United States Patent [19]
Grohe et al.


[54] 7-AMINO-1-CYCLOPROPYL-4-OXO-1, 4-DIHYDROQUINOLINE-AND NAPHTHYRIDINE-SCARBOXYLIC ACIDS AND ANTI-BACTERIAL AGENTS CONTAINING THESE COMPOUNDS


[21] Appl. No.: 654,923
[22] Filing Date: May 25, 1984

Related U.S. Application Data


[56] References Cited

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3,946,713 7/1976 Ikuta et al. 346/363
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[57] ABSTRACT

The invention relates to 7-amino-1-cyclopropyl-4-oxo-1,4-dihydroquinoline (or quinoline)-carboxylic acids of Formula I as defined in the specification. Also included in the invention is a process for the preparation of said compounds of Formula I or Ia. Further, the invention includes compositions containing the compounds of Formula I or Ia and the use of said compositions as antibacterial agents.

22 Claims, No Drawings

This partial patent contains the key elements:

(1) classification codes ⇒ 514/300 is the main one
(2) Background
(3) Examples ⇒ aka “experimental”
(4) Claims ⇒ This is the most important and carefully written section. If something is not in the claims section, then it will not have any patent protection.
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7-AMINO-3-CYCLOPROPYL-4-OXO-1,
4-DIHYDRO-QUINOLINE-3-CARBONYL ACIDS AND
ANTIBACTERIAL AGENTS CONTAINING THESE
COMPONDS

This application is a continuation-in-part of our application
Ser. No. 292,560 filed Aug. 12, 1981, now aban-
10 doned and a continuation-in-part of our application Ser.
No. 436,112 filed Oct. 22, 1982 now abandoned.

The present invention relates to certain 7-aminoo-3-
cyclopropyl-4-oxo-4,6-dihydro-quinoline-3-carbonyl
15 acids with antibacterial properties [see J. Med. Chem., 12, 29,
1979; 36, 541-547 (1977); and it has also been disclosed that 1-
ethyl-1,4-dihydropyridine-6,7-diones have antibacterial
20 properties]. The compounds of the present invention are pro-
vided by the general formula 7-aminoo-3-cyclopropyl-4-
25 oxo-1,4-dihydroquinoline and 7-aminoo-3-carbonyl
acids of the formula

or a salt thereof,

in which A represents a nitrogen atom or C=O,

wherein R1 means a hydroxy, a nitro group or a halogen (preferably a chlorine or bromine atom),
or a nitro, carbamoyl, carboxyl or ester group,
or an acylamino, amino or (aryl or hydroxy)-amino group, or C=H, and A and Z are
30 not necessarily nitrogen atoms, and R1 and
R2 are identical or different and represent a hydroxyl atom or a straight-chain or branched alkyl (alkenyl or alkyl)
radical which has up to 12 carbon atoms and is optionally substituted by radical(s) selected from hydroxyl, alkoxy, alkoxycarbonyl or
dialkylamino with up to 3 carbon atoms in each radical, nitro, alkoxy carbonyl with 1 to 4 carbon atoms in the
40 alcohol part, or aryl or heteroaryl, or furthermore represent a cycloalky1 radical with 3 to 6 carbon atoms, or, to-
tgether with the nitrogen atom which they substitute and if necessary, a further hetero-aromatic (as oxygen or nitrogen) or a 2-membered ring which can be nitro substituent disubstituted or polystituted by radical(s) selected from alkyl or alkenyl with up to 6 carbon atoms, hydroxyl, alkoxy or alkoxycarbonyl radical with 1 to 3 carbon atoms, or alkylamino, alkoxy alkylamino, or alkylaminoalkoxycarbonyl radical with 1 to 4 carbon atoms in the alcohol part, nitro group and aryl, and which can furthermore posses a double bond, and R4 represents a hydroxy group, or a branch or straight chain alkyl, aralkyl or alkyl amine group which has up to 6 carbon atoms and is optionally
substituted by (radically) selected from hydroxyl, alk-
50 oxy, alkoxy carbonyl or dialkylamino groups per alkyl radical and alkoxycarbonyl with 1 to 4 carbon atoms in the alcohol part,
or represents an alkyl group which is optionally substituted in the aryl radical by C1-C8 alkyl, halogen, preferably chlorine, NO2 and/or NH2 and has up to 4 (preferably 1) carbon atoms in the aliphatic part, or an optionally substituted phenyl or naphthyl group in a heterocyclic radical (such as a radical of pyridine, pyrimidine, thiazol or benzoazole), or R4 denotes an alkoxycarbonyl group which is optionally substituted by an aryl radical and has 1 to 4 carbon atoms in the aliphatic part, an alkoxycarbonyl radical with 1 to 4 carbon atoms, an aryl radical, an optionally substituted C1-C8 alkyl or ar- or naph(C6) car-
tanyl radical, an C1-C8 alkyl or arylalkoxycarbonyl rad-
cal or an optionally substituted aminocarbonyl radical. As used herein and unless otherwise specified, the term "aryl" is preferably mono- or bi-cyclic aromatic aryl, such as phenyl or naphthyl; the term "alkyl" is preferably mono- or bi-cyclic aromatic aryl-C1-C8 alkyl, such as benzyl, phenethyl, naphthyl, methyl- and naphthyl-ethyl; the term "heteroaryl" is preferably mono- or bi-cyclic, 3, 4, 5- or 6- heteroaryl, such as pyridine, pyrimidine and furan, and the term "aromatic" is preferably benzenoid or naphthyl.

The compounds of the present invention have a spec-
rific antibacterial action against both gram positive and
gram negative bacteria, including pseudomonas aer-
15 genea, to that of the known quinolines and azaquinol-
one-carboxylic acids.

The aforementioned aryl radicals, preferably the phenyl or naphthyl radical, are optionally substi-
tuted disubstituted or polysubstituted by sub-
30 stituent(s) selected from halogen(s) (preferably fluoro, chlorine and/or bromine), alkoxy, alkyl or alkenyl, with 1 to 3 carbon atoms, aralkoxycarbonyl with 1 to 4 carbon atoms, aryloxycarbonyl, or alkyl or arylamino or alkylaminoalkoxycarbonyl radical with 1 to 4 carbon atoms in the alcohol part.

Further according to the present invention and within the scope of the above formulae, there are also provided as new com-
posed 1-cyclopropyl-6-oxo-1,4-dihydro-4-oxo-
quinoline-1-carboxylic acid of the general formula

(2)

or its salt.

in which R1 denotes a hydroxy group or a methyl, ethyl or trifluoromethyl group.

Suitable salts are those of inorganic or organic acids,
55 p.e. hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, phosphoric acid, oxalic acid, nico-
tinic acid, maleic acid and the like. Suitable salts are furthermore those of amino acids or organic bases, p.e. KOH, NaOH.
The ingredient can also be made up in microencapsu-
lated form together with one or several of the above-
mentioned diluents.

The diluents to be used in pharmaceutical composi-
tions adapted to be formed into suppositories can, for
example, be the usual water-soluble diluents such as
polyethylene glycols and fats (e.g. cocoa oil and high
esters (e.g. C12-16 alcohol with C16-18 fatty acid) or mixtures
of these diluents or their esters). 

The pharmaceutical compositions which are esti-
mated on the basis of these diluents, e.g. with
polyethylene glycols, may also be used in the above-
manner. However, it is also possible to use the
above-mentioned diluents which are present in
the pharmaceutical compositions. For example, the use of the
above-mentioned diluents may be used together with the
above-mentioned diluents which are present in
the pharmaceutical compositions. For example, the use of the
above-mentioned diluents may be used together with the
above-mentioned diluents which are present in
the pharmaceutical compositions. For example, the use of the
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above-mentioned diluents which are present in
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above-mentioned diluents may be used together with the
above-mentioned diluents which are present in

The pharmaceutical compositions which are powders
and sprays can, for example, contain the usual diluents,
e.g. lactose, talc, silicic acid, aluminium hydroxide, calcium
silicates, and polyalcohols or mixtures of these
substances. 

Acetaldehyde sprays can, for example, contain the
usual propellants, e.g. dichlorofluorocarbons.

The pharmaceutical compositions which are solu-
tions and emulsions can, for example, contain the cat-
ionic diluents (with, of course, the above-mentioned
exclusion of solvents having a molecular weight below
200 and except in the presence of a surface-active agent),
such as solvents, suspending agents and emulsifiers. 

Cyclic examples of such diluents are water, ethyl alcohol,
isoamyl alcohol, ethyl carbitol, ethyl lactate, benzyl
alcohol, safflower oil, propylene glycol, 1,3-buty-
lactone, glycylidene dimethyl etheramine, oils (for example
ground nuts oil, glicerol, lauryldihydrofatty acids), alcohol,
propylene glycol and fatty acid esters of herbal or
mixtures thereof. 

For parenteral administration, solutions and emul-
sions should be sterile, and, if appropriate, blood-so-
containing.

The pharmaceutical compositions which are sus-
pensions can contain the usual diluents, such as liquid di-
rides, e.g. water, ethyl alcohol, propylene glycol, sur-
face-active agents (e.g. ethylated mono-esters) alcohols,
polysaccharides stearite and surfactants, starches,
hydrocrystalline cellulose, aluminium hydroxide, buns,
together with gases or mixtures thereof.

All the pharmaceutical compositions according to
the invention can also contain the following agents and preser-
vatives as well as perfumes and flavouring additions
(e.g. peppermint oil and menthol oil) and sweetening
agents, e.g. saccharin.

The pharmaceutical compositions according to
the invention generally contain from 0.1 to 90.0% usually
from 0.5 to 95.0% of the active ingredient by weight of
the total composition.

In addition to a component of the invention, the phar-
macological compositions and medicaments according to
the invention can also contain other pharmacologically
active compounds. They may also contain a plurality of
components of the like kind.

Any diluents in the medicaments of the present inven-
tion may be any of those mentioned above in relation to the
pharmaceutical compositions of the previous inven-
tion. Such medicaments may include solvents of molecu-
lar weight less than 200 as diluent.

The discrete droplets portions containing the exc-
ipients according to the invention will generally be
adapted by virtue of their shape or packaging for medi-
cal administration and may, for example, any of the
following tablets (including biometrics and granulates),
pills, dragees, capsules, suppositories and ampoules.

Some of these forms may be made up directly re-
lease of the active ingredient in a form of a pharma-
aceutical composition (e.g. granulates) and then form-
ing the composition into the medicament (e.g. tab-
lets).

The invention further provides a method of con-
stanting the above-mentioned diseases in waste-blooded
animals, which comprises administering to the animals
a component of the invention or in admixture with a
diluent or in a form of a medicament according to the
invention.

The provision of new bacillus for combating bacteria which are resistant to known bacillus as is
the case with competing of the printing invention is an
eminent of the state of the art.

The following examples illustrated but do not limit the
invention.

EXAMPLE 1

7-[4-(Methylsulpho) 1-cyclopenta -4-oxo-14-
hydroxy-13,14-dihydro-13,14-dihydrofumaroyl-3-carboxyl acid (a com-
pound of formula (I) which is KPaN=4-carboxyl-
piperazino. (A=H and B=CH).

A suspension of 2.46 g of 7-alpha-methylfuran-14-
ol-1,4-oxo-14-1,4-dihydro-13,14-dihydrofumaroyl-3-carboxyl
acid and 2.5 g of N-(4-methylpip-
erazino) -1-cyclopenta-4-oxo-1,4-dihydro-13,14-dihydrofumaroyl-
3-carboxyl (94% of the theoretical yield) of 7-[4-(Methyl-
sulpho) 1-cyclopenta -4-oxo-1,4-dihydro-13,14-dihydro-
13,14-dihydrofumaroyl-3-carboxyl acid of melting point 300° C.
(1-hydrochloride) (decomposition) were obtained.

EXPERIMENTAL METHOD

The carbonylic acids of Example 2 to 10 were ob-
tained by a procedure analogous to that in Example 1.

They are summarized in Table 1. The labeling of the
radicals R1 and R2 relates to the formula (I) of the de-
scription.

<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
<th>R1</th>
<th>R2</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>CH</td>
<td>CH3</td>
<td>CH3</td>
</tr>
<tr>
<td>3</td>
<td>CH</td>
<td>CH3</td>
<td>CH3</td>
</tr>
<tr>
<td>4</td>
<td>CH</td>
<td>CH3</td>
<td>CH3</td>
</tr>
<tr>
<td>5</td>
<td>CH</td>
<td>CH3</td>
<td>CH3</td>
</tr>
<tr>
<td>6</td>
<td>CH</td>
<td>CH3</td>
<td>CH3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
<th>R1</th>
<th>R2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>OH</td>
<td>CH3</td>
<td>CH3</td>
</tr>
<tr>
<td>2</td>
<td>OH</td>
<td>CH3</td>
<td>CH3</td>
</tr>
<tr>
<td>3</td>
<td>OH</td>
<td>CH3</td>
<td>CH3</td>
</tr>
<tr>
<td>4</td>
<td>OH</td>
<td>CH3</td>
<td>CH3</td>
</tr>
<tr>
<td>5</td>
<td>OH</td>
<td>CH3</td>
<td>CH3</td>
</tr>
</tbody>
</table>

The carbonylic acids of Example 2 to 10 were ob-
tained by a procedure analogous to that in Example 1.

They are summarized in Table 1. The labeling of the
radicals R1 and R2 relates to the formula (I) of the de-
scription.
<table>
<thead>
<tr>
<th>Example No.</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>Decomposition Temp. (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>N</td>
<td>CH₃</td>
<td>C₆H₄N⁺NCH₂CH₂⁺</td>
<td>(hydrochloride)</td>
</tr>
<tr>
<td>2</td>
<td>N</td>
<td>H</td>
<td>C₆H₄N⁺NCH₂CH₂⁺</td>
<td>(hydrochloride)</td>
</tr>
<tr>
<td>3</td>
<td>N</td>
<td>H</td>
<td>C₆H₄N⁺NCH₂CH₂⁺</td>
<td>(hydrochloride)</td>
</tr>
<tr>
<td>4</td>
<td>CF</td>
<td>H</td>
<td>C₆H₄N⁺NCH₂CH₂⁺</td>
<td>(hydrochloride)</td>
</tr>
<tr>
<td>5</td>
<td>CF</td>
<td>CH₃</td>
<td>C₆H₄N⁺NCH₂CH₂⁺</td>
<td>(hydrochloride)</td>
</tr>
<tr>
<td>6</td>
<td>CN</td>
<td>N</td>
<td>C₆H₄N⁺NCH₂CH₂⁺</td>
<td>(hydrochloride)</td>
</tr>
<tr>
<td>7</td>
<td>CN</td>
<td>N</td>
<td>C₆H₄N⁺NCH₂CH₂⁺</td>
<td>(hydrochloride)</td>
</tr>
</tbody>
</table>

#### EXAMPLE 25

Preparation of precursors

6-Chloro-4-CON₂-methoxy carbonyl-A^-ethyl-2-amino-4-propylidene-3-carboxylic acid methyl ester (a compound of formula V) in which R = methyl and X = chloride.

A mixture of 26.6 g of β-cyclopropylamino-propionic acid methyl ester and 21 g of triethylamine was rapidly added dropwise to a solution of 41.2 g of 4,6-dichloro-3-pyridine-1-carboxylic acid methyl ester in 150 ml of toluene at 10 to 20 °C, whilst cooling with ice and stirring. The ice-bath was removed and the mixture was stirred at room temperature for 4 hours and heated to the boiling point under reflux for 3 hours. The resulting suspension was washed with water and dried with Na₂SO₄, and the solvent was distilled off in vacuo. 59 g of the title compound were obtained as a brown oil. (b) The β-cyclopropylamino-propionic acid methyl ester.

This compound, used as a reagent in Example 25(a), was prepared as follows:

86 g of freshly distilled methyl acetate which had been cooled to -60 °C was added dropwise to a solution, which had been cooled to -60 °C to -70 °C, of 57 g of cyclopropylamine in 150 ml of ethanol in the course of about 3 hours. The mixture was then allowed to slowly rise to room temperature overnight; the solvent was distilled off in vacuo and the residue was then fractionated. 95 g of β-cyclopropylamino-propionic acid methyl ester was passed over 85°-90°C, 22 mm Hg. (A) 7-Chloro-1-cyclopropyl-4-CON₂-1,2,3,6-tetrahydro-1,6-methylenedioxy-3-carboxylic acid methyl ester (a compound of formula VII) in which R = methoxy and X = chloride.

99 g of crude 6-chloro-4-(N₂-methoxy carbonyl-3-pyridine-1-carboxylic acid methyl ester were distilled in 240 ml of anhydrous toluene, and 33 g of p-toluene sulfonic acid were rapidly added, whilst stirring. The mixture was left to stand overnight, 20 g of glacial acetic acid and 160 ml of water were added, the plates were separated, the toluene solution was washed again with water and dried with Na₂SO₄ and the toluene was stripped off in vacuo. After recrystallisation from methanol, 18 g of the carboxylic acid and 25 ml of melting point 140° to 157° C. were obtained.

(5) 7-Chloro-1-cyclopropyl-4-CON₂-1,4-dihydro-1,6-ethylenedioxy-3-carboxylic acid methyl ester (a compound of formula VIII) in which R = methoxy and X = chloride.

5.8 g of the tetrahydroxyphenylacetic acid methyl ester prepared according to Example 25(b) were dialysed in 200 ml of methylene chloride, and a solution of 5.9 g of benzene in 40 ml of CH₂Cl₂ was added in further 10 minutes. 8 g of triethylamine were added and the ice-bath was removed. The mixture was subsequently stirred for 3 hours, washed twice with water and dried with Na₂SO₄, the solvent was distilled off in vacuo and the residue was recrystallised from dimethyl formamide/ethanol. 8.8 g of 7-Chloro-1-cyclopropyl-4-CON₂-1,4-dihydro-1,6-ethylenedioxy-3-carboxylic acid methyl ester of melting point 275° to 277° C. (decomp.) were obtained.

(6) 7-Chloro-1-cyclopropyl-4-CON₂-1,4-dihydro-1,6-ethylenedioxy-3-carboxylic acid (a compound of formula (II) in which R = H, A = N, Z = CH and X = chloride).

A solution of 5.7 g of potassium hydroxide in 300 ml of water was added to 27.85 g of the ester prepared according to Example 16(d). The mixture was heated to 85° to 95° C for 30 minutes, whilst stirring, and the resulting solution was filtered at room temperature and acidified with glacial acetic acid. The precipitate was filtered off, washed with water and dried at calcium chloride in a vacuum drying cabinet. 20 g of pure 7-chloro-1-cyclopropyl-4-CON₂-1,4-dihydro-1,6-ethylenedioxy-3-carboxylic acid of melting point 235° to 237° C. were obtained. (including prevention, relief and cure of the so-called carcinoma-in-situ, which comprises administration to the animal a compound of the invention alone or in admixture with a diluent or in the form of a medicament according to the invention.

The present invention further provides a feed additive comprising an active compound of the present invention in admixture with a diluent or in the form of a medicament according to the invention.

The Examples which follow illustrate the invention further.
fluoro-benzoyl-malonic acid in 30 ml of water. The solution was heated at the boil for 3 hours while stirring thoroughly, and, when cold, was extracted several times with anhydrous ether, the mounted CHCl₃ solutions were washed once with saturated NaCl solution and dried with Na₂SO₄ and the solution was distilled off in vacuo. Fractionation of the residue under a fine vacuum gave 21.8 g of ethyl 2,4-dichloro-5-fluoro-benzoyl acetic acid IX of boiling point 127° to 127.5° C. (0.10 Ib.).

A mixture of 21.1 g of ethyl 2,4-dichloro-5-fluoro-benzoyl-acetic, 16.65 g of ethyl dioxime and 18.3 g of acetic anhydride was heated at 150° C. for 3 hours. The xylene-constituents were then distilled off under a water-jacket vacuum and finally under a fine vacuum, at a bath temperature of 120° C. 253 g of crude ethyl 2,4-dichloro-5-fluoro-benzoyl-2,3-ethylene-acrylate remained. It was sufficiently pure for the further reactions.

4.3 g of cyclopropylacetic acid was added dropwise to a solution of 24.9 g of ethyl 2,4-dichloro-5-fluoro-benzoyl-2,3-ethylene-acrylate (R₁= C₂H₅) in 100 ml of anhydrous diethylene, while cooling with ice and stirring. When the exothermic reaction had ceased, the mixture was stirred again for another hour at room temperature, the solvent was stripped off in vacuo, and the residue was recrystallized from cyclohexane/petroleum ether, 22.9 g of ethyl 2,4-dichloro-5-fluoro-benzoyl-3,5-cyclopropylacetoxy-acrylate (R₂= C₂H₅) of melting point 85° to 90° C. were obtained.

3.46 g of 60 percent sodium hydride were added in portions to a solution of 31.9 g of ethyl 2,4-dichloro-5-fluoro-benzoyl-3,5-cyclopropylacetoxy-acrylate (R₂= C₂H₅) in 100 ml of anhydrous diethylene, while cooling with ice and stirring. The mixture was then stirred at room temperature for 30 minutes and under reflux for 2 hours, and the solution was stripped off in vacuo. The residue (46.2 g) was suspended in 150 ml of water, 6.65 g of caustic potash were added, and the mixture was heated to 85° C. The warm solution was filtered, and the residue was rinsed with H₂O. The filtrate was then acidified to pH=4 with 2 with monochromatous hydrochloric acid, while cooling with ice, and the precipitate was filtered off under suction, washed with water and dried in vacuo at 100° C. 37.7 g of ethyl-2-cyclopropyl-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid (R₂= C₂H₅) of melting point 204° to 207° C. were obtained in this manner.

The present invention also comprises pharmaceutically acceptable bioprecursors of the active compounds of the present invention. The following example shows the recipe of a tablet according to the present invention.

The present invention also comprises pharmaceutically acceptable bioprecursors of the active compounds of the present invention. The following example shows the recipe of a tablet according to the present invention.

1-Cyclopropyl-4-fluoro-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid

<table>
<thead>
<tr>
<th>Component</th>
<th>Active Ingredient</th>
<th>Excipient</th>
</tr>
</thead>
<tbody>
<tr>
<td>polyvinylpyrrolidone (PVP)</td>
<td>5%</td>
<td>40%</td>
</tr>
<tr>
<td>Avicel</td>
<td>3%</td>
<td>5%</td>
</tr>
<tr>
<td>pregelatinized starch</td>
<td>4%</td>
<td>2%</td>
</tr>
<tr>
<td>magnesium stearate</td>
<td>1%</td>
<td>2%</td>
</tr>
<tr>
<td>tablet without film coating</td>
<td>100.0 g</td>
<td>15.0 g</td>
</tr>
<tr>
<td>film coating</td>
<td>15.0 g</td>
<td>25.0 g</td>
</tr>
</tbody>
</table>

The present invention also comprises pharmaceutically acceptable bioprecursors of the active compounds of the present invention. The following example shows the recipe of a tablet according to the present invention.

1-Cyclopropyl-4-fluoro-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid

1. Compound which is a 7-azetin-1-yl-cyclopropyl-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid of the formula

For the purpose of this specification the term "pharmaceutically acceptable bioprecursor" of an active compound of the invention means a compound having a structural formula different from the active compound but which nonetheless, upon administration to a warm-blooded animal is converted in this patient's body to the active compound.

The improved bacterial action of the compounds of Example 1 according to the present invention is particularly clear in the following bioassay Example, in which it was compared with 5-phenylazo-4-ethyl-5-ethyl-2,3- 4-disordopyrigo 2,3-pyridine-3-carboxylic acid ("phenylid acid") or the known compound 1-ethyl-1-methyl-1-phenylpyridyl-4-ene-3-carboxylic acid ("phenylid acid") and ethylpyrigo 2,3-pyridine-3-carboxylic acid ("pyrididine acid").

The ager dilution test was carried out by the Denley multipoint inoculation method and the results were as shown in the following Table.

<table>
<thead>
<tr>
<th>Minimum inhibitory concentrations (mg/ml)</th>
<th>in an agar dilution test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Component</td>
<td>50</td>
</tr>
<tr>
<td>Antibiotic</td>
<td>1.5</td>
</tr>
<tr>
<td>5-phenylazo-4-ethyl-5-ethyl-2,3-disordopyrigo 2,3-pyridine-3-carboxylic acid (&quot;phenylid acid&quot;)</td>
<td>1.5</td>
</tr>
<tr>
<td>ethylpyrigo 2,3-pyridine-3-carboxylic acid (&quot;pyrididine acid&quot;)</td>
<td>1.5</td>
</tr>
</tbody>
</table>

What is claimed is:

1. A compound which is a 7-azetin-1-yl-cyclopropyl-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid of the formula

2. or a pharmaceutically acceptable acid salt or an alkaloid for alkaline earth metal salt thereof, in which A represents a nitrogen atom or CR₃, wherein R₃ represents nitrogen or a heterocyclic nitrogen atom or a carbocyclic or a cycloalkyl group, and Z represents an amino group or a carbocyclic or a cycloalkyl group, and R₃ represents an amino group or an amino-carbon or a heterocyclic nitrogen atom or a carbocyclic or a cycloalkyl group, and Z represents an amino group or an amino-carbon or a heterocyclic nitrogen atom or a carbocyclic or a cycloalkyl group.
and R are identical or different and represent a hydrogen atom or a straight-chain or branched alkyl, alkenyl or alkynyl radical which has up to 12 carbon atoms and is optionally substituted by radicals selected from hydroxyl, alkyl, alkoxy, alkenyloxy, alkynyl, dialkylamino, or dialkylamino with 1 to 3 carbon atoms in each alkyl, alkenyl, or alkynyl group, and mono- or bicyclic carboxylic acid, or further more represents a cyclic alkyl radical with 3 to 5 carbon atoms, or, together with the aromatic atom which they substitute or together with a further heteroatom selected from the group consisting of N, O and S form a 3-membered to 7-membered ring which can be substituted by radicals selected from alkyl or alkenyl with 1 to 4 carbon atoms, hydroxy, alkoxy or alkylamino with 1 to 3 carbon atoms, alkylcarboxyl with 1 to 4 carbon atoms in the alcohol part, and mono- or bi-cyclic carboxylic acid.

2. A compound according to claim 1, in which R represents C(O)R and R represents a fluoro or chloro atom.

3. A compound according to claim 1 or 2, in which R and R together with the nitrogen atom which they substitute and oxygen, sulphur or R substituted nitrogen as a further heteroatom form a 3-membered or 7-membered ring which may be substituted by radicals selected from alkyl or alkenyl with up to 6 carbon atoms, hydroxy, alkoxy or alkylamino with 1 to 3 carbon atoms, alkylcarboxyl with 1 to 4 carbon atoms in the alcohol part, and mono- or bi-cyclic carboxylic acid.

4. A compound according to claim 1 or 2, in which R substitutes or forms a straight-chain alkyl group which has up to 6 carbon atoms or a branched or straight-chain alkyl which has up to 6 carbon atoms which is substituted by radicals selected from hydroxyl, alkyl, alkenyl, alkylcarboxyl or dialkylamino with 1 to 3 carbon atoms per alkyl radical, and alkylcarboxyl with 1 to 4 carbon atoms in the alcohol part, or represents a phenyl or benzyl group which has up to 4 carbon atoms is the aromatic part, or an optionally substituted phenyl or napthalene group or pyridine, pyrimidine, thiazole or benzothiazole, or

R represents an alkoxyalkyl group which is optionally substituted by a mono- or bi-cyclic carboxylic acid radical and has 1 to 6 carbon atoms in a alcohol part an alkynyl radical with 1 to 6 carbon atoms, a benzy1 or napthyl radical, an alkyl-, phenyl- or napthylphenyl radical, and an aromatic radical.

4. A compound according to claim 3, in which R represents a radical of pyridine, pyrimidine, thiazole or benzothiazole.

5. A 1-cyclopentyl-6-fluoro-1,4-dihydro-4-oxo-7-piperazino-quinolino-3-carboxylic acid and of the formula

5. OR or salts and/or hydrates thereof,

6. A compound according to claim 1 which is 7-(4-{methyl(phenyl)azo}-1-cyclopropyl-4-oxo-1,4-dihydro-naphthyl-3-one-3-carboxylic acid.

7. A compound according to claim 1 which is 7-piperazino-1-cyclopropyl-4-oxo-1,4-dihydro-naphthyl-3-one-3-carboxylic acid.

8. A compound according to claim 1 which is 7-(4-formyl(phenyl)azo)-1-cyclopropyl-4-oxo-1,4-dihydro-naphthyl-3-one-3-carboxylic acid.

9. A compound according to claim 1 which is 7-piperazino-1-cyclopropyl-4-oxo-1,4-dihydro-6-fluoroquinoline-3-carboxylic acid.

10. A compound according to claim 1 which is 7-(4-hydroxy(phenyl)azo)-1-cyclopropyl-4-oxo-1,4-dihydro-naphthyl-3-one-3-carboxylic acid.

11. A compound according to claim 1 which is 7-piperazino-1-cyclopropyl-4-oxo-1,4-dihydro-6-epoxoquinoline-3-carboxylic acid.

12. A compound according to claim 1 which is 7-(4-cyano-1-nitro)-1,4-dihydro-6-fluoroquinoline-3-carboxylic acid.

13. A compound according to claim 1 which is 7-cyano-1-cyclopropyl-4-oxo-1,4-dihydro-6-fluoroquinoline-3-carboxylic acid.

14. A compound according to claim 1 which is 7-(4-formyl(phenyl)azo)-1-cyclopropyl-4-oxo-1,4-dihydro-naphthyl-3-one-3-carboxylic acid.

15. A compound according to claim 1 which is 7-(4-formyl(phenyl)azo)-1-cyclopropyl-4-oxo-1,4-dihydro-naphthyl-3-one-3-carboxylic acid.

16. A pharmaceutical composition comprising as an active ingredient an antibacterial effective amount of R according to claim 1 admixed with an inert pharmaceutical carrier.

17. A pharmaceutical composition according to claim 16 in the form of a sterile or pharmaceutically inert aqueous solution.

18. A composition according to claim 16 or 17 containing from 0.1 to 5% by weight of the said active ingredient.

19. A medicament in dosage unit form comprising an antibacterial effective amount of R according to claim 1 admixed with an inert pharmaceutical carrier.

20. A medicament of claim 19 in the form of tablets, pills, dragees, capsules, aerosols, or suppositories.

21. A method of treating bacterial infections in warm-blood animals which comprises administering to the animal an antibacterial effective amount of R as an active compound according to claim 1 either alone or in admixture with a different or in the form of a medicament.

22. An animal feed, food concentrate or drinking water comprising an active compound according to claim 1.