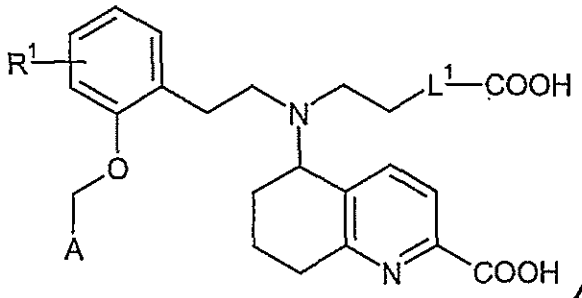
Patent Claims

~~1. Compound of the formula (I)~~



(I),

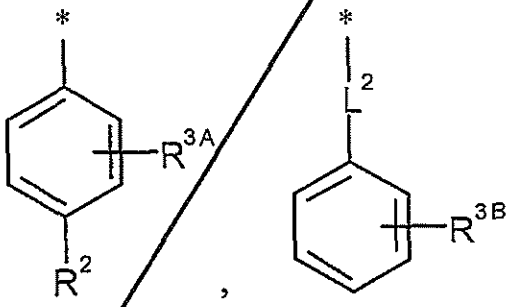
in which

R^1 represents hydrogen or fluorine,

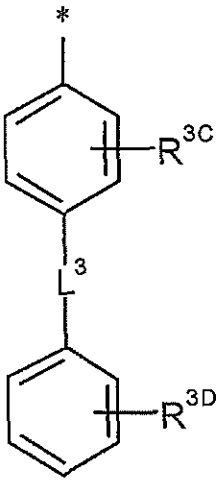
L^1 represents ethane-1,2-diyl or 1,4-phenylene,

and

A represents a group of the formula



or



in which

* denotes the respective point of attachment to the remainder of the molecule,

L^2 represents straight-chain (C_1-C_6)-alkanediyl,

~~L^3 represents a bond, -O-, -CH_2-, -CH_2-CH_2- or -CH=CH-,~~

R^2 represents (C_1-C_4)-alkyl which may be substituted up to six times by fluorine,

or

represents (C_3-C_6)-cycloalkyl which may be mono- or disubstituted by identical or different radicals selected from the group consisting of fluorine, difluoromethyl, trifluoromethyl and (C_1-C_4)-alkyl,

or

represents 4- to 6-membered heterocyclyl which contains one or two identical or different hetero ring members selected from the group consisting of $N(R^4)$, O, S and $S(O)_2$ where

R^4 represents (C_1-C_4)-alkyl or (C_1-C_4)-alkylcarbonyl or, in the case that $N(R^4)$ represents a ring nitrogen atom by means of which said heterocyclyl is attached to the adjacent phenyl group, is not present,

or

represents 5-membered heteroaryl which contains one, two or three identical or different ring heteroatoms selected from the group consisting of N, O and S and may optionally be fused to a phenyl ring,

where the heteroaryl ring and the optionally fused phenyl ring may each be mono- or disubstituted by identical or different radicals selected from the group consisting of fluorine, chlorine, cyano, difluoromethyl, trifluoromethyl, (C_1-C_4)-alkyl, difluoromethoxy, trifluoromethoxy and (C_1-C_4)-alkoxy,

or represents chlorine,

and

R^{3A}, R^{3B}, R^{3C} and R^{3D} independently of one another represent hydrogen or a substituent selected from the group consisting of fluorine, chlorine, bromine, cyano, (C_1-C_4)-alkyl, difluoromethyl, trifluoromethyl, (C_1-C_4)-alkoxy, difluoromethoxy and trifluoromethoxy,

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

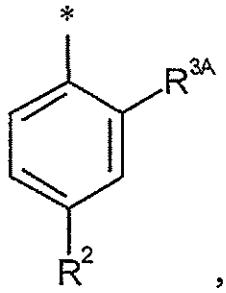
2. Compound of the formula (I) according to Claim 1 in which

R^1 represents hydrogen or fluorine,

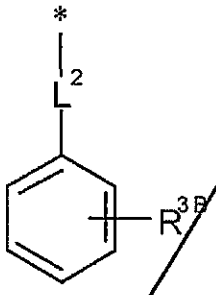
L^1 represents ethane-1,2-diyl or 1,4-phenylene,

and

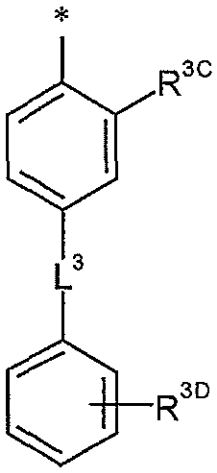
A represents a group of the formula



,



or



in which

* denotes the respective point of attachment to the remainder of the molecule,

L^2 represents straight-chain (C_3-C_5)-alkanediyl,

L^3 represents a bond, -CH_2-CH_2- or -CH=CH-,

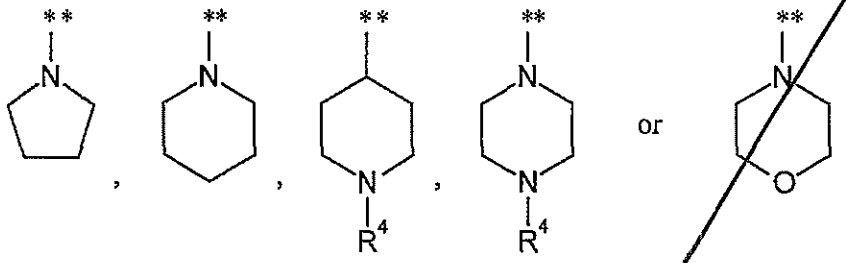
R^2 represents (C_1-C_4)-alkyl which may be substituted up to three times by fluorine,

or

represents cyclopentyl or cyclohexyl which may be mono- or disubstituted by identical or different radicals selected from the group consisting of fluorine, methyl and trifluoromethyl,

~~or~~

~~represents 5- or 6-membered heterocyclyl of the formula~~



in which

** denotes the respective point of attachment to the adjacent phenyl group

and

R^4 represents methyl, acetyl or propionyl,

or

represents 5-membered heteroaryl selected from the group consisting of 1,2-oxazolyl, 1,3-oxazolyl, 1,2-thiazolyl, 1,3-thiazolyl, 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,4-thiadiazolyl and 1,3,4-thiadiazolyl,

where the heteroaryl groups mentioned may each be substituted by methyl or trifluoromethyl

and

where 1,2-oxazolyl, 1,3-oxazolyl, 1,2-thiazolyl and 1,3-thiazolyl may be fused with a phenyl ring which for its part may be substituted by fluorine, chlorine, cyano, methyl, trifluoromethyl or trifluoromethoxy,

R^{3A} represents hydrogen, fluorine, chlorine, methyl or trifluoromethyl,

R^{3B} represents hydrogen, fluorine, chlorine, methyl, trifluoromethyl, methoxy or trifluoromethoxy,

R^{3C} represents hydrogen, fluorine, chlorine, methyl or trifluoromethyl,

~~and~~

R^{3D} represents hydrogen, fluorine, chlorine, cyano, methyl, trifluoromethyl, methoxy or trifluoromethoxy,

and salts, solvates and solvates of the salts thereof.

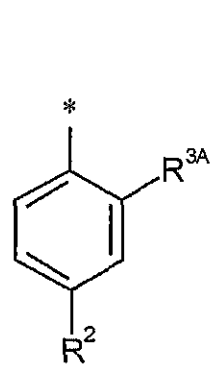
3. Compound of the formula (I) according to Claim 1 or 2 in which

R^1 represents hydrogen or fluorine,

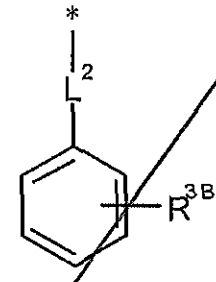
L^1 represents ethane-1,2-diyl or 1,4-phenylene,

and

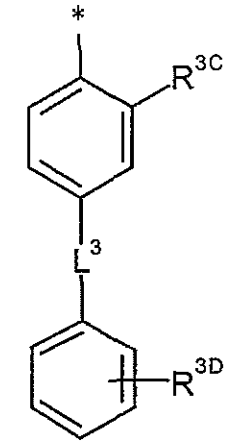
A represents a group of the formula



,



or



in which

* denotes the respective point of attachment to the remainder of the molecule,

L^2 represents straight-chain (C_3-C_5)-alkanediyl,

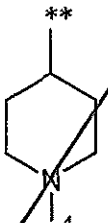
L^3 represents a bond, $-CH_2-CH_2-$ or -CH=CH-,

R^2 represents (C_1-C_4)-alkyl which may be substituted up to three times by fluorine,

or

~~represents cyclopentyl or cyclohexyl which may be mono- or disubstituted~~ by identical or different radicals selected from the group consisting of fluorine, methyl and trifluoromethyl,

or



represents 6-membered heterocyclyl of the formula in which

** denotes the point of attachment to the adjacent phenyl group

and

R^4 represents methyl, acetyl or propionyl,

or

represents 1,3-benzoxazol-2-yl, 1,2-benzoxazol-3-yl or 1,3-benzothiazol-2-yl which may be substituted by a radical selected from the group consisting of fluorine, chlorine, cyano, methyl, trifluoromethyl and trifluoromethoxy,

R^{3A} represents hydrogen, fluorine, chlorine, methyl or trifluoromethyl,

R^{3B} represents hydrogen, fluorine, chlorine, methyl, trifluoromethyl or trifluoromethoxy,

R^{3C} represents hydrogen, fluorine, chlorine, methyl or trifluoromethyl,

and

R^{3D} represents hydrogen, fluorine, chlorine, cyano, methyl, trifluoromethyl or trifluoromethoxy,

and salts, solvates and solvates of the salts thereof.

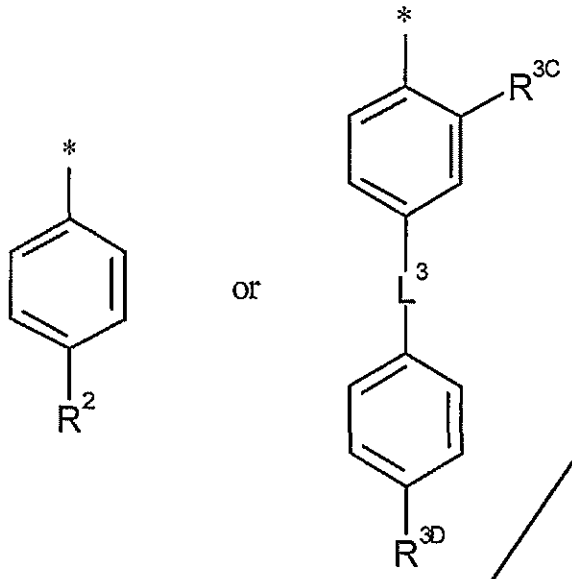
4. Compound of the formula (I) according to Claim 1, 2 or 3 in which

~~R^1 represents hydrogen or fluorine,~~

L^1 represents ethane-1,2-diyl or 1,4-phenylene,

and

A represents a group of the formula



or

in which

* denotes the respective point of attachment to the remainder of the molecule,

L^3 represents a bond or $-CH_2-CH_2-$,

R^2 represents *tert*-butyl, cyclohexyl, 4-(trifluoromethyl)cyclohexyl or 1,3-benzoxazol-2-yl which may be substituted by chlorine, cyano, methyl or trifluoromethyl,

R^{3C} represents hydrogen or chlorine,

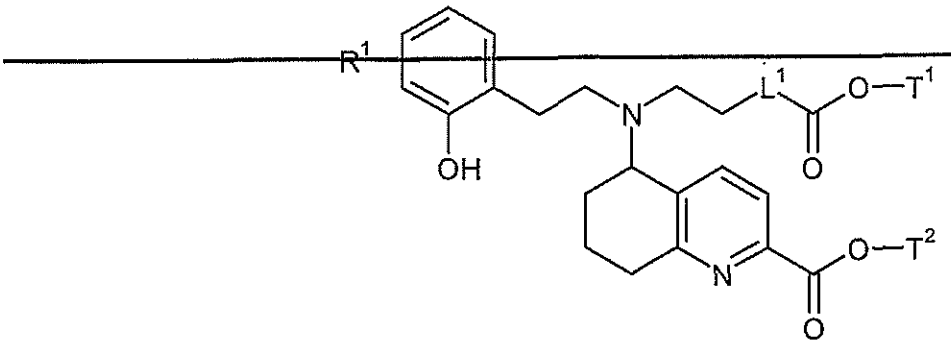
and

R^{3D} represents hydrogen, fluorine or trifluoromethyl,

and salts, solvates and solvates of the salts thereof.

5. Process for preparing a compound of the formula (I) as defined in any of Claims 1 to 4, characterized in that either

[A] a compound of the formula (II)



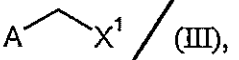
(II),

in which R^1 and L^1 have the meanings given in any of Claims 1 to 4

and

T^1 and T^2 are identical or different and represent (C_1-C_4)-alkyl,

is reacted in the presence of a base with a compound of the formula (III)



(III),

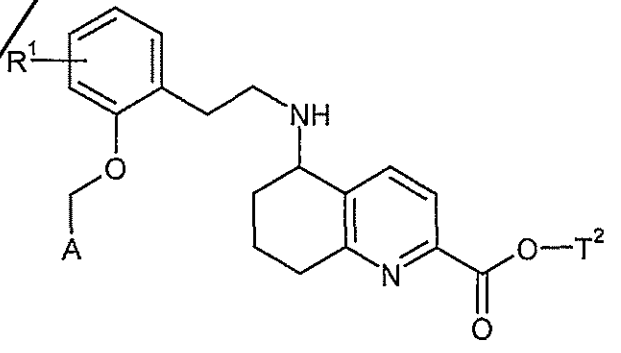
in which A has the meanings given in any of Claims 1 to 4

and

X^1 represents a leaving group such as, for example, chlorine, bromine, iodine, mesylate, triflate or tosylate,

or

[B] a compound of the formula (IV)



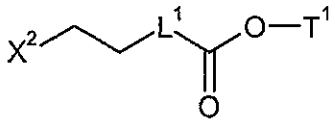
(IV),

in which R^1 and A have the meanings given in any of Claims 1 to 4

and

T^2 represents (C_1-C_4)-alkyl,

is reacted in the presence of a base with a compound of the formula (V)



(V),

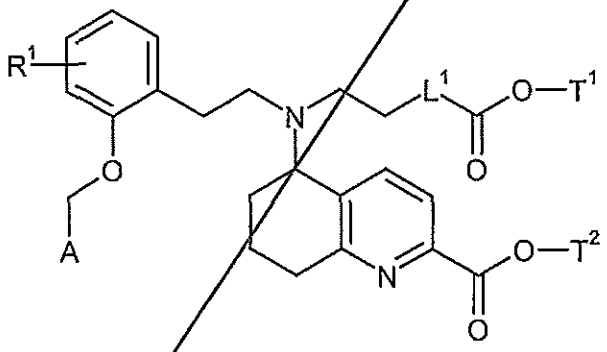
in which L^1 has the meanings given in any of Claims 1 to 4,

T^1 represents (C_1-C_4)-alkyl,

and

X^2 represents a leaving group such as, for example, chlorine, bromine, iodine, mesylate, triflate or tosylate,

and the respective resulting compound of the formula (VI)



(VI),

in which R^1, A, L^1, T^1 and T^2 have the meanings given above,

is then converted by hydrolysis of the ester groupings $-C(O)OT^1$ and $-C(O)OT^2$ into the corresponding dicarboxylic acid of the formula (I)

and the compounds of the formula (I) obtained in this manner are optionally separated into their enantiomers and/or diastereomers and/or optionally converted with the appropriate (i) solvents and/or (ii) bases or acids into their solvates, salts and/or solvates of the salts.

6. Compound as defined in any of Claims 1 to 4 for the treatment and/or prevention of diseases.

7. Compound as defined in any of Claims 1 to 4 for use in a method for the treatment and/or prevention of primary and secondary forms of pulmonary hypertension, heart failure,

~~angina pectoris, hypertension, thromboembolic disorders, ischaemias, vascular disorders,~~ impaired microcirculation, renal insufficiency, fibrotic disorders and arteriosclerosis.

8. Use of a compound as defined in any of Claims 1 to 4 for the preparation of medicament for the treatment and/or prevention of primary and secondary forms of pulmonary hypertension, heart failure, angina pectoris, hypertension, thromboembolic disorders, ischaemias, vascular disorders, impaired microcirculation, renal insufficiency, fibrotic disorders and arteriosclerosis.

9. Medicament, comprising a compound as defined in any of Claims 1 to 4 in combination with one or more inert non-toxic pharmaceutically suitable auxiliaries.

10. Medicament, comprising a compound as defined in any of Claims 1 to 4 in combination with one or more further active compounds selected from the group consisting of organic nitrates, NO donors, PDE 5 inhibitors, prostacyclin analogues, IP receptor agonists, endothelin receptor antagonists, guanylate cyclase stimulators, tyrosine kinase inhibitors, anti-obstructive agents, anti-inflammatory and/oder immunsuppressive agents, antithrombotic agents, agents for lowering blood pressure and agents that alter fat metabolism.

11. Medicament according to Claim 9 or 10 for the treatment and/or prevention of primary and secondary forms of pulmonary hypertension, heart failure, angina pectoris, hypertension, thromboembolic disorders, ischaemias, vascular disorders, impaired microcirculation, ~~renal insufficiency, fibrotic disorders and arteriosclerosis.~~

~~11.~~ 12. Method for the treatment and/or prevention of primary and secondary forms of pulmonary hypertension, heart failure, angina pectoris, hypertension, thromboembolic disorders, ischaemias, vascular disorders, impaired microcirculation, renal insufficiency, fibrotic disorders and arteriosclerosis in humans and animals by administration of an effective amount of at least one compound ~~as defined in any of Claims 1 to 4 or of a medicament as defined in any of Claims 9 to 11.~~