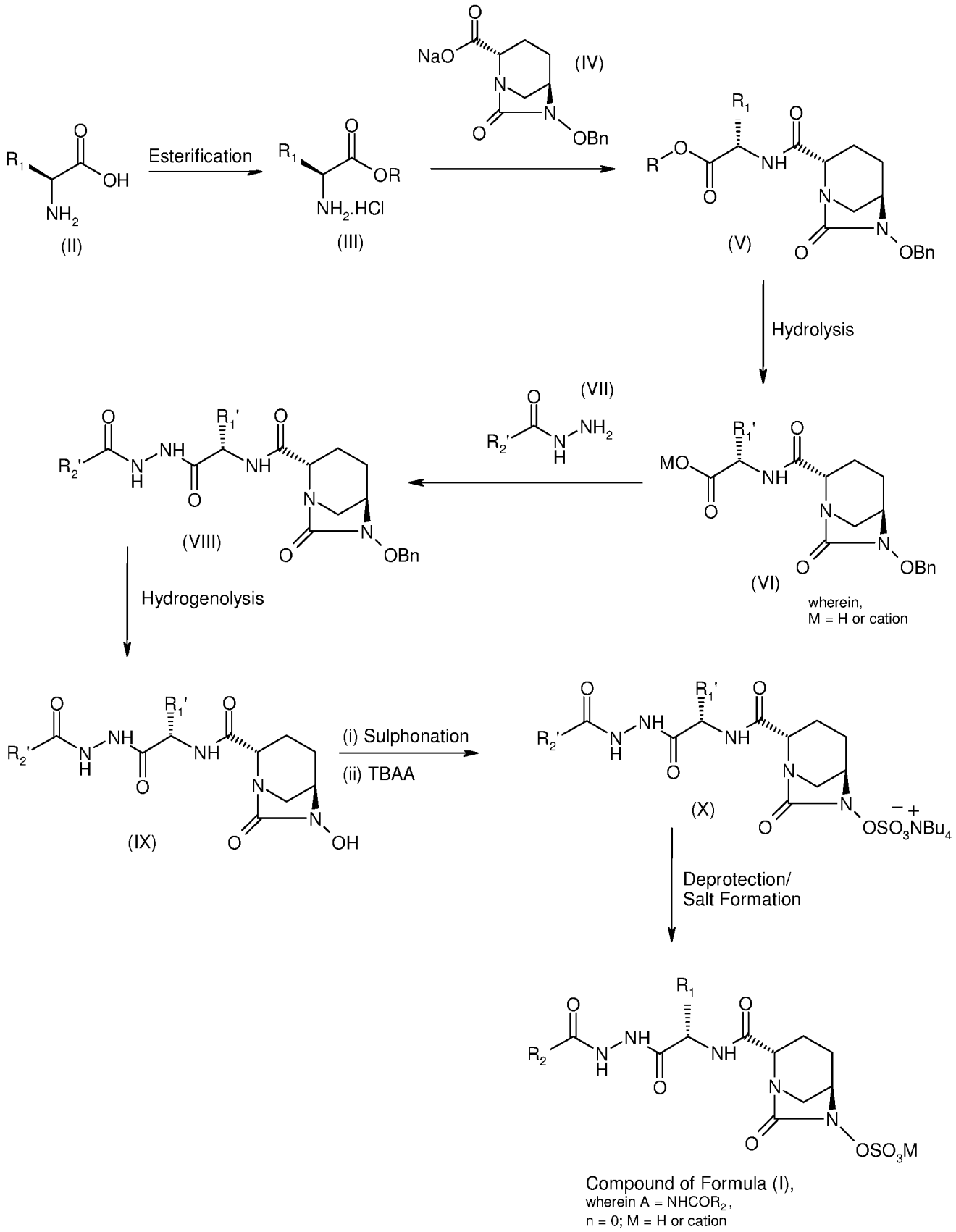
In some other embodiments, there are provided pharmaceutical compositions comprising: (a) a compound of Formula (I) or a stereoisomer or a pharmaceutically acceptable derivative thereof, and (b) at least one beta-lactamase inhibitor or a pharmaceutically acceptable derivative thereof.

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.

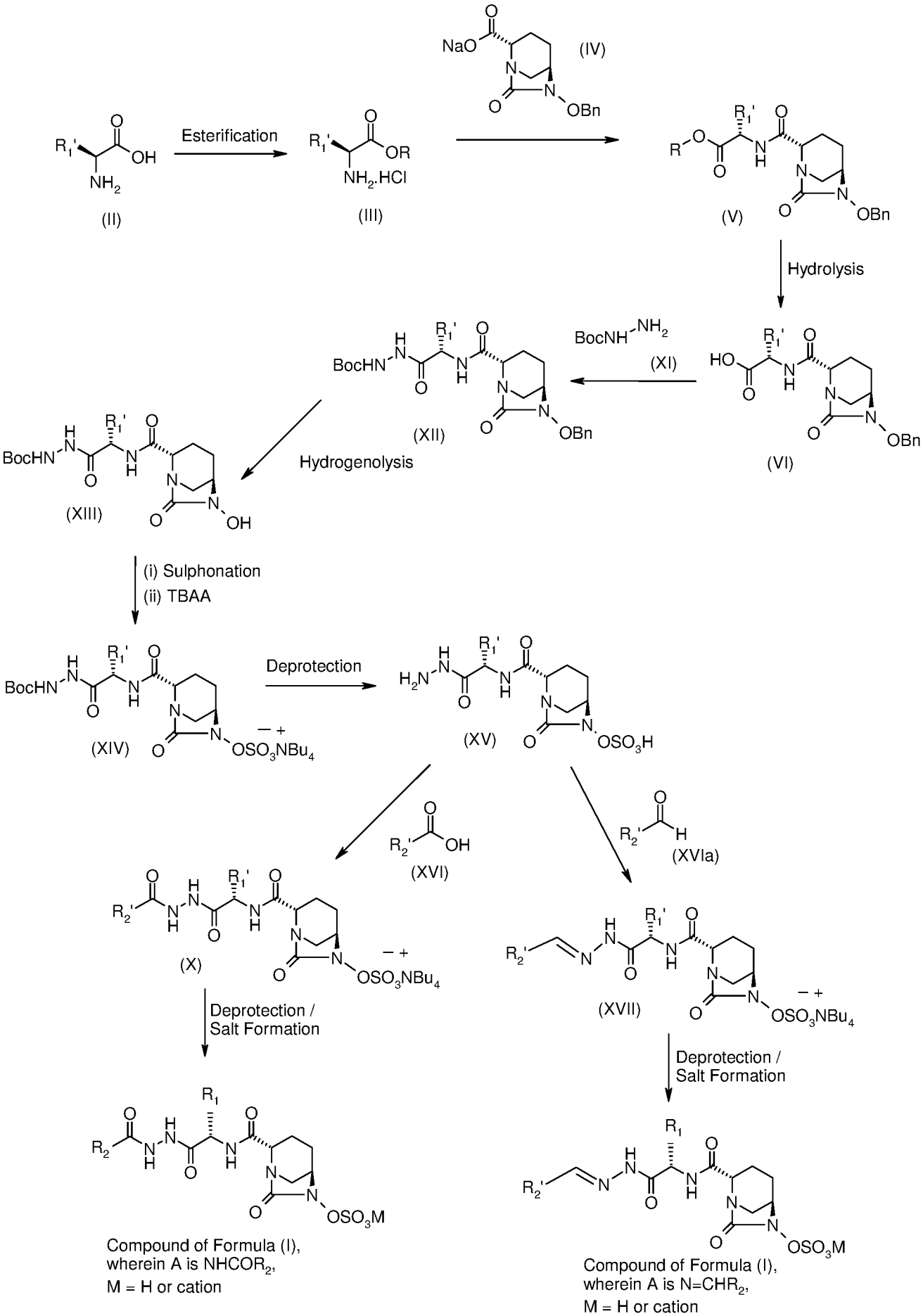
In some other embodiments, there are provided pharmaceutical compositions comprising: (a) a compound of Formula (I) or a stereoisomer or a pharmaceutically acceptable derivative thereof, and (b) at least one antibacterial agent or a pharmaceutically acceptable derivative thereof.

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.

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.


Esterification
(II)
(III)
(IV)
(V)
Hydrolysis
(VI)
wherein,
M = H or cation
(VII)
(VIII)
Hydrogenolysis
(IX)
(i) Sulphonation
(ii) TBAA
(X)
Deprotection/
Salt Formation
Compound of Formula (I),
wherein A = NHCOR2,
n = 0; M = H or cation

Scheme 1


Esterification
(II)
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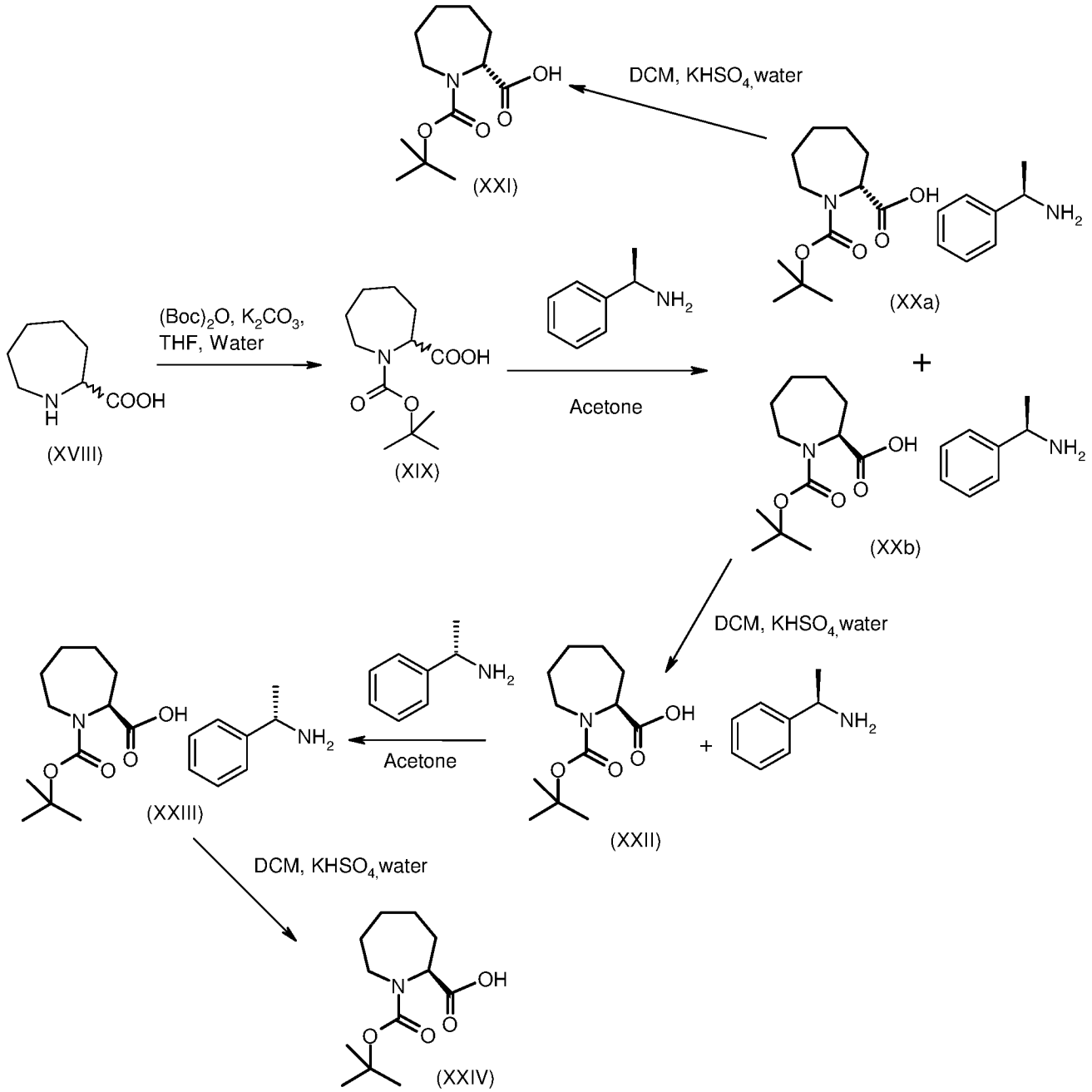
Hydrolysis
(VI)
(XI)
(XII)
Hydrogenolysis
(XIII)
(i) Sulphonation
(ii) TBAA
(XIV)
Deprotection
(XV)
(XVI)
(XVIa)
(X)
(XVII)
Deprotection / Salt Formation
Deprotection / Salt Formation
Compound of Formula (I), wherein A is NHCOR2, M = H or cation
Compound of Formula (I), wherein A is N=CHR2, M = H or cation

Scheme 2



Scheme 3

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.

Preparation of intermediates for compound of Formula (I) with azepane moiety

A. Preparation of (*R*)-1-(*tert*-butoxycarbonyl)-azepane-2-carboxylic acid (XXI)

Step 1: Preparation of 1-(*tert*-butoxycarbonyl)-azepane-2-carboxylic acid (XIX): To a stirred solution of a mixture of water (15 ml) and tetrahydrofuran (25 ml) were added azepane-2-carboxylic acid (Prepared as per procedure given in patent US20110212942) (2.5 g, 17.48 mmol) and potassium carbonate (6.03 g, 43.7 mmol) followed by drop-wise addition of Boc anhydride (7.6 g, 34.9 mmol) over a period of 30 minutes at 25-30°C. The reaction mixture was stirred further for 16 hours. The resulting mixture was diluted with ethyl acetate (25 ml) and the organic layer was separated. The aqueous layer was acidified to pH~2 using 5% aqueous potassium hydrogen sulpahte ($KHSO_4$) and the resulting mixture extracted with ethyl acetate (2 × 25 ml). The combined extracts were dried over anhydrous sodium sulfate. The solvents were evaporated under reduced pressure to obtain 3.5 g of 1-(*tert*-butoxycarbonyl)-azepane-2-carboxylic acid (XIX) as a white solid in 82% yield.

Step 2: Preparation of salt of 1-(*tert*-butoxycarbonyl)-azepane-2-carboxylic acid and (R)-α-methyl benzyl amine: A stirred solution of 1-(*tert*-butoxycarbonyl)-azepane-2-carboxylic acid (48.5 g, 199.5 mmol) in acetone (728 ml) was charged R-methylbenzyl amine (24.5 g, 199.5 mmol) and the stirring continued further for 3 hours. The separated solid was filtered on buckner funnel and the residue washed with 2 × 50 ml acetone. The solid was dried under reduced pressure till a constant weight to obtain the salt of (*R*)-1-(*tert*-butoxycarbonyl)-azepane-2-carboxylic acid and (*R*)-α-methyl

benzyl amine (XXa) (31 g, 42.6 % yield). The filtrate was concentrated under reduced pressure to obtain a 35g salt of (*S*)-1-(*tert*-butoxycarbonyl)-azepane-2-carboxylic acid and (*R*)-α-methyl benzyl amine (XXb) in 48% yield.

Step 3: Preparation of (*R*)-1-(*tert*-butoxycarbonyl)-azepane-2-carboxylic acid (XXI): A biphasic mixture of dichloromethane (310 ml) and water (310 ml) was charged the salt of (*R*)-1-(*tert*-butoxycarbonyl)-azepane-2-carboxylic acid and (*R*)-α-methyl benzyl amine (XXa; 31 g; 85 mmol). The resulting biphasic solution was then acidified by addition of an aqueous solution of potassium hydrogen sulphate to pH~2. The dichloromethane layer was separated and the aqueous layer re-extracted with fresh dichloromethane (310 ml). The combined extracts were dried over anhydrous sodium sulphate and the solvent evaporated under reduced pressure to obtain 18.5 g of (*R*)-1-(*tert*-butoxycarbonyl)-azepane-2-carboxylic acid (XXI) as a white solid in 82% yield.

(The same procedure of salt formation with *R*-(α)- methyl benzyl amine and further breaking of salt with potassium hydrogen sulfate was repeated to obtain the required chiral purity of (*R*)-1-(*tert*-butoxycarbonyl)-azepane-2-carboxylic acid (XXI) (15.2 g, 89 % yield).

Analysis:

Mass: 244.2 (M+1); for Molecular Formula of $C_{12}H_{24}NO_4$ and Molecular Weight of 243;

SOR$[\alpha]^{20}$ *c* = 1.0, MeOH: +61.39°.

(Literature value $[\alpha]^{20}$ *c* = 1.0, MeOH: -59.1° *J. Org. Chem.* 2001, *66,* 9056-9062 for S isomer)

B. Preparation of (*S*)-1-(*tert*-butoxycarbonyl)-azepane-2-carboxylic acid (XXIV)

Step 1: Preparation of (*S*)-1-(*tert*-butoxycarbonyl)-azepane-2-carboxylic acid (XXII): To a stirred biphasic mixture of dichloromethane (350 ml) and water (350 ml) was charged salt of (*S*)-1-(*tert*-butoxycarbonyl)-azepane-2-carboxylic acid and *R*-α-methyl benzyl amine (XXb) (35 g 85 mmol). The biphasic solution was then acidified by addition of potassium hydrogen sulfate to pH~2. The dichloromethane layer was separated and the aqueous layer re-extracted with dichloromethane (350 ml). The combined organic extracts were dried over anhydrous sodium sulfate and the solvent evaporated under reduced pressure to obtain 22 g of (*S*)-1-(*tert*-butoxycarbonyl)-azepane-2-carboxylic acid (XXII) in 94% yield.

Step 2: Preparation of salt of (*S*)-1-(*tert*-butoxycarbonyl)-azepane-2-carboxylic acid and (S)-α-methyl benzyl amine (XXIII): To a stirred solution of (*S*)-1-(*tert*-butoxycarbonyl)-azepane-2-carboxylic acid (22 g, 90.5 mmol) in acetone (220 ml) was charged *S*-α-methyl benzyl amine (10.95 g, 90.5 mmol) at room temperature. Stirring was further continued for 3 more hours and then the separated solid filtered on buckner funnel under suction and the solid washed with 2 × 40 ml of acetone. The solid precipitates of the salt were dried under reduced pressure till constant weight to obtain 24 g of the salt of (*S*)-1-(*tert*-butoxycarbonyl)-azepane-2-carboxylic acid and (*S*)-α-methyl benzyl amine (XXIII) in 72% yield.

Step 3: Preparation of (*S*)-1-(*tert*-butoxycarbonyl)-azepane-2-carboxylic acid (XXIV): To a stirred biphasic mixture of dichloromethane (240 ml) and water (240 ml) was charged salt of (*S*)-1-(*tert*-butoxycarbonyl)-azepane-2-carboxylic acid and (*S*)-α-methyl benzyl amine (24 g 65.9 mmol) at room temperature. The resulting biphasic solution was then acidified with potassium hydrogen sulfate to pH~2. The dichloromethane layer was separated and water layer re-extracted with dichloromethane (240 ml). The combined extracts were dried over anhydrous sodium sulfate and the solvent evaporated under reduced pressure to obtain 15.6 g of (*S*)-1-(*tert*-butoxycarbonyl)-azepane-2-carboxylic acid (XXIV) in 97% yield.

(The same procedure of salt formation with (*S*)-(α)- methyl benzyl amine and further breaking of salt with $KHSO_4$ is repeated twice to get required chiral purity of (*S*)-1-(*tert*-butoxycarbonyl)-azepane-2-carboxylic acid (12.5 g, 80% yield).

Analysis:

Mass: 244.2(M+1) for Molecular Formula of $C_{12}H_{24}NO_4$ and Molecular Weight of 243;

SOR $[\alpha]^{20}$ *c* = 1.0, MeOH : -63.49°.

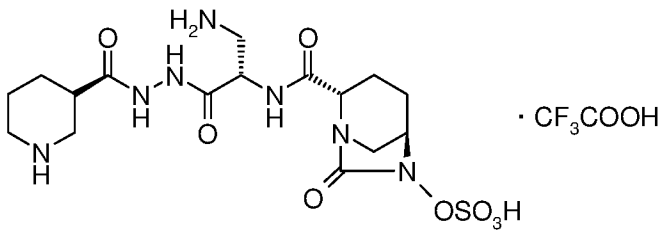
(Literature value $[\alpha]^{20}$ *c* = 1.0, MeOH : -59.1° *J. Org. Chem.* 2001, *66,* 9056-9062 for S isomer)

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

General procedure for removal of protecting groups from sodium salt: Trifluoroacetic acid (3.75 ml) was added slowly to the solution of methoxymethyl ether/ triethylsilyl protected sodium salt (2 mmol) in dichloromethane (7.5 ml) under stirring in argon atmosphere at 0°C. Stirring was continued further for 1 hour at 0°C, The progress of reaction was monitored by mass spectra. After complete consumption of starting material the solvent from reaction mixture was evaporated under reduced pressure (4 mm Hg) at 25°C and the residue triturated with diethyl ether (6 ml), stirred for 10 minutes and the separated solid filtered (in some cases the solvent is decanted and the residue processed further). The solid was then stirred with acetonitrile (6 ml), filtered (or decanted) and washed with fresh diethyl ether. The solid was dried under reduced pressure, to obtain the sodium salt.

Example 1

Synthesis of (2*S*,5*R*)-N-[(2*S*)-3-amino-1-[(3*R*)-3-(hydrazinylcarbonyl)piperidine]-1-oxopropan-2-yl]-6-sulfooxy-7-oxo-1,6-diazabicyclo[3.2.1]octane-2-carboxamide trifluoroacetic acid salt



Step 1: **Synthesis of (2*S*)-4-amino-2-[{9*H*-fluoren-9yl-methanol}amino]-4-oxobutanoic acid:** To a stirred solution of *L*-aspragine monohydrate (25 g, 166.6 mmol) in 1:1 mixture of water (250 ml) and tetrahydrofuran (250 ml) was added sodium bicarbonate (28 g, 333.3 mmol) in one portion followed by addition of *N*-(9-fluorenylmethoxycarbonyloxy)succinimide (61.78 g, 183.3 mmol). The resulting mixture was stirred at room temperature. The reaction was monitored by mass spectrometry. After the completion of reaction, the reaction mixture was acidified to pH of 1 by addition of 5% potassium hydrogen sulphate solution in water. The separated solid was filtered under suction and the obtained solid was further washed with 2 × 250 ml water and dried under reduced pressure to obtain 50 g of the titled product as white solid in 74% yield.

Analysis:

Mass: 355.3 (M+1); for Molecular Formula of $C_{19}H_{18}N_2O_5$ and Molecular Weight of 354.

Step 2: **Synthesis of (2*S*)-3-amino-2-[{9H-fluoren-9yl-methanol}amino]propanoic acid hydrochloride salt:** To suspension of (2*S*)-4-amino-2-[{9*H*-fluoren-9yl-methanol}amino]-4-oxobutanoic acid (30g, 84.74 mmoles) in a mixture of water (10 ml) and N,N'-dimethylformamide (25 ml) was added iodobenzene diacetate (32.74 g, 101.6 mmol) at 0°C under stirring. The resulting mixture was stirred at 0°C for 10 minutes and pyridine (20.4 ml, 254 mmoles) was added. The progress of reaction was monitored by mass spectrometry. After the completion of reaction, the reaction mixture was concentrated under reduced pressure (4 mm Hg) and residue was diluted with 2N

hydrochloric acid (25 ml). The aqueous reaction mixture was extracted with 2 × 25 ml diethyl ether. The aqueous layer was then concentrated under reduced pressure (4 mm Hg) to obtain 15.2 g of the titled product as a white solid 49% yield.

Analysis:

Mass: 327.3 (M+1); for Molecular Formula of $C_{18}H_{18}N_2O_4$.HCl and Molecular Weight of 362.5.

Step 3: Synthesis of (2*S*)-3[{*tert*-butoxycarbonyl}-amino]-2-[{9*H*-fluoren-9yl-methanol}amino] propanoic acid: To a (2*S*)-3-amino-2-[{9*H*-fluoren-9yl-methanol}amino]propanoic acid as hydrochloride salt (15 g, 41.3 mmoles) in a 1:1 mixture of water (150 mL) and tetrahydrofuran (150 ml) was added solid sodium bicarbonate (6.95g, 82.7 mmol) at 0°C under stirring. Boc anhydride (10.82 g, 49.6 mmol) was added drop-wise to it. The reaction mixture was allowed to warm to room temperature and stirred for 16 hours. The reaction mixture was extracted with 250 ml of diethyl ether. The aqueous layer was acidified to pH of 1 by addition of 5% potassium hydrogen sulphate solution followed by extraction with 2 × 250 ml ethyl acetate and 250 ml dichloromethane. The combined extracts were dried over anhydrous sodium sulphate and the solvent evaporated under reduced pressure to obtain the 13.08 g of titled product, as a white solid in 67% yield.

Analysis:

Mass: 427.3 (M+1); for Molecular Formula of $C_{23}H_{26}N_2O_6$ and for Molecular Weight of 426.

Step 4: Synthesis of ethyl (2*S*)-3[{*tert*-butoxycarbonyl}-amino]-2-[{9*H*-fluoren-9yl-methanol}amino]propanoate: To a solution of (2*S*)-3[{*tert*-butoxycarbonyl}-amino]-2-[{9*H*-fluoren-9yl-methanol} amino] propanoic acid (13 g, 30.5 mmol) in *N,N*'-dimethylformamide (130 ml) was added potassium carbonate (4.63 g, 33.5 mmol). The resulting mixture was cooled to 0°C and ethyl iodide (7.14 g, 45.7 mmol) was added drop-wise. The reaction mixture was allowed to warm to room temperature and stirred at ambient temperature for 16 hours. The resulting mixture was diluted with water (700 ml). The resulting mixture was extracted with 3 × 250 ml of ethyl acetate. The combined extracts were dried over anhydrous sodium sulphate and the solvent evaporated under reduced pressure to provide 10.5 g of the titled product as oil in 76% yield.

Analysis:

Mass: 455.5 (M+1); for Molecular Formula of $C_{25}H_{30}N_2O_6$ and Molecular Weight of 454.

Step 5: Synthesis of ethyl (2*S*)-2-amino-3-[{*tert*-butoxycarbonyl}-amino]propanoate: To a solution of ethyl (2*S*)-3[{*tert*-butoxycarbonyl}-amino]-2-[{9*H*-fluoren-9-yl-methanol}amino] propanoate (10 g, 22.0 mmol) in dichloromethane (200 ml) was added piperidine (3.74 g, 44.0 mmol). The reaction mixture was stirred at ambient temperature. The progress of reaction was monitored by mass spectrometry. After completion of reaction, the reaction mixture was concentrated under reduced pressure and residue was diluted with 200 ml of 5% potassium hydrogen sulphate. The resulting mixture was extracted with 2 × 150 ml of ethyl acetate. The aqueous layer was basified with solid sodium bicarbonate and extracted with 2 × 50 ml of dichloromethane. The combined dichloromethane extracts were dried over anhydrous sodium sulphate and the solvent was evaporated under reduced pressure to provide 4.1 g of the titled product as oil in 76% yield.

Analysis:

Mass: 233.2 (M+1) for Molecular Formula of $C_{10}H_{20}N_2O_4$ and Molecular Weight of 232.

Step 6: Synthesis of ethyl (2*S*)-3-[{*tert*-butoxycarbonyl}-amino]2-({[2S,5R)-6-benzyloxy-7-oxo-1,6diazabicyclo[3.2.1]oct-2yl]carbonyl}amino)propanoate: To a solution of (2*S*,5*R*)-6-benzyloxy-7-oxo-1,6-diazabicyclo[3.2.1]octane-2-carboxylic acid sodium salt (5.65 g, 18.9 mmol) in N,N'dimethylformamide (25 ml) was added ethyl (2*S*)-2-amino-3-[{*tert*-butoxycarbonyl}-amino]propanoate (4 g, 17.2 mmol). To this reaction mixture EDC.HCl (4.93 g, 25.8 mmol), hydroxy benzotriazile (2.32 g, 17.2 mmol) N-Methyl morpholine (5.8 ml, 51.7 mmol) were added successively at room temperature. The reaction mixture was allowed to stir for 16 hours. The resulting mixture was

diluted with 250 ml of water. The aqueous mixture was extracted with 2 × 100 ml of ethyl acetate. The combined extracts were dried over anhydrous sodium sulphate and the solvent evaporated under reduced pressure to obtain a crude product (~8 g). This was purified by column chromatography over silica gel (100-200 mesh size) by eluting with a v/v 1:1 mixture of hexane: acetone. The combined solvent fractions were evaporated to provide 5.5 g of the titled product as white solid in 65% yield.

Analysis:

Mass: 491.5 (M+1) for Molecular Formula of $C_{24}H_{34}N_4O_7$ and Molecular Weight of 490.

Step 7: Synthesis of (2*S*,5*R*)-*N*-[(2*S*)-3-[{*tert*-butoxycarbonyl}-amino]-1-[{*tert*-butyl-(3*R*)-3-(hydrazinylcarbonyl)piperidine-1-carboxylate)-1-oxopropan-2-yl]-6-benzyloxy-7-oxo-1,6-diazabicyclo [3.2.1]octane-2-carboxamide: To a stirred solution of ethyl (2*S*)-3-[{*tert*-butoxycarbonyl}-amino]2-({[2*S*,5*R*)-6-benzyloxy-7-oxo-1,6diazabicyclo[3.2.1]oct-2yl]carbonyl} amino)propanoate (1 g, 2.0 mmol) in tetrahydrofuran (10 ml) was added a solution of lithium hydroxide monohydrate (100 mg, 2.2 mmol) dissolved in water (1 ml) at 0°C. The reaction was monitored by thin layer chromatography (acetone: hexane 1:1). After the completion of reaction, the mixture was diluted with 10 ml of diethyl ether and stirred further for 10 minutes. Organic layer was separated. To the aqueous layer were added successively EDC.HCl (857 mg, 4.48 mmol), *tert*-butyl-(3*R*)-3-(hydrazinylcarbonyl)piperidine-1-carboxylate (500 mg, 2.0 mmol)(prepared as per Patent WO 2013/030733) followed by addition of hydroxyl benzotriazole (275 mg, 2.0 mmol). The resulting mixture was stirred at room temperature for 16 hours. The completion of reaction was monitored by mass spectrometry. The reaction mixture was extracted with 2 × 20 ml of ethyl acetate. The combined extracts were dried over anhydrous sodium sulphate and the solvent evaporated under reduced pressure to get crude product (~900 mg). This crude product was purified by column chromatography over silica gel (100-200 mesh) and was eluted with a v/v 1:1 mixture of hexane: acetone (5:5) and evaporation of the solvent from the combined fractions gave the 600 mg of the titled product as white solid in 42% yield.

Analysis:

Mass: 688.6 (M+1); for Molecular Formula of $C_{33}H_{49}N_7O_9$ and Molecular Weight of 687.

Step 8: Synthesis of (2*S*,5*R*)-*N*-[(2*S*)-3-[{*tert*-butoxycarbonyl}-amino]-1-[{*tert*butyl-(3*R*)-3-(hydrazinylcarbonyl) piperidine-1-carboxylate)-1-oxopropan-2-yl]-6-sulfooxy-7-oxo-1,6-diazabicyclo [3.2.1]octane-2-carboxamide tetrabutylammonium salt:

Part 1:

A solution of (2*S*,5*R*)-*N*-[(2*S*)-3-[{*tert*-butoxycarbonyl}-amino]-1-[{*tert*-butyl-(3*R*)-3-(hydrazinylcarbonyl)piperidine-1-carboxylate)-1-oxopropan-2-yl]-6-benzyloxy-7-oxo-1,6-diazabicyclo [3.2.1]octane-2-carboxamide (600 mg, 0.873 mmol) in a 1:1 mixture of dichloromethane (3 ml) and N,N'dimethylformamide (3 ml) containing 10% palladium over carbon (180 mg, 50% wet) was hydrogenated at 55 psi for 2 hours at 25°C. The resulting mixture was filtered through a celite pad. The residue was washed with additional dichloromethane (90 ml). The solvent from the combined filtrate was evaporated under reduced pressure to obtain the debenzylated product as oil, which was used as such for the next reaction without further purification.

Part 2:

To a stirred solution of (2*S*,5*R*)-*N*-[(2*S*)-3-[{*tert*-butoxycarbonyl}-amino]-1-[{*tert*-butyl-(3*R*)-3-(hydrazinylcarbonyl)piperidine-1-carboxylate)-1-oxopropan-2-yl]-6-hydroxy-7-oxo-1,6-diazabicyclo[3.2.1]octane-2-carboxamide (526 mg, 0.873 mmoles) in N,N'dimethylformamide (6 ml) was added sulphur trioxide dimethylformamide complex (160 mg, 1.04 mmol) in one portion, at 0°C under argon atmosphere. The reaction mass was stirred at the same temperature for 30 minutes and allowed to warm to room temperature. After 2 hours of stirring, to the resulting reaction mass was added a solution of tetrabutylammonium acetate (316 mg, 1.04 mmol) in water (1.2 ml). After 2 hours the solvent from the reaction mixture was evaporated under reduced pressure to obtain an oily residue.

The oily mass was co-evaporated with xylene (2×10 ml) to obtain thick mass. This mass was partitioned between a 1:1 mixture of dichloromethane (50 ml) and water (50 ml). The organic layer was separated and the aqueous layer re-extracted with dichloromethane (50 ml). The combined organic extracts were washed with water (3×25 ml) and dried over anhydrous sodium sulphate. The solvent was evaporated under reduced pressure to obtain crude product (~ 1.05 g). This was purified by column chromatography over silica-gel (100-200 mesh) by eluting with 3% methanol in chloroform. The evaporation of the combined solvent fractions under reduced pressure gave 610 mg of the titled product as white foam in 74% yield.

Analysis:

Mass: 678.3 (M+1); for Molecular Formula of $C_{27}H_{45}N_7O_8.C_{16}H_{36}N$ and Molecular Weight of 677.

Step 9: Synthesis of (2*S*,5*R*)-*N*-[(2*S*)-3-amino-1-[(3*R*)-3-(hydrazinylcarbonyl) piperidine]-1-oxopropan-2-yl]-6-sulfooxy-7-oxo-1,6diazabicyclo[3.2.1]octane-2-carboxamide trifluoroacetic acid salt: To a stirred solution of (2*S*,5*R*)-*N*-[(2*S*)-3-[{*tert*-butoxycarbonyl}-amino]-1-[{*tert*-butyl-(3*R*)-3-(hydrazinylcarbonyl)piperidine-1-carboxylate)-1-oxopropan-2-yl]-6-sulfooxy-7-oxo-1,6-diazabicyclo [3.2.1]octane-2-carboxamide tetrabutylammonium salt (610 mg, 0.652 mmol) in dichloromethane (1 ml) was added trifluoroacetic acid (6 ml) drop wise at -10°C over a period of 30 minutes under argon atmosphere. The resulting mass was further stirred at same temperature for 1 hour. The progress of reaction was monitored by mass spectrometry. After complete consumption of starting material the resulting mixture was concentrated under reduced pressure to obtain oily residue. To this was added 10 ml of acetonitrile and the mixture stirred well and solvent evaporated under reduced pressure to remove traces of trifluoroactetic acid. The resulting oily residue was diluted with 25 ml of diethyl ether and stirred for 30 minutes. The ether layer was removed by decantation from the precipitated solid. This procedure was repeated twice again with diethyl ether (2 × 25 ml). The solid thus obtained was filtered and washed with fresh diethyl ether (2 × 25 ml). The solid was dried at 25 °C under reduced pressure to obtain 140 mg of (2*S*,5*R*)-*N*-[(2*S*)-3-amino]-1-[(3*R*)-3-(hydrazinylcarbonyl)piperidine]-1-oxopropan-2-yl]-6-sulfooxy-7-oxo-1,6diazabicyclo [3.2.1]octane-2-carboxamide trifluoroacetic acid salt as a white solid, in 38% yield with HPLC purity of 96.77%.

Analysis:

Mass: 478.4(M+1), 476.2(M-1) as free acid; for Molecular Formula of $C_{16}H_{27}N_7O_8S.C_2HF_3O_2$ and Molecular Weight of 591;

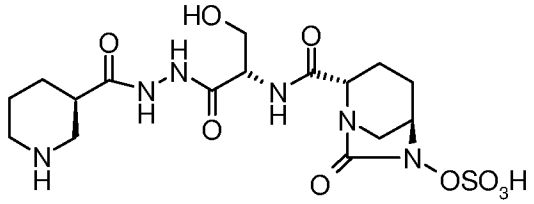
Melting point: 187-189°C (decomposes)

^{1}H NMR (DMSO, D_2O exchange): δ 4.65 (m, 1H), 4.02 (bs, 1H), 3.94 (d, 1H), 3.27-2.91 (m, 8H), 2.70(m, 1H) 2.15(m, 1H) 1.91-1.60 (m, 7H)

Purity as determined by HPLC: 96.77%.

Example 2

(2*S*,5*R*)-N-[(2*S*)-3-hydroxy-1-[(3*R*)-3-(hydrazinylcarbonyl)piperidine]-1-oxopropan-2-yl]-7-oxo-6-sulfooxy-1,6-diazabicyclo[3.2.1]octane-2-carboxamide



Step 1: Synthesis of 2-amino-3-hydroxy-propionic acid methyl ester hydrochloride: 2-Amino-3-hydroxy-propionic acid methyl ester hydrochloride was prepared by procedure described by Nasir, Baig R. B. et al from Synlett, (8), 1227-1232; 2009.

Step 2: **Synthesis of methyl (*R*)-2-(benzyloxycarbonyl) amino-3-hydroxypropanoate:** Methyl (*R*)-2-(benzyloxycarbonyl) amino-3-hydroxypropanoate was prepared by procedure described by Iwashita, Masazumi et al from Journal of Medicinal Chemistry, 52(19), 5837-5863; 2009.

Step 3: **Synthesis of methyl 2-(((benzyloxy)carbonyl)amino)-3- (methoxymethoxy) propanoate:** Methyl 2-(((benzyloxy)carbonyl)amino)-3-(methoxymethoxy)propanoate was prepared according to PCT International Patent Application No. 2013064231.

Step 4: **Synthesis of (2*S*)-2-{[(benzyloxy) carbonyl] amino}-3- (methoxymethoxy) propanoic acid lithium salt:** A solution of lithium hydroxide (1.26 g, 0.030 mol) in (15 ml) of water was added slowly to a stirred solution of methyl 2-(((benzyloxy)carbonyl)amino)-3-(methoxymethoxy) propanoate (5.96 g, 0.020 mol) in tetrahydrofuran (60 ml) at 0°C. The stirring was continued further for 2 hour at same temperature. The solvent was evaporated under reduced pressure to obtain the titled product which was taken for next step without workup.

Step 5: **Synthesis of 3-[*N*'-(2-benzyloxycarbonylamino-3-methoxymethoxy-propionyl)-hydrazinocarbonyl]-piperidine-1-carboxylic acid *tert*-butyl ester:** To a stirred solution of (2*S*)-2-{[(benzyloxy)carbonyl]amino}-3-(methoxymethoxy)propanoic acid lithium salt (5.78 g, 0.020 mol) in N, N-dimethylformamide (25 ml) were successively added HOBt (2.7 g, 0.020 mol), EDC hydrochloride (7.69 g, 0.040 mol) and N-methylmorpholine (4.08 g, 0.040 mol) at 25°C. The reaction mixture was stirred for 15 minutes and a solution of (*R*)-*N*-*tert*-butoxycarbonyl-piperidin-3-carboxylic acid hydrazide (4.87 g, 0.040 mol) in *N, N*-dimethylformamide (10 ml) was added in small portions. The reaction mixture was stirred at 25°C for 18 hours and the resulting mixture was poured into water (175 ml), stirred well and the mixture extracted with ethyl acetate (2 × 200 ml). The ethyl acetate layer was washed with water (100 ml) and brine (100 ml). The solvent was evaporated under reduced pressure and the residue was purified by column chromatography over silica gel. The elution was carried using v/v mixture of 10% acetone in hexane. The collected fractions were concentrated to provide 5 g of the titled product as white solid in 49% yield.

Analysis:

Mass: 509.5 (M+1) for Molecular Formula of $C_{24}H_{36}N4O_8$ and Molecular Weight of 508.58.

Step 6: **Synthesis of 3-[*N*'-(2-amino-3-methoxymethoxy-propionyl)-hydrazinocarbonyl]-piperidine-1-carboxylic acid *tert*-butyl ester:** To a solution of 3-[*N*'-(2-benzyloxycarbonylamino-3-methoxymethoxy-propionyl)-hydrazinocarbonyl]-piperidine-1-carboxylic acid *tert*-butyl ester (5 g, 0.0098 mol) in methanol (50 ml) was added 10% palladium on carbon (500 mg) and the suspension was stirred under atmospheric hydrogen pressure at a temperature of about 25°C for 2 hours. The catalyst was filtered over a celite bed and catalyst containing bed was washed with additional methanol (50 ml). The filtrate was concentrated under reduced pressure to provide a white foam, which was triturated with diethyl ether (10ml) to provide 3.5 g of the titled product as semi solid in 95% yield.

Step 7: **Synthesis of 3-(*N*'-{2-[(6-benzyloxy-7-oxo-1,6-diaza-bicyclo[3.2.1]octane-2-carbonyl)-amino]-3-methoxymethoxy-propionyl}-hydrazinocarbonyl)-piperidine-1-carboxylic acid tert-butyl ester:** To a stirred solution of trans-6-benzyloxy-7-oxo-l,6-diaza-bicyclo[3.2.1]octane-2-carboxylic acid sodium salt (prepared as per the procedure disclosed in WO2014135929) (2.79 g, 0.00936 mol) in *N, N*-dimethylformamide (5 ml), were added successively HOBt (1.26 g, 0.00936 mol), EDC hydrochloride (3.59 g, 0.0187 mol) and N-methylmorpholine (1.91 g, 0.0187 mol) at 25°C. The reaction mixture was stirred for 15 minutes and a solution of 3-[*N*'-(2-amino-3-methoxymethoxy-propionyl)-hydrazinocarbonyl]-piperidine-1-carboxylic acid *tert*-butyl ester (3.5 g, 0.00936 mol) dissolved in *N, N*-dimethylformamide (2 ml) was added in small portions. The reaction mixture was stirred at 25°C for 18 hours and the resulting mixture was poured into water (100 ml), stirred well and the mixture extracted with ethyl acetate (2 × 100 ml). The ethyl acetate layer was

washed with water (100 ml) and brine (50 ml). The solvent was evaporated under reduced pressure; the obtained residue was purified by column chromatography over silica gel and eluted with v/v mixture of 10% acetone in hexane. The collected fractions were concentrated to provide 2.5 g of 3-(*N*'-{2-[(6-benzyloxy-7-oxo-1,6-diaza-bicyclo[3.2.1]octane-2-carbonyl)-amino]-3-methoxymethoxy-propionyl}-hydrazinocarbonyl)-piperidine-1-carboxylic acid *tert*-butyl ester as white solid in 42% yield.

Analysis:

Mass: 633.4 (M+1); for Molecular Formula of $C_{30}H_{44}N_6O_9$ and Molecular Weight of 632.72

Step 8: Synthesis of 3-(*N*'-{2-[(6-hydroxy-7-oxo-1,6-diaza-bicyclo[3.2.1]octane-2-carbonyl)-amino]-3-methoxymethoxy-propionyl}-hydrazinocarbonyl)-piperidine-1-carboxylic acid *tert*-butyl ester: To a solution of 3-(*N*'-{2-[(6-benzyloxy-7-oxo-1,6-diaza-bicyclo[3.2.1]octane-2-carbonyl)-amino]-3-methoxymethoxy-propionyl}-hydrazinocarbonyl)-piperidine-1-carboxylic acid *tert*-butyl ester (2.5 g, 0.0039 mol) in methanol (25 ml) was added 10% palladium on carbon (250 mg). The suspension was stirred under atmospheric hydrogen pressure at a temperature of about 25°C for 2 hours. The catalyst was filtered over a celite bed and catalyst containing bed was washed with additional methanol (25 ml). The filtrate was concentrated under reduced pressure to provide white foam, which was triturated with diethyl ether (5 ml) to obtain 2 g of the titled product in 93% yield.

Analysis:

Mass: 543.5(M+1); for Molecular Formula of $C_{23}H_{38}N_6O_9$ and Molecular Weight of 542.59.

Step 9 & Step 10: Synthesis of tetrabutylammonium salt of 3-(*N*'-{3-methoxymethoxy-2-[(7-oxo-6-sulfooxy-1,6-diaza-bicyclo[3.2.1]octane-2-carbonyl)-amino]-propionyl}-hydrazinocarbonyl)-piperidine-1-carboxylic acid tert-butyl ester: 3-(*N*'-{2-[(6-Hydroxy-7-oxo-1,6-diaza-bicyclo[3.2.1]octane-2-carbonyl)-amino]-3-methoxy methoxy-propionyl}-hydrazinocarbonyl)-piperidine-1-carboxylic acid *tert*-butyl ester (2.0 g, 0.00368 mol) was dissolved in pyridine (10 ml) and to the stirred clear solution was added pyridine sulfur trioxide complex (2.93 g, 0.0184 mol). The mixture was stirred for 1 hour at room temperature. The obtained suspension was filtered and the solids were washed with dichloromethane (20 ml). The filtrate was evaporated under reduced pressure and the residue was stirred in 0.5N aqueous potassium dihydrogen phosphate solution (100 ml) for 30 minutes. The solution was washed with ethyl acetate (50 ml × 3) and layers were separated. To the aqueous layer was added tetrabutylammonium sulphate (1.24 g, 0.00368 mol) and stirred for 3 hours at 25°C. The resulting mixture was extracted with dichloromethane (100 ml × 2). The combined organic extract was washed with brine (50 ml) and dried over anhydrous sodium sulfate and the solvent evaporated under reduced pressure to obtain a semi-solid, that was triturated with diethyl ether and the separated solid was filtered to obtain a white solid. This solid was purified by column chromatography using silica gel (60-120 mesh size) and eluted with a v/v mixture of dichloromethane: methanol (95:5). The combined fractions were evaporated to provide 950 mg of the titled product as viscous oil in 30% yield.

Analysis:

Mass: 621.5 (M-1) as a free sulphonic acid; for Molecular Formula of $C_{39}H_{73}N_7O_{12}S$ and Molecular Weight of 864.12.

Step 11: Synthesis of sulfuric acid mono-(2-{1-hydroxymethyl-2-oxo-2-[N'-(piperidine-3-carbonyl)-hydrazino]-ethylcarbamoyl}-7-oxo-1,6-diaza-bicyclo[3.2.1]oct-6-yl) ester: To a cooled (-10°C), stirred solution of tetrabutylammonium salt of 3-(*N*'-{3-methoxymethoxy-2-[(7-oxo-6-sulfooxy-1,6-diaza-bicyclo[3.2.1]octane-2-carbonyl)-amino]-propionyl}-hydrazinocarbonyl)-piperidine-1-carboxylic acid tert-butyl ester (950 mg, 0.00109 mol) in dichloromethane (5 ml) was added trifluoroacetic acid (5 ml) drop-wise. After stirring for 30 minutes at -10°C the solvent was evaporated under reduced pressure. The residue obtained was triturated with diethyl ether to obtain a white solid. The solid was washed with diethyl ether (3 ×10 ml), acetonitrile (2 × 5 ml) and dichloromethane (2 × 5 ml). The residual solid was then dried under reduced pressure to provide 150 mg of the titled product in 28% yield.

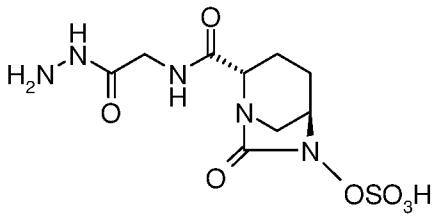
Analysis:

Mass: 479.4 (M+1) for Molecular Formula of $C_{16}H_{26}N_6O_9S$ and Molecular Weight of 478.47;

^{1}H-NMR (DMSO-D_6): δ 10.04-10.20 (m, 2H), 9.99 (s, 1H), 8.84 (s, 1H), 8.43 (brs, 2H), 7.77 (d, 1H, J = 8.4 Hz), 4.38-4.50 (m, 1H), 3.99 (s, 1H), 3.87 (d, 1H), 3.62-3.72 (m, 2H), 3.10-3.30 (m, 3H), 2.86-3.06 (m, 3H), 2.67 (brs, 1H), 2.08-2.16 (m, 1H), 1.52-1.98 (m, 6H).

Example 3

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



Step 1: Synthesis of ethyl aminoacetate hydrochloride: To the solution of glycine (40 g, 0.53 mol) in ethanol (400 ml), thionyl chloride (158.49 g, 1.33 mol) was added at 0°C under stirring. The solution was then allowed to warm to room temperature and stirred further for 16 hours. The completion of the reaction was monitored with thin layer chromatography. The resulting reaction mixture was concentrated under reduced pressure and the residual oil was diluted with diethyl ether (200 ml) and the mixture stirred for 15 minutes and the separated solid was filtered and the residue was washed with additional diethyl ether (40 ml). The solid obtained was dried under reduced pressure to obtain 62 g of the titled product as a white solid in 84% yield.

Step 2: Synthesis of ethyl ({[(2*S*,5*R*)-6-(benzyloxy)-7-oxo-1,6-diazabicyclo[3.2.1]oct-2-yl]carbonyl}amino)acetate: EDC.HCl (96.05 g, 0.50 mol), *N,N*-diisopropylethylamine (129.90 g, 1.0 mol) and HOBT (45.26 g, 0.33 mol) were added successively to a stirred solution of (2*S*,5*R*)-6-benzyloxy-7-oxo-1,6-diazabicyclo[3.2.1]octane-2-carboxylic acid sodium salt (100 g, 0.33 mol) in dimethyl formamide (1 L) at 25°C. Ethyl aminoacetate hydrochloride (37.0 g, 0.34 mol) was then added and stirring was continued further for 16 hours. The completion of the reaction was confirmed by thin layer chromatography. The resulting mixture was slowly poured into 6 L of water and the mixture was stirred for 1 hour. The mixture was extracted with ethyl acetate (2 × 500 ml). The extract was dried over sodium sulfate. The solvent was evaporated under reduced pressure to obtain 82 g of the titled product as a white solid in 69% yield.

Step 3: Synthesis of lithium ({[(2*S*,5*R*)-6-(benzyloxy)-7-oxo-1,6-diazabicyclo[3.2.1]oct-2-yl]carbonyl}amino)acetate: A solution of lithium hydroxide (4.0 g, 96 mmol) in 70 ml of water was added slowly to stirred solution of above obtained ester compound of step 2 (35 g, 96 mmol) in tetrahydrofuran (350 ml) at 0°C. After stirring for 1 hour at 0°C, the thin layer chromatography indicated the completion of the reaction. Ethyl acetate (350 ml) and water (280 ml) were added to the reaction mixture and stirred for 5 minutes and separated. The aqueous layer was taken for next step as such (Considered the yield as 100%, 32.85 g).

Step 4: Synthesis of *tert*-butyl 2-[({[(2*S*,5*R*)-6-(benzyloxy)-7-oxo-1,6-diazabicyclo[3.2.1]oct-2-yl]carbonyl}amino)acetyl]hydrazinecarboxylate: EDC.HCl (40.68 g, 213 mmol), and HOBT (13.07 g, 96 mmol) were added to the stirred solution of above obtained lithium salt compound (water layer from step 3) (32.85 g, 96 mmol) at room temperature. To thisreaction mixture was added *tert*-butyl hydrazine carboxylate (12.79 g, 96 mmol) and stirred for 16 hours. The completion of the reaction was monitored with thin layer chromatography. The resulting mixture was extracted with ethyl acetate (2 x

200 ml), dried over sodium sulfate, and the solvent evaporated under reduced pressure to obtain thick oil. This was purified by column chromatography over silica gel (60-120 mesh size) and elution was carried with mixture of ethyl acetate and hexane (20: 80) as an eluent. Evaporation of the solvents from the combined fractions gave 24 g of the titled product as white solid in 55% yield.

Step 5: Synthesis of *tert*-butyl 2-[({[(2*S*,5*R*)-6-hydroxy-7-oxo-1,6-diazabicyclo[3.2.1]oct-2-yl]carbonyl}amino)acetyl]hydrazinecarboxylate: To a solution of above obtained compound (24 g, 53 mmol) in methanol (240 ml) was added 10% palladium over carbon (50% wet) (2.4 g) and was hydrogenated under hydrogen balloon pressure under stirring for 3 hours at 25°C. The completion of the reaction was monitored by thin layer chromatography. After completion, the resulting mixture was filtered through celite bed and the residue washed with 50 ml of methanol. The filtrate was evaporated under reduced pressure to obtain 18.16 g of the titled product as white solid in 95% yield.

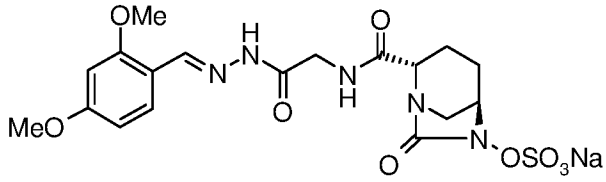
Step 6: Synthesis of tetrabutylammonium salt of [*tert*-butyl 2-[({[(2*S*,5*R*)-6-sulfooxy-7-oxo-1,6-diazabicyclo[3.2.1]oct-2-yl]carbonyl}amino)acetyl]hydrazinecarboxylate]: Pyridine sulphur trioxide complex (42.66 g, 268 mmol) was added to a stirred solution of hydroxy compound obtained in step-5 (18.16 g, 53 mmol) in pyridine (190 ml) under argon atmosphere at 25°C. Stirring was continued further for 16 hours at 25°C until thin layer chromatography indicated the completion of reaction. The resulting mixture was filtered under suction and the residue was washed with 20 ml dichloromethane. The combined filtrate was evaporated under reduced pressure to obtain thick oil. The oil was dissolved in 0.5M potassium dihydrogen phosphate solution (1.8 L) and stirred 0.5 hour at 25°C. The resulting mixture was washed with ethyl acetate (200 ml). To the aqueous layer tetrabutylammonium hydrogen sulphate (18.2 g, 53 mmol) was added and the mixture was stirred further for 3 hours at 25°C. The resulting mixture was extracted with 2 × 200 ml of dichloromethane. The organic layer was dried over sodium sulfate and the solvent evaporated under reduced pressure to obtain oil. This was purified by column chromatography over silica gel (60-120 mesh size) using mixture of dichloromethane: methanol (95: 5) as an eluent. Evaporation of the combined fractions gave 18 g of the product as white solid in 78% yield.

Step 7: Synthesis of (2*S*,5*R*)-*N*-(2-hydrazinyl-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo [3.2.1]octane-2-carboxamide: Trifluoroacetic acid (45 ml) was added slowly to a stirred solution of above obtained tetrabutylammonium acetate salt (18 g, 26 mmol) in dichloromethane (90 ml) under argon atmosphere, at 0°C. After 1 hour, the progress of reaction was monitored by mass spectra. The resulting reaction mass was evaporated under reduced pressure and the residue was triturated with diethyl ether (180 ml) by stirring for 10 minutes. The separated solid was filtered and the solid was then stirred with acetonitrile (180 ml), filtered and washed with acetonitrile (10 ml). The solid was dried under reduced pressure to obtain 7.8 g of the product as white solid in 84% yield.

Analysis:
Melting Point: 178-182°C;
Mass: 338.2 (M+1); for Molecular Formula of $C_9H_{15}N_5O_7S$ and Molecular Weight of 337.31;
^{1}H NMR (400 MHz, DMSOD6): δ 8.6-8.8 (2H, m), 4.30 (1H, s), 3.73-3.83 (2H, m), 3.37-3.39 (1H, m), 3.16 (2H, t, J=8.0), 2.77 (1H, s), 2.13-2.07 (2H, m), 1.82 (2H, s), 1.56-1.58 (1H, m), 1.28-1.36 (1H, m);
Purity as determined by HPLC: 91.63%.

Example 4

Synthesis of sodium salt of (2*S*,5*R*)-*N*-{2-[(2*E*/*Z*)-2-(2,4-dimethoxybenzylidenehydrazino]-2-oxoethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide:



Step 1: Synthesis of tetrabutylammonium salt of (2*S*,5*R*)-*N*-{2-[(2*E*/*Z*)-2-(2,4-dimethoxybenzylidenehydrazino]-2-oxoethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide: To a stirred solution of 2,4 dimethoxy benzaldehyde (0.542 g, 3.3 mmol) in tetrahydrofuran (10 ml.), was added *N, N*-diisopropyl ethyl amine (1.0 g, 7.0 mmol) followed by the addition of (2*S*,5*R*)-*N*-(2-hydrazino-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide (1 g, 3.0mmol) at 25°C. The reaction mixture was stirred for 16 hours and to the resulting mixture was added a solution of tetrabutylammonium acetate (0.3 g, 3.0 mmol) in tetrahydrofuran (10 ml.) and stirring continued further for 24 hours. The solvent was evaporated under reduced pressure and the residue was taken up in dichloromethane (20 ml) and washed with 10% aqueous potassium hydrogen sulfate solution (3 ml × 2) and finally organic layer was washed with water (5 ml). The organic layer was separated and dried over anhydrous sodium sulfate and evaporated under reduced pressure to yield a semi solid residue. This was purified by column chromatography over silica-gel (60-120 mesh) by eluting with mixture of methanol in dichloromethane (5: 95). The combined fractions were evaporated under reduced pressure to obtain 1.1 g of tetrabutylammonium salt of (2*S*,5*R*)-*N*-{2-[(2*E,Z*)-2-(2,4-dimethoxybenzylidenehydrazino]-2-oxoethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide as a white solid in 51% yield.

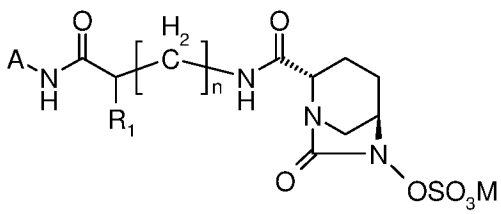
Step-2: Synthesis of sodium salt of (2*S*,5*R*)-*N*-{2-[(2*E*/*Z*)-2-(2,4-dimethoxybenzylidenehydrazino]-2-oxoethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide: A solution of tetrabutyl ammonium salt of (2*S*,5*R*)-*N*-{2-[(2*E*/*Z*)-2-(2,4-dimethoxybenzylidenehydrazino]-2-oxoethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide (1 g) in tetrahydrofuran (2 ml) diluted to 20 ml using water and passed through INDION 225 Na ION exchange resin with 10% tetrahydrofuran in water as eluent. The fractions containing compound were evaporated under reduced pressure to obtain the 0.485 g of the titled product as white solid in 67% yield.

Analysis:

Mass: 486.2 (M+1) as free acid, for Molecular Formula of $C_{18}H_{22}N_5O_9SNa$ and Molecular Weight of 507.46;

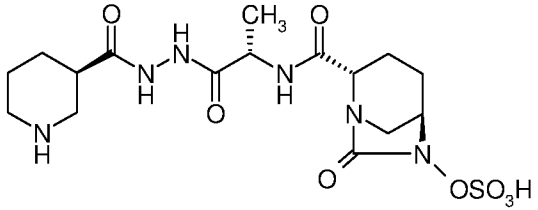
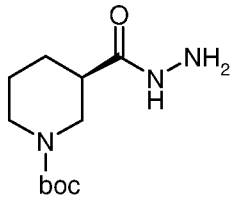
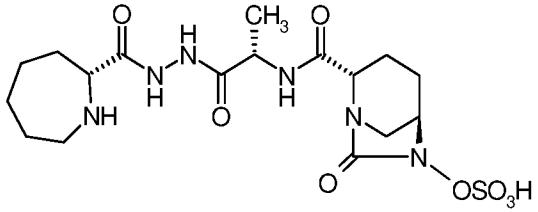
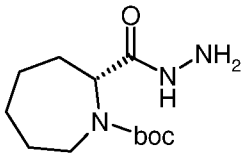
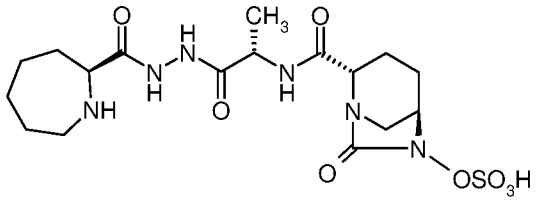
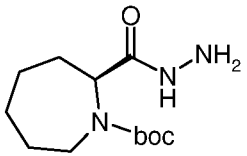
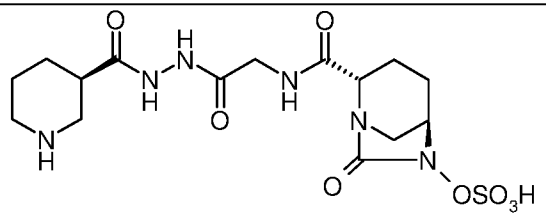
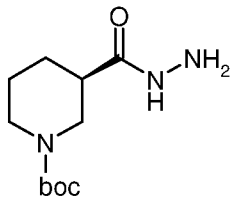
^{1}H NMR (DMSO-d_6): δ 11.43 (1H, s), 8.20 (1H, s), 8.03 (1H, t, J=5.2 Hz), 7.73 (1H, d, J=8.8 Hz), 6.62 (2H, s), 4.30 (1H, dd, J=6 Hz), 4.14 (1H, dd, J=5.6Hz), 4.00 (1H, s), 3.84 (4H, s), 3.78 (3H, s), 3.10 (2H, dd, J= 11.6, 10.8Hz), 2.15-2.12 (1H, m), 1.85-1.58 (3H, m).

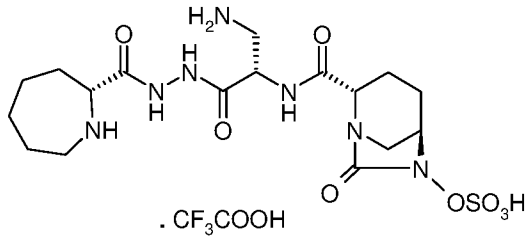
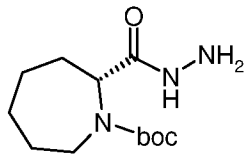
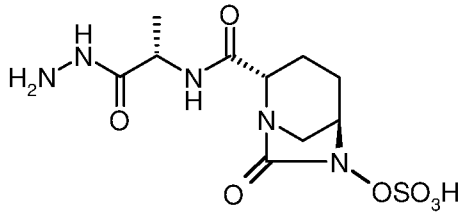
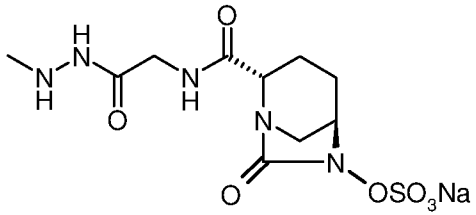
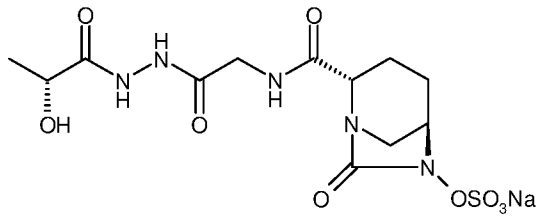
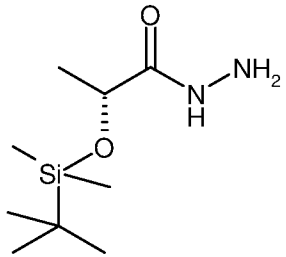
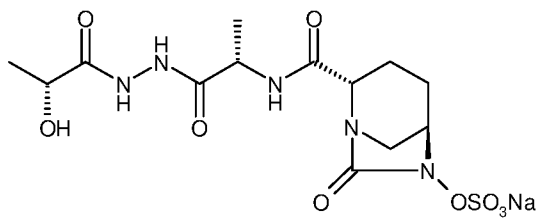
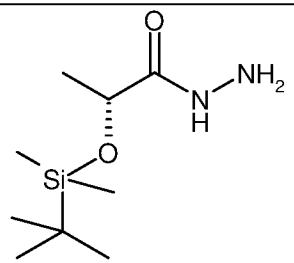
Compounds 5 to 25, 33, 37, 43 and 45 to 48 (Table 1) were prepared by using the procedure described in Example 1 and using corresponding hydrazine compound of Formula (VII) in place of *tert*-butyl (2*S*)-2-[(aminooxy)methyl]pyrolidine-1-carboxylate. Compounds 26 to 32, 34 to 36, 38 to 42, 44 and 49 to 57 (Table 1) were prepared by following the procedure described in Example 4. For the compounds wherein M = Na, the corresponding tetrabutylammonium salt was passed through sodium resin (as per step 2 of Example 4), followed by deprotection step to provide the final compounds representative of compound of Formula (I).

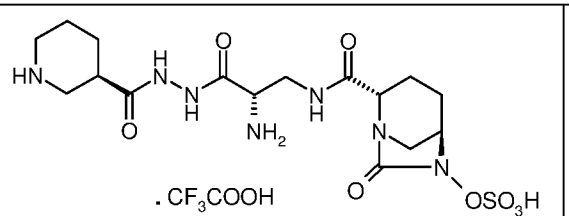
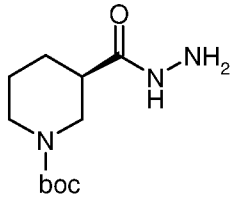
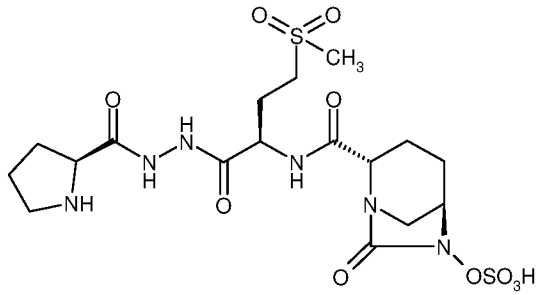
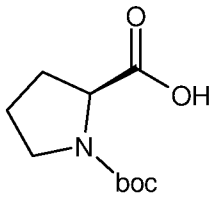
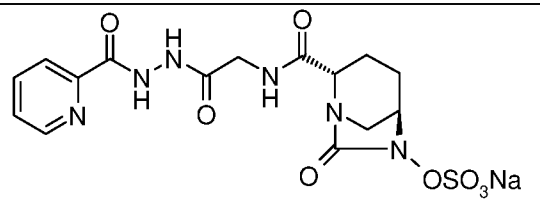
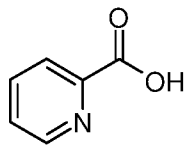
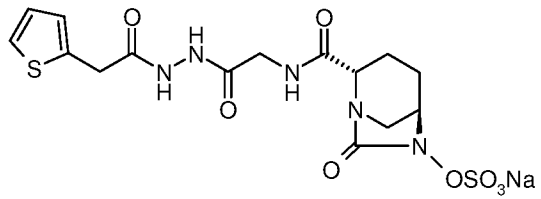
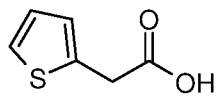
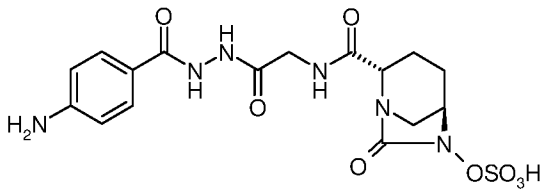
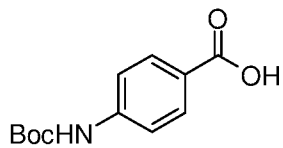


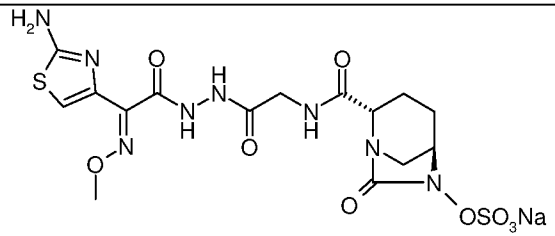
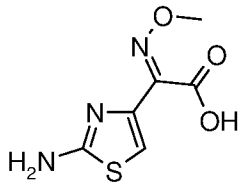
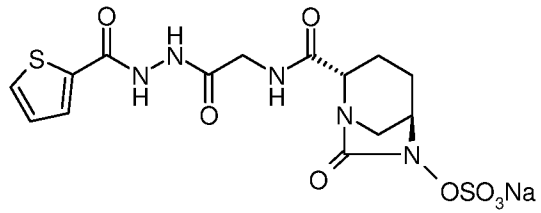
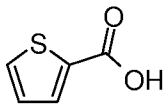
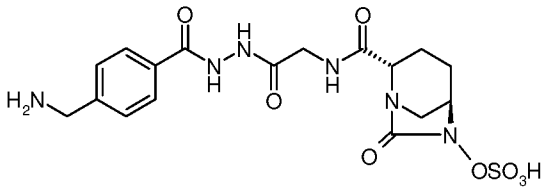
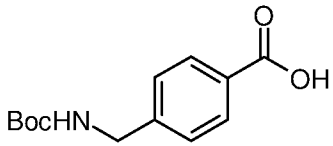
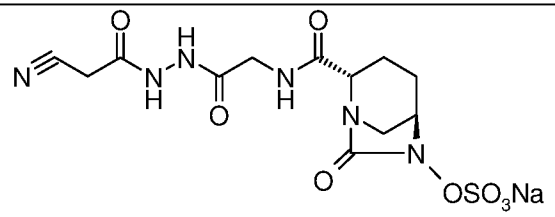
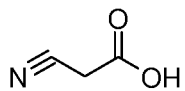
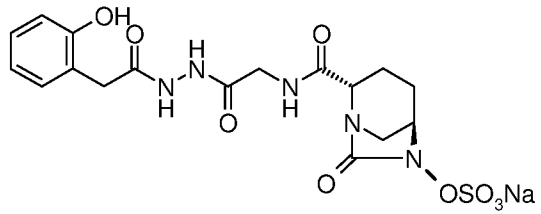
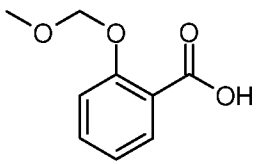
Formula (I)

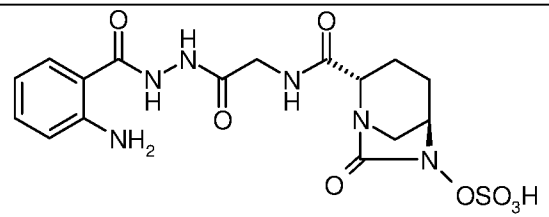
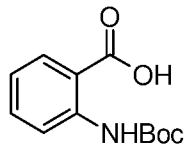
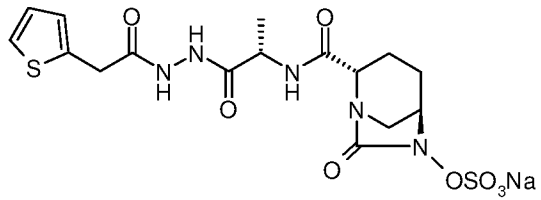
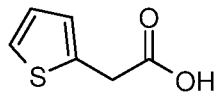
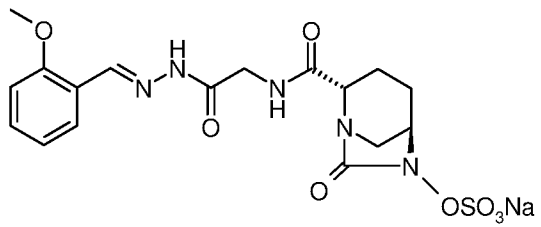
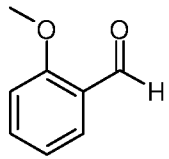
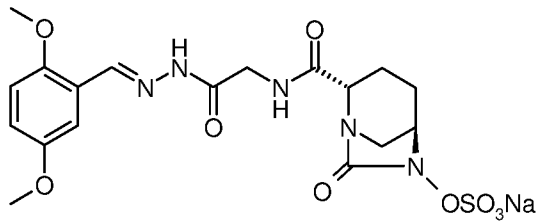
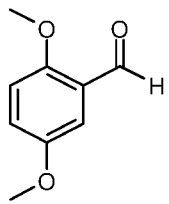
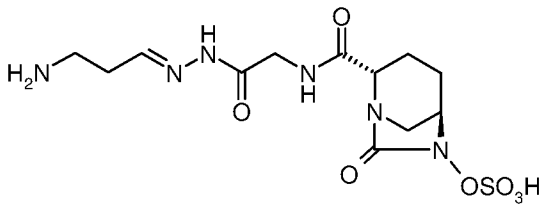
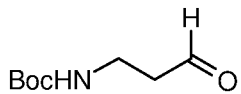
Table-1

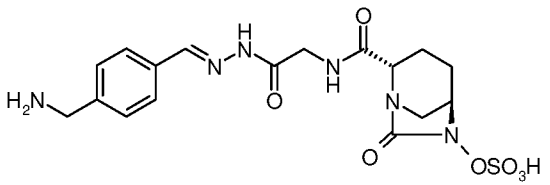
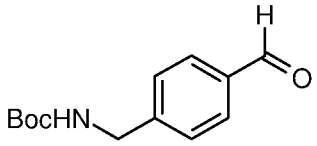
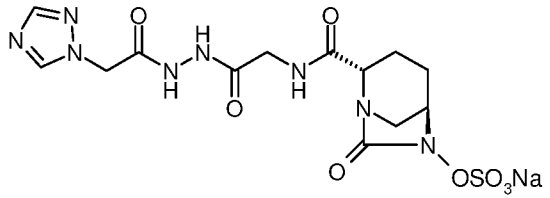
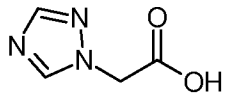
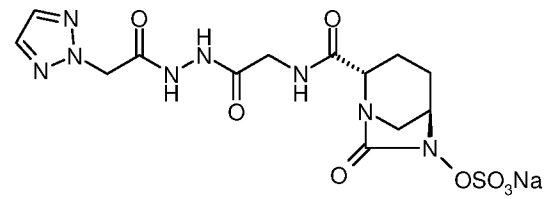
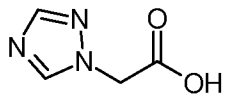
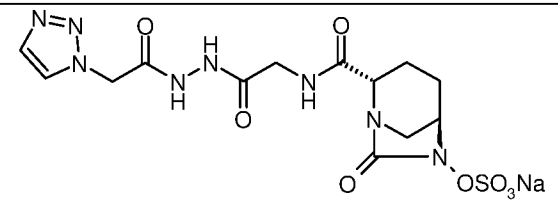
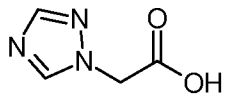
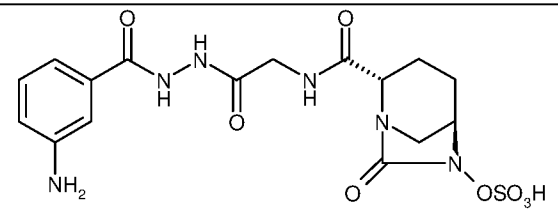
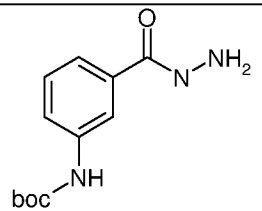
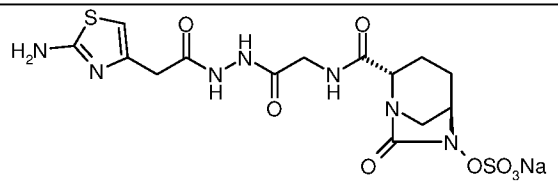
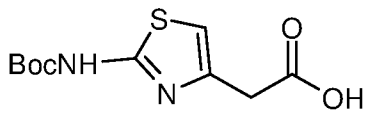
Example No.	Structure	Coupling Reagent	H^1 NMR (DMSO-d_6)	Mass (as free acid) Molecular Formula
5.			δ 10.06 (1H, s), 9.92 (1H, s), 8.42 (1H, s), 7.98 (1H, d, J=8.0 Hz), 3.99-4.39 (1H, m), 3.99 (1H, s), 3.79-3.81 (1H, m), 2.91-33.22 (7H, m), 2.67 (1H, s), 2.02-2.05 (1H, m), 1.62-1.90 (7H, m), 1.29-1.31 (3H, d, J=7.6 Hz)	463.4 (M+1) $C_{16}H_{26}N_6O_8S$
6.			δ 4.40 (m, 1H), 4.02 (bs, 1H), 3.94 (dd, 1H), 3.81(d, 1H), 3.17-2.93 (m, 4H), 2.15-2.03 (m, 2H), 1.87-1.55 (m, 10H), 1.33 (d, 3H)	477.4 (M+1), 475.5 (M-1) $C_{17}H_{28}N_6O_8S$
7.			δ 4.40 (m, 1H), 4.00 (bs, 1H), 3.93 (dd, 1H), 3.82(d, 1H), 3.17-2.94 (m, 4H), 2.18-2.0 (m, 2H), 1.86-1.53 (m, 10H), 1.36 (d, 3H)	477.4 (M+1), 475.5 (M-1) $C_{17}H_{28}N_6O_8S$
8.			δ 10.1 (s, 1H), 9.9 (s, 1H), 8.4 (s, 1H), 8.3 (s, 1H), 3.99 (s, 1H), 3.68-3.87 (m, 3H), 2.89-3.33 (m, 6H), 2.6 (s, 1H), 2.08-2.13 (m, 1H), 1.79-1.88 (m, 3H), 1.55-1.67 (m, 3H).	449.3 (M+1) $C_{15}H_{24}N_6O_8S$

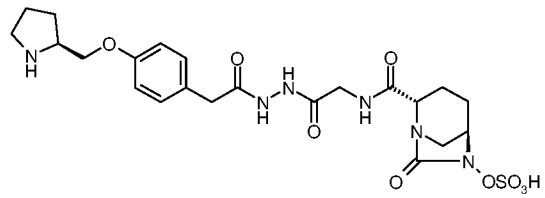
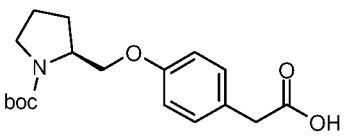
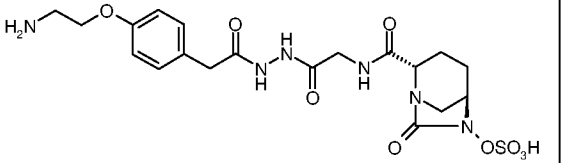
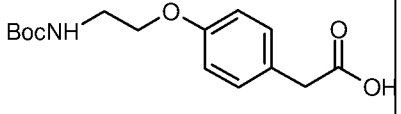
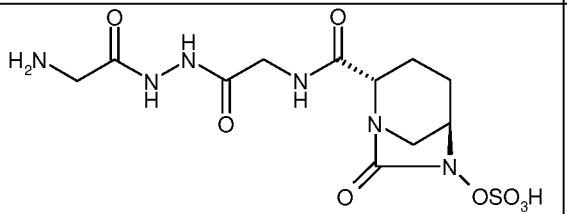
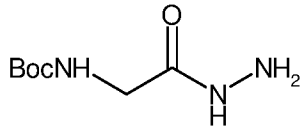
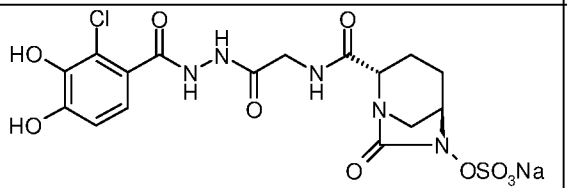
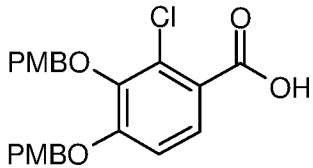
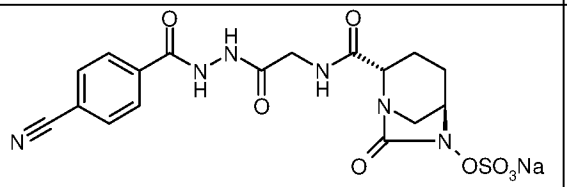
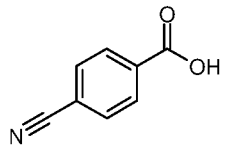
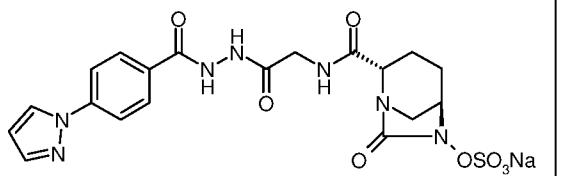
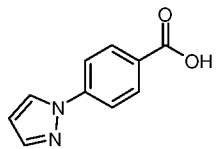
9.			δ 4.68 (m, 1H), 4.03 (bs, 1H), 3.95 (d, 1H), 3.26-2.99 (m, 7H), 2.18(m, 2H) 1.87-1.58 (m, 10H)	492.4 (M+1), 490.4 (M-1) $C_{17}H_{29}N_7O_8S.C_2HO_2F_3$
10.		$BocNHNH_2$	δ 10.7 (1H, s), 8.33 (1H, d, J=7.6 Hz), 4.38-4.34 (2H, m), 4.00 (1H, s), 3.84-3.82 (2H, d J=6.8 Hz), 3.03-2.93 (2H, m), 2.07-2.00 (2H, m), 1.86 (1H, s), 1.70-1.62 (2H, m), 1.32 (3H, d, J=7.2 Hz).	352.2 (M+1) $C_{10}H_{17}N_5O_7S$
11.		$BocN(CH_3)NH_2$	^{1}H NMR (400MHz, DMSO-d_6): δ 11.07 (1H, s), 8.38-8.41 (1H, m), 4.01 (1H, s), 3.76-3.89 (3H, m), 3.03 (2H, s), 2.74 (3H, s), 2.07-2.13 (1H, m), 1.54-1.85 (3H, m).	352.1 (M+1) $C_{10}H_{16}N_5O_7SNa$
12.			δ 9.75 (brs, 2H), 8.13 (t, 1H, *J*= 5.6 Hz), 5.46 (s, 1H), 4.09-4.05 (m, 2H), 3.78-3.45 (m, 2H), 3.37 (s, 2H), 3.11-2.98 (m, 2H), 2.13-2.08 (m, 1H), 1.83-1.55 (m, 3H), 1.23 (d, 3H, *J*= 6.4 Hz).	410.2 (M+1) $C_{12}H_{18}N_5O_9SNa$
13.			δ 9.78 (brs, 2H), 7.86 (d, 1H, *J*=7.6 Hz), 5.45 (s, 1H), 4.40-4.34 (m, 1H), 4.06-3.99 (m, 2H), 3.79 (d, 1H, *J*=6.4 Hz), 3.04-2.91 (m, 2H), 2.07-2.04 (m, 1H), 1.86-1.58 (m, 3H), 1.29-1.22 (m, 6H).	424.2 (M+1) $C_{13}H_{20}N_5O_9SNa$

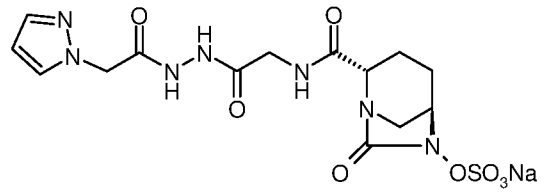
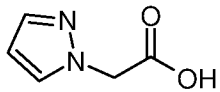
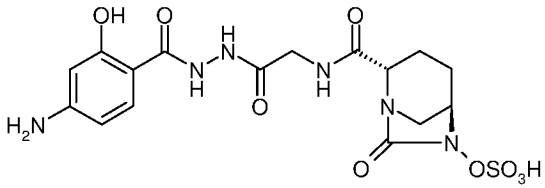
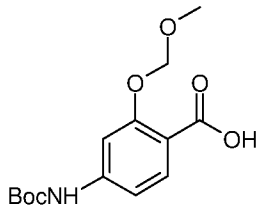
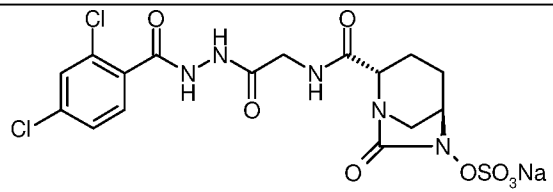
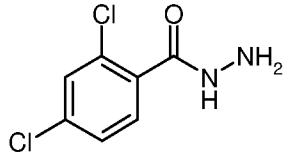
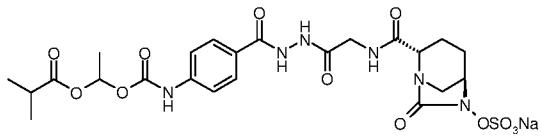
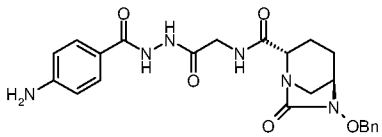
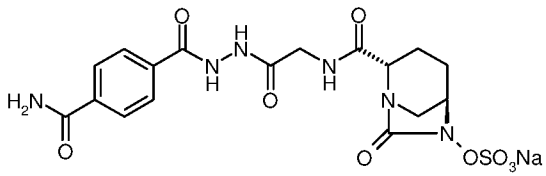
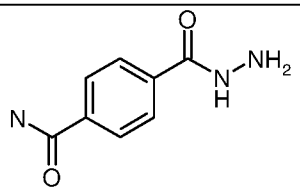
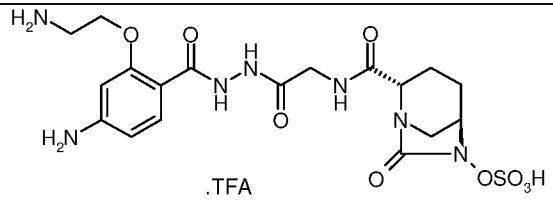
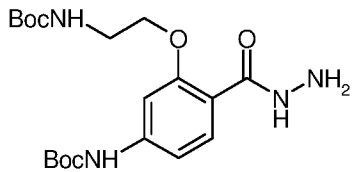
14.			δ 3.99 (m, 1H), 3.80 (m, 2H), 3.55 (m, 1H), 3.46-3.15 (m, 6H), 3.02-2.86 (m, 2H) 2.71(m, 1H) 2.12 (m, 1H), 1.93-1.60 (m, 7H)	478.3(M+1), 476.3(M-1) $C_{16}H_{27}N_7O_8S.C_2HF_3O_2$
15.			δ 4.42-4.43 (m, 1H), 4.17-4.19 (m, 1H), 4.00 (bs, 1H), 3.83-3.85 (d, 1H), 3.15-3.24 (m, 3H), 3.04-3.07 (m, 1H), 2.99 (s, 3H), 2.31-2.33 (m, 2H), 2.02-2.18 (m, 3H), 1.83-1.91 (m, 3H), 1.65-1.71 (m, 3H), 1.30-1.33 (m, 1H).	539.3 (M-1) $C_{17}H_{28}N_6O_{10}S_2$
16.			δ 10.45 (s, 1H), 10.11 (s, 1H), 8.66-8.67 (d, 1H), 8.19 (s, 1H), 8.01-8.02 (d, 1H), 7.63-7.65 (s, 1H), 3.60-3.98 (m, 4H), 2.98-3.13 (m, 2H), 2.10-2.11 (m, 1H), 1.57-1.83 (d, 3H).	441.2 (M-1) $C_{15}H_{17}N_6O_8SNa$
17.			δ 10.15 (s, 1H), 9.97 (s, 1H), 8.17-8.19 (t, 1H), 7.35-7.37 (t, 1H), 6.96 (s, 2H), 3.98 (s, 1H), 3.69-3.98 (m, 5H), 2.97-3.10 (m, 3H), 2.07-2.13 (m, 1H), 1.83 (s, 1H), 1.55-1.70 (m, 2H).	462.2 (M+1) $C_{15}H_{18}N_5O_8S_2Na$
18.			δ 9.82-9.94 (q, 2H), 8.18-8.21 (t, 1H), 7.60-7.66 (t, 2H), 6.60-6.69 (q, 2H), 3.88-3.98 (m, 7H), 2.97-3.43 (m, 2H), 2.09-2.13 (m, 1H), 1.84-1.86 (s, 1H), 1.58-1.68 (m, 2H).	457.2 (M+1) $C_{16}H_{20}N_6O_8S$

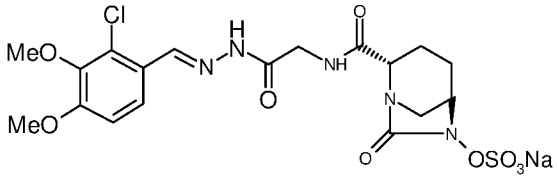
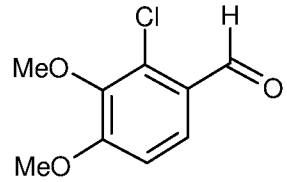
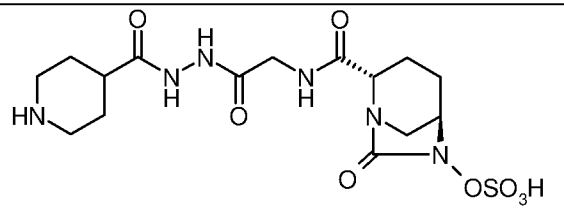
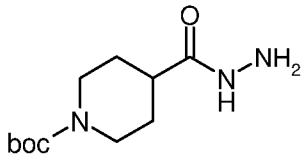
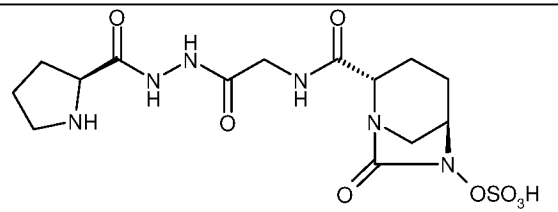
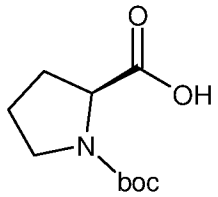
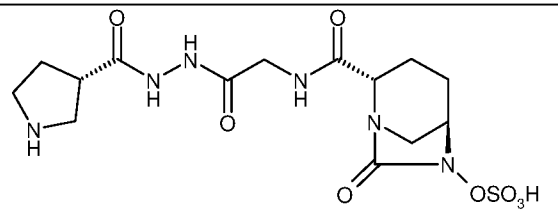
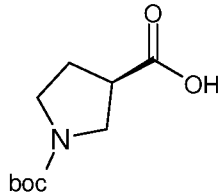
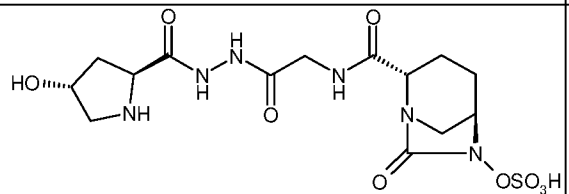
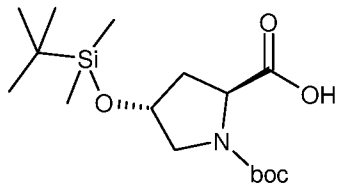
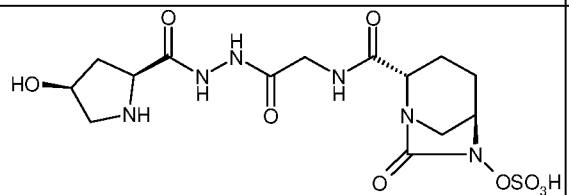
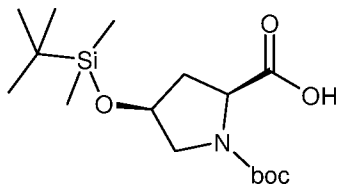
19.			δ 10.43 (s, 1H), 10.14 (s, 1H), 8.20-8.23 (s, 1H), 7.18-7.21 (d, 2H), 3.99 (s, 1H), 3.83 (s, 3H), 3.02 (s, 2H), 2.08-2.13 (m, 1H), 1.83 (s, 1H), 1.57-1.71 (m, 2H).	521.2 (M+1) $C_{15}H_{19}N_8O_9S_2Na$
20.			δ 10.2 (1H, s), 10.0 (1H, s), 7.97 (1H, d, J= 7.2 Hz), 7.36-7.37 (1H, s), 6.95 (1H, s), 4.35-4.39 (1H, m), 3.98 (1H, s), 3.80 (1H, d, J=6.8), 3.66 (2H, s), 2.93-3.02 (2H, m), 2.03-2.05 (1H, m), 1.84 (1H, s), 1.61-1.70 (2H, m), 1.29 (3H, d, J=7.2 Hz).	448.42 (M+1) $C_{14}H_{16}N_5O_8S_2Na$
21.			δ 10.21 (s, 1H), 10.01 (s, 1H), 8.23-8.26 (s, 3H), 7.90-7.92 (d, 2H), 7.55-7.57 (d, 2H), 4.10 (s, 2H), 3.76-3.83 (m, 4H), 3.10-3.13 (d, 1H), 2.98-3.01 (d, 2H), 2.07-2.13 (m, 1H), 1.85 (s, 1H), 1.57-1.69 (m, 2H)..	471.2 (M+1) $C_{17}H_{22}N_6O_8S$
22.			δ 10.12 (2H, s), 8.20 (1H, s), 3.97 (1H, s), 3.86-3.66 (3H, m), 3.58 (2H, s), 3.02 (2H, dd, J=12, 11.6 Hz), 2.10-2.06 (1H, m), 1.82-1.54 (3H, m).	405.2 (M+1) $C_{12}H_{15}N_6O_8SNa$
23.			δ 9.92 (2H, s), 8.16 (1H, t, J=5.6 Hz), 7.11 (1H, d J=6.8 Hz), 7.02 (1H, t, J=7.2 Hz), 6.76-6.68 (m, 2H), 4..33 (1H, br s,), 3.97 (1H, s), 3.85-3.67 (3H, m), 3.44-3.41 (2H, m), 3.02 (2H, dd, 12 J=6.8 Hz), 2.11-2.06 (2H, m), 1.83 (1H, m), 1.70-1.50 (2H, m).	472.2 (M+1) $C_{17}H_{20}N_5O_9SNa$

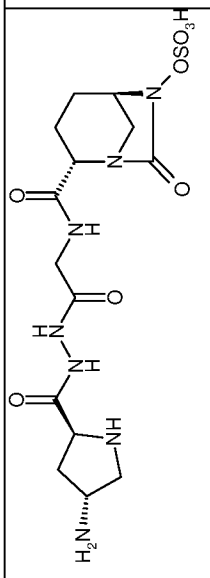
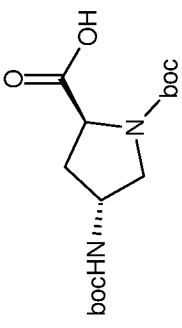
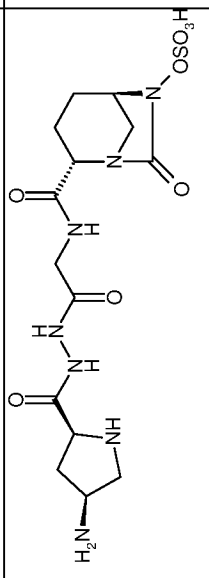
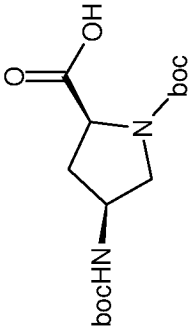
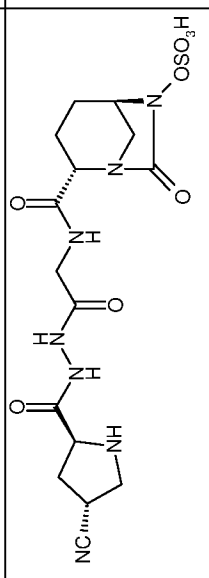
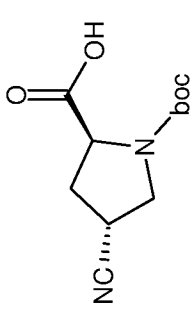
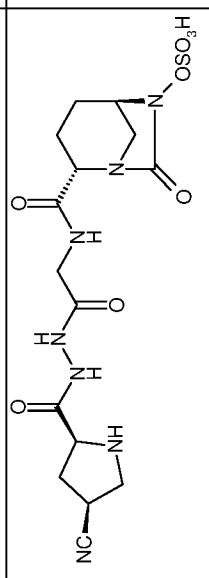
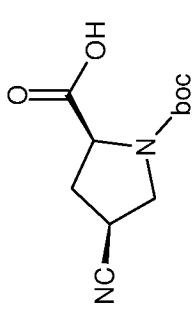
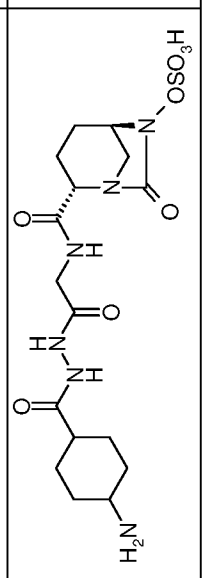
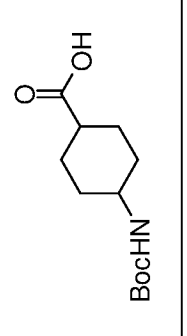
24.			δ 10.12 (1H, s), 9.85 (1H, s), 8.22 (1H, m), 7.53 (1H, d, J=7.6 Hz), 7.18 (1H, m), 6.73 (1H, d, J=8.0 Hz), 6.58-6.50 (1H, m), 3.76-3.99 (5H, m), 3.01-3.13 (3H, m), 2.03-2.05 (2H, m), 1.40-1.85 (2H, m).	457.44(M+1) $C_{16}H_{20}N_6O_8S$
25.			δ 10.2 (1H, s), 10.0 (1H, s), 8.0 (1H, s), 7.4 (1H, s), 7.1 (1H, s), 6.9 (1H, s), 4.39-4.35 (1H, m), 3.98 (1H, s), 3.79-381 (1H, s), 3.66 (2H, s), 2.93-3.03 (2H, m), 2.07-2.03 (1H, m), 1.84 (1H, s)1.63-1.68 (2H, m), 1.30-1.28 (3H, d, J=7.6 Hz).	476.2 (M+1) $C_{16}H_{20}N_5O_8S_2.Na$
26.			δ 11.42 (1H, s), 8.34 (1H, s), 8.06 (1H, t, J=5.6 Hz), 7.80 (1H, t, J=8 Hz), 7.40 (1H, t, J=8 Hz), 7.09 (1H, d, J=8.8 Hz), 7.0 (1H, t, J=7.2 Hz), 4.33 (1H, dd, J=6.4, 17.6 Hz), 4.16 (1H, dd, J=5.6, 17.6 Hz), 4.01 (1H, s), 3.90-3.76 (4H, m), 3.20-3.01 (2H, m), 2.17-2.10 (1H, m), 1.85-1.57 (3H, m).	456.2 (M+1) $C_{17}H_{20}N_5O_8SNa$
27.			δ 11.43 (1H, s), 8.30 (1H, s), 8.08 (1H, s), 7.31 (1H, s), 7.05-6.97 (2H, m), 4.25 (2H, dd, J=6, 5.2 Hz), 4.00 (1H, s), 3.85 (4H, s), 3.74 (3H, s), 3.19 (2H, dd, J= 12, 11.2 Hz), 2.15-2.12 (1H, m), 1.85-1.58 (3H, m).	486.2 (M+1) $C_{18}H_{22}N_5O_9SNa$
28.			δ 11.18 (1H, s), 8.02 (1H, t, J=5.6 Hz), 7.66 (3H, s), 7.28 (1H, s), 4.24 (1H, dd, J=5.6, 6 Hz), 4.04 (1H, d, J=5.2Hz), 3.99 (1H, s), 3.81-3.68 (3H, m), 3.13-3.00 (4H, m), 2.11-2.05 (1H, m), 1.83-1.54 (3H, m).	393.2 (M+1) $C_{12}H_{20}N_6O_7S$

29.			δ 11.51 (1H, s), 8.26 (1H, s), 8.12 (3H, s), 8.01 (1H, s), 7.74 (2H, d, J=8.4 Hz), 7.50 (2H, d, J=6, 17.2 Hz), 4.38 (1H, dd, J=6 Hz), 4.18 (1H, dd, J=5.2Hz), 4.07 (1H, d, J=5.6Hz), 4.01 (1H, s), 3.89-3.78 (2H, m), 3.17-3.01 (2H, m), 2.15-2.11 (1H, m), 1.85-1.58 (3H, m).	455.3 (M+1) $C_{17}H_{22}N_6O_7S$
30.			δ 10.30 (2H, br s), 8.49 (1H, s), 8.18 (1H, t), 7.94 (1H, s), 4.97 (2H, s), 3.97 (1H, s), 3.86-3.67 (3H, m), 3.02 (2H, dd, J=12, 11.6 Hz), 2.09-2.06 (1H, m), 1.81-1.54 (3H, m).	445.3 (M-1) $C_{13}H_{17}N_8O_8SNa$
31.			δ 10.32 (2H, br s), 8.18 (1H, t), 7.78 (2H, s), 5.16 (2H, s), 3.97 (1H, s), 3.86-3.68 (3H, m), 3.02 (2H, dd, J=12, 12.4 Hz), 2.11-2.06 (1H, m), 1.82-1.55 (3H, m).	445.3 (M-1) $C_{13}H_{17}N_8O_8SNa$
32.			δ 10.30 (2H, br s), 8.20 (1H, t), 8.07 (1H, s), 7.71 (1H, s), 5.15 (2H, s), 3.97 (1H, s), 3.86-3.67 (3H, m), 3.02 (2H, dd, J=12, 11.6 Hz), 2.11-2.06 (1H, m), 1.81-1.53 (3H, m).	445.3 (M-1) $C_{13}H_{17}N_8O_8SNa$
33.			δ 10.42 (1H, s), 10.05 (1H, s), 8.24 (1H, t, J=4 Hz), 7.32-7.70 (4H, m), 3.76-3.99 (8H, m), 2.98-3.16 (3H, m), 1.55-2.13 (4H, m).	457.4 (M+1) $C_{16}H_{20}N_6O_8S$
34.			δ 10.10 (1H, s), 9.95 (1H, s), 8.17 (1H, t, J=4 Hz), 6.85 (2H, s), 6.29 (1H, s), 3.69-3.99 (4H, m), 2.97-3.27 (5H, m), 1.55-2.13 (4H, m).	478.3 (M+1) $C_{14}H_{18}N_7O_8S_2Na$

35.			δ 7.32-7.34 (2H, d, J=8.4Hz), 7.03-7.05 (2H, d, J=8.4Hz), 4.39-4.41 (1H, m), 4.10-4.23 (5H, m), 3.67 (2H,s), 3.33-3.42 (3H, m), 3.16-3.24 (2H, m), 1.65-2.29 (8H, m)	553.4 (M-1) $C_{22}H_{30}N_6O_9S$
36.			δ 7.33-7.35 (2H, d, J=7.6Hz), 7.04-7.06 (2H, d, J=8.0Hz), 4.19-4.31 (3H, m), 4.10-4.20 (2H, m), 3.67 (2H, bs), 3.44-3.47 (2H, m), 3.33-3.36 (1H, m), 3.16-3.24 (2H, m), 1.82-2.25 (4H, m)	513.3 (M-1) $C_{19}H_{26}N_6O_9S$
37.			δ 10.30 (1H, s), 10.90 (1H, s), 7.95-8.22 (4H, m), 3.50-3.98 (5H, m), 2.96-3.09 (2H, m), 1.53-2.10 (4H, m).	393.2 (M-1) $C_{11}H_{18}N_6O_8S$
38.			δ 9.99 (2H, s), 9.25 (1H, s), 8.19 (1H, t, J=4 Hz), 6.75-6.83 (2H, m), 3.72-3.99 (3H, m), 2.99-3.11 (2H, m), 1.58-2.13 (4H, m).	508.2 (M+1) $C_{16}H_{17}N_6O_{10}SClNa$
39.			δ 10.6 (1H, s), 10.2 (1H, s), 7.28-8.29 (5H, m), 3.77-3.99 (3H, m), 2.79-3.13 (2H, m), 2.36 (1H, s), 1.56-2.15 (4H, m).	467.2 (M+1) $C_{17}H_{17}N_6O_8SNa$
40.			δ 10.21 (bs, 1H), 10.02 (bs, 1H), 8.62 (d, 1H), 8.25 (t, 1H), 7.98-8.02 (m, 3H), 7.80 (s, 1H), 6.59 (s, 1H), 3.91-3.99 (m, 2H), 3.31-3.83 (m, 2H), 3.02-3.11 (m, 1H), 2.67-2.99 (m, 1H), 2.10-2.14 (m, 1H), 1.56-1.85 (m, 3H)	506.2(M-1) $C_{19}H_{20}N_7O_8SNa$

41.			δ 10.15 (2H, bs), 8.19 (1H, t),7.72, (1H, s), 7.43 (1H, s), 6.25 (1H, s), 4.86 (2H, s), 3.99 (1H, s), 3.79-3.88 (3H, m), 3.69-3.75 (1H, m), 3.08-3.11 (1H, m), 2.08-2.13 (1H, m), 1.77 (1H, m), 1.72-1.76 (2H, m)	444.2 (M-1). $C_{14}H_{18}N_7O_8SNa$
42.			δ 10.42 (1H, s), 10.05 (1H, s), 8.24 (1H, t, J=4 Hz), 7.32-7.70 (4H, m), 3.76-3.99 (8H, m), 2.98-3.16 (3H, m), 1.55-2.13 (4H, m)	473.2 (M+1) $C_{16}H_{20}N_6O_9S$
43.			δ 10.4 (1H, s), 10.2 (1H, s), 8.24 (1H, s), 7.71 (1H, s), 7.48-7.54 (2H, m), 4.0 (1H, s), 3.58-3.93 (3H, m), 3.0-3.11 (2H, m), 1.56-2.13 (4H, m)	510.1 (M+1) $C_{16}H_{16}N_5O_8SCl_2Na$
44.			δ 9.95-10.2 (3H, m), 8.20 (1H, s), 7.81 (2H, d, J=9.2 Hz), 6.77 (2H, d, J=8.4 Hz), 6.77 (1H, d, J=5.6 Hz), 3.58-3.96 (7H, m), 2.99-3.11 (3H, m), 1.73-2.06 (6H, m), 1.45 (3H, d, J=5.6 Hz)	615.2 (M+1) $C_{23}H_{29}N_6O_{12}SNa$
45.			δ 9.82-9.94 (2H, m), 8.18-8.21 (1H, m), 7.60-7.66 (2H, m), 6.60-6.69 (2H, m), 3.88-3.98 (7H, m), 2.97-3.43 (2H, m), 2.09-2.13 (1H, m), 1.86 (1H, s), 1.58-1.68 (2H, m)	483.3 (M-1) $C_{17}H_{19}N_6NaO_9S$
46.			δ 10.66 (1H, s), 9.72 (1H, s), 8.19 (1H, s), 7.92 (3H, s), 7.45 (1H, s, J=8.4 Hz), 6.23-6.27 (2H, m), 5.85 (2H, s), 3.34-4.19 (8H, m), 3.04 (2H, s), 1.57-2.13 (4H, m)	516.2 (M+1) $C_{20}H_{26}F_3N_6N_7O_{11}S$

47.			δ 11.53 (1H, s), 8.49 (1H, s), 8.31 (1H, s), 8.08 (1H, t, J=6 Hz), 7.70 (1H, d, J=12 Hz), 7.15 (1H, t, J=8 Hz), 4.32-4.38 (1H, m), 4.11-4.16 (1H, m), 4.01 (1H, s), 3.88 (3H, s), 3.76 (3H, s), 3.19-3.01 (2H, m), 2.32-1.58 (4H, m)	520.2 (M+1) $C_{18}H_{21}N_5O_9SClNa$
48.			δ 9.92 (bs, 2H), 8.20 (t, 2H), 4.00 (bs, 1H), 3.70-3.88 (m, 3H), 3.30 (m, 2H), 2.89-3.09 (m, 3H), 2.08-2.12 (m, 1H), 1.56-1.87 (m, 5H)	447.4(M-H) $C_{15}H_{23}N_6O_8S$
49.			-	435.3 (M+1) $C_{14}H_{22}N_6O_8S$
50.			δ 9.98 (bs, 2H), 8.65(bs, 2H), 8.20 (t, 2H), 4.00 (bs, 1H), 3.70-3.89 (m, 3H), 3.36-3.70 (m, 1H), 2.98-3.27 (m, 5H), 2.08-2.20 (m, 2H), 1.84-2.00 (m, 2H), 1.54-1.74 (m, 2H)	433.3 (M-H) $C_{14}H_{22}N_6O_8S$
51.			-	449.3 (M-1) $C_{14}H_{22}N_6O_9S$
52.			-	449.3 (M-1) $C_{14}H_{22}N_6O_9S$

53.			-	451.3 (M+1) $C_{14}H_{23}N_6O_8S$
54.			-	451.3 (M+1) $C_{14}H_{23}N_6O_8S$
55.			-	460.4 (M-1) $C_{15}H_{21}N_7O_8S$
56.			-	460.4(M+1) $C_{14}H_{22}N_7O_8S$
57.			-	463.2 (M+1) $C_{16}H_{26}N_6O_8S$

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 104 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 35ºC 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.

The combinations of compounds according to present invention were also tested for their antibacterial activity in combination with Ceftazidime against various bacterial strains. The plates were poured with MHA containing doubling concentration range of Ceftazidime in combination with constant concentration (4 µg/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 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	16	> 32	> 32	> 32
4.	Example 4	> 32	> 32	> 32	16	> 32	> 32	> 32
5.	Example 5	> 32	32	32	> 32	> 32	32	32
6.	Example 6	> 32	32	32	> 32	> 32	32	32
7.	Example 7	> 32	> 32	> 32	> 32	> 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 12	> 32	> 32	> 32	32	> 32	> 32	> 32
13.	Example 13	> 32	> 32	> 32	> 32	> 32	> 32	> 32
14.	Example 14	> 32	> 32	> 32	> 32	> 32	> 32	> 32
15.	Example 15	> 32	> 32	> 32	> 32	> 32	> 32	> 32
16.	Example 16	> 32	> 32	> 32	16	> 32	> 32	> 32
17.	Example 17	> 32	> 32	> 32	16	> 32	> 32	> 32

18.	Example 18	> 32	> 32	> 32	8	> 32	> 32	> 32
19.	Example 19	> 32	> 32	> 32	32	> 32	> 32	> 32
20.	Example 20	> 32	> 32	> 32	> 32	> 32	> 32	> 32
21.	Example 21	> 32	> 32	> 32	32	> 32	> 32	> 32
22.	Example 22	> 32	> 32	> 32	> 32	> 32	> 32	> 32
23.	Example 23	> 32	> 32	> 32	32	> 32	> 32	> 32
24.	Example 24	> 32	> 32	> 32	32	> 32	> 32	> 32
25.	Example 25	> 32	> 32	> 32	32	> 32	> 32	> 32
26.	Example 26	> 32	> 32	> 32	16	> 32	> 32	> 32
27.	Example 27	> 32	> 32	> 32	16	> 32	> 32	> 32
28.	Example 28	> 32	> 32	> 32	16	> 32	> 32	> 32
29.	Example 29	> 32	> 32	> 32	16	> 32	> 32	> 32
30.	Ceftazidime	32	> 32	32	> 32	> 32	> 32	> 32

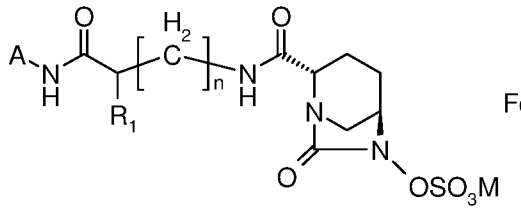
Table 3. Antibacterial activity of representative compounds according to the invention in combination with Ceftazidime

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
1.	Ceftazidime alone	32	> 32	32	> 32	> 32	> 32	> 32
2.	Ceftazidime + Example 2 (4mcg/ml)	0.5	8	1	1	8	32	32
3.	Ceftazidime + Example 3 (4mcg/ml)	1	4	0.25	1	-	8	8
4.	Ceftazidime + Example 4 (4mcg/ml)	0.5	2	0.25	0.5	4	2	2
5.	Ceftazidime + Example 5 (4mcg/ml)	2	4	0.5	1	8	32	32
6.	Ceftazidime + Example 6 (4mcg/ml)	4	16	1	1	> 32	> 32	> 32
7.	Ceftazidime + Example 7 (4mcg/ml)	4	16	2	2	> 32	> 32	> 32
8.	Ceftazidime + Example 8 (4mcg/ml)	1	2	0.5	0.5	4	4	4
9.	Ceftazidime + Example 10 (4mcg/ml)	1	4	0.5	1	-	16	16
10.	Ceftazidime + Example 12 (4mcg/ml)	1	8	0.5	1	8	16	16
11.	Ceftazidime + Example 18 (4mcg/ml)	0.25	1	0.06	0.5	2	4	2
12.	Ceftazidime + Example 19 (4mcg/ml)	0.5	4	0.5	0.5	8	16	8
13.	Ceftazidime + Example 20 (4mcg/ml)	1	4	0.5	-	-	-	-
14.	Ceftazidime + Example 23 (4mcg/ml)	1	4	0.5	1	4	8	8

15.	Ceftazidime + Example 24 (4mcg/ml)	1	8	0.25	1	4	8	16
16.	Ceftazidime + Example 26 (4mcg/ml)	1	4	0.25	1	4	8	4
17.	Ceftazidime + Example 27 (4mcg/ml)	1	4	0.25	1	4	16	8
18.	Ceftazidime + Example 28 (4mcg/ml)	0.5	2	0.25	0.5	4	4	4
19.	Ceftazidime + Example 29 (4mcg/ml)	0.5	1	0.25	0.5	2	2	4
20.	Ceftazidime + Example 30 (4mcg/ml)	1	8	0.5	2	4	16	16
21.	Ceftazidime + Example 33(4mcg/ml)	1	4	0.25	2	4	1	8
22.	Ceftazidime + Example 34(4mcg/ml)	1	4	0.5	2	4	16	16
23.	Ceftazidime + Example 39(4mcg/ml)	1	8	0.5	2	4	16	8
24.	Ceftazidime + Example 40(4mcg/ml)	1	16	0.25	2	16	>32	32

CLAIMS

1. A compound of Formula (I):



Formula (I)

or a stereoisomer or a pharmaceutically acceptable derivative thereof;

wherein:

A is $NHCOR_2$, NR_2R_3 or $N=CHR_2$;

R_1 is:

(a) hydrogen,
(b) C_1-C_6 alkyl optionally substituted with one or more substituents independently selected from OR_4, NR_4R_5, SR_4, SOR_4, SO_2R_4, CN, halogen, $COOR_4$, $CONR_4R_5$, NR_4COR_5, or $NR_4CONR_5R_6$,
(c) NR_4R_5,
(d) CN,
(e) SOR_4,
(f) SO_2R_4 or
(g) OR_4;

R_2 and R_3 are each independently:

(a) hydrogen,
(b) C_1-C_6 alkyl optionally substituted with one or more substituents independently selected from OR_4, NR_4R_5, SR_5, SOR_4, SO_2R_4, CN, halogen, $COOR_4$, $CONR_4R_5$, NR_4COR_5, $NR_4CONR_5R_6$, $=NOCH_3$, heterocyclyl, cycloalkyl, aryl or heteroaryl,
(c) cycloalkyl optionally substituted with one or more substituents independently selected from OR_4, NR_4R_5, SR_4, SOR_4, SO_2R_4, CN, $(CH_2)_mNR_4R_5$, halogen, $COOR_4$, $CONR_4R_5$, NR_4COR_5 or $NR_4CONR_5R_6$,
(d) heterocycloalkyl optionally substituted with one or more substituents independently selected from OR_4, NR_4R_5, SR_4, SOR_4, SO_2R_4, CN, $(CH_2)_mNR_4R_5$, halogen, $COOR_4$, $CONR_4R_5$, NR_4COR_5 or $NR_4CONR_5R_6$,
(e) aryl optionally substituted with one or more substituents independently selected from OR_4, NR_4R_5, SR_4, SOR_4, SO_2R_4, CN, $(CH_2)_mNR_4R_5$, halogen, $COOR_4$, $CONR_4R_5$, NR_4COR_5 or $NR_4CONR_5R_6$,
(f) heteroaryl optionally substituted with one or more substituents independently selected from OR_4, NR_4R_5, SR_4, SOR_4, SO_2R_4, CN, $(CH_2)_mNR_4R_5$, halogen, $COOR_4$, $CONR_4R_5$, NR_4COR_5 or $NR_4CONR_5R_6$ or
(g) R_2 and R_3 are joined together to form a four to seven member ring;

R_4, R_5 and R_6 are each independently:

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

n is 0,1,2 or 3;
m is 1 to 6;

M is hydrogen or a cation.

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

(2*S*,5*R*)-*N*-[(2*S*)-3-Amino-1-[(3*R*)-3-(hydrazinylcarbonyl)piperidine]-1-oxopropan-2-yl] -7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-[(2*S*)-3-Hydroxy-1-[(3*R*)-3-(hydrazinylcarbonyl)piperidine]-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-{2-[(3*R*)-piperidine-3-ylcarbonyl]hydrazinyl}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*R*)-Azepan-2-yl-carbonyl]hydrazinyl}-1-oxo-propan-2-yl]-2-methyl-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*, 5*R*)-*N*-[(2*S*)-1-{(2*S*)-Azepan-2-yl-carbonyl]hydrazinyl}-1-oxo-propan-2-yl]-2-methyl-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*- (2-Oxo-2-{2-[(3*R*)-piperidin-3-ylcarbonyl]hydrazinyl}ethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-[(2*S*)-3-Amino-1-[(2*R*)-2-(hydrazinylcarbonyl azepane]-1-oxopropan-2-yl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*- (2-Hydrazinyl-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo [3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-[(2*S*)-1-Hydrazinyl-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-[2-(thiophen-2-ylacetyl)hydrazinyl] propan-2-yl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-[(2*R*)-1-[(2*S*)-(Pyrrolidineacetyl)hydrazinyl]-4-(methylsulfonyl) -1-oxobutan-2-yl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-[(2*S*)-2-Amino-1-[(3*R*)-3-(hydrazinylcarbonyl) piperidine]-1-oxopropan-2-yl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-3-carboxamide;
(2*S*, 5*R*)-*N*- (2-{2-[(2*R*)-2-Hydroxypropanoyl]hydrazinyl}-2-oxoethyl) -7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*- {2-[2-(Aminoacetyl)hydrazinyl]-2-oxoethyl}-7-oxo-6-(sulfooxy) -1,6-diazabicyclo [3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*- {2-[2-(Hydroxyacetyl)hydrazinyl]-2-oxoethyl}-7-oxo-6-(sulfooxy) -1,6-diazabicyclo [3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-{2-Oxo-2-[2-(pyridin-2-ylcarbonyl)hydrazinyl]ethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*- {2-Oxo-2-[2-(thiophen-2-ylacetyl)hydrazinyl]ethyl}-7-oxo -6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*- [(2*S*)-1-{2-[(2*R*)-2-Hydroxypropanoyl]hydrazinyl}-1-oxopropan-2-yl] -7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;
(2*S*,5*R*)-*N*-(2-{2-[(4-Aminophenyl)carbonyl] hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(2*E*)-2-(2-Amino-1,3-thiazol-4-yl)-2-(methoxyimino) acetyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)--1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*) -*N*-{2-Oxo-2-[2-(thiophen-2-ylcarbonyl)hydrazinyl]ethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-[2-(2-{[4-(Aminomethyl)phenyl]carbonyl}hydrazinyl) -2-oxoethyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

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

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

(2*S*,5*R*)-*N*- {[2-Oxo-(2-hydroxyphen-2-ylcarbonyl)hydrazinyl]ethyl}-7-oxo-6- (sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

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

(2*S*,5*R*)-*N*- {2-Oxo-2-[2-(pyridin-3-ylcarbonyl)hydrazinyl]ethyl-7-oxo-6- (sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

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

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

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

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

(2*S*,5*R*)-*N*-{2-[(2*E*)-2-(2',4'-Dimethoxybenzylidenehydrazinyl]-2-oxoethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-2-({2-[(2*E*)-2-(3-Aminopropylidene)hydrazinyl]-2-oxoethyl}carbamoyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-{2-[(2*E*)-2-(4' Methylaminobenzylidenehydrazinyl]-2-oxoethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-{2-[2-(1*H*-1,2,4-Triazol-1-ylcarbonyl)hydrazinyl]-2-oxo-ethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-{2-[2-(2*H*-1,2,3-Triazol-2-ylcarbonyl)hydrazinyl]-2-oxo-ethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-{2-[2-(1*H*-1,2,3-Triazol-1-ylcarbonyl)hydrazinyl]-2-oxo-ethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(3-Aminophenyl)carbonyl] hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(2*E*)-2-(2-Amino-1,3-thiazol-4-yl)-2-oxoethyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)- *N*-(2-{2-[(4-(2*S*)-2-(Phenoxymethyl)pyrrolidine)acetyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)- *N*-(2-{2-[(4-(2-[(2-Phenoxyethanamine)acetyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

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

(2*S*,5*R*)-*N*-(2-{2-[(2-Chloro-3,4-dihydroxyphenyl)carbonyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(4-Cyanophenyl)carbonyl] hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(4-Amino-2-hydroxyphenyl)carbonyl] hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(2,4-Dichlorophenyl)carbonyl] hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(4-{1-[(2-Methylpropanoyl)oxy]ethoxy}carbonyl) phenyl)carbonyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1] octane-2-carboxamide1-(carbamoyloxy) ethyl 2-methylpropanoate;

(2*S*,5*R*)-*N*-(2-{2-[(4-Carboxamidophenyl)carbonyl] hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(4-Amino-2-aminoethoxyphenyl)carbonyl] hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[Piperidin-4-ylcarbonyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(3*R*)-Pyrrolidin-2-ylcarbonyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

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

(2*S*,5*R*)-*N*-(2-{2-[(2*S*,4*R*)-4-Hydroxypyrrolidin-2-ylcarbonyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(2*S*,4*S*)-4-Hydroxypyrrolidin-2-ylcarbonyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(2*S*,4*R*)-4-Cyanopyrrolidin-2-ylcarbonyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(2*S*,4*S*)-4-Cyanopyrrolidin-2-ylcarbonyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

(2*S*,5*R*)-*N*-(2-{2-[(4-Aminocylohexane-4-yl)carbonyl]hydrazinyl}-2-oxoethyl)-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:

Trifluoroacetate salt of (2*S*,5*R*)-*N*-[(2*S*)-3-amino-1-[(3*R*)-3-(hydrazinylcarbonyl)piperidine]-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*)-3-hydroxy-1-[(3*R*)-3-(hydrazinylcarbonyl)piperidine]-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-{2-[(3*R*)-piperidine-3-ylcarbonyl]hydrazinyl}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*R*)-azepan-2-yl-carbonyl]hydrazinyl}-1-oxo-propan-2-yl]-2-methyl-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*S*)-azepan-2-yl-carbonyl]hydrazinyl}-1-oxo-propan-2-yl]-2-methyl-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-[(3*R*)-piperidin-3-ylcarbonyl]hydrazinyl}ethyl)-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-[(2*R*)-2-(hydrazinylcarbonyl azepane]-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-hydrazinyl-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*)-1-hydrazinyl-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-[2-(thiophen-2-ylacetyl)hydrazinyl] 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*R*)-1-[(2*S*)-(pyrrolidineacetyl)hydrazinyl]-4-(methylsulfonyl) -1-oxobutan-2-yl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Trifluoroacetate salt of (2*S*,5*R*)-*N*-[(2*S*)-2-Amino-1-[(3*R*)-3-(hydrazinylcarbonyl) piperidine]-1-oxopropan-2-yl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-3-carboxamide;

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

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

Sodium salt of (2*S*,5*R*)-*N*- {2-[2-(hydroxyacetyl)hydrazinyl]-2-oxoethyl}-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-(pyridin-2-ylcarbonyl)hydrazinyl]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-(thiophen-2-ylacetyl)hydrazinyl]ethyl}-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-[(2*R*)-2-hydroxypropanoyl]hydrazinyl}-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-{2-[(4-aminophenyl)carbonyl] hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-(2-{2-[(2*E*)-2-(2-amino-1,3-thiazol-4-yl)-2-(methoxyimino) acetyl]hydrazinyl}-2-oxoethyl)-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-(thiophen-2-ylcarbonyl)hydrazinyl]ethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*-[2-(2-{[4-(aminomethyl)phenyl]carbonyl}hydrazinyl) -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*)-1-[2-(cyanoacetyl)hydrazinyl]-1-oxoethyl}-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-(cyanoacetyl)hydrazinyl]-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-oxo-(2-hydroxyphen-2-ylcarbonyl)hydrazinyl]ethyl}-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)-*N*- (2-{2-[(2-aminophenyl)carbonyl]hydrazinyl}-2-oxoethyl)-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-(pyridin-3-ylcarbonyl)hydrazinyl]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-({[(3*R*)-piperidin-3-ylcarbonyl]hydrazinyl}-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-(2-methylhydrazinyl)-2-oxoethyl]-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

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

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

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

Sodium salt of (2*S*,5*R*)-2-({2-[(2*E*)-2-(3-aminopropylidene)hydrazinyl]-2-oxoethyl}carbamoyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

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

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

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

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

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

Sodium salt of (2*S*,5*R*)-*N*-(2-{2-[(2*E*)-2-(2-amino-1,3-thiazol-4-yl)-2-oxoethyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

Sodium salt of (2*S*,5*R*)- *N*-(2-{2-[(4-(2*S*)-2-(phenoxymethyl)pyrrolidine)acetyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

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

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

Sodium salt of (2*S*,5*R*)-*N*-(2-{2-[(2-chloro-3,4-dihydroxyphenyl)carbonyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

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

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

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

Sodium salt of (2*S*,5*R*)-*N*-(2-{2-[(4-{1-[(2-methylpropanoyl)oxy]ethoxy}carbonyl) phenyl)carbonyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1] octane-2-carboxamide1-(carbamoyloxy) ethyl 2-methylpropanoate;

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

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

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

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

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

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

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

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

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

Sodium salt of (2*S*,5*R*)-*N*-(2-{2-[(4-aminocylohexane-4-yl)carbonyl]hydrazinyl}-2-oxoethyl)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide;

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, 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/IB2016/053974

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

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

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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
19 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

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PCT/IB2016/053974

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