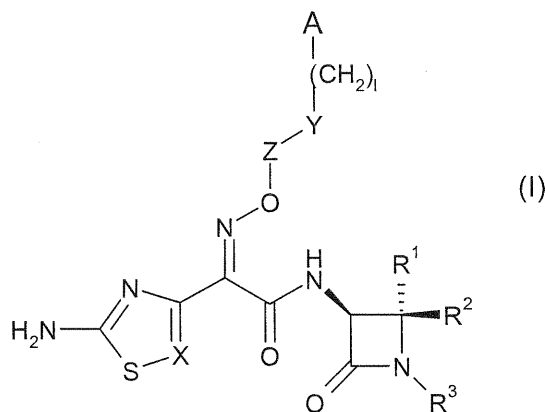


[0005] The attempt to enhance the cellular uptake of the β -lactams by using iron-siderophore uptake systems in microorganisms is one concept that has been explored in the monobactam field by Basilea (WO 2007065288), Naeja Pharmaceuticals (WO 2002022613) and Squibb & Sons (US 5290929, EP 531976, EP 484881). The heteroaryl units mimicing siderophores can also be attached to the side-chain as hydrazides as demonstrated by Squibb & Sons (US 5318963, US 5112968). Recently, Pfizer re-investigated monocarbams, monocyclic β -lactams that carry a sulfonylaminocarbonyl activating group at the N1-position (WO 2010070523). Additionally, in WO 2008116813 Basilea has described combination therapy approaches using a combination of monobactams with carbapenems.

[0006] In view of the increasing resistance development of pathogenic bacteria against known antibacterial agents, including multiple resistances, there is an ongoing need to find novel antibacterial substances, in particular compounds that have different structural motives.

SUMMARY

In an aspect, there is provided compound of formula



in which

R¹ and R² independently of one another represent hydrogen, aminocarbonyl or (C₁-C₄)-alkyl, or

R¹ and R² together with the carbon atom to which they are bonded form a (C₃-C₈)-cycloalkyl,

R³ represents -(CH₂)_m-(SO₂)OH or -O-(CH₂)_o-(SO₂)OH,

wherein m and o independently of one another represent an integer 0, 1, 2 or 3, and

wherein any CH₂-group contained in the residues which R³ represents may be substituted with one or two (C₁-C₄)-alkyl-residues,

X represents CR⁴ or N,

R⁴ represents hydrogen or halogen,

Z represents a bond or an alkyl-chain having one, two, three or four carbon atoms,

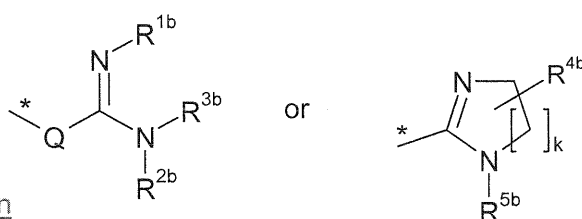
whereby the alkyl-chain may be substituted with one, two, three or four substituents, selected independently of one another from the group consisting of carboxy, aminocarbonyl and (C₁-C₄)-alkyl,

whereby alkyl in turn may be substituted with a substituent selected from the group consisting of hydroxy, carboxy and aminocarbonyl,

Y represents a bond, O, NH or S,

A represents (C₆-C₁₀)-aryl or 5- to 10-membered heteroaryl,

whereby aryl and heteroaryl are substituted with a substituent of the following formula



wherein

R^{1b}, R^{2b} and R^{3b} independently of one another represent hydrogen, amino, hydroxy, (C₁-C₄)-alkyl, (C₁-C₄)-alkoxy, (C₃-C₆)-cycloalkyl, 4-, 5- 6- or 7-membered heterocyclyl or 5- or 6-membered heteroaryl,

whereby amino and hydroxy may be substituted with one or two substituents selected independently of one another from the group consisting of carbonyl, (C₁-C₄)-alkylcarbonyl, mono- or di-(C₁-C₄)-alkylaminocarbonyl, and (C₁-C₄)-alkyl,

whereby alkoxy, heterocyclyl and heteroaryl may be substituted with one, two or three substituents selected independently of one another from the group consisting of halogen, hydroxy, amino, carbonyl, carboxy, (C₁-C₄)-alkylcarbonyl, (C₁-C₄)-alkoxy, mono- or di-(C₁-C₄)-alkylamino, mono- or di-(C₁-C₄)-alkylaminocarbonyl, -NH-CH(=NH), -NH-C(=NH)(NH₂), -C(=NH)CH₃ and (C₁-C₄)-alkyl, and

whereby alkyl and cycloalkyl may be substituted with one, two or three substituents selected independently of one another from the group consisting of halogen, hydroxy, amino, carbonyl, carboxy, carbonyloxy, aminocarbonyl, carbonylamino, (C₁-C₄)-alkylcarbonyl, (C₁-C₄)-alkoxy, mono- or di-(C₁-C₄)-alkylamino, mono- or di-(C₁-C₄)-alkylaminocarbonyl, -NH-CH(=NH), -NH-C(=NH)(NH₂), -CH(=NH)CH₃, (C₆-C₁₀)-aryl, 5- or 6-membered heteroaryl and 5- or 6-membered heterocyclyl,

whereby heteroaryl and heterocyclyl in turn may be substituted with (C₁-C₄)-alkyl, and

whereby amino in turn may be substituted with 5- or 6-membered heteroaryl, or

R^{2b} and R^{3b} together with the nitrogen atom to which they are bonded form a 5- to 7-membered heterocycle including one, two or three further heteroatoms selected from the series N, O and S and R^{1b} is as defined above,

R^{4b} represents hydrogen, amino, hydroxy, (C₁-C₄)-alkyl or (C₁-C₄)-alkoxy,

whereby amino and hydroxy may be substituted with one or two substituents selected independently of one another from the group consisting of (C₁-C₄)-alkylcarbonyl, mono- or di-(C₁-C₄)-alkylaminocarbonyl and (C₁-C₄)-alkyl,

whereby alkoxy may be substituted with one, two or three substituents selected independently of one another from the group consisting of halogen, hydroxy, amino, carbonyl, carboxy, (C₁-C₄)-alkylcarbonyl, (C₁-C₄)-alkoxy, mono- or di-(C₁-C₄)-alkylamino, mono- or di-(C₁-C₄)-alkylaminocarbonyl, -NH-CH(=NH), -NH-C(=NH)(NH₂), -CH(=NH)CH₃ and (C₁-C₄)-alkyl, and

whereby alkyl may be substituted with one, two or three substituents selected independently of one another from the group consisting of halogen, hydroxy, amino, carbonyl, carboxy, aminocarbonyl, (C₁-C₄)-alkylcarbonyl, (C₁-C₄)-alkoxy, mono- or di-(C₁-C₄)-alkylamino, mono- or di-(C₁-C₄)-alkylaminocarbonyl, -NH-CH(=NH), -NH-C(=NH)(NH₂), -CH(=NH)CH₃, (C₁-C₄)-alkyl, (C₆-C₁₀)-aryl and 5- or 6-membered heteroaryl,

R^{5b} represents hydrogen or (C₁-C₄)-alkyl,

Q represents a bond, CH₂ or NH,

k represents an integer 1 or 2, and

* is the linkage site to the residue represented by A, and

whereby aryl and heteroaryl further may be substituted with one or two substituents selected independently of one another from the group consisting of halogen, cyano, amino, hydroxy, (C₁-C₄)-alkyl, (C₁-C₄)-alkoxy, mono- or di-(C₁-C₄)-alkylamino, amino-(C₁-C₄)-alkyl, hydroxy-(C₁-C₄)-alkyl or carboxy,

whereby alkyl, alkoxy, alkylamino, aminoalkyl, hydroxyalkyl and carboxy in turn may be substituted with a substituent selected from the group consisting of halogen, (C₁-C₄)-alkyl and carbonyl, and

l represents an integer 0, 1, 2 or 3,

and the salts thereof, the solvates thereof and the solvates of the salts thereof.

In another aspect, there is provided compound which is

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-(4-carbamimidoyl-3-hydroxyphenoxy)ethoxy]imino)-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

(2S,3S)-3-([(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-(4-carbamimidoyl-3-hydroxyphenoxy)ethoxy]imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-([(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-[(6-carbamimidoylpyridin-3-yl)oxy]ethoxy]imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-[(6-carbamimidoylpyridin-3-yl)oxy]ethoxy]imino)-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

(2S,3S)-3-([(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-[(5-carbamimidoylpyridin-2-yl)oxy]ethoxy]imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-([(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-[(4-carbamimidoylphenyl)sulfanyl]ethoxy]imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-[(4-carbamimidoylphenyl)sulfanyl]ethoxy]imino)-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

(2S,3S)-3-([(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-[(4-carbamimidoylphenyl)amino]ethoxy]imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-([(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-(4-carbamimidoylphenoxy)ethoxy]imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-(4-carbamimidoylphenoxy)ethoxy]imino)-N-[(2R,3S)-2-methyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

(2R,3S)-3-([2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-(4-carbamimidoylphenoxy)ethoxy]imino)-acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

[2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-(4-carbamimidoylphenoxy)ethoxy]imino)acetyl]amino)-2-methyl-4-oxoazetidin-1-yl]oxy}methanesulfonic acid

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-(4-carbamimidoyl-3-methylphenoxy)ethoxy]imino)-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

(2S,3S)-3-([2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-(4-carbamimidoyl-3-methylphenoxy)ethoxy]imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-(4-carbamimidoylpyridin-4-yl)oxy]ethoxy]imino)-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-(4-carbamimidoylphenoxy)ethoxy]imino)-N-[2-oxo-1-(sulfooxy)-1-azaspiro[3.4]oct-3-yl]ethanamide

(2S,3S)-3-([2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-(4-carbamimidoylphenoxy)-2-methyl-propoxy]imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-([2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([1-(4-carbamimidoylphenoxy)-2-methylpropan-2-yl]oxy]imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-([2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-(4-carbamimidoyl-2-fluorophenoxy)ethoxy]imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-([2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-(4-carbamimidoyl-2-chlorophenoxy)ethoxy]imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-([2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-(4-(N-hydroxycarbamidoyl)-phenoxy]ethoxy]imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-(4-carbamimidoylpyridin-2-yl)oxy]ethoxy]imino)-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]-2-([4-[N-(piperidin-4-yl)carbamimidoyl]phenoxy]ethoxy]imino)ethanamide

(2Z)-2-([2-(4-[N-(2-Aminoethyl)carbamimidoyl]phenoxy)ethoxy]imino)-2-(2-amino-1,3-thiazol-4-yl)-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-(4-(4,5-dihydro-1H-imidazol-2-yl)phenoxy]ethoxy]imino)-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

(2S and 2R)-2-([2-(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-[(2S,3S)-2-methyl-4-oxo-1-sulfoazetidin-3-yl]amino)-2-oxoethylidene]amino)oxy)-3-(4-carbamidinoyl-phenoxy)propanoic acid

(2S and 2R)-2-([2-(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)-azetidin-3-yl]amino)-2-oxoethylidene]amino)oxy)-3-(4-carbamimidoylphenoxy)propanoic acid

(2S,3S)-3-([(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({2-[(6-carbamimidoylpyridazin-3-yl)oxy]ethoxy}-imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({2-[(6-carbamimidoylpyridazin-3-yl)oxy]-ethoxy}imino)-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

(2S,3S)-3-([(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({2-[(5-carbamimidoylpyrazin-2-yl)oxy]-ethoxy}imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-([(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({2-[(4-carbamimidoyl-1,3-thiazol-2-yl)oxy]-ethoxy}imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-([(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-(2-[(4-carbamimidoylthiophen-2-yl)methoxy]-imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({2-[(6-carbamimidoyl-5-hydroxypyridin-3-yl)oxy]ethoxy}-imino)-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

(2S and 2R)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)-azetidin-3-yl]amino}-2-oxoethylidene]amino}oxy)-3-(4-carbamimidoyl-3-hydroxyphenoxy)propanoic acid

(2S,3S)-3-([(2Z)-2-([2-(2-Amino-4-carbamimidoylphenoxy)ethoxy]imino)-2-(2-amino-1,3-thiazol-4-yl)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S and 2R)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)-azetidin-3-yl]amino}-2-oxoethylidene]amino}oxy)-3-[(6-carbamimidoylpyridin-3-yl)oxy]propanoic acid

(2S, 3S)-3-([(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({3-(4-carbamimidoylphenoxy)propoxy}-imino)-acetyl]-amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-N-[(3S)-1-hydroxy-2,2-dimethyl-4-oxoazetidin-3-yl]-2-({2-[4-(N-2-[(iminomethyl)amino]ethyl)carbamimidoyl]phenoxy]ethoxy}imino)ethanamide

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]-2-([2-(4-[N-[(3S)-pyrrolidin-3-yl]carbamimidoyl]phenoxy)ethoxy]imino)ethanamide

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-(4-[N-2-(dimethylamino)ethyl]carbamimidoyl]phenoxy)-ethoxy]imino)-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-([2-(4-carbamimidoylphenoxy)ethoxy]imino)-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

(4S)-4-({[4-[2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)-azetidin-3-yl]amino}-2-oxo-ethylidene]-amino}-oxy)-ethoxy]-phenyl](imino)methyl]-amino)-N,N-dimethyl-L-prolinamide

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]-2-([2-(4-[N-[(3S)-1-ethanimidoylpyrrolidin-3-yl]carbamimidoyl]phenoxy)ethoxy]imino)ethanamide

(2R and 2S)-3-{4-[N-(2-Aminoethyl)carbamimidoyl]phenoxy}-2-({[(1Z)-1-(2-amino-1,3-thiazol-4-yl)-2-({[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino}-2-oxoethylidene]-amino}-oxy)-propanoic acid

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({[(2R and 2S)-1-(4-carbamimidoylphenoxy)-3-hydroxypropan-2-yl]oxy}imino)-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

3-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-({[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino}-2-oxoethylidene]amino}oxy)-4-(4-carbamimidoylphenoxy)butanoic acid

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({[2-(4-carbamimidoylphenoxy)ethoxy]imino}-N-[(2S,3S)-2-methyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

(2R,3S)-3-({[(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({[3-(4-carbamimidoylphenoxy)propoxy]imino}-acetyl]amino}-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-({[(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({[2-(2-bromo-4-carbamimidoylphenoxy)ethoxy]imino}acetyl]amino}-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-({[(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({[2-(4-carbamimidamidophenoxy)ethoxy]imino}acetyl]amino}-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-({[(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({[3-(4-carbamimidamidophenoxy)propoxy]imino}acetyl]amino}-2-methyl-4-oxoazetidine-1-sulfonic acid

(2Z)-2-(5-Amino-1,2,4-thiadiazol-3-yl)-2-({[2-(4-carbamimidoylphenoxy)ethoxy]imino}-N-[(2S,3S)-1-hydroxy-2-methyl-4-oxoazetidin-3-yl]ethanamide

(2S,3S)-3-({[(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({[2-(3-carbamimidoylphenoxy)ethoxy]imino}acetyl]amino}-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-({[(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({[2-{4-[N-(propan-2-yl)carbamimidoyl]phenoxy}ethoxy]imino}acetyl]amino}-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-({[(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({[4-carbamimidoylbenzyl]oxy]imino}acetyl]amino}-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-({[(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({[2-{4-carbamimidoylthiophen-2-yl]methoxy]ethoxy]imino}acetyl]amino}-2-methyl-4-oxoazetidine-1-sulfonic acid

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({[4-carbamimidoylbenzyl]oxy]imino}-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({[3-(4-carbamimidoylphenoxy)propoxy]imino}-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

(2S,3S)-3-({[(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({[2-{4-carbamimidoyl-2-(hydroxymethyl)phenoxy]ethoxy]imino}acetyl]amino}-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-({[(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({[2-{4-carbamimidoyl-2-[(formyloxy)methyl]phenoxy]ethoxy]imino}acetyl]amino}-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-([(2Z)-2-(2-Amino-5-chloro-1,3-thiazol-4-yl)-2-[2-(4-carbamimidoylphenoxy)ethoxy]imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-([(2Z)-2-({2-[4-(2-Amino-2-iminoethyl)phenoxy]ethoxy}imino)-2-(2-amino-1,3-thiazol-4-yl)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-([(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-[2-[4-[(2-formylhydrazinyl)(imino)methyl]phenoxy]ethoxy]imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-([(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-[2-[4-[hydrazinyl(imino)methyl]phenoxy]ethoxy]imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-([(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({2-[(5-carbamimidoyl-1,3,4-thiadiazol-2-yl)oxy]ethoxy}imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-([(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-[2-(4-carbamimidoylphenoxy)ethoxy]imino)acetyl]amino)-2-carbamoyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-([(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({2-[(3-carbamimidoyl-1,2-oxazol-5-yl)oxy]ethoxy}imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-([(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({2-[4-(N-methylcarbamimidoyl)phenoxy]ethoxy}imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-([(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-[2-[4-[N-(2-hydroxyethyl)carbamimidoyl]phenoxy]ethoxy]imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-([(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-[2-[4-[N-[2-(formyloxy)ethyl]carbamidoyl]phenoxy]ethoxy]imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-([(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({2-[(3-carbamimidoyl-1-methyl-1H-pyrazol-5-yl)oxy]ethoxy}imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

(2S,3S)-3-([(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({2-[(5-carbamimidoyl-1-methyl-1H-pyrazol-3-yl)oxy]ethoxy}imino)acetyl]amino)-2-methyl-4-oxoazetidine-1-sulfonic acid

N-[4-[2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino)-2-oxoethylidene]amino}oxy)ethoxy]phenyl](imino)methyl]glycine

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({2-[(2-carbamimidoyl-5-methyl-1,3-thiazol-4-yl)oxy]ethoxy}imino)-N-[[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino)-2-oxoethylidene]amino}oxy)-3-(4-carbamimidoylphenoxy)propanamide

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-N-[[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]-2-[2-[4-[N-(pyridin-2-ylmethyl)carbamimidoyl]phenoxy]ethoxy]imino]ethanamide

[(2S,3S)-3-([(2Z)-2-[2-[4-[N-(2-Aminoethyl)carbamimidoyl]phenoxy]ethoxy]imino)-2-(2-amino-1,3-thiazol-4-yl)acetyl]amino)-2-methyl-4-oxoazetidin-1-yl]oxy]methanesulfonic acid

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-[(2-{4-[N-(2-carbamimidamidoethyl)carbamimidoyl]-phenoxy}ethoxy)imino]-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

1-(2-{[4-[2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino]-2-oxoethylidene]amino}oxy)ethoxy]phenyl}{(imino)-methyl]amino}ethyl)-1-methylpyrrolidinium chloride

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]-2-[(2-{4-[imino(piperazin-1-yl)methyl]phenoxy}ethoxy)imino]ethanamide

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-({[1-(4-carbamimidoylphenoxy)-(2R and 2S)-4-hydroxybutan-2-yl]oxy}imino)-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

(2Z)-2-{[2-({6-[N-(2-Aminoethyl)carbamimidoyl]pyridin-3-yl}oxy)ethoxy]imino}-2-(2-amino-1,3-thiazol-4-yl)-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

(2Z)-2-[(2-{4-[N-(3-Aminopropyl)carbamimidoyl]phenoxy}ethoxy)imino]-2-(2-amino-1,3-thiazol-4-yl)-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-[(2-{4-[N-(1,3-diaminopropan-2-yl)carbamimidoyl]-phenoxy}ethoxy)imino]-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

(2Z)-2-{[2-(4-{N-[(2R)-1-Amino-3-hydroxypropan-2-yl]carbamimidoyl]phenoxy}ethoxy)imino]-2-(2-amino-1,3-thiazol-4-yl)-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

(2Z)-2-({2-[4-(5-Amino-1,4,5,6-tetrahydropyrimidin-2-yl)]phenoxy}ethoxy)imino)-2-(2-amino-1,3-thiazol-4-yl)-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

(2R and 2S) 3-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino]-2-oxoethylidene]amino}oxy)-2-(4-carbamimidoylphenoxy)propanoic acid

(2S)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino]-2-oxoethylidene]amino}oxy)-3-(4-{N-[(3R)-piperidin-3-yl]carbamimidoyl}phenoxy)-propanoic acid

(2R)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]-amino]-2-oxoethylidene]amino}oxy)-3-(4-{N-[(3R)-piperidin-3-yl]carbamimidoyl}phenoxy)-propanoic acid

{[(3S)-3-({[(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-[(4-carbamimidoylbenzyl]oxy)imino}acetyl]amino)-2,2-dimethyl-4-oxoazetidin-1-yl]oxy}methanesulfonic acid

(2Z)-2-[(2-{4-[5-(Aminomethyl)-4,5-dihydro-1H-imidazol-2-yl]phenoxy}ethoxy)imino]-2-(2-amino-1,3-thiazol-4-yl)-N-[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]ethanamide

(3S)-3-({[(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-[(2-{4-[N-(pyrazolidin-4-yl)carbamimidoyl]-phenoxy}ethoxy)imino]acetyl]amino)-2,2-dimethyl-4-oxoazetidine-1-sulfonic acid

(2S)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-({[(3S)-2,2-dimethyl-4-oxo-1-sulfoazetidin-3-yl]-amino}-2-oxoethylidene)amino}oxy]-3-(4-{N-[(3S)-pyrrolidin-3-yl]carbamidoyl}phenoxy)propanoic acid

(2S)-3-{4-[N-(2-Amino-2-methylpropyl)carbamidoyl]phenoxy}-2-({[(1Z)-1-(2-amino-1,3-thiazol-4-yl)-2-({[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino}-2-oxoethylidene)amino}oxy]propanoic acid

(2S)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-({[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino}-2-oxoethylidene)amino}oxy]-3-(4-{N-[2-(methylamino)ethyl]carbamidoyl}phenoxy)propanoic acid

(2S)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-({[(3S)-2,2-dimethyl-4-oxo-1-sulfoazetidin-3-yl]amino}-2-oxoethylidene)amino}oxy]-3-(4-{N-[(3R)-pyrrolidin-3-yl]carbamidoyl}phenoxy)propanoic acid

(2S)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-({[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino}-2-oxoethylidene)amino}oxy]-3-{4-[N-(piperidin-3-yl)carbamidoyl]phenoxy}propanoic acid

(2S)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-({[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino}-2-oxoethylidene)amino}oxy]-3-{4-[N-(pyrrolidin-2-ylmethyl)-carbamidoyl]phenoxy}propanoic acid

(2S)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-({[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino}-2-oxoethylidene)amino}oxy]-3-{4-[N-(piperidin-2-ylmethyl)-carbamidoyl]phenoxy}propanoic acid

(2S)-3-{4-[N-(trans-(R,R and S,S)-2-Aminocyclopropyl)carbamidoyl]phenoxy}-2-({[(1Z)-1-(2-amino-1,3-thiazol-4-yl)-2-({[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino}-2-oxoethylidene)amino}oxy]propanoic acid

(2S)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-({[(3S)-2,2-dimethyl-4-oxo-1-sulfoazetidin-3-yl]-amino}-2-oxoethylidene)amino}oxy]-3-(4-{N-[(3S)-1-methylpyrrolidin-3-yl]carbamidoyl}-phenoxy)-propanoic acid

(2S)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-({[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino}-2-oxoethylidene)amino}oxy]-3-{4-[N-(1,3-diaminopropan-2-yl)carbamidoyl]phenoxy}propanoic acid

(2R)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-({[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino}-2-oxoethylidene)amino}oxy]-3-{4-[N-(1,3-diaminopropan-2-yl)-carbamidoyl]phenoxy}propanoic acid

(2S)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-({[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino}-2-oxoethylidene)amino}oxy]-3-{4-[N-(1H-imidazol-2-ylmethyl)-carbamidoyl]phenoxy}propanoic acid

(2R)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-({[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino}-2-oxoethylidene)amino}oxy]-3-{4-[N-(1H-imidazol-2-ylmethyl)-carbamidoyl]phenoxy}propanoic acid

(2S)-3-{4-[N-(4-Aminopyrrolidin-3-yl)carbamimidoyl]phenoxy}-2-({[(1Z)-1-(2-amino-1,3-thiazol-4-yl)-2-({[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino}-2-oxoethylidene]amino}oxy)propanoic acid

(2S)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-({[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino}-2-oxoethylidene]amino}oxy)-3-{4-[N-(azetidin-3-yl)carbamimidoyl]phenoxy}propanoic acid

(2S)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-({[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino}-2-oxoethylidene]amino}oxy)-3-{4-[N-(piperidin-4-yl)carbamimidoyl]phenoxy}propanoic acid

(2S)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-({[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino}-2-oxoethylidene]amino}oxy)-3-{4-[N-(azetidin-3-yl)carbamimidoyl]phenoxy}propanoic acid

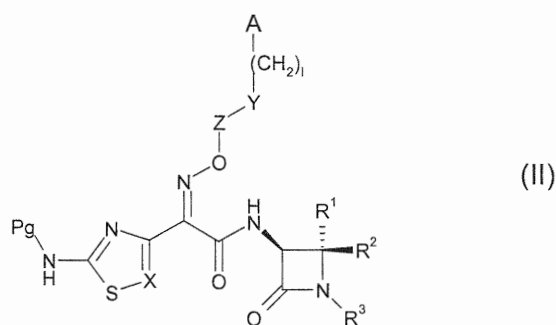
(2S)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-({[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino}-2-oxoethylidene]amino}oxy)-3-{4-[N-[2-(pyrimidin-2-ylamino)ethyl]carbamimidoyl]-phenoxy}propanoic acid

(2R)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-({[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino}-2-oxoethylidene]amino}oxy)-3-{4-[N-[2-(pyrimidin-2-ylamino)ethyl]carbamimidoyl]-phenoxy}propanoic acid

and the salts thereof, the solvates thereof and the solvates of the salts thereof.

In yet another aspect, there is provided the use of a compound as disclosed herein for the manufacture of a medicament for treating and/or preventing diseases, in particular bacterial infections, especially with Gram- negative bacteria.

In yet another aspect, there is provided a method for the preparation of a compound of formula (I) as disclosed above comprising removing the protecting group from a compound of formula



in which Pg represents a protecting group and R¹-R³, A, l, X, Y and Z are as defined above.

In yet another aspect, there is provided the use of a compound as disclosed herein for the manufacture of a medicament for the treatment and/or prophylaxis of diseases.

In yet another aspect, there is provided the use of a compound as disclosed herein for the manufacture of a medicament for the treatment and/or prophylaxis of bacterial infections.

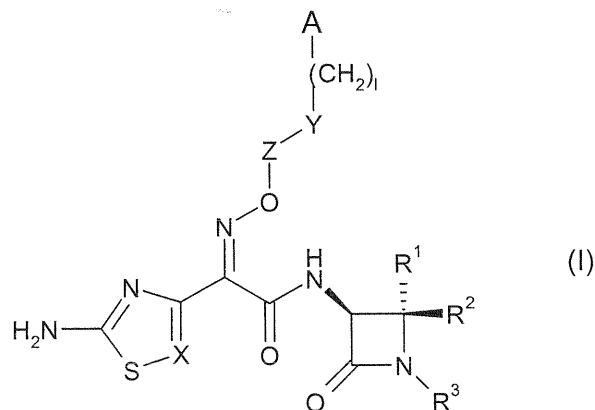
In yet another aspect, there is provided a medicament comprising at least one compound as disclosed herein in combination with at least one further active compound.

In yet another aspect, there is provided a medicament comprising at least one compound as disclosed herein in combination with at least one inert, non-toxic, pharmaceutically acceptable excipient.

In yet another aspect, there is provided the use of a medicament as disclosed herein for the manufacture of a medicament for treating and/or preventing bacterial infections.

DETAILED DESCRIPTION

[0007] The present invention relates to compounds of formula (I)



in which

(2S)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-{{[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino}-2-oxoethylidene]amino}oxy)-3-{4-[N-(azetidin-3-yl)carbamimidoyl]phenoxy}propanoic acid

(2S)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-{{[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino}-2-oxoethylidene]amino}oxy)-3-{4-[N-(piperidin-4-yl)carbamimidoyl]phenoxy}propanoic acid

(2S)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-{{[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino}-2-oxoethylidene]amino}oxy)-3-{4-[N-(azetidin-3-yl)carbamimidoyl]phenoxy}propanoic acid

(2S)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-{{[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino}-2-oxoethylidene]amino}oxy)-3-{4-{N-[2-(pyrimidin-2-ylamino)ethyl]carbamimidoyl}-phenoxy}propanoic acid

(2R)-2-({[(1Z)-1-(2-Amino-1,3-thiazol-4-yl)-2-{{[(3S)-2,2-dimethyl-4-oxo-1-(sulfooxy)azetidin-3-yl]amino}-2-oxoethylidene]amino}oxy)-3-{4-{N-[2-(pyrimidin-2-ylamino)ethyl]carbamimidoyl}-phenoxy}propanoic acid

and the salts thereof, the solvates thereof and the solvates of the salts thereof.

9. Use of a Ccompound according to any one of claims 1 to 8 for ~~use in the manufacture of a medicament for a method of~~ treating and/or preventing diseases, in particular bacterial infections, especially with Gram- negative bacteria.

in which R^1 , R^2 and R^3 are as defined in claim 1.

- ~~12.~~ ~~Use of a compound according to any one of claims 1 to 9 for the treatment and/or prophylaxis of diseases.~~
- ~~13~~12. Use of a compound according to any one of claims 1 to ~~9~~8 for the manufacture of a medicament for the treatment and/or prophylaxis of diseases.
- ~~14~~13. Use of a compound according to any one of claims 1 to ~~9~~8 for the manufacture of a medicament for the treatment and/or prophylaxis of bacterial infections.
- ~~15~~14. Medicament comprising at least one compound according to any one of claims 1 to ~~9~~8 in combination with at least one further active compound.
- ~~16~~15 Medicament according to claim ~~15~~14, characterized in that the further active compound is a β -lactamase inhibitor.
- ~~17~~16. Medicament comprising at least one compound according to any one of claims 1 to ~~9~~8 in combination with at least one inert, non-toxic, pharmaceutically acceptable excipient.
- ~~18~~17. Use of a Medicament according to any one of claims ~~15~~14 to ~~17~~16 for ~~use in the manufacture of a medicament for a method of treating and/or preventing bacterial infections.~~
- ~~19.~~ ~~Method for controlling bacterial infections in humans and animals by administering an antibacterially effective amount of at least one compound according to any one of claims 1 to 9 or a medicament according to any one of claims 15 to 18.~~