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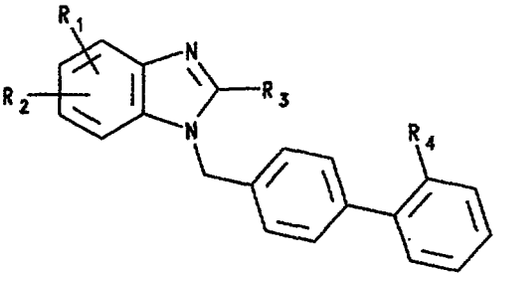
DR. KARL THOMAE GMBH
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Case 5/1057-FL-Eu

Benzimidazoles, pharmaceutical compositions containing these compounds and processes for preparing them

EP-A-0 392 317 has already described benzimidazoles which are valuable angiotensin antagonists.

It has now been found that the new benzimidazoles of general formula



(I)

the 1,3-isomer mixtures and addition salts thereof, particularly, for pharmaceutical use, the physiologically acceptable addition salts thereof with inorganic or organic acids or bases, are even more useful angiotensin antagonists, particularly angiotensin-II antagonists.

In general formula I above:

R_1 in the 4-position represents a fluorine, chlorine or bromine atom, a C_{1-4}-alkyl, a cycloalkyl, fluoromethyl, difluoromethyl or trifluoromethyl group and

R_2 represents a C_{3-5}-alkoxy group substituted in the 3-, 4- or 5-position by an imidazolyl group, or R_2 may

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represent a C_{2-5}-alkoxy group substituted in the 2-, 3-, 4- or 5-position by a benzimidazolyl or tetrahydrobenzimidazolyl group, or, if R_4 represents a 1H-tetrazolyl group, R_2 may also represent a 2-(imidazol-1-yl)ethoxy group,

or, R_2 may represent a C_{1-4}-alkylsulphonyloxy group, a benzenesulphonyloxy or phenylalkanesulphonyloxy group,

or, R_2 may represent an acylamino group optionally substituted at the nitrogen atom by a C_{1-6}-alkyl group or by a phenyl, cycloalkyl, phenylalkyl, cycloalkylalkyl, bicyclohexyl or biphenyl group, in which the acyl group is a C_{1-7}-alkanoyl group, a C_{2-4}(alkoxycarbonyl) group, a C_{1-6}-alkylsulphonyl group, a benzoyl, benzenesulphonyl, phenylalkanesulphonyl, naphthalenesulphonyl, cycloalkylcarbonyl, phenylalkanoyl or cycloalkylalkanoyl group, in which the above-mentioned phenyl nuclei may each be mono- or disubstituted by a fluorine, chlorine or bromine atom or by a methyl or methoxy group and the substituents may be identical or different,

or, R_2 may represent a phthalimino, homophthalimino, 2-carboxyphenylcarbonyl-amino or 2-carboxyphenylmethylamino group, in which a carbonyl group in a phthalimino group may be replaced by a methylene, alkyl-methylene or dialkyl-methylene group, and a methylene group in a homophthalimino group may be substituted by one or two alkyl groups, and additionally the above-mentioned phenyl nuclei may be mono- or disubstituted by alkyl or alkoxy groups, whilst the substituents may be identical or different, and at the same time may be totally or partially hydrogenated,

or, R_2 may represent a 5-, 6- or 7-membered alkyleneimino or alkenyleneimino group optionally substituted by one or two alkyl groups or by a tetramethylene or

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pentamethylene group, in which a methylene group may be replaced by a carbonyl or sulphonyl group,

or, R_2 may represent a bicycloalkane-2,3-dicarboxylic acid imino or bicycloalkene-2,3-dicarboxylic acid imino group, wherein the bicycloalkane and bicycloalkene moieties may each contain 9 or 10 carbon atoms, may be substituted by 1, 2 or 3 methyl groups and may have an endomethylene group replaced by an oxygen atom,

or, R_2 may represent an amidino group optionally substituted by one or two C_{1-6} alkyl groups,

a glutaric acid imino group wherein the n-propylene group may be perfluorinated, or may be substituted by one or two alkyl groups or by a tetramethylene or pentamethylene group,

a maleic acid imido group optionally mono- or di-substituted by an alkyl or phenyl group, whilst the substituents may be identical or different,

or, R_2 may represent a 5-membered heteroaromatic ring bound via a carbon atom or via an imino group and containing an imino group, an oxygen or sulphur atom, or an imino group and an oxygen, sulphur or nitrogen atom, or R_2 represents a 6-membered heteroaromatic ring bound via a carbon atom and containing 1 or 2 nitrogen atoms, whilst the abovementioned heteroaromatic rings may be substituted in the carbon structure by a C_{1-6} alkyl or by a phenylalkyl group, and an n-propylene or n-butylene group may be linked to the 6-membered heteroaromatic rings via two adjacent carbon atoms or a 1,3-butadienyl group may be linked both to the 5-membered and to the 6-membered heteroaromatic rings via two adjacent carbon atoms or an n-butylene or 1,3-butadienyl group is linked thereto via an imino group and an adjacent carbon atom

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and, in an anellated pyridine ring thus formed, a methine group may be replaced by a nitrogen atom and a vinylene group in the 3-, 4-position relative to the nitrogen atom of the pyridine ring formed may be replaced by a sulphur atom or in an anellated phenyl ring thus formed, one or two methine groups may be replaced by N-atoms, whilst additionally the above-mentioned fused aromatic or heteroaromatic rings may be monosubstituted in their carbon structures by a fluorine, chlorine or bromine atom or by an alkyl, alkoxy, hydroxy, phenyl, nitro, amino, alkylamino, dialkylamino, alkanoylamino, cyano, carboxy, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, fluoromethyl, difluoromethyl, trifluoromethyl, alkanoyl, aminosulphonyl, alkylaminosulphonyl or dialkylaminosulphonyl group or may be disubstituted by fluorine or chlorine atoms or by methyl, methoxy or hydroxy groups, and two methyl substituents in the 1,2-position relative to each other may be linked by a methylene or ethylene bridge and an -NH- group optionally present in an imidazole ring may be substituted by a C_{1-6}-alkyl group, by a phenylalkyl group or by a cycloalkyl group, or

R_2 may represent a pyrrolidine, piperidine or pyridine ring bound via a carbon atom, in which a phenyl group may be condensed onto the pyridine ring via two adjacent carbon atoms and a methylene group adjacent to the N-atom in a pyrrolidine or piperidine ring may be replaced by a carbonyl group,

R_2 may represent an imidazolidinedione group optionally substituted by an alkyl, phenylalkyl, tetramethylene, pentamethylene or hexamethylene group,

R_2 may represent a pyridazin-3-one or dihydro-pyridazin-3-one group which may be substituted in the 2-position

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by an optionally phenyl substituted alkyl group and additionally, in the carbon skeleton, by 1 or 2 alkyl groups,

R_2 may represent an R_7-NR_6-CO-NR_5- group wherein

R_5 represents a hydrogen atom, a C_{1-8}-alkyl group, a C_{5-7} cycloalkyl group or a phenylalkyl group,

R_6 represents a hydrogen atom, a C_{1-8}-alkyl group, a C_{3-5}-alkenyl group, a phenyl group, a phenylalkyl group or a C_{5-7}-cycloalkyl group,

R_7 represents a hydrogen atom or a C_{1-6}-alkyl group or

one of the groups R_5, R_6 or R_7 may also represent a bicyclohexyl or biphenylyl group or

R_6 and R_7 together with the nitrogen atom between them represent a straight-chained C_{4-6}-alkyleneimino group or a morpholino group or

R_5 and R_6 together represent a C_{2-4}-alkylene group,

R_2 may represent a 1H,3H-quinazolin-2,4-dion-3-yl or pentamethylene-oxazolin-2-yl group, or

R_1 represents a hydrogen atom or in the 5-, 6- or 7-position R_1 may represent a fluorine, chlorine or bromine atom, a C_{1-4}-alkyl group, a fluoromethyl, difluoromethyl or trifluoromethyl group and

R_2 represents a 5-membered heteroaromatic ring bound via a carbon atom or via an imino group and containing an imino group, an oxygen or sulphur atom or, an imino group and an oxygen, sulphur or nitrogen atom, or R_2

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represents a 6-membered heteroaromatic ring bound via a carbon atom and containing 1 or 2 nitrogen atoms, whilst the above mentioned heteroaromatic rings may be substituted in the carbon skeleton by a C_{1-6} alkyl or by a phenylalkyl group, and an n-propylene or n-butylene group may be linked via two adjacent carbon atoms to the 6-membered heteroaromatic rings or a 1,3-butadienyl group may be linked to both the 5-membered and 6-membered heteroaromatic rings via two adjacent carbon atoms or an n-butylene or 1,3-butadienyl group may be linked to said 5-membered and 6-membered heteroaromatic rings via an imino group and an adjacent carbon atom and, in an anellated pyridine ring thus formed, a methine group may be replaced by a nitrogen atom and a vinylene group in the 3-, 4-position relative to the nitrogen atom of the pyridine ring formed may be replaced by a sulphur atom or in an anellated phenyl ring thus formed, one or two methine groups may be replaced by N-atoms, whilst additionally the above-mentioned fused aromatic or heteroaromatic rings may be monosubstituted on the carbon skeleton by a fluorine, chlorine or bromine atom or by an alkyl, alkoxy, hydroxy, phenyl, nitro, amino, alkylamino, dialkylamino, alkanoylamino, cyano, carboxy, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, fluoromethyl, difluoromethyl, trifluoromethyl, alkanoyl, aminosulphonyl, alkylaminosulphonyl or dialkylamino-sulphonyl group or may be disubstituted by fluorine or chlorine atoms or by methyl, methoxy or hydroxy groups, and two methyl substituents in the 1,2-position relative to each other may be linked by a methylene or ethylene bridge and an -NH- group optionally present in an imidazole ring may be substituted by a C_{1-6}-alkyl group, by a phenylalkyl group or by a cycloalkyl group, whilst if

(i) R_1 represents a hydrogen atom, R_3 represents an n-

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propyl group and R_4 represents a carboxy group, R_2 cannot represent a 3-methyl-imidazo[4,5-b]pyridin-2-yl or 3-n-hexyl-imidazo[4,5-b]pyridin-2-yl group in the 6-position, or if

(ii) R_1 represents a hydrogen atom, R_3 represents an n-propyl or n-butyl group and R_4 represents a 1H-tetrazolyl group, R_2 cannot represent a benzoxazol-2-yl group in the 5- or 6-position, or if

(iii) R_1 represents a hydrogen atom, R_3 represents an n-propyl group and R_4 represents a carboxy group, R_2 cannot represent a 1-methylbenzimidazol-2-yl group in the 5- or 6-position or, cannot represent a 1-n-butyl-benzimidazol-2-yl, 1,5-dimethylbenzimidazol-2-yl or 1-methyl-5-trifluoromethyl-benzimidazol-2-yl group in the 6-position, or if

(iv) R_1 represents a hydrogen atom, R_3 represents an n-butyl group and R_4 represents a carboxy or 1H-tetrazolyl group, R_2 cannot represent a 1-methylbenzimidazol-2-yl group in the 6-position, or if

(v) R_1 represents a hydrogen atom, R_3 represents an n-butyl group and R_4 represents a carboxy group, R_2 cannot represent a benzimidazol-2-yl group in the 6-position,

or, R_2 may represent a pyrrolidine, piperidine or pyridine ring bound via a carbon atom, in which a phenyl group may be condensed onto the pyridine ring via 2 adjacent carbon atoms and a methylene group adjacent to the N-atom in a pyrrolidine or piperidine ring may be replaced by a carbonyl group,

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R_3 represents a hydrogen atom or a C_{1-5}-alkyl group in which a methylene group may be replaced by an oxygen or sulphur atom, or a C_{3-5}cycloalkyl group, and

R_4 represents a carboxy, cyano, 1H-tetrazolyl or 1-triphenylmethyltetrazolyl group, a C_{2-5}(alkoxycarbonyl) group, an alkanesulphonylaminocarbonyl, arylsulphonylamino-carbonyl or trifluoromethanesulphonylaminocarbonyl group,

whilst, unless otherwise specified, an alkanoyl, alkyl or alkoxy moiety mentioned hereinbefore may contain in each case 1 to 3 carbon atoms and a cycloalkyl moiety mentioned hereinbefore may contain 3 to 7 carbon atoms in each case.

As examples of the definitions of the groups R_1 to R_3 mentioned hereinbefore:

R_1 may represent a hydrogen, fluorine, chlorine or bromine atom, a methyl, ethyl, n-propyl, isopropyl, isobutyl, n-butyl, 1-methyl-n-propyl, 2-methyl-n-propyl, tert.butyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, fluoromethyl, difluoromethyl or trifluoromethyl group,

R_2 may represent a 3-(imidazol-1-yl)propoxy, 4-(imidazol-1-yl)butoxy, 5-(imidazol-1-yl)pentoxy, 2-(benzimidazol-1-yl)ethoxy, 3-(benzimidazol-1-yl)-propoxy, 4-(benzimidazol-1-yl)butoxy, 5-(benzimidazol-1-yl)-pentoxy, 2-(tetrahydrobenzimidazol-1-yl)ethoxy, 3-(tetrahydrobenzimidazol-1-yl)propoxy, 4-(tetrahydro-benzimidazol-1-yl)butoxy, 5-(tetrahydrobenzimidazol-1-yl)pentoxy, methanesulphonyloxy, ethanesulphonyloxy, n-propanesulphonyloxy, isopropanesulphonyloxy, n-butanesulphonyloxy, benzenesulphonyloxy, 4-fluorobenzenesulphonyloxy, 4-bromobenzenesulphonyloxy,

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4-methylbenzenesulphonyloxy, 4-methoxybenzene-sulphonyloxy, 3,4-dichlorobenzenesulphonyloxy, phenyl-methanesulphonyloxy, 2-phenylethanesulphonyloxy, 3-phenylpropanesulphonyloxy, formylamino, acetylamino, propionylamino, butanoylamino, isobutanoylamino, pentanoylamino, 3-methyl-butanoylamino, hexanoylamino, methoxycarbonylamino, ethoxycarbonylamino, n-propoxycarbonylamino, isopropoxycarbonylamino, methane-sulphonylamino, ethanesulphonylamino, n-propane-sulphonylamino, isopropanesulphonylamino, n-butane-sulphonylamino, n-pentanesulphonylamino, n-hexane-sulphonylamino, benzamido, benzenesulphonylamido, 4-fluorobenzenesulphonamido, 4-chlorobenzenesulphonamido, 4-bromobenzenesulphonamido, 4-methylbenzenesulphonamido, 4-methoxybenzenesulphonamido, phenylmethanesulphonyl-amido, 2-phenylethanesulphonylamido, 3-phenylpropane-sulphonylamido, naphthalen-1-yl-sulphonamido, naphthalen-2-yl-sulphonylamido, cyclopentylcarbonyl-amido, cyclohexylcarbonylamido, cycloheptylcarbonyl-amido, phenylacetylamido, 3-phenylpropionylamido, cyclopentylacetylamido, 3-cyclopentylpropionylamido, cyclohexylacetylamido, 3-cyclohexylpropionylamido, cycloheptylacetylamido, 3-cycloheptylpropionylamido, N-methyl-formylamino, N-methyl-acetylamino, N-methyl-propionylamino, N-methyl-butanoylamino, N-methyl-isobutanoylamino, N-methyl-pentanoylamino, N-methyl-3-methyl-butanoylamino, N-methyl-hexanoylamino, N-methyl-methoxycarbonylamino, N-methyl-ethoxycarbonylamino, N-methyl-n-propoxycarbonylamino, N-methyl-isopropoxy-carbonylamino, N-methyl-methanesulphonylamino, N-methyl-ethanesulphonylamino, N-methyl-n-propanesulphonylamino, N-methyl-isopropanesulphonylamino, N-methyl-n-butane-sulphonylamino, N-methyl-n-pentanesulphonylamino, N-methyl-n-hexanesulphonylamino, N-methyl-benzamido, N-methyl-benzenesulphonylamido, N-methyl-4-fluorobenzene-sulphonamido, N-methyl-4-chlorobenzenesulphonamido, N-methyl-4-bromobenzenesulphonamido, N-methyl-4-

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methylbenzenesulphonamido, N-methyl-4-methoxybenzene-sulphonamido, N-methyl-phenylmethanesulphonylamido, N-methyl-2-phenylethanesulphonylamido, N-methyl-3-phenylpropanesulphonylamido, N-methyl-naphthalen-1-yl-sulphonamido, N-methyl-naphthalen-2-yl-sulphonylamido, N-methyl-cyclopentylcarbonylamido, N-methyl-cyclohexyl-carbonylamido, N-methyl-cycloheptylcarbonylamido, N-methyl-phenylacetylamido, N-methyl-3-phenylpropionyl-amido, N-methyl-cyclopentylacetylamido, N-methyl-3-cyclopentylpropionylamido, N-methyl-cyclohexylacetyl-amido, N-methyl-3-cyclohexylpropionylamido, N-methyl-cycloheptylacetylamido, N-methyl-3-cycloheptylpropionyl-amido, N-ethyl-formylamino, N-ethyl-acetylamino, N-ethyl-propionylamino, N-ethyl-butanoylamino, N-ethyl-isobutanoylamino, N-ethyl-pentanoylamino, N-ethyl-3-methyl-butanoylamino, N-ethyl-hexanoylamino, N-ethyl-methoxycarbonylamino, N-ethyl-ethoxycarbonylamino, N-ethyl-n-propoxycarbonylamino, N-ethyl-isopropoxy-carbonylamino, N-ethyl-methanesulphonylamino, N-ethyl-ethanesulphonylamino, N-ethyl-n-propanesulphonylamino, N-ethyl-isopropanesulphonylamino, N-ethyl-n-butanesulphonylamino, N-ethyl-n-pentanesulphonylamino, N-ethyl-n-hexanesulphonylamino, N-ethyl-benzamido, N-ethyl-benzenesulphonylamido, N-ethyl-4-fluorobenzene-sulphonamido, N-ethyl-4-chlorobenzenesulphonamido, N-ethyl-4-bromobenzenesulphonamido, N-ethyl-4-methylbenzenesulphonamido, N-ethyl-4-methoxybenzenesulphonamido, N-ethyl-phenylmethanesulphonylamido, N-ethyl-2-phenylethanesulphonylamido, N-ethyl-3-phenylpropane-sulphonylamido, N-ethyl-naphthalen-1-yl-sulphonamido, N-ethyl-naphthalen-2-yl-sulphonylamido, N-ethyl-cyclopentylcarbonylamido, N-ethyl-cyclohexylcarbonyl-amido, N-ethyl-cycloheptylcarbonylamido, N-ethyl-phenylacetylamido, N-ethyl-3-phenyl-propionylamido, N-ethyl-cyclopentylacetylamido, N-ethyl-3-cyclopentyl-propionylamido, N-ethyl-cyclohexylacetylamido, N-ethyl-

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3-cyclohexylpropionylamido, N-ethyl-cycloheptylacetyl-amido, N-ethyl-3-cycloheptylpropionylamido, N-n-propyl-formylamino, N-n-propyl-acetylamino, N-n-propyl-propionylamino, N-n-propyl-butanoylamino, N-n-propyl-isobutanoylamino, N-n-propyl-pentanoylamino, N-n-propyl-(3-methyl-butanoyl)amino, N-n-propyl-hexanoylamino, N-isopropyl-formylamino, N-isopropyl-acetylamino, N-isopropyl-propionylamino, N-isopropyl-butanoylamino, N-isopropyl-isobutanoylamino, N-isopropyl-pentanoylamino, N-isopropyl-(3-methyl-butanoyl)amino, N-isopropyl-hexanoylamino, N-n-butyl-formylamino, N-n-butyl-acetylamino, N-n-butyl-propionylamino, N-n-butyl-butanoylamino, N-n-butyl-isobutanoylamino, N-n-butyl-pentanoylamino, N-n-butyl-(3-methyl-butanoyl)amino, N-n-butyl-hexanoylamino, N-isobutyl-formylamino, N-isobutyl-acetylamino, N-isobutyl-propionylamino, N-isobutyl-butanoylamino, N-isobutyl-isobutanoylamino, N-isobutyl-pentanoylamino, N-n-pentyl-formylamino, N-n-pentyl-acetylamino, N-n-pentyl-propionylamino, N-n-pentyl-butanoylamino, N-n-pentyl-isobutanoylamino, N-n-pentyl-pentanoylamino, N-(1-methyl-butyl)-formylamino, N-(1-methyl-butyl)-acetylamino, N-(1-methyl-butyl)-propionylamino, N-(1-methyl-butyl)-butanoylamino, N-(1-methyl-butyl)-isobutanoylamino, N-(1-methyl-butyl)-pentanoylamino, N-(2-methyl-butyl)-formylamino, N-(2-methyl-butyl)-acetylamino, N-(2-methyl-butyl)-propionylamino, N-(2-methyl-butyl)-butanoylamino, N-(2-methyl-butyl)-isobutanoylamino, N-(2-methyl-butyl)-pentanoylamino, N-(3-methyl-butyl)-formylamino, N-(3-methyl-butyl)-acetylamino, N-(3-methyl-butyl)-propionylamino, N-(3-methyl-butyl)-butanoylamino, N-(3-methyl-butyl)-isobutanoylamino, N-(3-methyl-butyl)-pentanoylamino, N-n-hexyl-formylamino, N-n-hexyl-acetylamino, N-n-hexyl-propionylamino, N-n-hexyl-butanoylamino, N-n-hexyl-isobutanoylamino, N-n-hexyl-pentanoylamino, N-n-propyl-cyclohexylcarbonylamino, N-n-propyl-cyclohexylacetylamino, N-n-propyl-3-

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(cyclohexyl)propionylamino, N-isopropyl-cyclohexylcarbonylamino, N-isopropyl-cyclohexylacetylamino, N-isopropyl-3-(cyclohexyl)-propionylamino, N-n-butyl-cyclohexylcarbonylamino, N-n-butyl-cyclohexylacetylamino, N-n-butyl-3-(cyclohexyl)-propionylamino, N-isobutyl-cyclohexylcarbonylamino, N-isobutyl-cyclohexylacetylamino, N-isobutyl-3-(cyclohexyl)propionylamino, N-n-pentyl-cyclohexyl-carbonylamino, N-n-pentyl-cyclohexylacetylamino, N-n-pentyl-3-(cyclohexyl)propionylamino, N-n-hexyl-cyclohexylcarbonylamino, N-n-hexyl-cyclohexylacetyl-amino, N-n-hexyl-3-(cyclohexyl)propionylamino, phthalimino, 5-methoxy-phthalimino, 5,6-dimethoxy-phthalimino, 6-methoxy-phthalimino, homophthalimino, 4,4-dimethyl-homophthalimino, 7-methoxy-homophthalimino, 6,7-dimethoxy-homophthalimino, 7-methoxy-4,4-dimethyl-homophthalimino, 6,7-dimethoxy-4,4-dimethyl-homophthalimino, 1,2,3,6-tetrahydrophthalimino, hexahydrophthalimino, cis-hexahydrophthalimino, trans-hexahydrophthalimino, 1-oxo-isoindolin-2-yl, 3,4-dimethyl-phthalimino, 4,5-dimethyl-1,2,3,6-tetrahydrophthalimino, 4,5-dimethyl-hexahydro phthalimino, 4,5-dimethyl-1-oxo-isoindolin-2-yl, 3,4-dimethoxy-phthalimino, 4,5-dimethoxy-1,2,3,6-tetrahydrophthalimino, 4,5-dimethoxy-hexahydro phthalimino, 4,5-dimethoxy-1-oxo-isoindolin-2-yl, 2-carboxyphenylmethylamino, 2-carboxyphenylmethylene-carbonylamino, pyrrolidino, 2-methylpyrrolidino, 3-ethylpyrrolidino, 3-isopropylpyrrolidino, piperidino, 3-methylpiperidino, 4-methylpiperidino, 4-ethylpiperidino, 4-isopropylpiperidino, hexamethyleneimino, 3-methyl-hexamethyleneimino, 4-methylhexamethyleneimino, 3-ethylhexamethyleneimino, 4-isopropylhexamethyleneimino, 3,3-dimethyl-pyrrolidino, 3,4-dimethyl-pyrrolidino, 3,3-dimethyl-piperidino, 3,4-dimethyl-piperidino, 4,4-dimethyl-piperidino, 3,3-dimethyl-hexamethyleneimino, 3,4-dimethyl-hexamethyleneimino, 4,4-dimethyl-

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hexamethyleneimino, 3,5-dimethyl-hexamethyleneimino, 3,3-tetramethylene-pyrrolidino, 3,3-pentamethylene-pyrrolidino, 3,3-tetramethylene-piperidino, 3,3-pentamethylene-piperidino, 4,4-tetramethylene-piperidino, 4,4-pentamethylene-piperidino, 3,3-tetramethylene-hexamethyleneimino, 3,3-pentamethylene-hexamethyleneimino, 4,4-tetramethylene-hexamethylene-imino, 4,4-pentamethylene-hexamethyleneimino, 2-oxo-pyrrolidino, 2-oxo-piperidino, 2-oxo-hexamethyleneimino, propanesultam-1-yl, butanesultam-1-yl, pentanesultam-1-yl, endo-bicyclo[2.2.2]oct-5-ene-2,3-dicarboxylic acid imino, methyl-5-norbornene-2,3-dicarboxylic acid imino, 3,6-endoxo-1,2,3,6-tetrahydrophthalimino, 5-norbornen-endo-2,3-dicarboxylic acid imino, glutarimino, 3,3-tetramethylene-glutarimino, 3,3-pentamethylene-glutarimino, 2,2-dimethyl-glutarimino, 3-methyl-glutarimino, 3,3-dimethyl-glutarimino, 3-ethyl-glutarimino, 3-ethyl-3-methyl-glutarimino, 1,3-cyclopentanedicarbonylimino, 2,4-dimethyl-glutarimino, 2,4-di-n-propyl-glutarimino, glutaramino, 3,3-tetramethylene-glutaramino, 3,3-pentamethylene-glutaramino, 2,2-dimethyl-glutaramino, 3-methyl-glutaramino, 3,3-dimethyl-glutaramino, 3-ethyl-glutaramino, 3-ethyl-3-methyl-glutaramino, 1,3-cyclopentanedicarbonylamino, 2,4-dimethyl-glutaramino, 2,4-di-n-propyl-glutaramino, maleic acid amido, maleic acid imido, 2-methyl-maleic acid amido, 3-methyl-maleic acid amido, 2-methyl-maleic acid imido, 2-phenyl-maleic acid amido, 3-phenyl-maleic acid amido, 2-phenyl-maleic acid imido, 2,3-dimethyl-maleic acid amido, 3-methyl-2-phenyl-maleic acid amido, 2-methyl-3-phenyl-maleic acid amido, 2-methyl-3-phenyl-maleic acid imido, 2,3-diphenyl-maleic acid amido, 2,3-diphenyl-maleic acid amido, pyrrolidin-2-yl, pyrrolidin-2-on-5-yl, piperidin-2-yl, piperidin-2-on-1-yl, piperidin-2-on-6-yl, quinolin-2-yl, isoquinolin-1-yl, isoquinolin-3-yl, pyridin-2-yl, 4-methylimidazol-2-yl, 1-methylimidazol-4-

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yl, 1-methylimidazol-5-yl, 1-n-hexylimidazol-4-yl, 1-n-hexylimidazol-5-yl, 1-benzylimidazol-4-yl, 1-benzylimidazol-5-yl, 1,2-dimethylimidazol-4-yl, 1,2-dimethylimidazol-5-yl, 1-n-pentyl-2-methyl-imidazol-4-yl, 1-n-pentyl-2-methyl-imidazol-5-yl, 1-n-butyl-2-methyl-imidazol-4-yl, 1-n-butyl-2-methyl-imidazol-5-yl, 1-benzyl-2-methyl-imidazol-4-yl, 1-benzyl-2-methyl-imidazol-5-yl, benzimidazol-2-yl, 1-methylbenzimidazol-2-yl, 1-ethylbenzimidazol-2-yl, 1-n-propylbenzimidazol-2-yl, 1-isopropylbenzimidazol-2-yl, 1-n-butylbenzimidazol-2-yl, 1-isobutylbenzimidazol-2-yl, 1-n-pentylbenzimidazol-2-yl, 1-n-hexylbenzimidazol-2-yl, 1-cyclopropyl-benzimidazol-2-yl, 1-cyclobutyl-benzimidazol-2-yl, 1-cyclopentylbenzimidazol-2-yl, 1-cyclohexylbenzimidazol-2-yl, 5-nitro-benzimidazol-2-yl, 5-amino-benzimidazol-2-yl, 5-acetamido-benzimidazol-2-yl, 5-methyl-benzimidazol-2-yl, 5-methoxy-benzimidazol-2-yl, 5-ethoxy-benzimidazol-2-yl, 1-methyl-5-methoxy-benzimidazol-2-yl, 1,5-dimethyl-benzimidazol-2-yl, 1,6-dimethyl-benzimidazol-2-yl, 1,4-dimethyl-benzimidazol-2-yl, 5,6-dimethyl-benzimidazol-2-yl, 1,5,6-trimethyl-benzimidazol-2-yl, 5-chloro-benzimidazol-2-yl, 5-chloro-1-methyl-benzimidazol-2-yl, 6-chloro-1-methyl-benzimidazol-2-yl, 5,6-dichloro-1-methyl-benzimidazol-2-yl, 5-dimethylamino-benzimidazol-2-yl, 5-dimethylamino-1-ethyl-benzimidazol-2-yl, 5,6-dimethoxy-1-methyl-benzimidazol-2-yl, 5,6-dimethoxy-1-ethyl-benzimidazol-2-yl, 5-fluoro-1-methyl-benzimidazol-2-yl, 6-fluoro-1-methyl-benzimidazol-2-yl, 5-trifluoromethyl-benzimidazol-2-yl, 5-trifluoromethyl-1-methyl-benzimidazol-2-yl, 4-cyano-1-methyl-benzimidazol-2-yl, 5-carboxy-1-methyl-benzimidazol-2-yl, 5-aminocarbonyl-benzimidazol-2-yl, 5-aminocarbonyl-1-methyl-benzimidazol-2-yl, 5-dimethylaminosulphonyl-1-methyl-benzimidazol-2-yl, 5-methoxycarbonyl-1-methyl-benzimidazol-2-yl, 5-methylaminocarbonyl-1-methyl-benzimidazol-2-yl, 5-dimethylaminocarbonyl-1-methyl-

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benzimidazol-2-yl, 4,6-difluoro-1-methyl-benzimidazol-2-yl, 5-acetyl-1-methyl-benzimidazol-2-yl, 5,6-dihydroxy-1-methyl-benzimidazol-2-yl, imidazo[1,2-a]pyridin-2-yl, 5-methyl-imidazo[1,2-a]pyridin-2-yl, 6-methyl-imidazo[1,2-a]-pyridin-2-yl, 7-methyl-imidazo[1,2-a]-pyridin-2-yl, 8-methyl-imidazo[1,2-a]pyridin-2-yl, 5,7-dimethyl-imidazo[1,2-a]pyridin-2-yl, 6-aminocarbonyl-imidazo[1,2-a]pyridin-2-yl, 6-chloro-imidazo[1,2-a]-pyridin-2-yl, 6-bromo-imidazo[1,2-a]pyridin-2-yl, 5,6,7,8-tetrahydro-imidazo[1,2-a]pyrimidin-2-yl, imidazo[1,2-a]pyrimidin-2-yl, 5,7-dimethyl-imidazo[1,2-a]pyrimidin-2-yl, imidazo[4,5-b]pyridin-2-yl, 1-methyl-imidazo[4,5-b]pyridin-2-yl, 1-n-hexyl-imidazo[4,5-b]pyridin-2-yl, 1-cyclopropyl-imidazo[4,5-b]pyridin-2-yl, 1-cyclohexyl-imidazo[4,5-b]-pyridin-2-yl, 4-methyl-imidazo[4,5-b]pyridin-2-yl, 6-methyl-imidazo[4,5-b]pyridin-2-yl, 1,4-dimethyl-imidazo[4,5-b]pyridin-2-yl, 1,6-dimethyl-imidazo[4,5-b]-pyridin-2-yl, imidazo[4,5-c]pyridin-2-yl, 1-methyl-imidazo[4,5-c]pyridin-2-yl, 1-n-hexyl-imidazo[4,5-c]-pyridin-2-yl, 1-cyclopropyl-imidazo[4,5-c]pyridin-2-yl, 1-cyclohexyl-imidazo[4,5-c]pyridin-2-yl, imidazo[2,1-b]-thiazol-6-yl, 3-methyl-imidazo[2,1-b]thiazol-6-yl, 2-phenyl-imidazo[2,1-b]thiazol-6-yl, 3-phenyl-imidazo[2,1-b]thiazol-6-yl, 2,3-dimethyl-imidazo[2,1-b]-thiazol-6-yl, 2,3-trimethylene-imidazo[2,1-b]thiazol-6-yl, 2,3-tetramethylene-imidazo[2,1-b]thiazol-6-yl, imidazo[1,2-c]pyrimidin-2-yl, imidazo[1,2-a]pyrazin-2-yl, imidazo[1,2-b]pyridazin-2-yl, imidazo[4,5-c]pyridin-2-yl, purin-8-yl, imidazo[4,5-b]pyrazin-2-yl, imidazo[4,5-c]pyridazin-2-yl, imidazo[4,5-d]pyridazin-2-yl, imidazolidin-2,4-dion-3-yl, 5-methyl-imidazolidin-2,4-dion-3-yl, 5-ethyl-imidazolidin-2,4-dion-3-yl, 5-n-propyl-imidazolidin-2,4-dion-3-yl, 5-benzyl-imidazolidin-2,4-dion-3-yl, 5-(2-phenylethyl)-imidazolidin-2,4-dion-3-yl, 5-(3-phenylpropyl)-imidazolidin-2,4-dion-3-yl, 5,5-tetramethylene-

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imidazolidin-2,4-dion-3-yl, 5,5-pentamethylene-imidazolidin-2,4-dion-3-yl, 5,5-hexamethylene-imidazolidin-2,4-dion-3-yl, 1-methyl-imidazolidin-2,4-dion-3-yl, 1-benzyl-imidazolin-2,4-dion-3-yl, 4,5-dihydro-2H-pyridazin-3-on-6-yl, 2-methyl-4,5-dihydro-2H-pyridazin-3-on-6-yl, 2-ethyl-4,5-dihydro-2H-pyridazin-3-on-6-yl, 2-n-propyl-4,5-dihydro-2H-pyridazin-3-on-6-yl, 2-isopropyl-4,5-dihydro-2H-pyridazin-3-on-6-yl, 2-benzyl-4,5-dihydro-2H-pyridazin-3-on-6-yl, 2-(2-phenylethyl)-4,5-dihydro-2H-pyridazin-3-on-6-yl, 2-(3-phenylpropyl)-4,5-dihydro-2H-pyridazin-3-on-6-yl, 4-methyl-4,5-dihydro-2H-pyridazin-3-on-6-yl, 5-methyl-4,5-dihydro-2H-pyridazin-3-on-6-yl, 4,4-dimethyl-4,5-dihydro-2H-pyridazin-3-on-6-yl, 5,5-dimethyl-4,5-dihydro-2H-pyridazin-3-on-6-yl, 4,5-dimethyl-4,5-dihydro-2H-pyridazin-3-on-6-yl, 2,4-dimethyl-4,5-dihydro-2H-pyridazin-3-on-6-yl, 2,5-dimethyl-4,5-dihydro-2H-pyridazin-3-on-6-yl, 2,4,5-trimethyl-4,5-dihydro-2H-pyridazin-3-on-6-yl, 2,4,4-trimethyl-4,5-dihydro-2H-pyridazin-3-on-6-yl, 2,5,5-trimethyl-4,5-dihydro-2H-pyridazin-3-on-6-yl, 2H-pyridazin-3-on-6-yl, 2-methyl-pyridazin-3-on-6-yl, 2-ethyl-pyridazin-3-on-6-yl, 2-n-propyl-pyridazin-3-on-6-yl, 2-isopropyl-pyridazin-3-on-6-yl, 2-benzyl-pyridazin-3-on-6-yl, 2-(2-phenylethyl)-pyridazin-3-on-6-yl, 2-(3-phenylpropyl)-pyridazin-3-on-6-yl, 4-methyl-pyridazin-3-on-6-yl, 5-methyl-pyridazin-3-on-6-yl, 4,5-dimethyl-pyridazin-3-on-6-yl, 2,4-dimethyl-pyridazin-3-on-6-yl, 2,5-dimethyl-pyridazin-3-on-6-yl, 2,4,5-trimethyl-pyridazin-3-on-6-yl, aminocarbonylamino, methylaminocarbonylamino, dimethylaminocarbonylamino, N-methylaminocarbonyl-methylamino, N-(dimethylaminocarbonyl)-methylamino, N-dimethylaminocarbonyl-ethylamino, N-dimethylamino-carbonyl-isopropylamino, N-(dimethylaminocarbonyl)-n-pentylamino, N-methylaminocarbonyl-ethylamino, N-methylaminocarbonyl-n-pentylamino, N-methylamino-carbonyl-n-hexylamino, N-methylaminocarbonyl-n-

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octylamino, N-methylaminocarbonyl-cyclohexylamino, ethylaminocarbonylamino, N-ethylaminocarbonyl-methylamino, N-ethylaminocarbonyl-ethylamino, N-ethylaminocarbonyl-n-hexylamino, N-ethylaminocarbonyl-n-heptylamino, N-ethylaminocarbonyl-cyclohexylamino, diethylaminocarbonylamino, N-(diethylaminocarbonyl)-methylamino, N-(diethylaminocarbonyl)-ethylamino, N-(diethylaminocarbonyl)-n-butylamino, N-(diethylaminocarbonyl)-n-hexylamino, N-(diethylaminocarbonyl)-n-octylamino, isopropylaminocarbonylamino, N-isopropylaminocarbonyl-methylamino, n-butylaminocarbonylamino, N-(n-butylaminocarbonyl)-methylamino, N-(n-butylaminocarbonyl)-ethylamino, N-(n-butylaminocarbonyl)-isopropylamino, N-(n-butylaminocarbonyl)-n-butylamino, N-(n-butylaminocarbonyl)-n-hexylamino, N-(n-butylaminocarbonyl)-cyclohexylamino, N-(di-(n-butyl)-aminocarbonyl)-amino, N-(di-(n-butyl)-aminocarbonyl)-methylamino, N-(di-(n-butyl)-aminocarbonyl)-ethylamino, N-(di-(n-butyl)-aminocarbonyl)-n-butylamino, N-(di-(n-butyl)-aminocarbonyl)-n-hexylamino, N-(n-pentylaminocarbonyl)-methylamino, N-(n-pentylaminocarbonyl)-ethylamino, N-(n-hexylaminocarbonyl)-ethylamino, n-hexylaminocarbonylamino, n-heptylaminocarbonylamino, n-octylaminocarbonylamino, N-(n-hexylaminocarbonyl)-n-butylamino, N-(n-hexylaminocarbonyl)-n-pentylamino, N-(n-hexylaminocarbonyl)-n-hexylamino, N-(n-hexylaminocarbonyl)-cyclohexylamino, di-(n-hexyl)-aminocarbonylamino, N-(di-(n-hexyl)-aminocarbonyl)-methylamino, N-((n-hexyl)-methylaminocarbonyl)-amino, cyclohexylaminocarbonylamino, N-cyclohexylaminocarbonyl-methylamino, N-cyclohexylaminocarbonyl-ethylamino, N-cyclohexylaminocarbonyl-n-butylamino, N-cyclohexylaminocarbonyl-isobutylamino, N-cyclohexylaminocarbonyl-n-pentylamino, N-cyclohexylaminocarbonyl-n-hexylamino, N-cyclohexylaminocarbonyl-cyclohexylamino, N-(ethyl-cyclohexylaminocarbonyl)-methylamino, N-(propyl-cyclohexylaminocarbonyl)-methylamino, N-(n-butyl-

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cyclohexylaminocarbonyl)-methylamino, allylaminocarbonylamino, benzylaminocarbonylamino, N-benzylaminocarbonyl-isobutylamino, phenylaminocarbonyl-amino, pyrrolidinocarbonylamino, pyrrolidinocarbonyl-methylamino, piperidinocarbonylamino, hexamethylene-iminocarbonylamino, morpholinocarbonylamino, 3,4,5,6-tetrahydro-2-pyrimidon-1-yl, 3-methyl-3,4,5,6-tetrahydro-2-pyrimidon-1-yl, 3-ethyl-3,4,5,6-tetrahydro-2-pyrimidon-1-yl, 3-n-propyl-3,4,5,6-tetrahydro-2-pyrimidon-1-yl, 3-isopropyl-3,4,5,6-tetrahydro-2-pyrimidon-1-yl, 3-n-butyl-3,4,5,6-tetrahydro-2-pyrimidon-1-yl, 3-isobutyl-3,4,5,6-tetrahydro-2-pyrimidon-1-yl, 3-n-pentyl-3,4,5,6-tetrahydro-2-pyrimidon-1-yl, 3-n-hexyl-3,4,5,6-tetrahydro-2-pyrimidon-1-yl, 3-cyclopentyl-3,4,5,6-tetrahydro-2-pyrimidon-1-yl, 3-cyclohexyl-3,4,5,6-tetrahydro-2-pyrimidon-1-yl, 3-cycloheptyl-3,4,5,6-tetrahydro-2-pyrimidon-1-yl, 3-benzyl-3,4,5,6-tetrahydro-2-pyrimidon-1-yl, 3,4,5,6-tetrahydro-2(1H)-pyrimidon-1-yl, 3-methyl-3,4,5,6-tetrahydro-2(1H)-pyrimidon-1-yl, 3-ethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidon-1-yl, 3-n-propyl-3,4,5,6-tetrahydro-2(1H)-pyrimidon-1-yl, 3-isopropyl-3,4,5,6-tetrahydro-2(1H)-pyrimidon-1-yl, 3-benzyl-3,4,5,6-tetrahydro-2(1H)-pyrimidon-1-yl, 3-(2-phenylethyl)-3,4,5,6-tetrahydro-2(1H)-pyrimidon-1-yl or 3-(3-phenylpropyl)-3,4,5,6-tetrahydro-2(1H)-pyrimidon-1-yl group, and

R_3 may represent a hydrogen atom, a methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, tert.butyl, n-pentyl, 1-methyl-butyl, 2-methyl-butyl, 3-methyl-butyl, cyclopropyl, cyclobutyl, cyclopentyl, methoxy, ethoxy, n-propoxy, isopropoxy, methylmercapto, ethylmercapto, n-propylmercapto, isopropylmercapto or n-butylmercapto group.

Preferred compounds of general formula I above are those

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wherein

R_1 in the 4-position represents a fluorine, chlorine or bromine atom, a C_{1-3}-alkyl group, a cycloalkyl, fluoromethyl, difluoromethyl or trifluoromethyl group and

R_2 represents a C_{3-5}-alkoxy group substituted in the 3-, 4- or 5-position by an imidazolyl group, or R_2 may represent a C_{2-5}-alkoxy group substituted in the 2-, 3-, 4- or 5-position by a benzimidazolyl or tetrahydrobenzimidazolyl group,

an acylamino group optionally substituted at the nitrogen atom by a C_{1-5}-alkyl group, wherein the acyl group is a C_{2-7}-alkanoyl group, a C_{2-4}(alkoxycarbonyl) group, a C_{1-3}-alkylsulphonyl group or a benzenesulphonyl group,

a phthalimino or homophthalimino group, wherein a carbonyl group in a phthalimino group may be replaced by a methylene group and a methylene in a homophthalimino group may be substituted by one or two alkyl groups,

a 5-, 6- or 7-membered alkyleneimino or alkenyleneimino group, optionally substituted by one or two alkyl groups or by a tetramethylene or pentamethylene group, wherein a methylene group may be replaced by a carbonyl or sulphonyl group,

a glutaric acid imino group wherein the n-propylene group may be perfluorinated, or may be substituted by one or two alkyl groups or by a tetramethylene or pentamethylene group,

a maleic acid imido group optionally mono- or disubstituted by an alkyl or phenyl group, whilst the

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substituents may be identical or different,

an amidino group optionally substituted by one or two C_{1-4} alkyl groups,

a benzimidazol-2-yl group optionally substituted in the 1-position by C_{1-6}-alkyl or a cycloalkyl group, whilst the phenyl nucleus of an abovementioned benzimidazole group may additionally be substituted by a fluorine atom or by a methyl or trifluoromethyl group, or R_2 may represent an imidazo[2,1-b]thiazol-6-yl, imidazo[1,2-a]pyridin-2-yl, 5,6,7,8-tetrahydro-imidazo[1,2-a]pyridin-2-yl, imidazo[1,2-a]pyrimidin-2-yl, imidazo[4,5-b]pyridin-2-yl, imidazo[4,5-c]pyridin-2-yl, imidazo[1,2-c]pyrimidin-2-yl, imidazo[1,2-a]pyrazin-2-yl, imidazo[1,2-b]-pyridazin-2-yl, imidazo[4,5-c]pyridin-2-yl, purin-8-yl, imidazo[4,5-b]pyrazin-2-yl, imidazo[4,5-c]pyridazin-2-yl or imidazo[4,5-d]pyridazin-2-yl group, or a carbon attached pyrrolidine, piperidine or pyridine ring in which a phenyl group may be condensed onto the pyridine ring via two adjacent carbon atoms and a methylene group adjacent to the N-atom in a pyrrolidine or piperidine ring may be replaced by a carbonyl group,

a carbon attached imidazolyl group optionally substituted in the 1-position by a C_{1-3}-alkyl group or by a benzyl group, which may also be substituted in the carbon skeleton by a C_{1-3}-alkyl group,

an imidazolidindione group optionally substituted by an alkyl, phenylalkyl, tetramethylene, pentamethylene or hexamethylene group,

a pyridazin-3-one or dihydro-pyridazin-3-one group which may be substituted in the 2-position by a methyl or benzyl group,

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an R_7-NR_6-CO-NR_5- group wherein

R_5 represents a hydrogen atom, a C_{1-5}-alkyl group, a cyclohexyl or benzyl group,

R_6 represents a hydrogen atom, a C_{1-6}-alkyl group, an allyl, cyclohexyl, benzyl or phenyl group,

R_7 represents a hydrogen atom or a C_{1-3}-alkyl group or

R_6 and R_7 together with the nitrogen atom between them represent an unbranched C_{4-6}-alkyleneimino group or a morpholino group or

R_5 and R_6 together represent a C_{2-3}-alkylene group, or

R_1 represents a hydrogen atom or in the 5-, 6- or 7-position R_1 may represent a fluorine, chlorine or bromine atom, a C_{1-4}-alkyl or a trifluoromethyl group and

R_2 represents a benzimidazol-2-yl group optionally substituted in the 1-position by a C_{1-6}-alkyl group or by a cycloalkyl group, whilst the phenyl nucleus of an abovementioned benzimidazole group may additionally be substituted by a fluorine atom or by a methyl or trifluoromethyl group, or R_2 may represent an imidazo[2,1-b]thiazol-6-yl, imidazo[1,2-a]pyridin-2-yl, 5,6,7,8-tetrahydro-imidazo[1,2-a]pyridin-2-yl, imidazo[1,2-a]pyrimidin-2-yl, imidazo[4,5-b]pyridin-2-yl, imidazo[4,5-c]pyridin-2-yl, imidazo[1,2-c]pyrimidin-2-yl, imidazo[1,2-a]pyrazin-2-yl, imidazo[1,2-b]-pyridazin-2-yl, imidazo[4,5-c]-pyridin-2-yl, purin-8-yl, imidazo[4,5-b]pyrazin-2-yl, imidazo[4,5-c]pyridazin-2-yl or imidazo[4,5-d]-pyridazin-2-yl group, or a carbon attached pyrrolidine, piperidine or pyridine ring in

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which a phenyl group may be condensed onto the pyridine ring via 2 adjacent carbon atoms and a methylene group adjacent to the N-atom in a pyrrolidine or piperidine ring may be replaced by a carbonyl group, or a carbon attached imidazolyl group optionally substituted in the 1-position by a C_{1-3} alkyl group or by a benzyl group which may also be substituted in the carbon skeleton by a C_{1-3} alkyl group, whilst if

(v) R_1 represents a hydrogen atom, R_3 represents an n-butyl group and R_4 represents a carboxy group, R_2 cannot represent a benzimidazol-2-yl group in the 6-position,

R_3 represents a C_{1-5}-alkyl group or a C_{3-5}-cycloalkyl group and

R_4 represents a carboxy or 1H-tetrazolyl group,

the 1-, 3-isomer mixtures thereof and the addition salts thereof, more particularly for pharmaceutical use the physiologically acceptable addition salts thereof with inorganic or organic acids or bases,

whilst, unless otherwise specified, an alkanoyl, alkyl or alkoxy moiety as mentioned hereinbefore may in each case contain 1 to 3 carbon atoms and a cycloalkyl moiety mentioned above may contain from 3 to 7 carbon atoms.

Particularly preferred compounds of general formula I above are those wherein

R_1 in the 4-position represents a chlorine atom, a C_{1-3}-alkyl or a trifluoromethyl group and

R_2 represents a C_{3-5}-alkoxy substituted in the 3-, 4- or 5-position by an imidazolyl group, or R_2 may represent a

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C_{2-5}-alkoxy group substituted in the 2-, 3-, 4- or 5-position by a benzimidazolyl or tetrahydrobenzimidazolyl group,

a C_{2-5}(alkanoylamino) group or an N-benzenesulphonyl-methylamino group,

a phthalimino or homophthalimino group, wherein a carbonyl group in a phthalimino group may be replaced by a methylene group,

a 5-, 6- or 7-membered alkyleneimino group wherein a methylene group is replaced by a carbonyl or sulphonyl group,

a glutaric acid imino group wherein the n-propylene group may be substituted by one or two alkyl groups or by a tetramethylene or pentamethylene group,

a maleic acid imido group optionally mono- or disubstituted by an alkyl or phenyl group, whilst the substituents may be identical or different,

a benzimidazol-2-yl group optionally substituted in the 1-position by a C_{1-6}-alkyl or by a cycloalkyl group, whilst the phenyl nucleus of an abovementioned benzimidazole group may additionally be substituted by a fluorine atom or by a methyl or trifluoromethyl group, or R_2 may represent an imidazo[2,1-b]thiazol-6-yl, imidazo[1,2-a]pyridin-2-yl, 5,6,7,8-tetrahydro-imidazo[1,2-a]pyridin-2-yl, imidazo[1,2-a]pyrimidin-2-yl, imidazo[4,5-b]pyridin-2-yl, imidazo[4,5-c]pyridin-2-yl, imidazo[1,2-c]pyrimidin-2-yl, imidazo[1,2-a]pyrazin-2-yl, imidazo[1,2-b]-pyridazin-2-yl, imidazo[4,5-c]pyridin-2-yl, purin-8-yl, imidazo[4,5-b]pyrazin-2-yl, imidazo[4,5-c]pyridazin-2-yl or imidazo[4,5-d]pyridazin-2-yl group, or a carbon

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attached pyrrolidine, piperidine or pyridine ring in which a phenyl group may be condensed onto the pyridine ring via two adjacent carbon atoms and a methylene group adjacent to the N-atom in a pyrrolidine or piperidine ring may be replaced by a carbonyl group,

or an imidazol-4-yl group substituted in the 1-position by a C_{1-3} alkyl group or by a benzyl group which may also be substituted in the carbon skeleton by a C_{1-3} alkyl group,

a pyridazin-3-one or dihydro-pyridazin-3-one group which may be substituted in the 2-position by a methyl or benzyl group,

an R_7-NR_6-CO-NR_5- group wherein

R_5 represents a hydrogen atom, a C_{1-5}-alkyl, a cyclohexyl or benzyl group,

R_6 represents a hydrogen atom, a C_{1-6}-alkyl group, an allyl, cyclohexyl, benzyl or phenyl group,

R_7 represents a hydrogen atom or a C_{1-3}-alkyl group or

R_6 and R_7 together with the nitrogen atom between them represent an unbranched C_{4-6}-alkyleneimino group or a morpholino group or

R_5 and R_6 together represent a C_{2-3}-alkylene group, or

R_1 represents a hydrogen atom or, in the 5-, 6- or 7-position R_1 represents a C_{1-4}-alkyl group or a trifluoromethyl group and

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R_2 represents a benzimidazol-2-yl group optionally substituted in the 1-position by a C_{1-6}-alkyl group or by a cycloalkyl group, whilst the phenyl nucleus of one of the abovementioned benzimidazole groups may additionally be substituted by a fluorine atom or by a methyl or trifluoromethyl group, or R_2 may represent an imidazo[2,1-b]thiazol-6-yl, imidazo[1,2-a]pyridin-2-yl, 5,6,7,8-tetrahydro-imidazo[1,2-a]pyridin-2-yl, imidazo[1,2-a]pyrimidin-2-yl, imidazo[4,5-b]pyridin-2-yl, imidazo[4,5-c]pyridin-2-yl, imidazo[1,2-c]pyrimidin-2-yl, imidazo[1,2-a]pyrazin-2-yl, imidazo[1,2-b]-pyridazin-2-yl, imidazo[4,5-c]-pyridin-2-yl, purin-8-yl, imidazo[4,5-b]pyrazin-2-yl, imidazo[4,5-c]pyridazin-2-yl or imidazo[4,5-d]pyridazin-2-yl group, or a carbon attached pyrrolidine, piperidine or pyridine ring in which a phenyl group may be condensed onto the pyridine ring via two adjacent carbon atoms and a methylene group adjacent to the N-atom in a pyrrolidine or piperidine ring may be replaced by a carbonyl group, or an imidazol-4-yl group substituted in the 1-position by a C_{1-3} alkyl group or by a benzyl group which may also be substituted in the carbon skeleton by a C_{1-3} alkyl group, whilst if

(v) R_1 represents a hydrogen atom, R_3 represents an n-butyl group and R_4 represents a carboxy group, R_2 cannot represent a benzimidazol-2-yl group in the 6-position,

R_3 represents a C_{1-5}-alkyl group or a C_{3-5}-cycloalkyl group and

R_4 represents a carboxy or 1H-tetrazolyl group,

especially those compounds of general formula I above wherein

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R_1 in the 4-position represents a methyl group or a chlorine atom and

R_2 represents a C_{3-5}-alkoxy group substituted in the 3-, 4- or 5-position by an imidazolyl group or R_2 may represent, a C_{2-5}-alkoxy group substituted in the 2-, 3-, 4- or 5-position by a benzimidazolyl or tetrahydrobenzimidazolyl group,

a C_{2-5}(alkanoyl) group or an N-benzenesulphonyl-methylamino group,

a phthalimino or homophthalimino group, wherein a carbonyl group in a phthalimino group may be replaced by a methylene group,

a 5-, 6- or 7-membered alkyleneimino group, wherein a methylene group is replaced by a carbonyl or sulphonyl group,

a maleic acid imido group optionally mono- or disubstituted by an alkyl or phenyl group, whilst the substituents may be identical or different,

a benzimidazol-2-yl group optionally substituted in the 1-position by a C_{1-3}-alkyl group, whilst the phenyl nucleus of an abovementioned benzimidazole group may additionally be substituted by a fluorine atom, or R_2 may represent an imidazo[1,2-a]-pyridin-2-yl group, 5,6,7,8-tetrahydro-imidazo[1,2-a]-pyridin-2-yl, imidazo[1,2-a]pyrimidin-2-yl or imidazo[2,1-b]thiazol-6-yl group,

an imidazol-4-yl group substituted in the 1-position by a C_{1-3} alkyl group,

a pyridazin-3-one or dihydro-pyridazin-3-one group which

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may be substituted in the 2-position by a methyl or benzyl group, or

R_1 represents a hydrogen atom or, in the 5-, 6- or 7-position R_1 may represent a methyl group and

R_2 represents a benzimidazol-2-yl group optionally substituted in the 1-position by a C_{1-3}-alkyl group, whilst the phenyl nucleus may additionally be substituted by a fluorine atom, or R_2 may represent an imidazo[1,2- a]pyridin-2-yl group, an imidazol-4-yl group substituted in the 1-position by a C_{1-3} alkyl group, whilst if

(v) R_1 represents a hydrogen atom, R_3 represents an n-butyl group and R_4 represents a carboxy group, R_2 cannot represent a benzimidazol-2-yl group in the 6-position,

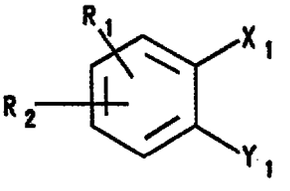
R_3 represents a C_{1-5}-alkyl group or a C_{3-5}-cycloalkyl group and

R_4 represents a carboxy or 1H-tetrazolyl group,

the 1-, 3-isomer mixtures thereof and the addition salts thereof, more particularly for pharmaceutical use the physiologically acceptable salts thereof with inorganic or organic acids or bases.

According to the invention, the compounds are obtained by the following processes:

a) Cyclising a compound of general formula

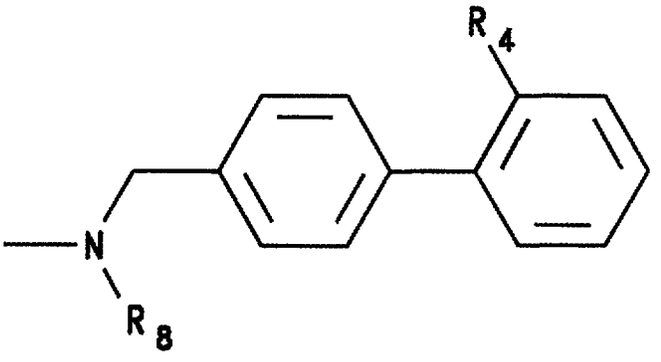


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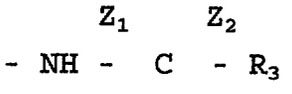
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wherein
R_1 and R_2 are defined as hereinbefore,

one of the groups X_1 or Y_1 represents a group of general formula



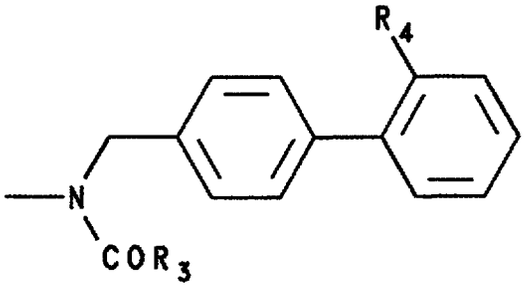
and the other group X_1 or Y_1 represents a group of the general formula



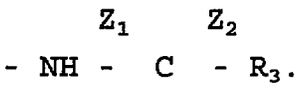
wherein

R_2 and R_4 are defined as hereinbefore,
R_8 represents a hydrogen atom or an R_3CO- group, wherein R_3 is defined as hereinbefore,
Z_1 and Z_2, which may be identical or different, represent optionally substituted amino groups or hydroxy or mercapto groups optionally substituted by lower alkyl groups or
Z_1 and Z_2 together represent an oxygen or sulphur atom, an optionally C_{1-3}-alkyl substituted imino group, or a C_{2-3}-alkylenedioxy or C_{2-3}-alkylenedithio group,
but one of the groups X_1 or Y_1 must represent a group of general formula

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or



The cyclisation is conveniently carried out in a solvent or mixture of solvents such as ethanol, isopropanol, glacial acetic acid, benzene, chlorobenzene, toluene, xylene, glycol, glycolmonomethylether, diethyleneglycol-dimethylether, sulpholane, dimethylformamide, tetraline or in an excess of the acylating agent used to prepare the compound of general formula II, e.g. in the corresponding nitrile, anhydride, acid halide, ester or amide, e.g. at temperatures between 0 and 250°C, but preferably at the boiling temperature of the reaction mixture, optionally in the presence of a condensing agent such as phosphorusoxychloride, thionylchloride, sulphurylchloride, sulphuric acid, p-toluenesulphonic acid, methanesulphonic acid, hydrochloric acid, phosphoric acid, polyphosphoric acid, acetic anhydride or optionally in the presence of a base such as potassium ethoxide or potassium tert.-butoxide. However, cyclisation may also be carried out without a solvent and/or condensing agent.

However, it is particularly advantageous to carry out the reaction by preparing a compound of general formula II in the reaction mixture by reducing a corresponding o-nitro-amino compound, optionally in the presence of a carboxylic acid of general formula R_3COOH, or by acylation of a corresponding o-diamino compound. When

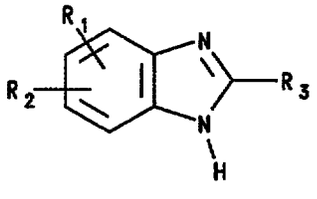
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the reduction of the nitro group is broken off at the hydroxylamine stage, the N-oxide of a compound of general formula I is obtained in the subsequent cyclisation. The resulting N-oxide is then converted by reduction into a corresponding compound of general formula I.

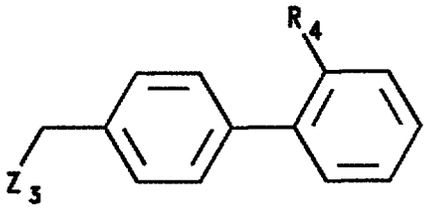
The subsequent reduction of the N-oxide of formula I obtained is preferably carried out in a solvent such as water, water/ethanol, methanol, glacial acetic acid, ethyl acetate or dimethylformamide with hydrogen in the presence of a hydrogenation catalyst such as Raney nickel, platinum or palladium/charcoal, with metals such as iron, tin or zinc in the presence of an acid such as acetic, hydrochloric or sulphuric acid, with salts such as iron(II)sulphate, tin(II)chloride or sodium dithionite, or with hydrazine in the presence of Raney nickel at temperatures between 0 and 50°C, but preferably at ambient temperature.

b) Reaction of a benzimidazole of general formula



(III)

wherein
R_1 to R_3 are defined as hereinbefore, with a biphenyl compound of general formula



(IV)

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wherein
R_4 is defined as hereinbefore and
Z_3 represents a nucleophilic leaving group such as a halogen atom, e.g. a chlorine, bromine or iodine atom, or a substituted sulphonyloxy group, e.g. a methanesulphonyloxy, phenylsulphonyloxy or p-toluenesulphonyloxy group.

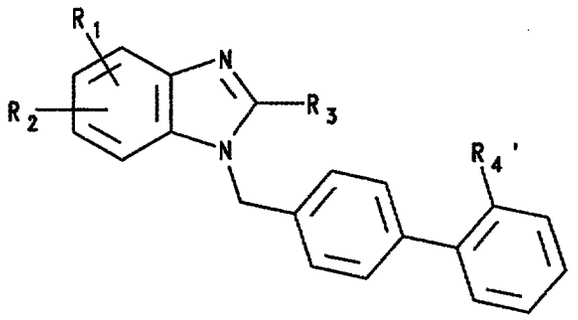
The reaction is conveniently carried out in a solvent or mixture of solvents such as methylene chloride, diethylether, tetrahydrofuran, dioxane, dimethyl-sulphoxide, dimethylformamide or benzene, optionally in the presence of an acid binding agent such as sodium carbonate, potassium carbonate, sodium hydroxide, potassium tert.-butoxide, triethylamine or pyridine, whilst the latter two may simultaneously also be used as solvent, preferably at temperatures between 0 and 100°C, e.g. at temperatures between ambient temperature and 50°C.

In the reaction, a mixture of the 1- and 3- isomers is preferably obtained which can if desired subsequently be resolved into the corresponding 1- and 3- isomers, preferably by chromatography using a substrate such as silica gel or aluminium oxide.

c) In order to prepare a compound of general formula I wherein R_4 represents a carboxy group:

Converting a compound of general formula

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(V)

wherein
R_1 to R_3 are defined as hereinbefore and
R_4' represents a group which may be converted into a carboxy group by hydrolysis, thermolysis or hydrogenolysis.

For example, functional derivatives of the carboxy group such as unsubstituted or substituted amides, esters, thiolesters, orthoesters, iminoethers, amidines or anhydrides, a nitrile group or a tetrazolyl group may be converted into a carboxy group by hydrolysis, esters with tertiary alcohols, e.g. tert.butylester, may be converted into a carboxy group by thermolysis and esters with aralkanols, e.g. benzylester, may be converted into a carboxy group by hydrogenolysis.

The hydrolysis is conveniently carried out in the presence of an acid such as hydrochloric, sulphuric, phosphoric, trichloroacetic or trifluoroacetic acid in the presence of a base such as sodium hydroxide or potassium hydroxide in a suitable solvent such as water, water/methanol, ethanol, water/ethanol, water/isopropanol or water/dioxane at temperatures between -10°C and 120°C, e.g. at temperatures between ambient temperature and the boiling temperature of the reaction mixture. When hydrolysis is carried out in the presence of an organic acid such as trichloroacetic or trifluoroacetic acid, any alcoholic hydroxy groups present may optionally be simultaneously converted into

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a corresponding acyloxy group such as a trifluoroacetoxy group.

If R_4' in a compound of general formula V represents a cyano or aminocarbonyl group, these groups may also be converted into a carboxy group with a nitrite, e.g. sodium nitrite, in the presence of an acid such as sulphuric acid, which may also be simultaneously used as solvent, at temperatures between 0 and 50°C.

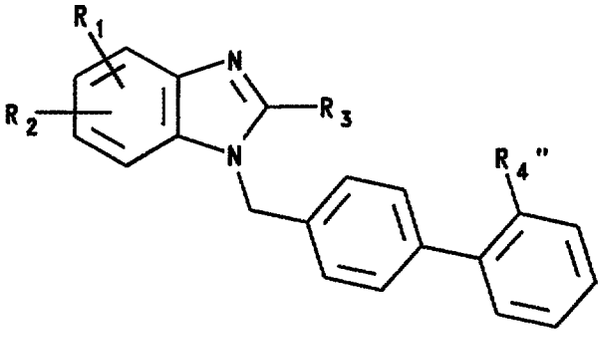
If R_4' in a compound of general formula V represents, for example, a tert.-butyloxycarbonyl group, the tert.-butyl group may also be thermally cleaved, optionally in an inert solvent such as methylene chloride, chloroform, benzene, toluene, tetrahydrofuran or dioxane and preferably in the presence of a catalytic amount of an acid such as p-toluenesulphonic acid, sulphuric, phosphoric or polyphosphoric acid, preferably at the boiling temperature of the solvent used, e.g. at temperatures between 40°C and 100°C.

If R_4' in a compound of general formula V represents, for example, a benzyloxycarbonyl group, the benzyl group may also be hydrogenolytically cleaved in the presence of a hydrogenation catalyst such as palladium/charcoal in a suitable solvent such as methanol, ethanol, ethanol/water, glacial acetic acid, ethyl acetate, dioxane or dimethylformamide, preferably at temperatures between 0 and 50°C, e.g. at ambient temperature, under a hydrogen pressure of 1 to 5 bar. During hydrogenolysis, other groups may be reduced at the same time, e.g. a nitro group may be reduced to an amino group, a benzyloxy group to a hydroxy group, a vinylidene group to the corresponding alkylidene group or a cinnamic acid group to the corresponding phenyl-propionic acid group, or they may be replaced by hydrogen atoms, e.g. a halogen may be replaced by a hydrogen atom.

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d) In order to prepare a compound of general formula I wherein R_4 represents a 1H-tetrazolyl group:

Cleaving of a protective group from a compound of general formula



(VI)

wherein
R_1, R_2 and R_3 are defined as hereinbefore and
R_4" represents a 1H-tetrazolyl group protected in the 1- or 3-position by a protecting group.

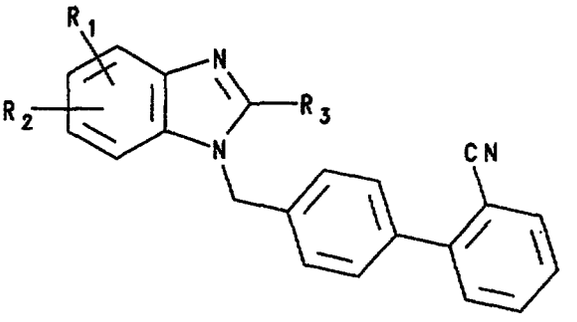
Suitable protecting groups include, for example, triphenylmethyl, tributyl tin or triphenyl tin groups.

The cleaving of a protective group used is preferably carried out in the presence of a hydrohalic acid, preferably in the presence of hydrochloric acid, in the presence of a base such as sodium hydroxide or alcoholic ammonia, in a suitable solvent such as methylene chloride, methanol, methanol/ammonia, ethanol or isopropanol at temperatures between 0 and 100°C, but preferably at ambient temperature or, if the reaction is carried out in the presence of alcoholic ammonia, at elevated temperatures, e.g. at temperatures between 100 and 150°C, preferably at temperatures between 120 and 140°C.

e) In order to prepare a compound of general formula I wherein R_4 represents a 1H-tetrazolyl group:

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Reaction of a compound of general formula



(VII)

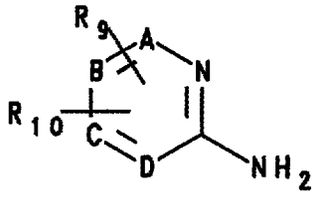
wherein
R_1 to R_3 are defined as hereinbefore, with hydrazoic acid or the salts thereof.

The reaction is preferably carried out in a solvent such as benzene, toluene or dimethylformamide at temperatures between 80 and 150°C, preferably at 125°C. Conveniently, either the hydrazoic acid is liberated during the reaction from an alkali metal azide, e.g. sodium azide, in the presence of a weak acid such as ammonium chloride or a tetrazolide salt obtained in the reaction mixture during the reaction with a salt of hydrazoic acid, preferably with aluminium azide or tributyl tin azide, which is also preferably produced in the reaction mixture by reacting aluminium chloride or tributyl tin chloride with an alkali metal azide such as sodium azide, is subsequently liberated by acidification with a dilute acid such as 2N hydrochloric or 2N sulphuric acid.

f) In order to prepare compounds of general formula I wherein R_2 represents one of the above-mentioned imidazo[1,2-a]pyridin-2-yl, imidazo[1,2-a]pyrimidin-2-yl, imidazo[1,2-c]pyrimidin-2-yl, imidazo[1,2-a]pyrazin-2-yl, imidazo[1,2-b]pyridazin-2-yl or imidazo[2,1-b]-thiazol-6-yl groups:

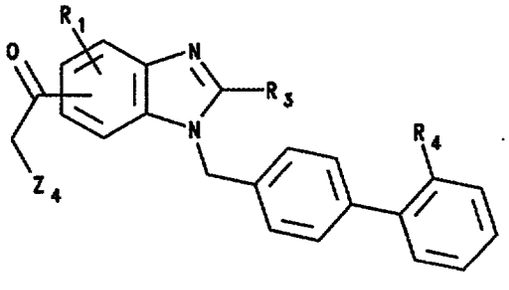
Reaction of a compound of general formula

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(VIII)

wherein
one of the groups A, B, C or D represents a methine group or a nitrogen atom and
the remaining groups A, B, C or D represent methine groups or A and B each represent a methine group and the -C=D- group represents a sulphur atom,
R_9 represents a hydrogen, fluorine, chlorine or bromine atom, an alkyl, alkoxy, hydroxy, phenyl, nitro, amino, alkylamino, dialkylamino, alkanoylamino, cyano, carboxy, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, trifluoromethyl, alkanoyl, aminosulphonyl, alkylaminosulphonyl or dialkylamino-sulphonyl group and
R_{10} represents a hydrogen, fluorine or chlorine atom, or a methyl, methoxy or hydroxy group, whilst if R_9 and R_{10} represent adjacent methyl groups these may be linked together by a methylene or ethylene group,
with a compound of general formula



(IX)

wherein
R_1, R_3 and R_4 are defined as hereinbefore and
Z_4 represents a nucleophilic leaving group such as a halogen atom, e.g. a chlorine or bromine atom.

The reaction is expediently carried out in a solvent or mixture of solvents such as ethanol, isopropanol,

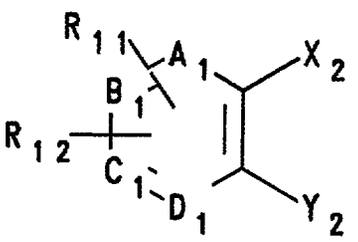
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benzene, glycol, glycolmonomethylether, dimethylformamide or dioxane, e.g. at temperatures between 0 and 150°C, preferably at temperatures between 20 and 100°C. However, the reaction may also be carried out without solvents.

g) In order to prepare compounds of general formula I wherein R_2 represents one of the above-mentioned benzimidazol-2-yl, imidazo[4,5-b]pyridin-2-yl, imidazo[4,5-c]pyridin-2-yl, imidazo[4,5-b]pyrazin-2-yl, imidazo[4,5-c]pyridazin-2-yl, imidazo[4,5-d]pyridazin-2-yl or purin-8-yl groups:

Cyclisation of a compound of general formula



(X)

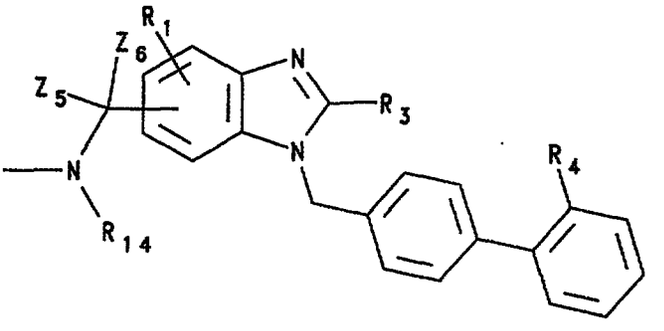
wherein
none, one or two of the groups A_1, B_1, C_1 or D_1 represent a nitrogen atom and
the remaining groups A_1, B_1, C_1 or D_1 represent methine groups,
R_{11} represents a hydrogen, fluorine, chlorine or bromine atom or an alkyl, alkoxy, hydroxy, phenyl, nitro, amino, alkylamino, dialkylamino, alkanoylamino, cyano, carboxy, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, trifluoromethyl, alkanoyl, aminosulphonyl, alkylaminosulphonyl or dialkylaminosulphonyl group and

R_{12} represents a hydrogen, fluorine or chlorine atom or a methyl, methoxy or hydroxy group,
one of the groups X_2 or Y_2 represents an R_{13}-NH- group and

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the other X_2 or Y_2 group represents a group of general formula



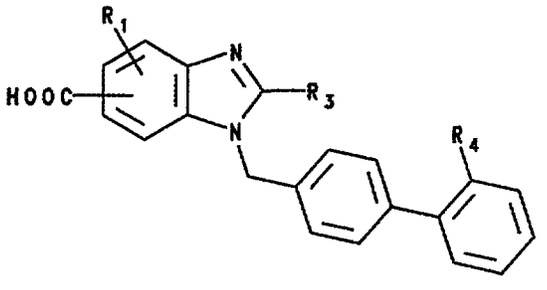
wherein R_1, R_3 and R_4 are defined as hereinbefore,
one of the groups R_{13} or R_{14} represents a hydrogen atom and the other R_{13} or R_{14} group represents a hydrogen atom, a C_{1-6}-alkyl group or a cycloalkyl group,
Z_5 and Z_6, which may be identical or different, represent optionally substituted amino groups or hydroxy or mercapto groups optionally substituted by lower alkyl groups or
Z_5 and Z_6 together represent an oxygen or sulphur atom, an optionally C_{1-3}-alkyl substituted imino group, or an alkylenedioxy or alkylenedithio group each having 2 or 3 carbon atoms, optionally with subsequent hydrolysis.

The cyclisation is conveniently carried out in a solvent or mixture of solvents such as ethanol, isopropanol, glacial acetic acid, benzene, chlorobenzene, toluene, xylene, glycol, glycolmonomethylether, diethyleneglycol-dimethylether, sulpholan, dimethylformamide, tetralin or in an excess of the acylating agent used to prepare the compound of general formula X, e.g. in the corresponding nitrile, anhydride, acid halide, ester or amide, e.g. at temperatures between 0 and 250°C, but preferably at the boiling temperature of the reaction mixture, optionally in the presence of a condensing agent such as phosphorus oxychloride, thionylchloride, sulphurylchloride, sulphuric acid, p-toluenesulphonic acid, methanesulphonic acid, hydrochloric acid, phosphoric

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acid, polyphosphoric acid, acetic acid anhydride or optionally in the presence of a base such as potassium ethoxide or potassium tert.-butoxide. However, the cyclisation may also be carried out without a solvent and/or condensing agent.

However, it is particularly advantageous to perform the reaction by preparing a compound of general formula X in the reaction mixture by reducing a corresponding o-nitro-amino compound, optionally in the presence of a carboxylic acid of general formula



(XI)

wherein
R_1, R_3 and R_4 are defined as hereinbefore, or by acylating a corresponding o-diamino compound with a carboxylic acid of general formula XI.

When the reduction of the nitro group is broken off at the hydroxylamine stage, subsequent cyclisation produces the N-oxide of a compound of general formula I. The N-oxide thus obtained is then converted by reduction into a corresponding compound of general formula I.

The subsequent reduction of an N-oxide thus obtained is preferably carried out in a solvent such as water, water/ethanol, methanol, glacial acetic acid, ethyl acetate or dimethylformamide with hydrogen in the presence of a hydrogenation catalyst such as Raney nickel, platinum or palladium/charcoal, with metals such as iron, tin or zinc in the presence of an acid such as acetic, hydrochloric or sulphuric acid, with salts such

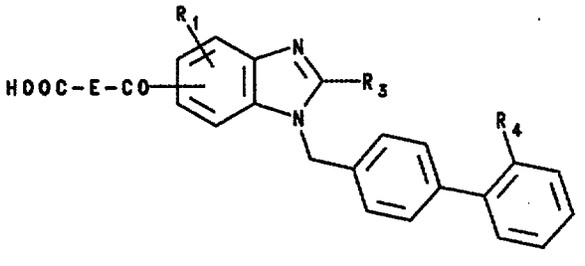
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as iron(II)sulphate, tin(II)chloride or sodium dithionite, or with hydrazine in the presence of Raney nickel at temperatures between 0 and 50°C, but preferably at ambient temperature.

The subsequent hydrolysis is conveniently carried out either in the presence of an acid such as hydrochloric, sulphuric, phosphoric, trichloroacetic or trifluoroacetic acid in the presence of a base such as sodium hydroxide or potassium hydroxide in a suitable solvent such as water, water/methanol, ethanol, water/ethanol, water/isopropanol or water/dioxane at temperatures between -10°C and 120°C, e.g. at temperatures between ambient temperature and the boiling temperature of the reaction mixture. When hydrolysis is carried out in the presence of an organic acid such as trichloroacetic or trifluoroacetic acid, any alcoholic hydroxy groups present may simultaneously be converted into a corresponding acyloxy group such as the trifluoroacetoxy group.

h) In order to prepare compounds of general formula I wherein R_2 represents a dihydro-pyridazin-3-one or pyridazin-3-one group which may be substituted in the 2-position by an optionally phenyl-substituted C_{1-3}-alkyl group or in the carbon structure by one or two C_{1-3}-alkyl groups:

Reaction of a carboxylic acid of general formula



(XII)

wherein

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R_1, R_3 and R_4 are defined as hereinbefore and
E represents an ethylene or ethenylene group optionally substituted by one or two C_{1-3}-alkyl groups, or the reactive acid derivatives thereof such as the esters, amides or halides thereof, with a hydrazine of general formula

$$H_2N - NHR_{15} \qquad (XIII)$$

wherein
R_{15} represents a hydrogen atom or an optionally phenyl-substituted C_{1-3}-alkyl group.

The reaction is conveniently carried out in a solvent such as methanol, ethanol, isopropanol, glacial acetic acid or propionic acid and/or in an excess of the hydrazine or hydrazine hydrate used at temperatures between 0 and 200°C, e.g. at temperatures between 20 and 150°C, but preferably at the boiling temperature of the reaction mixture, and optionally in the presence of an acid such as sulphuric or p-toluenesulphonic acid as condensing agent. The reaction may, however, also be carried out without a solvent.

In the reactions described hereinbefore, any reactive groups present such as hydroxy, amino or alkylamino groups may be protected during the reaction by conventional protecting groups which are split off again after the reaction.

Examples of protecting groups for a hydroxy group are trimethylsilyl, acetyl, benzoyl, methyl, ethyl, tert.-butyl, benzyl and tetrahydropyranyl groups and protecting groups for an amino, alkylamino or imino group include the acetyl, benzoyl, ethoxycarbonyl and benzyl groups.

The optional subsequent cleaving of a protecting group is preferably carried out by hydrolysis in an aqueous

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solvent, e.g. in water, isopropanol/water, tetrahydrofuran/water or dioxane/water, in the presence of an acid such as hydrochloric or sulphuric acid or in the presence of an alkali metal base such as sodium hydroxide or potassium hydroxide at temperatures between 0 and 100°C, preferably at the boiling temperature of the reaction mixture. However, a benzyl group is preferably split off by hydrogenolysis, e.g. with hydrogen in the presence of a catalyst such as palladium/charcoal in a solvent such as methanol, ethanol, ethyl acetate or glacial acetic acid, optionally with the addition of an acid such as hydrochloric acid at temperatures between 0 and 50°C, but preferably at ambient temperature, under a hydrogen pressure of 1 to 7 bar, preferably 3 to 5 bar.

An isomer mixture of a compound of general formula I thus obtained may if desired be resolved by chromatography using a substrate such as silica gel or aluminium oxide.

Moreover, the compounds of general formula I obtained may be converted into the acid addition salts thereof, more particularly for pharmaceutical use the physiologically acceptable salts thereof with inorganic or organic acids. Suitable acids for this purpose include hydrochloric, hydrobromic, sulphuric, phosphoric, fumaric, succinic, lactic, citric, tartaric or maleic acid.

Furthermore, the new compounds of general formula I thus obtained, if they contain a carboxy or 1H-tetrazolyl group, may if desired subsequently be converted into the salts thereof with inorganic or organic bases, more particularly for pharmaceutical use into the physiologically acceptable addition salts thereof. Suitable bases include for example sodium hydroxide,

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potassium hydroxide, cyclohexylamine, ethanolamine, diethanolamine and triethanolamine.

The compounds of general formulae II to XIII used as starting materials are known from the literature in some cases or may be obtained by methods known from the literature.

Thus, for example, a compound of general formula II is obtained by alkylation of a corresponding o-amino-nitro compound and subsequent reduction of the nitro group.

A compound of general formula III, V, VI, VII, IX, X or XII used as starting material is obtained by acylation of a corresponding o-phenylenediamine or a corresponding o-amino-nitro compound, followed by reduction of the nitro group and subsequent cyclisation of an o-diamino-phenyl compound thus obtained, optionally followed by the cleaving of any protecting group used or by cyclisation of a correspondingly substituted benzimidazole with a corresponding amine or by NH-alkylation of a corresponding 1H-benzimidazole, whilst the isomer mixture thus obtained may subsequently be resolved by conventional methods, e.g. chromatography. Some of the starting compounds mentioned above are described in EP-A-0 392 317.

For example, 2-n-butyl-5-(imidazo[1,2-a]pyridin-2-yl)-3H-benzimidazole is obtained by reacting p-amino-acetophenone with butyric acid chloride, followed by nitration, bromination, cyclisation with 2-aminopyridine to form the 6-n-butanoylamido-3-(imidazo[1,2-a]pyridin-2-yl)-nitrobenzene, which is subsequently converted into the desired compound by cyclisation, after reduction of the nitro group, or

2-n-butyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-1H-

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benzimidazole may be obtained by nitration of methyl 3-methyl-4-n-butanoylamido-benzoate, subsequent reduction of the nitro group and cyclisation to yield 2-n-butyl-4-methyl-6-methoxycarbonyl-1H-benzimidazole, which is then converted into the desired compound using 2-methylamino-aniline with cyclisation.

A benzimidazole in which the alkoxy group is substituted in the 2-, 3-, 4- or 5-position by an imidazole group may be obtained for example by reaction of a corresponding 7-hydroxy-benzimidazole, as described in EP-A-0 392 317, by reaction with a corresponding α, ω-dihaloalkane and subsequent reaction with a corresponding imidazole.

The new compounds of general formula I and the physiologically acceptable salts thereof have valuable pharmacological properties. They are angiotensin antagonists, particularly angiotensin-II-antagonists.

By way of example, the following compounds were tested for their biological effects as described hereinafter:

A = 4'-[[2-n-butyl-7-[3-(imidazol-1-yl)-propyloxy]-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid,

B = 4'-[[2-n-butyl-7-[3-(benzimidazol-1-yl)-propyloxy]-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid trifluoroacetate,

C = 4'-[[2-n-butyl-4-methyl-7-[4-(tetrahydro-benzimidazol-1-yl)-butoxy]-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid,

D = 4'-[[2-n-propyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-

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carboxylic acid,

E = 4'-[[2-n-propyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl,

F = 4'-[[2-n-propyl-4-methyl-6-(1-oxo-isoindolin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl,

G = 4'-[[2-n-propyl-4-methyl-6-(butanesultam-1-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl,

H = 4'-[[2-n-butyl-6-(2,3-dimethylmaleic acid imino)-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid semihydrate,

I = 4'-[[2-n-butyl-6-(isopropylcarbonylamino)-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid,

J = 4'-[[2-n-butyl-4-methyl-6-(morpholinocarbonylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid,

K = 4'-[[2-n-butyl-6-(cyclohexylaminocarbonylamino)-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid semitrifluoroacetate,

L = 4'-[[2-n-butyl-7-[3-(imidazol-1-yl)-propyloxy]-4-methyl-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl,

M = 4'-[(2-cyclopropyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid,

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N = 4'-[(2-n-propyl-4-methyl-6-(1-methyl-5-fluoro-benzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid,

O = 4'-[(2-n-propyl-4-methyl-6-(imidazo[1,2-a]pyrimidin-2-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl,

P = 4'-[(2-n-propyl-4-methyl-6-(5,6,7,8-tetrahydro-imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid,

Q = 4'-[(2-n-propyl-4-methyl-6-(5,6,7,8-tetrahydro-imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl,

R = 4'-[(2-n-propyl-4-chloro-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl-hydrochloride and

S = 4'-[[2-n-propyl-4-methyl-6-(imidazo[2,1-b]thiazol-6-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

Description of method: Angiotensin II-receptor bonding

The tissue (rats lung) is homogenised in Tris-buffer (50 mMol Tris, 150 mMol NaCl, 5 mMol EDTA, pH 7.40) and centrifuged twice for 20 minutes at 20,000 x g. The finished pellets are resuspended in incubating buffer (50 mMol Tris, 5 mMol $MgCl_2$, 0.2% BSA, pH 7.40) 1:75, based on the moist weight of the tissue. Each 0.1 ml of homogenate is incubated for 60 minutes at 37°C with 50 pM [^{125}I]-antiotensin II (NEN, Dreieich, FRG) with increasing concentrations of the test substance in a total volume of 0.25 ml. Incubation is ended by rapid filtration through glass fibre filter mats. The filters are each washed with 4 ml of ice cold buffer (25 mMol

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Tris, 2.5 mMol $MgCl_2$, 0.1% BSA, pH 7.40). The bound radioactivity is measured using a gamma-counter. The corresponding IC_{50} value is obtained from the dose-activity curve.

In the test described, substances A to S show the following IC_{50} values:

Substance	IC_{50} [nM]
A	510.0
B	52.0
C	130.0
D	3.7
E	14.0
F	5.0
G	1.2
H	20.0
I	6.6
J	3.5
K	17.0
L	240.0
M	12.0
N	26.0
O	3.4
P	1.2
Q	1.7
R	20.0
S	7.8

In addition, compounds D, E, F, G, H, M and O were tested on conscious renally hypertensive rats for their effect after oral administration using methods known from the literature. At a dosage of 10 mg/kg these compounds exhibited a hypotensive effect.

Moreover, when the above-mentioned compounds were administered in a dose of 30 mg/kg i.v. no toxic side

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effects, e.g. negative inotropic effects or disorders in heart rhythm, were observed. The compounds are therefore well tolerated.

In view of their pharmacological properties, the new compounds and the physiologically acceptable addition salts thereof are suitable for the treatment of hypertension and cardiac insufficiency and also for treating ischaemic peripheral circulatory disorders, myocardial ischaemia (angina), for the prevention of the progression of cardiac insufficiency after myocardial infarction and for treating diabetic nephropathy, glaucoma, gastrointestinal diseases and bladder diseases.

The new compounds and the physiologically acceptable addition salts thereof are also suitable for treating pulmonary diseases, e.g. lung oedema and chronic bronchitis, for preventing arterial re-stenosis after angioplasty, for preventing thickening of blood vessel walls after vascular operations, and for preventing arteriosclerosis and diabetic angiopathy. In view of the effects of angiotensin on the release of acetyl-choline and dopamine in the brain, the new angiotensin antagonists are also suitable for alleviating central nervous system disorders, e.g. depression, Alzheimer's disease, Parkinson syndrome, bulimia and disorders of cognitive function.

The dosage required to achieve these effects in adults is appropriately, when administered intravenously, 20 to 100 mg, preferably 30 to 70 mg, and, when administered orally, 50 to 200 mg, preferably 75 to 150 mg, 1 to 3 times a day. For this purpose, the compounds of general formula I prepared according to the invention, optionally in conjunction with other active substances, such as hypotensives, diuretics and/or calcium

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antagonists, may be incorporated together with one or more inert conventional carriers and/or diluents, e.g. with corn starch, lactose, glucose, microcrystalline cellulose, magnesium stearate, polyvinylpyrrolidone, citric acid, tartaric acid, water, water/ethanol, water/glycerol, water/sorbitol, water/polyethylene-glycol, propylene-glycol, cetylstearyl alcohol, carboxymethylcellulose or fatty substances such as hard fat or suitable mixtures thereof, in conventional galenic preparations such as plain or coated tablets, capsules, powders, suspensions or suppositories.

Additional active substances which may be included in the combinations mentioned above might be, for example, bendroflumethiazide, chlorothiazide, hydrochloro-thiazide, spironolactone, benzothiazide, cyclothiazide, ethacrinic acid, furosemide, metoprolol, prazosine, atenolol, propranolol, (di)hydralazine-hydrochloride, diltiazem, felodipin, nicardipin, nifedipin, nisoldipin and nitrendipin. The dosage for these active substances is appropriately one fifth of the lowest recommended dose up to 1/1 of the normally recommended dose, i.e., for example, 15 to 200 mg of hydrochlorothiazide, 125 to 2000 mg of chlorothiazide, 15 to 200 mg of ethacrinic acid, 5 to 80 mg of furosemide, 20 to 480 mg of propranolol, 5 to 60 mg of felodipine, 5 to 60 mg of nifedipin or 5 to 60 mg of nitrendipin.

The Examples which follow are intended to illustrate the invention:

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Example 1

4'-[[2-n-Butyl-7-[5-(imidazol-1-yl)-pentyloxy]-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid hydrate

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0.7 g (1.15 mMol) of tert.-butyl 4'-[[2-n-butyl-7-[5-(imidazol-1-yl)-pentyloxy]-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate are dissolved in 35 ml of methylene chloride, 5 ml of trifluoroacetic acid are added and the mixture is stirred for 12 hours at ambient temperature. It is diluted with methylene chloride and extracted with water and with saturated sodium bicarbonate solution. The organic phase is dried over sodium sulphate and evaporated down in vacuo. The crude product thus obtained is purified over a silica gel column (particle size: 0.063-0.02 mm, ethyl acetate/ethanol/ammonia - 90:10:0.1) and crystallised from acetone.

Yield: 0.19 g (29.9% of theory),

Melting point: 185-187°C

$C_{34}H_{38}N_4O_3 \times H_2O$ (550.70)

Calculated:	C 71.81	H 7.09	N 9.85
Found:	72.03	7.19	9.71

Mass spectrum: m/e = M^+ 550

The following compounds are obtained analogously to Example 1:

4'-[[2-n-butyl-4-methyl-6-(4,5-dihydro-2H-pyridazin-3-on-6-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(4,5-dihydro-2H-pyridazin-3-on-6-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-ethyl-4-methyl-6-(4,5-dihydro-2H-pyridazin-3-on-

6-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-butyl-4-methyl-6-(phenylaminocarbonylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-ethyl-4-methyl-6-(cyclohexylaminocarbonylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(cyclohexylaminocarbonyl-amino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-butyl-4-methyl-6-(cyclohexylaminocarbonyl-amino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(methylaminocarbonyl-methylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(n-pentylaminocarbonyl-methylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(n-pentylaminocarbonylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(n-butylaminocarbonyl-methylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(benzylaminocarbonylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(allylaminocarbonylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

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4'-[[2-n-propyl-4-methyl-6-(cyclohexylaminocarbonyl-methylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(dimethylaminocarbonyl-methylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(dimethylaminocarbonylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(cyclohexylaminocarbonyl-n-butylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(methylaminocarbonyl-cyclohexylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(methylaminocarbonyl-benzylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(n-hexylaminocarbonyl-cyclohexylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(cyclohexylaminocarbonyl-ethylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(dimethylaminocarbonyl-n-pentylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(morpholinocarbonylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

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4'-[[2-n-propyl-4-methyl-6-(pyrrolidinocarbonylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(pyrrolidinocarbonyl-methylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(piperidinocarbonylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(3-benzyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinon-1-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

Example 2

4'-[[2-n-Butyl-7-[3-(imidazol-1-yl)-propyloxy]-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.-butyl 4'-[[2-n-butyl-7-[3-(imidazol-1-yl)-propyloxy]-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 69.4% of theory,
Melting point: 208-210°C
$C_{32}H_{34}N_4O_3$ (522.64)
Calculated: C 73.54 H 6.56 N 10.72
Found: 73.45 6.62 10.60
R_f value: 0.50 (silica gel; ethyl acetate/ethanol/ammonia = 50:45:5)

Example 3

4'-[[2-n-Butyl-7-[3-(benzimidazol-1-yl)-propyloxy]-4-methylbenzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid trifluoroacetate

---

Prepared analogously to Example 1 from tert.-butyl 4'-

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[[2-n-butyl-7-[3-(benzimidazol-1-yl)-propyloxy]-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 87.8% of theory,
Melting point: 221-223°C
$C_{36}H_{36}N_4O_3 \times CF_3COOH$ (686.72)
Calculated: C 66.46 H 5.43 N 8.15
Found: 66.58 5.62 8.31
R_f value: 0.45 (silica gel; ethyl acetate/ethanol/ammonia = 50:45:5)

Example 4

4'-[[2-n-Butyl-7-[4-(imidazol-1-yl)-butyloxy]-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid hydrate

---

Prepared analogously to Example 1 from tert.-butyl 4'-[[2-n-butyl-7-[4-(imidazol-1-yl)-butyloxy]-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 68.5% of theory,
Melting point: 126-128°C
$C_{33}H_{36}N_4O_3 \times H_2O$ (554.68)
Calculated: C 71.46 H 6.91 N 10.10
Found: 71.63 7.02 9.98
Mass spectrum: m/e = 536

Example 5

4'-[[2-n-Butyl-7-[2-(benzimidazol-1-yl)-ethoxy]-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.-butyl 4'-[[2-n-butyl-7-[2-(benzimidazol-1-yl)-ethoxy]-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.

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Yield: 78.1% of theory,
Melting point: 167-169°C
$C_{35}H_{34}N_4O_3$ (558.68)
Calculated: C 75.25 H 6.13 N 10.03
Found: 75.03 6.17 9.95

Example 6

4'-[[2-n-Butyl-7-[5-(benzimidazol-1-yl)-pentyloxy]-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.-butyl 4'-[[2-n-butyl-7-[5-(benzimidazol-1-yl)-pentyloxy]-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.

Example 7

4'-[[2-n-Butyl-7-[4-(benzimidazol-1-yl)-butyloxy]-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.-butyl 4'-[[2-n-butyl-7-[4-(benzimidazol-1-yl)-butyloxy]-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.

Example 8

4'-[[2-n-Butyl-4-methyl-7-[4-(tetrahydrobenzimidazol-1-yl)-butyloxy]-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.-butyl 4'-[[2-n-butyl-4-methyl-7-[4-(tetrahydrobenzimidazol-1-yl)-butyloxy]-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.

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Yield: 86% of theory,
Melting point: 229-231°C
$C_{37}H_{42}N_4O_3$ (590.76)
Calculated: C 75.23 H 7.17 N 9.48
Found: 75.34 7.06 9.38

Example 9

4'-[[2-n-Propyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.-butyl 4'-[[2-n-propyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in dimethylformamide.
Yield: 63.9% of theory,
Melting point: 261-263°C
$C_{33}H_{30}N_4O_2$ (514.60)
Calculated: C 77.02 H 5.87 N 10.89
Found: 76.90 5.85 10.99

The following compounds are obtained analogously to Example 9:

4'-[[2-n-propyl-4-methyl-6-(1-n-propylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(1-n-hexylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(1-cyclopropylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(1-cyclohexylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

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Example 10

4'-[[2-n-Propyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

4.3 g (66 mMol) of sodium azide and 3.5 g (66 mMol) of ammonium chloride are added to a solution of 1.60 g (3.3 mMol) of 4'-[[2-n-propyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-2-cyano-biphenyl in 50 ml of dimethylformamide and the mixture is stirred for 24 hours at 140°C. Then water is added and the precipitate is removed by suction filtering. The crude product thus obtained is purified by chromatography over silica gel (300 g of silica gel, methylene chloride + 6% ethanol).
Yield: 900 mg (51% of theory),
Melting point: 228-230°C
$C_{33}H_{30}N_8$ (538.70)

Calculated:	C 73.58	H 5.61	N 20.80
Found:	73.48	5.55	20.70

The following compounds are obtained analogously to Example 10:

4'-[[2-n-propyl-4-methyl-6-(1-n-hexylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(1-cyclobutylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(1-cyclohexylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-4-methyl-7-[2-(imidazol-1-yl)-ethoxy]-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

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4'-[[2-n-butyl-7-[3-(imidazol-1-yl)-propyloxy]-4-methyl-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-7-[4-(imidazol-1-yl)-butyloxy]-4-methyl-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-4-methyl-7-[5-(imidazol-1-yl)-pentyloxy]-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-7-[2-(benzimidazol-1-yl)-ethoxy]-4-methyl-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-4-methyl-7-[3-(benzimidazol-1-yl)-propyloxy]-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-7-[4-(benzimidazol-1-yl)-butyloxy]-4-methyl-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-4-methyl-7-[5-(benzimidazol-1-yl)-pentyloxy]-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-7-[2-(4,5,6,7-tetrahydrobenzimidazol-1-yl)-ethoxy]-4-methyl-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-4-methyl-7-[3-(tetrahydrobenzimidazol-1-yl)-propyloxy]-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-7-[4-(tetrahydrobenzimidazol-1-yl)-butyloxy]-4-methyl-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

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4'-[[2-n-butyl-4-methyl-7-[5-(tetrahydrobenzimidazol-1-yl)-pentyloxy]-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-4-methyl-6-(phenylaminocarbonylamino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-ethyl-4-methyl-6-(cyclohexylaminocarbonylamino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-propyl-4-methyl-6-(cyclohexylaminocarbonylamino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-4-methyl-6-(cyclohexylaminocarbonyl-amino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(methylaminocarbonyl-methylamino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(n-pentylaminocarbonyl-methylamino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(n-pentylaminocarbonylamino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(n-butylaminocarbonyl-methylamino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(benzylaminocarbonylamino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(allylaminocarbonylamino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

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4'-[[2-n-propyl-4-methyl-6-(cyclohexylaminocarbonyl-methylamino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(dimethylaminocarbonylmethyl-amino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(dimethylaminocarbonylamino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(cyclohexylaminocarbonyl-n-butylamino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(methylaminocarbonyl-cyclohexylamino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(methylaminocarbonyl-benzylamino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(n-hexylaminocarbonyl-cyclohexylamino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(cyclohexylaminocarbonyl-ethylamino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(dimethylaminocarbonyl-n-pentylamino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(morpholinocarbonylamino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

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4'-[[2-n-propyl-4-methyl-6-(pyrrolidinocarbonylamino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(pyrrolidinocarbonyl-methylamino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(piperidinocarbonyl-methylamino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(3-benzyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinon-1-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

Example 11

4'-[(2-n-Propyl-4-methyl-6-phthalimino-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[(2-n-propyl-4-methyl-6-phthalimino-benzimidazol-1-yl)-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 6.8% of theory,
Melting point: sintering from 160°C
$C_{33}H_{27}N_7O_2$ (553.60)

Calculated:	C 71.59	H 4.92	N 17.71
Found:	71.39	4.88	17.54

Example 12

4'-[(2-n-Butyl-4-methyl-6-phthalimino-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[(2-n-butyl-4-methyl-6-phthalimino-benzimidazol-1-yl)-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 7.1% of theory,

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Melting point: sintering from 150°C

$C_{34}H_{29}N_7O_2$ (567.70)

Calculated:	C 71.94	H 5.15	N 17.27
Found:	71.75	5.19	17.22

Example 13

4'-[[2-n-Propyl-4-methyl-6-(1-oxo-isoindolin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[[2-n-propyl-4-methyl-6-(1-oxo-isoindolin-2-yl)-benzimidazol-1-yl]-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.

Yield: 25.0% of theory,

Melting point: sintering from 170°C

$C_{33}H_{29}N_7O$ (539.60)

Calculated:	C 73.45	H 5.42	N 18.17
Found:	73.20	5.41	18.33

Example 14

4'-[[2-n-Butyl-4-methyl-6-(1-oxo-isoindolin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[[2-n-butyl-4-methyl-6-(1-oxo-isoindolin-2-yl)-benzimidazol-1-yl]-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.

Yield: 21.0% of theory,

Melting point: sintering from 165°C

$C_{34}H_{31}N_7O$ (553.70)

Calculated:	C 73.76	H 5.64	N 17.71
Found:	73.58	5.33	17.41

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Example 15

4'-[[2-n-Propyl-4-methyl-6-(butanesultam-1-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[[2-n-propyl-4-methyl-6-(butanesultam-1-yl)-benzimidazol-1-yl]-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 49.0% of theory,
Melting point: Sintering from 186°C
$C_{29}H_{31}N_7O_2S$ (541.70)

Calculated:	C	64.30	H	5.77	N	18.10	S 5.92
Found:		64.10		5.39		18.01	5.98

Example 16

4'-[[2-Ethyl-4-methyl-6-(butanesultam-1-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[[2-ethyl-4-methyl-6-(butanesultam-1-yl)-benzimidazol-1-yl]-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 60.0% of theory,
Melting point: amorphous, sintering from 194°C
$C_{28}H_{29}N_7O_2S$ (527.70)

Calculated:	C	63.74	H	5.54	N	18.58	S 6.08
Found:		63.83		5.66		18.41	5.82

Example 17

4'-[[2-n-Butyl-4-methyl-6-(butanesultam-1-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[[2-n-butyl-4-methyl-6-(butanesultam-1-yl)-benzimidazol-1-yl]-methyl]-2-cyano-biphenyl and sodium azide in dimethyl-formamide.

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Yield: 48.0% of theory,
Melting point: amorphous, sintering from 183°C
$C_{30}H_{33}N_7O_2S$ (555.70)

Calculated:	C	64.84	H	5.99	N	17.64	S 5.77
Found:		64.53		5.66		17.63	5.55

Example 18

4'-[[2-n-Propyl-4-ethyl-6-(butanesultam-1-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[[2-n-propyl-4-ethyl-6-(butanesultam-1-yl)-benzimidazol-1-yl]-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 27.0% of theory,
Melting point: amorphous, sintering from 189°C
$C_{30}H_{33}N_7O_2S$ (555.70)

Calculated:	C	64.84	H	5.99	N	17.64	S 5.77
Found:		64.81		5.68		17.87	5.31

Example 19

4'-[[2-Ethyl-4-ethyl-6-(butanesultam-1-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[[2-ethyl-4-ethyl-6-(butanesultam-1-yl)-benzimidazol-1-yl]-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 39.0% of theory,
Melting point: amorphous, sintering from 212°C
$C_{29}H_{31}N_7O_2S$ (541.70)

Calculated:	C	64.30	H	5.77	N	18.10	S 5.92
Found:		64.30		5.51		17.99	5.59

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Example 20

4'-[[2-n-Propyl-4-isopropyl-6-(butanesultam-1-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[[2-n-propyl-4-isopropyl-6-(butanesultam-1-yl)-benzimidazol-1-yl]-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 22.0% of theory,
Melting point: amorphous
$C_{31}H_{35}N_7O_2S$ (569.70)

Calculated:	C	65.35	H	6.19	N	17.21	S 5.63
Found:		65.13		6.10		17.54	5.40

Example 21

4'-[[2-Ethyl-4-isopropyl-6-(butanesultam-1-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[[2-ethyl-4-isopropyl-6-(butanesultam-1-yl)-benzimidazol-1-yl]-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 24.0% of theory,
Melting point: amorphous, sintering from 209°C
$C_{30}H_{33}N_7O_2S$ (555.70)

Calculated:	C	64.84	H	5.99	N	17.64	S 5.77
Found:		64.99		5.71		17.43	5.71

Example 22

4'-[[2-n-Propyl-4-trifluoromethyl-6-(butanesultam-1-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[[2-n-propyl-4-trifluoromethyl-6-(butanesultam-1-yl)-benzimidazol-1-yl]-methyl]-2-cyano-biphenyl and sodium azide in

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dimethyl-formamide.
Yield: 17.0% of theory,
Melting point: 199-203°C
$C_{29}H_{28}F_3N_7O_2S$ (595.70)

Calculated:	C	58.48	H	4.74	N	16.46
Found:		58.28		4.43		16.22

Example 23

4'-[[2-n-Propyl-4-methyl-6-(N-benzenesulphonyl-methylamino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[[2-n-propyl-4-methyl-6-(N-benzenesulphonyl-methylamino)-benzimidazol-1-yl]-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 42.0% of theory,
Melting point: 161-163°C
$C_{32}H_{31}N_7O_2S$ (577.70)

Calculated:	C	66.53	H	5.41	N	16.97	S	5.55
Found:		66.32		5.36		16.70		5.31

Example 24

4'-[[2-n-Butyl-4-methyl-6-(N-benzenesulphonyl-methylamino)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[[2-n-butyl-4-methyl-6-(N-benzenesulphonyl-methylamino)-benzimidazol-1-yl]-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 37.0% of theory,
Melting point: 150-153°C
$C_{33}H_{33}N_7O_2S$ (591.70)

Calculated:	C	66.98	H	5.62	N	16.57
Found:		66.71		5.38		16.39

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The following compounds are obtained analogously to Example 24:

4'-[[2-ethyl-4-methyl-6-(4,5-dihydro-2H-pyridazin-3-on-6-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(4,5-dihydro-2H-pyridazin-3-on-6-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-4-methyl-6-(4,5-dihydro-2H-pyridazin-3-on-6-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(3-benzyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinon-1-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-ethyl-4-methyl-6-(3-benzyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinon-1-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

Example 25

4'-[[2-n-Butyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.-butyl 4'-[[2-n-butyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 48.0% of theory,
Melting point: 233-235°C
$C_{34}H_{32}N_4O_2$ (528.70)

Calculated:	C 77.25	H 6.10	N 10.60
Found:	77.10	5.98	10.46

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Example 26

4'-[[2-n-Butyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[[2-n-butyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 41.0% of theory,
Melting point: 235-237°C
$C_{34}H_{32}N_8$ (552.70)

Calculated:	C 73.89	H 5.84	N 20.28
Found:	73.67	5.81	19.93

The following compounds are obtained analogously to Example 26:

4'-[[2-n-butyl-4-methyl-6-(1-ethylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-4-methyl-6-(1-cyclopropylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-4-methyl-6-(1-n-pentylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-4-methyl-6-(1-cyclopentylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

Example 27

4'-[[2-n-Propyl-4-methyl-6-(2-oxo-piperidin-1-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[[2-n-propyl-

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4-methyl-6-(2-oxo-piperidin-1-yl)-benzimidazol-1-yl]-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 51.0% of theory,
Melting point: amorphous, from 140°C (sintering)
$C_{30}H_{31}N_7O$ (505.60)
Calculated: C 71.26 H 6.18 N 19.39
Found: 71.08 6.22 19.47

Example 28

4'-[[2-n-Butyl-4-methyl-6-(2-oxo-piperidin-1-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[[2-n-butyl-4-methyl-6-(2-oxo-piperidin-1-yl)-benzimidazol-1-yl]-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 39.0% of theory,
Melting point: amorphous, from 128°C (sintering)
$C_{31}H_{33}N_7O$ (519.70)
Calculated: C 71.65 H 6.40 N 18.87
Found: 71.44 6.23 18.59

Example 29

4'-[[2-n-Propyl-4-methyl-6-(2-oxo-piperidin-1-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared from 4'-[[2-n-propyl-4-methyl-6-(2-oxo-piperidin-1-yl)-benzimidazol-1-yl]-methyl]-2-(2-triphenylmethyl-tetrazol-5-yl)biphenyl by cleaving the triphenylmethyl group with methanolic hydrochloric acid.
Yield: 51.0% of theory,
Melting point: amorphous, sintering from 115°C
$C_{30}H_{31}N_7O$ (505.60)
Calculated: C 71.26 H 6.18 N 19.39
Found: 71.51 6.39 19.09

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Example 30

4'-[[2-n-Propyl-6-(imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.-butyl 4'-[[2-n-propyl-6-(imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 54.0% of theory,
Melting point: 202-204°C
$C_{31}H_{26}N_4O_2$ (486.60)

Calculated:	C 76.52	H 5.39	N 11.52
Found:	76.33	5.32	11.30

The following compounds may be prepared analogously to Example 30:

4'-[[2-n-propyl-6-(8-methyl-imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-butyl-6-(6-methyl-imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-6-(5,7-dimethyl-imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-6-(6-aminocarbonyl-imidazo[1,2-a]-pyridin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-butyl-6-(6-chloro-imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-6-(imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

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4'-[[2-n-propyl-6-(imidazo[2,1-b]thiazol-6-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-butyl-6-(2,3-dimethyl-imidazo[2,1-b]thiazol-6-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

Example 31

4'-[[2-n-Butyl-6-(imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.-butyl 4'-[[2-n-butyl-6-(imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 41.0% of theory,
Melting point: 193-195°C
$C_{32}H_{28}N_4O_2$ (500.60)

Calculated:	C 76.78	H 5.64	N 11.19
Found:	76.73	5.48	11.00

Example 32

4'-[[2-n-Propyl-6-(imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[[2-n-propyl-6-(imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 28.0% of theory,
Melting point: 187-189°C
$C_{31}H_{26}N_8$ (510.60)

Calculated:	C 72.92	H 5.13	N 21.95
Found:	72.80	4.97	21.74

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The following compounds may be prepared analogously to Example 32:

4'-[[2-n-propyl-6-(7-methyl-imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-6-(5-methyl-imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-6-(6-bromo-imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-6-(5,7-dimethyl-imidazo[1,2-a]pyrimidin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-6-(3-methyl-imidazo[2,1-b]thiazol-6-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-6-(2-phenyl-imidazo[2,1-b]thiazol-6-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

Example 33

4'-[[2-n-Butyl-6-(imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[[2-n-butyl-6-(imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 23.0% of theory,
Melting point: 170-173°C
$C_{32}H_{28}N_8$ (524.60)

Calculated:	C 73.26	H 5.38	N 21.36
Found:	73.09	5.32	21.20

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Example 34

4'-[[2-n-Propyl-4-methyl-6-(imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.-butyl 4'-[[2-n-propyl-4-methyl-6-(imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 38.0% of theory,
Melting point: 195-197°C (after evaporation and without recrystallisation)
Melting point: 299-303°C (methylene chloride/ethanol = 20:1)
$C_{32}H_{28}N_4O_2$ (500.60)

Calculated:	C 76.78	H 5.64	N 11.19
Found:	76.55	5.61	10.87

The following compounds may be prepared analogously to Example 34:

4'-[[2-n-propyl-4-methyl-6-(8-methyl-imidazo[1,2-a]-pyridin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-butyl-4-methyl-6-(7-methyl-imidazo[1,2-a]-pyridin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-butyl-4-methyl-6-(6-methyl-imidazo[1,2-a]-pyridin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(5-methyl-imidazo[1,2-a]-pyridin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(5,7-dimethyl-imidazo-[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-

biphenyl-2-carboxylic acid

4'-[[2-ethyl-4-methyl-6-(6-aminocarbonyl-imidazo-[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-ethyl-4-methyl-6-(6-chloro-imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

Example 35

4'-[[2-n-Propyl-4-methyl-6-(imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[[2-n-propyl-4-methyl-6-(imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 21.0% of theory,
Melting point: sintering from 181°C
$C_{32}H_{28}N_8$ (524.60)

Calculated:	C 73.26	H 5.38	N 21.36
Found:	73.10	5.24	21.13

The following compounds may be prepared analogously to Example 35:

4'-[[2-n-propyl-4-methyl-6-(5-methyl-imidazo[1,2-a]-pyridin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(imidazo[1,2-a]pyrimidin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

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Example 36

4'-[[2-n-Butyl-4-methyl-6-(imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.-butyl 4'-[[2-n-butyl-4-methyl-6-(imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 51.0% of theory,
Melting point: 194-197°C
$C_{33}H_{30}N_4O_2$ (514.60)

Calculated:	C 77.02	H 5.88	N 10.89
Found:	76.81	5.78	10.64

The following compounds are obtained analogously to Example 36:

4'-[[2-n-propyl-6-(pyrrolidin-2-on-5-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-6-(pyrrolidin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-6-(quinolin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-butyl-6-(quinolin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-6-(isoquinolin-3-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-ethyl-6-(isoquinolin-3-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

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Example 37

4'-[[2-n-Butyl-4-methyl-6-(imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[[2-n-butyl-4-methyl-6-(imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 26.0% of theory,
$C_{33}H_{30}N_8$ (538.60)

Calculated:	C 73.58	H 5.61	N 20.80
Found:	73.39	5.40	20.92

The following compounds are obtained analogously to Example 37:

4'-[[2-n-propyl-6-(pyrrolidin-2-on-5-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-6-(pyrrolidin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-6-(piperidin-2-on-6-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-6-(piperidin-2-on-6-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-6-(piperidin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-6-(piperidin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-ethyl-6-(pyridin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

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4'-[[2-n-propyl-6-(pyridin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-6-(pyridin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-6-(quinolin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-6-(quinolin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-6-(isoquinolin-3-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-ethyl-6-(isoquinolin-3-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

Example 38

4'-[[2-n-Butyl-4-methyl-6-(2,2-dimethylpropionylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.-butyl 4'-[[2-n-butyl-4-methyl-6-(2,2-dimethylpropionylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.

Example 39

4'-[[2-n-Butyl-7-[2-(tetrahydrobenzimidazol-1-yl)-ethoxy]-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.-butyl 4'-[[2-n-butyl-7-[2-(tetrahydrobenzimidazol-1-yl)-ethoxy]-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene

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chloride.
Yield: 81% of theory,
Melting point: 236-237°C
$C_{35}H_{38}N_4O_3$ (562.71)
Calculated: C 74.71 H 6.81 N 9.96
Found: 74.51 6.79 9.98

Example 40

4'-[[2-n-Butyl-4-methyl-7-[5-(tetrahydrobenzimidazol-1-yl)-pentyloxy]-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.-butyl 4'-[[2-n-butyl-4-methyl-7-[5-(tetrahydrobenzimidazol-1-yl)-pentyloxy]-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.

Example 41

4'-[[2-n-Butyl-7-[3-(tetrahydrobenzimidazol-1-yl)-propyloxy]-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.-butyl 4'-[[2-n-butyl-7-[3-(tetrahydrobenzimidazol-1-yl)-propyloxy]-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.

Example 42

4'-[[2-n-Propyl-4-methyl-6-(imidazo[1,2-a]pyrimidin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.-butyl 4'-

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[[2-n-propyl-4-methyl-6-(imidazo[1,2-a]pyrimidin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 47% of theory,
Melting point: 224-226°C (after evaporation and without recrystallisation)
Melting point: 294-297°C (methylene chloride/ethanol = 20:1)
$C_{31}H_{27}N_5O_2$ (501.60)

Calculated:	C	74.23	H	5.43	N	13.96
Found:		74.10		5.31		13.66

Example 43

4'-[[2-n-Propyl-4-methyl-6-(imidazo[2,1-b]thiazol-6-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.-butyl 4'-[[2-n-propyl-4-methyl-6-(imidazo[2,1-b]thiazol-6-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 43% of theory,
Melting point: 192-195°C (after evaporation and without recrystallisation)
Melting point: >300°C (methylene chloride/ethanol - 20:1)
$C_{30}H_{26}N_4O_2S$ (506.64)

Calculated:	C	71.12	H	5.17	N	11.06	S 6.33
Found:		70.97		5.19		10.88	6.09

The following compounds may be prepared analogously to Example 43:

4'-[[2-n-propyl-4-methyl-6-(3-methyl-imidazo[2,1-b]-thiazol-6-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

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4'-[[2-n-propyl-4-methyl-6-(2,3-dimethyl-imidazo[2,1-b]-thiazol-6-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-butyl-4-methyl-6-(2,3-trimethylene-imidazo-[2,1-b]thiazol-6-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(2,3-tetramethylene-imidazo[2,1-b]thiazol-6-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-ethyl-4-methyl-6-(2-phenyl-imidazo[2,1-b]-thiazol-6-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

Example 44

4'-[[2-n-Propyl-4-methyl-6-(imidazo[2,1-b]thiazol-6-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[[2-n-propyl-4-methyl-6-(imidazo[2,1-b]thiazol-6-yl)-benzimidazol-1-yl]-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 21% of theory,
Melting point: amorphous, sintering from 196°C
$C_{30}H_{26}N_8S$ (530.67)

Calculated:	C 67.90	H 4.94	N 21.12	S 6.04
Found:	67.77	4.84	21.00	5.87

The following compounds may be prepared analogously to Example 44:

4'-[[2-n-propyl-4-methyl-6-(3-methyl-imidazo[2,1-b]-thiazol-6-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

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4'-[[2-n-butyl-4-methyl-6-(2,3-dimethyl-imidazo[2,1-b]-thiazol-6-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-4-methyl-6-(2,3-trimethylene-imidazo-[2,1-b]thiazol-6-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-ethyl-4-methyl-6-(2,3-tetramethylene-imidazo-[2,1-b]thiazol-6-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(2-phenyl-imidazo[2,1-b]-thiazol-6-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

Example 45

4'-[[2-n-Propyl-4-methyl-6-(benzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[[2-n-propyl-4-methyl-6-(benzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-2-cyano-biphenyl and sodium azide in dimethyl-formamide.
Yield: 28% of theory,
Melting point: 202-205°C
$C_{32}H_{28}N_8$ (524.64)

Calculated:	C 73.26	H 5.38	N 21.36
Found:	73.01	5.22	21.56

The following compounds are obtained analogously to Example 45:

4'-[[2-ethyl-4-methyl-6-(benzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-butyl-4-methyl-6-(benzimidazol-2-yl)-

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benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(1-n-hexyl-benzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(1-cyclopropyl-benzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[[2-n-propyl-4-methyl-6-(1-cyclohexyl-benzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

Example 46

4'-[[2-n-Propyl-4-methyl-6-(benzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.-butyl 4'-[[2-n-propyl-4-methyl-6-(benzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 43% of theory,
Melting point: 239-242°C
$C_{32}H_{28}N_4O_2$ (500.61)

Calculated:	C 76.78	H 5.64	N 11.19
Found:	76.55	5.60	11.41

The following compounds are obtained analogously to Example 46:

4'-[[2-ethyl-4-methyl-6-(benzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-butyl-4-methyl-6-(benzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

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4'-[[2-n-propyl-4-methyl-6-(1-n-hexyl-benzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(1-cyclopropyl-benzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

4'-[[2-n-propyl-4-methyl-6-(1-cyclohexyl-benzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

Example 47

4'-[[2-n-Butyl-7-[3-(imidazol-1-yl)-propyloxy]-4-methyl-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared from 4'-[[2-n-butyl-7-[3-(imidazol-1-yl)-propyloxy]-4-methyl-benzimidazol-1-yl]-methyl]-2-(1-triphenylmethyl-tetrazol-5-yl)-biphenyl by cleaving the 1-triphenylmethyl group by means of ethanol/hydrochloric acid.
Yield: 89.8% of theory,
Melting point: 83-87°C
$C_{32}H_{34}N_8O \times 1.5\ H_2O$ (573.69)

Calculated:	C 66.99	H 6.50	N 19.53
Found:	66.83	6.52	19.43

Example 48

4'-[[6-(N-Benzenesulphonyl-methylamino)-2-n-butyl-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.butyl 4'-[[6-(N-benzenesulphonylmethylamino)-2-n-butyl-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 95.6% of theory,
Melting point: 211-212°C

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$C_{33}H_{33}N_3O_4S$ (567.70)

Calculated:	C	69.80	H	5.86	N	7.40	S 5.65
Found:		69.52		5.92		7.33	5.84

Example 49

4'-[[6-(N-Benzenesulphonyl-n-pentylamino)-2-n-butyl-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.butyl 4'-[[6-(N-benzenesulphonyl-n-pentylamino)-2-n-butyl-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 81.8% of theory,
Melting point: 232-233°C
$C_{37}H_{41}N_3O_4S$ (623.81)

Calculated:	C	71.24	H	6.62	N	6.74	S 5.14
Found:		71.30		6.77		6.68	5.33

Example 50

4'-[[2-n-Butyl-6-(isopropylcarbonylamino)-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.butyl 4'-[[2-n-butyl-6-(isopropylcarbonylamino)-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 86.3% of theory,
Melting point: 313-315°C
$C_{30}H_{33}N_3O_3$ (483.61)

Calculated:	C	74.51	H	6.88	N	8.69	
Found:		74.37		7.10		8.74	

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Example 51

4'-[[2-n-Butyl-6-(2,3-dimethylmaleic acid imino)-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid-semihydrate

---

Prepared analogously to Example 1 from tert.butyl 4'-[[2-n-butyl-6-(2,3-dimethylmaleic acid imino)-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 88.9% of theory,
Melting point: 321-322°C
$C_{32}H_{31}N_3O_4 \times 0.5\ H_2O$ (530.62)

Calculated:	C 72.43	H 6.08	N 7.92
Found:	72.89	6.16	7.89

Example 52

4'-[[6-(2,3-Dimethylmaleic acid imino)-2-n-propyl-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid semihydrate

---

Prepared analogously to Example 1 from tert.butyl 4'-[[6-(2,3-dimethylmaleic acid imino)-2-n-propyl-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 75.4% of theory,
Melting point: 329-331°C
$C_{31}H_{29}N_3O_4 \times 0.5\ H_2O$ (516.60)

Calculated:	C 72.08	H 5.85	N 8.13
Found:	72.04	5.84	7.96

Example 53

4'-[(6-Acetamino-2-n-butyl-4-methyl-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid trifluoroacetate semihydrate

---

Prepared analogously to Example 1 from tert.butyl 4'-

[(6-acetamino-2-n-butyl-4-methyl-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 95.7% of theory,
Melting point: 112-114°C (amorphous)
$C_{28}H_{29}N_3O_3$ x CF_3COOH x 0.5 H_2O (578.59)
Calculated: C 62.28 H 5.40 N 7.26.
Found: 62.57 5.46 7.21

Example 54

4'-[[2-n-Butyl-4-methyl-6-(morpholinocarbonylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.butyl 4'-[[2-n-butyl-4-methyl-6-(morpholinocarbonylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 80.9% of theory,
Melting point: 279-281°C
$C_{31}H_{34}N_4O_4$ (526.64)
Calculated: C 70.70 H 6.51 N 10.64
Found: 70.48 6.50 10.51

Example 55

4'-[[2-n-Butyl-6-(cyclohexylaminocarbonylamino)-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid semitrifluoroacetate

---

Prepared analogously to Example 1 from tert.butyl 4'-[[2-n-butyl-6-(cyclohexylaminocarbonylamino)-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 76.9% of theory,
Melting point: 288-289°C
$C_{33}H_{38}N_4O_3$ x 0.5 CF_3COOH (595.70)
Calculated: C 68.55 H 6.51 N 9.41.

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Found: 69.08 7.02 9.65

Example 56

4'-[[2-n-Propyl-4-isopropyl-6-(1-oxo-isoindolin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

Prepared analogously to Example 10 from 4'-[[2-n-propyl-4-isopropyl-6-(1-oxo-isoindolin-2-yl)-benzimidazol-1-yl]-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 14% of theory,
Melting point: amorphous
$C_{35}H_{33}N_7O$ (567.71)
Calculated: C 74.05 H 5.86 N 17.27
Found: 73.97 5.82 17.26
Mass spectrum: M^+ = 567

Example 57

4'-[[2-n-Propyl-5-(imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid

Prepared analogously to Example 1 from tert.butyl 4'-[[2-n-propyl-5-(imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 32% of theory,
Melting point: 250-253°C
$C_{31}H_{26}N_4O_2$ (486.60)
Calculated: C 76.52 H 5.39 N 11.52
Found: 76.28 5.47 11.27

Example 58

4'-[(2-n-Propyl-4-ethyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

Prepared analogously to Example 1 from tert.butyl 4'-

[(2-n-propyl-4-ethyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 64% of theory,
Melting point: 217-219°C
$C_{34}H_{32}N_4O_2$ (528.70)

Calculated:	C 77.24	H 6.10	N 10.60
Found:	77.12	6.09	10.75

Example 59

4'-[(2-n-Propyl-4-ethyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[(2-n-propyl-4-ethyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 15% of theory,
Melting point: 215-217°C
$C_{34}H_{32}N_8$ (552.70)

Calculated:	C 73.89	H 5.84	N 20.28
Found:	73.66	6.02	20.56

Example 60

4'-[(2-Cyclopropyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.butyl 4'-[(2-cyclopropyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 52% of theory,
Melting point: 244-246°C
$C_{33}H_{28}N_4O_2$ (512.60)

Calculated:	C 77.32	H 5.51	N 10.93

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Found: 77.75 5.71 10.94

Example 61

4'-[(2-Cyclopropyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[(2-cyclopropyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 59% of theory,
Melting point: 245-247°C
$C_{33}H_{28}N_8$ (536.65)
Calculated: C 73.86 H 5.26 N 20.88
Found: 73.95 5.42 20.90

Example 62

4'-[(2-Cyclobutyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.butyl 4'-[(2-cyclobutyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 63% of theory,
Melting point: 189-191°C
$C_{34}H_{30}N_4O_2$ (526.60)
Calculated: C 77.55 H 5.74 N 10.64
Found: 77.35 5.92 10.40

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Example 63

4'-[(2-Cyclobutyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[(2-cyclobutyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 61% of theory,
Melting point: 197-199°C
$C_{34}H_{30}N_8$ (550.70)

Calculated:	C 74.16	H 5.49	N 20.35
Found:	74.12	5.74	20.67

Example 64

4'-[(2-n-Propyl-4-methyl-6-(1-methyl-5-fluoro-benzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.butyl 4'-[(2-n-propyl-4-methyl-6-(1-methyl-5-fluoro-benzimidazol-2-yl)-benzimidazol-1-y)-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 34% of theory,
Melting point: 250-252°C
$C_{33}H_{29}FN_4O_2$ (532.60)

Calculated:	C 74.42	H 5.49	N 10.52
Found:	74.14	5.64	10.54

The following compounds are obtained analogously to Example 64:

4'-[(2-n-propyl-4-methyl-6-(pyridin-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

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4'-[(2-n-propyl-4-methyl-6-(quinolin-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

4'-[(2-n-propyl-4-methyl-6-(isoquinolin-3-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

4'-[(2-n-propyl-4-methyl-6-(isoquinolin-1-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

Example 65

4'-[(2-n-Propyl-4-methyl-6-(imidazo[1,2-a]pyrimidin-2-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[(2-n-propyl-4-methyl-6-(imidazo[1,2-a]pyrimidin-2-yl)-benzimidazol-1-yl)-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 16.5% of theory,
Melting point: from 275°C (decomp.)
$C_{31}H_{27}N_9 \times H_2O$ (543.65)

Calculated:	C 68.49	H 5.38	N 23.19
Found:	68.25	5.50	23.37

The following compounds are obtained analogously to Example 65:

4'-[(2-n-propyl-4-methyl-6-(pyridin-2-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[(2-n-propyl-4-methyl-6-(quinolin-2-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[(2-n-propyl-4-methyl-6-(isoquinolin-3-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[(2-n-propyl-4-methyl-6-(isoquinolin-1-yl)-

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benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

Example 66

4'-[(2-n-Propyl-4-methyl-6-(5,6,7,8-tetrahydro-imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.butyl 4'-[(2-n-propyl-4-methyl-6-(5,6,7,8-tetrahydro-imidazo-[1,2-a]pyridin-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 67% of theory,
Melting point: from 240°C (sinters)
$C_{32}H_{32}N_4O_2$ (504.64)

Calculated:	C 76.16	H 6.39	N 11.10
Found:	75.94	6.46	11.20

The following compounds are obtained analogously to Example 66:

4'-[(2-n-butyl-4-methyl-6-(5,6,7,8-tetrahydro-imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

4'-[(2-ethyl-4-methyl-6-(5,6,7,8-tetrahydro-imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

Example 67

4'-[(2-n-Propyl-4-methyl-6-(5,6,7,8-tetrahydro-imidazo-[1,2-a]pyridin-2-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[(2-n-propyl-4-methyl-6-(5,6,7,8-tetrahydro-imidazo[1,2-a]pyridin-2-

yl)-benzimidazol-1-yl)-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 73.5% of theory,
Melting point: from 275°C (decomp.)
$C_{32}H_{32}N_8$ (528.67)
Calculated: C 72.70 H 6.10 N 21.20
Found: 72.40 6.07 21.48

The following compounds are obtained analogously to Example 67:

4'-[(2-n-butyl-4-methyl-6-(5,6,7,8-tetrahydro-imidazo-[1,2-a]pyridin-2-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[(2-ethyl-4-methyl-6-(5,6,7,8-tetrahydro-imidazo-[1,2-a]pyridin-2-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

Example 68

4'-[(2-n-Propyl-4-methyl-6-(1-methyl-6-fluoro-benzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.butyl 4'-[(2-n-propyl-4-methyl-6-(1-methyl-6-fluoro-benzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 76% of theory,
Melting point: 243-245°C
$C_{33}H_{29}FN_4O_2$ (532.60)
Calculated: 74.42 H 5.49 N 10.52
Found: 74.74 5.52 10.77
Mass spectrum: m/e = 532

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Example 69

4'-[(2-n-Propyl-4-chloro-6-(1-oxo-isoindolin-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.butyl 4'-[(2-n-propyl-4-chloro-6-(1-oxo-isoindolin-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 7.5% of theory,
Melting point: 209-210°C
$C_{32}H_{26}ClN_3O_3$ (536.04)
Mass spectrum: m/e = 535/537
R_f value: 0.25 (silica gel; methylene chloride/ethanol = 9:1)

Example 70

4'-[(2-n-Propyl-4-chloro-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.butyl 4'-[(2-n-propyl-4-chloro-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 52.7% of theory,
Melting point: 292-295°C
$C_{32}H_{27}CN_4O_2$ (535.06)
R_f value: 0.30 (silica gel; methylene chloride/ethanol = 19:1)

Calculated:	C 71.90	H 5.08	N 10.45	Cl 6.63
Found:	71.29	5.21	10.40	6.76

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Example 71

4'-[(2-n-Propyl-4-chloro-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl hydrochloride

---

Prepared analogously to Example 10 from 4'-[(2-n-propyl-4-chloro-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 54.8% of theory,
Melting point: sintering from 204°C
$C_{32}H_{27}ClN_8$ x HCl (595.55)
R_f value: 0.20 (silica gel; petroleum ether/ethyl acetate = 1:1 and 1% glacial acetic acid)

Calculated:	C 62.55	H 4.71	N 18.85	Cl 11.85
Found:	62.34	4.97	18.84	11.57

Example 72

4'-[(2-n-Propyl-4-chloro-6-(1-oxo-isoindolin-2-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[(2-n-propyl-4-chloro-6-(1-oxo-isoindolin-2-yl)-benzimidazol-1-yl)-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 24.6% of theory,
Melting point: 246-248°C
$C_{32}H_{26}ClN_7O$ (560.08)
R_f value: 0.15 (silica gel; methylene chloride/ethanol = 9:1)

Calculated:	C 69.00	H 4.67	N 17.55	Cl 6.40
Found:	68.26	4.75	17.73	6.97

The following compound is obtained analogously to Example 72:

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4'-[(2-n-propyl-4-methyl-6-(4-methyl-imidazol-2-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

Example 73

4'-[(2-n-Propyl-4-chloro-6-(cyclohexylaminocarbonyl-amino)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

---

Prepared analogously to Example 1 from tert.butyl 4'-[(2-n-propyl-4-chloro-6-(cyclohexylaminocarbonylamino)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 75% of theory,
Melting point: 222-224°C
$C_{31}H_{33}ClN_4O_3$ (545.09)
R_f value: 0.15 (silica gel; methylene chloride/ethanol = 19:1)

Calculated:	C 68.50	H 6.10	N 10.30	Cl 6.48
Found:	68.89	5.98	10.02	7.04

Example 74

4'-[(2-n-Propyl-4-methyl-6-amidino-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid hydrate

---

a) Methyl 4'-[(2-n-propyl-4-methyl-6-amidino-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylate

2.1 g (5 mMol) of methyl 4'-[(2-n-propyl-4-methyl-6-cyano-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylate are dissolved in 250 ml of methanol at ambient temperature with stirring. Hydrogen chloride is introduced at 10-20°C for 3 hours whilst cooling with ice. The mixture is then stirred for a further 3 hours at ambient temperature. The solvent is distilled off in vacuo, the residue is twice mixed with ether and concentrated by evaporation. The iminoether formed is

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taken up in 250 ml of methanol and mixed with 10.0 g of ammonium carbonate. The reaction mixture is stirred for 12 hours at ambient temperature. After the solvent has been removed in vacuo the residue is purified over a silica gel column (particle size 0.063-0.032 mm), using as eluant mixtures of methylene chloride and methanol of increasing polarity (9:1 and 8:2). The uniform fractions are evaporated down in vacuo.
Yield: 1.5 g (58% of theory)
R_f value: 0.15 (silica gel; eluant: methylene chloride/methanol = 9:1)

b) 4'-[(2-n-Propyl-4-methyl-6-amidino-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

0.51 g (1.0 mMol) of methyl 4'-[(2-n-propyl-4-methyl-6-amidino-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylate are dissolved in 6 ml of tetrahydrofuran, 2.8 ml of 1.4 M aqueous lithium hydroxide solution and 3 ml of water are added and the mixture is stirred for 2 days at ambient temperature. Then a solution of 300 mg of ammonium chloride in 4 ml of water is added. The mixture is stirred for 5 minutes, the precipitate formed is suction filtered, washed with acetone and dried over potassium hydroxide.
Yield: 0.25 g (59% of theory),
Melting point: 270-271°C (decomp.)
$C_{26}H_{26}N_4O_2 \times H_2O$ (426.53)
Calculated: C 70.25 H 6.35 N 12.60
Found: 70.04 6.23 12.50
R_f value: 0.55 (silica gel; eluant: methylene chloride/methanol/ammonia = 2:1:0.25)

The following compound is obtained analogously to Example 74:

4'-[(2-n-propyl-4-methyl-6-(3-methyl-imidazol-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

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Example 75

4'-[(2-n-Propyl-4-methyl-6-(1-methyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

---

a) 3-Methyl-4-butyrylamino-5-nitro-acetophenone
32.6 g (148 mmol) of 3-methyl-4-butyrylamino-acetophenone are added in batches at -15°C to 300 ml of fuming nitric acid with stirring, and stirred for a further 30 minutes at -15°C. The reaction mixture is then poured onto 3 litres of ice, with stirring, the crude product precipitated is suction filtered, washed with 400 ml of water, dried and purified by recrystallisation from ethanol/diethylether (1:1).
Yield: 23.8 g (61.0% of theory),
R_f value: 0.32 (silica gel; methylene chloride),
R_f value: 0.48 (silica gel; methylene chloride/methanol = 50:1).

b) 3-Methyl-4-butyrylamino-5-nitro-ω-bromoacetophenone
A solution of 16.0 g (200 mmol) of bromine in 140 ml of dioxane is added dropwise to a solution of 23.8 g (90 mmol) of 3-methyl-4-butyrylamino-5-nitro-acetophenone in 900 ml of dichloromethane at ambient temperature, with stirring, so slowly that total decolorisation of the reaction mixture occurs constantly. The mixture is then stirred for a further two hours, then the reaction mixture is evaporated to dryness in vacuo, the residue obtained is triturated with about 20 ml of dichloromethane/diethylether (1:1), suction filtered and then dried. 23g (74% of theory) of 3-methyl-4-butyrylamino-5-nitro-ω-bromoacetophenone are thus obtained, still containing about 10% starting material. The product is further reacted without any more purification.
R_f value: 0.69 (silica gel; methylene chloride/methanol = 50:1)

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R_f value: 0.84 (silica gel; methylene chloride/methanol = 9:1).

c) 2-Butyrylamino-3-nitro-5-(imidazo-4-yl)-toluene

A solution of 6.8 g (20 mmol) of 3-methyl-4-butyrylamino-5-nitro-ω-bromoacetophenone in 20 ml of formamide is heated to 140°C for two hours. The cooled solution is then poured into about 50 ml of 1N ammonia and stirred for about 15 minutes. The crude product precipitated is suction filtered, washed with about 50 ml of water and dried. In this way, 4.4 g (75% of theory) of the product are obtained, which is further reacted without any more purification.

R_f value: 0.29 (silica gel; methylene chloride/methanol = 9:1)

d) 2-Butyrylamino-3-nitro-5-(1-methyl-imidazol-4-yl)-toluene

1.3 g (9.5 mmol) of methyliodide are added dropwise at ambient temperature to a solution of 2.5 g (8.7 mmol) of 2-butyrylamino-3-nitro-5-(imidazol-4-yl)-toluene and 5.2 g (30 mmol) of potassium carbonate dihydrate in 30 ml of dimethylsulfoxide and the mixture is then stirred for two hours. The reaction mixture is then stirred into about 150 ml of water and extracted four times with 25 ml of ethylacetate. The organic extracts are washed with about 30 ml of water, dried and evaporated down. The crude product thus obtained is purified by column chromatography (300 g of silica gel, eluant: methylene chloride/methanol = 30:1).

Yield: 640 mg (24% of theory),

R_f value: 0.54 (silica gel; methylene chloride/methanol = 9:1)

e) 2-Butyrylamino-3-amino-5-(1-methyl-imidazol-4-yl)-toluene

640 mg (2.1 mmol) of 2-butyrylamino-3-nitro-5-(1-methyl-imidazol-4-yl)-toluene are hydrogenated in 30 ml of

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methanol after the addition of about 200 mg of palladium/charcoal (20%) at ambient temperature under a hydrogen pressure of 5 bar. After all the hydrogen has been absorbed the catalyst is removed by filtering and the filtrate is evaporated down. The crude product obtained is further reacted without any more purification.
Yield: 600 mg (100% of theory),
R_f value: 0.23 (silica gel; methylene chloride/methanol = 9:1)

f) 2-n-Propyl-4-methyl-6-(1-methyl-imidazol-4-yl)-benzimidazole
600 mg (2.1 mmol) of 2-butyrylamino-3-amino-5-(1-methyl-imidazol-4-yl)-toluene are refluxed for one hour in 10 ml of glacial acetic acid. Then the mixture is evaporated to dryness in vacuo, the residue is mixed with about 15 ml of water, made alkaline with ammonia and extracted four times with about 10 ml of ethylacetate. The organic extracts are washed with about 15 ml of water, dried and finally evaporated down. The crude product thus obtained is further reacted without any more purification.
Yield: 420 mg (79% of theory),
R_f value: 0.37 (silica gel; methylene chloride/methanol = 9:1)

g) Tert.butyl-4'-[(2-n-propyl-4-methyl-6-(1-methyl-imidazol-4-yl)-benzimidazol-1-yl)methyl]-biphenyl-2-carboxylate
280 mg (0.8 mmol) of tert.butyl-4'-bromomethyl-biphenyl-2-carboxylate are added to a solution of 200 mg (0.79 mmol) of 2-n-propyl-4-methyl-6-(1-methyl-imidazol-4-yl)-benzimidazole and 90 mg (0.8 mmol) of potassium tert.butoxide in 5 ml of dimethylsulfoxide and the mixture is stirred for 90 minutes at ambient temperature, then stirred into about 40 ml of water, extracted four times with about 10 ml of ethylacetate,

then the organic extracts are washed with 10 ml of water, dried and evaporated to dryness. The crude product thus obtained is purified by column chromatography (100 g silica gel, eluant: dichloromethane/methanol = 30:1).
Yield: 230 mg (56% of theory),
R_f value: 0.61 (silica gel; methylene chloride/methanol = 9:1)

h) 4'-[2-n-Propyl-4-methyl-6-(1-methyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid
A solution of 230 mg (0.44 mmol) of tert.butyl-4'-[(2-n-propyl-4-methyl-6-(1-methyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylate and 2 ml of trifluoroacetic acid in 10 ml of dichloromethane was stirred overnight at ambient temperature and then evaporated to dryness. The residue was dissolved in about 5 ml of dilute sodium hydroxide solution, the solution was neutralised with acetic acid, the precipitate was suction filtered, washed with water and dried.
Yield: 120 mg (59% of theory);
Melting point: 293-295°C
R_f value: 0.39 (silica gel; methylene chloride/methanol = 9:1)

The following compounds are obtained analogously to Example 75:

4'-[(2-n-propyl-4-methyl-6-(1-ethyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

4'-[(2-n-propyl-4-methyl-6-(1-n-hexyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

4'-[(2-n-propyl-4-methyl-6-(1-benzyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

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4'-[(2-n-propyl-4-methyl-6-(1-isopropyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

4'-[(2-n-propyl-4-methyl-6-(1-cyclohexyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

Example 76

4'-[(2-n-Propyl-4-methyl-6-(1-methyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

---

Prepared analogously to Example 10 from 4'-[(2-n-propyl-4-methyl-6-(1-methyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 24% of theory
M.p.: 255-257°C
R_f value: 0.24 (silica gel; methylene chloride/methanol = 9:1)
$C_{29}H_{28}N_8 \times H_2O$ (506.62)

Calculated:	C 68.75	H 5.97	N 22.12
Found:	68.90	5.97	22.03

The following compounds are obtained analogously to Example 76:

4'-[(2-n-propyl-4-methyl-6-(1-ethyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

4'-[(2-n-propyl-4-methyl-6-(1-n-hexyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

4'-[(2-n-propyl-4-methyl-6-(1-benzyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

4'-[(2-n-propyl-4-methyl-6-(1-isopropyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

This Sheet Has Been Replaced

4'-[(2-n-propyl-4-methyl-6-(1-cyclohexyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

Example 77

4'-[2-Ethyl-4-methyl-6-(5,6,7,8-tetrahydro-imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

Prepared analogously to Example 10 from 4'-[(2-ethyl-4-methyl-6-(5,6,7,8-tetrahydro-imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl)methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 21% of theory
M.p.: amorphous
R_f value: 0.27 (silica gel; methylene chloride/ethanol = 9:1)
$C_{31}H_{30}N_8$ (514.64)

Calculated:	C 72.35	H 5.88	N 21.78
Found:	72.01	5.82	22.44

Example 78

4'-[(2-n-Propyl-4-methyl-6-(8-methyl-imidazo-[1,2-a]-pyridin-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

Prepared analogously to Example 1 from tert.butyl 4'-[(2-n-propyl-4-methyl-6-(8-methyl-imidazo-[1,2-a]-pyridin-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 87% of theory
M.p.: 295-297°C
R_f value: 0.34 (silica gel; methylene chloride/ethanol = 9:1)
$C_{33}H_{30}N_4O_2 \times H_2O$ (532.65)

Calculated:	C 74.41	H 6.06	N 10.52

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Found: 74.81 6.05 10.43

Example 79

4'-[(2-n-Propyl-4-methyl-6-(2-pyridyl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

Prepared analogously to Example 10 from 4'-[(2-n-propyl-4-methyl-6-(2-pyridyl)-benzimidazol-1-yl)-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 56% of theory,
Melting point: from 136°C (decomp.)
$C_{30}H_{27}N_7 \times 0.5\ H_2O$ (494.60)
Calculated: C 72.85 H 5.71 N 19.83
Found: 72.45 6.01 19.83

Example 80

4'-[(2-n-Propyl-4-methyl-6-(8-methyl-imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

Prepared analogously to Example 10 from 4'-[(2-n-propyl-4-methyl-6-(8-methyl-imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl)-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.
Yield: 19% of theory
Melting point: amorphous
R_f value: 0.36 (silica gel; methylene chloride/ethanol = 9:1)
$C_{33}H_{30}N_8$ (538.61)
Mass spectrum: m/e = 538

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Example 81

4'-[(2-Ethyl-4-methyl-6-(5,6,7,8-tetrahydro-imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

Prepared analogously to Example 1 from tert.butyl 4'-[2-ethyl-4-methyl-6-(5,6,7,8-tetrahydro-imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 50% of theory
Melting point: >300°C
R_f value: 0.16 (silica gel; methylene chloride/ethanol = 9:1)

Example 82

4'-[(2-n-Propyl-4-methyl-6-(1-isopropyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

Prepared analogously to Example 1 from tert.butyl 4'-[(2-n-propyl-4-methyl-6-(1-isopropyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylate and trifluoroacetic acid in methylene chloride.
Yield: 84% of theory
M.p.: 285-286°C
R_f value: 0.55 (silica gel; methylene chloride/methanol = 9:1)

Example 83

4'-[(2-n-Propyl-4-methyl-6-(1-isopropyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

Prepared analogously to Example 10 from 4'-[(2-n-propyl-4-methyl-6-(1-isopropyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-2-cyano-biphenyl and sodium azide in

dimethylformamide.
Yield: 18% of theory
M.p.: amorphous
R_f value: 0.29 (silica gel; methylene chloride/methanol = 9:1)
$C_{31}H_{32}N_8$ (516.66)
Mass spectrum: m/e = 516

Example 84

4'-[(2-n-Propyl-4-methyl-6-(1-n-hexyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

Prepared analogously to Example 1 from tert.butyl 4'-[(2-n-propyl-4-methyl-6-(1-n-hexyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-biphenyl and trifluoroacetic acid in methylene chloride.

Example 85

4'-[(2-n-Propyl-4-methyl-6-(1-benzyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

Prepared analogously to Example 1 from tert.butyl 4'-[(2-n-propyl-4-methyl-6-(1-benzyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-biphenyl and trifluoroacetic acid in methylene chloride.

Example 86

4'-[(2-n-Propyl-4-methyl-6-(1-n-hexyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

Prepared analogously to Example 10 from 4'-[(2-n-propyl-4-methyl-6-(1-n-hexyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.

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Example 87

4'-[(2-n-Propyl-4-methyl-6-(1-benzyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl

Prepared analogously to Example 10 from 4'-[(2-n-propyl-4-methyl-6-(1-benzyl-imidazol-4-yl)-benzimidazol-1-yl)-methyl]-2-cyano-biphenyl and sodium azide in dimethylformamide.

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In the Examples of Pharmaceutical Formulations which follow, any suitable compound of formula I, particularly those compounds wherein R_4 represents a carboxy- or 1H-tetrazolyl group, may be used as the active substance:

Example 1

Ampoules containing 50 mg of active substance per 5 ml

Active substance	50 mg
KH_2PO_4	2 mg
$Na_2HPO_4 \times 2H_2O$	50 mg
NaCl	12 mg
Water for injections ad	5 ml

Preparation:

The buffer substances and isotonic substance are dissolved in some of the water. The active substance is added and, once it has been completely dissolved, water is added to make up the required volume.

Example II

Ampoules containing 100 mg of active substance per 5 ml

Active substance	100 mg
Methyl glucamine	35 mg
Glycofurol	1000 mg
Polyethyleneglycol-polypropylene-glycol block polymer	250 mg
Water for injections ad	5 ml

Preparation:

Methyl glucamine is dissolved in some of the water and

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the active substance is dissolved with stirring and heating. After the addition of solvents, water is added to make up the desired volume.

Example III

Tablets containing 50 mg of active substance

Active substance	50.0 mg
Calcium phosphate	70.0 mg
Lactose	40.0 mg
Corn starch	35.0 mg
Polyvinylpyrrolidone	3.5 mg
Magnesium stearate	1.5 mg
	200.0 mg

Preparation:

The active substance, $CaHPO_4$, lactose and corn starch are uniformly moistened with an aqueous PVP solution. The mass is passed through a 2 mm screen, dried at 50°C in a circulating air dryer and screened again.

After the lubricant has been added, the granules are compressed in a tablet making machine.

Example IV

Coated tablets containing 50 mg of active substance

Active substance	50.0 mg
Lysine	25.0 mg
Lactose	60.0 mg
Corn starch	34.0 g
Gelatin	10.0 mg
Magnesium stearate	1.0 mg
	180.0 mg

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Preparation:

The active substance is mixed with the excipients and moistened with an aqueous gelatin solution. After screening and drying the granules are mixed with magnesium stearate and compressed to form tablet cores.

The cores thus produced are covered with a coating by known methods. A colouring may be added to the coating suspension or solution.

Example V

Coated tablets containing 100 mg of active substance

Active substance	100.0 mg
Lysine	50.0 mg
Lactose	86.0 mg
Corn starch	50.0 mg
Polyvinylpyrrolidone	2.8 mg
Microcrystalline cellulose	60.0 mg
Magnesium stearate	1.2 mg
	350.0 mg

Preparation:

The active substance is mixed with the excipients and moistened with an aqueous PVP solution. The moist mass is passed through a 1.5 mm screen and dried at 45°C. After drying, it is screened again and the magnesium stearate is added. This mixture is compressed into cores.

The cores thus produced are covered with a coating by known methods. Colourings may be added to the coating suspension or solution.

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Example VI

Capsules containing 250 mg of active substance

Active substance	250.0 mg
Corn starch	68.5 mg
Magnesium stearate	1.5 mg
	320.0 mg

Preparation:

The active substance and corn starch are mixed together and moistened with water. The moist mass is screened and dried. The dry granules are screened and mixed with magnesium stearate. The final mixture is packed into size 1 hard gelatine capsules.

Example VII

Oral suspension containing 50 mg of active substance per 5 ml

Active substance	50.0 mg
Hydroxyethylcellulose	50.0 mg
Sorbic acid	5.0 mg
70% sorbitol	600.0 mg
Glycerol	200.0 mg
Flavouring	15.0 mg
Water ad	5.0 ml

Preparation:

Distilled water is heated to 70°C. Hydroxyethyl-cellulose is dissolved therein with stirring. With the addition of sorbitol solution and glycerol the mixture is cooled to ambient temperature. At ambient

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temperature, sorbic acid, flavouring and active substance are added. The suspension is evacuated with stirring to remove any air. One dose of 50 mg is contained in 5.0 ml.

Example VIII

Suppositories containing 100 mg of active substance

Active substance	100.0 mg
Solid fat	1600.0 mg
	1700.0 mg

Preparation:

The hard fat is melted. At 40°C the ground active substance is homogeneously dispersed in the melt. It is cooled to 38°C and poured into slightly chilled suppository moulds.

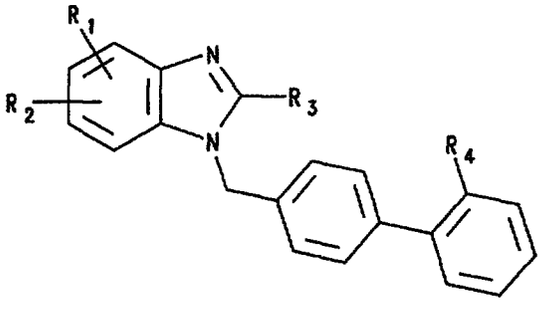
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Patent Claims

1. Benzimidazoles of general formula



(I)

wherein

R_1 in the 4-position represents a fluorine, chlorine or bromine atom, a C_{1-4}-alkyl, a cycloalkyl, fluoromethyl, difluoromethyl or trifluoromethyl group and

R_2 represents a C_{3-5}-alkoxy group substituted in the 3-, 4- or 5-position by an imidazolyl group, or R_2 may represent a C_{2-5}-alkoxy group substituted in the 2-, 3-, 4- or 5-position by a benzimidazolyl or tetrahydrobenzimidazolyl group, or, if R_4 represents a 1H-tetrazolyl group, R_2 may also represent a 2-(imidazol-1-yl)-ethoxy group,

a C_{1-4}-alkylsulphonyloxy group, a benzenesulphonyloxy or phenylalkanesulphonyloxy group,

an acylamino group optionally substituted at the nitrogen atom by a C_{1-6}-alkyl group or by a phenyl, cycloalkyl, phenylalkyl, cycloalkylalkyl, bicyclohexyl or biphenyl group, in which the acyl group is a C_{1-7}-alkanoyl group, a C_{2-4}(alkoxycarbonyl) group, a C_{1-6}-alkylsulphonyl group, a benzoyl, benzenesulphonyl, phenylalkanesulphonyl, naphthalenesulphonyl, cycloalkylcarbonyl, phenylalkanoyl or cycloalkylalkanoyl

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group, in which the above-mentioned phenyl nuclei may each be mono- or disubstituted by a fluorine, chlorine or bromine atom or by a methyl or methoxy group and the substituents may be identical or different,

a phthalimino, homophthalimino, 2-carboxyphenylcarbonyl-amino or 2-carboxyphenylmethylamino group, in which a carbonyl group in a phthalimino group may be replaced by a methylene, alkyl-methylene or dialkyl-methylene group, and a methylene group in a homophthalimino group may be substituted by one or two alkyl groups, and additionally the above-mentioned phenyl nuclei may be mono- or disubstituted by alkyl or alkoxy groups, whilst the substituents may be identical or different, and at the same time may be totally or partially hydrogenated,

a 5-, 6- or 7-membered alkyleneimino or alkenyleneimino group optionally substituted by one or two alkyl groups or by a tetramethylene or pentamethylene group, in which a methylene group may be replaced by a carbonyl or sulphonyl group,

a bicycloalkane-2,3-dicarboxylic acid imino or bicycloalkene-2,3-dicarboxylic acid imino group, wherein the bicycloalkane and bicycloalkene moieties may each contain 9 or 10 carbon atoms, may be substituted by 1, 2 or 3 methyl groups and may have an endomethylene group replaced by an oxygen atom,

an amidino group optionally substituted by one or two C_{1-6} alkyl groups,

a glutaric acid imino group wherein the n-propylene group may be perfluorinated, or may be substituted by one or two alkyl groups or by a tetramethylene or pentamethylene group,

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a maleic acid imido group optionally mono- or di-substituted by an alkyl or phenyl group, whilst the substituents may be identical or different,

a 5-membered heteroaromatic ring bound via a carbon atom or via an imino group and containing an imino group, an oxygen or sulphur atom, or an imino group and an oxygen, sulphur or nitrogen atom, or R_2 may represent a 6-membered heteroaromatic ring bound via a carbon atom and containing 1 or 2 nitrogen atoms, whilst the abovementioned heteroaromatic rings may be substituted in the carbon structure by a C_{1-6} alkyl or by a phenylalkyl group, and an n-propylene or n-butylene group may be linked to the 6-membered heteroaromatic rings via two adjacent carbon atoms or a 1,3-butadienyl group may be linked both to the 5-membered and to the 6-membered heteroaromatic rings via two adjacent carbon atoms or an n-butylene or 1,3-butadienyl group is linked thereto via an imino group and an adjacent carbon atom and, in an anellated pyridine ring thus formed, a methine group may be replaced by a nitrogen atom and a vinylene group in the 3-, 4-position relative to the nitrogen atom of the pyridine ring formed may be replaced by a sulphur atom or in an anellated phenyl ring thus formed, one or two methine groups may be replaced by N-atoms, whilst additionally the above-mentioned fused aromatic or heteroaromatic rings may be monosubstituted in the carbon structure by a fluorine, chlorine or bromine atom or by an alkyl, alkoxy, hydroxy, phenyl, nitro, amino, alkylamino, dialkylamino, alkanoylamino, cyano, carboxy, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, fluoromethyl, difluoromethyl, trifluoromethyl, alkanoyl, aminosulphonyl, alkylaminosulphonyl or dialkylaminosulphonyl group or may be disubstituted by fluorine or chlorine atoms or by methyl, methoxy or hydroxy groups, and two methyl substituents in the 1,2-

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position relative to each other may be linked by a methylene or ethylene bridge and an -NH- group optionally present in an imidazole ring may be substituted by a C_{1-6}-alkyl group, by a phenylalkyl group or by a cycloalkyl group, or

a pyrrolidine, piperidine or pyridine ring bound via a carbon atom, in which a phenyl group may be condensed onto the pyridine ring via two adjacent carbon atoms and a methylene group adjacent to the N-atom in a pyrrolidine or piperidine ring may be replaced by a carbonyl group,

an imidazolidinedione group optionally substituted by an alkyl, phenylalkyl, tetramethylene, pentamethylene or hexamethylene group,

a pyridazin-3-one or dihydro-pyridazin-3-one group which may be substituted in the 2-position by an optionally phenyl substituted alkyl group and additionally, in the carbon skeleton, by 1 or 2 alkyl groups,

an R_7-NR_6-CO-NR_5- group wherein

R_5 represents a hydrogen atom, a C_{1-8}-alkyl group, a C_{5-7} cycloalkyl group or a phenylalkyl group,

R_6 represents a hydrogen atom, a C_{1-8}-alkyl group, a C_{3-5}-alkenyl group, a phenyl group, a phenylalkyl group or a C_{5-7}-cycloalkyl group,

R_7 represents a hydrogen atom or a C_{1-6}-alkyl group or

one of the groups R_5, R_6 or R_7 may also represent a bicyclohexyl or biphenylyl group or

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R_6 and R_7 together with the nitrogen atom between them represent an unbranched C_{4-6}-alkyleneimino group or a morpholino group or

R_5 and R_6 together represent a C_{2-4}-alkylene group,

or, R_2 may represent a 1H,3H-quinazolin-2,4-dion-3-yl or pentamethylene-oxazolin-2-yl group or

R_1 represents a hydrogen atom or in the 5-, 6- or 7-position R_1 may represent a fluorine, chlorine or bromine atom, a C_{1-4}-alkyl group, a fluoromethyl, difluoromethyl or trifluoromethyl group and

R_2 represents a 5-membered heteroaromatic ring bound via a carbon atom or via an imino group and containing an imino group, an oxygen or sulphur atom or, an imino group and an oxygen, sulphur or nitrogen atom, or R_2 represents a 6-membered heteroaromatic ring bound via a carbon atom and containing 1 or 2 nitrogen atoms, whilst the abovementioned heteroaromatic rings may be substituted in the carbon skeleton by a C_{1-6} alkyl or by a phenylalkyl group and an n-propylene or n-butylene group may be linked via two adjacent carbon atoms to the 6-membered heteroaromatic rings or a 1,3-butadienyl group may be linked to both the 5-membered and 6-membered heteroaromatic rings via two adjacent carbon atoms or an n-butylene or 1,3-butadienyl group may be linked to said 5-membered and 6-membered heteroaromatic rings via an imino group and an adjacent carbon atom and, in an anellated pyridine ring thus formed, a methine group may be replaced by a nitrogen atom and a vinylene group in the 3-, 4-position relative to the nitrogen atom of the pyridine ring formed may be replaced by a sulphur atom or in an anellated phenyl ring thus formed, one or two methine groups may be replaced by N-atoms, whilst additionally the above-

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mentioned fused aromatic or heteroaromatic rings may be monosubstituted on the carbon skeleton by a fluorine, chlorine or bromine atom or by an alkyl, alkoxy, hydroxy, phenyl, nitro, amino, alkylamino, dialkylamino, alkanoylamino, cyano, carboxy, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, fluoromethyl, difluoromethyl, trifluoromethyl, alkanoyl, aminosulphonyl, alkylaminosulphonyl or dialkylamino-sulphonyl group or may be disubstituted by fluorine or chlorine atoms or by methyl, methoxy or hydroxy groups, and two methyl substituents in the 1,2-position relative to each other may be linked by a methylene or ethylene bridge and an -NH- group optionally present in an imidazole ring may be substituted by a C_{1-6}-alkyl group, by a phenylalkyl group or by a cycloalkyl group, whilst if

(i) R_1 represents a hydrogen atom, R_3 represents an n-propyl group and R_4 represents a carboxy group, R_2 cannot represent a 3-methyl-imidazo[4,5-b]pyridin-2-yl or 3-n-hexyl-imidazo[4,5-b]pyridin-2-yl group in the 6-position, or if

(ii) R_1 represents a hydrogen atom, R_3 represents an n-propyl or n-butyl group and R_4 represents a 1H-tetrazolyl group, R_2 cannot represent a benzoxazol-2-yl group in the 5- or 6-position, or if

(iii) R_1 represents a hydrogen atom, R_3 represents an n-propyl group and R_4 represents a carboxy group, R_2 cannot represent a 1-methylbenzimidazol-2-yl group in the 5- or 6-position and cannot represent a 1-n-butyl-benzimidazol-2-yl, 1,5-dimethylbenzimidazol-2-yl or 1-methyl-5-trifluoromethyl-benzimidazol-2-yl group in the 6-position, or if

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(iv) R_1 represents a hydrogen atom, R_3 represents an n-butyl group and R_4 represents a carboxy or 1H-tetrazolyl group, R_2 cannot represent a 1-methylbenzimidazol-2-yl group in the 6-position, or if

(v) R_1 represents a hydrogen atom, R_3 represents an n-butyl group and R_4 represents a carboxy group, R_2 cannot represent a benzimidazol-2-yl group in the 6-position,

or, R_2 may represent a pyrrolidine, piperidine or pyridine ring bound via a carbon atom, in which a phenyl group may be condensed onto the pyridine ring via 2 adjacent carbon atoms and a methylene group adjacent to the N-atom in a pyrrolidine or piperidine ring may be replaced by a carbonyl group,

R_3 represents a hydrogen atom or a C_{1-5}-alkyl group in which a methylene group may be replaced by a sulphur atom, or R_3 may represent a C_{3-5}cycloalkyl group, and

R_4 represents a carboxy, cyano, 1H-tetrazolyl or 1-triphenylmethyltetrazolyl group, a C_{2-5}(alkoxycarbonyl) group, an alkanesulphonylaminocarbonyl, arylsulphonylamino-carbonyl or trifluoromethanesulphonylaminocarbonyl group,.

the 1-, 3-isomer mixtures thereof and the addition salts thereof with inorganic or organic acids or bases,

whilst, unless otherwise specified, an alkanoyl, alkyl or alkoxy moiety mentioned hereinbefore may contain in each case 1 to 3 carbon atoms and a cycloalkyl moiety mentioned hereinbefore may contain 3 to 7 carbon atoms in each case.

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2. Benzimidazoles of general formula I according to claim 1, wherein

R_1 in the 4-position represents a fluorine, chlorine or bromine atom, a C_{1-3}-alkyl group, a cycloalkyl, fluoromethyl, difluoromethyl or trifluoromethyl group and

R_2 represents a C_{3-5}-alkoxy group substituted in the 3-, 4- or 5-position by an imidazolyl group, or R_2 may represent a C_{2-5}-alkoxy group substituted in the 2-, 3-, 4- or 5-position by a benzimidazolyl or tetrahydrobenzimidazolyl group,

an acylamino group optionally substituted at the nitrogen atom by a C_{1-5}-alkyl group, wherein the acyl group is a C_{2-7}-alkanoyl group, a C_{2-4}(alkoxycarbonyl) group, a C_{1-3}-alkylsulphonyl group or a benzenesulphonyl group,

a phthalimino or homophthalimino group, wherein a carbonyl group in a phthalimino group may be replaced by a methylene group and a methylene in a homophthalimino group may be substituted by one or two alkyl groups,

a 5-, 6- or 7-membered alkyleneimino or alkenyleneimino group, optionally substituted by one or two alkyl groups or by a tetramethylene or pentamethylene group, wherein a methylene group may be replaced by a carbonyl or sulphonyl group,

a glutaric acid imino group wherein the n-propylene group may be perfluorinated, or may be substituted by one or two alkyl groups or by a tetramethylene or pentamethylene group,

a maleic acid imido group optionally mono- or

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disubstituted by an alkyl or phenyl group, whilst the substituents may be identical or different,

an amidino group optionally substituted by one or two C_{1-4} alkyl groups,

a benzimidazol-2-yl group optionally substituted in the 1-position by C_{1-6}-alkyl or a cycloalkyl group, whilst the phenyl nucleus of an abovementioned benzimidazole group may additionally be substituted by a fluorine atom or by a methyl or trifluoromethyl group, R_2 may represent an imidazo[2,1-b]thiazol-6-yl, imidazo[1,2-a]pyridin-2-yl, 5,6,7,8-tetrahydro-imidazo[1,2-a]pyridin-2-yl, imidazo[1,2-a]pyrimidin-2-yl, imidazo[4,5-b]pyridin-2-yl, imidazo[4,5-c]pyridin-2-yl, imidazo[1,2-c]pyrimidin-2-yl, imidazo[1,2-a]pyrazin-2-yl, imidazo[1,2-b]-pyridazin-2-yl, imidazo[4,5-c]pyridin-2-yl, purin-8-yl, imidazo[4,5-b]pyrazin-2-yl, imidazo[4,5-c]pyridazin-2-yl or imidazo[4,5-d]pyridazin-2-yl group, or a carbon attached pyrrolidine, piperidine or pyridine ring in which a phenyl group may be condensed onto the pyridine ring via two adjacent carbon atoms and a methylene group adjacent to the N-atom in a pyrrolidine or piperidine ring may be replaced by a carbonyl group,

a carbon attached imidazolyl group optionally substituted in the 1-position by a C_{1-3}-alkyl group or by a benzyl group, and which may also be substituted in the carbon skeleton by a C_{1-3}-alkyl group,

an imidazolidindione group optionally substituted by an alkyl, phenylalkyl, tetramethylene, pentamethylene or hexamethylene group,

a pyridazin-3-one or dihydro-pyridazin-3-one group which may be substituted in the 2-position by a methyl or benzyl group,

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an R_7-NR_6-CO-NR_5- group wherein

R_5 represents a hydrogen atom, a C_{1-5}-alkyl group, a cyclohexyl or benzyl group,

R_6 represents a hydrogen atom, a C_{1-6}-alkyl group, an allyl, cyclohexyl, benzyl or phenyl group,

R_7 represents a hydrogen atom or a C_{1-3}-alkyl group or

R_6 and R_7 together with the nitrogen atom between them represent an unbranched C_{4-6}-alkyleneimino group or a morpholino group or

R_5 and R_6 together represent a C_{2-3}-alkylene group, or

R_1 represents a hydrogen atom or in the 5-, 6- or 7- R_1 may represent position a fluorine, chlorine or bromine atom, a C_{1-4}-alkyl or a trifluoromethyl group and

R_2 represents a benzimidazol-2-yl group optionally substituted in the 1-position by a C_{1-6}-alkyl group or by a cycloalkyl group, whilst the phenyl nucleus of an abovementioned benzimidazole group may additionally be substituted by a fluorine atom or by a methyl or trifluoromethyl group, or R_2 may represent an imidazo[2,1-b]thiazol-6-yl, imidazo[1,2-a]pyridin-2-yl, 5,6,7,8-tetrahydro-imidazo[1,2-a]pyridin-2-yl, imidazo[1,2-a]pyrimidin-2-yl, imidazo[4,5-b]pyridin-2-yl, imidazo[4,5-c]pyridin-2-yl, imidazo[1,2-c]pyrimidin-2-yl, imidazo[1,2-a]pyrazin-2-yl, imidazo[1,2-b]-pyridazin-2-yl, imidazo[4,5-c]-pyridin-2-yl, purin-8-yl, imidazo[4,5-b]pyrazin-2-yl, imidazo[4,5-c]pyridazin-2-yl or imidazo[4,5-d]-pyridazin-2-yl group, or a carbon attached pyrrolidine, piperidine or pyridine ring in

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which a phenyl group may be condensed onto the pyridine ring via 2 adjacent carbon atoms and a methylene group adjacent to the N-atom in a pyrrolidine or piperidine ring may be replaced by a carbonyl group, or a carbon attached imidazolyl group optionally substituted in the 1-position by a C_{1-3} alkyl group or by a benzyl group which may also be substituted in the carbon skeleton by a C_{1-3} alkyl group, whilst if

(v) R_1 represents a hydrogen atom, R_3 represents an n-butyl group and R_4 represents a carboxy group, R_2 cannot represent a benzimidazol-2-yl group in the 6-position,

R_3 represents a C_{1-5}-alkyl group or a C_{3-5}-cycloalkyl group and

R_4 represents a carboxy or 1H-tetrazolyl group,

the 1-, 3-isomer mixtures thereof and the addition salts thereof with inorganic or organic acids or bases,

whilst, unless otherwise specified, an alkanoyl, alkyl or alkoxy moiety as mentioned hereinbefore may in each case contain 1 to 3 carbon atoms and a cycloalkyl moiety mentioned above may contain from 3 to 7 carbon atoms.

3. Benzimidazoles of general formula I according to claim 1, wherein

R_1 in the 4-position represents a chlorine atom, or a C_{1-3}-alkyl or a trifluoromethyl group and

R_2 represents a C_{3-5}-alkoxy substituted in the 3-, 4- or 5-position by an imidazolyl group, or R_2 may represent a C_{2-5}-alkoxy group substituted in the 2-, 3-, 4- or 5-position by a benzimidazolyl or tetrahydrobenzimidazolyl

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group,

a C_{2-5}(alkanoyl)amino group or an N-benzenesulphonyl-methylamino group,

a phthalimino or homophthalimino group, wherein a carbonyl group in a phthalimino group may be replaced by a methylene group,

a 5-, 6- or 7-membered alkyleneimino group wherein a methylene group is replaced by a carbonyl or sulphonyl group,

a glutaric acid imino group wherein the n-propylene group may be substituted by one or two alkyl groups or by a tetramethylene or pentamethylene group,

a maleic acid imido group optionally mono- or disubstituted by an alkyl or phenyl group, whilst the substituents may be identical or different,

a benzimidazol-2-yl group optionally substituted in the 1-position by a C_{1-6}-alkyl or by a cycloalkyl group, whilst the phenyl nucleus of an abovementioned benzimidazole group may additionally be substituted by a fluorine atom or by a methyl or trifluoromethyl group, or R_2 may represent an imidazo[2,1-b]thiazol-6-yl, imidazo[1,2-a]pyridin-2-yl, 5,6,7,8-tetrahydro-imidazo[1,2-a]pyridin-2-yl, imidazo[1,2-a]pyrimidin-2-yl, imidazo[4,5-b]pyridin-2-yl, imidazo[4,5-c]pyridin-2-yl, imidazo[1,2-c]pyrimidin-2-yl, imidazo[1,2-a]pyrazin-2-yl, imidazo[1,2-b]-pyridazin-2-yl, imidazo[4,5-c]pyridin-2-yl, purin-8-yl, imidazo[4,5-b]pyrazin-2-yl, imidazo[4,5-c]pyridazin-2-yl or imidazo[4,5-d]pyridazin-2-yl group, or a carbon attached pyrrolidine, piperidine or pyridine ring in which a phenyl group may be condensed onto the pyridine

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ring via two adjacent carbon atoms and a methylene group adjacent to the N-atom in a pyrrolidine or piperidine ring may be replaced by a carbonyl group,

or an imidazol-4-yl group substituted in the 1-position by a C_{1-3} alkyl group or by a benzyl group which may also be substituted in the carbon skeleton by a C_{1-3} alkyl group,

a pyridazin-3-one or dihydro-pyridazin-3-one group which may be substituted in the 2-position by a methyl or benzyl group,

an R_7-NR_6-CO-NR_5- group wherein

R_5 represents a hydrogen atom, a C_{1-5}-alkyl group, a cyclohexyl or benzyl group,

R_6 represents a hydrogen atom, a C_{1-6}-alkyl group, an allyl, cyclohexyl, benzyl or phenyl group,

R_7 represents a hydrogen atom or a C_{1-3}-alkyl group or

R_6 and R_7 together with the nitrogen atom between them represent an unbranched C_{4-6}-alkyleneimino group or a morpholino group or

R_5 and R_6 together represent a C_{2-3}-alkylene group, or

R_1 represents a hydrogen atom or, in the 5-, 6- or 7-position R_1 represents a C_{1-4}-alkyl group or a trifluoromethyl group and

R_2 represents a benzimidazol-2-yl group optionally substituted in the 1-position by a C_{1-6}-alkyl group or by

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a cycloalkyl group, whilst the phenyl nucleus of an abovementioned benzimidazole group may additionally be substituted by a fluorine atom or by a methyl or trifluoromethyl group, or R_2 may represent an imidazo[2,1-b]thiazol-6-yl, imidazo[1,2-a]pyridin-2-yl, 5,6,7,8-tetrahydro-imidazo[1,2-a]pyridin-2-yl, imidazo[1,2-a]pyrimidin-2-yl, imidazo[4,5-b]pyridin-2-yl, imidazo[4,5-c]pyridin-2-yl, imidazo[1,2-c]pyrimidin-2-yl, imidazo[1,2-a]pyrazin-2-yl, imidazo[1,2-b]-pyridazin-2-yl, imidazo[4,5-c]-pyridin-2-yl, purin-8-yl, imidazo[4,5-b]pyrazin-2-yl, imidazo[4,5-c]pyridazin-2-yl or imidazo[4,5-d]pyridazin-2-yl group, or a carbon attached pyrrolidine, piperidine or pyridine ring in which a phenyl group may be condensed onto the pyridine ring via two adjacent carbon atoms and a methylene group adjacent to the N-atom in a pyrrolidine or piperidine ring may be replaced by a carbonyl group, or an imidazol-4-yl group substituted in the 1-position by a C_{1-3} alkyl group or by a benzyl group which may also be substituted in the carbon skeleton by a C_{1-3} alkyl group, whilst if

(v) R_1 represents a hydrogen atom, R_3 represents an n-butyl group and R_4 represents a carboxy group, R_2 cannot represent a benzimidazol-2-yl group in the 6-position,

R_3 represents a C_{1-5}-alkyl group or a C_{3-5}-cycloalkyl group and

R_4 represents a carboxy or 1H-tetrazolyl group,

the 1-, 3-isomer mixtures thereof and the addition salts thereof with inorganic or organic acids or bases.

4. Benzimidazoles of general formula I according to claim 1, wherein

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R_1 in the 4-position represents a methyl group or a chlorine atom and

R_2 represents a C_{3-5}-alkoxy group substituted in the 3-, 4- or 5-position by an imidazolyl group, or R_2 may represent a C_{2-5}-alkoxy group substituted in the 2-, 3-, 4- or 5-position by a benzimidazolyl or tetrahydrobenzimidazolyl group,

a C_{2-5}(alkanoyl)amino group or an N-benzenesulphonyl-methylamino group,

a phthalimino or homophthalimino group, wherein a carbonyl group in a phthalimino group may be replaced by a methylene group,

a 5-, 6- or 7-membered alkyleneimino group, wherein a methylene group is replaced by a carbonyl or sulphonyl group,

a maleic acid imido group optionally mono- or disubstituted by an alkyl or phenyl group, whilst the substituents may be identical or different,

a benzimidazol-2-yl group optionally substituted in the 1-position by a C_{1-3}-alkyl group, whilst the phenyl nucleus of an abovementioned benzimidazole group may additionally be substituted by a fluorine atom, or R_2 may represent an imidazo[1,2-a]-pyridin-2-yl group, 5,6,7,8-tetrahydro-imidazo[1,2-a]-pyridin-2-yl, imidazo[1,2-a]pyrimidin-2-yl or imidazo[2,1-b]thiazol-6-yl group,

an imidazol-4-yl group substituted in the 1-position by a C_{1-3} alkyl group,

a pyridazin-3-one or dihydro-pyridazin-3-one group which

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may be substituted in the 2-position by a methyl or benzyl group, or

R_1 represents a hydrogen atom or, in the 5-, 6- or 7-position R_1 may represent a methyl group and

R_2 represents a benzimidazol-2-yl group optionally substituted in the 1-position by a C_{1-3}-alkyl group, whilst the phenyl nucleus may additionally be substituted by a fluorine atom, or R_2 may represent an imidazo[1,2-a]pyridin-2-yl group, an imidazol-4-yl group substituted in the 1-position by a C_{1-3} alkyl group, whilst if

(v) R_1 represents a hydrogen atom, R_3 represents an n-butyl group and R_4 represents a carboxy group, R_2 cannot represent a benzimidazol-2-yl group in the 6-position,

R_3 represents a C_{1-5}-alkyl group or a C_{3-5}-cycloalkyl group and

R_4 represents a carboxy or 1H-tetrazolyl group,

the 1-, 3-isomer mixtures thereof and the salts thereof with inorganic or organic acids or bases.

5. The following benzimidazoles of general formula I according to claim 1:

(a) 4'-[[2-n-propyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid,

(b) 4'-[[2-n-propyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl,

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(c) 4'-[[2-n-propyl-4-methyl-6-(1-oxo-isoindolin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl,

(d) 4'-[[2-n-propyl-4-methyl-6-(butanesultam-1-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl,

(e) 4'-[[2-n-butyl-6-(2,3-dimethylmaleic acid imino)-4-methylbenzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid,

(f) 4'-[[2-n-butyl-6-(isopropylcarbonylamino)-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid,

(g) 4'-[[2-n-butyl-4-methyl-6-(morpholinocarbonylamino)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid,

(h) 4'-[[2-n-butyl-6-(cyclohexylaminocarbonylamino)-4-methyl-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid,

(i) 4'-[(2-cyclopropyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid,

(j) 4'-[(2-n-propyl-4-methyl-6-(1-methyl-5-fluoro-benzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid,

(k) 4'-[(2-n-propyl-4-methyl-6-(imidazo[1,2-a]pyrimidin-2-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl,

(l) 4'-[(2-n-propyl-4-methyl-6-(4,5,6,7-tetrahydro-imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid,

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(m) 4'-[(2-n-propyl-4-methyl-6-(4,5,6,7-tetrahydro-imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl,

(n) 4'-[(2-n-propyl-4-chloro-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-2-(1H-tetrazol-5-yl)-biphenyl,

(o) 4'-[[2-n-propyl-4-methyl-6-(imidazo[2,1-b]thiazol-6-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid,

(p) 4'-[[2-ethyl-4-methyl-6-(butanesultam-1-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl,

(q) 4'-[[2-n-butyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl,

(r) 4'-[[2-n-propyl-6-(imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl,

(s) 4'-[[2-n-propyl-4-methyl-6-(imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid,

(t) 4'-[[2-n-propyl-4-methyl-6-(imidazo[1,2-a]pyridin-2-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl,

(u) 4'-[[2-n-propyl-4-methyl-6-(imidazo[2,1-b]thiazol-6-yl)-benzimidazol-1-yl]-methyl]-2-(1H-tetrazol-5-yl)-biphenyl and

(v) 4'-[(2-n-propyl-4-methyl-6-(1-methyl-6-fluoro-

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benzimidazol-2-yl)-benzimidazol-1-yl)-methyl]-biphenyl-2-carboxylic acid

the 1-, 3-isomer mixtures thereof and the salts thereof with inorganic or organic acids or bases.

6. Physiologically acceptable addition salts of the compounds according to at least one of claims 1 to 5 with inorganic or organic acids or bases.

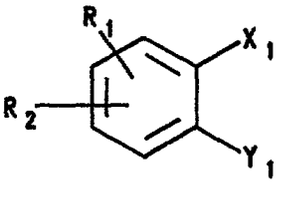
7. Pharmaceutical compositions containing a compound according to at least one of claims 1 to 5 or a physiologically acceptable addition salt according to claim 6 optionally together with one or more inert carriers and/or diluents.

8. Use of a compound according to at least one of claims 1 to 6 for preparing a pharmaceutical composition with an angiotensin-antagonist activity.

9. Process for preparing a pharmaceutical composition according to claim 8, characterised in that a compound according to at least one of claims 1 to 6 is incorporated in one or more inert carriers and/or diluents by a non-chemical method.

10. Process for preparing the benzimidazoles according to claims 1 to 6, characterised in that

a) a compound of general formula

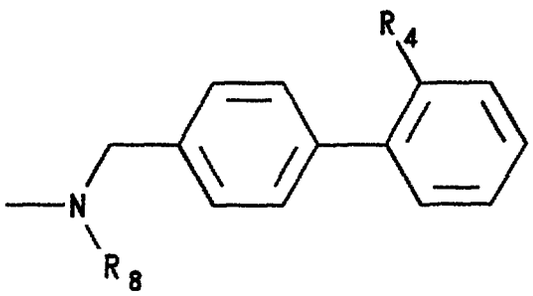


(II)

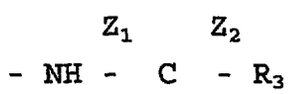
wherein
R_1 and R_2 are defined as in claims 1 to 5,

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one of the groups X_1 or Y_1 represents a group of general formula

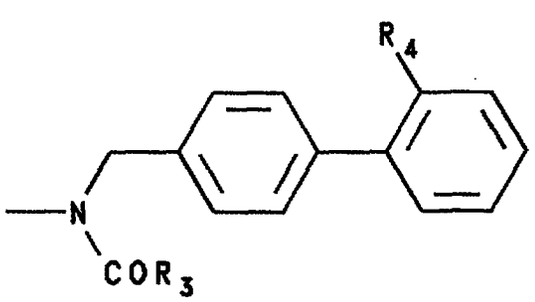


and the other group X_1 or Y_1 represents a group of the general formula



wherein

R_2 and R_4 are defined as in claims 1 to 5,
R_8 represents a hydrogen atom or an R_3CO- group, wherein R_3 is defined as hereinbefore,
Z_1 and Z_2, which may be identical or different, represent optionally substituted amino groups or hydroxy or mercapto groups optionally substituted by lower alkyl groups or
Z_1 and Z_2 together represent an oxygen or sulphur atom, an optionally C_{1-3}-alkyl substituted imino group, an alkylenedioxy or alkylenedithio group, each having 2 or 3 carbon atoms, but one of the groups X_1 or Y_1 must represent a group of general formula



or

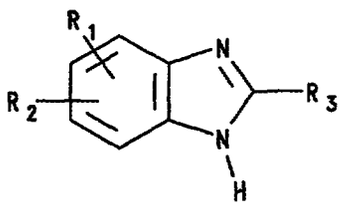
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$$-NH-\underset{Z_1}{\overset{Z_2}{C}}-R_3,$$

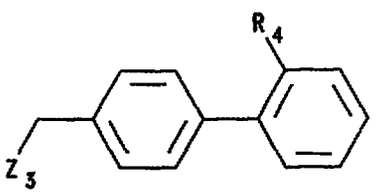
is cyclised and a corresponding N-oxide which might thus be obtained is reduced or

b) a benzimidazole of general formula



(III)

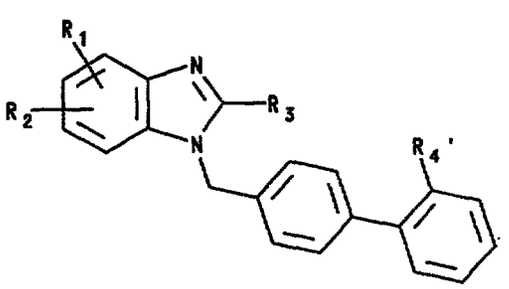
wherein
R_1 to R_3 are defined as in claims 1 to 5,
is reacted with a biphenyl compound of general formula



(IV)

wherein
R_4 is defined as in claims 1 to 5 and
Z_3 represents a nucleophilic leaving group, or

c) in order to prepare a compound of general formula I wherein R_4 represents a carboxy group, a compound of general formula



(V)

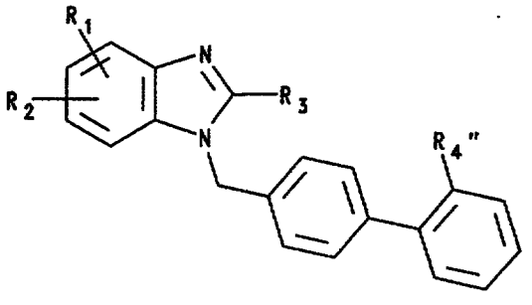
wherein

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R_1 to R_3 are defined as in claims 1 to 5 and
R_4' represents a group which may be converted into a carboxy group by hydrolysis, thermolysis or hydrogenolysis, is converted into a corresponding carboxy compound or

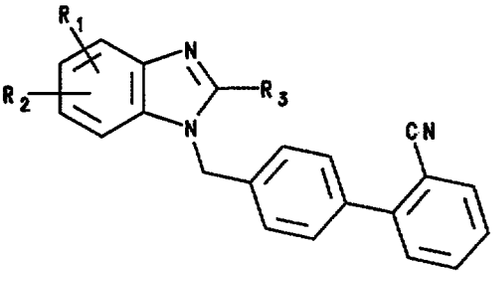
d) in order to prepare a compound of general formula I wherein R_4 represents a 1H-tetrazolyl group, a protecting group is split off from a compound of general formula



(VI)

wherein
R_1, R_2 and R_3 are defined as in claims 1 to 5 and
R_4'' represents a 1H-tetrazolyl group protected in the 1- or 3-position by a protecting group, or

e) in order to prepare a compound of general formula I wherein R_4 represents a 1H-tetrazolyl group, a compound of general formula



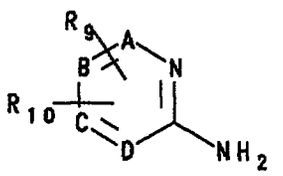
(VII)

wherein
R_1 to R_3 are defined as in claims 1 to 5, is reacted with hydrazoic acid or the salts thereof or

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f) in order to prepare compounds of general formula I wherein R_2 represents one of the imidazo[1,2-a]-pyridin-2-yl, imidazo[1,2-a]pyrimidin-2-yl, imidazo[1,2-c]-pyrimidin-2-yl, imidazo[1,2-a]pyrazin-2-yl, imidazo-[1,2-b]pyridazin-2-yl or imidazo[2,1-b]thiazol-6-yl groups mentioned in claims 1 to 5,

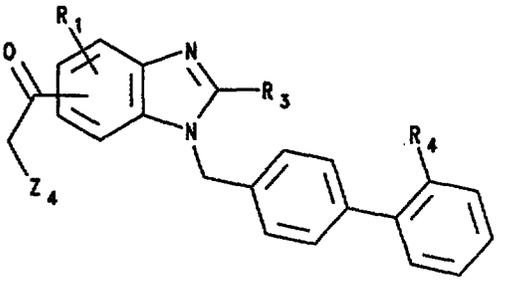
a compound of general formula



(VIII)

wherein
one of the groups A, B, C or D represents a methine group or a nitrogen atom and
the remaining groups A, B, C or D represent methine groups or
A and B each represent methine and the -C=D- group represents a sulphur atom,
R_9 represents a hydrogen, fluorine, chlorine or bromine atom or an alkyl, alkoxy, hydroxy, phenyl, nitro, amino, alkylamino, dialkylamino, alkanoylamino, cyano, carboxy, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, trifluoromethyl, alkanoyl, aminosulphonyl, alkylaminosulphonyl or dialkylamino-sulphonyl group and
R_{10} represents a hydrogen, fluorine or chlorine atom or a methyl, methoxy or hydroxy group, whilst if R_9 and R_{10} represent adjacent methyl groups, these may be linked together by a methylene or ethylene group,
is reacted with a compound of general formula

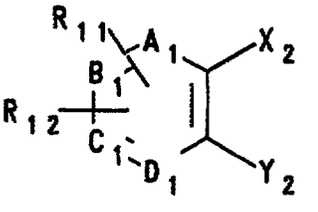
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(IX)

wherein
R_1, R_3 and R_4 are defined as in claims 1 to 5 and
Z_4 represents a nucleophilic leaving group such as a halogen atom,
e.g. a chlorine or bromine atom, or

g) in order to prepare compounds of general formula I wherein R_2 represents one of the benzimidazol-2-yl, imidazo[4,5-b]pyridin-2-yl, imidazo[4,5-c]pyridin-2-yl, imidazo[4,5-b]pyrazin-2-yl, imidazo[4,5-c]pyridazin-2-yl, imidazo[4,5-d]pyridazin-2-yl or purin-8-yl groups mentioned in claims 1 to 5,
a compound of general formula

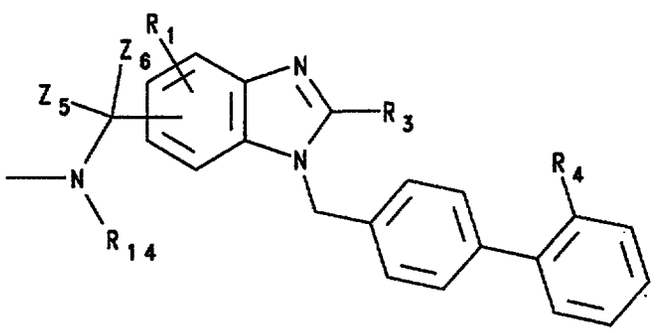


(X)

wherein
none, one or two of the groups A_1, B_1, C_1 or D_1 represents a nitrogen atom and
the remaining groups A_1, B_1, C_1 or D_1 represent methine groups,
R_{11} represents a hydrogen, fluorine, chlorine or bromine atom or an alkyl, alkoxy, hydroxy, phenyl, nitro, amino, alkylamino, dialkylamino, alkanoylamino, cyano, carboxy, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, trifluoromethyl, alkanoyl,

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aminosulphonyl, alkylaminosulphonyl or dialkylamino-sulphonyl group and
R_{12} represents a hydrogen, fluorine or chlorine atom or a methyl, methoxy or hydroxy group,
one of the groups X_2 or Y_2 represents an R_{13}-NH- group and
the other X_2 or Y_2 group represents a group of general formula

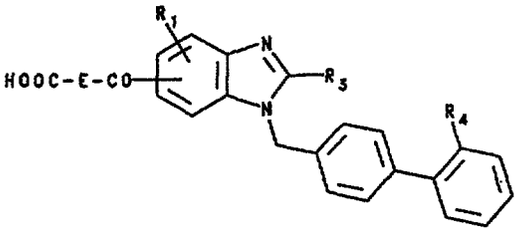


wherein
R_1, R_3 and R_4 are defined as in claims 1 to 5,
one of the groups R_{13} or R_{14} represents a hydrogen atom and the other R_{13} or R_{14} group represents a hydrogen atom, a C_{1-6}-alkyl group or a cycloalkyl group,
Z_5 and Z_6, which may be identical or different, represent optionally substituted amino groups or hydroxy or mercapto groups optionally substituted by lower alkyl groups or
Z_5 and Z_6 together represent an oxygen or sulphur atom, an optionally C_{1-3}-alkyl substituted imino group, an alkylenedioxy or alkylenedithio group each having 2 or 3 carbon atoms,
is cyclised and a corresponding N-oxide which might be obtained is reduced and a compound thus obtained is optionally subsequently hydrolysed, or

h) in order to prepare compounds of general formula I wherein R_2 represents a dihydro-pyridazin-3-one or pyridazin-3-one group which may be substituted in the 2-position by a C_{1-3}-alkyl group optionally substituted by

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a phenyl group, or in the carbon structure by one or two alkyl groups each having 1 to 3 carbon atoms,
a carboxylic acid of general formula



(XII)

wherein
R_1, R_3 and R_4 are defined as in claims 1 to 5 and
E represents an ethylene or ethenylene group optionally substituted by one or two C_{1-3}alkyl groups, or the reactive acid derivatives thereof such as the esters, amides or halides thereof,
is reacted with a hydrazine of general formula

$$H_2N - NHR_{15} \qquad (XIII)$$

wherein
R_{15} represents a hydrogen atom or a C_{1-3}-alkyl group optionally substituted by a phenyl group,

and if necessary a protecting group used during the reactions a) to h) in order to protect reactive groups is cleaved and/or

if desired a 1-, 3-isomer mixture of a compound of general formula I thus obtained is resolved by isomer separation into the 1- and 3-isomers or

a compound of general formula I thus obtained is converted into an addition salt thereof, more particularly for pharmaceutical use a physiologically acceptable salt thereof with an inorganic or organic acid or base.

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