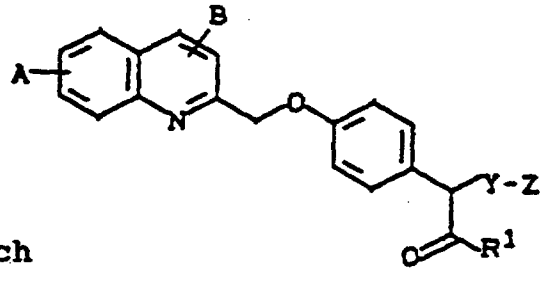
The invention relates to substituted 4-(quinolin-2-yl-methoxy)phenylacetic acids, esters and amides thereof, processes for their preparation and their use in medicaments.

It is known that 3-(quinolin-2-yl-methoxy)phenylacetic acid and 2-[3-(quinolin-2-yl-methoxy)phenyl]propionic acid and methyl and ethyl esters thereof have an anti-inflammatory and antiallergic action [compare EP-A 181,568].

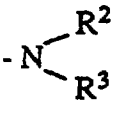
Substituted 4-(quinolin-2-yl-methoxy)-phenylacetic acids and esters and amides thereof, of the general formula (I)



(I)

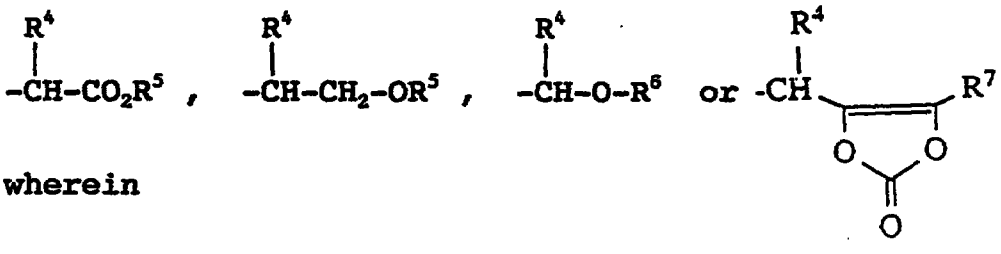
in which

R^1 - represents a group of the formula

$-OR^2$ or  , wherein

R^2 and R^3 are identical or different and

- represent hydrogen, C_1-C_6-alkyl benzyl, phenyl or a group of the formula



wherein

R^4 - represents hydrogen, C_1-C_6-alkyl, phenyl or benzyl, which can optionally be substituted by hydroxyl, C_1-C_6-alkoxycarbonyl, carboxyl, C_1-C_6-alkylthio, thienyl, furyl, pyridyl, pyrimidyl,

pyrazinyl, pyridazinyl, quinolyl, isoquinolyl, quinazolyl, quinoxalyl, thiazolyl, benzothiazolyl, isothiazolyl, oxazolyl, benzoxazolyl, isoxazolyl, imidazolyl, benzimidazolyl, pyrazolyl, indolyl and isoindolyl or carbymoyl,

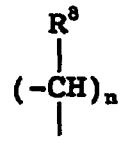
R^5 - represents hydrogen, C_1-C_6-alkyl, phenyl or benzyl

R^6- represents a group of the formula $-COR^5$ or $-CO_2R^5$, wherein R^5 has the abovementioned meaning,

and

R^7 - represents hydrogen, C_1-C_6-alkyl or phenyl,

Y - represents a group of the formula



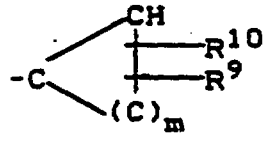
, wherein

R^8 - represents hydrogen, C_1-C_6-alkyl or phenyl

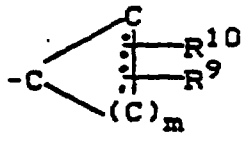
and

n - - denotes a number from 0 to 5,

Z - represents norbornyl, or
represents a group of the formula



or



wherein

R^9 and R^{10} are identical or different and denote hydrogen, C_1-C_6-alkyl or phenyl, or

R^9 and R^{10} can together form a saturated carbocyclic ring having up to 6 carbon atoms and

m denotes a number from 1 to 6,

and

A and B are identical or different and denote hydrogen, methyl, ethyl, fluorine, chlorine or bromine,

and salts thereof

have been found.

In comparison with the compounds known from EP-A 181,568, the quinolines of the general formula (I) according to the invention surprisingly have a higher in vitro activity than leucotriene synthesis inhibitors and a more potent in vivo action following oral administration.

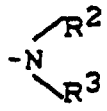
Physiologically acceptable salts are preferred in the context of the present invention. Physiologically acceptable salts of the substituted 4-(quinolin-2-yl-methoxy)-phenylacetic acids, esters and amides can be salts of the substances according to the invention with mineral acids, carboxylic acids or sulphonic acids. Particularly preferred salts are, for example, those with hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, ethanesulphonic acid, toluenesulphonic acid, benzenesulphonic acid, naphthalenedisulphonic acid, acetic acid, propionic acid, lactic acid, tartaric acid, citric acid, fumaric acid, maleic acid or benzoic acid.

Salts in the context of the present invention are furthermore salts of monovalent metals, such as alkali metals and ammonium salts. Sodium, potassium and ammonium salts

are preferred.

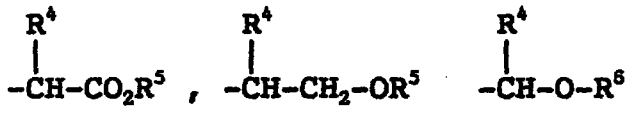
Preferred compounds of the general formula (I) are those in which

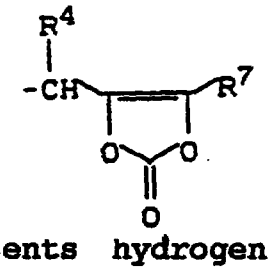
R^1 - represents a group of the formula

$-OR^2$ or  , wherein

R^2 and R^3 are identical or different and

- represent hydrogen, methyl, ethyl, propyl, isopropyl, butyl, tert.-butyl, phenyl or benzyl, or represent a group of the formula



or  , wherein

R^4 - represents hydrogen, methyl, ethyl, propyl, isopropyl, butyl, tert.-butyl, benzyl or phenyl, which can optionally be substituted by hydroxyl, methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, carboxyl, methylthio, ethylthio, propylthio, imidazolyl or carbamoyl,

R^5 - represents hydrogen, methyl, ethyl, propyl, isopropyl, butyl, tert.-butyl, phenyl or benzyl,

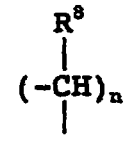
R^6 - represents a group of the formula $-COR^5$ or $-CO_2R^5$, wherein

R^5 has the abovementioned meaning,

and

R^7 - represents hydrogen, methyl, ethyl, propyl, isopropyl, butyl, tert. butyl or phenyl,

Y - represents a group of the formula



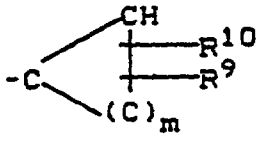
, wherein

R^8 - represents hydrogen, methyl, ethyl, propyl, isopropyl, butyl, tert.-butyl or phenyl,

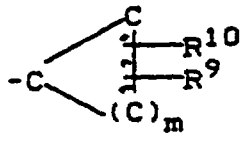
and

n - denotes a number from 0 to 5,

Z - represents norbornyl or
represents a group of the formula



or



,

wherein

R^9 and R^{10} are identical or different and denote hydrogen, methyl, ethyl, n-propyl, iso-propyl, butyl or tert.-butyl, or

R^9 and R^{10} can together form a saturated carbocyclic ring having up to 6 carbon atoms and

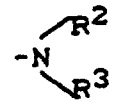
m - denotes a number from 1 to 6,

A and B are identical or different and denote hydrogen, methyl, ethyl, fluorine or chlorine,

and salts thereof.

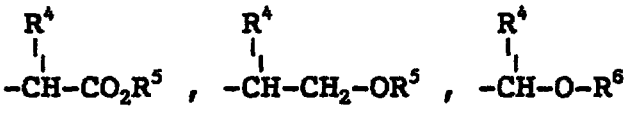
Particularly preferred compounds of the general formula (I) are those in which

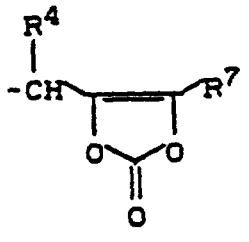
R^1 - represents a group of the formula

$-OR^2$ or  , wherein

R^2 and R^3 are identical or different and

- represent hydrogen or methyl, or
- represent a group of the formula



or  , wherein

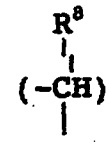
R^4 - represents hydrogen, methyl or phenyl,

R^5 - represents hydrogen, methyl, ethyl, tert.-butyl or benzyl,

R^6 - represents a group of the formula $-COR^5$, wherein R^5 has the abovementioned meaning, and

R^7 - represents methyl,

Y - represents a group of the formula

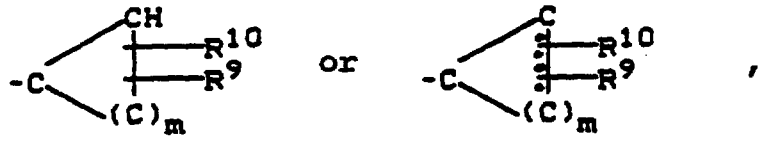
 , wherein

R^8 - represents hydrogen or methyl,

and

n denotes a number 0 or 1,

Z - represents norbornyl, or
represents a group of the formula



wherein

R^9 and R^{10} are identical or different and denote hydrogen or methyl, or

R^9 and R^{10} together form a cyclohexyl ring, and

m - denotes a number 1, 2, 3, 4 or 5,

A and B denote hydrogen or fluorine,

and salts thereof.

The compounds according to the invention can be in stereoisomeric forms which either behave as image and mirror image (enantiomers) or do not behave as image and mirror image (diastereomers). The invention relates both to the antipodes and to the racemic forms as well as the diastereomer mixtures. The racemic forms, like the diastereomers, can be resolved into the stereoisomerically uniform constituents in a known manner (compare E.L. Eliel, Stereochemistry of Carbon Compounds, McGraw Hill, 1962).

The following active compounds may be mentioned specifically:

methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-3-cyclopropyl-propionate
methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-3-cyclohexyl-propionate

methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cyclopentyl-acetate

methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cyclohexyl-acetate

methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cycloheptyl-acetate

2-[4-(quinolin-2-yl-methoxy)phenyl]-3-cyclopropyl-propionic acid

2-[4-(quinolin-2-yl-methoxy)phenyl]-3-cyclohexyl-propionic acid

2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cyclopentyl-acetic acid

2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cyclohexyl-acetic acid

2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cycloheptyl-acetic acid

methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-(cyclohex-2-enyl)-acetate

benzyloxycarbonylmethyl 2-[4-(quinolin-2-yl-methoxy)-phenyl]-2-cyclopropyl-propionate

benzyloxycarbonylmethyl 2-[4-(quinolin-2-yl-methoxy)-phenyl]-2-cyclopentyl-acetate

2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cyclopentylacetic acid methoxycarbonylmethylamide

methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-(1-decalinyl)-acetate

tert.-butoxycarbonylmethyl 2-[4-(quinolin-2-yl-methoxy)-phenyl]-2-cyclopentyl-acetate

pivaloyloxymethyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cyclopentyl-acetate

methoxycarbonylmethyl 2-[4-(quinolin-2-yl-methoxy)-phenyl]-2-cyclopentyl-acetate

2-[4-(quinolin-2-yl-methoxy)phenyl]-2-(1-decalinyl)-acetic acid

2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cyclopentyl-acetic acid carboxymethylamide

sodium 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cyclopentyl-acetate

methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-3-cyclopentyl-propionate

2-[4-(quinolin-2-yl-methoxy)phenyl]-3-cyclopentyl-propionic acid

2-[4-(quinolin-2-yl-methoxy)phenyl]-2-(cyclohex-2-enyl)-acetic acid

carboxymethyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cyclopentylacetate

methyl 2-[4-(6-fluoroquinolin-2-yl-methoxy)phenyl-2-cyclopentylacetate

2-[4-(6-fluoroquinolin-2-yl-methoxy)phenyl-2-cyclopentyl-acetic acid

methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-norbornyl-acetate

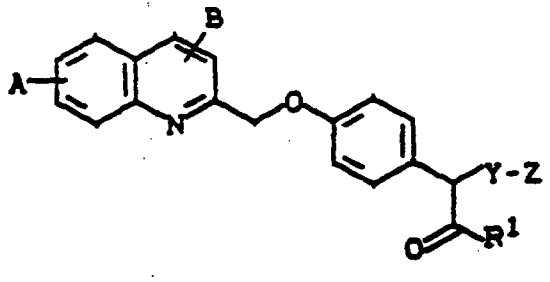
2-[4-(quinolin-2-yl-methoxy)phenyl]-2-norbornyl-acetic acid

2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cyclopentyl-acetic acid [(L)-2-hydroxy-1-phenylethyl]amide
(both diastereomers)

(+)-4-[2-(quinolin-2-yl-methoxy)phenyl]-2-cyclopentyl-acetic acid and

(-)-4-[2-(quinolin-2-yl-methoxy)phenyl]-2-cyclopentyl-acetic acid

Processes for the preparation of the compounds of the general formula (I)



(I)

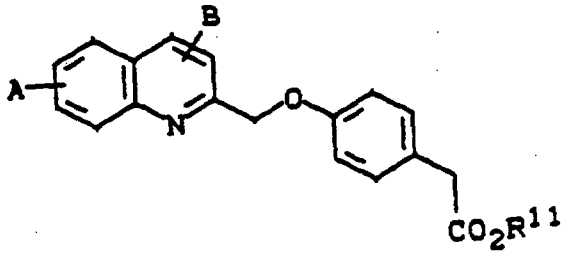
in which

A, B, R^1, Y and Z have the abovementioned meaning,

have furthermore been found,

which are characterised in that

[A] 4-(quinolin-2-yl-methoxy)phenylacetic acid esters of the general formula (Ia)



(Ia)

in which

R^{11} - represents alkyl and

A and B have the abovementioned meaning,

are alkylated with compounds of the general formula (II)

$$Y\text{-}Z\text{-}X \qquad (II)$$

in which

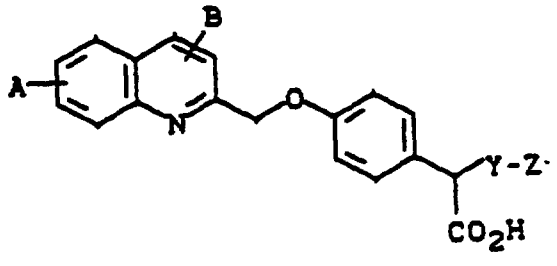
Y and Z have the abovementioned meaning and

X - represents chlorine, bromine or iodine,

and in the case of the acids the esters are hydrolyzed,

or in that

[B] the acids of the general formula (Ib)



(Ib)

in which

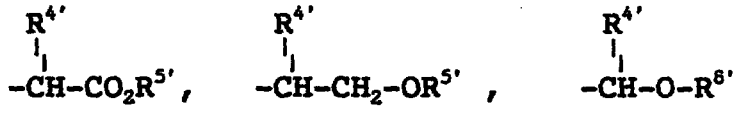
A, B, Y and Z have the abovementioned meaning,

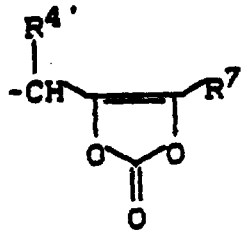
are esterified with compounds of the general formula (III)

$$X\text{-}R^{12} \qquad \text{(III)}$$

in which

R^{12} - represents a group of the formula



or  , wherein

$R^{4'}$ - represents alkyl, aralkyl or aryl, which can optionally be substituted by hydroxyl, carboxyl, alkoxycarbonyl, alkylthio, heteroaryl or aminocarbonyl,

$R^{5'}$ - represents alkyl, aryl or aralkyl,

$R^{6'}$ - represents a group of the formula $-COR^{5'}$ or $-CO_2R^{5'}$, wherein

$R^{5'}$ has the abovementioned meaning,

$R^{7'}$ - represents alkyl or aryl,

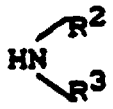
and

X has the abovementioned meaning,

and in the case of the acids the esters are subjected to hydrogenolytic cleavage,

or in that

[C] the acids of the general formula (Ib) are amidated with amines of the general formula (IV)



(IV)

in which

R^2 and R^3 have the abovementioned meaning,

with the proviso that R^5 does not denote hydrogen if R^2 or R^3 represents the group



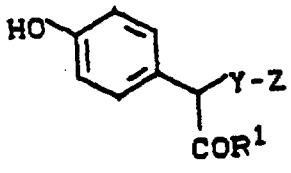
wherein

R^4 and R^5 have the abovementioned meaning,

in the presence of customary activating reagents, and in the case of the acids the esters are hydrolyzed

or in that

[D] phenols of the general formula (V)



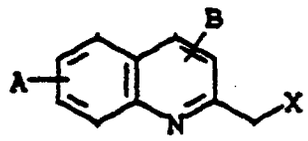
(V)

in which

R^1, Y and Z have the abovementioned meaning

are etherified with

2-halogenomethylquinolines of the formula (VI)



(VI)

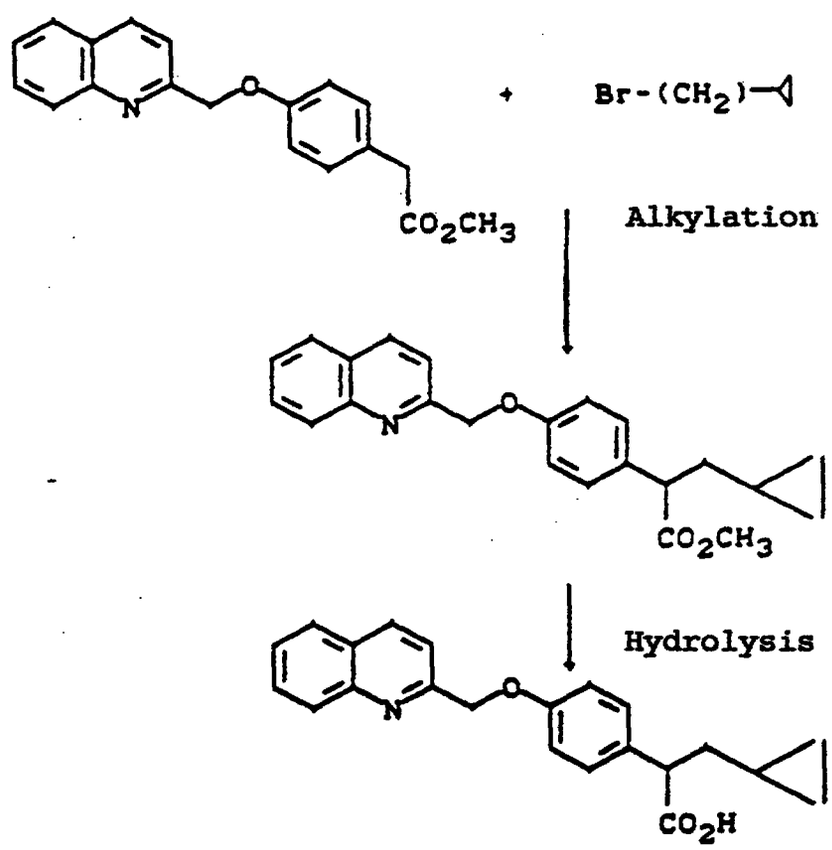
in which

A, B and X have the abovementioned meaning,

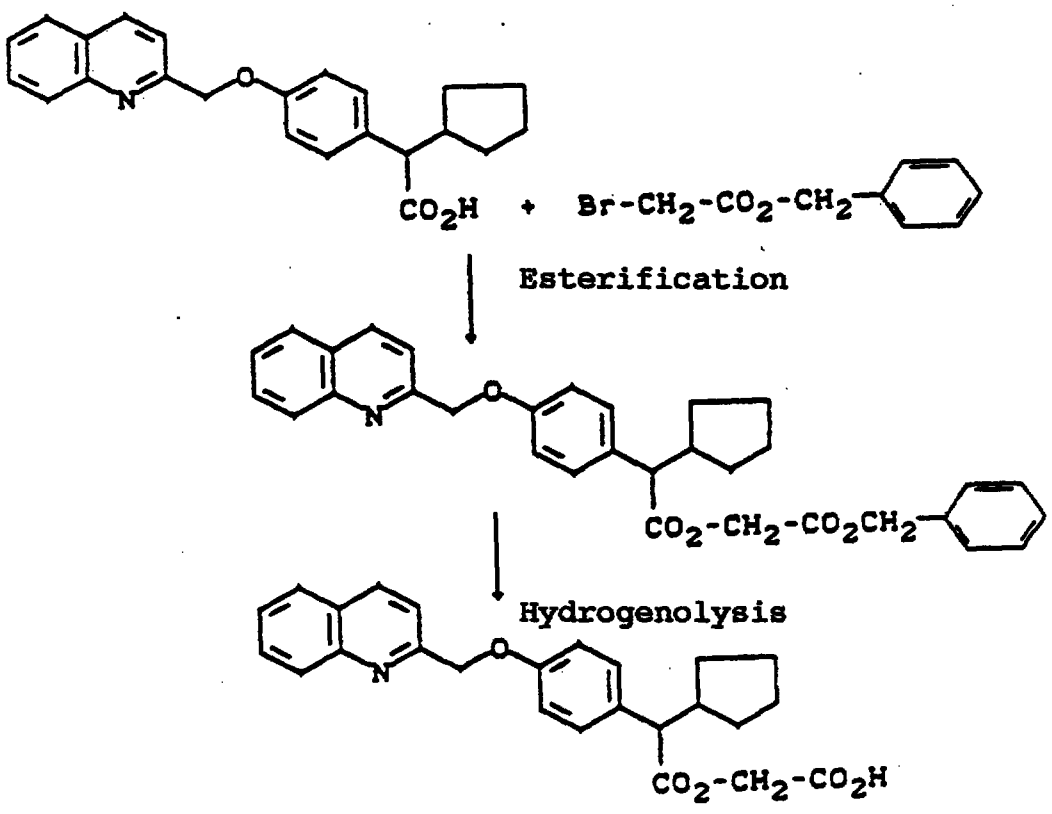
and in the case of the acids the esters are hydrolyzed.

The processes according to the invention can be illustrated by the following equations:

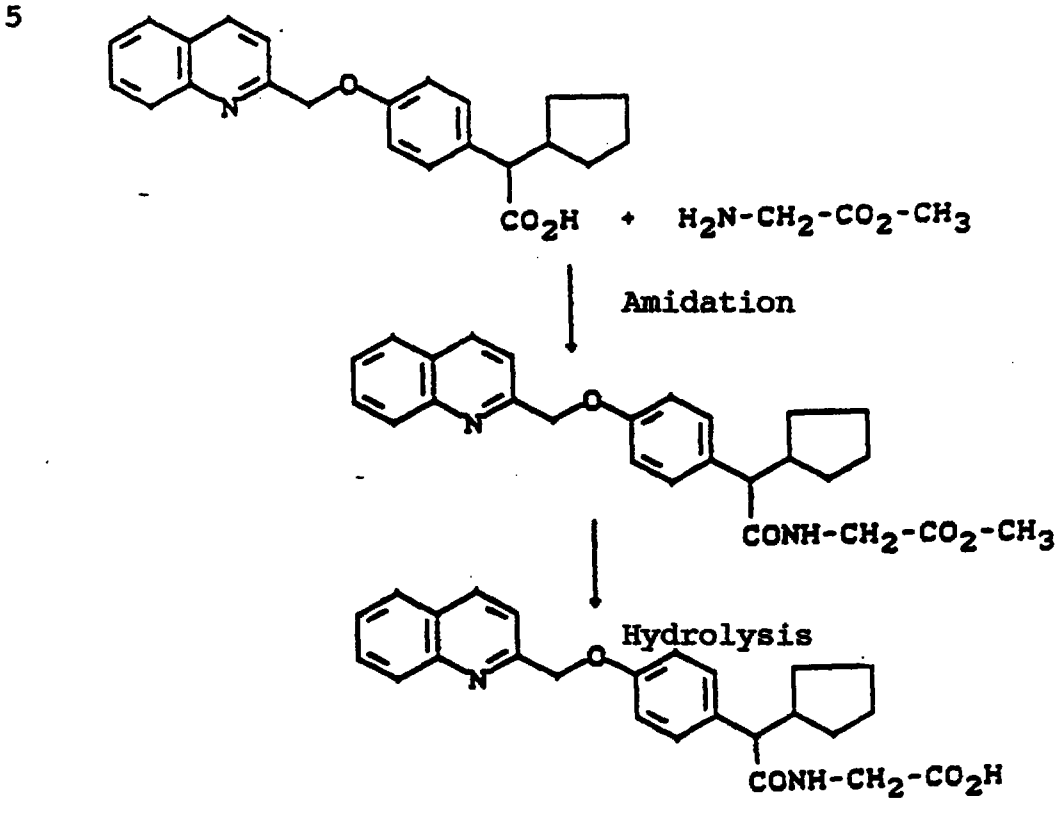
[A]



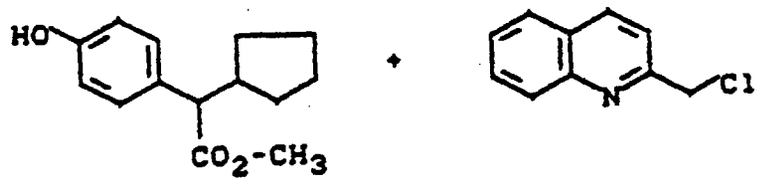
[B]


CO2H + Br-CH2-CO2-CH2
Esterification
CO2-CH2-CO2CH2
Hydrogenolysis
CO2-CH2-CO2H

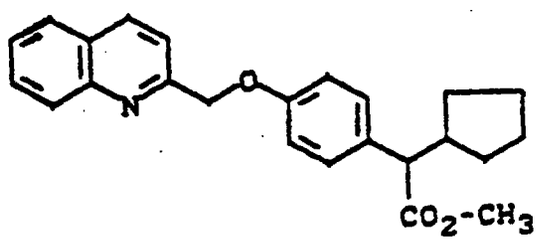
[C]


CO2H + H2N-CH2-CO2-CH3
Amidation
CONH-CH2-CO2-CH3
Hydrolysis
CONH-CH2-CO2H

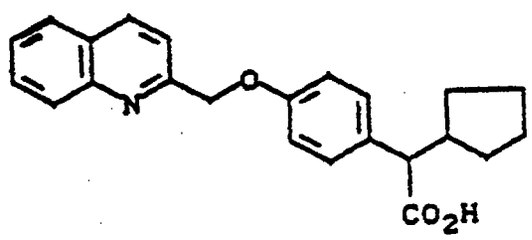
[D]



O-Alkylation



Hydrolysis



The alkylation of the C-H acid compounds (formula Ia) with alkyl halides is in general carried out in inert solvents in the presence of a base.

Suitable solvents for this reaction are all the inert organic solvents, depending on the nature of the alkylating agent. These solvents include, preferably, ethers, such as diethyl ether, dioxane or tetrahydrofuran, or hydrocarbons, such as benzene, toluene or xylene, or dimethylformamide or hexamethylphosphoric acid triamide, or mixtures of the solvents mentioned.

Suitable bases are the customary basic compounds. These include, preferably, alkali metal hydrides, such as sodium hydride, alkali metal amides, such as sodium amide or lithium diisopropylamide, alkali metal alcoholates, such as sodium methanolate, sodium ethanolate, potassium methanolate, potassium ethanolate or potassium tert.-butylate, or organic amines, such as trialkylamines, for example triethylamine, or organolithium compounds, such as butyllithium or phenyllithium.

The alkylation of the CH-acid compounds is in general carried out in a temperature range from 0°C to 150°C, preferably from 10°C to 100°C.

The alkylation of the CH-acid compounds is in general carried out under normal pressure. However, it is also possible to carry out the process under reduced pressure or increased pressure (for example in a range from 0.5 to 5 bar).

In general, 0.5 to 5, preferably 1 to 2, mol of halide are employed per mol of the reaction partner. The base is in general employed in an amount of 0.5 to 5 mol, preferably 1 to 3 mol, based on the halide.

The hydrolysis of the carboxylic acid esters is carried out by customary methods, by treating the esters with customary bases in inert solvents, it being possible for the salts initially formed to be converted into the free carboxylic acids by treatment with acid.

Suitable bases for the hydrolysis are the customary inorganic bases. These include, preferably, alkali metal hydroxides or alkaline earth metal hydroxides, such as, for example, sodium hydroxide, potassium hydroxide or barium hydroxide, or alkali metal carbonates, such as sodium or potassium carbonate or sodium bicarbonate, or alkali metal alcoholates, such as sodium ethanolate, sodium methanolate, potassium ethanolate, potassium methanolate or potassium tert.-butanolate. Sodium hydroxide or potassium hydroxide are particularly preferably employed.

Suitable solvents for the hydrolysis are water or the organic solvents customary for hydrolysis. These include, preferably, alcohols, such as methanol, ethanol, propanol, isopropanol or butanol, or ethers, such as

tetrahydrofuran or dioxane, or dimethylformamide or dimethylsulphoxide. Alcohols, such as methanol, ethanol, propanol or isopropanol, are particularly preferably used. It is likewise possible to employ mixtures of the solvents mentioned.

The hydrolysis is in general carried out in a temperature range from 0°C to +100°C, preferably from +20°C to +80°C.

The hydrolysis is in general carried out under normal pressure. However, it is also possible to carry out the hydrolysis under reduced pressure or under increased pressure (for example from 0.5 to 5 bar).

In carrying out the hydrolysis, the base is in general employed in an amount of 1 to 3 mol, preferably 1 to 1.5 mol, per mol of the ester or lactone. Molar amounts of the reactants are particularly preferably used.

In carrying out the hydrolysis, the salts of the compounds according to the invention are formed in the first step as intermediate products which can be isolated. The acids according to the invention are obtained by treatment of the salts with customary inorganic acids. These include, preferably, mineral acids, such as, for example, hydrochloric acid, hydrobromic acid, sulphuric acid or phosphoric acid. In the preparation of the carboxylic acids it has proved advantageous here for the basic reaction mixture of the hydrolysis to be acidified in a second step without the salts being isolated. The acids can then be isolated in the customary manner.

The esterification of the carboxylic acids is carried out by customary methods by treating the acids with alkyl halides in inert solvents, if appropriate in the presence of a base.

Suitable bases are the customary organic amines. These include, preferably, alkylamines, such as triethylamine, diisopropylamine, dicyclohexylamine and ethyldiisopropylamine.

Suitable solvents here are all the inert organic solvents. These include, preferably, ethers, such as diethyl ether, dioxane or tetrahydrofuran, or hydrocarbons, such as benzene, toluene or xylene, or dimethylformamide or mixtures of the solvents mentioned.

The esterification of the carboxylic acids is in general carried out in a temperature range from 0° to 150°C, preferably from 10°C to 100°C.

The esterification of the carboxylic acids is in general carried out under normal pressure. However, it is also possible to carry out the process under reduced pressure or increased pressure (for example in a range from 0.5 to 5 bar).

In general, 0.5 to 5, preferably 1 to 2, mol of halide per mol of the reaction partner are employed. The base is in general employed in an amount of 0.5 to 5 mol, preferably 1 to 3 mol, based on the halide.

In general, 0.01 to 1, preferably 0.05 to 0.5, mol of catalyst per mol of reaction partner is employed.

The hydrogenolytic cleavage of the benzyl esters is carried out by customary methods by hydrogenating the benzyl esters with hydrogen gas in an inert solvent in the presence of a catalyst.

Suitable catalysts are the customary metal catalysts, which are applied, if appropriate, to an inert carrier, such as, for example, charcoal, in variable concentrations. These catalysts preferably include palladium,

nickel and platinum, particularly preferably 5 to 15% strength palladium-on-active charcoal.

Suitable solvents here are all the inert organic solvents. These include, preferably, ethers, such as diethyl ether, dioxane or tetrahydrofuran, or hydrocarbons, such as benzene, toluene or xylene, or alcohols, such as methanol, ethanol or propanol, or low-boiling esters, such as ethyl acetate, or amines, such as triethylamine, or mixtures of the solvents mentioned.

The hydrogenolytic cleavage is in general carried out in a temperature range from 0°C to 150°C, preferably from 10°C to 100°C.

The hydrogenolytic cleavage is in general carried out with hydrogen under normal pressure. However, it is also possible to carry out the process under increased pressure (for example in a range from 1 to 10 bar).

In general, 0.01 to 1, preferably 0.05 to 0.5, mol of catalyst per mol of reaction partner is employed.

The amidation of the compounds (Ib) with amines is in general carried out in inert solvents in the presence of a base.

Suitable solvents here are all the inert organic solvents, depending on the nature of the amine. These include, preferably, ethers, such as diethyl ether, dioxane or tetrahydrofuran, hydrocarbons, such as benzene, toluene or xylene, or dimethylformamide or mixtures of the solvents mentioned. Dimethylformamide is particularly preferred.

Suitable bases are the customary basic compounds. These include, preferably, organic amines, such as trialkylamines, for example triethylamine.

Suitable amine components are, in addition to the customary amines, such as, for example, propylamine, dimethylamine or diethylamine, also optically active amino acid esters, such as, for example, the esters of alanine, leucine, methionine, threonine, tyrosine, cystine, glycine, isoleucine, lysine, phenylalanine, phenylglycine or valine, or amino-alcohols, such as, for example, 2-aminoethanol or phenylglycinol/alamine, it being possible for the latter to be prepared in optically pure form by reduction of the corresponding amino acid by a known method (compare G.C. Barrett, Chemistry and Biochemistry of the Amino Acids, Chapman and Hall, 1985).

The diastereomeric amides of the compounds of the formula (I) can thus be prepared by a process analogous to process [C] described above by using the abovementioned amine components. After resolution of the diastereomers by the customary methods listed above and subsequent hydrolysis, the pure enantiomers of the compounds of the formula (I) according to the invention are obtained.

Activating reagents which are used are in general the customary peptide-coupling reagents. These include, preferably, carbodiimides, such as, for example, diisopropylcarbodiimide, dicyclohexylcarbodiimide or N-(3-dimethylaminoisopropyl)-N'-ethylcarbodiimide hydrochloride, or carbonyl compounds, such as carbonyldiimidazole or 1,2-oxalium compounds, such as 2-ethyl-5-phenyl-1,2-oxazolium-3-sulphonate, or propanephosphonic anhydride or isobutyl chloroformate or benzotriazolyloxy-tris-(dimethylamino)-phosphonium hexafluorophosphate or phosphoric acid diphenyl ester-amide or methanesulphonyl chloride, if appropriate in the presence of bases, such as triethylamine or N-ethylmorpholine or N-methylpiperidine or dicyclohexylcarbodiimide and N-hydroxysuccinimide.

The hydrolysis is in general carried out with inorganic or organic acids, such as hydrochloric acid, hydrobromic

acid, sulphuric acid, phosphoric acid, formic acid, acetic acid, propionic acid, methanesulphonic acid or trifluoroacetic acid, or mixtures of the acids mentioned.

The amidation of the compounds of the general formula (I) according to the invention is in general carried out in a temperature range from 0°C to +150°C, preferably from 0°C to +50°C.

The amidation is in general carried out under normal pressure. However, it is also possible to carry out the process under reduced pressure or under increased pressure (for example in a range from 0.5 to 5 bar).

The esters of the general formula (Ia) used as starting compounds are also prepared from the known 4-hydroxyphenylacetic acids by etherification with 2-halogenomethylquinolines of the general formula (VI) analogously to process D.

The etherification can be carried out in inert organic solvents, if appropriate in the presence of a base.

Solvents for the etherification can be inert organic solvents which do not change under the reaction conditions. These include, preferably, ethers, such as, for example, dioxane, tetrahydrofuran or diethyl ether, halogenohydrocarbons, such as methylene chloride, chloroform, carbon tetrachloride, 1,2-dichloroethane or trichloroethylene, hydrocarbons, such as benzene, xylene, toluene, hexane, cyclohexane or petroleum fractions, nitromethane, dimethylformamide, acetonitrile, acetone or hexamethylphosphoric acid triamide. It is also possible to employ mixtures of the solvents.

Inorganic or organic bases can be employed as bases for the etherification. These include, preferably, alkali metal hydroxides, such as, for example, sodium hydroxide

or potassium hydroxide, alkaline earth metal hydroxides, such as, for example, barium hydroxide, alkali metal carbonates, such as sodium carbonate or potassium carbonate, alkaline earth metal carbonates, such as calcium carbonate, or organic amines (trialkyl(C_1-C_6)amines), such as triethylamine, or heterocyclic compounds, such as pyridine, methyl-piperidine, piperidine or morpholine.

It is also possible for alkali metals, such as sodium, and hydrides thereof, such as sodium hdyride, to be employed as bases.

The etherification to prepare compounds of the formula (Ia) is in general carried out in a temperature range from 0°C to 150°C, preferably from 10°C to 100°C, and in general under normal pressure. However, it is also possible to carry out the process under reduced pressure or increased pressure (for example in a range from 0.5 to 5 bar).

In general, 0.5 to 5, preferably 1 to 2, mol of halide per mol of reaction partner is employed. The base is in general employed in an amount of 0.5 to 5 mol, preferably 1 to 3 mol, based on the halide.

4-Hydroxyphenylacetic acid esters are known or can be prepared by customary methods from the corresponding phenols, suitable protective groups being split off [compare H. Beyer, Lehrbuch der organischen Chemie (Textbook of Organic Chemistry), S. Hirzel Verlag, Stuttgart; Protective Groups in Organic Synthesis, J. Wiley & Sons, 1981, New York].

The substituted 4-hydroxyphenylacetic acid esters of the general formula (V) are in most cases new and can be prepared from the abovementioned 4-hydroxyphenylacetic acid esters by alkylation by known methods (compare Ferri, Reaktionen der organischen Synthese, Georg Thieme

Verlag, Stuttgart, 1978).

2-Halogenomethylquinolines of the formula (VI), such as, for example, 2-chloromethylquinoline, are known and can be prepared by customary methods [compare Chem. Berichte. 120, 649, 1987].

The compounds of the formula (II) and (III) are known or can be prepared by customary halogenation methods [compare Organikum VEB Deutscher Verlag der Wissenschaften, Berlin 1977].

The acids, esters and amides according to the invention can be employed as active compounds in medicaments. The substances have an action in particular as inhibitors of enzymatic reactions in the context of arachidonic acid metabolism, in particular of 5-lipoxygenase.

The compounds according to the invention exhibit a good action following oral administration in lipoxygenase-sensitive test models.

They are therefore preferably suitable for treatment and prevention of diseases of the respiratory tract, such as allergies/asthma, bronchitis, emphysemas, shock lung, pulmonary hypertension, inflammations/rheumatism and oedemas, thromboses and thromboembolisms, ischaemias (peripheral, cardiac and cerebral circulation disturbances), cardiac and cerebral infarctions, disturbances in cardiac rhythm, angina pectoris and arteriosclerosis, for tissue transplants, dermatoses, such as psoriasis, and metastases and for cytoprotection in the gastrointestinal tract.

The new active compounds can be converted into the customary formulations, such as tablets, capsules, coated tablets, pills, granules, aerosols, syrups, emulsions, suspensions and solutions, in a manner which is known per

se using inert non-toxic pharmaceutically suitable excipients or solvents. The therapeutically active compound should in each case be present in the total mixture here in a concentration of about 0.5 to 90% by weight, preferably 10 to 70% by weight, that is to say in amounts which suffice to achieve the stated dosage range.

The formulations are prepared, for example, by extending the active compounds with solvents and/or excipients, if appropriate using emulsifying agents and/or dispersing agents, and, for example, in the case where water is used as a diluent, organic solvents can be used, if appropriate, as auxiliary solvents.

Examples of auxiliaries which may be mentioned are: water, non-toxic organic solvents, such as paraffins (for example petroleum fractions), vegetable oils (for example groundnut/sesame oil), alcohols (for example ethyl alcohol and glycerol) and glycols (for example propylene glycol and polyethylene glycol), solid excipients, such as natural rock powders (for example kaolins, aluminas, talc and chalk), synthetic rock powders (for example highly disperse silicic acid and silicates), sugars (for example sucrose, lactose and glucose), emulsifying agents (for example polyoxyethylene fatty acid esters, polyoxyethylene fatty alcohol ethers, alkylsulphonates and arylsulphonates), dispersing agents (for example lignin-sulphite waste liquors, methylcellulose, starch and polyvinylpyrrolidone) and lubricants (for example magnesium stearate, talc, stearic acid and sodium lauryl sulphate.

Administration can be effected in the customary manner, preferably orally or parenterally, in particular perlingually or intravenously. In the case of oral use, tablets can of course also contain, in addition to the excipients mentioned, additives such as sodium citrate, calcium carbonate and dicalcium phosphate, together with

various additional substances, such as starch, preferably potato starch, gelatine and the like. Lubricants, such as magnesium stearate, sodium lauryl sulphate and talc, can moreover be co-used for tablet-making. In the case of aqueous suspensions and/or elixirs intended for oral use, various agents for improving the taste or dyestuffs can be added to the active compounds in addition to the abovementioned auxiliaries.

In the case of parenteral use, solutions of the active compounds can be used, employing suitable liquid excipients.

In general, it has proved advantageous in the case of intravenous administration to administer amounts of about 0.01 to 10 mg/kg, preferably 0.01 to 5 mg/kg of body weight to achieve effective results. In the case of oral administration, the dosage is in general about 0.1 to 200 mg/kg, preferably 1 to 100 mg/kg of body weight.

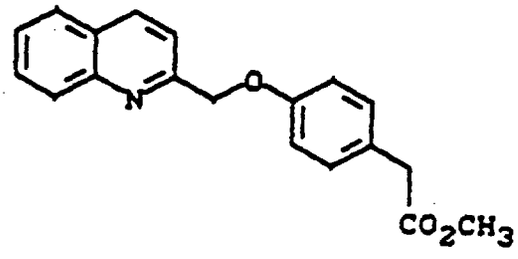
Nevertheless, it may at times be necessary to deviate from the amounts mentioned, and in particular to do so as a function of the body weight or nature of the administration route, the individual behaviour towards the medicament, the nature of its formulation and the time or interval at which administration takes place. Thus it can in some cases suffice to manage with less than the abovementioned minimum amount, whereas in other cases the upper limit mentioned must be exceeded. Where relatively large amounts are administered, it may be advisable to divide these into several individual doses over the course of the day.

The acids and esters according to the invention can be used both in human medicine and in veterinary medicine.

Preparation Examples

Example 1 (starting compound)

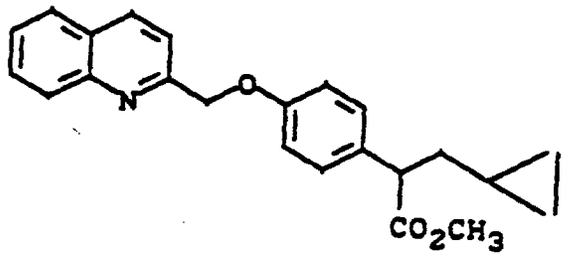
Methyl 4-(quinolin-2-yl-methoxy)phenylacetate



200 g (1.2 mol) of methyl 4-hydroxyphenylacetate and 166 g (1.2 mol) of potassium carbonate are stirred in 2 l of dimethylformamide at 25°C for 1 hour. After addition of 214 g (1.2 mol) of 2-chloromethylquinoline, the mixture is heated to 50°C for 15 hours. After concentration in vacuo, the residue is partitioned between water and ethyl acetate and the organic phase is dried over sodium sulphate and concentrated. The product which remains is recrystallized from methanol.
Yield: 293 g (79% of theory)
Melting point: 71 - 73°C

Example 2

Methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-3-cyclopropyl-propionate



15.4 g (50 mmol) of methyl 4-(quinolin-2-yl-methoxy)-phenylacetate are added dropwise to a suspension of 1.5 g (55 mmol) of sodium hydride in 60 ml of dimethylformamide at 0°C under an inert gas. When the evolution of hydrogen has ended, the mixture is subsequently stirred at 25°C

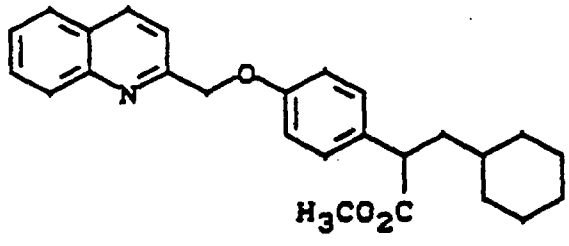
for 1 hour, 7.4 g (55 mmol) of (bromomethyl)-cyclopropane in 60 ml of dimethylformamide are added dropwise, while cooling with ice, and the mixture is stirred at 25°C for 16 hours. After the solvent has been evaporated off in vacuo, the residue is partitioned between ethyl acetate and water and the organic phase is dried over sodium sulphate and concentrated. The residue is recrystallized from methanol.

Yield: 15 g (83% of theory)

Melting point: 47°C

Example 3

Methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-3-cyclohexyl-propionate



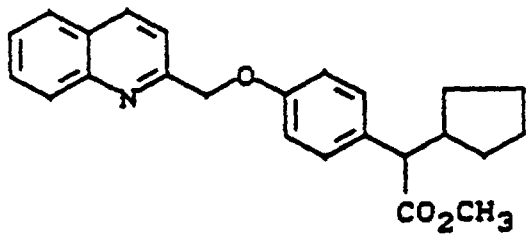
The preparation is carried out from 15.4 g (50 mmol) of methyl 4-(quinolin-2-yl-methoxy)phenylacetate and 9.74 g (55 mmol) of (bromomethyl)-cyclohexane analogously to the instructions of Example 2.

Yield: 15.9 g (79% of theory)

Melting point: 69°C

Example 4

Methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cyclopentyl-acetate



Process a)

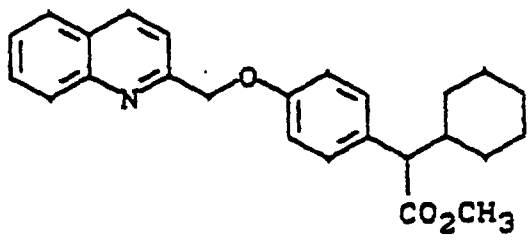
The preparation is carried out from 15.4 g (50 mmol) of methyl 4-(quinolin-2-yl-methoxy)phenylacetate and 8.2 g (55 mmol) of cyclopentyl bromide analogously to the instructions of Example 2.
Yield: 12.8 g (68% of theory)
Melting point: 94°C

Process b)

2.3 g (10 mmol) of methyl 2-(cyclopentyl-2(4-hydroxyphenyl)acetate are dissolved in 30 ml of dimethylformamide. After addition of 1.4 g (10 mmol) of potassium carbonate, the mixture is stirred at 60°C for 1 hour, a solution of 2.3 g (10 mmol) of 2-chloromethylquinoline in 20 ml of dimethylformamide is added dropwise and the mixture is stirred at 60°C for 15 hours. After cooling, the mixture is concentrated, the residue is taken up in ethyl acetate and the mixture is washed twice with water. After drying over sodium sulphate, the mixture is concentrated and the residue is recrystallized from methanol.
Yield: 3.18 g (85% of theory)

Example 5

Methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cyclohexylacetate



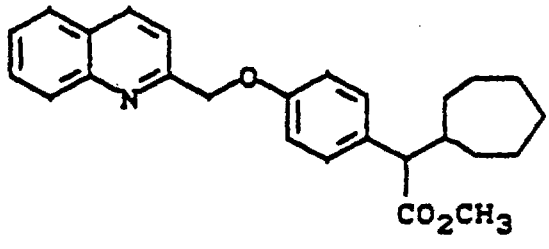
The preparation is carried out from 15.4 g (50 mmol) of methyl 4-(quinolin-2-yl-methoxy)phenylacetate and 11.55 g (55 mmol) of cyclohexyl iodide analogously to the instructions of Example 2.

Yield: 11.74 g (60% of theory)

Melting point: 92°C

Example 6

Methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cycloheptyl-acetate



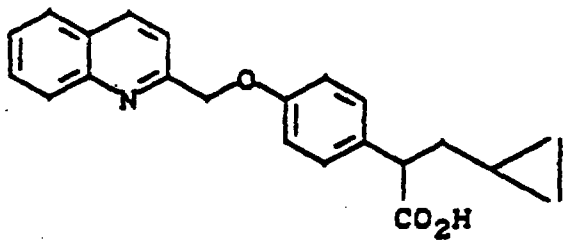
The preparation is carried out from 15.4 g (50 mmol) of methyl 4-(quinolin-2-yl-methoxy)phenylacetate and 9.07 g (55 mmol) of cycloheptyl bromide analogously to the instructions of Example 2.

Yield: 16 g (80% of theory)

Melting point: 81°C

Example 7

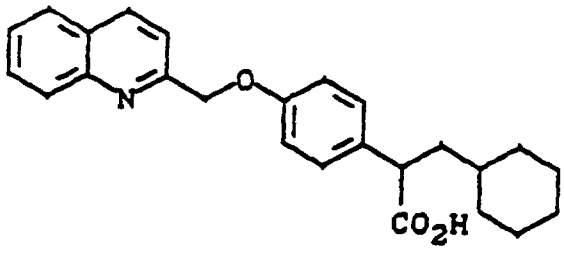
2-[4-(Quinolin-2-yl-methoxy)phenyl]-3-cyclopropyl-propionic acid



13.33 g (37 mmol) of methyl 2-[4-(quinolin-2-yl-methoxy)-phenyl]-3-cyclopropyl-propionate are heated under reflux in 200 ml of methanol and 55.4 ml of 1 molar sodium hydroxide solution for 10 hours. After cooling, the mixture is acidified with concentrated hydrochloric acid and the product which has precipitated is filtered off with suction and dried.
Yield: 12.5 g (98% of theory)
Melting point: 146°C

Example 8

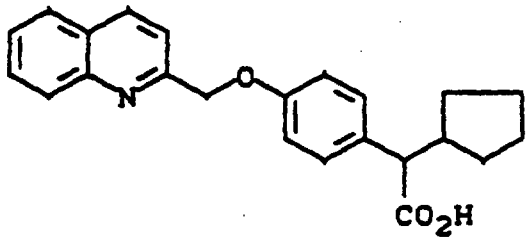
2-[4-(Quinolin-2-yl-methoxy)phenyl]-3-cyclohexylpropionic acid



The preparation is carried out from 6.25 g (15.5 mmol) of methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-3-cyclohexyl propionate analogously to the instructions of Example 7.
Yield: 5 g (83% of theory)
Melting point: 148 - 151°C

Example 9

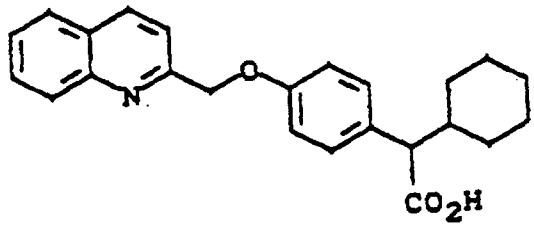
2-[4-(Quinolin-2-yl-methoxy)phenyl]-2-cyclopentylacetic acid



The preparation is carried out from 10.87 g (29 mmol) of methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cyclopentylacetate analogously to the instructions of Example 7.
Yield: 8.8 g (84% of theory)
Melting point: 183 - 185°C

Example 10

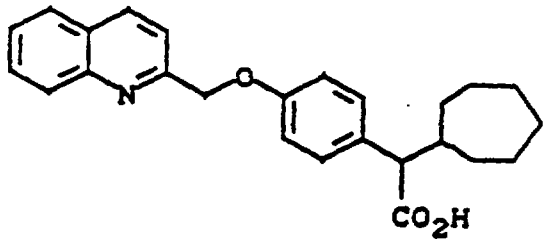
2-[4-(Quinolin-2-yl-methoxy)phenyl]-2-cyclohexylacetic acid



The preparation is carried out from 10 g (26 mmol) of methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cyclohexylacetate analogously to the instructions of Example 7.
Yield: 8.7 g (90% of theory)
Melting point: 201 - 207°C

Example 11

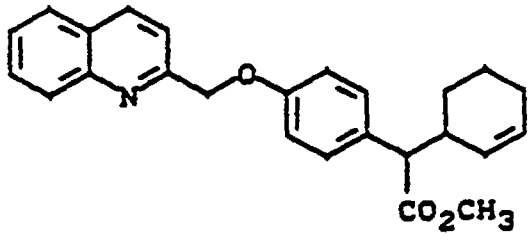
2-[4-(Quinolin-2-yl-methoxy)phenyl]-2-cycloheptylacetic acid



The preparation is carried out from 11 g (27 mmol) of methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cycloheptyl-acetate analogously to the instructions of Example 7.
Yield: 9.3 g (87% of theory)
Melting point: 176°C

Example 12

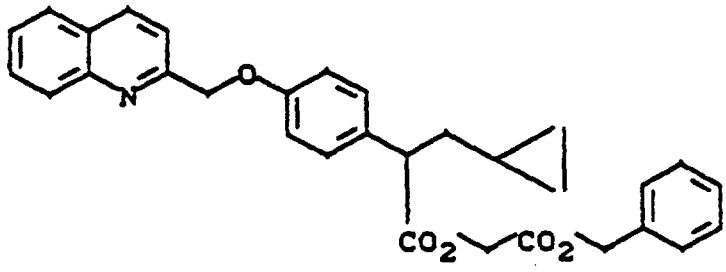
Methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cyclohex-2-enyl)acetate



The preparation is carried out from 15.4 g (50 mmol) of methyl 4-(quinolin-2-yl-methoxy)phenylacetate and 8.86 g (55 mmol) of 3-bromocyclohexene analogously to the instructions of Example 2.
Yield: 14.74 g (76% of theory)
Melting point: 102 - 104°C

Example 13

Benzyloxycarbonylmethyl 2-[4-(quinolin-2-yl-methoxy)-phenyl]-3-cyclopropylpropionate



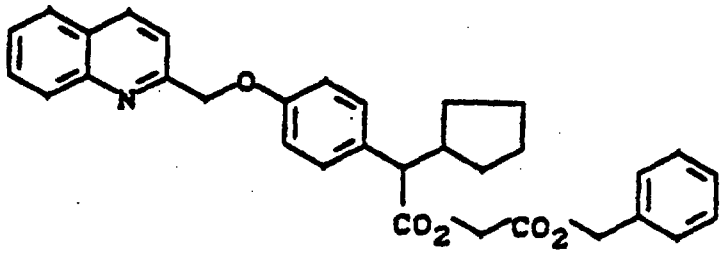
7 g of 2-[4-(quinolin-2-yl-methoxy)phenyl]-3-cyclopropyl-propionic acid, 5 g of benzyl bromoacetate and 4 g of dicyclohexylamine are heated under reflux in 100 ml of tetrahydrofuran for 15 hours. After cooling to 0°C, the salt which has precipitated is filtered off and the solvent is evaporated off in vacuo. The residue is chromatographed on silica gel using methylene chloride. An oil is obtained.

Yield: 9.27 g (93% of theory)

R_t (HPLC) = 4.30 minutes (RP 8, 7 µm; acetonitrile/water 70:30)).

Example 14

Benzyloxycarbonylmethyl 2-[4-(quinolin-2-yl-methoxy)-phenyl]-2-cyclopentylacetate



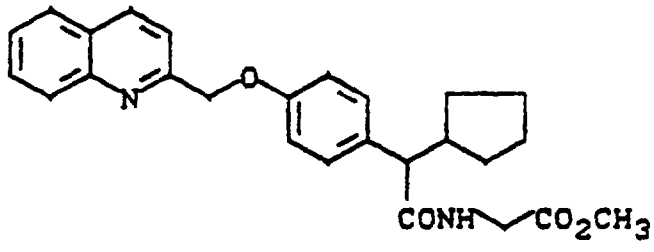
The preparation is carried out from 7.22 g (20 mmol) of 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cyclopentylacetic acid and 5 g (22 mmol) of benzyl bromoacetate analogously to the instructions of Example 13.

Yield: 8.03 g (79% of theory)

Melting point: 63 - 65°C (hydrochloride)

Example 15

2-[4-(Quinolin-2-yl-methoxy)phenyl]-2-cyclopentylacetic acid methyloxycarbonylmethylamide



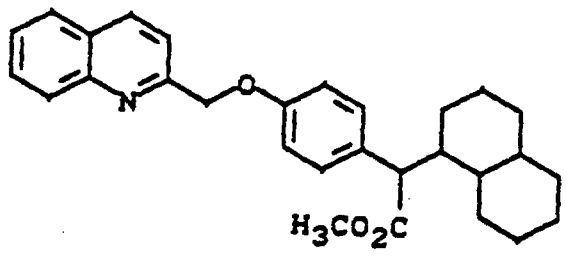
7.22 g (20 mmol) of 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cyclopentylacetic acid and 3.0 g (24 mmol) of glycine methyl ester hydrochloride are dissolved in 75 ml of dimethylformamide. After cooling to 0°C, 6.6 g (24 mmol) of phosphoric acid diphenyl ester-azide, dissolved in 25 ml of dimethylformamide, are added dropwise and the mixture is subsequently stirred for 30 minutes. 7.3 g (72 mmol) of triethylamine are then added dropwise and the mixture is subsequently stirred at 0°C for 4 hours and at 25°C for 15 hours. The reaction solution is poured onto 300 g of ice and extracted three times with ethyl acetate. The organic phases are washed once with 1 normal hydrochloric acid and once with water, dried over sodium sulphate and concentrated. The product is recrystallized from methanol.

Yield: 5.34 g (62% of theory)

Melting point: 134 - 136°C

Example 16

Methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-(1-decalinyl)-acetate



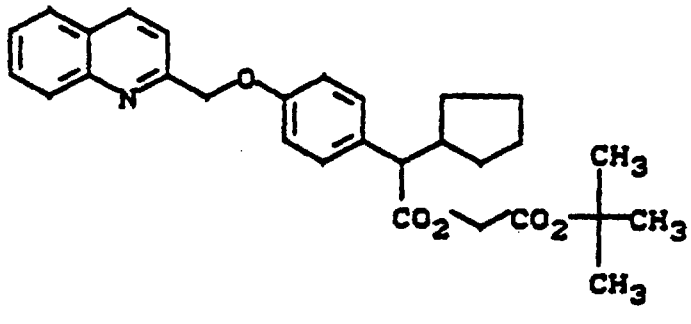
The preparation is carried out from 15.4 g (50 mmol) of methyl 4-(quinolin-2-yl-methoxy)phenyl-acetate and 9.55 g (55 mmol) of 1-chloro-decalin analogously to the instructions of Example 2.

Yield: 3.11 g (14% of theory)

Melting point: 118°C

Example 17

tert.-Butyloxycarbonylmethyl 2-[4-(quinolin-2-yl-methoxy)-phenyl]-2-cyclopentylacetate



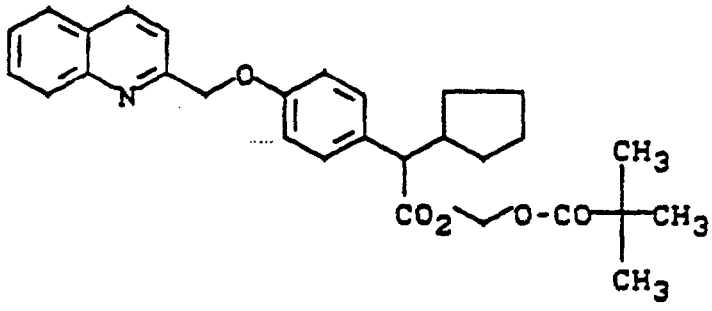
The preparation is carried out from 3 g (8.3 mmol) of 2-[4-(quinolin-2-yl-methoxy)-phenyl]-2-cyclopentyl-acetic acid and 1.77 g (9.1 mmol) of tert.-butylbromoacetate analogously to the instructions of Example 13.

Yield: 3.18 g (80.5% of theory)

Melting point: 88 - 91°C

Example 18

Pivaloyloxymethyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cyclopentylacetate



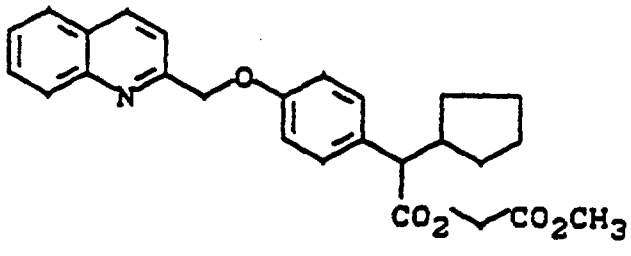
The preparation is carried out from 3 g (8.3 mmol) of 2-[4-(quinolin-2-yl-methoxy)-phenyl]-2-cyclopentyl-acetic acid and 1.37 g (9.1 mmol) of chloromethyl pivalate analogously to the instructions of Example 13.

Yield: 1.38 g (35% of theory)

Melting point: 30 - 32°C

Example 19

Methoxycarbonylmethyl 2-[4-(quinolin-2-yl-methoxy)-phenyl]-2-cyclopentyl-acetate



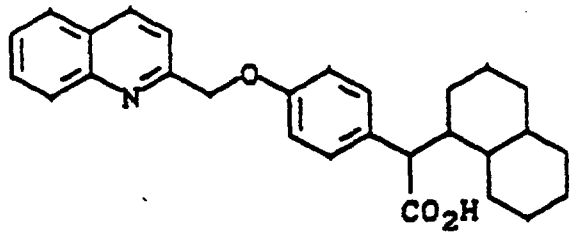
The preparation is carried out from 3 g (8.3 mmol) of 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cyclopentyl-acetic acid and 1.39 g (9.1 mmol) of methyl bromoacetate analogously to the instructions of Example 13.

Yield: 3.37 g (94% of theory)

Melting point: 90 - 93°C

Example 20

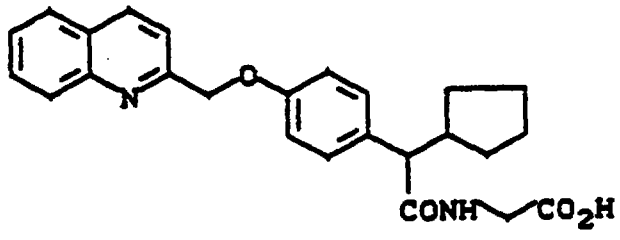
2-[4-(Quinolin-2-yl-methoxy)phenyl]-2-(1-decalinyl)-acetic acid



The preparation is carried out from 610 mg (1.37 mmol) of methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-(1-decalinyl)-acetate analogously to the instructions of Example 7.
Yield: 470 mg (80% of theory)
Melting point: 200 - 207°C

Example 21

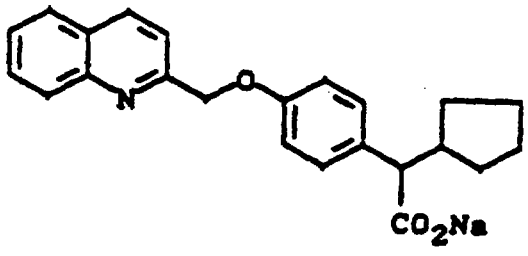
2-[4-(Quinolin-2-yl-methoxy)phenyl]-2-cyclopentylacetic acid carboxymethylamide



The preparation is carried out from 3 g (69 mmol) of 2-[4-(quinolin-2-yl-methoxy)-phenyl]-2-cyclopentyl-acetic acid methoxycarbonyl-methylamide analogously to the instructions of Example 7.
Yield: 2.47 g (85% of theory)
Melting point: 182 - 185°C

Example 22

Sodium 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cyclopentyl-acetate



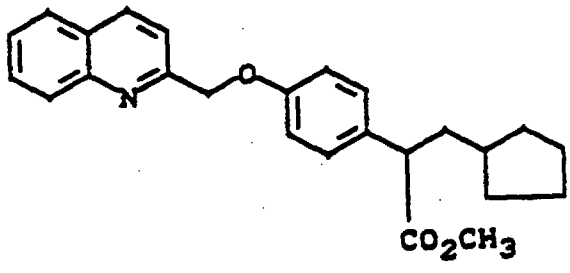
10 g (27.7 mmol) of 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cyclopentylacetic acid are dissolved in 100 ml of water. After addition of 27.7 ml of 1 normal sodium hydroxide solution, the mixture is stirred at 25°C for 1 hour and then concentrated and the residue is dried in vacuo at 100°C.

Yield: quantitative

Melting point: > 230°C

Example 23

Methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-3-cyclopentyl-propionate



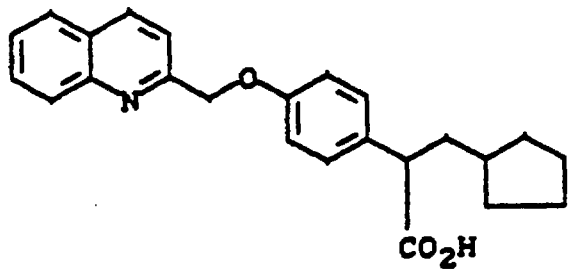
The preparation is carried out from 6.2 g (20 mmol) of methyl 4-(quinolin-2-yl-methoxy)phenylacetate and 3.3 g (20 mmol) of bromomethyl-cyclopentane analogously to the instructions of Example 2.

Yield: 5.1 g (65.5% of theory)

Melting point: 66 - 68°C

Example 24

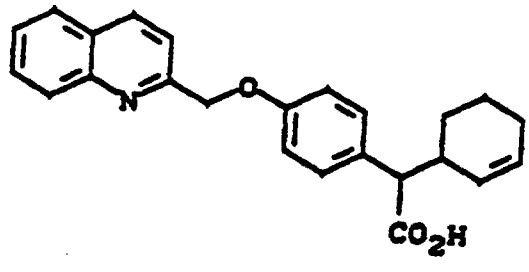
2-[4-(Quinolin-2-yl-methoxy)phenyl]-3-cyclopentyl-propionic acid



The preparation is carried out from 5 g (12.8 mmol) of methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-3-cyclopentyl-propionate analogously to the instructions of Example 7.
Yield: 2.5 g (52% of theory)
Melting point: 126 - 128°C

Example 25

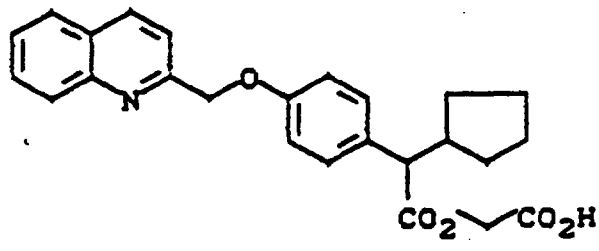
2-[4-(Quinolin-2-yl-methoxy)phenyl]-2-(cyclohex-2-enyl)-acetic acid



The preparation is carried out from 24.34 g (62.8 mmol) of methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-(cyclohex-2-enyl)-acetate analogously to the instructions of Example 7.
Yield: 18.3 g (78% of theory)
Melting point: 188 - 192°C

Example 26

Carboxymethyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-3-cyclopentylacetate



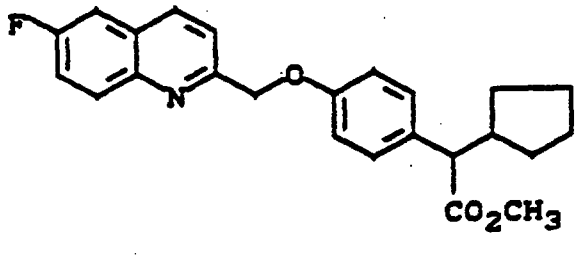
6.91 g (13.5 mmol) of benzyloxycarbonylmethyl 2-[4-(quinolin-2-yl-methoxy)-phenyl]-2-cyclopentyl-acetate are dissolved in 100 ml of ethyl acetate and 10 ml of triethylamine, 0.5 g of palladium catalyst (10% strength on charcoal) is added and hydrogenation is carried out under normal pressure at 25°C. After uptake of the theoretical amount of hydrogen, the catalyst is filtered off. After concentration in vacuo, the residue is recrystallized from methanol.

Yield: 3.15 g (55.6% of theory)

Melting point: 168 - 171°C

Example 27

Methyl 2-[4-(6-fluoroquinolin-2-yl-methoxy)phenyl]-2-cyclopentylacetate



4.68 g (20.4 mmol) of methyl 2-[4-hydroxyphenyl)-2-cyclopentylacetate are dissolved in 50 ml of dimethylformamide. After addition of 2.82 g (20.4 mmol) of potassium carbonate, the mixture is stirred at 50°C for

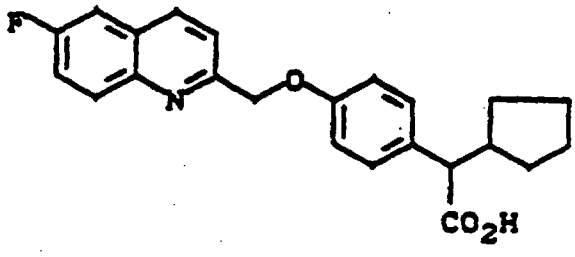
1 hour, 4 g (20.4 mmol) of 2-chloromethyl-6-fluoroquinoline are added and the mixture is stirred at 50°C for a further 15 hours. After concentrating in vacuo, the residue is partitioned between water and ethyl acetate, the organic phase is dried over sodium sulphate and concentrated and the residue is recrystallized from methanol.

Yield: 7.36 g (91.6% of theory)

Melting point: 117 - 119°C

Example 28

2-[4-(6-Fluoroquinolin-2-yl-methoxy)phenyl]-2-cyclopentylacetic acid



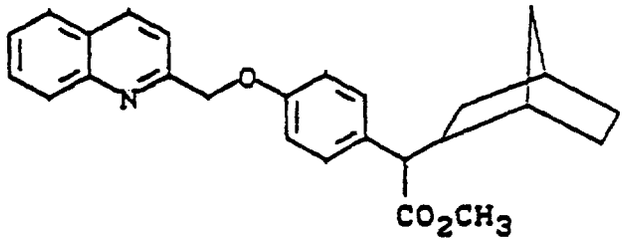
The preparation is carried out from 7 g (17.8 mmol) of methyl 2-[4-(fluoroquinolin-2-yl-methoxy)phenyl]-2-cyclopentyl-acetate analogously to the instructions of Example 7.

Yield: 4.51 g (67% of theory)

Melting point: 182 - 184°C

Example 29

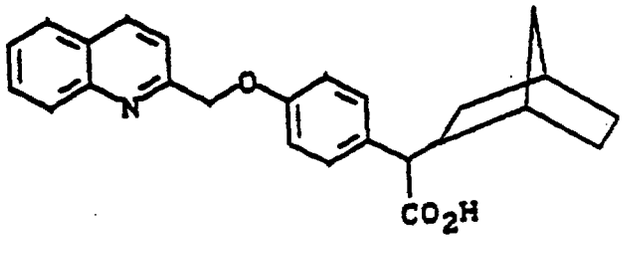
Methyl 2-[4-(quinolin-2-yl-methoxy)-phenyl]-2-norbornyl-acetate



The preparation is carried out from 6.2 g (20 mmol) of methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-acetate and 3.5 g (20 mmol) of exo-2-norbornyl chloride analogously to the instructions of Example 2. For purification, the product is chromatographed on silica gel 60 (eluent: toluene/ethyl acetate 9:1).
Yield: 0.2 g (2.5% of theory)
Melting point: 123 - 125°C

Example 30

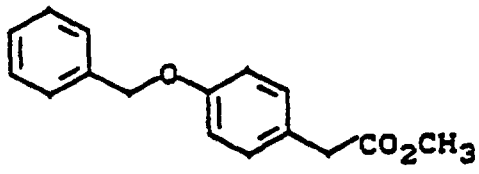
2-[4-(Quinolin-2-yl-methoxy)phenyl]-2-norbornyl-acetic acid



The preparation is carried out from 0.4 g (1 mmol) of methyl 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-norbornyl-acetate analogously to the instructions of Example 7.
Yield: 0.36 g (93% of theory)
Melting point: 158 - 160°C

Example 31

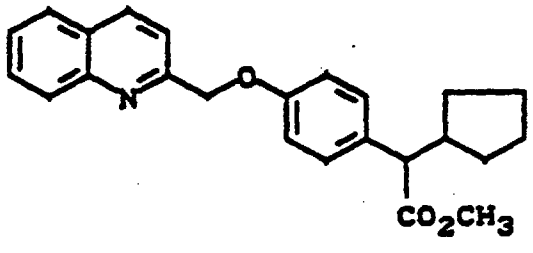
Methyl 4-benzyloxyphenylacetate



397 g of methyl 4-hydroxyphenylacetate and 330 g of potassium carbonate are stirred in 2 l of dimethylformamide at 25°C for 1 hour. 302 g of benzyl chloride are then added and the mixture is heated at 50°C for 15 hours. After concentrating in vacuo, the residue is partitioned between water and ethyl acetate and the organic phase is dried over sodium sulphate and concentrated. The product is recrystallized from methanol.
Yield: 511 g (83% of theory)
Melting point: 60°C

Example 32

Methyl 2-(4-benzyloxyphenyl)-2-cyclopentylacetate



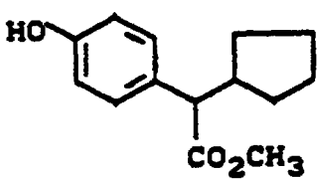
256.3 g (1 mol) of methyl 4-benzyloxyphenylacetate are dissolved in 1 l of dimethylformamide and the solution is added dropwise to a suspension of 24 g (1 mol) of sodium hydride in 100 ml of dimethylformamide at 0°C under an inert gas (argon). When the evolution of H_2 has ended, the mixture is subsequently stirred at 0°C for 2 hours. 149 g (1 mol) of cyclopentyl bromide, dissolved in 400 ml of dimethylformamide, are then added dropwise at the same temperature. When the addition has ended, the mixture is subsequently stirred at room temperature for 15 hours. The solvent is concentrated in vacuo and hot water (80°C)

is added to the residue. The mixture is cooled slowly, while stirring (KPG stirrer). The crystallized product is filtered off with suction, washed thoroughly with water, dried and recrystallized from methanol. Yield: 276 g (85% of theory)

Melting point: 77 - 78°C (methanol)

Example 33

2-Cyclopentyl-2-(4-hydroxyphenyl)

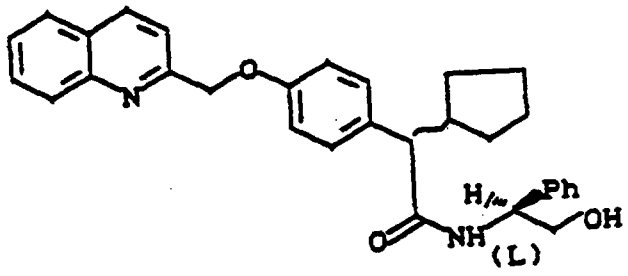


65 g (0.2 mol) of methyl 2-(4-benzyloxyphenyl)-2-cyclopentylacetate are dissolved in 100 ml of tetrahydrofuran, 200 ml of ethanol and 100 ml of triethylamine. After addition of 1.5 g of palladium catalyst (10% strength on charcoal), the mixture is hydrogenated under 3 bar of hydrogen for 2 hours. The catalyst is filtered off, the filtrate is concentrated and the residue is chromatographed on silica gel (eluent: methylene chloride). A viscous oil is obtained.

Yield: 43.7 g (93% of theory)

Examples 34 A and 34 B

Diastereomers of 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cyclopentylacetic acid [(L)-2-hydroxy-1-phenylethyl]amide



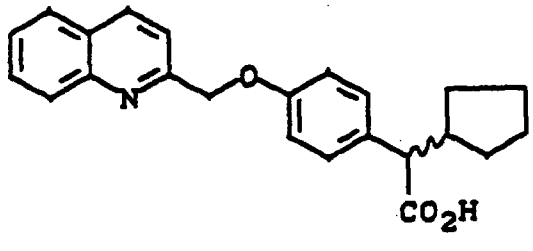
7.2 g (20 mmol) of 2-[4-(quinolin-2-yl-methoxy)phenyl]-2-cyclopentylacetic acid and 3.3 g (24 mmol) of (L)-phenyl-glycinol are dissolved in 100 ml of dimethylformamide. 6.6 g (24 mmol) of phosphoric acid diphenyl ester-azide in 25 ml of dimethylformamide are slowly added dropwise to the solution, which has been cooled to -10°C, 4.8 g (48 mmol) of triethylamine are then added and the mixture is stirred at -10°C for 15 hours. The reaction mixture is poured onto ice and the crude product is filtered off, washed with water and dried. Recrystallization three times from ethanol gives diastereomer 34 A. Diastereomer 34 B is obtained by recrystallization of the combined mother liquors three times from methylene chloride.

Example 34 A: Yield: 1.93 g (20.1% of theory)
Melting point: 201 - 203°C (EtOH)

Example 34 B: Yield: 1.52 g (15.8% of theory)
Melting point: 158 - 159°C (CH_2Cl_2)

Example 35

(+)-4-(2-Quinolin-2-yl-methoxy)phenyl]-2-cyclopentyl-acetic acid



(+)-Enantiomer

4.8 g (10 mmol) of diastereomer A from Example 34 are heated under reflux in 50 ml of dioxane and 50 ml of 5 normal sulphuric acid for 24 hours. After cooling to 0°C, the pH is brought to 3 with 5 normal sodium hydroxide solution. The product is filtered off with suction and recrystallized from ethanol.

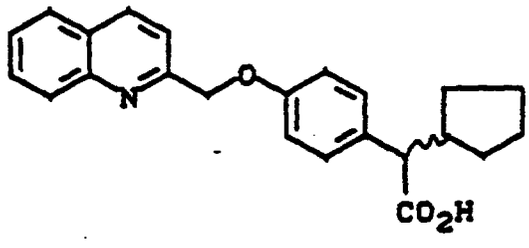
Yield: 2.38 g (65.8% of theory)

α_D^{25} = +40.9 (c = 1, $CHCl_3$)

Melting point: 170 - 172°C

Example 36

(-)-4-[2-Quinolin-2-yl-methoxy)-phenyl]-2-cyclopentyl-acetic acid



(-)-Enantiomer

The preparation of compound 36 is carried out analogously to the instructions of Example 35 using 4.8 g (10 mmol) of diastereomer B from Example 34.

Yield: 2.28 g (63.2% of theory)

α_D^{25} = - 40.7 (C = 1, $CHCl_3$)

Melting point: 170 - 172°C

Example 37 (use example)

The release of leucotriene B_4 (LTB_4) from polymorphonuclear rat leucocytes (PMN) following addition of substances and a Ca-ionophor was determined by means of reverse phase HPLC by the method of Borgeat, P. et al, Proc. Nat. Acad. Sci. (USA) 76, 2148-2152 (1979) as a measure of lipoxygenase inhibition.

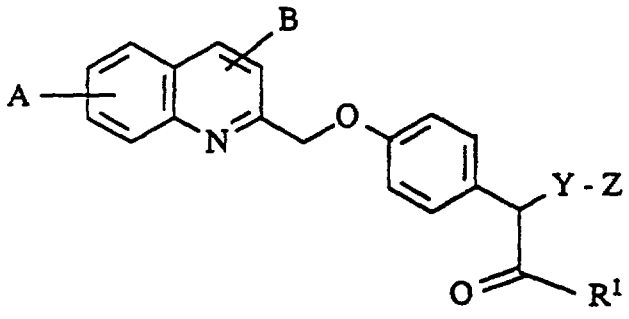
The values achieved in this test with some compounds according to the invention are listed by way of example in Table 1:

Table 1 Lipoxygenase inhibition

Example No.	LO inhibition IC_{50} (μM)
7	0.14
8	0.01
9	0.04

Patent Claims for the Contracting States: AT, BE, CH, DE, FR, GB, GR, IT, LI, NL, SE

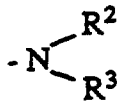
1. Substituted 4-(quinolin-2-yl-methoxy)phenyl-acetic acid derivatives of the formula



(I)

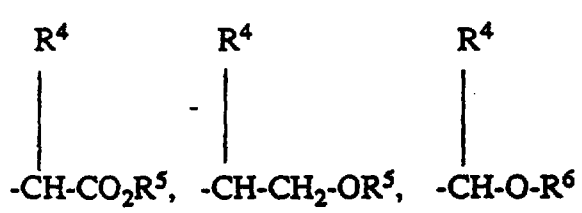
wherein

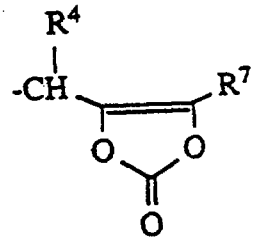
R^1 - represents a group of the formula

$-OR^2$ or  , wherein

R^2 and R^3 are identical or different and

- represent hydrogen, C_1-C_6-alkyl benzyl, phenyl or a group of the formula



or 

wherein

R^4 - represents hydrogen, C_1-C_6-alkyl, phenyl or benzyl, which can optionally be substituted by hydroxyl, C_1-C_6-alkoxycarbonyl, carboxyl, C_1-C_6-alkylthio, thienyl, furyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, quinolyl, isoquinolyl, quinazolyl,

quinoxalyl, thiazolyl, benzothiazolyl, isothiazolyl, oxazolyl, benzoxazolyl, isoxazolyl, imidazolyl, benzimidazolyl, pyrazolyl, indolyl and isoindolyl or carbymoyl,

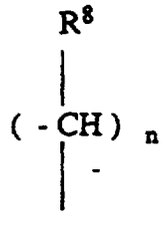
R^5 - represents hydrogen, C_1-C_6-alkyl, phenyl or benzyl,

R^6 - represents a group of the formula $-COR^5$ or $-CO_2R^5$, wherein R^5 has the abovementioned meaning,

and

R^7 - represents hydrogen, C_1-C_6-alkyl or phenyl,

Y - represents a group of the formula



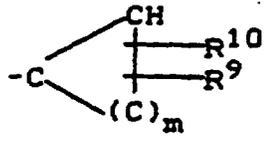
, wherein

R^8 - represents hydrogen, C_1-C_6-alkyl or phenyl,

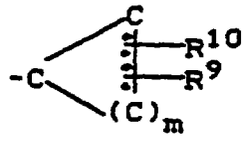
and

n - denotes a number from 0 to 5,

Z - represents norbornyl, or
represents a group of the formula



or



wherein

R^9 and R^{10} are identical or different and denote

hydrogen, C_1-C_6-alkyl or phenyl, or

R^9 and R^{10} can together form a saturated carbocyclic ring having up to 6 carbon atoms and

m denotes a number from 1 to 6,

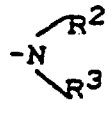
and

A and B are identical or different and denote hydrogen, methyl, ethyl, fluorine, chlorine or bromine,

and salts thereof.

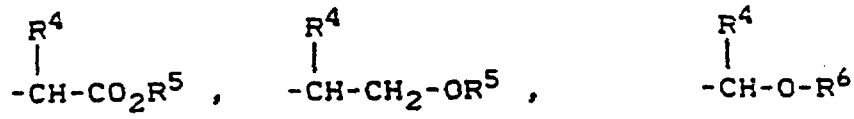
2. Substituted 4-(quinolin-2-yl-methoxy)phenyl-acetic acid derivatives of the formula (I) according to Claim 1, wherein

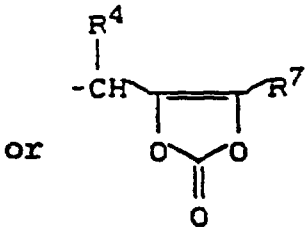
R^1 - represents a group of the formula

$-OR^2$ or  , wherein

R^2 and R^3 are identical or different and

- represent hydrogen, methyl, ethyl, propyl, isopropyl, butyl, tert.-butyl, phenyl or benzyl, or represent a group of the formula





, wherein

R^4 - represents hydrogen, methyl, ethyl, propyl, isopropyl, butyl, tert.-butyl, benzyl or phenyl, which can optionally be substituted by hydroxyl, methoxycarbonyl, ethoxycarbonyl propoxycarbonyl, carboxyl, methylthio, ethylthio, propylthio, imidazolyl or carbamoyl

R^5 - represents hydrogen, methyl, ethyl, propyl, isopropyl, butyl, tert.-butyl, phenyl or benzyl,

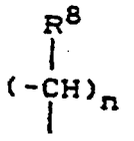
and

R^6 - represents a group of the formula $-COR^5$ or $-CO_2R^5$, wherein R^5 has the abovementioned meaning,

and

R^7 - represents hydrogen, methyl, ethyl, propyl, isopropyl, butyl, tert.butyl or phenyl,

Y - represents a group of the formula

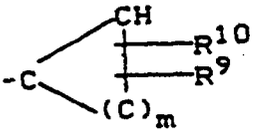
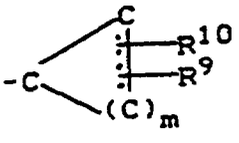

, wherein

R^8 - represents hydrogen, methyl, ethyl, propyl, isopropyl, butyl, tert.-butyl or phenyl,

and

n - denotes a number from 0 to 5,

Z - represents norbornyl or
represents a group of the formula


or

,

wherein

R^9 and R^{10} are identical or different and denote hydrogen, methyl, ethyl, n-propyl, isopropyl, butyl or tert.-butyl, or

R^9 and R^{10} can together form a saturated carbocyclic ring having up to 6 carbon atoms and

m - denotes a number from 1 to 6,

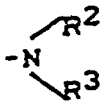
and

A and B are identical or different and denote hydrogen, methyl, ethyl, fluorine or chlorine,

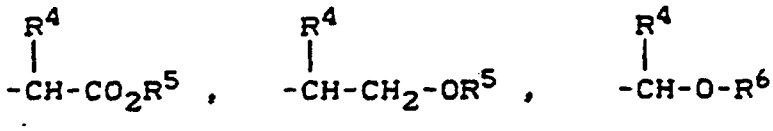
and salts thereof.

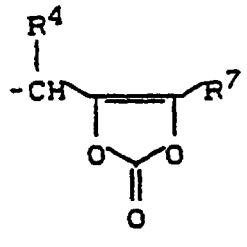
3. Substituted 4-(quinolin-2-yl-methoxy)phenylacetic acid derivatives according to Claim 1, wherein

R^1 - represents a group of the formula

$-OR^2$ or  , wherein

R^2 and R^3 are identical or different and
- represent hydrogen or methyl, or
represent a group of the formula



or  , wherein

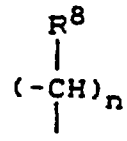
R^4 - represents hydrogen, methyl or phenyl,

R^5 - represents hydrogen, methyl, ethyl, tert.-butyl or benzyl,

R^6 - represents a group of the formula $-COR^5$, wherein R^5 has the abovementioned meaning, and

R^7 - represents methyl,

Y - represents a group of the formula



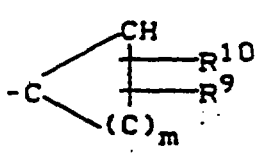
, wherein

R^8 - represents hydrogen or methyl,

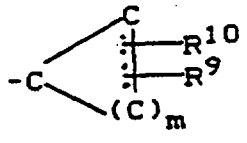
and

n - denotes a number 0 or 1,

Z - represents norbornyl, or
represents a group of the formula



or



,

wherein

R^9 and R^{10} are identical or different and denote hydrogen or methyl, or

R^9 and R^{10} together form a cyclohexyl ring, and

m - denotes a number 1, 2, 3, 4 or 5,

A and B denote hydrogen or fluorine,

and salts thereof.

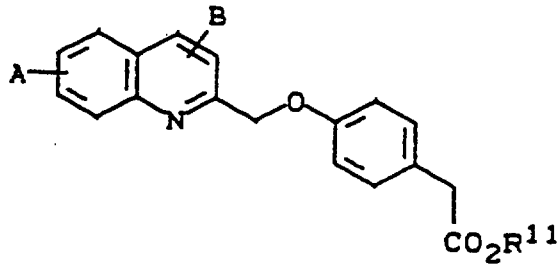
4. (+)-4-[(2-Quinolin-2-yl-methoxy)phenyl]-2-cyclopentyl-acetic acid according to Claim 1.

5. (-)-4-[(2-Quinolin-2-yl-methoxy)phenyl]-2-cyclopentyl-acetic acid according to Claim 1.

* C L M S *

6. Process for the preparation of substituted 4-(quinolin-2-yl-methoxy)phenyl-acetic acid derivatives according to Claim 1, characterized in that

[A] 4-(quinolin-2-yl-methoxy)phenylacetic acid esters of the general formula (Ia)



(Ia)

in which

R^{11} - represents alkyl and

A and B have the abovementioned meaning,

are alkylated with compounds of the general formula (II)

$$Y\text{-}Z\text{-}X \qquad (II)$$

in which

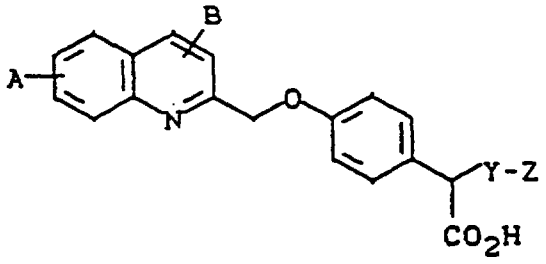
Y and Z have the abovementioned meaning and

X - represents chlorine, bromine or iodine,

and in the case of the acids the esters are hydrolyzed,

or in that

[B] the acids of the general formula (Ib)



(Ib)

in which

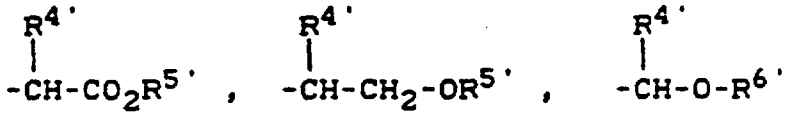
A, B, Y and Z have the abovementioned meaning,

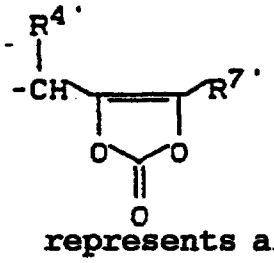
are esterified with compounds of the general formula (III)

$$X\text{-}R^{12} \qquad (III)$$

in which

R^{12} - represents a group of the formula



or  , wherein

$R^{4'}$ - represents alkyl, aralkyl or aryl, which can optionally be substituted by hydroxyl, carboxyl, alkoxycarbonyl, alkylthio, heteroaryl or aminocarbonyl,

$R^{5'}$ - represents alkyl, aryl or aralkyl,

$R^{6'}$ - represents a group of the formula $-COR^{5'}$ or $-CO_2R^{5'}$, wherein

$R^{5'}$ has the abovementioned meaning,

$R^{7'}$ - represents alkyl or aryl,

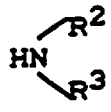
and

X has the abovementioned meaning,

and in the case of the acids the esters are subjected to hydrogenolytic cleavage,

or in that

[C] the acids of the general formula (Ib) are amidated with amines of the general formula (IV)

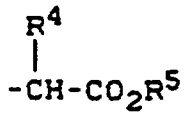


(IV)

in which

R^2 and R^3 have the abovementioned meaning,

with the proviso that R^5 does not denote hydrogen if R^2 or R^3 represents the group



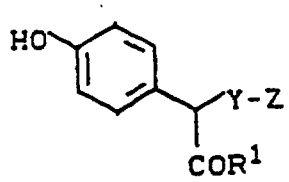
wherein

R^4 and R^5 have the abovementioned meaning,

in the presence of customary activating reagents, and in the case of the acids the esters are hydrolyzed

or in that

[D] phenols of the general formula (V)



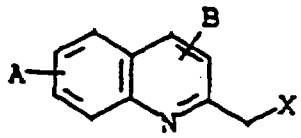
(V)

in which

R^1, Y and Z have the abovementioned meaning

are etherified with

2-halogenomethylquinolines of the formula (VI)



(VI)

in which

A, B and X have the abovementioned meaning,

and in the case of the acids the esters are hydrolyzed.

7. Process according to Claim 6, characterized in that it is carried out in the temperature range from 0 to 150°C.

8. Medicaments containing substituted 4-(quinolin-2-yl-methoxy)phenyl-acetic acid derivatives according to Claims 1 to 5.

* C L M S *

9. Medicaments according to Claim 8, containing 0.5 to 90% by weight of substituted 4-(quinolin-2-yl-methoxy)phenyl-acetic acid derivatives.

10. Use of substituted 4-(quinolin-2-yl-methoxy)phenyl-acetic acid derivatives according to Claims 1 to 5 for the preparation of medicaments.