The following statement is a full description of this invention, including the best method of performing it known to us:

NEW CYCLOALKANO-QUINOLONE DERIVATIVES AND THE PREPARATION THEREOF

(ADDITIONAL TO 431609)

DR. PHIL. HERBERT BERGER, DR. PHIL. ALFRED RHOMBERG, DR. ING. KURT STACH, DR. MED. WOLFGANG VOMEL AND DR. MED. VET. WINFRIEDE SAUER

The following statement is a full description of this invention, including the best method of performing it known to us:

X620-73-ND-14P.C.
The present invention is concerned with new cycloalkano-quinolone derivatives and with the preparation thereof and is also concerned with pharmaceutical compositions with an anti-microbial activity containing the new cycloalkano-quinolone derivatives.

In Parent Specification No. 1,210,638, there are described and claimed cycloalkano-quinolone derivatives of the general formula:

\[
\text{R}_1 \text{COY} \\
\text{R}_2 \text{N}_x \text{X} \\
\text{R}_3
\]

wherein one of the symbols \( \text{R}_1 \) and \( \text{R}_2 \) represents a hydrogen or halogen atom or a nitro, amino or hydroxyl group or an acylamino, acyloxy, alkoxy or aryloxy radical, while the other one, together with \( \text{R}_3 \) forms an aliphatic bridge containing 2 - 6 carbon atoms, \( \text{X} \) is a hydrogen atom or an alkyl or alkenyl radical containing up to 4 carbon atoms and \( \text{Y} \) is a hydroxyl or amino group or an alkoxy radical containing up to 4 carbon atoms; and the pharmacologically compatible salts thereof. The Parent Specification also describes and claims processes for the preparation of the compounds of general formula (I), as well as pharmaceutical compositions containing compounds of general formula (I).

We have now found that a series of new cycloalkano-quinolone derivatives, which are not covered by the above-mentioned Parent Specification and in which \( \text{Y} \) is always a hydroxyl group, also possess \textit{in vitro} and \textit{in vivo} a
surprisingly high anti-microbial activity which, in some cases, is superior to that of the compounds according to the above-mentioned Parent Specification.

The new cycloalkano-quinolone derivatives according to the present invention are compounds of the general formula:

\[
\begin{align*}
\text{R'} & \text{COOH} \\
\text{R'} & \text{N} \\
\text{R'} & \text{2 X'}
\end{align*}
\]

wherein one of the symbols \( R'_1 \) and \( R'_2 \) represents a hydrogen atom, while the other one, together with \( R'_3 \), forms an aliphatic bridge containing 3 - 5 carbon atoms and \( X' \) is a lower alkyl radical substituted by a halogen atom, a hydroxyl group or an acyloxy, alkoxy, aryloxy, aralkoxy, mercapto, alkylmercapto, alkyl-sulphonyl or aryl-sulphonyl radical; and the pharmacologically compatible salts thereof.

The new compounds according to the present invention can be prepared, for example, by reacting cycloalkano-quinolones of the general formula:

\[
\begin{align*}
\text{R'} & \text{COY'} \\
\text{R'} & \text{N} \\
\text{R'} & \text{2 H}
\end{align*}
\]

wherein \( R'_{1}, R'_{2} \) and \( R'_{3} \) have the same meanings as above.
and \( Y' \) is a hydroxyl group or an alkoxy radical, with compounds of the general formula:

\[
X' - Z
\]

(III),

wherein \( X' \) has the same meaning as above and \( Z \) is a reactive residue, the possibly esterified 3-carboxylic is then hydrolysed under basic conditions and, if desired, a substituent in the group \( X' \) is chemically changed in known manner and/or, if desired, the compounds of general formula (I') are converted into salts by reaction with pharmacologically compatible bases.

For the N-alkylation of the compounds (II) with the reactive compounds (III), it is particularly preferred to use those in which \( Z \) is a halogen atom or a sulphonic acid radical. The symmetrical esters of sulphuric acid can, of course, also be used. Furthermore, the corresponding epoxides can be used for the introduction of \( \beta \)-hydroxy-alkyl substituents.

The reaction is preferably carried out in a high boiling, inert solvent, such as dimethyl sulphoxide or dimethyl formamide, with the addition of a weak base for the removal of liberated acid.

A number of substituents in the N-alkyl radical can subsequently be favourably changed. Thus, for example, a hydroxyl substituent can be acylated with a reactive acid derivative. As reactive derivative for this purpose, there is preferably used an anhydride or acid halide, preferably in an inert solvent and with the addition of a weak base. By reaction with a gaseous hydrogen halide, the hydroxyl group can also be converted into the corresponding halo compound, the water thereby formed preferably
being removed by azeotropic distillation. Stronger alkyl-
lation agents, for example the alkyl halides and alkyl
sulphonates, convert hydroxyl and mercapto substituents
into the corresponding alkoxy and alkylthio compounds,
respectively. On the other hand, it is possible to split
off an alkoxy or aralkoxy substituent by boiling with a
hydrohalic acid, without any noticeable attack on the
remainder of the molecule occurring. Furthermore, a halo-
alkyl radical can be converted into an alkylthio or arylthio
radical by reaction with an alkali metal salt of an
appropriate mercaptan. The alkyl-sulphonyl radical can be
obtained, for example, by oxidation of the corresponding
alkylthio radical, potassium permanganate or hydrogen
peroxide thereby being suitable oxidation agents.

The conversion of the cycloalkano-quinolones (I')
into their pharmacologically compatible salts can be carried
out, for example, by mixing a solution or suspension of a
compound (I') in a polar solvent with one equivalent of a
pharmacologically compatible base, followed by evaporation
of the resultant solution.

As pharmacologically compatible bases there may be
mentioned, by way of example, the alkali metal, magnesium,
calcium and ammonium hydroxides and carbonates.

The compounds of general formula (I') and the salts
thereof can be administered enterally and parenterally in
the form of solutions, suspensions or in solid form, by
admixture with solid or liquid pharmaceutical diluents or
carriers. Preferably, they are administered in the form
of tablets or dragees with a content of active material
per tablet or dragee of 100 - 500 mg. The tablets and
dragees can contain further solid carrier materials, such as starch, lactose, methyl-cellulose, talc, highly-dispersed silicic acid, high molecular weight fatty acids, magnesium stearate, gelatine, solid high molecular weight polymers (such as polyethylene glycols) and possibly also flavouring and colouring agents.

Suspensions are preferably administered with a content of active material of 20 - 100 mg./ml., using water as the suspension agent. High molecular weight, water-soluble materials, such as cellulose ethers or polyethylene oxide, can be added for the stabilisation of the suspensions. Furthermore, sweetening agents, flavouring agents, odoriferous agents and edible dyestuffs can also be added.

For injection solutions, it is preferable to use the more readily soluble salts of the compounds (I') in aqueous solution in amounts of from 10 to 100 mg./dose. Such injection solutions preferably also contain the conventional additives, such as stabilising agents, solubilising agents, buffers and mannitol or sodium chloride in the amount necessary for the production of an isotonic solution.

The following Examples are given for the purpose of illustrating the present invention:-

Example 1.

2.57 g. 3-carbethoxy-4-hydroxy-cyclopentano-(h)-quinoline, 7 g. potassium carbonate and 830 mg. potassium iodide are suspended in 12 ml. dimethyl formamide and, while stirring at 100°C., a mixture of 13.2 g. 1-iodo-2-
benzyloxyethane and 12 ml. dimethyl formamide added dropwise within the course of 7 hours. Inorganic material is removed by hot filtration of the reaction mixture, the residue is then washed with hot dimethyl formamide and the filtrate, together with the washings, is evaporated in a rotary evaporator.

An oily residue is obtained which contains a comparatively large amount of excess 1-iodo-2-benzyloxyethane. This is then distilled off at a pressure of 0.5 mm.Hg. and at a bath temperature of about 160°C. The residue is heated under reflux for 2.5 hours with a mixture of 30 ml. 2N sodium hydroxide solution and 30 ml. ethanol. The alcohol is thereafter evaporated off in a vacuum and the residue mixed with 30 ml. water and 30 ml. ethylene chloride and boiled for about 2 - 3 minutes. While still hot, the water is separated off in a separating funnel and the ethylene chloride phase extracted three times with 30 ml. amounts of hot water. The aqueous phases are combined and the oily sodium salt of the desired quinolone which precipitates out is brought into solution by heating, whereafter the hot solution is acidified to a pH value of 1 - 2 with concentrated hydrochloric acid. The precipitated quinolone carboxylic acid is filtered off and boiled out twice with 16 ml. amounts of dioxan. The dioxan extracts are combined and then evaporated to dryness. There is thus obtained 1.1 g. 1-β-benzyloxyethyl-7-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4), which has a melting point of 152 - 160°C. After recrystallisation from alcohol/dioxan, the product has a melting point of 163 - 164°C.
Example 2.

1-\(\beta\)-Ethoxyethyl\(\beta\)-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4).

1.3 g. 3-carbethoxy-4-hydroxy-cyclopentano-(h)-quinoline, 5.25 g. potassium carbonate and 0.5 g. potassium iodide are suspended in 13 ml. dimethyl formamide and, while stirring at 100 - 110°C., a mixture of 4.05 g. 1-chloro-2-ethoxyethane and 10.5 ml. dimethyl formamide is added dropwise within the course of 7 hours. Inorganic material is removed by hot filtration, the residue is washed with hot dimethyl formamide and the filtrate, together with the washings, is evaporated in a vacuum. The evaporation residue is heated under reflux for half an hour in a mixture of 20 ml. 2N sodium hydroxide solution and 5 ml. dioxan. After cooling, the reaction mixture is acidified with 5N hydrochloric acid and the carboxylic acid which separates out is filtered off and dried. There are obtained 700 mg. crude 1-\(\beta\)-ethoxyethyl\(\beta\)-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4). After recrystallisation from a mixture of dioxan and dimethyl sulfoxide (2:1), there are obtained 350 mg. of pure product, which has a melting point of 159 - 160°C.

Example 3.

1-\(\beta\)-Phenoxyethyl\(\beta\)-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4).

1.3 g. 3-carbethoxy-4-hydroxy-cyclopentano-(h)-quinoline, 5.25 g. potassium carbonate and 0.5 g. potassium iodide are suspended in 13 ml. dimethyl formamide and a mixture of 5.8 g. 1-chloro-2-phenoxy-ethane and 15 ml. dimethyl formamide introduced portionwise, with stirring and at a temperature of 100 - 110°C., within a period of
7 hours (about 0.7 ml. of the mixture every 15 minutes).

Inorganic material is filtered off with suction from the hot reaction mixture, the residue is washed through with hot dimethyl formamide and the filtrate, together with the washings, is evaporated in a vacuum. The evaporation residue is boiled under reflux for half an hour in a mixture of 20 ml. 2N sodium hydroxide solution and 5 ml. dioxan. After cooling, the reaction mixture is acidified with 5N hydrochloric acid and the 1-(β-phenoxethyl)-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4) which precipitates out is filtered off and dried. The yield is 350 mg. and the compound is obtained in chromatographically pure form. The compound can be recrystallised from dimethyl sulphoxide. It has a melting point of 239 - 240°C.

Example 4.

1-(β-Methoxyethyl)-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4).

14.48 g. 3-carbethoxy-4-hydroxy-cyclopentano-(h)-quinoline, 59.2 g. potassium carbonate and 5.64 g. potassium iodide are suspended in 145 ml. dimethyl formamide and a mixture of 40 g. 1-chloro-2-methoxyethane and 128 ml. dimethyl formamide added dropwise, with stirring and at a temperature of 100 - 110°C., within the course of 7 hours. Inorganic material is filtered off with suction from the hot reaction mixture, the residue is washed through with hot dimethyl formamide and the filtrate, together with the washings, is evaporated in a vacuum. The evaporation residue is boiled under reflux for half an hour in a mixture of 115 ml. 2N sodium hydroxide solution and 28 ml. dioxan. After cooling, the reaction mixture is acidified.
with 5N hydrochloric acid to a pH value of 2 and the carboxylic acid which precipitates out is filtered off and dried. There are obtained 7.0 g. 1-\[\beta\]-methoxyethyl\(\beta\)-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4). The compound can be recrystallised from dimethyl sulphoxide, whereinafter it has a melting point of 222. – 226°C.

**Example 5.**

1-\[\beta\]-Hydroxyethyl\(\beta\)-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4).

**Variant a.**

2.5 g. 1-\[\beta\]-methoxyethyl\(\beta\)-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4) are heated to 100 – 110°C for 1.25 hours with 25 ml. 48% aqueous hydrobromic acid. The reaction mixture is then poured into 125 ml. water and solid material is filtered off with suction and dried. There are obtained 2.2 g. almost pure 1-\[\beta\]-hydroxyethyl\(\beta\)-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4). After recrystallisation from a mixture of di\(\phi\)xan and dimethyl formamide, the compound has a melting point of 240 – 244°C.

**Variant b.**

1 g. 1-\[\beta\]-benzylxoyethyl\(\beta\)-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4) are boiled under reflux for 1.5 hours in 15 ml. concentrated hydrochloric acid. 15 ml. water are then added thereto and the crystals which separate are filtered off with suction. There is obtained 0.71 g. 1-\[\beta\]-hydroxyethyl\(\beta\)-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4), which has a melting point of 233 – 235°C.
Example 6.

1-α-Acetoxy-ethyl-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4).

0.7 g. 1-α-hydroxyethyl-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4) is boiled under reflux for 1 hour in 8.25 ml. acetyl chloride. Subsequently, excess acetyl chloride is evaporated off and the evaporation residue triturated with water. The solid material is filtered off and boiled out twice with a mixture of benzene and dioxan (1:4). The benzene-dioxan extracts are freed from undissolved components by hot filtration and then evaporated. There is obtained 0.45 g. 1-α-acetoxy-ethyl-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4) which only contains traces of impurities. After recrystallisation from, for example, a mixture of dioxan and isopropanol, the compound has a melting point of 180 - 186°C., sintering above 170°C.

Example 7.

1-α-Tosyloxy-ethyl-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4).

100 mg. 1-α-hydroxyethyl-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4) are suspended in 2 ml. anhydrous pyridine and 418 mg. p-toluene-sulphonyl chloride added portionwise, while stirring and at ambient temperature, within the course of 20 minutes. Thereafter, the reaction mixture is stirred for a further 45 minutes at ambient temperature and poured on to ice and the solid material is filtered off with suction and washed with some isopropanol and ether. After recrystallisation from dimethyl formamide, there are obtained 70 mg. 1-α-tosyloxy-ethyl-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4),
which melts at 237 - 238°C. (decomp.).

Example 8.
1-β-Chloroethyl]-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4).

500 mg. 1-β-hydroxyethyl]-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4) are heated to 140°C. in 10 ml. nitrobenzene and, at the same time, gaseous hydrogen chloride is passed therethrough. The progress of the reaction is followed chromatographically. The reaction is finished when no more starting material is detected in the chromatogram. The water formed during the halogenation reaction must be continuously removed by distillation during the whole course of the reaction. When the reaction is completed, the reaction mixture is diluted with about 50 ml. ligroin, a brown oil thereby separating out. The supernatant ligroin/nitrobenzene solution is decanted off and the oil remaining behind is triturated with isopropanol and crystallised. There are obtained 310 mg. of almost pure 1-β-chloroethyl]-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4). After recrystallisation from dimethyl formamide/dioxan (3:7), it has a melting point of 252 - 253°C.

Example 9.
1-/β-(Chloroacetoxy)-ethyl]-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4).

273 mg. 1-β-hydroxyethyl]-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4) and 3 g. chloroacetyl chloride are heated, while stirring, to 120°C. for 10 minutes. The reaction mixture is then evaporated to dryness and the oily evaporation residue is mixed with ice.
Crystallisation thereby occurs. The crystals (about 320 mg.) are filtered off with suction, washed with water and thereafter with some isopropanol and subsequently recrystallised from dioxan. There are obtained 200 mg. 1-\(\beta\)-(chloroacetox)-ethyl\(\gamma\)-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4), which has a melting point of 163 - 165°C.

Example 10.

1-\(\beta\)-Benzoyloxy-ethyl\(\gamma\)-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4).

75 mg. 1-\(\beta\)-hydroxyethyl\(\gamma\)-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4) are dissolved in 1 ml. 5N potassium hydroxide solution, whereafter 100 mg. benzoyl chloride are added, with shaking, at ambient temperature. A white precipitate is formed which is filtered off and triturated with 2N hydrochloric acid. Excess hydrochloric acid is removed by filtration and there are obtained 90 mg. chromatographically pure 1-\(\beta\)-benzoyloxy-ethyl\(\gamma\)-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4). After recrystallisation from a mixture of dioxan and water (4:1), the compound has a melting point of 221 - 222°C.

Example 11.

1-\(\beta\)-Methylthio-ethyl\(\gamma\)-1,4-dihydro-3-carboxy-cyclopentano-(g)-quinolone-(4).

0.916 g. 3-carboxy-4-hydroxy-cyclopentano-(g)-quinoline, 2.8 g. potassium carbonate and 0.35 g. potassium iodide are suspended in 10 ml. dimethyl formamide and a mixture of 3.16 g. 1-chloro-2-methylthioethane in 17 ml. dimethyl formamide are introduced, with stirring and at a temperature of 130°C., within the course of 4 hours. The reaction mixture is further stirred for 45 minutes at 130°C., inorganic material is then filtered off with suction.
and the filtrate is evaporated to dryness in a vacuum. The evaporation residue is boiled under reflux for 15 minutes in a mixture of 12 ml. 2N sodium hydroxide solution and 3 ml. alcohol, whereafter 15 ml. water are added and the reaction mixture acidified with concentrated hydrochloric acid to a pH value of 1 - 2. The 1-\(\beta\)-methylthio-ethyl1\,4-dihydro-3-carboxy-cyclopentano-(g)-quinolone-(4) which precipitates out, is filtered off and dried. The yield is 1.05 g. The chromatographically almost pure compound can be recrystallised from dimethyl sulphoxide and then has a melting point of 217 - 220°C.

Example 12.

1-\(\beta\)-Methylsulphonylethyl1\,4-dihydro-3-carboxy-cyclopentano-(g)-quinolone-(4).

300 mg. 1-\(\beta\)-methylthioethyl1\,4-dihydro-3-carboxy-cyclopentano-(g)-quinolone-(4) are boiled for 20 minutes in a mixture of 1 ml. 30% hydrogen peroxide and 4.5 ml. glacial acetic acid. Upon cooling the reaction mixture, pure 1-\(\beta\)-methylsulphonylethyl1\,4-dihydro-3-carboxy-cyclopentano-(g)-quinolone-(4) crystallises out. This is filtered off and has a melting point of 258°C. (decomp.). The yield is 300 mg.

Example 13.

1-\(\beta\)-n-Butylthioethyl1\,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4).

100 mg. 1-\(\beta\)-chloroethyl1\,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4) are suspended in 1 ml. dioxan and 1 ml. of a 35.3% methanolic solution of sodium n-butyl mercaptide (prepared from a sodium methanolate solution into which is introduced the stoichiometric amount of n-butyl mercaptan) is added, a clear solution thereby
being obtained. The reaction mixture is heated to 60°C. for 2 hours, 3 ml. water are subsequently added thereto and the mixture is extracted with ether and the aqueous phase acidified with 5N hydrochloric acid. The semi-crystalline material obtained is filtered off with suction and triturated with isopropanol. There are thus obtained 50 mg. of chromatographically pure 1-β-n-butylthioethyl\(\beta\) 1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4). This compound can be recrystallised from dioxan, whereafter it has a melting point of 180 - 182°C.

Example 14.
1-β-Ethoxy-ethyl\(\beta\) 1,4-dihydro-3-carboxy-cyclohexano-(g)-quinolone-(4).

0.9 g. 3-carbethoxy-4-hydroxy-cyclohexano-(g)-quinoline, 3.5 g. potassium carbonate and 0.35 g. potassium iodide are suspended in 9 ml. dimethyl formamide and a mixture of 2.7 g. 1-chloro-2-ethoxy-ethane and 6.8 ml. dimethyl formamide added dropwise, with stirring and at a temperature of 100 - 110°C, within the course of 7 hours. Inorganic material is then filtered off with suction, the residue is washed through with hot dimethyl formamide and the filtrate, together with the washings, is evaporated in a vacuum. The evaporation residue is boiled under reflux for 1 hour in a mixture of 2 ml. 2N sodium hydroxide solution and 1.5 ml. dioxan. After cooling, the reaction mixture is acidified with 5N hydrochloric acid and the carboxylic acid which precipitates out is filtered off and dried. There are obtained 850 mg. chromatographically pure 1-β-ethoxy-ethyl\(\beta\) 1,4-dihydro-3-carboxy-cyclohexano-(g)-quinolone, which, after recrystallisation from dimethyl sulfoxide, has a melting point of 206 - 208°C.
Example 15.

1-/β-Methylthioethyl]-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4).

1.0 g. 1-/β-chloroethyl]-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4) is suspended in 10 ml. dioxan and a solution of 2.4 g. solid sodium methyl mercaptide in 10 ml. methanol is added thereto. After stirring the reaction mixture for 2 hours at 60°C, it is cooled, 20 ml. water are added thereto and then it is acidified with 5N hydrochloric acid. The 1-/β-methylthioethyl]-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4) which separates out is filtered off and dried. The yield is 950 mg. The product can be recrystallised from dimethyl sulphoxide, whereafter it has a melting point of 228 - 230°C.
THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. Cycloalkano-quinolone derivatives of the general formula:

```
R'1
\|  \|  \|  \|  \|  \|  \|
R'3 C COOH
R'2
```

wherein one of the symbols $R'_{1}$ and $R'_{2}$ represents a hydrogen atom, while the other one, together with $R'_{3}$, forms an aliphatic bridge containing 3 - 5 carbon atoms and $X'$ is a lower alkyl radical substituted by a halogen atom, a hydroxyl group or an acyloxy, alkoxy, aryloxy, aralkoxy, mercapto, alkylmercapto, alkyl-sulphonyl or aryl-sulphonyl radical; and the pharmacologically acceptable salts thereof.

2. 1-$\beta$-Benzyloxyethyl$^\gamma$-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4).

3. 1-$\beta$-Ethoxyethyl$^\gamma$-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4).

4. 1-$\beta$-Phenoxyethyl$^\gamma$-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4).

5. 1-$\beta$-Methoxyethyl$^\gamma$-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4).

6. 1-$\beta$-Hydroxyethyl$^\gamma$-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4).

7. 1-$\beta$-Acetoxy-ethyl$^\gamma$-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4).

8. 1-$\beta$-Tosyloxy-ethyl$^\gamma$-1,4-dihydro-3-carboxy-cyclopentano-(h)-quinolone-(4).
9. $1-\beta$-Chloroethyl-$1,4$-dihydro-$3$-carboxy-cyclopentano-(h)-quinolone-(4).

10. $1-\beta$-(Chloroacetoxy)-ethyl-$1,4$-dihydro-$3$-carboxy-cyclopentano-(h)-quinolone-(4).

11. $1-\beta$-Benzoyloxy-ethyl-$1,4$-dihydro-$3$-carboxy-cyclopentano-(h)-quinolone-(4).

12. $1-\beta$-Methylthioethyl-$1,4$-dihydro-$3$-carboxy-cyclopentano-(g)-quinolone-(4).

13. $1-\beta$-Methylsulphonylethyl-$1,4$-dihydro-$3$-carboxy-cyclopentano-(g)-quinolone-(4).

14. $1-\beta$-Butylthioethyl-$1,4$-dihydro-$3$-carboxy-cyclopentano-(h)-quinolone-(4).

15. $1-\beta$-Ethoxy-ethyl-$1,4$-dihydro-$3$-carboxy-cyclohexano-(g)-quinolone-(4).

16. $1-\beta$-Methylthioethyl-$1,4$-dihydro-$3$-carboxy-cyclopentano-(h)-quinolone-(4).

17. Process for the preparation of compounds of the general formula given in claim 1, wherein a cycloalkano-quinolone of the general formula:

\[
\begin{array}{c}
\text{R'}_1 \\
\text{R'}_2 \\
\text{R'}_3 \\
\end{array}
\]

in which $\text{R'}_1$, $\text{R'}_2$ and $\text{R'}_3$ have the same meanings as in claim 1 and $\text{Y'}$ is a hydroxyl group or an alkoxy radical, is reacted with a compound of the general formula:

\[
\text{X'} - \text{Z},
\]

in which $\text{X'}$ has the same meaning as in claim 1 and $\text{Z}$ is a reactive residue, whereafter, when the product obtained
contains an esterified 3-carboxylic acid group, this is hydrolysed under basic conditions in order to liberate the carboxylic acid group and, if desired, a substituent in the group X' is chemically changed in known manner and/or, if desired, the product obtained is reacted with a pharmacologically compatible base in order to give the corresponding salt.

18. Process according to claim 17, wherein the reaction is carried out in a high boiling, inert solvent, with the addition of a weak base.

19. Process according to claim 18, wherein the solvent used is dimethyl sulphoxide or dimethyl formamide.

20. Process for the preparation of compounds according to claim 1, substantially as hereinbefore described and exemplified.

21. Compounds according to claim 1, whenever prepared by the process according to any of claims 17 – 20.

22. Pharmaceutical compositions, containing at least one compound according to claim 1, in admixture with a solid or liquid pharmaceutical diluent or carrier.