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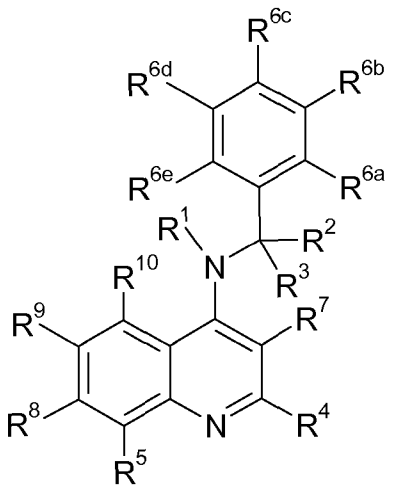
(54) Title: 4-BENZYLAMINOQUINOLINES, PHARMACEUTICAL COMPOSITIONS CONTAINING THEM, AND THEIR USE IN THERAPY



(I)

(57) Abstract: The present invention relates to 4-benzylamino-quinolines of the formula (I) or physiologically tolerated salts thereof. The invention relates to pharmaceutical compositions comprising such quinolines, and the use of such quinolines for therapeutic purposes. The quinolines are GIyTI inhibitors.

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4-Benzylaminoquinolines, pharmaceutical compositions containing them, and their use in therapy

Background Of The Invention

The present invention relates to 4-benzylaminoquinolines, pharmaceutical compositions comprising such quinolines, and the use of such quinolines for therapeutic purposes. The quinolines are GlyT1 inhibitors.

Dysfunction of glutamatergic pathways has been implicated in a number of disease states in the human central nervous system (CNS) including but not limited to schizophrenia, cognitive deficits, dementia, Parkinson disease, Alzheimer disease and bipolar disorder. A large number of studies in animal models lend support to the NMDA hypofunction hypothesis of schizophrenia.

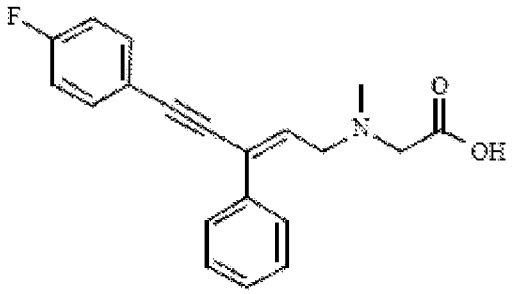
NMDA receptor function can be modulated by altering the availability of the co-agonist glycine. This approach has the critical advantage of maintaining activity-dependent activation of the NMDA receptor because an increase in the synaptic concentration of glycine will not produce an activation of NMDA receptors in the absence of glutamate. Since synaptic glutamate levels are tightly maintained by high affinity transport mechanisms, an increased activation of the glycine site will only enhance the NMDA component of activated synapses.

Two specific glycine transporters, GlyT1 and GlyT2 have been identified and shown to belong to the Na/Cl-dependent family of neurotransmitter transporters which includes taurine, gamma-aminobutyric acid (GABA), proline, monoamines and orphan transporters. GlyT1 and GlyT2 have been isolated from different species and shown to have only 50% identity at the amino acid level. They also have a different pattern of expression in mammalian central nervous system, with GlyT2 being expressed in spinal cord, brainstem and cerebellum and GlyT1 present in these regions as well as forebrain areas such as cortex, hippocampus, septum and thalamus. At the cellular level, GlyT2 has been reported to be expressed by glycinergic nerve endings in rat spinal cord whereas GlyT1 appears to be preferentially expressed by glial cells. These expression studies have led to the suggestion that GlyT2 is predominantly responsible for glycine uptake at glycinergic synapses whereas GlyT1 is involved in monitoring glycine concentration in the vicinity of NMDA receptor expressing synapses. Recent functional studies in rat have shown that blockade of GlyT1 with the potent inhibitor (N-[3-(4'-fluorophenyl)-3-(4'-phenylphenoxy)propyl])sarcosine (NFPS) potentiates NMDA receptor activity and NMDA receptor-dependent long-term potentiation in rat.

Molecular cloning has further revealed the existence of three variants of GlyT1, termed GlyT-1a, GlyT-1b and GlyT-1c, each of which displays a unique distribution in the brain and peripheral tissues. The variants arise by differential splicing and exon usage, and differ in their N-terminal regions.

The physiological effects of GlyT1 in forebrain regions together with clinical reports showing the beneficial effects of GlyT1 inhibitor sarcosine in improving symptoms in schizophrenia patients suggest that selective GlyT1 inhibitors represent a new class of antipsychotic drugs.

Glycine transporter inhibitors are already known in the art, for example:



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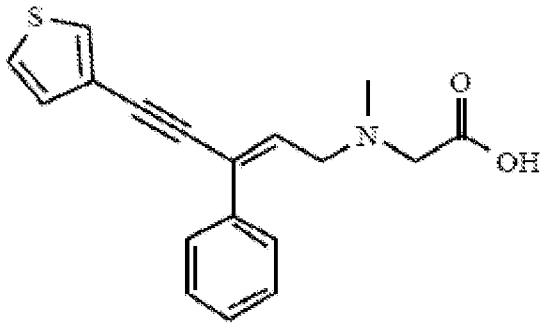

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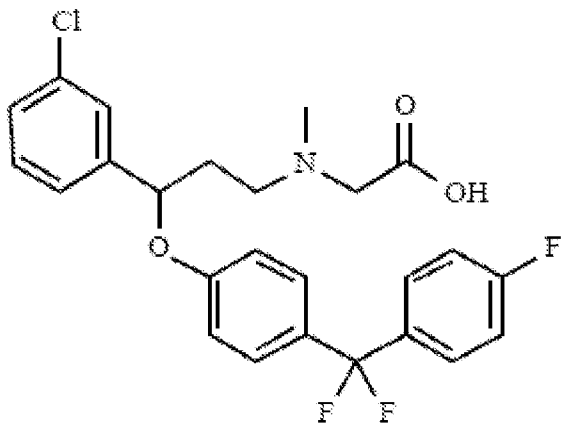

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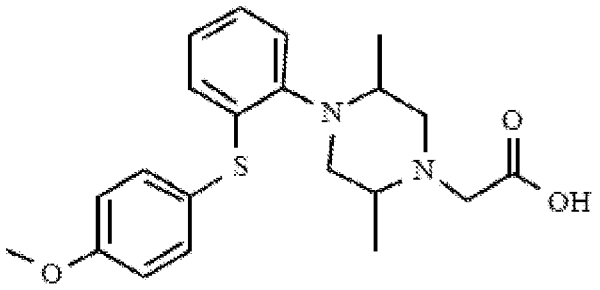

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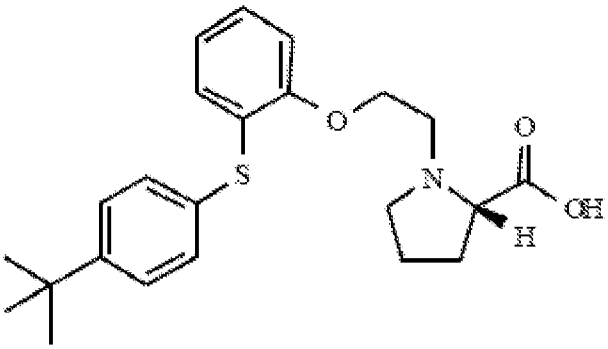

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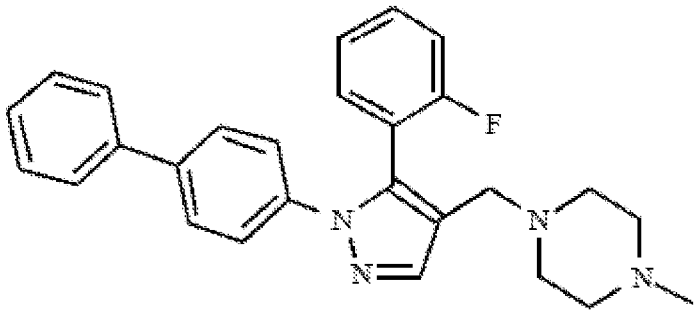

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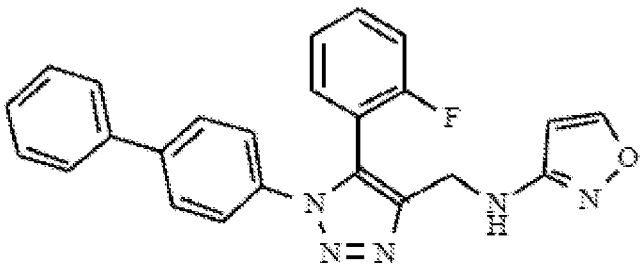

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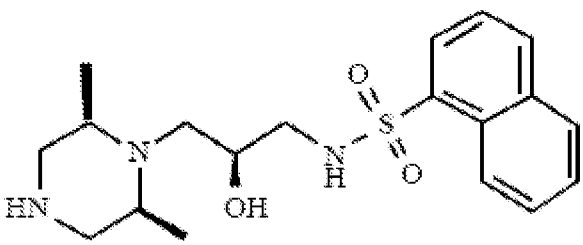

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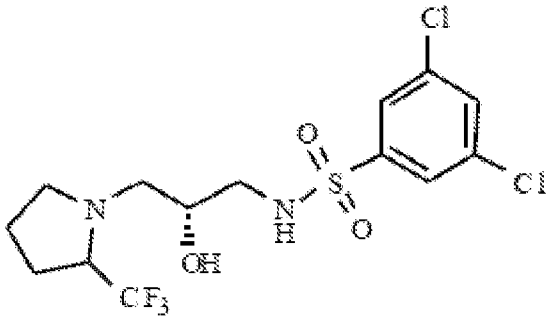

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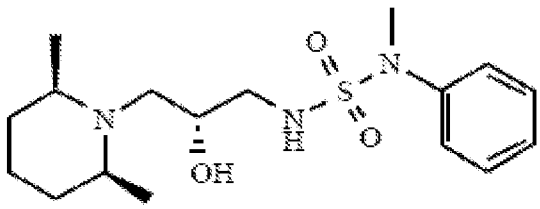

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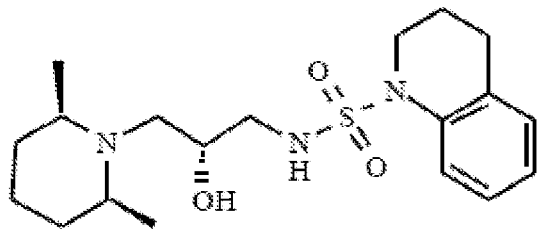

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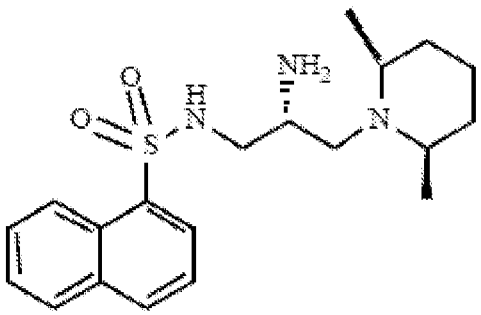

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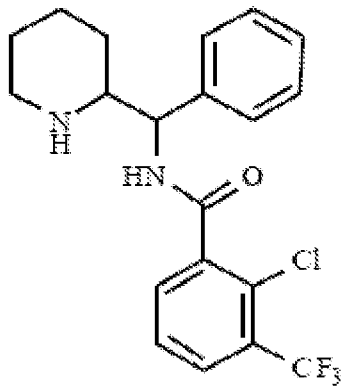

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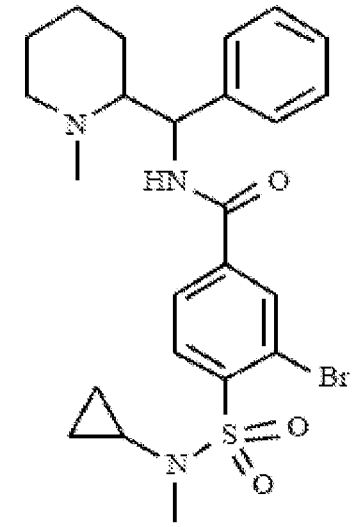

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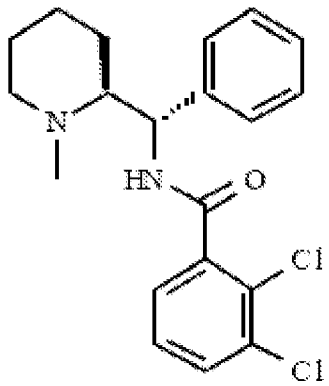

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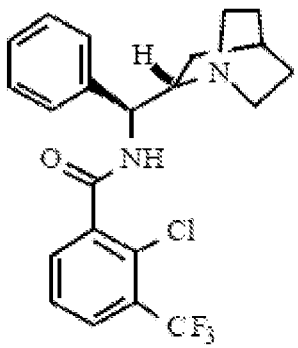

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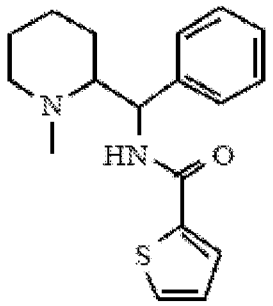

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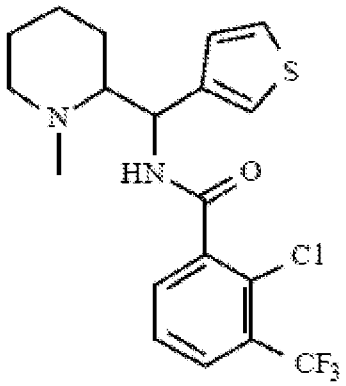

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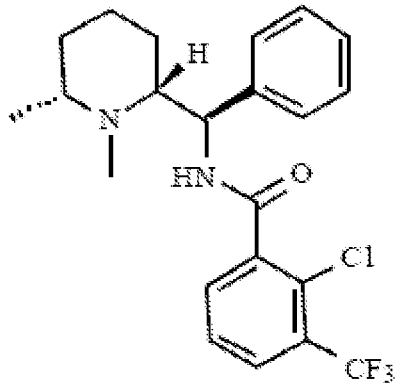

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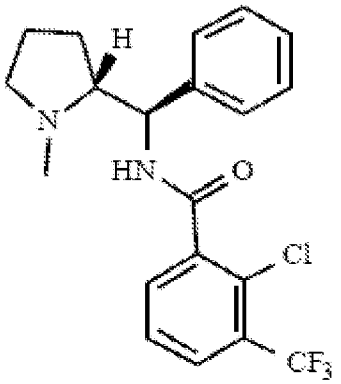

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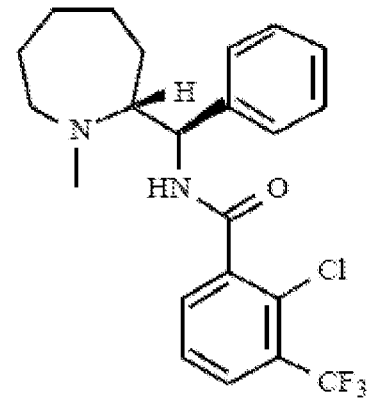

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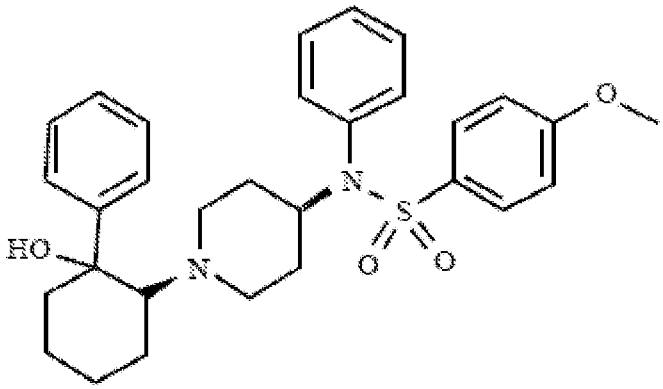

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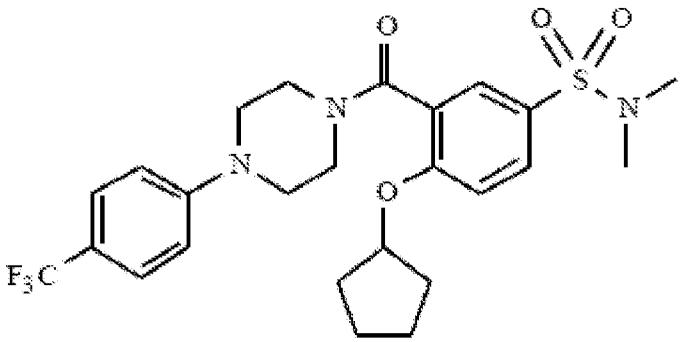

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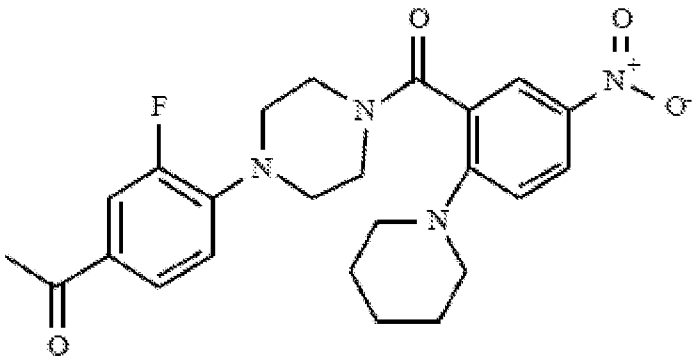

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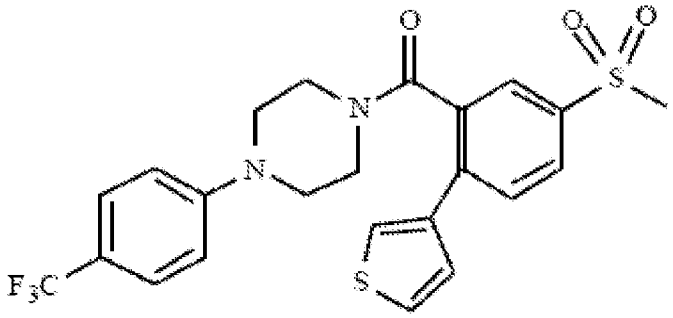

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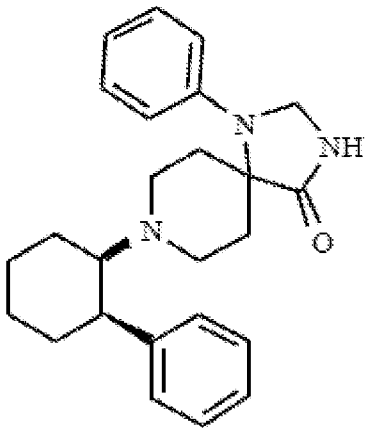

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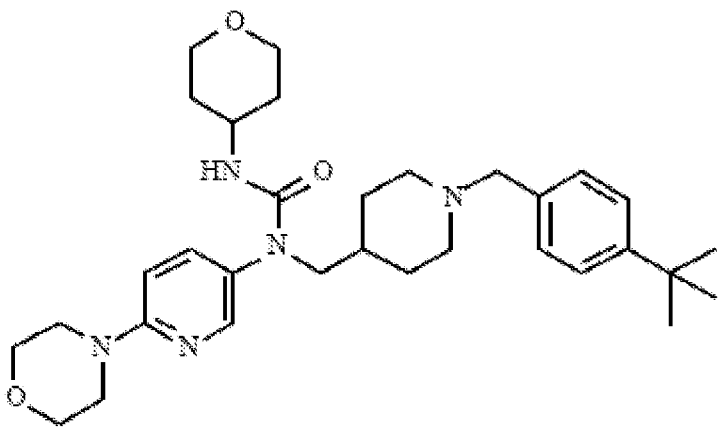

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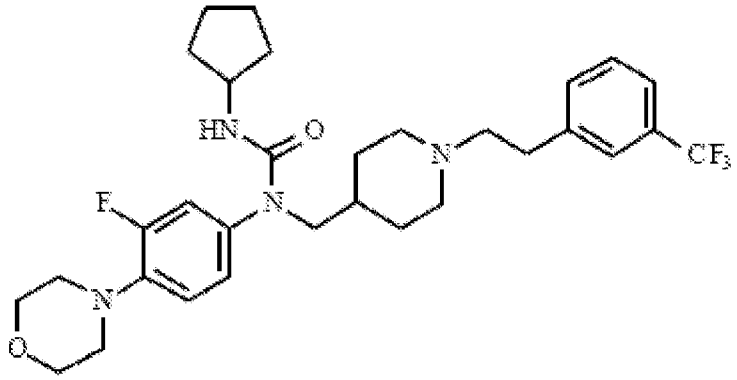

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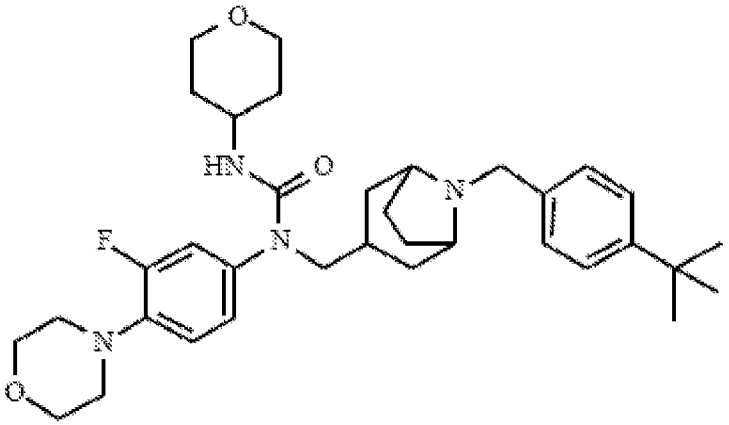

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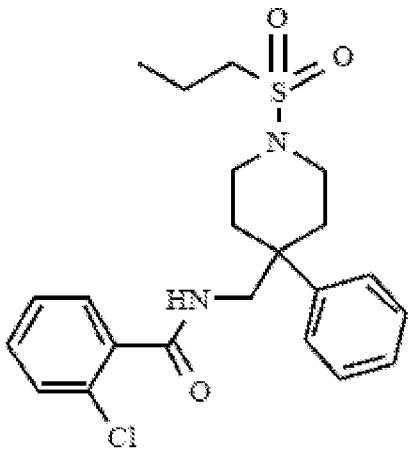

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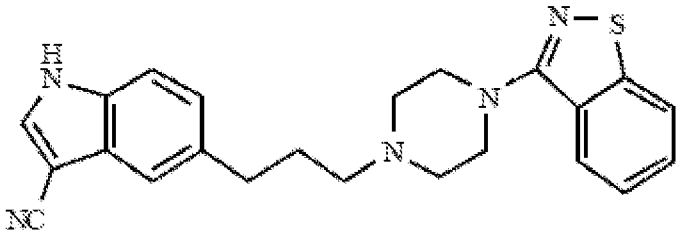

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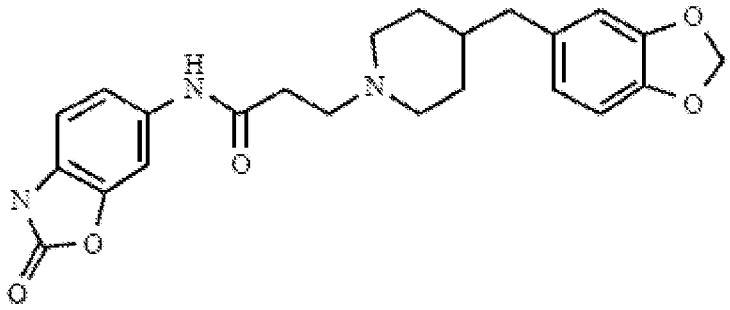

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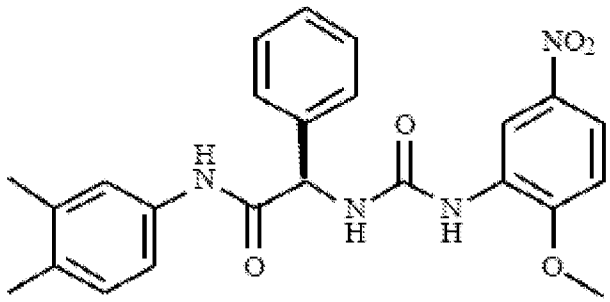


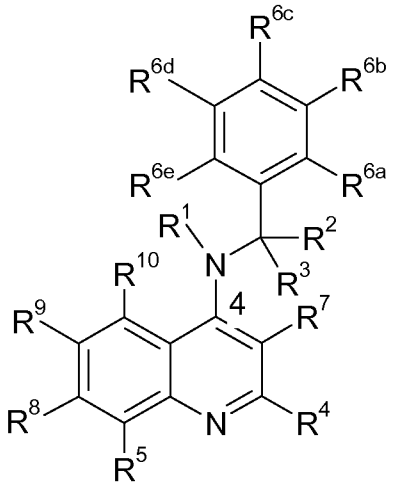
WO 2004022528

(see also Hashimoto K., Recent Patents on CNS Drug Discovery, 2006, 1, 43–53; Harsing L.G. et al., Current Medicinal Chemistry, 2006, 13, 1017–1044; Javitt D.C., Molecular Psychiatry (2004) 9, 984–997; Lindsley, C.W. et al., Current Topics in Medicinal Chemistry, 2006, 6, 771–785; Lindsley C.W. et al., Current Topics in Medicinal Chemistry, 2006, 6, 1883–1896).

It was one object of the present invention to provide further glycine transporter inhibitors.

Summary Of The Invention

The present invention relates to 4-benzylaminoquinolines of the formula (I)



(I)

wherein

R^1 is hydrogen, alkyl, aryl;

R^2, R^3
are independently hydrogen, alkyl, C_3-C_{12}-cycloalkyl, aryl, aminocarbonyl, amino or heterocyclyl;

R^4 is alkyl, halogenated alkyl, alkoxy, dialkylamino, arylamino or sulfonylamino;

R^5 is hydrogen, halogen, alkyl, hydroxy, alkoxy, substituted alkoxy, aryloxy, heteroaryloxy, alkylthio, alkylsulfinyl, alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, amino, substituted amino or heterocyclyl;

R^{6a}, R^{6b}, R^{6c}, R^{6d}, R^{6e}
are independently hydrogen, halogen, alkyl, halogenated alkyl, hydroxyalkyl, alkoxycarbonyl, (halogenated alkoxy)carbonyl, cyano, alkoxy, halogenated alkoxy, aryl, alkylthio, (halogenated alkyl)thio, nitro, amino, alkylamino, (halogenated alkyl)amino, dialkylamino, di-(halogenated alkyl)amino, alkylcarbonylamino, (halogenated alkyl)carbonylamino, alkylsulfonylamino, (halogenated alkyl)sulfonylamino or arylsulfonylamino; or

R^{6a}, R^2
together are alkylene; or

R^{6a} and R^{6b} or R^{6b} and R^{6c}
together with the carbon atoms to which they are attached form an anellated aryl ring; or
together are alkylenedioxo; and

R^7, R^8, R^9, R^{10}
are independently hydrogen, halogen, alkyl or alkoxy,

wherein alkyl, alkylene, alkoxycarbonyl, aminocarbonyl, aryl, alkoxy, alkylenedioxo, aryloxy, heteroaryloxy, alkylthio, alkylsulfinyl, alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, amino, alkylamino, dialkylamino, alkylcarbonylamino, arylamino, sulfonylamino, alkylsulfonylamino, arylsulfonylamino and heterocyclyl may be substituted,

or a physiologically tolerated salt thereof.

Said compounds, i.e., the 4-benzylaminoquinolines and their physiologically tolerated acid addition salts, are glycine transporter inhibitors and thus uselful as pharmaceuticals.

The present invention thus also relates to pharmaceutical compositions which comprises an inert carrier and a compound of formula (I).

In particular, said compounds, i.e., the 4-benzylaminoquinolines and their physiologically tolerated acid addition salts, are inhibitors of the glycine transporter GlyT1.

The present invention thus further relates to the use of the compounds of formula (I) in the manufacture of a medicament for inhibiting the glycine transporter GlyT1 and corresponding methods of inhibiting the glycine transporter GlyT1.

Glycine transport inhibitors and in particular inhibitors of the glycine transporter GlyT1 are known to be useful in treating a variety of neurologic and psychiatric disorders.

The present invention thus further relates to the the compounds of formula (I) for use in treating a neurologic or psychiatric disorder.

The present invention thus further relates to the use of the compounds of formula (I) in the manufacture of a medicament for treating a neurologic or psychiatric disorder and corresponding methods of treating said disorders.

In one aspect of the present invention the following compounds and their physiologically tolerated salts are excluded, but not their use as defined herein:

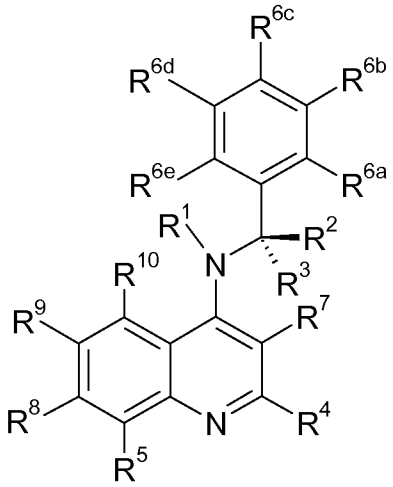
a) 4'-[[(2-methyl-4-quinolinyl)amino]methyl]-[1,1'-biphenyl]-2-carboxylic acid, 1,1-dimethylethyl ester
b) 2-methyl-N-[[2'-[1-(triphenylmethyl)-1H-tetrazol-5-yl][1,1'-biphenyl]-4-yl]methyl]-4-quinolinamine,
c) 2-methyl-N-[[3'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-4-quinolinamine,
d) 4'-[[(2-methyl-4-quinolinyl)amino]methyl]-[1,1'-biphenyl]-2-carboxylic acid,
e) 4'-[[(2-methyl-4-quinolinyl)amino]methyl]-[1,1'-biphenyl]-3-carboxylic acid, 1,1-dimethylethyl ester
f) 2-methyl-N-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-4-quinolinamine,
g) 4'-[[(8-methoxy-2-methyl-4-quinolinyl)amino]methyl]-[1,1'-biphenyl]-2-carboxylic acid,
h) 8-methoxy-2-methyl-N-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-4-quinolinamine,
i) 4'-[[(2-methyl-4-quinolinyl)amino]methyl]-N-(methylsulfonyl)-[1,1'-biphenyl]-2-carboxamide,
j) 4'-[[(2-methyl-4-quinolinyl)amino]methyl]-[1,1'-biphenyl]-2-carboxylic acid,
k) 4'-[[(2-methyl-4-quinolinyl)amino]methyl]-[1,1'-biphenyl]-2-carboxylic acid, methyl ester
l) N-[(2-methylphenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
m) N-[(2-methoxyphenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
n) N-[(2-ethylphenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
o) N-[(2-bromophenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
p) N-[(2,6-dichlorophenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
q) N-[(2,6-dimethoxyphenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
r) N-[(2,6-dimethylphenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
s) N-[(2,3-dimethylphenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
t) N-[(2,4-dimethylphenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
u) N-[(2,5-dimethylphenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
v) N-[(2-chlorophenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
w) N-[(2-fluorophenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
x) N-[(2-chloro-6-fluorophenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
y) N-[(2,6-difluorophenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
z) N-[[2-(trifluoromethyl)phenyl]methyl]-8-methoxy-2-methyl-4-quinolinamine,
aa) 4-[[(8-methoxy-2-methyl-4-quinolinyl)amino]methyl]-3-methyl-phenol,
ab) 4-[(p-chlorobenzyl)amino]-quinaldine,
ac) N-[(1S)-1-phenylethyl]-2-methyl-4-quinolinamine,
ad) N-(phenylmethyl)-2-methyl-4-quinolinamine,

ae) 4-[[1-(3,4-dimethoxyphenyl)hexyl]amino]-2-methyl-8-quinolinol,
af) 4-[[1-(2-hexyl-4,5-dimethoxyphenyl)ethyl]amino]-2-methyl-8-quinolinol,
ag) 4-[[1-(3,4-dimethoxyphenyl)hexyl]amino]-2-methyl-8-quinolinol,
ah) 4-[[1-(2-hexyl-4,5-dimethoxyphenyl)ethyl]amino]-2-methyl-4-quinolinol,
ai) N-[1-(3,4-dimethoxyphenyl)hexyl]-8-methoxy-2-methyl-4-quinolinamine,
aj) N-[1-(2-hexyl-4,5-dimethoxyphenyl)ethyl]-8-methoxy-2-methyl-4-quinolinamine.

Detailed Description Of The Invention

Provided that the 4-benzylaminoquinolines of the formula (I) of a given constitution may exist in different spatial arrangements, for example if they possess one or more centers of asymmetry, polysubstituted rings or double bonds, or as different tautomers, it is also possible to use enantiomeric mixtures, in particular racemates, diastereomeric mixtures and tautomeric mixtures, preferably, however, the respective essentially pure enantiomers, diastereomers and tautomers of the compounds of formula (I) and/or of their salts.

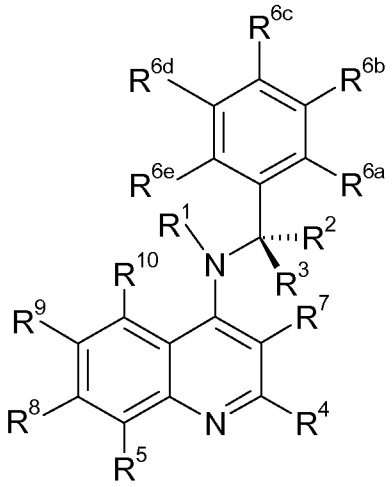
According to one embodiment, an enantiomer of the 4-benzylaminoquinolines of the present invention has the following formula (Ia):



(Ia)

wherein R^1, R^2, R^3, R^4, R^5, R^{6a}, R^{6b}, R^{6c}, R^{6d}, R^{6e}, R^7, R^8, R^9, R^{10} are as defined herein.

According to a further embodiment, an enantiomer of the 4-benzylaminoquinolines of the present invention has the following formula (Ib):



(Ib)

wherein R^1, R^2, R^3, R^4, R^5, R^{6a}, R^{6b}, R^{6c}, R^{6d}, R^{6e}, R^7, R^8, R^9, R^{10} are as defined herein.

The physiologically tolerated salts of the 4-benzylaminoquinolines of the formula (I) are especially acid addition salts with physiologically tolerated acids. Examples of suitable physiologically tolerated organic and inorganic acids are hydrochloric acid, hydrobromic acid, phosphoric acid, sulfuric acid, C_1-C_4-alkylsulfonic acids, such as methanesulfonic acid, cycloaliphatic sulfonic acids, such as S-(+)-10-campher sulfonic acid, aromatic sulfonic acids, such as benzenesulfonic acid and toluenesulfonic acid, di- and tricarboxylic acids and hydroxycarboxylic acids having 2 to 10 carbon atoms, such as oxalic acid, malonic acid, maleic acid, fumaric acid, lactic acid, tartaric acid, citric acid, glycolic acid, adipic acid and benzoic acid. Other utilizable acids are described, e.g., in Fortschritte der Arzneimittelforschung [Advances in drug research], Volume 10, pages 224 ff., Birkhäuser Verlag, Basel and Stuttgart, 1966.

The organic moieties mentioned in the above definitions of the variables are - like the term halogen – collective terms for individual listings of the individual group members. The prefix C_n-C_m indicates in each case the possible number of carbon atoms in the group.

Unless indicated otherwise, the term "substituted" means that a radical is substituted with 1, 2 or 3, especially 1, substituent selected from the group consisting of halogen, C_1-C_4-alkyl, C_1-C_4-alkenyl, OH, SH, CN, CF_3, O-CF_3, COOH, O-CH_2-COOH, C_1-C_6-alkoxy, C_1-C_6-alkylthio, C_3-C_7-cycloalkyl, COO-C_1-C_6-alkyl, $CONH_2$, CONH-C_1-C_6-alkyl, SO_2NH-C_1-C_6-alkyl, CON-(C_1-C_6-alkyl)$_2$, SO_2N-(C_1-C_6-alkyl)$_2$, NH_2, NH-C_1-C_6-alkyl, N-(C_1-C_6-alkyl)$_2$, NH-(C_1-C_4-alkyl-C_6-C_{12}-aryl), NH-CO-C_1-C_6-alkyl, NH-SO_2-C_1-C_6-alkyl, SO_2-C_1-C_6-alkyl, C_6-C_{12}-aryl, O-C_6-C_{12}-aryl, O-CH_2-C_6-C_{12}-aryl, CONH-C_6-C_{12}-aryl, SO_2NH-C_6-C_{12}-aryl, CONH-C_5-C_{12}-hetaryl, SO_2NH-C_5-C_{12}-hetaryl, SO_2-C_6-C_{12}-aryl, NH-SO_2-C_6-C_{12}-aryl, NH-CO-C_6-C_{12}-aryl, NH-SO_2-C_5-C_{12}-hetaryl and NH-CO-C_5-C_{12}-hetaryl, wherein aryl and

hetaryl in turn may be unsubstituted or substituted with 1, 2 oder 3 substiuents selected from the group consisting of halogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy and C_1-C_4-haloalkoxy.

The term halogen denotes in each case fluorine, bromine, chlorine or iodine, in particular fluorine or chlorine.

C_1-C_4-Alkyl is a straight-chain or branched alkyl group having from 1 to 4 carbon atoms. Examples of an alkyl group are methyl, C_2-C_4-alkyl such as ethyl, n-propyl, iso-propyl, n-butyl, 2-butyl, iso-butyl or tert-butyl. C_1-C_2-Alkyl is methyl or ethyl, C_1-C_3-alkyl is additionally n-propyl or isopropyl.

C_1-C_6-Alkyl is a straight-chain or branched alkyl group having from 1 to 6 carbon atoms. Examples include methyl, C_2-C_4-alkyl as mentioned herein and also pentyl, 1-methylbutyl, 2-methylbutyl, 3-methylbutyl, 2,2-dimethylpropyl, 1-ethylpropyl, hexyl, 1,1-dimethylpropyl, 1,2-dimethylpropyl, 1-methylpentyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl, 1,1-dimethylbutyl, 1,2-dimethylbutyl, 1,3-dimethylbutyl, 2,2-dimethylbutyl, 2,3-dimethylbutyl, 3,3-dimethylbutyl, 1-ethylbutyl, 2-ethylbutyl, 1,1,2-trimethylpropyl, 1,2,2-trimethylpropyl, 1-ethyl-1-methylpropyl and 1-ethyl-2-methylpropyl.

Halogenated C_1-C_4-alkyl is a straight-chain or branched alkyl group having 1 to 4 carbon atoms, preferably 1 to 3 carbon atoms, more preferably 1 or 2 carbon atoms, wherein at least one, e.g. 1, 2, 3, 4 or all of the hydrogen atoms are replaced by 1, 2, 3, 4 or a corresponding number of identical or different halogen atoms, such as in halogenomethyl, dihalogenomethyl, trihalogenomethyl, (R)-1-halogenoethyl, (S)-1-halogenoethyl, 2-halogenoethyl, 1,1-dihalogenoethyl, 2,2-dihalogenoethyl, 2,2,2-trihalogenoethyl, (R)-1-halogenopropyl, (S)-1-halogenopropyl, 2-halogenopropyl, 3-halogenopropyl, 1,1-dihalogenopropyl, 2,2-dihalogenopropyl, 3,3-dihalogenopropyl, 3,3,3-trihalogenopropyl, (R)-2-halogeno-1-methylethyl, (S)-2-halogeno-1-methylethyl, (R)-2,2-dihalogeno-1-methylethyl, (S)-2,2-dihalogeno-1-methylethyl, (R)-1,2-dihalogeno-1-methylethyl, (S)-1,2-dihalogeno-1-methylethyl, (R)-2,2,2-trihalogeno-1-methylethyl, (S)-2,2,2-trihalogeno-1-methylethyl, 2-halogeno-1-(halogenomethyl)ethyl, 1-(dihalogenomethyl)-2,2-dihalogenoethyl, (R)-1-halogenobutyl, (S)-1-halogenobutyl, 2-halogenobutyl, 3-halogenobutyl, 4-halogenobutyl, 1,1-dihalogenobutyl, 2,2-dihalogenobutyl, 3,3-dihalogenobutyl, 4,4-dihalogenobutyl, 4,4,4-trihalogenobutyl, etc. Particular examples include the fluorinated C_1-C_4 alkyl groups as defined, such as trifluoromethyl.

Hydroxy-C_1-C_4-alkyl is a straight-chain or branched alkyl group having 1 to 4 carbon atoms, preferably 1 to 3 carbon atoms, more preferably 1 or 2 carbon atoms, wherein one or

two hydrogen atoms are replaced by one or two hydroxyl groups, such as in hydroxymethyl, (R)-1-hydroxyethyl, (S)-1-hydroxyethyl, 2-hydroxyethyl, (R)-1-hydroxypropyl, (S)-1-hydroxypropyl, 2-hydroxypropyl, 3-hydroxypropyl, (R)-2-hydroxy-1-methylethyl, (S)-2-hydroxy-1-methylethyl, 2-hydroxy-1-(hydroxymethyl)ethyl, (R)-1-hydroxybutyl, (S)-1-hydroxybutyl, 2-hydroxybutyl, 3-hydroxybutyl, 4-hydroxybutyl.

C_1-C_6-Alkoxy-C_1-C_4-alkyl is a straight-chain or branched alkyl group having 1 to 4 carbon atoms, preferably 1 to 3 carbon atoms, more preferably 1 or 2 carbon atoms, wherein one or two hydrogen atoms are replaced by one or two alkoxy groups having 1 to 6, preferably 1 to 4, in particular 1 or 2 carbon atoms, such as in methoxymethyl, (R)-1-methoxyethyl, (S)-1-methoxyethyl, 2-methoxyethyl, (R)-1-methoxypropyl, (S)-1-methoxypropyl, 2-methoxypropyl, 3-methoxypropyl, (R)-2-methoxy-1-methylethyl, (S)-2-methoxy-1-methylethyl, 2-methoxy-1-(methoxymethyl)ethyl, (R)-1-methoxybutyl, (S)-1-methoxybutyl, 2-methoxybutyl, 3-methoxybutyl, 4-methoxybutyl, ethoxymethyl, (R)-1-ethoxyethyl, (S)-1-ethoxyethyl, 2-ethoxyethyl, (R)-1-ethoxypropyl, (S)-1-ethoxypropyl, 2-ethoxypropyl, 3-ethoxypropyl, (R)-2-ethoxy-1-methylethyl, (S)-2-ethoxy-1-methylethyl, 2-ethoxy-1-(ethoxymethyl)ethyl, (R)-1-ethoxybutyl, (S)-1-ethoxybutyl, 2-ethoxybutyl, 3-ethoxybutyl, 4-ethoxybutyl.

Amino-C_1-C_4-alkyl is a straight-chain or branched alkyl group having 1 to 4 carbon atoms, preferably 1 to 3 carbon atoms, more preferably 1 or 2 carbon atoms, in particular 1 or two carbon atoms, wherein one hydrogen atom is replaced by an amino group, such as in aminomethyl, 2-aminoethyl.

C_1-C_6-Alkylamino-C_1-C_4-alkyl is a straight-chain or branched alkyl group having 1 to 4 carbon atoms, preferably 1 to 3 carbon atoms, more preferably 1 or 2 carbon atoms, in particular 1 or two carbon atoms, wherein one hydrogen atom is replaced by a C_1-C_6-alkylamino group, in particular by a C_1-C_4-alkylamino group, such as in methylaminomethyl, ethylaminomethyl, n-propylaminomethyl, iso-propylaminomethyl, n-butylaminomethyl, 2-butylaminomethyl, iso-butylaminomethyl or *tert*-butylaminomethyl.

Di-C_1-C_6-alkylamino-C_1-C_4-alkyl is a straight-chain or branched alkyl group having 1 to 4 carbon atoms, preferably 1 to 3 carbon atoms, more preferably 1 or 2 carbon atoms, in particular 1 or two carbon atoms, wherein one hydrogen atom is replaced by a di-C_1-C_6-alkylamino group, in particular by a di-C_1-C_4-alkylamino group, such as in dimethylaminomethyl.

C_1-C_6-Alkylcarbonylamino-C_1-C_4-alkyl is a straight-chain or branched alkyl group having 1 to 4 carbon atoms, preferably 1 to 3 carbon atoms, more preferably 1 or 2 carbon atoms,

in particular 1 or two carbon atoms, wherein one hydrogen atom is replaced by a C_1-C_6-alkylcarbonylamino group, in particular by a C_1-C_4-alkylcarbonylamino group, such as in methylcarbonylaminomethyl, ethylcarbonylaminomethyl, n-propylcarbonylaminomethyl, iso-propylcarbonylaminomethyl, n-butylcarbonylaminomethyl, 2-butylcarbonylaminomethyl, iso-butylcarbonylaminomethyl or *tert*-butylcarbonylaminomethyl.

C_1-C_6-Alkylsulfonylamino-C_1-C_4-alkyl is a straight-chain or branched alkyl group having 1 to 4 carbon atoms, preferably 1 to 3 carbon atoms, more preferably 1 or 2 carbon atoms, in particular 1 or two carbon atoms, wherein one hydrogen atom is replaced by a C_1-C_6-alkylsulfonylamino group, in particular by a C_1-C_4-alkylsulfonylamino group, such as in methylsulfonylaminomethyl, ethylsulfonylaminomethyl, n-propylsulfonylaminomethyl, iso-propylsulfonylaminomethyl, n-butylsulfonylaminomethyl, 2-butylsulfonylaminomethyl, iso-butylsulfonylaminomethyl or *tert*-butylsulfonylaminomethyl.

(C_6-C_{12}-aryl-C_1-C_6-alkyl)amino-C_1-C_4 alkyl is a straight-chain or branched alkyl group having 1 to 4 carbon atoms, preferably 1 to 3 carbon atoms, more preferably 1 or 2 carbon atoms, in particular 1 or two carbon atoms, wherein one hydrogen atom is replaced by a (C_6-C_{12}-aryl-C_1-C_6-alkyl)amino group, in particular a (C_6-C_{12}-aryl-C_1-C_2-alkyl)amino group, such as in benzylaminomethyl.

C_3-C_{12}-heterocyclyl-C_1-C_4-alkyl is a straight-chain or branched alkyl group having 1 to 4 carbon atoms, preferably 1 to 3 carbon atoms, more preferably 1 or 2 carbon atoms, in particular 1 or two carbon atoms, wherein one hydrogen atom is replaced by C_3-C_{12}-heterocyclyl, such as in N-pyrrolidinylmethyl, N-piperidinylmethyl or N-morpholinylmethyl.

C_3-C_{12}-Cycloalkyl is a cycloaliphatic radical having from 3 to 12 carbon atoms. In particular, 3 to 6 carbon atoms form the cyclic structure, such as cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl. The cyclic structure may be unsubstituted or may carry 1, 2, 3 or 4 C_1-C_4 alkyl radicals, preferably one or more methyl radicals.

C_1-C_6-alkylcarbonyl is a radical of the formula R-C(O)-, wherein R is an alkyl radical having from 1 to 6, preferably from 1 to 4, in particular 1 or 2 carbon atoms as defined herein. Examples include acetyl, propionyl, n-butyryl, 2-methylpropionyl and pivaloyl.

C_6-C_{12}-arylcarbonyl is a radical of the formula R-C(O)-, wherein R is an aryl radical having from 6 to 12 carbon atoms as defined herein. Examples include benzoyl.

C_1-C_6-alkoxycarbonyl is a radical of the formula R-O-C(O)-, wherein R is an alkyl radical having from 1 to 6, preferably from 1 to 4, in particular 1 or 2 carbon atoms as defined herein. Examples include methoxycarbonyl.

Halogenated C_1-C_6-alkoxycarbonyl is a C_1-C_6-alkoxycarbonyl as defined herein, wherein at least one, e.g. 1, 2, 3, 4 or all of the hydrogen atoms are replaced by 1, 2, 3, 4 or a corresponding number of identical or different hydrogen atoms.

C_6-C_{12}-Aryloxycarbonyl is a radical of the formula R-O-C(O)-, wherein R is an aryl radical having from 6 to 12 carbon atoms as defined herein. Examples include phenoxycarbonyl.

Cyano is -C≡N.

Aminocarbonyl is $NH_2C(O)$-.

C_1-C_6-Alkylaminocarbonyl is a radical of the formula R-NH-C(O)-, wherein R is an alkyl radical having from 1 to 6, preferably from 1 to 4, in particular 1 or 2 carbon atoms as defined herein. Examples include methylaminocarbonyl.

(Halogenated C_1-C_4-alkyl)aminocarbonyl is a C_1-C_4-alkylaminocarbonyl as defined herein, wherein at least one, e.g. 1, 2, 3, 4 or all of the hydrogen atoms are replaced by 1, 2, 3, 4 or a corresponding number of identical or different hydrogen atoms.

C_6-C_{12}-Arylaminocarbonyl is a radical of the formula R-NH-C(O)-, wherein R is an aryl radical having from 6 to 12 carbon atoms as defined herein. Examples include phenylaminocarbonyl.

C_2-C_6-Alkenyl is a singly unsaturated hydrocarbon radical having 2, 3, 4, 5 or 6 carbon atoms, e.g. vinyl, allyl (2-propen-1-yl), 1-propen-1-yl, 2-propen-2-yl, methallyl (2-methylprop-2-en-1-yl) and the like. C_3-C_4-Alkenyl is, in particular, allyl, 1-methylprop-2-en-1-yl, 2-buten-1-yl, 3-buten-1-yl, methallyl, 2-penten-1-yl, 3-penten-1-yl, 4-penten-1-yl, 1-methylbut-2-en-1-yl or 2-ethylprop-2-en-1-yl.

C_1-C_4-Alkylene is straight-chain or branched alkylene group having from 1 to 4 carbon atoms. Examples include methylene and ethylene.

C_6-C_{12}-Aryl is a 6- to 12-membered, in particular 6- to 10-membered, aromatic cyclic radical. Examples include phenyl and naphthyl.

Hydroxy is –OH.

C_1-C_6-Alkoxy is a a radical of the formula R-O-, wherein R is a straight-chain or branched alkyl group having from 1 to 6, in particular 1 to 4 carbon atoms. Examples include methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, 2-butoxy, iso-butoxy (2-methylpropoxy), tert.-butoxy, pentyloxy, 1-methylbutoxy, 2-methylbutoxy, 3-methylbutoxy, 2,2-dimethylpropoxy, 1-ethylpropoxy, hexyloxy, 1,1-dimethylpropoxy, 1,2-dimethylpropoxy, 1-methylpentyloxy, 2-methylpentyloxy, 3-methylpentyloxy, 4-methylpentyloxy, 1,1-dimethylbutyloxy, 1,2-dimethylbutyloxy, 1,3-dimethylbutyloxy, 2,2-dimethylbutyloxy, 2,3-dimethylbutyloxy, 3,3-dimethylbutyloxy, 1-ethylbutyloxy, 2-ethylbutyloxy, 1,1,2-trimethylpropoxy, 1,2,2-trimethylpropoxy, 1-ethyl-1-methylpropoxy and 1-ethyl-2-methylpropoxy.

Halogenated C_1-C_6-alkoxy is a straight-chain or branched alkoxy group having from 1 to 6, preferably from 1 to 4, in particular 1 or 2 carbon atoms, wherein at least one, e.g. 1, 2, 3, 4 or all of the hydrogen atoms are replaced by 1, 2, 3, 4 or a corresponding number of identical or different halogen atoms, such as in halogenomethoxy, dihalogenomethoxy, trihalogenomethoxy, (R)-1-halogenoethoxy, (S)-1-halogenoethoxy, 2-halogenoethoxy, 1,1-dihalogenoethoxy, 2,2-dihalogenoethoxy, 2,2,2-trihalogenoethoxy, (R)-1-halogenopropoxy, (S)-1-halogenopropoxy, 2-halogenopropoxy, 3-halogenopropoxy, 1,1-dihalogenopropoxy, 2,2-dihalogenopropoxy, 3,3-dihalogenopropoxy, 3,3,3-trihalogenopropoxy, (R)-2-halogeno-1-methylethoxy, (S)-2-halogeno-1-methylethoxy, (R)-2,2-dihalogeno-1-methylethoxy, (S)-2,2-dihalogeno-1-methylethoxy, (R)-1,2-dihalogeno-1-methylethoxy, (S)-1,2-dihalogeno-1-methylethoxy, (R)-2,2,2-trihalogeno-1-methylethoxy, (S)-2,2,2-trihalogeno-1-methylethoxy, 2-halogeno-1-(halogenomethyl)ethoxy, 1-(dihalogenomethyl)-2,2-dihalogenoethoxy, (R)-1-halogenobutoxy, (S)-1-halogenobutoxy, 2-halogenobutoxy, 3-halogenobutoxy, 4-halogenobutoxy, 1,1-dihalogenobutoxy, 2,2-dihalogenobutoxy, 3,3-dihalogenobutoxy, 4,4-dihalogenobutoxy, 4,4,4-trihalogenobutoxy, etc. Particular examples include the fluorinated C_1-C_4 alkoxy groups as defined, such as trifluoromethoxy.

C_1-C_6-Hydroxyalkoxy is an alkoxy radical having from 1 to 6, preferably from 1 to 4 carbon atoms as defined herein, wherein one or two hydrogen atoms are replaced by hydroxy. Examples include 2-hydroxyethoxy, 3-hydroxypropoxy, 2-hydroxypropoxy, 1-methyl-2-hydroxyethoxy and the like.

C_1-C_6-Alkoxy-C_1-C_4-alkoxy is an alkoxy radical having from 1 to 4 carbon atoms, preferably 1 or 2 carbon atoms as defined herein, wherein one or two hydrogen atoms are replaced by one or two alkoxy radicals having from 1 to 6, preferably from 1 to 4 carbon

atoms as defined herein. Examples include methoxymethoxy, 2-methoxyethoxy, 1-methoxyethoxy, 3-methoxypropoxy, 2-methoxypropoxy, 1-methyl-1-methoxyethoxy, ethoxymethoxy, 2-ethoxyethoxy, 1-ethoxyethoxy, 3-ethoxypropoxy, 2-ethoxypropoxy, 1-methyl-1-ethoxyethoxy and the like.

Amino-C_1-C_4 alkoxy is an alkoxy radical having from 1 to 4, preferably 1 or 2 carbon atoms as defined herein, wherein one hydrogen atom is replaced by an amino group. Examples include 2-aminoethoxy.

C_1-C_6-Alkylamino-C_1-C_4-alkoxy is an alkoxy radical having from 1 to 4, preferably 1 or 2 carbon atoms as defined herein, wherein one hydrogen atom is replaced by an alkylamino group having from 1 to 6, preferably from 1 to 4 carbon atoms as defined herein. Examples include methylaminomethoxy, ethylaminomethoxy, n-propylaminomethoxy, isopropylaminomethoxy, n-butylaminomethoxy, 2-butylaminomethoxy, isobutylaminomethoxy, *tert*-butylaminomethoxy, 2-(methylamino)ethoxy, 2-(ethylamino)ethoxy, 2-(n-propylamino)ethoxy, 2-(iso-propylamino)ethoxy, 2-(n-butylamino)ethoxy, 2-(2-butylamino)ethoxy, 2-(iso-butylamino)ethoxy, 2-(*tert*-butylamino)ethoxy.

Di-C_1-C_6-alkylamino-C_1-C_4-alkoxy is an alkoxy radical having from 1 to 4, preferably 1 or 2 carbon atoms as defined herein, wherein one hydrogen atom is replaced by a dialkylamino group having from 1 to 6, preferably from 1 to 4 carbon atoms as defined herein. Examples include dimethylaminomethoxy, diethylaminomethoxy, N-methyl-N-ethylamino)ethoxy, 2-(dimethylamino)ethoxy, 2-(diethylamino)ethoxy, 2-(N-methyl-N-ethylamino)ethoxy.

C_1-C_6-Alkylcarbonylamino-C_1-C_4-alkoxy is an alkoxy radical having from 1 to 4, preferably 1 or 2 carbon atoms as defined herein, wherein one hydrogen atom is replaced by an alkylcarbonylamino group wherein the alkyl group has from 1 to 6, preferably from 1 to 4 carbon atoms as defined herein. Examples include methylcarbonylaminomethoxy, ethylcarbonylaminomethoxy, n-propylcarbonylaminomethoxy, isopropylcarbonylaminomethoxy, n-butylcarbonylaminomethoxy, 2-butylcarbonylaminomethoxy, iso-butylcarbonylaminomethoxy, *tert*-butylcarbonylaminomethoxy, 2-(methylcarbonylamino)ethoxy, 2-(ethylcarbonylamino)ethoxy, 2-(n-propylcarbonylamino)ethoxy, 2-(iso-propylcarbonylamino)ethoxy, 2-(n-butylcarbonylamino)ethoxy, 2-(2-butylcarbonylamino)ethoxy, 2-(iso-butylcarbonylamino)ethoxy and 2-(*tert*-butylcarbonylamino)ethoxy.

C_6-C_{12}-Arylcarbonylamino-C_1-C_4-alkoxy is an alkoxy radical having from 1 to 4, preferably 1 or 2 carbon atoms as defined herein, wherein one hydrogen atom is replaced by a C_6-C_{12}-arylcarbonylamino group as defined herein. Examples include 2-(benzoylamino)ethoxy.

C_1-C_6-Alkoxycarbonylamino-C_1-C_4-alkoxy is an alkoxy radical having from 1 to 4, preferably 1 or 2 carbon atoms as defined herein, wherein one hydrogen atom is replaced by an alkoxycarbonylamino group wherein the alkoxy group has from 1 to 6, preferably from 1 to 4 carbon atoms as defined herein. Examples include methoxycarbonylaminomethoxy, ethoxycarbonylaminomethoxy, n-propoxycarbonylaminomethoxy, iso-propoxycarbonylaminomethoxy, n-butoxycarbonylaminomethoxy, 2-butoxycarbonylaminomethoxy, iso-butoxycarbonylaminomethoxy, *tert*-butoxycarbonylaminomethoxy, 2-(methoxycarbonylamino)ethoxy, 2-(ethoxycarbonylamino)ethoxy, 2-(n-propoxycarbonylamino)ethoxy, 2-(iso-propoxycarbonylamino)ethoxy, 2-(n-butoxycarbonylamino)ethoxy, 2-(2-butoxycarbonylamino)ethoxy, 2-(iso-butoxycarbonylamino)ethoxy and 2-(*tert*-butoxycarbonylamino)ethoxy.

C_3-C_{12}-Heterocyclyl-C_1-C_4-alkoxy is an alkoxy radical having from 1 to 4, preferably 1 or 2 carbon atoms as defined herein, wherein one hydrogen atom is replaced by a C_3-C_{12}-heterocyclyl group as defined herein. Examples include 2-(N-pyrrolidinyl)ethoxy, 2-(N-morpholinyl)ethoxy and 2-(N-imidazolyl)ethoxy.

C_1-C_6-Alkylsulfonylamino-C_1-C_4-alkoxy is an alkoxy radical having from 1 to 4, preferably 1 or 2 carbon atoms as defined herein, wherein one hydrogen atom is replaced by an alkylsulfonylamino group having from 1 to 6, preferably from 1 to 4 carbon atoms as defined herein. Examples include 2-(methylsulfonylamino)ethoxy, 2-(ethylsulfonylamino)ethoxy and 2-[(2-methylpropyl)sulfonylamino]ethoxy.

(Halogenated C_1-C_6-alkyl)sulfonylamino-C_1-C_4-alkoxy is an alkoxy radical having from 1 to 4, preferably 1 or 2 carbon atoms as defined herein, wherein one hydrogen atom is replaced by an alkylsulfonylamino group having from 1 to 6, preferably from 1 to 4 carbon atoms as defined herein, wherein the alkyl group is halogenated. Examples include 2-(trifluoromethylsulfonylamino)ethoxy.

C_6-C_{12}-Arylsulfonylamino-C_1-C_4-alkoxy is an alkoxy radical having from 1 to 4, preferably 1 or 2 carbon atoms as defined herein, wherein one hydrogen atom is replaced by a C_6-C_{12}-arylsulfonylamino group as defined herein. Examples include 2-(phenylsulfonylamino)ethoxy and 2-(naphthylsulfonylamino)ethoxy.

(C_6-C_{12}-Aryl-C_1-C_6-alkyl)sulfonylamino-C_1-C_4-alkoxy is an alkoxy radical having from 1 to 4, preferably 1 or 2 carbon atoms as defined herein, wherein one hydrogen atom is replaced by a (C_6-C_{12}-aryl-C_1-C_6-alkyl)sulfonylamino group, preferably by a (C_6-C_{12}-aryl-C_1-C_2-alkyl)sulfonylamino group. Examples include 2-(benzylsulfonylamino)ethoxy.

C_3-C_{12}-Heterocyclylsulfonylamino-C_1-C_4-alkoxy is an alkoxy radical having from 1 to 4, preferably 1 or 2 carbon atoms as defined herein, wherein one hydrogen atom is replaced by a C_3-C_{12}-heterocyclylsulfonylamino group as defined herein. Examples include 2-(pyridin-3-yl-sulfonylamino)ethoxy.

C_6-C_{12}-Aryl-C_1-C_4-alkoxy is an alkoxy radical having from 1 to 4, preferably 1 or 2 carbon atoms as defined herein, wherein one hydrogen atom is replaced by a C_6-C_{12}-aryl group as defined herein. Examples include benzyloxy.

C_1-C_2-Alkylenedioxo is a radical of the formula -O-R-O-, wherein R is a straight-chain or branched alkylene group having 1 or 2 carbon atoms as defined herein. Examples include methylenedioxo.

C_6-C_{12}-Aryloxy is a radical of the formula R-O-, wherein R is an aryl group having from 6 to 12, in particular 6 carbon atoms as defined herein. Examples include phenoxy.

C_3-C_{12}-Heterocyclyloxy is a radical of the formula R-O-, wherein R is a C_3-C_{12}-heterocyclyl group having from 3 to 12, in particular from 3 to 7 carbon atoms as defined herein. Examples include pyridin-2-yloxy.

C_1-C_6-Alkylthio is a radical of the formula R-S-, wherein R is an alkyl radical having from 1 to 6, preferably from 1 to 4 carbon atoms as defined herein. Examples include methylthio, ethylthio, propylthio, butylthio, pentylthio, 1-methylbutylthio, 2-methylbutylthio, 3-methylbutylthio, 2,2-dimethylpropylthio, 1-ethylpropylthio, hexylthio, 1,1-dimethylpropylthio, 1,2-dimethylpropylthio, 1-methylpentylthio, 2-methylpentylthio, 3-methylpentylthio, 4-methylpentylthio, 1,1-dimethylbutylthio, 1,2-dimethylbutylthio, 1,3-dimethylbutylthio, 2,2-dimethylbutylthio, 2,3-dimethylbutylthio, 3,3-dimethylbutylthio, 1-ethylbutylthio, 2-ethylbutylthio, 1,1,2-trimethylpropylthio, 1,2,2-trimethylpropylthio, 1-ethyl-1-methylpropyl and 1-ethyl-2-methylpropyl.

Halogenated C_1-C_6-alkylthio is a radical of the formula R-S-, wherein R is a halogenated alkyl radical having from 1 to 6, preferably from 1 to 4 carbon atoms as defined herein. Examples include halogenomethylthio, dihalogenomethylthio, trihalogenomethylthio, (R)-1-halogenoethylthio, (S)-1-halogenoethylthio, 2-halogenoethylthio, 1,1-

dihalogenoethylthio, 2,2-dihalogenoethylthio, 2,2,2-trihalogenoethylthio, (R)-1-halogenopropylthio, (S)-1-halogenopropylthio, 2-halogenopropylthio, 3-halogenopropylthio, 1,1-dihalogenopropylthio, 2,2-dihalogenopropylthio, 3,3-dihalogenopropylthio, 3,3,3-trihalogenopropylthio, (R)-2-halogeno-1-methylethylthio, (S)-2-halogeno-1-methylethylthio, (R)-2,2-dihalogeno-1-methylethylthio, (S)-2,2-dihalogeno-1-methylethylthio, (R)-1,2-dihalogeno-1-methylethylthio, (S)-1,2-dihalogeno-1-methylethylthio, (R)-2,2,2-trihalogeno-1-methylethylthio, (S)-2,2,2-trihalogeno-1-methylethylthio, 2-halogeno-1-(halogenomethyl)ethylthio, 1-(dihalogenomethyl)-2,2-dihalogenoethylthio, (R)-1-halogenobutylthio, (S)-1-halogenobutylthio, 2-halogenobutylthio, 3-halogenobutylthio, 4-halogenobutylthio, 1,1-dihalogenobutylthio, 2,2-dihalogenobutylthio, 3,3-dihalogenobutylthio, 4,4-dihalogenobutylthio, 4,4,4-trihalogenobutylthio, etc.. Particular examples include the fluorinated C_1-C_4 alkylthio groups as defined, such as trifluoromethylthio.

C_1-C_6-Alkylsulfinyl is a radical of the formula R-S(O)-, wherein R is an alkyl radical having from 1 to 6, preferably from 1 to 4 carbon atoms as defined herein. Examples include methylsulfinyl, ethylsulfinyl, propylsulfinyl, butylsulfinyl, pentylsulfinyl, 1-methylbutylsulfinyl, 2-methylbutylsulfinyl, 3-methylbutylsulfinyl, 2,2-dimethylpropylsulfinyl, 1-ethylpropylsulfinyl, hexylsulfinyl, 1,1-dimethylpropylsulfinyl, 1,2-dimethylpropylsulfinyl, 1-methylpentylsulfinyl, 2-methylpentylsulfinyl, 3-methylpentylsulfinyl, 4-methylpentylsulfinyl, 1,1-dimethylbutylsulfinyl, 1,2-dimethylbutylsulfinyl, 1,3-dimethylbutylsulfinyl, 2,2-dimethylbutylsulfinyl, 2,3-dimethylbutylsulfinyl, 3,3-dimethylbutylsulfinyl, 1-ethylbutylsulfinyl, 2-ethylbutylsulfinyl, 1,1,2-trimethylpropylsulfinyl, 1,2,2-trimethylpropylsulfinyl, 1-ethyl-1-methylpropyl and 1-ethyl-2-methylpropyl.

C_1-C_6-Alkylsulfonyl is a radical of the formula R-S$(O)_2$-, wherein R is an alkyl radical having from 1 to 6, preferably from 1 to 4 carbon atoms as defined herein. Examples include methylsulfonyl, ethylsulfonyl, propylsulfonyl, butylsulfonyl, pentylsulfonyl, 1-methylbutylsulfonyl, 2-methylbutylsulfonyl, 3-methylbutylsulfonyl, 2,2-dimethylpropylsulfonyl, 1-ethylpropylsulfonyl, hexylsulfonyl, 1,1-dimethylpropylsulfonyl, 1,2-dimethylpropylsulfonyl, 1-methylpentylsulfonyl, 2-methylpentylsulfonyl, 3-methylpentylsulfonyl, 4-methylpentylsulfonyl, 1,1-dimethylbutylsulfonyl, 1,2-dimethylbutylsulfonyl, 1,3-dimethylbutylsulfonyl, 2,2-dimethylbutylsulfonyl, 2,3-dimethylbutylsulfonyl, 3,3-dimethylbutylsulfonyl, 1-ethylbutylsulfonyl, 2-ethylbutylsulfonyl, 1,1,2-trimethylpropylsulfonyl, 1,2,2-trimethylpropylsulfonyl, 1-ethyl-1-methylpropyl and 1-ethyl-2-methylpropyl.

(Halogenated C_1-C_6-alkyl)sulfonyl is a C_1-C_6-alkylsulfonyl as defined herein, wherein at least one, e.g. 1, 2, 3, 4 or all of the hydrogen atoms are replaced by 1, 2, 3, 4 or a corresponding number of identical or different hydrogen atoms.

C_6-C_{12}-Arylsulfonyl is a radical of the formula R-S(O)$_2$-, wherein R is an aryl radical having from 6 to 12 carbon atoms as defined herein. Examples include phenylsulfonyl.

(C_6-C_{12}-Aryl-C_1-C_4-alkyl)sulfonyl is a radical of the formula R-S(O)$_2$-, wherein R is a C_6-C_{12}-aryl-C_1-C_4-alkyl radical, in particular a C_6-C_{12}-aryl-C_1-C_2-alkyl radical as defined herein. Examples include benzylsulfonyl.

C_3-C_{12}-Heterocyclylsulfonyl is a radical of the formula R-S(O)$_2$-, wherein R is C_3-C_{12}-heterocyclyl as defined herein.

Aminosulfonyl is NH_2-S(O)$_2$-.

C_1-C_6-Alkylaminosulfonyl is a radical of the formula R-NH-S(O)$_2$- wherein R is an alkyl radical having from 1 to 6, preferably from 1 to 4 carbon atoms as defined herein. Examples include methylaminosulfonyl, ethylaminosulfonyl, n-propylaminosulfonyl, iso-propylaminosulfonyl, n-butylaminosulfonyl, 2-butylaminosulfonyl, iso-butylaminosulfonyl and *tert*-butylaminosulfonyl.

Di-C_1-C_6-alkylaminosulfonyl is a radical of the formula RR'N-S(O)$_2$- wherein R and R' are independently of each other an alkyl radical having from 1 to 6, preferably from 1 to 4 carbon atoms as defined herein. Examples include dimethylaminosulfonyl, diethylaminosulfonyl and N-methyl-N-ethylaminosulfonyl.

C_6-C_{12}-Arylaminosulfonyl is a radical of the formula R-NH-S(O)$_2$- wherein R is an aryl radical having from 6 to 12, preferably 6 carbon atoms as defined herein.

Amino is NH_2.

C_1-C_6-Alkylamino is a radical of the formula R-NH- wherein R is an alkyl radical having from 1 to 6, in particular from 1 to 4 carbon atoms as defined herein. Examples include methylamino, ethylamino, n-propylamino, iso-propylamino, n-butylamino, 2-butylamino, iso-butylamino and *tert*-butylamino.

(Halogenated C_1-C_6-Alkyl)amino is a C_1-C_6-alkylamino as defined herein, wherein at least one, e.g. 1, 2, 3, 4 or all of the hydrogen atoms are replaced by 1, 2, 3, 4 or a corresponding number of identical or different hydrogen atoms.

Di-C_1-C_6-Alkylamino is a radical of the formula RR'N- wherein R and R' are independently of each other an alkyl radical having from 1 to 6, in particular from 1 to 4 carbon atoms as defined herein. Examples include dimethylamino, diethylamino and N-methyl-N-ethylamino.

Di-(halogenated C_1-C_6-alkyl)amino is a di-C_1-C_6-alkylamino as defined herein, wherein at least one, e.g. 1, 2, 3, 4 or all of the hydrogen atoms are replaced by 1, 2, 3, 4 or a corresponding number of identical or different hydrogen atoms.

C_1-C_6-Alkylcarbonylamino is a radical of the formula R-C(O)-NH-, wherein R is an alkyl radical having from 1 to 6, in particular from 1 to 4 carbon atoms as defined herein. Examples include acetamido (methylcarbonylamino), propionamido, n-butyramido, 2-methylpropionamido (isopropylcarbonylamino), 2,2-dimethylpropionamido and the like.

(Halogenated C_1-C_6-Alkyl)carbonylamino is a C_1-C_6-alkylcarbonylamino as defined herein, wherein at least one, e.g. 1, 2, 3, 4 or all of the hydrogen atoms are replaced by 1, 2, 3, 4 or a corresponding number of identical or different hydrogen atoms.

C_6-C_{12}-Arylcarbonylamino is a radical of the formula R-C(O)-NH-, wherein R is an aryl radical having from 6 to 12 carbon atoms as defined herein. Examples include phenylcarbonylamino.

C_1-C_6-Alkylsulfonylamino is a radical of the formula R-S(O)$_2$-NH-, wherein R is an alkyl radical having from 1 to 6, in particular from 1 to 4 carbon atoms as defined herein. Examples include methylsulfonylamino, ethylsulfonylamino, n-propylsulfonylamino, iso-propylsulfonylamino, n-butylsulfonylamino, 2-butylsulfonylamino, iso-butylsulfonylamino and *tert*-butylsulfonylamino.

(Halogenated C_1-C_6 alkyl)sulfonylamino is a C_1-C_6-alkylsulfonylamino as defined herein, wherein at least one, e.g. 1, 2, 3, 4 or all of the hydrogen atoms are replaced by 1, 2, 3, 4 or a corresponding number of identical or different hydrogen atoms.

C_6-C_{12}-Arylsulfonylamino is a radical of the formula R-S(O)$_2$-NH-, wherein R is an aryl radical having from 6 to 12 carbon atoms as defined herein. Examples include phenylsulfonylamino.

Nitro is $-NO_2$.

C_3-C_{12}-Heterocyclyl is a 3- to 12-membered heterocyclic radical including a saturated heterocyclic radical, which generally has 3, 4, 5, 6,or 7 ring forming atoms (ring members), an unsaturated non-aromatic heterocyclic radical, which generally has 5, 6 or 7 ring forming atoms, and a heteroaromatic radical (hetaryl), which generally has 5, 6 or 7 ring forming atoms. The heterocylcic radicals may be bound via a carbon atom (C-bound) or a nitrogen atom (N-bound). Preferred heterocyclic radicals comprise 1 nitrogen atom as ring member atom and optionally 1, 2 or 3 further heteroatoms as ring members, which are selected, independently of each other from O, S and N. Likewise preferred heterocyclic radicals comprise 1 heteroatom as ring member, which is selected from O, S and N, and optionally 1, 2 or 3 further nitrogen atoms as ring members.

Examples of C_3-C_{12}-heterocyclyl include:

C-bound 3-4-membered, saturated rings, such as
2-oxiranyl, 2-oxetanyl, 3-oxetanyl, 2-aziridinyl, 3-thiethanyl, 1-azetidinyl and 2-azetidinyl;

C-bound, 5-membered, saturated rings, such as
tetrahydrofuran-2-yl, tetrahydrofuran-3-yl, tetrahydrothien-2-yl, tetrahydrothien-3-yl, tetrahydropyrrol-2-yl, tetrahydropyrrol-3-yl, tetrahydropyrazol-3-yl, tetrahydro-pyrazol-4-yl, tetrahydroisoxazol-3-yl, tetrahydroisoxazol-4-yl, tetrahydroisoxazol-5-yl, 1,2-oxathiolan-3-yl, 1,2-oxathiolan-4-yl, 1,2-oxathiolan-5-yl, tetrahydroisothiazol-3-yl, tetrahydroisothiazol-4-yl, tetrahydroisothiazol-5-yl, 1,2-dithiolan-3-yl, 1,2-dithiolan-4-yl, tetrahydroimidazol-2-yl, tetrahydroimidazol-4-yl, tetrahydrooxazol-2-yl, tetrahydrooxazol-4-yl, tetrahydrooxazol-5-yl, tetrahydrothiazol-2-yl, tetrahydrothiazol-4-yl, tetrahydrothiazol-5-yl, 1,3-dioxolan-2-yl, 1,3-dioxolan-4-yl, 1,3-oxathiolan-2-yl, 1,3-oxathiolan-4-yl, 1,3-oxathiolan-5-yl, 1,3-dithiolan-2-yl, 1,3-dithiolan-4-yl and 1,3,2-dioxathiolan-4-yl;

C-bound, 6-membered, saturated rings, such as
tetrahydropyran-2-yl, tetrahydropyran-3-yl, tetrahydropyran-4-yl, piperidin-2-yl, piperidin-3-yl, piperidin-4-yl, tetrahydrothiopyran-2-yl, tetrahydrothiopyran-3-yl, tetrahydrothiopyran-4-yl, 1,3-dioxan-2-yl, 1,3-dioxan-4-yl, 1,3-dioxan-5-yl, 1,4-dioxan-2-yl, 1,3-dithian-2-yl, 1,3-dithian-4-yl, 1,3-dithian-5-yl, 1,4-dithian-2-yl, 1,3-oxathian-2-yl, 1,3-oxathian-4-yl, 1,3-oxathian-5-yl, 1,3-oxathian-6-yl, 1,4-oxathian-2-yl, 1,4-oxathian-3-yl, 1,2-dithian-3-yl, 1,2-dithian-4-yl, hexahydropyrimidin-2-yl, hexahydropyrimidin-4-yl, hexahydropyrimidin-5-yl, hexahydropyrazin-2-yl, hexahydropyridazin-3-yl, hexahydropyridazin-4-yl, tetrahydro-1,3-oxazin-2-yl, tetrahydro-1,3-oxazin-4-yl, tetrahydro-1,3-oxazin-5-yl, tetrahydro-1,3-oxazin-

6-yl, tetrahydro-1,3-thiazin-2-yl, tetrahydro-1,3-thiazin-4-yl, tetrahydro-1,3-thiazin-5-yl, tetrahydro-1,3-thiazin-6-yl, tetrahydro-1,4-thiazin-2-yl, tetrahydro-1,4-thiazin-3-yl, tetrahydro-1,4-oxazin-2-yl, tetrahydro-1,4-oxazin-3-yl, tetrahydro-1,2-oxazin-3-yl, tetrahydro-1,2-oxazin-4-yl, tetrahydro-1,2-oxazin-5-yl and tetrahydro-1,2-oxazin-6-yl;

N-bound, 5-membered, saturated rings, such as
tetrahydropyrrol-1-yl (pyrrolidin-1-yl), tetrahydropyrazol-1-yl, tetrahydroisoxazol-2-yl, tetrahydroisothiazol-2-yl, tetrahydroimidazol-1-yl, tetrahydrooxazol-3-yl and tetrahydrothiazol-3-yl;

N-bound, 6-membered, saturated rings, such as
piperidin-1-yl, hexahydropyrimidin-1-yl, hexahydropyrazin-1-yl (piperazin-1-yl), hexahydropyridazin-1-yl, tetrahydro-1,3-oxazin-3-yl, tetrahydro-1,3-thiazin-3-yl, tetrahydro-1,4-thiazin-4-yl, tetrahydro-1,4-oxazin-4-yl (morpholin-1-yl) and tetrahydro-1,2-oxazin-2-yl;

C-bound, 5-membered, partially unsaturated rings, such as
2,3-dihydrofuran-2-yl, 2,3-dihydrofuran-3-yl, 2,5-dihydrofuran-2-yl, 2,5-di-hydrofuran-3-yl, 4,5-dihydrofuran-2-yl, 4,5-dihydrofuran-3-yl, 2,3-dihydro-thien-2-yl, 2,3-dihydrothien-3-yl, 2,5-dihydrothien-2-yl, 2,5-dihydrothien-3-yl, 4,5-dihydrothien-2-yl, 4,5-dihydrothien-3-yl, 2,3-dihydro-1H-pyrrol-2-yl, 2,3-dihydro-1H-pyrrol-3-yl, 2,5-dihydro-1H-pyrrol-2-yl, 2,5-dihydro-1H-pyrrol-3-yl, 4,5-dihydro-1H-pyrrol-2-yl, 4,5-dihydro-1H-pyrrol-3-yl, 3,4-dihydro-2H-pyrrol-2-yl, 3,4-dihydro-2H-pyrrol-3-yl, 3,4-dihydro-5H-pyrrol-2-yl, 3,4-dihydro-5H-pyrrol-3-yl, 4,5-dihydro-1H-pyrazol-3-yl, 4,5-dihydro-1H-pyrazol-4-yl, 4,5-dihydro-1H-pyrazol-5-yl, 2,5-dihydro-1H-pyrazol-3-yl, 2,5-dihydro-1H-pyrazol-4-yl, 2,5-dihydro-1H-pyrazol-5-yl, 4,5-dihydroisoxazol-3-yl, 4,5-dihydroisoxazol-4-yl, 4,5-dihydroisoxazol-5-yl, 2,5-dihydroisoxazol-3-yl, 2,5-dihydroisoxazol-4-yl, 2,5-dihydroisoxazol-5-yl, 2,3-dihydroisoxazol-3-yl, 2,3-dihydroisoxazol-4-yl, 2,3-dihydroisoxazol-5-yl, 4,5-dihydroisothiazol-3-yl, 4,5-dihydroisothiazol-4-yl, 4,5-dihydroisothiazol-5-yl, 2,5-dihydroisothiazol-3-yl, 2,5-dihydroisothiazol-4-yl, 2,5-dihydroisothiazol-5-yl, 2,3-dihydroisothiazol-3-yl, 2,3-dihydroisothiazol-4-yl, 2,3-dihydroisothiazol-5-yl, 4,5-dihydro-1H-imidazol-2-yl, 4,5-dihydro-1H-imidazol-4-yl, 4,5-dihydro-1H-imidazol-5-yl, 2,5-dihydro-1H-imidazol-2-yl, 2,5-dihydro-1H-imidazol-4-yl, 2,5-dihydro-1H-imidazol-5-yl, 2,3-dihydro-1H-imidazol-2-yl, 2,3-dihydro-1H-imidazol-4-yl, 4,5-dihydro-oxazol-2-yl, 4,5-dihydrooxazol-4-yl, 4,5-dihydrooxazol-5-yl, 2,5-dihydrooxazol-2-yl, 2,5-dihydrooxazol-4-yl, 2,5-dihydrooxazol-5-yl, 2,3-dihydrooxazol-2-yl, 2,3-dihydrooxazol-4-yl, 2,3-dihydrooxazol-5-yl, 4,5-dihydrothiazol-2-yl, 4,5-dihydrothiazol-4-yl, 4,5-dihydrothiazol-5-yl, 2,5-dihydrothiazol-2-yl, 2,5-dihydrothiazol-4-yl, 2,5-dihydrothiazol-5-yl, 2,3-dihydrothiazol-2-yl, 2,3-dihydrothiazol-4-yl, 2,3-dihydrothiazol-5-yl, 1,3-dioxol-2-yl, 1,3-dioxol-4-yl, 1,3-dithiol-2-yl, 1,3-dithiol-4-yl, 1,3-oxathiol-2-yl, 1,3-oxathiol-4-yl and 1,3-oxathiol-5-yl;

C-bound, 6-membered, partially unsaturated rings, such as 2H-3,4-dihydropyran-6-yl, 2H-3,4-dihydropyran-5-yl, 2H-3,4-dihydropyran-4-yl, 2H-3,4-dihydropyran-3-yl, 2H-3,4-dihydropyran-2-yl, 2H-3,4-dihydrothiopyran-6-yl, 2H-3,4-dihydrothiopyran-5-yl, 2H-3,4-dihydrothiopyran-4-yl, 2H-3,4-dihydrothiopyran-3-yl, 2H-3,4-dihydrothiopyran-2-yl, 1,2,3,4-tetrahydropyridin-6-yl, 1,2,3,4-tetrahydropyridin-5-yl, 1,2,3,4-tetrahydropyridin-4-yl, 1,2,3,4-tetra-hydropyridin-3-yl, 1,2,3,4-tetrahydropyridin-2-yl, 2H-5,6-dihydropyran-2-yl, 2H-5,6-dihydropyran-3-yl, 2H-5,6-dihydropyran-4-yl, 2H-5,6-dihydropyran-5-yl, 2H-5,6-dihydropyran-6-yl, 2H-5,6-dihydrothiopyran-2-yl, 2H-5,6-dihydrothiopyran-3-yl, 2H-5,6-dihydrothiopyran-4-yl, 2H-5,6-dihydrothiopyran-5-yl, 2H-5,6-dihydrothiopyran-6-yl, 1,2,5,6-tetrahydropyridin-2-yl, 1,2,5,6-tetrahydropyridin-3-yl, 1,2,5,6-tetrahydropyridin-4-yl, 1,2,5,6-tetrahydropyridin-5-yl, 1,2,5,6-tetrahydropyridin-6-yl, 2,3,4,5-tetrahydropyridin-2-yl, 2,3,4,5-tetrahydropyridin-3-yl, 2,3,4,5-tetrahydropyridin-4-yl, 2,3,4,5-tetrahydropyridin-5-yl, 2,3,4,5-tetrahydropyridin-6-yl, 4H-pyran-2-yl, 4H-pyran-3-yl-, 4H-pyran-4-yl, 4H-thiopyran-2-yl, 4H-thiopyran-3-yl, 4H-thiopyran-4-yl, 1,4-dihydropyridin-2-yl, 1,4-dihydropyridin-3-yl, 1,4-dihydropyridin-4-yl, 2H-pyran-2-yl, 2H-pyran-3-yl, 2H-pyran-4-yl, 2H-pyran-5-yl, 2H-pyran-6-yl, 2H-thiopyran-2-yl, 2H-thiopyran-3-yl, 2H-thiopyran-4-yl, 2H-thiopyran-5-yl, 2H-thiopyran-6-yl, 1,2-dihydropyridin-2-yl, 1,2-dihydro-pyridin-3-yl, 1,2-dihydropyridin-4-yl, 1,2-dihydropyridin-5-yl, 1,2-dihydro-pyridin-6-yl, 3,4-dihydropyridin-2-yl, 3,4-dihydropyridin-3-yl, 3,4-dihydro-pyridin-4-yl, 3,4-dihydropyridin-5-yl, 3,4-dihydropyridin-6-yl, 2,5-dihydropyridin-2-yl, 2,5-dihydropyridin-3-yl, 2,5-dihydropyridin-4-yl, 2,5-dihydropyridin-5-yl, 2,5-dihydropyridin-6-yl, 2,3-dihydropyridin-2-yl, 2,3-dihydropyridin-3-yl, 2,3-dihydropyridin-4-yl, 2,3-dihydropyridin-5-yl, 2,3-dihydropyridin-6-yl, 2H-5,6-dihydro-1,2-oxazin-3-yl, 2H-5,6-dihydro-1,2-oxazin-4-yl, 2H-5,6-dihydro-1,2-oxazin-5-yl, 2H-5,6-dihydro-1,2-oxazin-6-yl, 2H-5,6-dihydro-1,2-thiazin-3-yl, 2H-5,6-dihydro-1,2-thiazin-4-yl, 2H-5,6-dihydro-1,2-thiazin-5-yl, 2H-5,6-dihydro-1,2-thiazin-6-yl, 4H-5,6-dihydro-1,2-oxazin-3-yl, 4H-5,6-dihydro-1,2-oxazin-4-yl, 4H-5,6-dihydro-1,2-oxazin-5-yl, 4H-5,6-dihydro-1,2-oxazin-6-yl, 4H-5,6-dihydro-1,2-thiazin-3-yl, 4H-5,6-dihydro-1,2-thiazin-4-yl, 4H-5,6-dihydro-1,2-thiazin-5-yl, 4H-5,6-dihydro-1,2-thiazin-6-yl, 2H-3,6-dihydro-1,2-oxazin-3-yl, 2H-3,6-dihydro-1,2-oxazin-4-yl, 2H-3,6-dihydro-1,2-oxazin-5-yl, 2H-3,6-dihydro-1,2-oxazin-6-yl, 2H-3,6-dihydro-1,2-thiazin-3-yl, 2H-3,6-dihydro-1,2-thiazin-4-yl, 2H-3,6-dihydro-1,2-thiazin-5-yl, 2H-3,6-dihydro-1,2-thiazin-6-yl, 2H-3,4-dihydro-1,2-oxazin-3-yl, 2H-3,4-dihydro-1,2-oxazin-4-yl, 2H-3,4-dihydro-1,2-oxazin-5-yl, 2H-3,4-dihydro-1,2-oxazin-6-yl, 2H-3,4-dihydro-1,2-thiazin-3-yl, 2H-3,4-dihydro-1,2-thiazin-4-yl, 2H-3,4-dihydro-1,2-thiazin-5-yl, 2H-3,4-dihydro-1,2-thiazin-6-yl, 2,3,4,5-tetrahydropyridazin-3-yl, 2,3,4,5-tetrahydropyridazin-4-yl, 2,3,4,5-tetrahydropyridazin-5-yl, 2,3,4,5-tetrahydropyridazin-6-yl, 3,4,5,6-tetrahydropyridazin-3-yl, 3,4,5,6-tetrahydropyridazin-4-yl, 1,2,5,6-tetrahydropyridazin-3-yl, 1,2,5,6-tetrahydropyridazin-4-yl, 1,2,5,6-tetra-hydropyridazin-5-yl, 1,2,5,6-tetrahydropyridazin-6-yl,

1,2,3,6-tetrahydro-pyridazin-3-yl, 1,2,3,6-tetrahydropyridazin-4-yl, 4H-5,6-dihydro-1,3-oxazin-2-yl, 4H-5,6-dihydro-1,3-oxazin-4-yl, 4H-5,6-dihydro-1,3-oxazin-5-yl, 4H-5,6-dihydro-1,3-oxazin-6-yl, 4H-5,6-dihydro-1,3-thiazin-2-yl, 4H-5,6-dihydro-1,3-thiazin-4-yl, 4H-5,6-dihydro-1,3-thiazin-5-yl, 4H-5,6-dihydro-1,3-thiazin-6-yl, 3,4,5-6-tetrahydropyrimidin-2-yl, 3,4,5,6-tetrahydropyrimidin-4-yl, 3,4,5,6-tetrahydropyrimidin-5-yl, 3,4,5,6-tetrahydropyrimidin-6-yl, 1,2,3,4-tetrahydropyrazin-2-yl, 1,2,3,4-tetrahydropyrazin-5-yl, 1,2,3,4-tetrahydro-pyrimidin-2-yl, 1,2,3,4-tetrahydropyrimidin-4-yl, 1,2,3,4-tetrahydropyrimidin-5-yl, 1,2,3,4-tetrahydropyrimidin-6-yl, 2,3-dihydro-1,4-thiazin-2-yl, 2,3-dihydro-1,4-thiazin-3-yl, 2,3-dihydro-1,4-thiazin-5-yl, 2,3-dihydro-1,4-thiazin-6-yl, 2H-1,3-oxazin-2-yl, 2H-1,3-oxazin-4-yl, 2H-1,3-oxazin-5-yl, 2H-1,3-oxazin-6-yl, 2H-1,3-thiazin-2-yl, 2H-1,3-thiazin-4-yl, 2H-1,3-thiazin-5-yl, 2H-1,3-thiazin-6-yl, 4H-1,3-oxazin-2-yl, 4H-1,3-oxazin-4-yl, 4H-1,3-oxazin-5-yl, 4H-1,3-oxazin-6-yl, 4H-1,3-thiazin-2-yl, 4H-1,3-thiazin-4-yl, 4H-1,3-thiazin-5-yl, 4H-1,3-thiazin-6-yl, 6H-1,3-oxazin-2-yl, 6H-1,3-oxazin-4-yl, 6H-1,3-oxazin-5-yl, 6H-1,3-oxazin-6-yl, 6H-1,3-thiazin-2-yl, 6H-1,3-oxazin-4-yl, 6H-1,3-oxazin-5-yl, 6H-1,3-thiazin-6-yl, 2H-1,4-oxazin-2-yl, 2H-1,4-oxazin-3-yl, 2H-1,4-oxazin-5-yl, 2H-1,4-oxazin-6-yl, 2H-1,4-thiazin-2-yl, 2H-1,4-thiazin-3-yl, 2H-1,4-thiazin-5-yl, 2H-1,4-thiazin-6-yl, 4H-1,4-oxazin-2-yl, 4H-1,4-oxazin-3-yl, 4H-1,4-thiazin-2-yl, 4H-1,4-thiazin-3-yl, 1,4-dihydropyridazin-3-yl, 1,4-dihydropyridazin-4-yl, 1,4-dihydropyridazin-5-yl, 1,4-dihydropyridazin-6-yl, 1,4-dihydropyrazin-2-yl, 1,2-dihydropyrazin-2-yl, 1,2-dihydropyrazin-3-yl, 1,2-dihydropyrazin-5-yl, 1,2-dihydropyrazin-6-yl, 1,4-dihydropyrimidin-2-yl, 1,4-dihydropyrimidin-4-yl, 1,4-dihydropyrimidin-5-yl, 1,4-dihydropyrimidin-6-yl, 3,4-dihydropyrimidin-2-yl, 3,4-dihydropyrimidin-4-yl, 3,4-dihydropyrimidin-5-yl and 3,4-dihydropyrimidin-6-yl;

N-bound, 5-membered, partially unsaturated rings, such as 2,3-dihydro-1H-pyrrol-1-yl, 2,5-dihydro-1H-pyrrol-1-yl, 4,5-dihydro-1H-pyrazol-1-yl, 2,5-dihydro-1H-pyrazol-1-yl, 2,3-dihydro-1H-pyrazol-1-yl, 2,5-dihydroisoxazol-2-yl, 2,3-dihydroisoxazol-2-yl, 2,5-dihydroisothiazol-2-yl, 2,3-dihydroisoxazol-2-yl, 4,5-dihydro-1H-imidazol-1-yl, 2,5-dihydro-1H-imidazol-1-yl, 2,3-dihydro-1H-imidazol-1-yl, 2,3-dihydrooxazol-3-yl and 2,3-dihydrothiazol-3-yl;

N-bound, 6-membered, partially unsaturated rings, such as 1,2,3,4-tetrahydropyridin-1-yl, 1,2,5,6-tetrahydropyridin-1-yl, 1,4-dihydro-pyridin-1-yl, 1,2-dihydropyridin-1-yl, 2H-5,6-dihydro-1,2-oxazin-2-yl, 2H-5,6-dihydro-1,2-thiazin-2-yl, 2H-3,6-dihydro-1,2-oxazin-2-yl, 2H-3,6-dihydro-1,2-thiazin-2-yl, 2H-3,4-dihydro-1,2-oxazin-2-yl, 2H-3,4-dihydro-1,2-thiazin-2-yl, 2,3,4,5-tetrahydropyridazin-2-yl, 1,2,5,6-tetrahydropyridazin-1-yl, 1,2,5,6-tetrahydropyridazin-2-yl, 1,2,3,6-tetrahydropyridazin-1-yl, 3,4,5,6-tetrahydropyrimidin-3-yl, 1,2,3,4-tetrahydropyrazin-1-yl, 1,2,3,4-tetrahydropyrimidin-1-yl, 1,2,3,4-tetrahydropyrimidin-3-yl, 2,3-dihdro-1,4-thiazin-4-yl, 2H-

1,2-oxazin-2-yl, 2H-1,2-thiazin-2-yl, 4H-1,4-oxazin-4-yl, 4H-1,4-thiazin-4-yl, 1,4-dihydropyridazin-1-yl, 1,4-dihydropyrazin-1-yl, 1,2-dihydropyrazin-1-yl, 1,4-dihydropyrimidin-1-yl and 3,4-dihydropyrimidin-3-yl.

C-bound, 5-membered, heteroaromatic rings, such as
2-furyl, 3-furyl, 2-thienyl, 3-thienyl, pyrrol-2-yl, pyrrol-3-yl, pyrazol-3-yl, pyrazol-4-yl, isoxazol-3-yl, isoxazol-4-yl, isoxazol-5-yl, isothiazol-3-yl, isothiazol-4-yl, isothiazol-5-yl, imidazol-2-yl, imidazol-4-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, 1,2,3-oxadiazol-4-yl, 1,2,3-oxadiazol-5-yl, 1,2,4-oxadiazol-3-yl, 1,2,4,-oxadiazol-5-yl, 1,3,4-oxadiazol-2-yl, 1,2,3-thiadiazol-4-yl, 1,2,3-thiadiazol-5-yl, 1,2,4-thiadiazol-3-yl, 1,2,4-thiadiazol-5-yl, 1,3,4-thiadiazolyl-2-yl, 1,2,3-triazol-4-yl, 1,2,4-triazol-3-yl and tetrazol-5-yl.

C-bound, 6-membered, heteroaromatic rings, such as
pyridin-2-yl, pyridin-3-yl, pyridin-4-yl (4-pyridyl), pyridazin-3-yl, pyridazin-4-yl, pyrimidin-2-yl, pyrimidin-4-yl, pyrimidin-5-yl, pyrazin-2-yl, 1,3,5-triazin-2-yl, 1,2,4-triazin-3-yl, 1,2,4-triazin-5-yl, 1,2,4-triazin-6-yl and 1,2,4,5-tetrazin-3-yl.

N-bound, 5-membered, heteroaromatic rings, such as
pyrrol-1-yl, pyrazol-1-yl, imidazol-1-yl, 1,2,3-triazol-1-yl, 1,2,4-triazol-1-yl and tetrazol-1-yl.

Heterocyclyl also includes bicyclic heterocycles, which comprise one of the described 5- or 6-membered heterocyclic rings and a further anellated, saturated or unsaturated or aromatic carbocycle, such as a benzene, cyclohexane, cyclohexene or cyclohexadiene ring, or a futher anellated 5- or 6-membered heterocyclic ring, this heterocyclic ring being saturated or unsaturated or aromatic. These include quinolinyl, isoquinolinyl, indolyl, indolizinyl, isoindolyl, indazolyl, benzofuryl, benzthienyl, benzo[b]thiazolyl, benzoxazolyl, benzthiazolyl and benzimidazolyl. Examples of 5- or 6-membered heteroaromatic compounds comprising an anellated cycloalkenyl ring include dihydroindolyl, dihydroindolizinyl, dihydroisoindolyl, dihydrochinolinyl, dihydroisoquinolinyl, chromenyl and chromanyl.

With respect to their capability of inhibiting glycine transporter 1, the variables R^1, R^2, R^3, R^4, R^5, R^{6a}, R^{6b}, R^{6c}, R^{6d}, R^{6e}, R^7, R^8, R^9 and R^{10} preferably have the following meanings which, when taken alone or in combination, represent particular embodiments of the 4-benzylaminoquinolines of the formula (I).

R^1 is hydrogen, C_1-C_6-alkyl, or C_6-C_{12}-aryl. Preferably, R^1 is hydrogen.

R^2 and R^3 are independently hydrogen, C_1-C_6-alkyl, substituted C_1-C_4-alkyl, C_3-C_{12}-cycloalkyl, C_6-C_{12}-aryl, aminocarbonyl, amino, or optionally substituted C_3-C_{12}-heterocyclyl.

More preferably, R^2 and R^3 are independently hydrogen, C_1-C_6-alkyl (e.g. methyl), substituted C_1-C_4-alkyl, C_3-C_{12}-cycloalkyl (e.g. cyclopropyl), aminocarbonyl (e.g. aminocarbonyl), or optionally substituted C_3-C_{12}-heterocyclyl (e.g. piperidin-2-yl, N-methylpiperidin-2-yl, N-allylpiperidin-2-yl, pyridin-4-yl, N-methylimidazol-2-yl). Preferred alkyl substitutents are C_1-C_6-alkoxy, amino (e.g. aminomethyl), C_1-C_6-alkylamino (e.g. isopropylaminomethyl), di-C_1-C_6-alkylamino (e.g. dimethylaminomethyl), (C_6-C_{12}-aryl-C_1-C_4-alkyl)amino (e.g. benzylaminomethyl), C_1-C_6-alkylcarbonylamino, C_1-C_6-alkylsulfonylamino or C_3-C_{12}-heterocyclyl (e.g. N-pyrrolidinylmethyl, N-piperidinylmethyl, N-morpholinylmethyl). More preferred alkyl substitutents are amino (e.g. aminomethyl), C_1-C_6-alkylamino (e.g. isopropylaminomethyl), di-C_1-C_6-alkylamino (e.g. dimethylaminomethyl), (C_6-C_{12}-aryl-C_1-C_4-alkyl)amino (e.g. benzylaminomethyl) or C_3-C_{12}-heterocyclyl (e.g. N-pyrrolidinylmethyl, N-piperidinylmethyl, N-morpholinylmethyl). Preferred heterocyclyl substituents are C_1-C_4-alkyl and C_2-C_4-alkenyl.

According to a particular embodiment, R^2 is hydrogen or C_1-C_3-alkyl, in particular hydrogen. R^3 is defined as above. Preferably, R^3 is C_1-C_2-alkyl substituted with amino (e.g. aminomethyl), C_1-C_4-alkylamino (e.g. isopropylaminomethyl), di-C_1-C_4-alkylamino (e.g. dimethylaminomethyl), (C_6-C_{12}-aryl-C_1-C_2-alkyl)amino (e.g. benzylaminomethyl) or C_3-C_{12}-heterocyclyl (e.g. N-pyrrolidinylmethyl, N-piperidinylmethyl, N-morpholinylmethyl), or R^3 is optionally substituted C_3-C_{12}-heterocyclyl (e.g. piperidin-2-yl, N-methylpiperidin-2-yl, N-allylpiperidin-2-yl). More preferably, R^3 is aminomethyl (e.g. aminomethyl), C_1-C_4-alkylaminomethyl (e.g. isopropylaminomethyl), di-C_1-C_4-alkylaminomethyl (e.g. dimethylaminomethyl), (C_6-C_{12}-aryl-C_1-C_2-alkyl)aminomethyl (e.g. benzylaminomethyl) or C_3-C_{12}-heterocyclylmethyl (e.g. N-pyrrolidinylmethyl, N-piperidinylmethyl, N-morpholinylmethyl), or R^3 is piperidinyl or piperidinyl substituted with C_1-C_4-alkyl or C_2-C_4-allyl.

R^4 is C_1-C_6-alkyl, halogenated C_1-C_6-alkyl, C_1-C_6-alkoxy, di-(C_1-C_6-alkyl)amino, C_6-C_{12}-arylamino or sulfonylamino.

More preferably, R^4 is methyl or dimethylamino.

R^5 is hydrogen, halogen, C_1-C_6-alkyl, hydroxy, C_1-C_6-alkoxy, substituted C_1-C_4-alkoxy, C_6-C_{12}-aryloxy, C_6-C_{12}-heteroaryloxy, C_1-C_6-alkylthio, C_1-C_6-alkylsulfinyl, C_1-C_6-alkylsulfonyl, aminosulfonyl, C_1-C_6-alkylaminosulfonyl, di-C_1-C_6-alkylaminosulfonyl, (optionally substituted C_6-C_{12}-aryl)aminosulfonyl, amino, substituted amino or optionally substituted C_3-C_{12}-

heterocyclyl. Preferred aryl substituents are halogen, in particular fluoro, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, in particular ethoxy, and C_1-C_4-haloalkoxy, in particular chloromethoxy. Preferred heterocyclyl substituents are halogen, in particular fluoro and chloro, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, in particular ethoxy, and C_1-C_4-haloalkoxy, in particular chloromethoxy.

According to a particular embodiment, R^5 is hydrogen or halogen (e.g. fluoro, chloro), preferably hydrogen.

According to a further particular embodiment, R^5 is hydroxy (e.g. hydroxy), C_1-C_6-alkoxy (e.g. methoxy, n-propyloxy, isopropyloxy, 2-methylpropyloxy), halogenated C_1-C_4-alkoxy (e.g. trifluoromethoxy), C_6-C_{12}-aryloxy (e.g. phenoxy) or C_6-C_{12}-heteroaryloxy (e.g. pyridin-2-yloxy), preferably C_1-C_2-alkoxy.

According to a further particular embodiment, R^5 is a group of the formula (II):

$$—A^1—A^2—A^3—R^{5a} \qquad (II)$$

wherein

A^1 is O, NR^{5b};

A^2 is optionally substituted C_1-C_4-alkylene;

A^3 is O, NR^{5b};

R^{5a} is hydrogen, C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl, C_6-C_{12}-arylcarbonyl, C_1-C_6-alkoxycarbonyl, halogenated C_1-C_4-alkoxycarbonyl, C_6-C_{12}-aryloxycarbonyl, C_1-C_6-alkylaminocarbonyl, (halogenated C_1-C_4-alkyl)aminocarbonyl, C_6-C_{12}-arylaminocarbonyl, C_1-C_6-alkylsulfonyl, (halogenated C_1-C_6-alkyl)sulfonyl, C_6-C_{12}-arylsulfonyl, (C_6-C_{12}-aryl-C_1-C_4-alkyl)sulfonyl, C_3-C_{12}-heterocyclylsulfonyl, C_6-C_{12}-aryl; and

R^{5b} is hydrogen, C_1-C_4-alkyl; or

R^{5a} and R^{5b}
together with the nitrogen atom to which they are attached are C_3-C_{12}-heterocyclyl.

Substituted C_1-C_4-alkylene is preferably C_1-C_4-alkylene substituted with halogen, C_1-C_4-alkyl or C_1-C_3-alkoxy.

A^1 in formula (II) is preferably oxygen.

A^2 in formula (II) is preferably C_1-C_2-alkylene.

A^3 in formula (II) is preferably NR^{5b}.

R^{5a} and R^{5b} in formula (II) are independently as defined above. R^{5a} is preferably C_1-C_4-alkylsulfonyl. R^{5b} is preferably hydrogen.

According to a further particular embodiment, R^5 is substituted C_1-C_4-alkoxy, such as C_1-C_4-alkoxy substituted with C_1-C_6-alkoxy (e.g. 2-methoxyethoxy), amino (e.g. 2-aminoethoxy), di-C_1-C_6-alkylamino (e.g. 2-(dimethylamino)ethoxy), C_1-C_6-alkylcarbonylamino (e.g. 2-(methylcarbonylamino)ethoxy, 2-(isopropylcarbonylamino)ethoxy), C_6-C_{12}-arylcarbonylamino (e.g. 2-(benzoylamino)ethoxy), C_1-C_6-alkoxycarbonylamino (e.g. 2-(t-butyloxycarbonylamino)ethoxy), C_3-C_{12}-heterocyclyl (e.g. 2-(N-pyrrolidinyl)ethoxy, 2-(N-morpholinyl)ethoxy, 2-(N-imidazolyl)ethoxy), C_1-C_6-alkylsulfonylamino (e.g. 2-(methylsulfonylamino)ethoxy, 2-(ethylsulfonylamino)ethoxy, 2-[(2-methylpropyl)sulfonylamino]ethoxy), (halogenated C_1-C_4-alkyl)sulfonylamino (e.g. 2-(trifluoromethylsulfonylamino)ethoxy), C_6-C_{12}-arylsulfonylamino (e.g. 2-(phenylsulfonylamino)ethoxy, 2-(naphthylsulfonylamino)ethoxy), (C_6-C_{12}-aryl-C_1-C_4-alkyl)sulfonylamino (e.g. 2-(benzylsulfonylamino)ethoxy), C_3-C_{12}-heterocyclylsulfonylamino (e.g. 2-(pyridin-3-yl-sulfonylamino)ethoxy) or C_6-C_{12}-aryl (e.g. benzyloxy); preferably, substituted C_1-C_2-alkoxy, such as C_1-C_2-alkoxy substituted with C_1-C_4-alkoxy (e.g. 2-methoxyethoxy), amino (e.g. 2-aminoethoxy), di-C_1-C_4-alkylamino (e.g. 2-(dimethylamino)ethoxy), C_1-C_4-alkylcarbonylamino (e.g. 2-(methylcarbonylamino)ethoxy, 2-(isopropylcarbonylamino)ethoxy), C_6-C_{12}-arylcarbonylamino (e.g. 2-(benzoylamino)ethoxy), C_1-C_4-alkoxycarbonylamino (e.g. 2-(t-butyloxycarbonylamino)ethoxy), C_3-C_{12}-heterocyclyl (e.g. 2-(N-pyrrolidinyl)ethoxy, 2-(N-morpholinyl)ethoxy, 2-(N-imidazolyl)ethoxy), C_1-C_4-alkylsulfonylamino (e.g. 2-(methylsulfonylamino)ethoxy, 2-(ethylsulfonylamino)ethoxy, 2-[(2-methylpropyl)sulfonylamino]ethoxy), (halogenated C_1-C_4-alkyl)sulfonylamino (e.g. 2-(trifluoromethylsulfonylamino)ethoxy), C_6-C_{12}-arylsulfonylamino (e.g. 2-(phenylsulfonylamino)ethoxy, 2-(naphthylsulfonylamino)ethoxy), (C_6-C_{12}-aryl-C_1-C_2-alkyl)sulfonylamino (e.g. 2-(benzylsulfonylamino)ethoxy), C_3-C_{12}-heterocyclylsulfonylamino (e.g. 2-(pyridin-3-yl-sulfonylamino)ethoxy), or C_6-C_{12}-aryl (e.g. benzyloxy); and even more preferably substituted ethoxy, such as C_1-C_6-alkoxy-ethoxy (e.g. 2-

methoxyethoxy), amino-ethoxy (e.g. 2-aminoethoxy), di-C_1-C_6-alkylamino-ethoxy (e.g. 2-(dimethylamino)ethoxy), C_1-C_6-alkylcarbonylamino-ethoxy (e.g. 2-(methylcarbonyl-amino)ethoxy, 2-(isopropylcarbonylamino)ethoxy), C_6-C_{12}-arylcarbonylamino-ethoxy (e.g. 2-(benzoylamino)ethoxy), C_1-C_6-alkoxycarbonylamino-ethoxy (e.g. 2-(t-butyloxycarbonylamino)ethoxy), C_3-C_{12}-heterocyclyl-ethoxy (e.g. 2-(N-pyrrolidinyl)ethoxy, 2-(N-morpholinyl)ethoxy, 2-(N-imidazolyl)ethoxy), C_1-C_6-alkylsulfonylamino-ethoxy (e.g. 2-(methylsulfonylamino)ethoxy, 2-(ethylsulfonylamino)ethoxy, 2-[(2-methylpropyl)sulfonylamino]ethoxy), (halogenated C_1-C_4-alkyl)sulfonylamino-ethoxy (e.g. 2-(trifluoromethylsulfonylamino)ethoxy), C_6-C_{12}-arylsulfonylamino-ethoxy (e.g. 2-(phenylsulfonylamino)ethoxy, 2-(naphthylsulfonylamino)ethoxy), (C_6-C_{12}-aryl-C_1-C_4-alkyl)sulfonylamino-ethoxy (e.g. 2-(benzylsulfonylamino)ethoxy), C_3-C_{12}-heterocyclylsulfonylamino-ethoxy (e.g. 2-(pyridin-3-yl-sulfonylamino)ethoxy).

According to a further particular embodiment, R^5 is a radical that is bound to the quinoline nucleus via a sulphur atom, such as C_1-C_6-alkylthio (e.g. methylthio), C_1-C_6-alkylsulfinyl (e.g. methylsulfinyl), C_1-C_6-alkylsulfonyl (e.g. methylsulfonyl), aminosulfonyl (e.g. amino-sulfonyl), C_1-C_6-alkylaminosulfonyl (e.g. isopropylaminosulfonyl), di-C_1-C_6-alkylaminosulfonyl (e.g. dimethylaminosulfonyl) or (optionally substituted C_6-C_{12}-aryl)aminosulfonyl (e.g. (4-chlorophenyl)aminosulfonyl).

According to a further particular embodiment, R^5 is amino (e.g. amino).

According to a further particular embodiment, R^5 is a substituted amino group, such as C_1-C_6-alkylamino (e.g. methylamino, ethylamino), di-C_1-C_6-alkylamino (e.g. dimethylamino), C_1-C_6-alkylcarbonylamino (e.g. methylcarbonylamino, isopropylcarbonylamino), C_6-C_{12}-arylcarbonylamino (e.g. phenylcarbonylamino), C_1-C_6-alkylsulfonylamino (e.g. methylsulfonylamino), C_6-C_{12}-arylsulfonylamino (e.g. phenylsulfonylamino), di-(C_1-C_6-alkylsulfonyl)amino (e.g. di(methylsulfonyl)amino), optionally substituted C_3-C_{12}-heterocyclyl (e.g. N-pyrrolidinyl, N-piperazinyl, 4-[(4-methylphenyl)sulfonyl]piperazinyl, morpholin-1-yl). Preferred heterocyclyl substituents are halogen, in particular fluoro and chloro, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, in particular ethoxy, and C_1-C_4-haloalkoxy, in particular chloromethoxy.

R^{6a}, R^{6b}, R^{6c}, R^{6d}, R^{6e} are independently hydrogen, halogen, C_1-C_6-alkyl, halogenated C_1-C_4-alkyl, C_1-C_4-hydroxyalkyl, C_1-C_6-alkoxycarbonyl, (halogenated C_1-C_4-alkoxy)carbonyl, cyano, C_1-C_6-alkoxy, halogenated C_1-C_4-alkoxy, optionally substituted C_6-C_{12}-aryl, C_1-C_4-alkylthio, (halogenated C_1-C_4-alkyl)thio, nitro, amino, C_1-C_6-alkylamino, (halogenated C_1-C_6-alkyl)amino, di-C_1-C_6-alkylamino, di-(halogenated C_1-C_6-alkyl)amino, C_1-C_6-

alkylcarbonylamino, (halogenated C_1-C_4-alkyl)carbonylamino, C_1-C_6-alkylsulfonylamino, (halogenated C_1-C_4-alkyl)sulfonylamino or C_6-C_{12}-arylsulfonylamino.

R^{6a} is preferably hydrogen, halogen (e.g. fluoro, bromo, chloro), C_1-C_6-alkyl (e.g. methyl), halogenated C_1-C_4-alkyl (e.g. trifluoromethyl), C_1-C_4-hydroxyalkyl, cyano, C_1-C_6-alkoxy (e.g. methoxy), optionally substituted C_6-C_{12}-aryl (e.g. 3,5-dichlorophenyl), amino, C_1-C_6-alkylamino, (halogenated C_1-C_6-alkyl)amino, di-C_1-C_6-alkylamino, di-(halogenated C_1-C_6-alkyl)amino, C_1-C_6-alkylcarbonylamino, (halogenated C_1-C_4-alkyl)carbonylamino, C_1-C_6-alkylsulfonylamino, (halogenated C_1-C_4-alkyl)sulfonylamino or C_6-C_{12}-arylsulfonylamino, more preferably hydrogen, halogen (e.g. fluoro, bromo, chloro), C_1-C_6-alkyl (e.g. methyl), halogenated C_1-C_4-alkyl (e.g. trifluoromethyl), C_1-C_6-alkoxy (e.g. methoxy) or optionally substituted C_6-C_{12}-aryl (e.g. 3,5-dichlorophenyl). Preferred aryl substituents are halogen, in particular fluoro and chloro, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, in particular ethoxy, and C_1-C_4-haloalkoxy, in particular chloromethoxy.

R^{6b} is preferably hydrogen, halogen (e.g. fluoro, chloro), C_1-C_6-alkyl (e.g. methyl), halogenated C_1-C_4-alkyl (e.g. trifluoromethyl), C_1-C_4-hydroxyalkyl, cyano, C_1-C_6-alkoxy (e.g. methoxy), nitro (e.g. nitro), amino, C_1-C_6-alkylamino, (halogenated C_1-C_6-alkyl)amino, di-C_1-C_6-alkylamino, di-(halogenated C_1-C_6-alkyl)amino, C_1-C_6-alkylcarbonylamino, (halogenated C_1-C_4-alkyl)carbonylamino, C_1-C_6-alkylsulfonylamino, (halogenated C_1-C_4-alkyl)sulfonylamino or C_6-C_{12}-arylsulfonylamino, more preferably hydrogen, halogen (e.g. fluoro, chloro), C_1-C_6-alkyl (e.g. methyl), halogenated C_1-C_4-alkyl (e.g. trifluoromethyl), C_1-C_6-alkoxy (e.g. methoxy) or nitro (e.g. nitro).

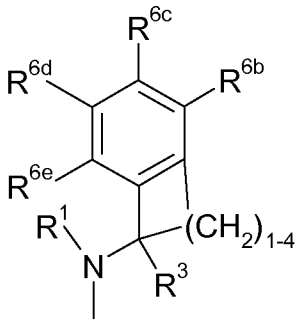
R^{6c} is preferably hydrogen, halogen (e.g. fluoro, bromo, chloro), C_1-C_6-alkyl (e.g. methyl, t-butyl), halogenated C_1-C_4-alkyl (e.g. trifluoromethyl), C_1-C_4-hydroxyalkyl, C_1-C_6-alkoxycarbonyl (e.g. methoxycarbonyl), cyano, C_1-C_6-alkoxy (e.g. methoxy), halogenated C_1-C_4-alkoxy (e.g. trifluoromethoxy), halogenated C_1-C_4-alkylthio (e.g. trifluoromethylthio), nitro (e.g. nitro), amino, C_1-C_6-alkylamino, (halogenated C_1-C_6-alkyl)amino, di-C_1-C_6-alkylamino, di-(halogenated C_1-C_6-alkyl)amino, C_1-C_6-alkylcarbonylamino, (halogenated C_1-C_4-alkyl)carbonylamino, C_1-C_6-alkylsulfonylamino, (halogenated C_1-C_4-alkyl)sulfonylamino or C_6-C_{12}-arylsulfonylamino, more preferably hydrogen, halogen (e.g. fluoro, bromo, chloro), C_1-C_6-alkyl (e.g. methyl, t-butyl), halogenated C_1-C_4-alkyl (e.g. trifluoromethyl), C_1-C_6-alkoxycarbonyl (e.g. methoxycarbonyl), C_1-C_6-alkoxy (e.g. methoxy), halogenated C_1-C_4-alkoxy (e.g. trifluoromethoxy), halogenated C_1-C_4-alkylthio (e.g. trifluoromethylthio) or nitro (e.g. nitro).

R^{6d} is preferably hydrogen, halogen (e.g. chloro), C_1-C_6-alkyl (e.g. methyl), halogenated C_1-C_4-alkyl, C_1-C_4-hydroxyalkyl, cyano, C_1-C_6-alkoxy (e.g. methoxy), nitro, amino, C_1-C_6-

alkylamino, (halogenated C_1-C_6-alkyl)amino, di-C_1-C_6-alkylamino, di-(halogenated C_1-C_6-alkyl)amino, C_1-C_6-alkylcarbonylamino, (halogenated C_1-C_4-alkyl)carbonylamino, C_1-C_6-alkylsulfonylamino, (halogenated C_1-C_4-alkyl)sulfonylamino or C_6-C_{12}-arylsulfonylamino, more preferably hydrogen, halogen (e.g. chloro), C_1-C_6-alkyl (e.g. methyl) or C_1-C_6-alkoxy (e.g. methoxy).

R^{6e} is preferably hydrogen, halogen, C_1-C_6-alkyl, halogenated C_1-C_4-alkyl, C_1-C_4-hydroxyalkyl, cyano, C_1-C_6-alkoxy, optionally substituted C_6-C_{12}-aryl, amino, C_1-C_6-alkylamino, (halogenated C_1-C_6-alkyl)amino, di-C_1-C_6-alkylamino, di-(halogenated C_1-C_6-alkyl)amino, C_1-C_6-alkylcarbonylamino, (halogenated C_1-C_4-alkyl)carbonylamino, C_1-C_6-alkylsulfonylamino, (halogenated C_1-C_4-alkyl)sulfonylamino or C_6-C_{12}-arylsulfonylamino, more preferably hydrogen.

Alternatively, R^{6a} and R^2 together are optionally substituted C_1-C_4-alkylene, preferably unsubstituted C_1-C_4-alkylene (e.g. ethylene), thereby forming a group of the formual (III):

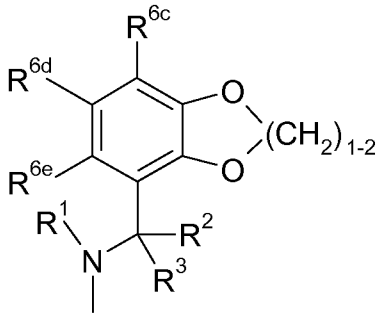


(III)

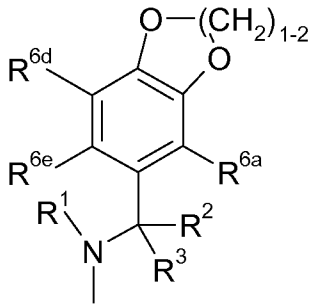
wherein R^1, R^3, R^{6b}, R^{6c}, R^{6d}, R^{6e} are as defined above (the group of formula (III) is bound to the quinoline nucleus).

Alternatively, R^{6a} and R^{6b} or R^{6b} and R^{6c}, preferably R^{6a} and R^{6b}, together with the carbon atoms to which they are attached form an anellated aryl ring, preferably an anellated C_5-C_{10}-aryl ring (e.g. benzene), R^{6a} or R^{6c}, and R^{6d} and R^{6e} being as defined herein.

Alternatively, R^{6a} and R^{6b} or R^{6b} and R^{6c}, preferably R^{6b} and R^{6c}, together are C_1-C_2-alkylenedioxo (e.g. methylenedioxo), thereby forming a group of the formual (IVa) or (IVb):



(IVa)



(IVb)

wherein R^1, R^2, R^3, R^{6a} or R^{6c}, R^{6d} and R^{6e} are as defined above (the group of formula (IIIa) or (IIIb) is bound to the quinoline nucleus).

According to a particular embodiment, at least one of R^{6a}, R^{6b}, R^{6c}, R^{6d}, R^{6e} is different from hydrogen. Preferably, at least one of R^{6a}, R^{6b}, R^{6c}, R^{6d}, R^{6e} is halogen (e.g. fluoro, bromo, chloro), C_1-C_4-hydroxyalkyl, cyano or nitro (e.g. nitro). More preferably, at least one of R^{6a}, R^{6b}, R^{6c}, R^{6d}, R^{6e} is halogen (e.g. fluoro, bromo, chloro) or nitro (e.g. nitro).

According to a further particular embodiment, at least one of R^{6a}, R^{6c} is different from hydrogen. Preferably, at least one of R^{6a}, R^{6c} is halogen (e.g. fluoro, bromo, chloro), C_1-C_4-hydroxyalkyl, cyano or nitro (e.g. nitro). More preferably, at least one of R^{6a}, R^{6c} is halogen (e.g. fluoro, bromo, chloro) or nitro (e.g. nitro).

According to a further particular embodiment, at least one of R^{6b}, R^{6c}, R^{6d} is different from hydrogen. Preferably, at least one of R^{6b}, R^{6c}, R^{6d} is halogen (e.g. fluoro, bromo, chloro), C_1-C_4-hydroxyalkyl; cyano or nitro (e.g. nitro). More preferably, at least one of R^{6b}, R^{6c}, R^{6d} is halogen (e.g. fluoro, bromo, chloro) or nitro (e.g. nitro).

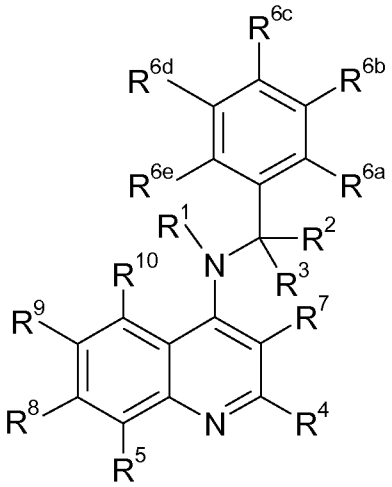
According to a further particular embodiment, at least one of R^{6b}, R^{6c} is different from hydrogen. Preferably, at least one of R^{6b}, R^{6c} is halogen (e.g. fluoro, bromo, chloro), C_1-C_4-hydroxyalkyl, cyano or nitro (e.g. nitro). More preferably, at least one of R^{6b}, R^{6c} is halogen (e.g. fluoro, bromo, chloro) or nitro (e.g. nitro).

According to a further particular embodiment, R^{6c} is different from hydrogen. Preferably, R^{6c} is halogen (e.g. fluoro, bromo, chloro), C_1-C_4-hydroxyalkyl; cyano or nitro (e.g. nitro). More preferably, R^{6c} is halogen (e.g. fluoro, bromo, chloro) or nitro (e.g. nitro).

According to a further particular embodiment, R^{6a}, R^{6e} are both hydrogen.

R^7, R^8, R^9, R^{10} are independently hydrogen, halogen, C_1-C_6-alkyl or C_1-C_6-alkoxy. Preferably, R^7, R^8, R^9, R^{10} are all hydrogen.

4-Benzylaminoquinoline of the formula (I)



(I)

wherein

R^1 is hydrogen;

R^2 is hydrogen, C_1-C_4-alkyl (e.g. methyl), amino-C_1-C_4-alkyl (e.g. aminomethyl), C_1-C_6-alkylamino-C_1-C_4-alkyl (e.g. isopropylaminomethyl), di-C_1-C_6-alkylamino-C_1-C_4-alkyl (e.g. dimethylaminomethyl), (C_6-C_{12}-aryl-C_1-C_4-alkyl)amino-C_1-C_4-alkyl (e.g. benzylaminomethyl), C_3-C_{12}-heterocyclyl-C_1-C_4-alkyl (e.g. N-pyrrolidinylmethyl, N-piperidinylmethyl, N-morpholinylmethyl), C_3-C_{12}-cycloalkyl (e.g. cyclopropyl), C_6-C_{12}-aryl (e.g. phenyl), aminocarbonyl (e.g. aminocarbonyl), C_3-C_{12}-heterocyclyl (e.g. piperidin-2-yl, N-methylpiperidin-2-yl, N-allylpiperidin-2- yl, pyridin-4-yl or N-methylimidazol-2-yl);

R^3 is hydrogen;

R^4 is methyl or dimethylamino;

R^5 is hydrogen, halogen (e.g. fluoro, chloro), C_1-C_6-alkyl (e.g. methyl), hydroxy (e.g. hydroxy), C_1-C_6-alkoxy (e.g. methoxy, n-propyloxy, isopropyloxy, 2-methyl-propyloxy), halogenated C_1-C_4-alkoxy (e.g. trifluoromethoxy), C_1-C_6-alkoxy-C_1-C_4-alkoxy (e.g. 2-methoxyethoxy), amino-C_1-C_4-alkoxy (e.g. 2-aminoethoxy), di-C_1-C_6-alkylamino-C_1-C_4-alkoxy (e.g. 2-(dimethylamino)ethoxy), C_1-C_6-alkylcarbonylamino-C_1-C_4-alkoxy (e.g. 2-(methylcarbonylamino)ethoxy, 2-(isopropylcarbo-

nylamino)ethoxy), (C_6-C_{12}-arylcarbonylamino-C_1-C_4-alkoxy (e.g. 2-(benzoylamino)ethoxy), C_1-C_6-alkoxycarbonylamino-C_1-C_4-alkoxy (e.g. 2-(t-butyloxycarbonylamino)ethoxy), C_3-C_{12}-heterocyclyl-C_1-C_4-alkoxy (e.g. 2-(N-pyrrolidinyl)ethoxy, 2-(N-morpholinyl)ethoxy, 2-(N-imidazolyl)ethoxy), C_1-C_6-alkylsulfonylamino-C_1-C_4-alkoxy (e.g. 2-(methylsulfonylamino)ethoxy, 2-(ethylsulfonylamino)ethoxy, 2-[(2-methylpropyl)sulfonylamino]ethoxy), (halogenated C_1-C_4-alkyl)sulfonylamino-C_1-C_4-alkoxy (e.g. 2-(trifluoromethylsulfonylamino)ethoxy), C_6-C_{12}-arylsulfonylamino-C_1-C_4-alkoxy (e.g. 2-(phenylsulfonylamino)ethoxy, 2-(naphthylsulfonylamino)ethoxy), (C_6-C_{12}-aryl-C_1-C_4-alkyl)sulfonylamino-C_1-C_4-alkoxy (e.g. 2-(benzylsulfonylamino)ethoxy), C_3-C_{12}-heterocyclylsulfonylamino-C_1-C_4-alkoxy (e.g. 2-(pyridin-3-yl-sulfonylamino)ethoxy), C_6-C_{12}-aryl-C_1-C_4-alkoxy (e.g. benzyloxy), C_6-C_{12}-aryloxy (e.g. phenoxy), C_6-C_{12}-heteroaryloxy (e.g. pyridin-2-yloxy), C_1-C_6-alkylthio (e.g. methylthio), C_1-C_6-alkylsulfinyl (e.g. methylsulfinyl), C_1-C_6-alkylsulfonyl (e.g. methylsulfonyl), aminosulfonyl (e.g. aminosulfonyl), C_1-C_6-alkylaminosulfonyl (e.g. isopropylaminosulfonyl), di-C_1-C_6-alkylaminosulfonyl (e.g. dimethylaminosulfonyl), (optionally substituted C_6-C_{12}-aryl)aminosulfonyl (e.g. (4-chlorophenyl)aminosulfonyl), amino (e.g. amino), C_1-C_6-alkylamino (e.g. methylamino, ethylamino), di-C_1-C_6-alkylamino (e.g. dimethylamino), C_1-C_6-alkylcarbonylamino (e.g. methylcarbonylamino, isopropylcarbonylamino), C_6-C_{12}-arylcarbonylamino (e.g. phenylcarbonylamino), C_1-C_6-alkylsulfonylamino (e.g. methylsulfonylamino), C_6-C_{12}-arylsulfonylamino (e.g. phenylsulfonylamino), di-(C_1-C_6-alkylsulfonyl)amino (e.g. di(methylsulfonyl)amino), optionally substituted C_3-C_{12}-heterocyclyl (e.g. N-pyrrolidinyl, N-piperazinyl or 4-[(4-methylphenyl)sulfonyl]piperazinyl, morpholin-1-yl);

R^{6a}, R^{6e}

are hydrogen;

R^{6b}, R^{6c}, R^{6d}

are indpendently hydrogen, halogen (e.g. fluoro, bromo, chloro), C_1-C_6-alkyl (e.g. methyl, t-butyl), halogenated C_1-C_4-alkyl (e.g. trifluoromethyl), C_1-C_6-alkoxycarbonyl (e.g. methoxycarbonyl), C_1-C_6-alkoxy (e.g. methoxy), halogenated C_1-C_4-alkoxy (e.g. trifluoromethoxy), halogenated C_1-C_4-alkylthio (e.g. trifluoromethylthio) or nitro (e.g. nitro), at least one of R^{6b}, R^{6c}, R^{6d} being different from hydrogen, and

R^7, R^8, R^9, R^{10}

are all hydrogen,

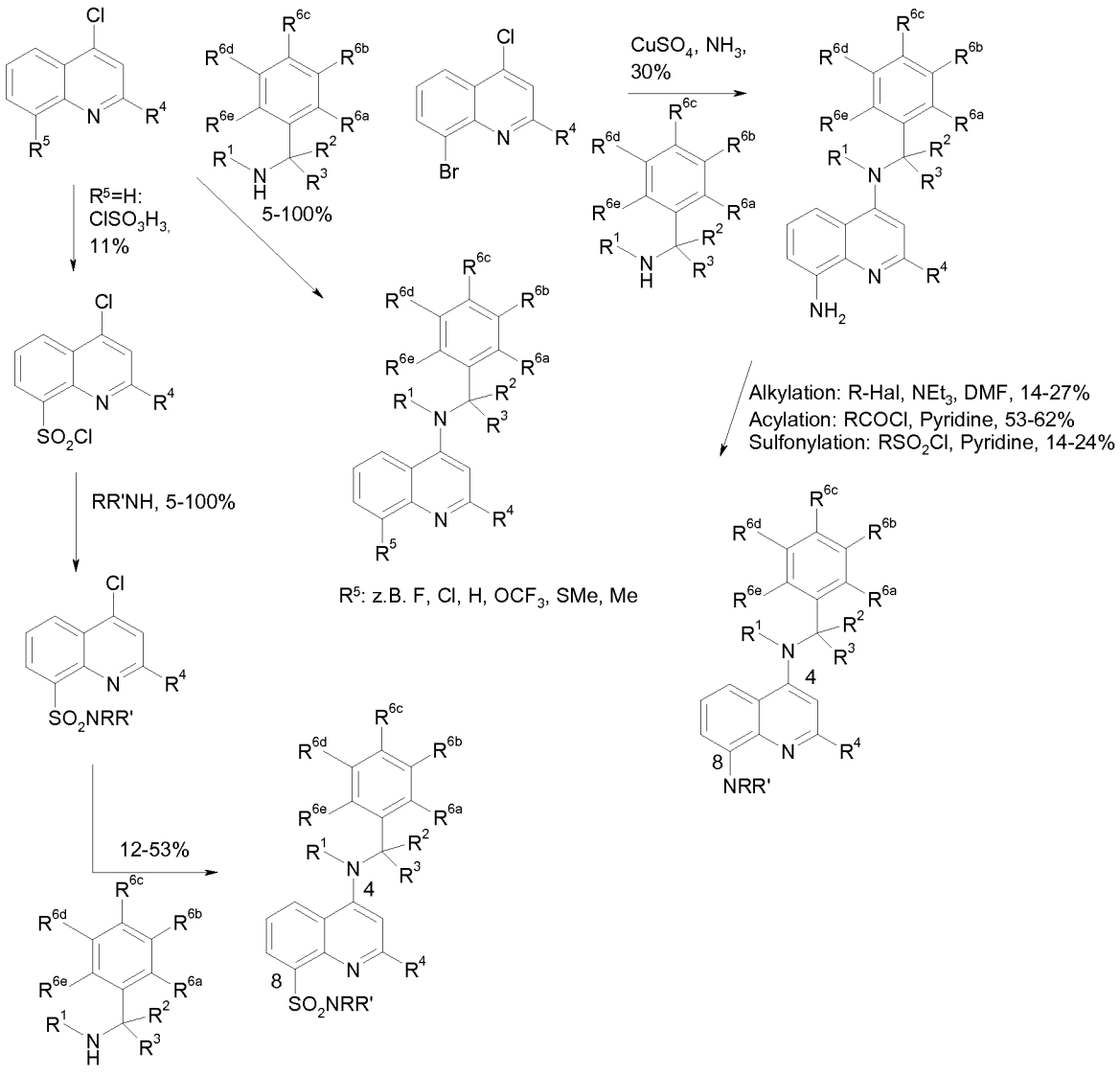
or a physiologically tolerated acid addition salt (e.g. trifluoroacetate, bromide, cloride) thereof, are particularly preferred compounds of the present invention.

Particular compounds of the present invention are the 4-benzylaminoquinolines disclosed in examples 1 to 96 and physiologically tolerated acid addition salts therof.

The compounds of the formula (I) can be prepared by analogy to methods which are well known in the art. A suitable method for the preparation of compounds of formula (I) is outlined in the following schemes.

The process depicted in scheme 1 is useful for obtaining 4-benzylaminochinolines having *N*-alkyl, *N*-aryl, amide or sulfonamide radicals in 8-position.

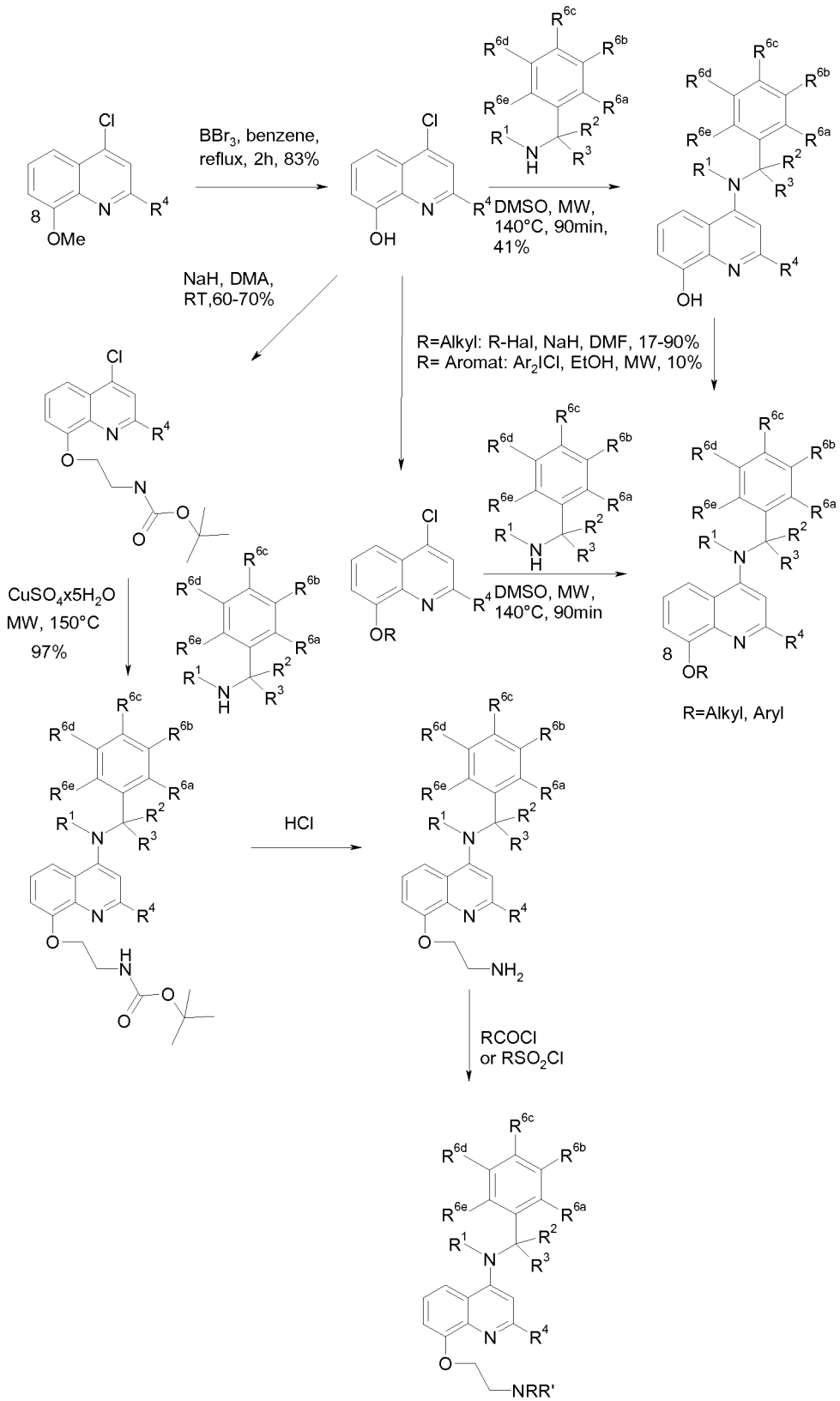
Scheme 1:



In scheme 1, the variables R^1, R^2, R^3, R^4, R^5, R^{6a}, R^{6b}, R^{6c}, R^{6d}, R^{6e} are as defined herein (unless indicated otherwise). Hal is chlorine or bromine. R, R' are independently hydrogene, C_1-C_6-alkyl or optionally substituted C_6-C_{12}-aryl as defined herein.

The process depicted in scheme 2 is useful for obtaining 4-benzylaminochinolines having ether radicals in 8-position.

Scheme 2:

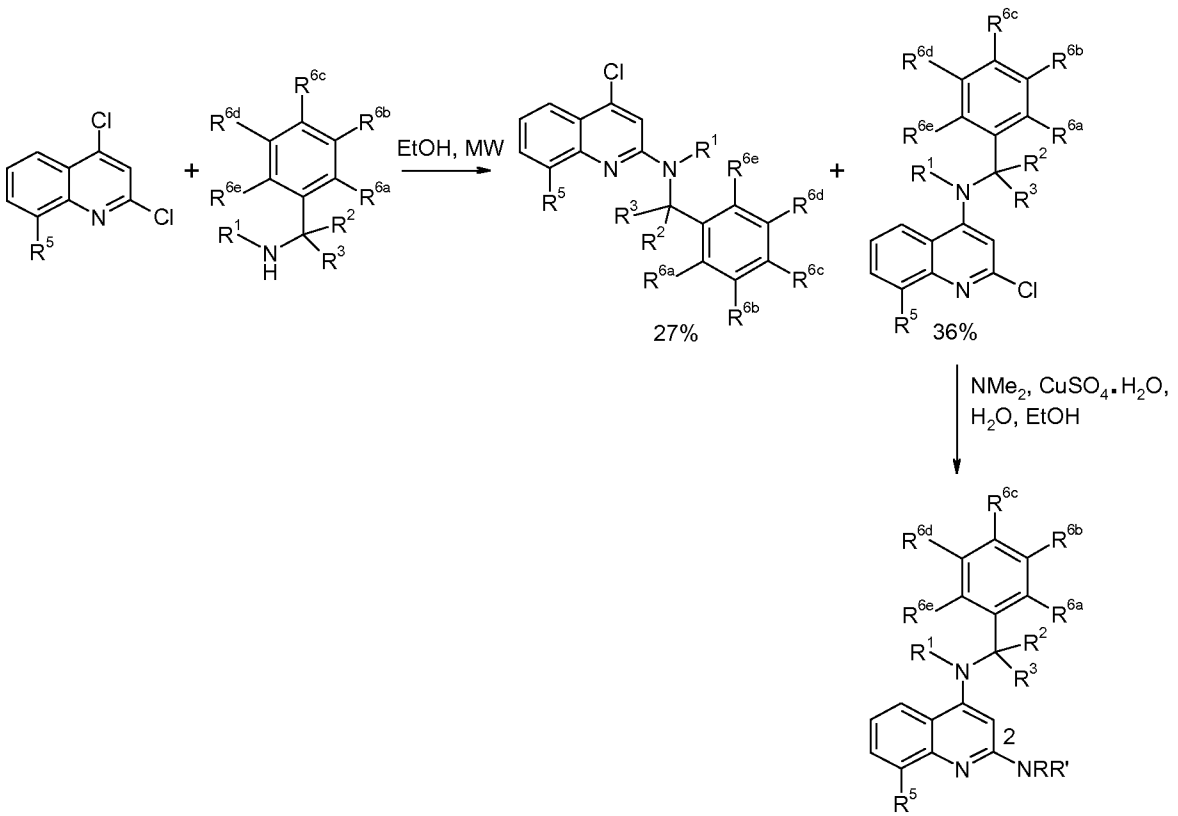


In scheme 2, the variables R^1, R^2, R^3, R^4, R^5, R^{6a}, R^{6b}, R^{6c}, R^{6d}, R^{6e} are as defined herein (unless indicated otherwise). Hal is chlorine or bromine. R, R' are independently hydrogen, C_1-C_6-akyl, C_1-C_6-alkylcarbonyl, C_1-C_6-alkenylcarbonyl, C_1-C_6-alkylsulfonyl, (halogenated

C_1-C_6-alkyl)sulfonyl, C_6-C_{12}-arylsulfonyl, (C_6-C_{12}-aryl C_1-C_4-alkyl)sulfonyl or C_3-C_{12}-heterocyclylsulfonyl.

4-Benzylaminochinolines having a dimethylamine radical in 2-position are obtainable by the process depicted in scheme 3.

Scheme 3:



In scheme 3, the variables R^1, R^2, R^3, R^4, R^5, R^{6a}, R^{6b}, R^{6c}, R^{6d}, R^{6e} are as defined herein (unless indicated otherwise). R, R' are independently C_1-C_6-alkyl.

The acid addition salts of the 4-benzylaminoquinolines of formula (I) are prepared in a customary manner by mixing the free base with a corresponding acid, optionally in solution in an organic solvent, for example a lower alcohol, such as methanol, ethanol or propanol, an ether, such as methyl *tert*-butyl ether or diisopropyl ether, a ketone, such as acetone or methyl ethyl ketone, or an ester, such as ethyl acetate.

The compounds of the formula (I) are capable of inhibiting the activity of glycine transporter, in particular glycine transporter 1 (GlyT1).

The utility of the compounds in accordance with the present invention as inhibiting the glycine transporter activity, in particular GlyT1 activity, may be demonstrated by methodology known in the art. For instance, human GlyT1c expressing recombinant hGlyT1c_5_CHO cells can be used for measuring glycine uptake and its inhibition (IC_{50}) by a compound of formula (I).

Amongst the compounds of the formula (I) those are preferred which achieve effective inhibition at low concentrations. In particular, compounds of the formula (I) are preferred which inhibit glycine transporter 1 (GlyT1) at a level of $IC_{50} < 1$ µMol, more preferably at a level of $IC_{50} < 0.5$ µMol, particularly preferably at a level of $IC_{50} < 0.2$ µMol and most preferably at a level of $IC_{50} < 0.1$ µMol.

The compounds of the formula (I) according to the present invention are thus uselful as pharmaceuticals.

The present invention therefore also relates to pharmaceutical compositions which comprise a carrier and a compound of the formula (I). Said carrier is preferably inert.

The present invention also relates to the use of the compounds of the formula (I) in the manufacture of a medicament for inhibiting the glycine transporter GlyT1, and to corresponding methods of inhibiting the glycine transporter GlyT1.

The NMDA receptor is central to a wide range of CNS processes, and its role in a variety of diseases in humans or other species has been described. GlyT1 inhibitors slow the removal of glycine from the synapse, causing the level of synaptic glycine to rise. This in turn increases the occupancy of the glycine binding site on the NMDA receptor, which increases activation of the NMDA receptor following glutamate release from the presynaptic terminal. Glycine transport inhibitors and in particular inhibitors of the glycine transporter GlyT1 are thus known to be useful in treating a variety of neurologic and psychiatric disorders.

The present invention thus further relates to the use of the compounds of the formula (I) for the manufacture of a medicament for treating a neurologic or psychiatric disorder, and to corresponding methods of treating said disorders.

According to a particular embodiment, the disorder is associated with glycinergic or glutamatergic neurotransmission dysfunction.

According to a further particular embodiment, the disorder is one or more of the following conditions or diseases: schizophrenia or a psychotic disorder including schizophrenia (paranoid, disorganized, catatonic or undifferentiated), schizophreniform disorder, schizoaffective disorder, delusional disorder, brief psychotic disorder, shared psychotic disorder, psychotic disorder due to a general medical condition and substance- induced psychotic disorder, including both the positive and the negative symptoms of schizophrenia and other psychoses; cognitive disorders including dementia (associated with Alzheimer's disease, ischemia, multi-infarct dementia, trauma, vascular problems or stroke, HIV disease, Parkinson's disease, Huntington's disease, Pick's disease, Creutzfeldt-Jacob disease, perinatal hypoxia, other general medical conditions or substance abuse); delirium, amnestic disorders or cognitive impairment including age related cognitive decline; anxiety disorders including acute stress disorder, agoraphobia, generalized anxiety disorder, obsessive-compulsive disorder, panic attack, panic disorder, post-traumatic stress disorder, separation anxiety disorder, social phobia, specific phobia, substance-induced anxiety disorder and anxiety due to a general medical condition; substance-related disorders and addictive behaviors (including substance-induced delirium, persisting dementia, persisting amnestic disorder, psychotic disorder or anxiety disorder; tolerance, dependence or withdrawal from substances including alcohol, amphetamines, cannabis, cocaine, hallucinogens, inhalants, nicotine, opioids, phencyclidine, sedatives, hypnotics or anxiolytics); obesity, bulimia nervosa and compulsive eating disorders; bipolar disorders, mood disorders including depressive disorders; depression including unipolar depression, seasonal depression and post-partum depression, premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PDD), mood disorders due to a general medical condition, and substance-induced mood disorders; learning disorders, pervasive developmental disorder including autistic disorder, attention deficit disorders including attention-deficit hyperactivity disorder (ADHD) and conduct disorder; movement disorders, including akinesias and akinetic-rigid syndromes (including Parkinson's disease, drug-induced parkinsonism, postencephalitic parkinsonism, progressive supranuclear palsy, multiple system atrophy, corticobasal degeneration, parkinsonism-ALS dementia complex and basal ganglia calcification), medication-induced parkinsonism (such as neuroleptic-induced parkinsonism, neuroleptic malignant syndrome, neuroleptic-induced acute dystonia, neuroleptic-induced acute akathisia, neuroleptic-induced tardive dyskinesia and medication-induced postural tremor), Gilles de la Tourette's syndrome, epilepsy, muscular spasms and disorders associated with muscular spasticity or weakness including tremors; dyskinesias [including tremor (such as rest tremor, postural tremor and intention tremor), chorea (such as Sydenham's chorea, Huntington's disease, benign hereditary chorea, neuroacanthocytosis, symptomatic chorea, drug-induced chorea and hemiballism), myoclonus (including generalised myoclonus and focal myoclonus), tics (including simple tics, complex tics and symptomatic tics), and dystonia (including generalised dystonia such as iodiopathic

dystonia, drug-induced dystonia, symptomatic dystonia and paroxymal dystonia, and focal dystonia such as blepharospasm, oromandibular dystonia, spasmodic dysphonia, spasmodic torticollis, axial dystonia, dystonic writer's cramp and hemiplegic dystonia)]; urinary incontinence; neuronal damage including ocular damage, retinopathy or macular degeneration of the eye, tinnitus, hearing impairment and loss, and brain edema; emesis; and sleep disorders including insomnia and narcolepsy.

The compounds of formula (I) are particularly useful in the treatment of schizophrenia, bipolar disorder, depression including unipolar depression, seasonal depression and postpartum depression, premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PDD), learning disorders, pervasive developmental disorder including autistic disorder, attention deficit disorders including Attention-Deficit/Hyperactivity Disorder, tic disorders including Tourette's disorder, anxiety disorders including phobia and post traumatic stress disorder, cognitive disorders associated with dementia, AIDS dementia, Alzheimer's, Parkinson's, Huntington's disease, spasticity, myoclonus, muscle spasm, tinnitus and hearing impairment and loss are of particular importance.

Particular cognitive disorders are dementia, delirium, amnestic disorders and cognitive impartment including age-related cognitive decline.

Particular anxiety disorders are generalized anxiety disorder, obsessive-compulsive disorder and panic attack.

Particular schizophrenia or psychosis pathologies are paranoid, disorganized, catatonic or undifferentiated schizophrenia and substance-induced psychotic disorder.

Particular neurologic disorders that can be treated with the compounds of of the formula (I) include in particular a cognitive disorder such as dementia, cognitive impairment, attention deficit hyperactivity disorder.

Particular psychiatric disorders that can be treated with the compounds of of the formula (I) include in particular an anxiety disorder, a mood disorder such as depression or a bipolar disorder, schizophrenia, a psychotic disorder.

Within the context of the treatment, the use according to the invention of the compounds of the formula (I) involves a method. In this method, an effective quantity of one or more compounds or the formula (I), as a rule formulated in accordance with pharmaceutical and veterinary practice, is administered to the individual to be treated, preferably a mammal, in particular a human being. Whether such a treatment is indicated, and in which form it is to

take place, depends on the individual case and is subject to medical assessment (diagnosis) which takes into consideration signs, symptoms and/or malfunctions which are present, the risks of developing particular signs, symptoms and/or malfunctions, and other factors.

As a rule, the treatment is effected by means of single or repeated daily administration, where appropriate together, or alternating, with other drugs or drug-containing preparations.

The invention also relates to the manufacture of pharmaceutical compositions for treating an individual, preferably a mammal, in particular a human being. Thus, the compounds of the formula (I) are customarily administered in the form of pharmaceutical compositions which comprise an inert carrier (e.g. a pharmaceutically acceptable excipient) together with at least one compound according to the invention and, where appropriate, other drugs. These compositions can, for example, be administered orally, rectally, transdermally, subcutaneously, intravenously, intramuscularly or intranasally.

Examples of suitable pharmaceutical formulations are solid medicinal forms, such as powders, granules, tablets, in particular film tablets, lozenges, sachets, cachets, sugar-coated tablets, capsules, such as hard gelatin capsules and soft gelatin capsules, suppositories or vaginal medicinal forms, semisolid medicinal forms, such as ointments, creams, hydrogels, pastes or plasters, and also liquid medicinal forms, such as solutions, emulsions, in particular oil-in-water emulsions, suspensions, for example lotions, injection preparations and infusion preparations, and eyedrops and eardrops. Implanted release devices can also be used for administering inhibitors according to the invention. In addition, it is also possible to use liposomes or microspheres.

When producing the compositions, the compounds according to the invention are optionally mixed or diluted with one or more carriers (excipients). Carriers (excipients) can be solid, semisolid or liquid materials which serve as vehicles, carriers or medium for the active compound.

Suitable carriers (excipients) are listed in the specialist medicinal monographs. In addition, the formulations can comprise pharmaceutically acceptable auxiliary substances, such as wetting agents; emulsifying and suspending agents; preservatives; antioxidants; antiirritants; chelating agents; coating auxiliaries; emulsion stabilizers; film formers; gel formers; odor masking agents; taste corrigents; resin; hydrocolloids; solvents; solubilizers; neutralizing agents; diffusion accelerators; pigments; quaternary ammonium compounds; refatting and overfatting agents; raw materials for ointments, creams or oils; silicone deriva-

tives; spreading auxiliaries; stabilizers; sterilants; suppository bases; tablet auxiliaries, such as binders, fillers, glidants, disintegrants or coatings; propellants; drying agents; opacifiers; thickeners; waxes; plasticizers and white mineral oils. A formulation in this regard is based on specialist knowledge as described, for example, in Fiedler, H.P., Lexikon der Hilfsstoffe für Pharmazie, Kosmetik und angrenzende Gebiete [Encyclopedia of auxiliary substances for pharmacy, cosmetics and related fields], 4th edition, Aulendorf: ECV-Editio-Cantor-Verlag, 1996.

The following examples serve to explain the invention without limiting it.

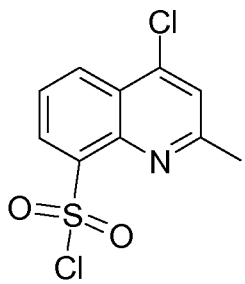
The compounds were characterized by mass spectrometry, generally recorded via HPLC-MS in a fast gradient on C18-material (electrospray-ionisation (ESI) mode).

Preparation Examples

Example 1:
4-(3,4-Dichlorobenzylamino)-2-methylquinoline-8-sulfonic dimethylamide

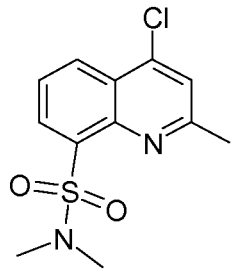
1.1 *4-Chloro-2-methylquinoline-8-sulfonyl chloride*

4-Chloro-2-methylquinoline (10.0 g, 0.056 mole) was added dropwise to chlorosulfonic



acid (61.3 g, 0.526 mole) under stirring at room temperature to undergo an exothermic reaction. The mixture was stirred at 110°C for 18 hrs. The content of the flask was poured into ice cold water and extracted with dichloromethane. The combined organic phases were concentrated and purified using silica gel chromatography, eluting with cyclohexane:ethyl acetate 80:20. The residue was extracted with cyclohexane to give 1.7 g (11%) of a yellowish solid.
ESI-MS [M+H]+=276.0/278.0calculated for $C_{10}H_7Cl_2NO_2S$ = 276 g/mole

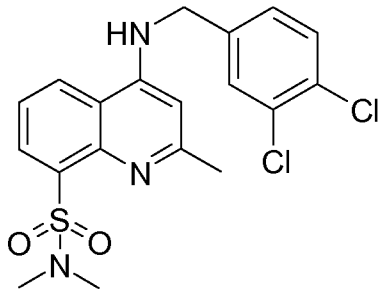
1.2 *4-Chloro-2-methylquinoline-8-sulfonic dimethylamide*



4-Chloro-2-methylquinoline-8-sulfonyl chloride (100 mg, 0.362 mmole) and a 40% solution of dimethylamine in water (408 mg, 3.62 mmole) were stirred at 60°C for 1 h. The content of the flask was filtered off and a white solid was obtained (103 mg, 100%).

ESI-MS [M+H]+ =285.1 calculated for $C_{12}H_{13}ClN_2O_2S$ = 285 g/ mole

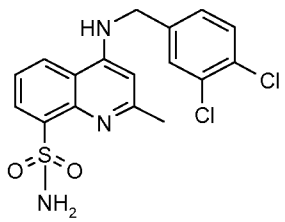
1.3 *4-(3,4-Dichlorobenzylamino)-2-methylquinoline-8-sulfonic dimethylamide*



4-Chloro-2-methylquinoline-8-sulfonic dimethylamide (80mg, 0.281 mmole) and 3,4-dichlorobenzylamine (100 mg, 0.568 mmole) were stirred at 155 °C for 10 min in a microwave oven. Methanol was added and the mixture was concentrated, mixed with dichloromethane and then filtered. The residue was purified using silica gel chromatography, eluting with dichloromethane:methanol 95:5. Precipitation in ethyl acetate gave a pink solid (15 mg, 13%).

ESI-MS [M+H]+ = 424.1/428.1 calculated for $C_{19}H_{19}Cl_2N_3O_2S$ = 424 g/ mole

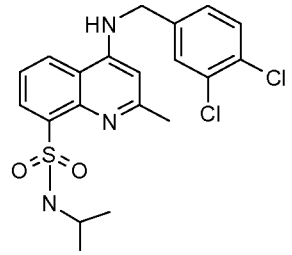
Example 2:
4-(3,4-Dichlorobenzylamino)-2-methylquinoline-8-sulfonamide



Preparation was made using a similar procedure as described in example 1, method 1.3. Starting materials were 4-chloro-2-methylquinoline-8-sulfonamide and dichlorobenzylamine.
Yield: 29%.

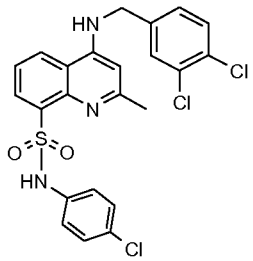
ESI-MS [M+H]+ =396.1/398.1 calculated for $C_{17}H_{15}Cl_2N_3O_2S$ = 396 g/ mole

Example 3:
4-(3,4-Dichlorobenzylamino)-2-methyl-quinoline-8-sulfonic isopropylamide



Preparation was made using a similar procedure as described in example 1, method 1.3. Starting materials were 4-chloro-2-methylquinoline-8-sulfonic isopropylamide and dichlorobenzylamine.
Yield: 53%.
ESI-MS [M+H]+ =438.4/440.4 calculated for $C_{20}H_{21}Cl_2N_3O_2S$ = 438 g/ mole

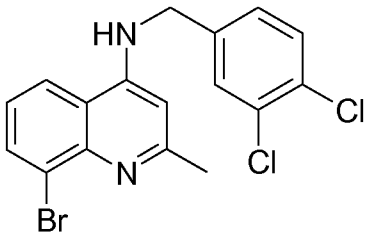
Example 4:
4-(3,4-Dichlorobenzylamino)-2-methylquinoline-8-sulfonic (4-chlorophenyl)-amide



Preparation was made using a similar procedure as described in example 1, method 1.3. Starting materials were 4-chloro-2-methylquinoline-8-sulfonic (4-chlorophenyl)-amide and dichlorobenzylamine.
Yield: 25%.
ESI-MS [M+H]+ =506.1/510.0 calculated for $C_{23}H_{18}Cl_3N_3O_2S$ = 507 g/ mole

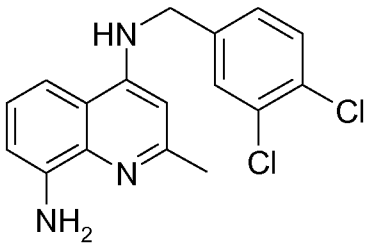
Example 5:
N*4*-(3,4-Dichlorobenzyl)-2-methylquinoline-4,8-diamine

5.1 *(8-Bromo-2-methylquinolin-4-yl)-(3,4-dichlorobenzyl)-amine*



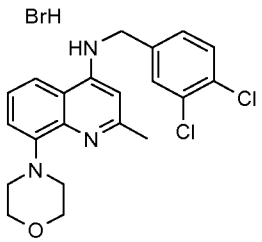
8-Bromo-4-chloro-2-methylquinoline (4.50 g, 17.5 mmole) and 3,4-dichlorobenzylamine (6.30 g, 35.8 mmole) in dimethylsulfoxide (6 mL) were stirred at 140°C for 2 h in a microwave oven. Water was added and the mixture was decanted to obtain an oily residue. The residue was washed with ethyl acetate to give a white solid (1.40 g, 20%).
ESI-MS [M+H]+ =395.1/397.1 calculated for $C_{17}H_{13}BrCl_2N_2$ = 396 g/ mole

5.2. *N*4*-(3,4-Dichlorobenzyl)-2-methylquinoline-4,8-diamine*



(8-Bromo-2-methylquinolin-4-yl)-(3,4-dichlorobenzyl)-amine (500 mg, 1.26 mmole), copper(II)sulphate pentahydrate (316 mg, 1.27 mmole) and ammonia (20% in water/ ethanol 1:1, 20 mL) were stirred in a microwave oven at 150°C for 5 hrs. The reaction mixture was dissolved in water and extracted with dichloromethane. The resulting organic phases were dried and purified using silica gel chromatography, eluting with dichloromethane:water 99:1. Precipitation in isopropyl ether gave a brownish solid (220 mg, 52%).
ESI-MS [M+H]+ =332.1/334.1 calculated for $C_{17}H_{15}Cl_2N_3$ = 332 g/ mole

Example 6:
(3,4-Dichlorobenzyl)-(2-methyl-8-morpholin-4-yl-quinolin-4-yl)-amine hydrobromide



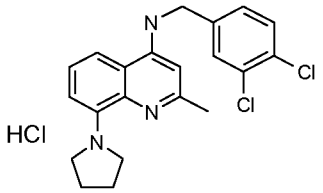
N*4*-(3,4-Dichlorobenzyl)-2-methylquinoline-4,8-diamine (60.0 mg, 0.181 mmole) and bis(2-bromoethyl)ether (83.7 mg, 0.361 mmole) in dimethylformamide (1 mL), were stirred at 100 °C for 90 min in a microwave oven. Water was added and the mixture was extracted with dichloromethane. The organic phases were washed with saturated NaCl solu-

tion, dried and the solvent was removed. The residue thus obtained was purified using silica gel chromatography, eluting with dichloromethane:water 90:10. Precipitation in ethyl acetate gave a brownish solid (15 mg, 17%).

ESI-MS [M+H]+ =402.1/406.0 calculated for $C_{21}H_{21}Cl_2N_3O$= 402 g/ mole

Example 7:

(3,4-Dichlorobenzyl)-(2-methyl-8-pyrrolidin-1-yl-quinolin-4-yl)-amine hydrochloride



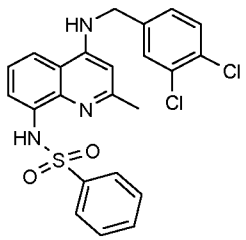
Preparation was made using a similar procedure as described in example 6. Starting materials were 8-bromo-2-methylquinolin-4-yl)-(3,4-dichlorobenzyl)-amine and 1,4-dibromobutane.

Yield: 28%.

ESI-MS [M+H]+ =386.1/390.1 calculated for $C_{21}H_{21}Cl_2N_3$= 386g/ mole

Example 8:

N-[4-(3,4-Dichlorobenzylamino)-2-methylquinolin-8-yl]-phenylsulfonamide

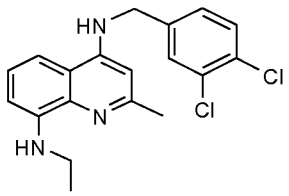


N*4*-(3,4-Dichlorobenzyl)-2-methylquinoline-4,8-diamine (60 mg, 0.181 mmole, example 5.1) and phenylsulfonylchloride (33.4 mg, 0.190 mmole) were dissolved in pyridine and stirred at RT for 76 hrs. The content of the flask was concentrated, 1N NaOH was added and the mixture was extracted using dichloromethane. The organic phase was washed with water and saturated NaCl solution and concentrated. The residue thus obtained was purified using silica gel chromatography, eluting with dichloromethane:water 95:5. Cristallisation from ethyl acetate:isopropyl ether 1:1 gave a yellow solid (21 mg, 25%).

ESI-MS [M+H]+ = 472.3/474.3 calculated for $C_{23}H_{19}Cl_2N_3O_2S$ = 472 g/ mole

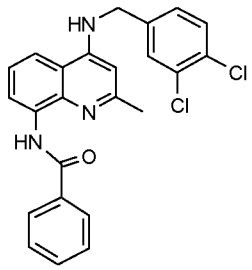
Example 9:

N*4*-(3,4-Dichlorobenzyl)-N*8*-ethyl-2-methylquinolin-4,8-diamine



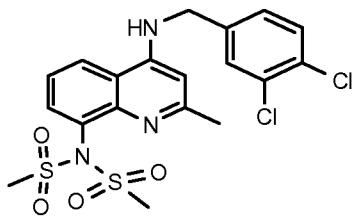
Preparation was made using a similar procedure as described in example 6. Starting materials were 8-bromo-2-methylquinolin-4-yl)-(3,4-dichlorobenzyl)-amine and bromoethane.
Yield: 17%.
ESI-MS [M+H]+ = 360.1/364.0 calculated for $C_{19}H_{19}Cl_2N_3$ = 360 g/ mole

Example 10:
N-[4-(3,4-Dichlorobenzylamino)-2-methylquinolin-8-yl]-benzamide



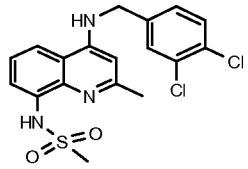
Preparation was made using a similar procedure as described in example 8. Starting materials were 8-bromo-2-methylquinolin-4-yl)-(3,4-dichlorobenzyl)-amine and benzoyl chloride.
Yield: 63%.
ESI-MS [M+H]+ =436.1/440.1 calculated for $C_{24}H_{19}Cl_2N_3O$ = 436 g/ mole

Example 11:
N-[4-(3,4-Dichlorobenzylamino)-2-methylquinolin-8-yl]-bismethanesulfonamide



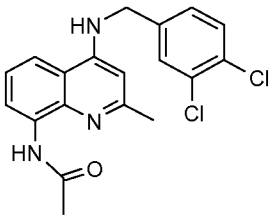
Preparation was made using a similar procedure as described in example 8. Starting materials were 8-bromo-2-methylquinolin-4-yl)-(3,4-dichlorobenzyl)-amine and methanesulfonyl chloride
Yield: 15%.
ESI-MS [M+H]+ =488.1/490.1 calculated for $C_{19}H_{19}Cl_2N_3O_4S_2$ = 488 g/ mole

Example 12:
N-[4-(3,4-Dichlorobenzylamino)-2-methylquinolin-8-yl]-methanesulfonamide



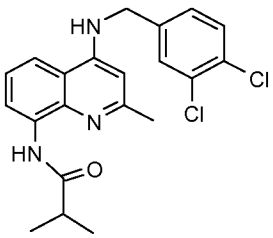
Preparation was made using a similar procedure as described in example 8. Starting materials were 8-bromo-2-methylquinolin-4-yl)-(3,4-dichlorobenzyl)-amine and methanesulfonyl chloride.
Yield: 17%.
ESI-MS [M+H]+ =410.1/414.1 calculated for $C_{18}H_{17}Cl_2N_3O_2S$ = 410 g/ mole

Example 13:
N-[4-(3,4-Dichlorobenzylamino)-2-methylquinolin-8-yl]-acetamide



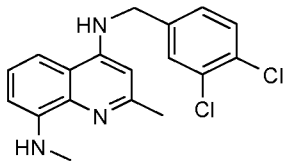
Preparation was made using a similar procedure as described in example 8. Starting materials were 8-bromo-2-methylquinolin-4-yl)-(3,4-dichlorobenzyl)-amine and acetylchloride.
Yield: 53%.
ESI-MS [M+H]+ =374.1/378.1 calculated for $C_{19}H_{17}Cl_2N_3O$ = 374 g/ mole

Example 14:
N-[4-(3,4-Dichlorobenzylamino)-2-methylquinolin-8-yl]-isobutyramide



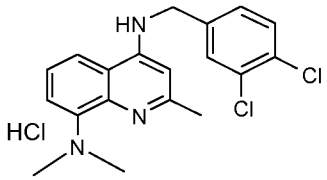
Preparation was made using a similar procedure as described in example 8. Starting materials were 8-bromo-2-methylquinolin-4-yl)-(3,4-dichlorobenzyl)-amine and isobutyrylchloride.
Yield: 58%.
ESI-MS [M+H]+ =402.1/406.1 calculated for $C_{21}H_{21}Cl_2N_3O$ = 402 g/ mole

Example 15:
N*4*-(3,4-Dichlorobenzyl)-N*8*-methyl-2-methylquinolin-4,8-diamine



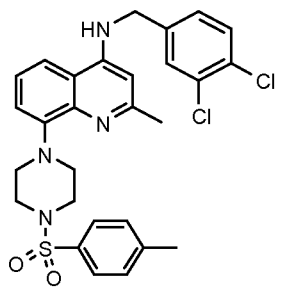
Preparation was made using a similar procedure as described in example 6. Starting materials were 8-bromo-2-methylquinolin-4-yl)-(3,4-dichlorobenzyl)-amine and iodomethane. Yield: 19%.
ESI-MS [M+H]+ =346.2 calculated for $C_{18}H_{17}Cl_2N_3$ = 346 g/ mole

Example 16:
N*4*-(3,4-Dichlorobenzyl)-N*8*-dimethyl-2-methylquinolin-4,8-diamine hydrochloride



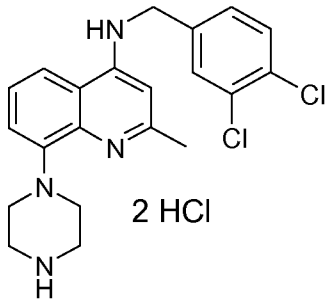
(3,4-Dichlorobenzyl)-(8-fluoro-2-methyl-quinolin-4-yl)-amine (100 mg, 0.298 mmole), a solution of dimethylamine in water (40%, 4 mL), copper(I)chloride (59 mg, 0.596 mmole), and copper(II)sulphate pentahydrate (150 mg, 0.601 mmole) were suspended with absolute ethanol (0.5 mL) and stirred at 155 °C for 7 hrs in a microwave oven. Water was added and the mixture was extracted using dichloromethane. The organic phases were washed with saturated NaCl solution, dried and the solvent was removed. The residue thus obtained was purified using silica gel chromatography, eluting with dichloromethane:water 99:1 to give a yellow salt (12 mg, 10%).
ESI-MS [M+H]+ =360.2/3.2 calculated for $C_{19}H_{19}Cl_2N_3$ = 360 g/ mole

Example 17:
(3,4-Dichlorobenzyl)-{2-methyl-8-[4-(toluene-4-sulfonyl)-piperazin-1-yl]-quinolin-4-yl}-amine



Preparation was made using a similar procedure as described in example 6. Starting materials were 8-bromo-2-methylquinolin-4-yl)-(3,4-dichlorobenzyl)-amine and N,N-bis(2-chloroethyl)-p-toluenesulfonamide.
Yield: 26%.
ESI-MS [M+H]+ =555.2/557.2 calculated for $C_{28}H_{28}Cl_2N_4O_2S$ = 556 g/ mole

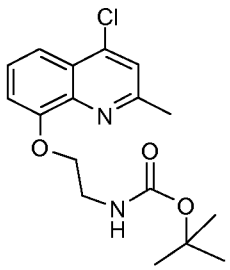
Example 18:
(3,4-Dichlorobenzyl)-(2-methyl-8-piperazin-1-yl-quinolin-4-yl)-amine dihydrochloride



(3,4-Dichlorobenzyl)-{2-methyl-8-[4-(toluene-4-sulfonyl)-piperazin-1-yl]-quinolin-4-yl}-amine (example 17, 40 mg, 0.072 mmole) and a mixture of HBr/glacial acetic acid (33%, 1 mL)/ 0.2 mL) were stirred at 70°C for 3 hrs. The content of the flask was diluted with water and extracted with ethyl acetate. The aqueous phase was alkalized and extracted with dichloromethane. The organic phases were washed with saturated NaCl solution and concentrated. The residue was crystallized as hydrochloride from isopropanol/isopropyl ether/ethanol/HCl to give a light fawn salt (17 mg, 50%).
ESI-MS [M+H]+ = 401.1/405.1 calculated for $C_{21}H_{22}Cl_2N_4$= 401 g/mole

Example 19:
{2-[4-(3,4-Dichlorobenzylamino)-2-methylquinolin-8-yloxy]-ethyl}-carbamate tert-butyl ester

19.1 *[2-(4-Chloro-2-methylquinolin-8-yloxy)-ethyl]-carbamate tert-butyl ester*

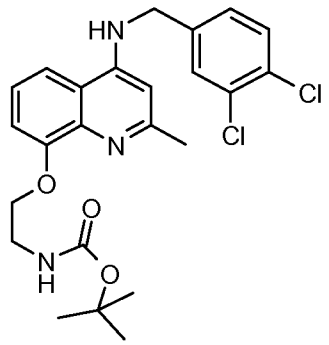


0.6 g Sodium hydride, free of paraffin, was suspended in dimethyl acetamide (50 mL), then 4-chloro-2-methylquinoline-8-ol (1,6 g, 8.26 mmole) was added at RT and the mixture was stirred for 1 h. 2-(boc-amino)ethylbromide was added dropwise and the mixture

was kept on stirring for 48 hrs. The content of the flask was poured into half concentrated NaCl solution and extracted with ethyl acetate. The organic phases were washed with water and saturated NaCl solution, dried and concentrated. Dimethyl acetamide was removed *in vacuo* and the residue was precipitated from isopropyl ether to give a light fawn solid (2.50 g, 90%).

ESI-MS [M+H]+ = 337.2 calculated for $C_{17}H_{21}ClN_2O_3$ = 337 g/ mole

19.2 *{2-[4-(3,4-Dichlorobenzylamino)-2-methylquinolin-8-yloxy]-ethyl}-carbamate tert-butyl ester*

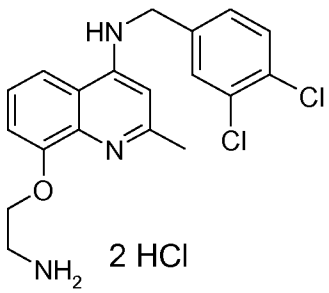


[2-(4-Chloro-2-methylquinolin-8-yloxy)-ethyl]-carbamate tert-butyl ester (1.30 g, 3.86 mmole), 3,4-dichlorobenzylamine (1.36 g, 7.72 mmole) and a catalytic effective amount of copper(II)sulphate pentahydrate in dimethylsulfoxide (0.2 mL) were stirred at 155 °C for 30 min in a microwave oven. The organic phases were washed with water and saturated NaCl solution, dried and the solvent was removed. The residue thus obtained was purified using silica gel chromatography, eluting with dichloromethane:water 90:10. Precipitation in ethyl acetate gave a brownish solid (230 mg, 13%).

ESI-MS [M+H]+ = 476.2/478.2 calculated for $C_{24}H_{27}Cl_2N_3O_3$ = 476 g/mole

Example 20:

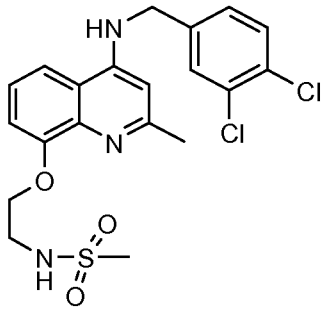
[8-(2-Aminoethoxy)-2-methylquinolin-4-yl]-(3,4-dichlorobenzyl)-amine dihydrochloride



[2-(4-Chloro-2-methylquinolin-8-yloxy)-ethyl]-carbamate tert-butyl ester (example 19, 230 mg, 0.483 mmole) was stirred in isopropanol/HCl (5-6N, 10 mL) at RT overnight. The content of the flask was diluted with isopropyl ether and the precipitated solid was filtered off to obtain a white salt (215 mg, 99%).

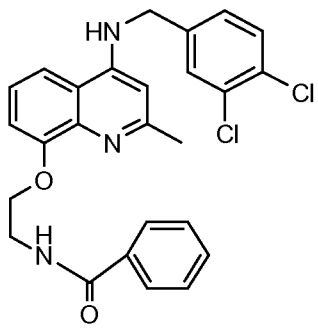
ESI-MS [M+H]+ =377.0/379.0 calculated for $C_{19}H_{19}Cl_2N_3O$ = 376 g/ mole

Example 21:
N-{2-[4-(3,4-Dichlorobenzylamino)-2-methylquinolin-8-yloxy]-ethyl}-ethanesulfonamide



[8-(2-Aminoethoxy)-2-methylquinolin-4-yl]-(3,4-dichlorobenzyl)-amine dihydrochloride (example 20, 60 mg, 0.160 mmole) and methanesulfonyl chloride (33.8 mg, 0.30 mmole) were dissolved in pyridine and stirred at RT for 12 hrs. The content of the flask was concentrated, mixed with 1N NaOH and extracted with dichloromethane. The organic layer was washed with water and saturated NaCl solution and concentrated. The residue thus obtained was purified using silica gel chromatography, eluting with dichloromethane:methanol 95:5. After precipitation in ethyl acetate a white solid was obtained (12 mg, 17%).
ESI-MS [M+H]+ =454.0/458.1 calculated for $C_{20}H_{21}Cl_2N_3O_3S$ = 454 g/ mole

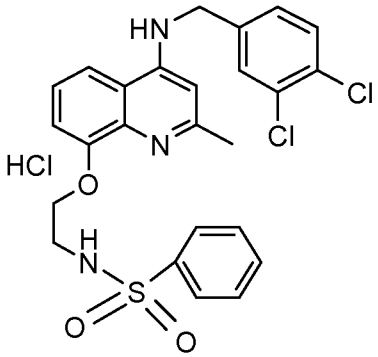
Example 22:
N-{2-[4-(3,4-Dichlorobenzylamino)-2-methylquinolin-8-yloxy]-ethyl}-phenylamide



Preparation was made using a similar procedure as described in example 21. Starting materials were [8-(2-aminoethoxy)-2-methylquinolin-4-yl]-(3,4-dichlorobenzyl)-amine dihydrochloride and benzoyl chloride.
Yield: 37%.
ESI-MS [M+H]+ =480.1/484.1 calculated for $C_{26}H_{23}Cl_2N_3O_2$ = 480 g/ mole

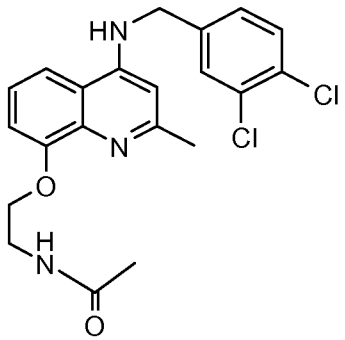
Example 23:

N-{2-[4-(3,4-Dichlorobenzylamino)-2-methylquinolin-8-yloxy]-ethyl}-benzamide hydrochloride



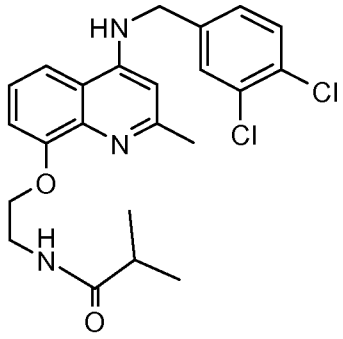
Preparation was made using a similar procedure as described in example 21. Starting materials were [8-(2-aminoethoxy)-2-methylquinolin-4-yl]-(3,4-dichlorobenzyl)-amine dihydrochloride and phenylsulfonyl chloride.
Yield: 8%.
ESI-MS [M+H]+ =516.1/520.0 calculated for $C_{25}H_{23}Cl_2N_3O_3S$= 516 g/ mole

Example 24:
N-{2-[4-(3,4-Dichlorobenzylamino)-2-methylquinolin-8-yloxy]-ethyl}-acetamide



Preparation was made using a similar procedure as described in example 21. Starting materials were [8-(2-aminoethoxy)-2-methylquinolin-4-yl]-(3,4-dichlorobenzyl)-amine dihydrochloride and acetylchloride.
Yield: 65%.
ESI-MS [M+H]+ =418.1/422.1 calculated for $C_{21}H_{21}Cl_2N_3O_2$ = 418 g/ mole

Example 26:
N-{2-[4-(3,4-Dichlorobenzylamino)-2-methylquinolin-8-yloxy]-ethyl}-isobutyramide



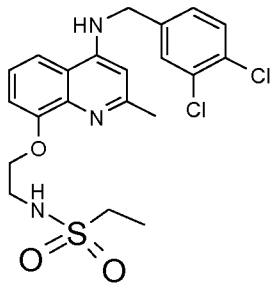
Preparation was made using a similar procedure as described in example 21. Starting materials were [8-(2-aminoethoxy)-2-methylquinolin-4-yl]-(3,4-dichlorobenzyl)-amine dihydrochloride and isobutyrylchloride.

Yield: 11%.

ESI-MS [M+H]+ =446.1/450.1 calculated for $C_{23}H_{25}Cl_2N_3O_2$ = 446 g/ mole

Example 27:

Ethanesulfonic {2-[4-(3,4-Dichloro-benzylamino)-2-methylquinolin-8-yloxy]-ethyl}-amide



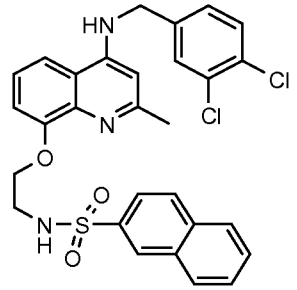
Preparation was made using a similar procedure as described in example 21. Starting materials were [8-(2-aminoethoxy)-2-methylquinolin-4-yl]-(3,4-dichlorobenzyl)-amine dihydrochloride and ethanesulfonyl chloride.

Yield: 19%.

ESI-MS [M+H]+ =468.0/472.0 calculated for $C_{21}H_{23}Cl_2N_3O_3S$ = 468 g/ mole

Example 28:

Naphthyl-2-sulfonic {2-[4-(3,4-dichlorobenzylamino)-2-methylquinolin-8-yloxy]-ethyl}-amide



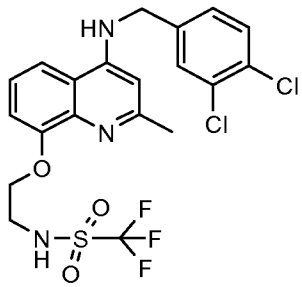
Preparation was made using a similar procedure as described in example 21. Starting materials were [8-(2-aminoethoxy)-2-methylquinolin-4-yl]-(3,4-dichlorobenzyl)-amine dihydrochloride and naphthyl-2-sulfonic chloride.

Yield: 27%.

ESI-MS [M+H]+ =566.1/570.1 calculated for $C_{29}H_{25}Cl_2N_3O_3S$ = 566 g/ mole

Example 29:

N-{2-[4-(3,4-Dichlorobenzylamino)-2-methylquinolin-8-yloxy]-ethyl}-C,C,C-trifluoromethanesulfonamide



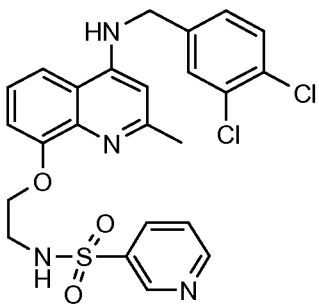
Preparation was made using a similar procedure as described in example 21. Starting materials were [8-(2-aminoethoxy)-2-methylquinolin-4-yl]-(3,4-dichlorobenzyl)-amine dihydrochloride and trifluoromethanesulfonyl chloride.

Yield: 40%.

ESI-MS [M+H]+ =508.0/512.0 calculated for $C_{20}H_{18}Cl_2F_3N_3O_3S$ = 508 g/ mole

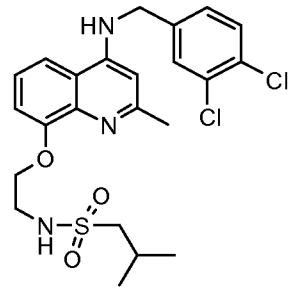
Example 30:

Pyridine-3-sulfonic {2-[4-(3,4-dichlorobenzylamino)-2-methylquinolin-8-yloxy]-ethyl}amide



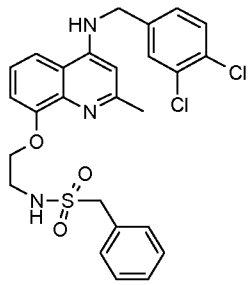
Preparation was made using a similar procedure as described in example 21. Starting materials were [8-(2-aminoethoxy)-2-methylquinolin-4-yl]-(3,4-dichlorobenzyl)-amine dihydrochloride and pyridine-3-sulfonyl chloride.
Yield: 28%.
ESI-MS [M+H]+ =517.0/521.0 calculated for $C_{24}H_{22}Cl_2N_4O_3S$ = 517 g/ mole

Example 31:
2-Methylpropane-1-sulfonic {2-[4-(3,4-dichlorobenzylamino)-2-methylquinolin-8-yloxy]-ethyl}-amide



Preparation was made using a similar procedure as described in example 21. Starting materials were [8-(2-aminoethoxy)-2-methylquinolin-4-yl]-(3,4-dichlorobenzyl)-amine dihydrochloride and isobutanesulfonyl chloride.
Yield: 14%.
ESI-MS [M+H]+ =496.1/500.1 calculated for $C_{23}H_{27}Cl_2N_3O_3S$ = 496 g/ mole

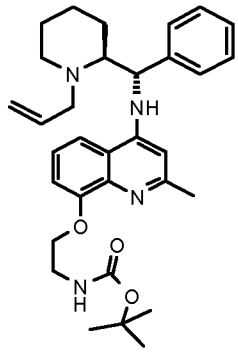
Example 32:
N-{2-[4-(3,4-Dichloro-benzylamino)-2-methylquinolin-8-yloxy]-ethyl}-C-phenyl-methanesulfonamide



Preparation was made using a similar procedure as described in example 21. Starting materials were [8-(2-aminoethoxy)-2-methylquinolin-4-yl]-(3,4-dichlorobenzyl)-amine dihydrochloride and phenylmethanesulfonyl chloride.
Yield: 3%.
ESI-MS [M+H]+ =530.1/534.1 calculated for $C_{26}H_{25}Cl_2N_3O_3S$ = 530 g/ mole

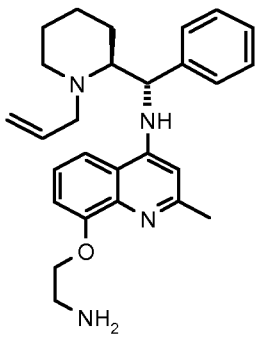
Example 33:

[2-(4-{[(S)-((S)-1-Allyl-piperidin-2-yl)-phenylmethyl]-amino}-2-methylquinolin-8-yloxy)-ethyl]-carbamate tert-butyl ester



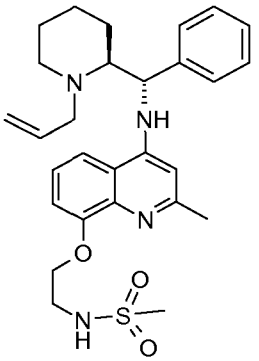
Preparation was made using a similar procedure as described in example 19, method 19.2. Starting materials were 2-(4-chloro-2-methylquinolin-8-yloxy)-ethyl]-carbamate tert-butyl ester (200 mg, 0.594 mmole) and C-[(S)-C-((S)-1-allyl-piperidin-2-yl)-C-phenyl]-methylamine (274 mg, 1.19 mmole).
Yield: 18%.
ESI-MS [M+H]+ =531.4 calculated for $C_{32}H_{42}N_4O_3$ = 531 g/ mole

Example 34:
[(S)-((S)-1-Allylpiperidin-2-yl)-phenylmethyl]-[8-(2-aminoethoxy)-2-methylquinolin-4-yl]-amine



Preparation was made using a similar procedure as described in example 19, method 19.2. Starting materials were 2-(4-chloro-2-methylquinolin-8-yloxy)-ethyl]-carbamate tert-butyl ester (200 mg, 0.594 mmole) and C-[(S)-C-((S)-1-allyl-piperidin-2-yl)-C-phenyl]-methylamine (274 mg, 1.19 mmole).
Yield: 78%.
ESI-MS [M+H]+ =431.4 calculated for $C_{27}H_{34}N_4O$ = 431 g/ mole

Example 35:
N-[2-(4-{[(S)-((S)-1-Allylpiperidin-2-yl)-phenylmethyl]-amino}-2-methylquinolin-8-yloxy)-ethyl]-methanesulfonamide



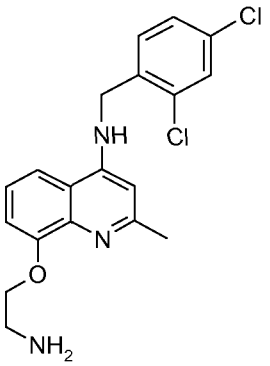
Preparation was made using a similar procedure as described in example 21. Starting materials were [(S)-((S)-1-allylpiperidin-2-yl)-phenylmethyl]-[8-(2-aminoethoxy)-2-methylquinolin-4-yl]-amine (example 34) and methanesulfonyl chloride.

Yield: 33%.

ESI-MS [M+H]+ =509.3 calculated for $C_{27}H_{35}ClN_4$ = 509 g/ mole

Example 36:

[8-(2-Aminoethoxy)-2-methylquinolin-4-yl]-(2,4-dichlorobenzyl)-amine



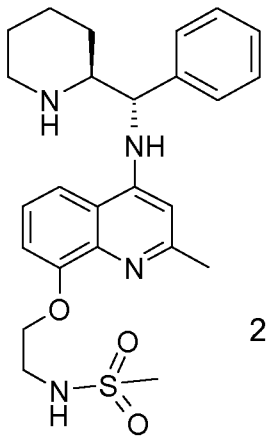
Preparation was made using a similar procedure as described in example 20. Starting materials were [2-(4-chloro-2-methylquinoline-8-yloxy)-ethyl]-carbamate tert-butyl ester and 2,4-dichlorobenzylamine.

Yield: 30%.

ESI-MS [M+H]+ = 376.2/378.2 calculated for $C_{19}H_{19}Cl_2N_3O$ = 376 g/ mole

Example 37:

N-(2-{2-Methyl-4-[((S)-phenyl-(S)-piperidin-2-yl-methyl)-amino]-quinolin-8-yloxy}-ethyl)-methanesulfonamide dihydrochloride



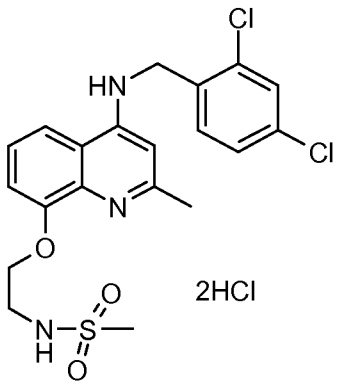
2HCl

Tris-(dibenzylidenaceton)-dipalladium(0) (19.0 mg, 0.021 mmole) and 1,4-bis-(diphenylphosphino)butane (9 mg, 0.021 mmole) were mixed with THF (10 mL). N-[2-(4-{[(S)-((S)-1-Allylpiperidin-2-yl)-phenylmethyl]-amino}-2-methylquinolin-8-yloxy)-ethyl]-methanesulfonamide (example 35, 130 mg, 0.256 mmole) in THF (5 mL) and 2-mercaptobenzoic acid (86.7 mg, 0.562 mmole) in THF (5 mL) were added and the mixture was stirred at RT for 2 hrs. The content of the flask was mixed with 1N NaOH and extracted with dichloromethane. The organic layer was washed with water and saturated NaCl solution and concentrated. The residue thus obtained was cystallized from isopropanol/water/HCl to obtain a white solid (42 mg, 30%).

ESI-MS [M+H]+ =469.3 calculated for $C_{25}H_{32}N_4O_3S$ = 469 g/ mole

Example 38:

N-{2-[4-(2,4-Dichlorobenzylamino)-2-methylquinolin-8-yloxy]-ethyl}-methanesulfonamide



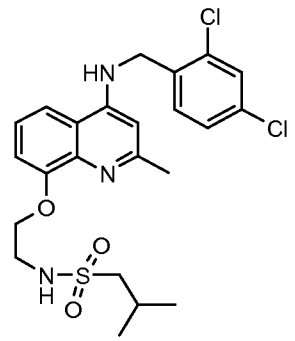
2HCl

Preparation was made using a similar procedure as described in example 21. Starting materials were [8-(2-aminoethoxy)-2-methylquinolin-4-yl]-(2,4-dichlorobenzyl)-amine (example 36) and methanesulfonyl chloride.

Yield: 32%.

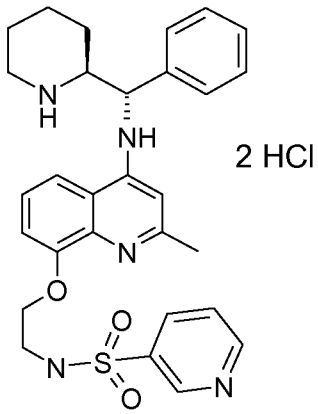
ESI-MS [M+H]+ =454.2/456.2 calculated for $C_{20}H_{20}Cl_2N_3O_3S$ = 454 g/ mole

Example 39:
2-Methylpropane-1-sulfonic {2-[4-(2,4-dichlorobenzylamino)-2-methylquinolin-8-yloxy]-ethyl}-amide



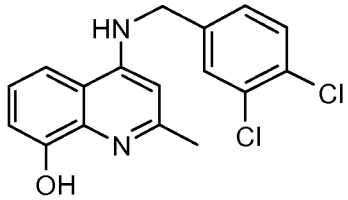
Preparation was made using a similar procedure as described in example 21. Starting materials were [8-(2-aminoethoxy)-2-methylquinolin-4-yl]-(2,4-dichlorobenzyl)-amine dihydrochloride (example 36) and isobutanesulfonyl chloride.
Yield: 25%.
ESI-MS [M+H]+ =496.3/498.2 calculated for $C_{23}H_{27}Cl_2N_3O_3S$ = 496 g/ mole

Example 40:
Pyridin-3-sulfonic (2-{2-methyl-4-[((S)-phenyl-(S)-piperidin-2-yl-methyl)-amino]-quinolin-8-yloxy}-ethyl)-amide dihydrochloride



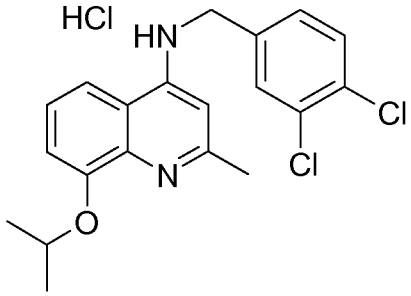
Preparation was made using a similar procedure as described in example 37. Starting materials were pyridine-3-sulfonic[2-(4-{[(S)-((S)-1-allylpiperidin-2-yl)-phenylmethyl]-amino}-2-methylquinolin-8-yloxy)-ethyl]-amide.
Yield: 34%.
ESI-MS [M+H]+ =532.2 calculated for $C_{29}H_{33}N_5O_3S$ = 532 g/ mole

Example 41:
4-(3,4-Dichlorobenzylamino)-2-methylquinolin-8-ol



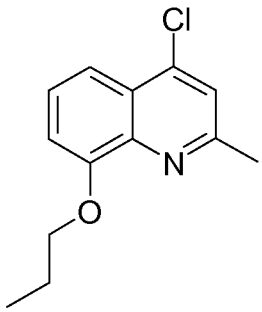
4-Chloro-8-hydroxy-2-methylquinoline (500 mg, 2.58 mmole) and 3,4-dichlorobenzylamine (910 mg, 5.16 mmole) in dimethylsulfoxide (5 mL) were stirred at 140 °C for 90 min in a microwave oven. Water was added and the mixture was decanted to obtain an oily residue. The residue was washed with ethyl acetate to give a brownish solid (350 mg, 41%).
ESI-MS [M+H]+ =333.1/337.0 calculated for $C_{17}H_{14}Cl_2N_2O$ = 333 g/ mole

Example 42:
(3,4-Dichlorobenzyl)-(8-isopropoxy-2-methylquinolin-4-yl)-amine hydrochloride



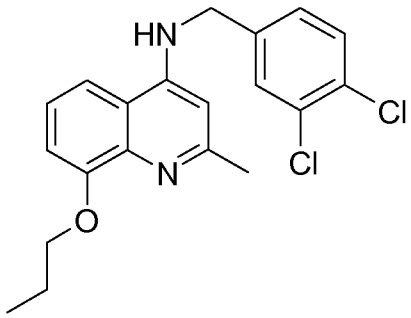
4-(3,4-Dichlorobenzylamino)-2-methylquinolin-8-ol (example 41, 70.0 mg, 0.210 mmole) was suspended in dimethylformamide (5 mL) and mixed with sodium hydride (60% in paraffin liq., 9.24 mg). After stirring for 30 min isopropyliodide (37.5 mg, 0.221 mmole) was added dropwise and the mixture was kept under stirring at RT for 16 hrs. Diluted NaCl solution was added and the mixture was extracted with ethyl acetate. The organic phases were dried and concentrated and the residue thus obtained was purified using silica gel chromatography, eluting with dichloromethane:methanol 90:10. Precipitation in Isopropanol/isopropyl ether/HCl gave a brownish salt (15 mg, 17%).
ESI-MS [M+H]+ =375.1/379.2 calculated for $C_{20}H_{20}Cl_2N_2O$ = 375 g/ mole

Example 43:
(3,4-Dichlorobenzyl)-(2-methyl-8-propoxyquinolin-4-yl)-amine
43.1 *4-Chloro-2-methyl-8-propoxyquinoline*



4-Chloro-8-hydroxy-2-methylquinoline (500 mg, 2.58 mmole) was suspended in dimethylformamide (4 mL) and mixed with sodium hydride (60% in paraffin liq., 113 mg). After stirring for 1 h, propyliodide (461 mg, 2.71 mmole) in dimethylformamide (1 mL) was added dropwise and the mixture was kept under stirring at RT for 16 hrs. Diluted NaCl solution was added and the mixture was extracted with ethyl acetate. The organic phases were dried, concentrated and the residue thus obtained was purified using silica gel chromatography, eluting with dichloromethane:methanol 95:5. Precipitation in isopropanol/isopropyl ether/HCl gave the product (300 mg, 49%).

43.2 *(3,4-Dichlorobenzyl)-(2-methyl-8-propoxyquinolin-4-yl)-amine*



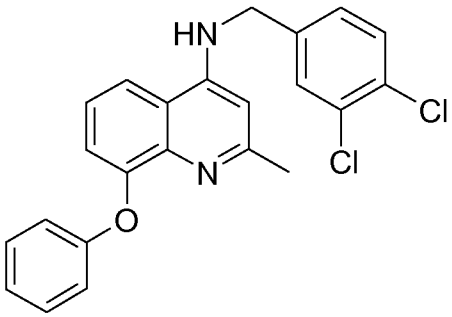
Preparation was made using a similar procedure as described in example 5, method 5.1. Starting materials were 4-chloro-2-methyl-8-propoxyquinoline and 3,4-dichlorobenzylamine. A catalytic effective amount of copper(II)sulphate hydrate was added to the reaction mixture. The product was purified using silica gel chromatography, eluting with dichloromethane:methanol 90:10.

Yield: 8%.

ESI-MS [M+H]+ =375.1/377.1 calculated for $C_{20}H_{20}Cl_2N_2O$ = 375 g/ mole

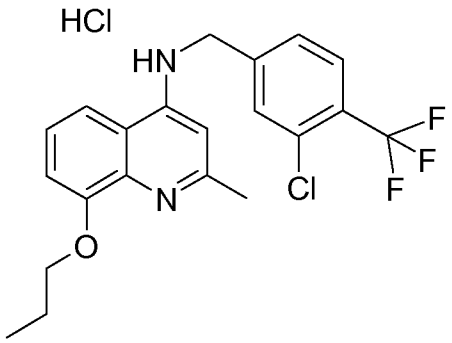
Example 44:

(3,4-Dichlorobenzyl)-(2-methyl-8-phenoxyquinolin-4-yl)-amine



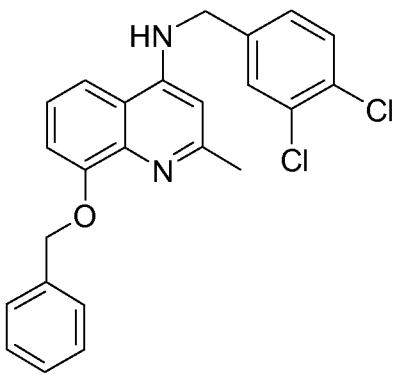
Preparation was made using a similar procedure as described in example 43, using 4-chloro-8-hydroxy-2-methylquinoline.
Yield: 25% in last step.
ESI-MS [M+H]+ = 409.1/411.1 calculated for $C_{23}H_{18}Cl_2N_2O$ = 409 g/ mole

Example 45:
(3-Chloro-4-trifluoromethylbenzyl)-(2-methyl-8-propoxyquinoline-4-yl)-amine hydrochloride



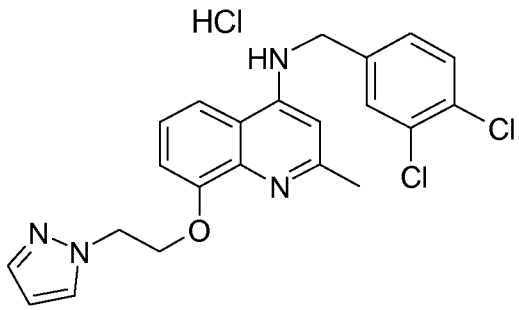
Preparation was made using a similar procedure as described in example 43, using 4-chloro-8-hydroxy-2-methylquinoline.
Yield: 25% in last step
ESI-MS [M+H]+ =409.2 calculated for $C_{21}H_{20}ClF_3N_2O$ = 409 g/ mole

Example 46:
(8-Benzyloxy-2-methylquinolin-4-yl)-(3,4-dichlorobenzyl)-amine



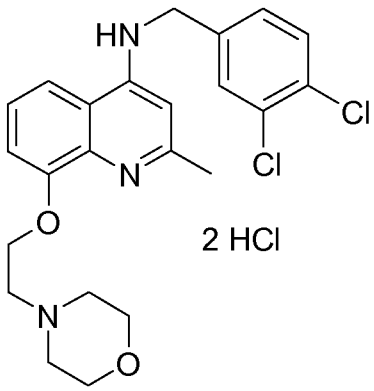
Preparation was made using a similar procedure as described in example 43, using 4-chloro-8-hydroxy-2-methylquinoline.
Yield: 11% in last step
ESI-MS [M+H]+ =423.3/425.3 calculated for $C_{24}H_{20}Cl_2N_2O$ = 423 g/ mole

Example 47:
(3,4-Dichlorobenzyl)-[2-methyl-8-(2-pyrazol-1-yl-ethoxy)-quinolin-4-yl]-amine hydrochloride



Preparation was made using a similar procedure as described in example 43, using 4-chloro-8-hydroxy-2-methylquinoline.
Yield: 35% in last step
ESI-MS [M+H]+ =427.4/429.4 calculated for $C_{22}H_{21}Cl_3N_4O$ = 427 g/ mole

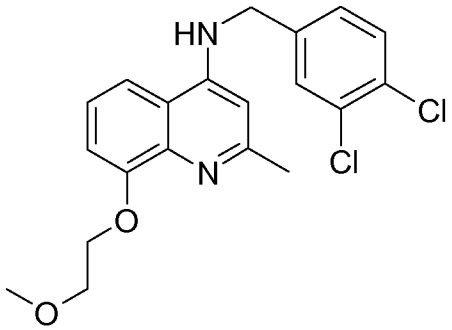
Example 48:
(3,4-Dichlorobenzyl)-[2-methyl-8-(2-morpholin-4-yl-ethoxy)-quinolin-4-yl]-amine dihydrochloride



Preparation was made using a similar procedure as described in example 43, using 4-chloro-8-hydroxy-2-methylquinoline.
Yield: 19% in last step
ESI-MS [M+H]+ = 446.3/448.4 calculated for $C_{23}H_{27}Cl_4N_3O_2$ = 446 g/ mole

Example 49:

(3,4-Dichlorobenzyl)-[8-(2-methoxyethoxy)-2-methylquinolin-4-yl]-amine



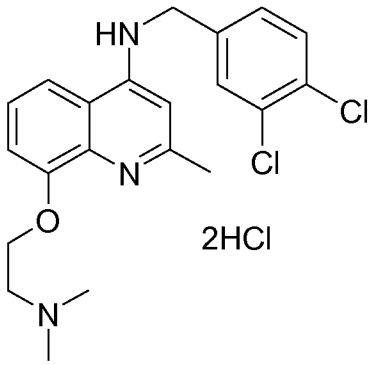
Preparation was made using a similar procedure as described in example 43, using 4-chloro-8-hydroxy-2-methylquinoline.

Yield: 28% in last step

ESI-MS [M+H]+ =391.1/393.1 calculated for $C_{20}H_{20}Cl_2N_2O_2$ = 391 g/ mole

Example 50:

(3,4-Dichlorobenzyl)-[8-(2-dimethylamino-ethoxy)-2-methylquinolin-4-yl]-amine dihydrochloride



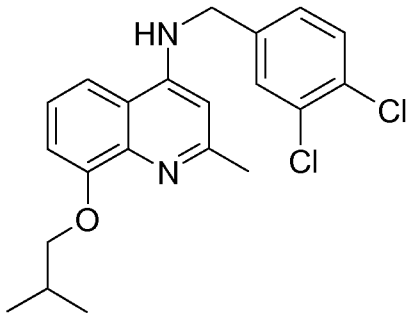
Preparation was made using a similar procedure as described in example 43, using 4-chloro-8-hydroxy-2-methylquinoline.

Yield: 20% in last step

ESI-MS [M+H]+ =404.2/406.2 calculated for $C_{21}H_{25}Cl_4N_3O$ = 404 g/ mole

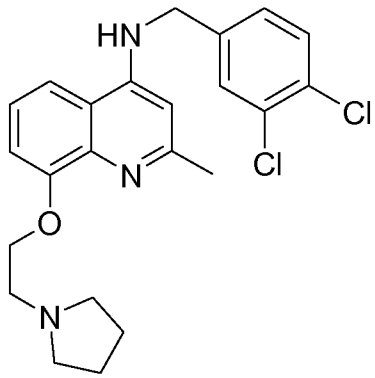
Example 51:

(3,4-Dichlorobenzyl)-(8-isobutoxy-2-methylquinolin-4-yl)-amine



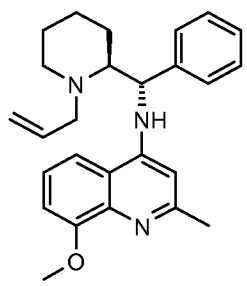
Preparation was made using a similar procedure as described in example 43, using 4-chloro-8-hydroxy-2-methylquinoline.
Yield: 48% in last step
ESI-MS [M+H]+ =389.2/391.2 calculated for $C_{21}H_{22}Cl_2N_2O$ = 389 g/ mole

Example 52:
(3,4-Dichlorobenzyl)-[2-methyl-8-(2-pyrrolidin-1-yl-ethoxy)-quinolin-4-yl]-amine



Preparation was made using a similar procedure as described in example 43, using 4-chloro-8-hydroxy-2-methylquinoline.
Yield: 32% in last step
ESI-MS [M+H]+ = 430.2/432.2 calculated for $C_{23}H_{25}Cl_2N_3O$ = 430 g/ mole

Example 53:
[(S)-((S)-1-Allylpiperidin-2-yl)-phenylmethyl]-(8-methoxy-2-methylquinolin-4-yl)-amine



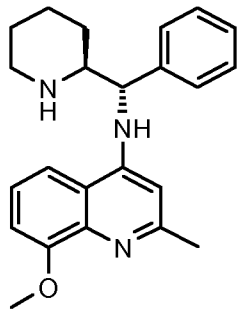
Preparation was made using a similar procedure as described in example 5, method 5.1. Starting materials were 4-chloro-8-hydroxy-2-methylquinoline) and C-[(S)-C-((S)-1-allyl-piperidin-2-yl)-C-phenyl]-methylamine. Acetonitrile was used as solvent instead of di-methylformamide.

Yield: 32%.

ESI-MS [M+H]+ = 402,2 calculated for $C_{26}H_{31}N_3O$ = 402 g/ mole

Example 54:

(8-Methoxy-2-methylquinolin-4-yl)-((S)-phenyl-(S)-piperidin-2-yl-methyl)-amine



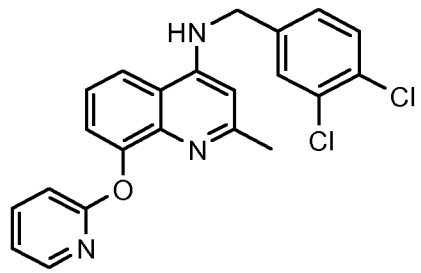
Preparation was made using a similar procedure as described in example 37, using [(S)-((S)-1-allyl-piperidin-2-yl)-phenyl]- (8-methoxy-2-methylquinolin-4-yl)-amine (example 53).

Yield: 37%.

ESI-MS [M+H]+ = 362,1 calculated for $C_{23}H_{29}Cl_2N_3O$ = 402 g/ mole

Example 55:

(3,4-Dichlorobenzyl)-[2-methyl-8-(pyridin-2-yloxy)-quinolin-4-yl]-amine

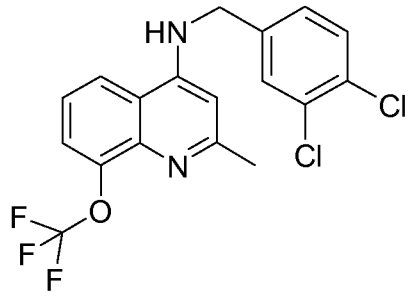


Preparation was made using a similar procedure as described in example 1, method 1.3. Starting materials were 4-chloro-2-methyl-8-(pyridin-2-yloxy)-quinoline and 3,4-dichlorobenzylamine.

Yield: 7%.

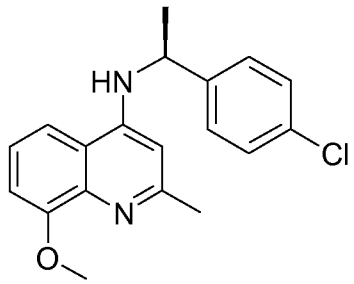
ESI-MS [M+H]+ =410.1/414.1 calculated for $C_{22}H_{17}Cl_2N_3O$ = 410 g/ mole

Example 56:
(3,4-Dichloro-benzyl)-(2-methyl-8-trifluoromethoxyquinolin-4-yl)-amine



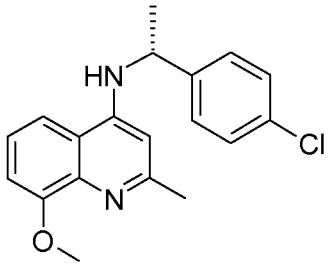
Preparation was made using a similar procedure as described in example 1, method 1.3. Starting materials were 4-chloro-2-methyl-8-trifluoromethoxyquinoline and 3,4-dichlorobenzylamine.
Yield: 5%.
ESI-MS [M+H]+ =401.1/405.1 calculated for $C_{18}H_{13}Cl_2F_3N_2O$ = 401 g/ mole

Example 57:
[(S)-1-(4-Chlorophenyl)-ethyl]-(8-methoxy-2-methylquinolin-4-yl)-amine



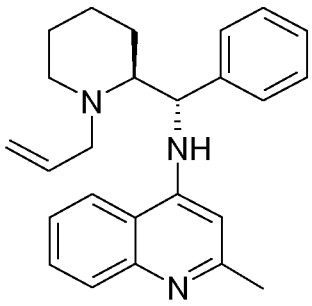
Preparation was made using a similar procedure as described in example 41. Starting materials were 4-chloro-8-methoxy-2-methylquinoline and (S)-1-(4-chloro-phenyl)-ethylamine.
Yield: 28%.
ESI-MS [M+H]+ =327.1/329.1 calculated for $C_{19}H_{19}ClN_2O$ = 327 g/ mole

Example 58:
[(R)-1-(4-Chlorophenyl)-ethyl]-(8-methoxy-2-methylquinolin-4-yl)-amine



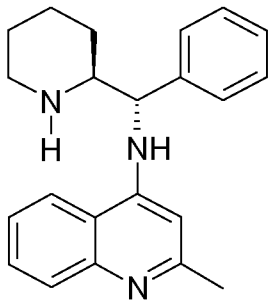
Preparation was made using a similar procedure as described in example 41. Starting materials were 4-chloro-8-methoxy-2-methylquinoline and (R)-1-(4-chloro-phenyl)-ethylamine.
Yield: 64%.
ESI-MS [M+H]+ =327.2 calculated for $C_{19}H_{19}ClN_2O$ = 327 g/ mole

Example 59:
[(S)-((S)-1-Allylpiperidin-2-yl)-phenylmethyl]-(2-methylquinolin-4-yl)-amine



Preparation was made using a similar procedure as described in example 5, method 5.1. Starting materials were 4-chloro-2-methylquinoline and C-[(S)-C-((S)-1-allylpiperidin-2-yl)-C-phenyl]-methylamine. Acetonitrile was used as solvent instead of dimethylformamide.
Yield: 64%.
ESI-MS [M+H]+ = 372,3/ 373,3 calculated for $C_{25}H_{29}N_3$ = 372 g/ mole

Example 60:
(2-Methylquinolin-4-yl)-((S)-phenyl-(S)-piperidin-2-yl-methyl)-amine

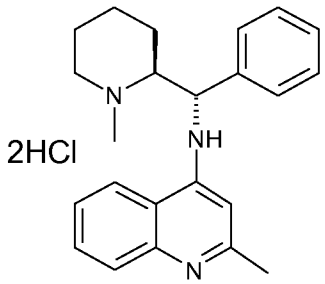


Preparation was made using a similar procedure as described in example 37, using [(S)-((S)-1-allylpiperidin-2-yl)-phenylmethyl]-(2-methylquinolin-4-yl)-amine (example 59). Yield: 60%.

ESI-MS $[M+H]^+$ = 332,2/ 333,3 calculated for $C_{22}H_{25}N_3$ = 331 g/ mole

Example 61:

(S)-((S)-1-Methylpiperidin-2-yl)-phenylmethyl]-(2-methylquinolin-4-yl)-amine dihydrochloride

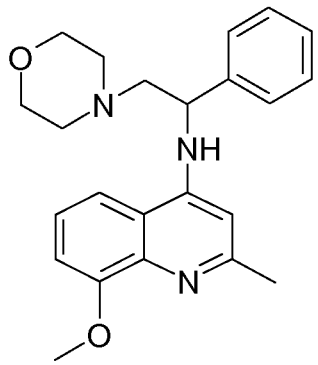


(2-Methylquinolin-4-yl)-((S)-phenyl-(S)-piperidin-2-yl-methyl)-amine (example 60, 27 mg, 0.08 mmole) was suspended in dichloromethane and mixed with paraformaldehyde (37%, 7 mg) and one drop of acetic acid. Sodium triacetoxyborohydride was added and the mixture was stirred for 14 hrs. The reaction mixture was washed with saturated $NaHCO_3$ solution, the watery phase was washed with dichloromethane and the combined organic phases were dried with sodium sulphate and concentrated. After purification using silica gel chromatography, eluting with dichloromethane:methanol 80:20, the product was precipitated in diethyl ether as hydrochloride (8,40 mg, 25%).

ESI-MS $[M+H]^+$ = 346,3/ 347,2 calculated for $C_{21}H_{27}N_3 \bullet 2HCl$ = 418 g/ mole

Example 62:

(8-Methoxy-2-methylquinolin-4-yl)-(2-morpholin-4-yl-1-phenyl)-ethylamine



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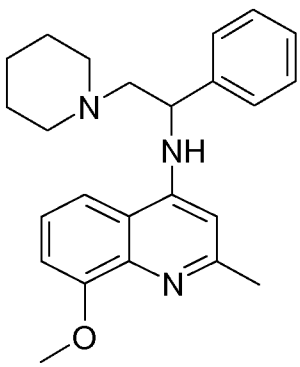
Preparation was made using a similar procedure as described in example 68. Starting materials were 4-chloro-2-methylquinoline and 2-morpholin-4-yl-1-phenyl-ethylamine. Yield: 17%.

ESI-MS $[M+H]^+$ = 378,1/ 379,1 calculated for $C_{23}H_{27}N_3O_2$ = 377 g/ mole

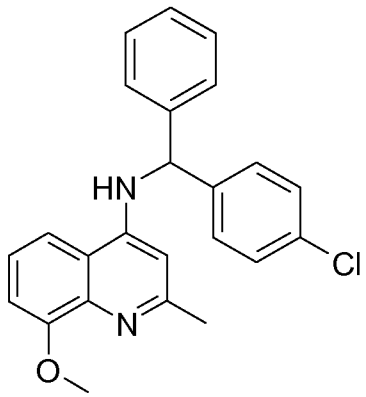
Example 63:
(8-Methoxy-2-methyl-quinolin-4-yl)-(1-phenyl-2-piperidin-1-yl)-ethylamine



Preparation was made using a similar procedure as described in example 68. Starting materials were 4-chloro-2-methylquinoline and 1-phenyl-2-piperidin-1-yl-ethylamine. Yield: 34%.

ESI-MS $[M+H]^+$ = 376,3/ 377,2 calculated for $C_{24}H_{29}N_3O$ = 376 g/ mole

Example 64:
[(4-Chlorophenyl)-phenylmethyl]-(8-methoxy-2-methylquinolin-4-yl)-amine



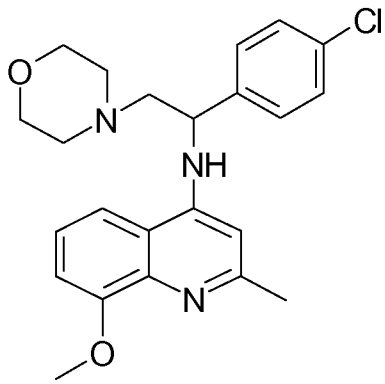
Preparation was made using a similar procedure as described in example 5, method 5.1. Starting materials were 4-chloro-2-methylquinoline and C-(4-chloro-phenyl)-C-phenyl-methylamine.

Yield: 57%.

ESI-MS [M+H]+ =389.2 calculated for $C_{24}H_{21}ClN_2O$ = 389 g/ mole

Example 65:

[1-(4-Chlorophenyl)-2-morpholin-4-yl-ethyl]-(8-methoxy-2-methylquinolin-4-yl)-amine



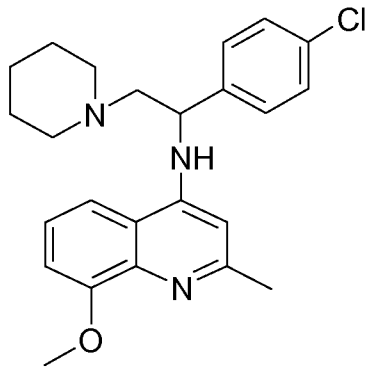
Preparation was made using a similar procedure as described in example 68. Starting materials were 4-chloro-2-methylquinoline and 1-(4-chlorophenyl)-2-morpholin-4-yl-ethylamine.

Yield: 29%.

ESI-MS $[M+H]^+$ = 412,1/ 414,1 calculated for $C_{23}H_{26}ClN_3O_2$ = 412 g/ mole

Example 66:

[1-(4-Chlorophenyl)-2-piperidin-1-yl-ethyl]-(8-methoxy-2-methylquinolin-4-yl)-amine



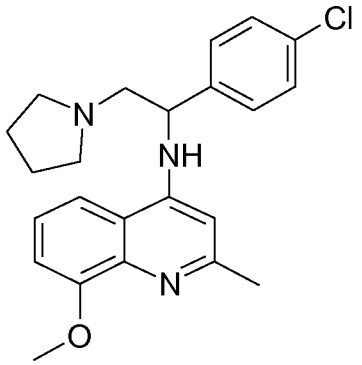
Preparation was made using a similar procedure as described in example 68. Starting materials were 4-chloro-2-methylquinoline and 1-(4-chlorophenyl)-2-piperidin-1-yl-ethylamine.

Yield: 84%.

ESI-MS [M+H]+ = 331,2/ 332,3 calculated for $C_{24}H_{28}ClN_3O$ = 410 g/ mole

Example 67:

[1-(4-Chloro-phenyl)-2-pyrrolidin-1-yl-ethyl]-(8-methoxy-2-methyl-quinolin-4-yl)-amine



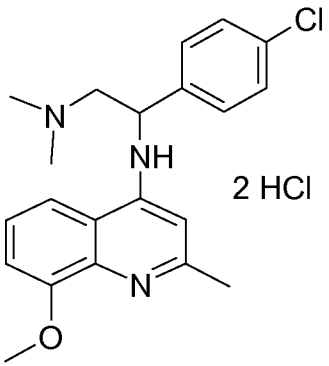
Preparation was made using a similar procedure as described in example 68. Starting materials were 4-chloro-2-methylquinoline and 1-(4-chlorophenyl)-2-pyrrolidin-1-yl-ethylamine.

Yield: 28%.

ESI-MS $[M+H]^+$ = 396,3/ 398,3 calculated for $C_{23}H_{26}ClN_3O$ = 396 g/ mole

Example 68:

(rac)-1-(4-Chlorophenyl)-N*1*-(8-methoxy-2-methylquinolin-4-yl)-N*2*,N*2*-dimethylethane-1,2-diamine dihydrochloride

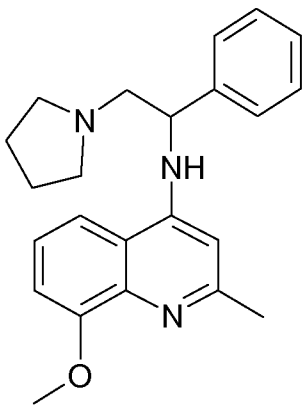


4-Chloro-8-methoxy-2-methylquinoline (2.00 g, 9.63 mmole), 1-(4-chlorophenyl)-N*2*,N*2*-dimethylethane-1,2-diamine (2.30 g, 11.6 mmole), sodium tert-butylate (1.3 g, 13.5 mmole), tris(dibenzylidenaceton)-dipalladium(0) (0.18 g, 0.193 mmole) and 2-dicyclohexyl-phosphino-2(N,N-dimethylamino)biphenyl (0.27 g, 0.674 mmole) were stirred at 150 °C under nitrogen atmosphere in a microwave oven for 30 min. The reaction mixture was dissolved in ethyl acetate and filtered. The filtrate was extracted with water. The organic phases were dried, concentrated and the residue was purified using silica gel chromatography, eluting with dichloromethane:methanol 90:10. Precipitation in isopropanol/HCl and in ethyl acetate gave the product (1.55 g, 36%).

ESI-MS $[M+H]^+$ = 370.1/ 372,1 calculated for $C_{21}H_{24}ClN_3O \bullet 2HCl$ = 442 g/ mole

Example 69:

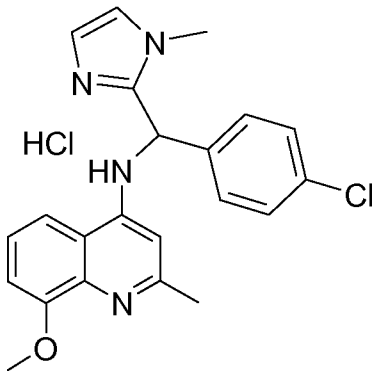
(8-Methoxy-2-methylquinolin-4-yl)-(1-phenyl-2-pyrrolidin-1-ylethyl)-amine



Preparation was made using a similar procedure as described in example 68. Starting materials were 4-chloro-2-methylquinoline and 1-phenyl-2-pyrrolidin-1-yl-ethylamine. Yield: 41%.

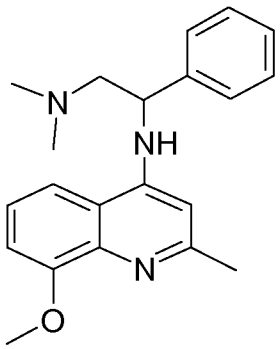
ESI-MS $[M+H]^+$ = 362,1/ 363,2 calculated for $C_{23}H_{27}N_3O$ = 361 g/ mole

Example 70:
[(4-Chlorophenyl)-(1-methyl-1H-imidazol-2-yl)-methyl]-(8-methoxy-2-methylquinoline-4-yl)-amine



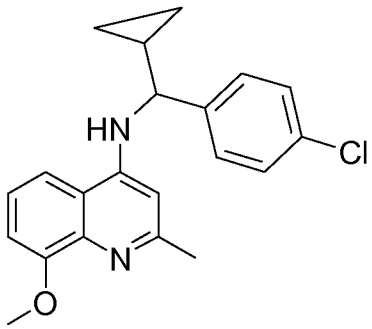
Preparation was made using a similar procedure as described in example 68. Starting materials were 4-chloro-2-methylquinoline and C-(4-chlorophenyl)-C-(1-methyl-1H-imidazol-2-yl)-methylamine.
Yield: 4%.
ESI-MS [M+H]+ =393.2/395.2 calculated for $C_{22}H_{21}ClN_4O$ = 393 g/ mole

Example 71:
N*1*-(8-Methoxy-2-methylquinolin-4-yl)-N*2*,N*2*-dimethyl-1-phenylethane-1,2-diamine



Preparation was made using a similar procedure as described in example 68. Starting materials were 4-chloro-2-methylquinoline and N*2*,N*2*-dimethyl-1-phenylethane-1,2-diamine.
Yield: 11%.
ESI-MS $[M+H]^+$ = 336,2/ 337,2 calculated for $C_{21}H_{25}N_3O$ = 335 g/ mole

Example 72:
[(4-Chlorophenyl)-cyclopropylmethyl]-(8-methoxy-2-methylquinolin-4-yl)-amine



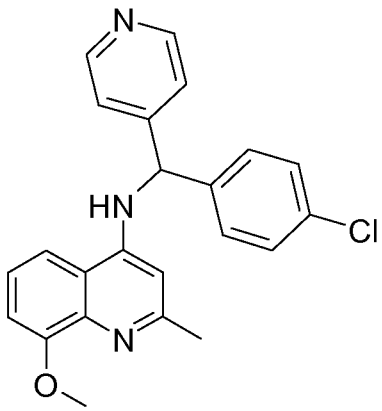
Preparation was made using a similar procedure as described in example 68. Starting materials were 4-chloro-2-methylquinoline and N*2*,N*2*-dimethyl-1-phenylethane-1,2-diamine.

Yield: 8%.

ESI-MS [M+H]+ =353.2/355.2 calculated for $C_{21}H_{22}Cl_2N_2O$ = 353 g/ mole

Example 73:

[(4-Chlorophenyl)-pyridin-4-ylmethyl]-(8-methoxy-2-methylquinolin-4-yl)-amine



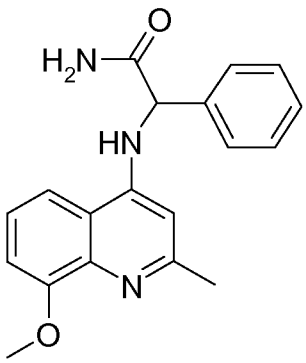
Preparation was made using a similar procedure as described in example 19, method 19.2. Starting materials were 4-chloro-8-methoxy-2-methylquinoline and C-(4-chloro-phenyl)-C-pyridin-4-yl-methylamine. Acetonitrile was used as solvent instead of dimethyl-formamide.

Yield: 2%.

ESI-MS [M+H]+ =390.2 calculated for $C_{23}H_{20}ClN_3O$ = 390 g/ mole

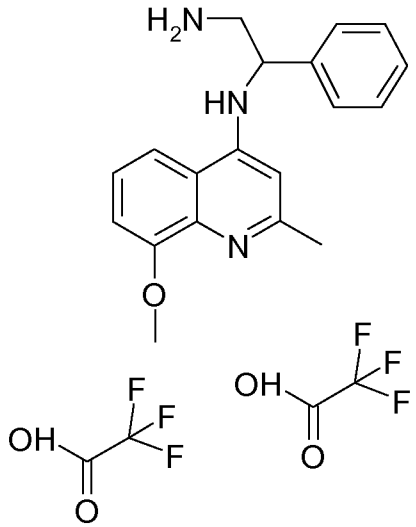
Example 74:

2-(8-Methoxy-2-methylquinolin-4-ylamino)-2-phenylacetamide



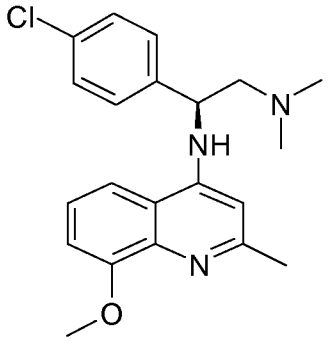
Preparation was made using a similar procedure as described in example 19, method 19.2. Starting materials were 4-chloro-8-methoxy-2-methylquinoline and 2-amino-2-phenyl-acetamide. Acetonitrile was used as solvent instead of dimethylformamide.
Yield: 59%.
ESI-MS [M+H]+ =322.3 calculated for $C_{19}H_{19}N_3O_2$ = 321 g/ mole

Example 75:
N*1*-(8-Methoxy-2-methylquinolin-4-yl)-1-phenylethane-1,2-diamine



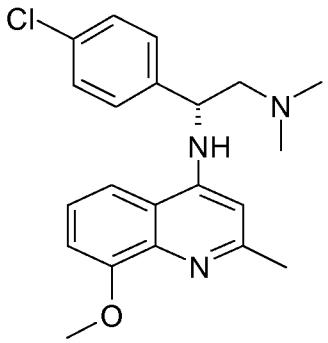
2-(8-Methoxy-2-methylquinolin-4-ylamino)-2-phenylacetamide (example 74, 430 mg, 1.33 mmole) was suspended in tetrahydrofurane (20 mL) and BH_3xSMe_2 (2M in tetrahydrofurane) was added dropwise. The mixture was refluxed under stirring for 1 h and then stirred at RT for 12 hrs. The content of the flask was carefully mixed with 2N HCl and refluxed for 2 hrs. The reaction mixture was alkalized and extracted with dichloromethane. The organic phases were dried and concentrated. The residue thus obtained was purified using HPLC (RP-18, eluting with water/acetonitrile) to obtain the product (12%, 83 mg).
ESI-MS [M+H]+ =294.1 calculated for $C_{22}H_{21}F_6N_3O_5$ = 293 g/ mole

Example 76:
(S)-1-(4-Chlorophenyl)-N*1*-(8-methoxy-2-methylquinolin-4-yl)-N*2*,N*2*-dimethylethane-1,2-diamine



Preparative chiral chromatography (Chiracel-OD, OD85-15) was used to separate 1-(4-chlorophenyl)-N*1*-(8-methoxy-2-methylquinoline-4-yl)-N*2*,N*2*-dimethylethane-1,2-diamine dihydrochloride (example 68, 200 mg) into its enantiomers. 42 mg (25%) of (S)-1-(4-chlorophenyl)-N*1*-(8-methoxy-2-methylquinoline-4-yl)-N*2*,N*2*-dimethylethane-1,2-diamine were obtained.
ESI-MS $[M+H]^+$ = 370.1/372,1 calculated for $C_{21}H_{24}ClN_3O$ = 370 g/ mole

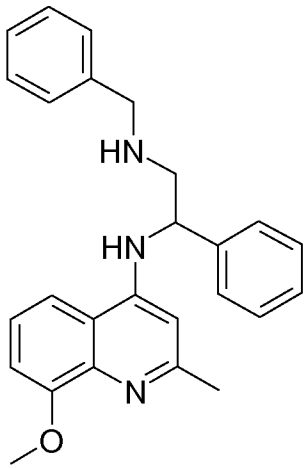
Example 77:
(R)-1-(4-Chlorphenyl)-N*1*-(8-methoxy-2-methylquinoline-4-yl)-N*2*,N*2*-dimethylethane-1,2-diamin



Preparative chiral chromatography (Chiracel-OD, OD85-15, n-hexane: isopropanol/ NEt_3 850:150:1) was used to separate 1-(4-chlorophenyl)-N*1*-(8-methoxy-2-methylquinoline-4-yl)-N*2*,N*2*-dimethylethane-1,2-diamine dihydrochloride (example 68, 200 mg) into its enantiomers. 37 mg (22%) of (R)-1-(4-chlorophenyl)-N*1*-(8-methoxy-2-methylquinoline-4-yl)-N*2*,N*2*-dimethylethane-1,2-diamine were obtained.
ESI-MS [M+H]+ = 370.1/ 372,1 calculated for $C_{21}H_{24}ClN_3O$ = 370 g/ mole

Example 78:

N*2*-Benzyl-N*1*-(8-methoxy-2-methylquinolin-4-yl)-1-phenylethane-1,2-diamine

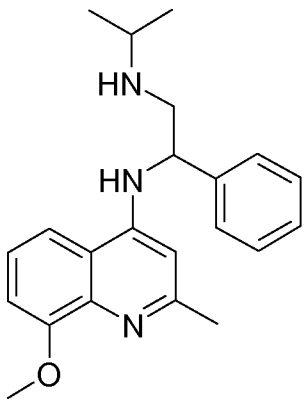


N*1*-(8-Methoxy-2-methylquinolin-4-yl)-1-phenylethane-1,2-diamine (Example 75, 150 mg, 0.488 mmole) and benzaldehyde were stirred at RT for 20 hrs. Molecular sieve (4A) was added and the mixture was heated to 60°C within 2 hrs. $NaBH_4$ was added and the mixture was stirred for 1 h at RT. The resulting mixture was filtered and extracted with dichloromethane. The organic phases were dried and concentrated. The residue was purified using preparative HPLC (RP-18, water/acetonitrile) to obtain the product (21 mg, 11%).

ESI-MS [M+H]+ = 398.3 calculated for $C_{26}H_{27}N_3O$ = 398 g/ mole

Example 79:

N*2*-Isopropyl-N*1*-(8-methoxy-2-methylquinolin-4-yl)-1-phenylethane-1,2-diamine

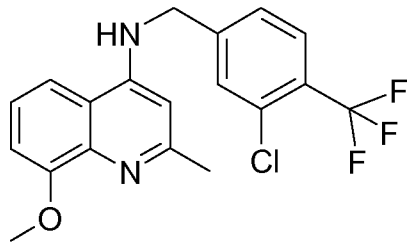


Preparation was made using a similar procedure as described in example 79. Starting materials were N*1*-(8-methoxy-2-methylquinolin-4-yl)-1-phenylethane-1,2-diamine (Example 75) and acetone.

Yield: 27%.

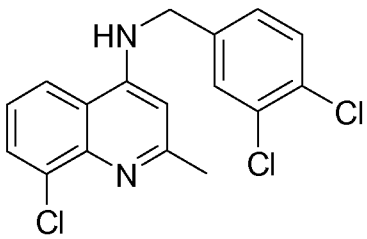
ESI-MS [M+H]+ =350.3 calculated for $C_{22}H_{27}N_3O$ = 349 g/ mole

Example 80:
(3-Chloro-4-trifluoromethylbenzyl)-(8-methoxy-2-methylquinolin-4-yl)-amine



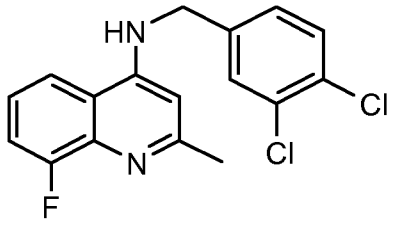
Preparation was made using a similar procedure as described in example 1, method 1.3. Starting materials were 4-chloro-8-methoxy-2-methylquinoline and 3-chloro-4-trifluoromethylbenzylamine.
Yield: 39%.
ESI-MS [M+H]+ =381.2 calculated for $C_{19}H_{16}ClF_3N_2O$ = 380 g/ mole

Example 81:
(8-Chlor-2-methylquinolin-4-yl)-(3,4-dichlorobenzyl)-amine



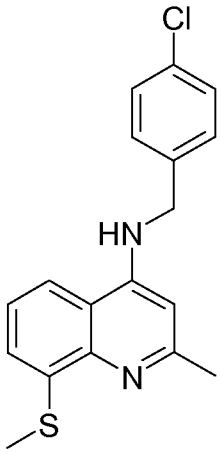
Preparation was made using a similar procedure as described in example 1, method 1.3. Starting materials were 4,8-dichloro-2-methylquinoline and 3,4-dichlorobenzylamine.
Yield: 6%.
ESI-MS [M+H]+ =351.1/353.1 calculated for $C_{17}H_{13}Cl_3N_2$ = 352 g/ mole

Example 82:
(3,4-Dichlorobenzyl)-(8-fluoro-2-methylquinolin-4-yl)-amine



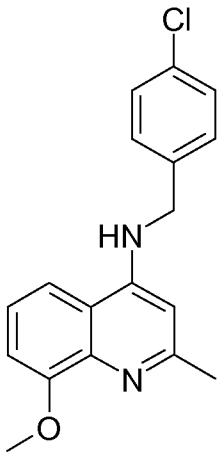
Preparation was made using a similar procedure as described in example 1, method 1.3. Starting materials were 4-chloro-8-fluoro-2-methylquinoline and 3,4-dichlorobenzylamine.
Yield: 24%.
ESI-MS [M+H]+ =335.1/337.1 calculated for $C_{17}H_{13}Cl_2FN_2$ = 335 g/ mole

Example 83:
(4-Chlorobenzyl)-(2-methyl-8-methylsulfanylquinolin-4-yl)-amine



Preparation was made using a similar procedure as described in example 1, method 1.3. Starting materials were 4-chloro-2-methyl-8-methylsulfanylquinoline and 4-chloro-benzylamine.
Yield: 19%.
ESI-MS [M+H]+ = 329,1 calculated for $C_{18}H_{17}ClN_2S$ = 329 g/ mole

Example 84:
(4-Chlorobenzyl)-(2-methyl-8-methoxyquinolin-4-yl)-amine

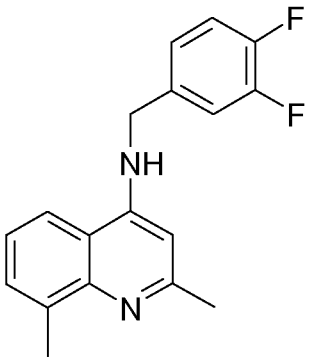


Preparation was made using a similar procedure as described in example 1, method 1.3. Starting materials were 4-chloro-2-methyl-8-methoxyquinoline and 4-chlorobenzylamine. Yield: 72%.

ESI-MS [M+H]+ = 313,0 calculated for $C_{18}H_{17}ClN_2O$ = 313 g/ mole

Example 85:

(3,4-Difluoro-benzyl)-(2,8-dimethyl-quinolin-4-yl)-amine

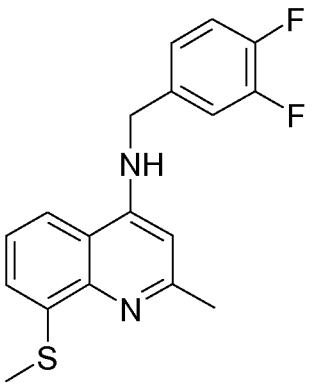


Preparation was made using a similar procedure as described in example 1, method 1.3. Starting materials were 4-chloro-2-methyl-8-methylquinoline and 3,4-difluorobenzylamine. Yield: 19%.

ESI-MS [M+H]+ = 299,1 calculated for $C_{18}H_{16}F_2N_2$ = 298 g/ mole

Example 86:

(3,4-Difluorobenzyl)-(2-methyl-8-methylsulfanylquinolin-4-yl)-amine



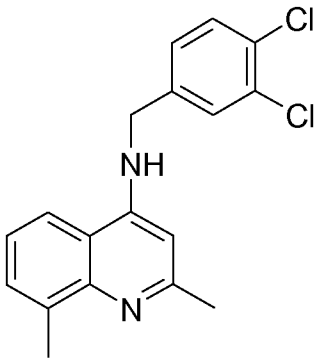
Preparation was made using a similar procedure as described in example 1, method 1.3. Starting materials were 4-chloro-2-methyl-8-methylsulfanylquinoline and 3,4-difluorobenzylamine.

Yield: 24%.

ESI-MS [M+H]+ = 331,0 calculated for $C_{18}H_{16}F_2N_2S$ = 330 g/ mole

Example 87:

(3,4-Dichlorobenzyl)-(2-methyl-8-methylquinolin-4-yl)-amine

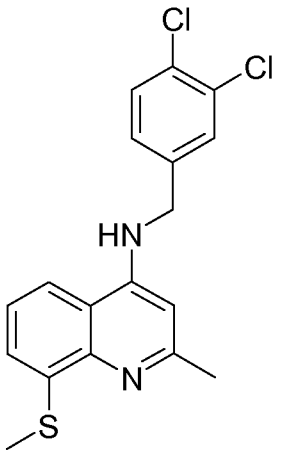


Preparation was made using a similar procedure as described in example 1, method 1.3. Starting materials were 4-chloro-2-methyl-8-methylquinoline and 3,4-dichlorobenzylamine. Yield: 24%.

ESI-MS [M+H]+ = 331,0 / 333,0 calculated for $C_{18}H_{16}Cl_2N_2$ = 331 g/ mole

Example 88:

(3,4-Dichlorobenzyl)-(2-methyl-8-methylsulfanylquinolin-4-yl)-amine



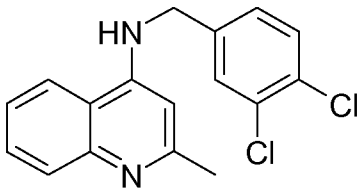
Preparation was made using a similar procedure as described in example 1, method 1.3. Starting materials were 4-chloro-2-methyl-8-methylsulfanylquinoline and 3,4-dichlorobenzylamine.

Yield: 48%.

ESI-MS [M+H]+ = 313,0 calculated for $C_{18}H_{16}Cl_2N_2S$ = 363 g/ mole

Example 89:

(3,4-Dichlorobenzyl)-(2-methylquinolin-4-yl)-amine



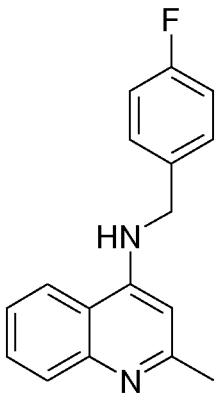
Preparation was made using a similar procedure as described in example 1, method 1.3. Starting materials were 4-chloro-2-methylquinoline and 3,4-dichlorobenzylamine.

Yield: 10%.

ESI-MS [M+H]+ = 317,0 / 319,0 calculated for $C_{17}H_{14}Cl_2N_2$= 317 g/ mole

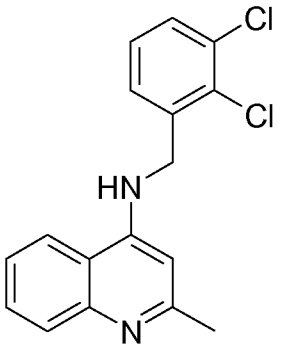
Example 90:

(4-Fluorobenzyl)-(2-methylquinoline-4-yl)-amine



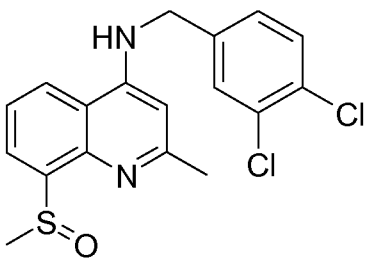
Preparation was made using a similar procedure as described in example 1, method 1.3. Starting materials were 4-chloro-2-methylquinoline and 4-fluorobenzylamine.
Yield: 47%.
ESI-MS [M+H]+ = 267,1 calculated for $C_{17}H_{15}FN_2$= 266 g/ mole

Example 91:
(2,3-Dichloro-benzyl)-(2-methylquinolin-4-yl)-amine



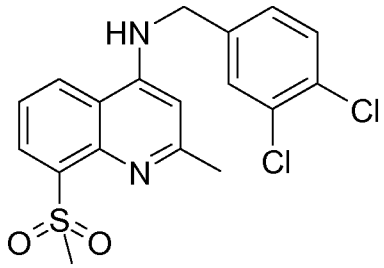
Preparation was made using a similar procedure as described in example 1, method 1.3. Starting materials were 4-chloro-2-methylquinoline and 2,3-dichlorobenzylamine.
Yield: 47%.
ESI-MS [M+H]+ = 317,0/ 319,0 calculated for $C_{17}H_{14}Cl_2N_2$= 317 g/ mole

Example 92:
(3,4-Dichlorobenzyl)-(8-methanesulfinyl-2-methylquinolin-4-yl)-amine



H_2O_2 (30%, 20.0 mg, 0.55 mmole) was added dropwise to a solution of (3,4-dichlorobenzyl)-(2-methyl-8-methylsulfanylquinolin-4-yl)-amine (100 mg, 0.275 mmole) in acetic acid (3.5 mL) at 0 °C. The mixture was stirred at RT for 16 hrs, concentrated by half, 2N NaOH was added and the resulting mixture was extracted with ethyl acetate. The organic phases were dried and concentrated. Precipitation in isopropyl ether gave the product as a white solid (37 mg, 35%).
ESI-MS [M+H]+ =379.1/383.1 calculated for $C_{18}H_{16}Cl_2N_2OS$= 379 g/ mole

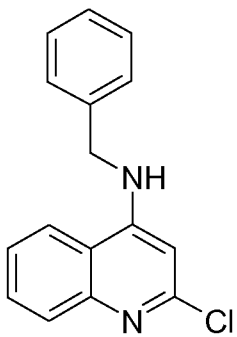
Example 93:
(3,4-Dichlorobenzyl)-(8-methanesulfonyl-2-methylquinolin-4-yl)-amine



H_2O_2 (30%, 18.0 mg, 0.53 mmole) was added dropwise to a solution of (3,4-dichlorobenzyl)-(8-methanesulfinyl-2-methylquinolin-4-yl)-amine (50 mg, 0.132 mmole) in acetic acid (3,5 mL) at 0 °C. The mixture was stirred at 70 °C for 16 hrs, concentrated by half, 2N NaOH was added and the resulting mixture was extracted with ethyl acetate. The organic phases were dried and concentrated. Precipitation in ethyl acetate gave the product as white solid (32 mg, 61%).
ESI-MS [M+H]+ =395.1/399.0 calculated for $C_{18}H_{16}Cl_2N_2O_2S$= 395 g/ mole

Example 94:
N*4*-Benzyl-N*2*,N*2*-dimethylquinoline-2,4-diamine

94.1 *Benzyl-(2-chloroquinolin-4-yl)-amine*

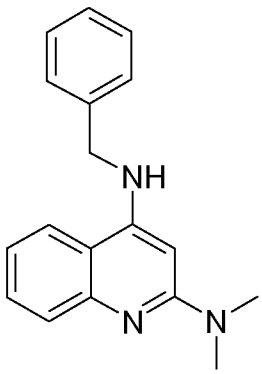


2,4-Dichloroquinoline (0.70 g, 3,53 mmole) and benzylamine (3,79 g, 35,3 mmole) in ethanol (2 mL) were stirred at 110 °C in a microwave oven for 1h. Water was added and

the mixture was extracted with ethyl acetate. The organic phases were washed with saturated NaCl solution, dried and concentrated. The residue thus obtained was purified using silica gel chromatography, eluting with dichloromethane:methanol 95:5 to give a white solid (330 mg, 35%).

ESI-MS [M+H]+ =269.1/271.0 calculated for $C_{16}H_{13}ClN_2$ = 269 g/ mole

94.2 *N*4*-Benzyl-N*2*,N*2*-dimethylquinoline-2,4-diamine*

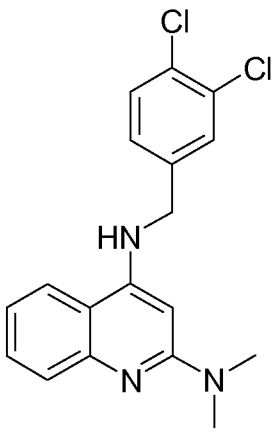


Benzyl-(2-chloroquinolin-4-yl)-amine (100 mg, 0.372 mmole), copper(II)sulphate pentahydrate (92.9 mg, 0.372 mmole) and dimethylamine (1M in MeOH, 3 mL) were stirred at 150 °C in a microwave oven for 5 hrs. The reaction mixture was dissolved with water and extracted with ethyl acetate. The residue obtained from the organic phases was purified using silica gel chromatography, eluting with dichloromethane:methanol 90:10. Precipitation in isopropyl ether gave a yellowish solid (70.0 mg, 68%).

ESI-MS [M+H]+ =278.2/279.2 calculated for $C_{18}H_{19}N_3$ = 277 g/ mole

Example 95:

N*4*-(3,4-Dichlorobenzyl)-N*2*,N*2*-dimethylquinoline-2,4-diamine

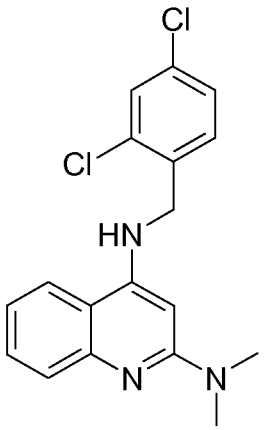


Preparation was made using a procedure similar to example 94. Yield of the desired product was 31% in the last step.

ESI-MS [M+H]+ =346.1/350.1 calculated for $C_{18}H_{17}Cl_2N_3$ = 346 g/ mole

Example 96:

N*4*-(2,4-Dichlorobenzyl)-N*2*,N*2*-dimethylquinoline-2,4-diamin



Preparation was made using a procedure similar to example 94. Yield of the desired product was 5% in the last step.

ESI-MS [M+H]+ =346.1/350.1 calculated for $C_{18}H_{17}Cl_2N_3$ = 346 g/ mole

Biological testing

1. Glycine uptake in recombinant hGlyT1 expressing cells:
Human GlyT1c expressing recombinant hGlyT1c_5_CHO cells were plated at 20,000 cells per well in 96 well Cytostar-T scintillation microplates (Amersham Biosciences) and cultured to sub-confluency for 24h. For glycine uptake assays the culture medium was aspirated and the cells were washed once with 100 µl HBSS (Gibco BRL, #14025-050) with 5 mM L-Alanine (Merck #1007). 80 µl HBSS buffer were added, followed by 10 µl inhibitor or vehicle (10% DMSO) and 10 µl [^{3}H]-glycine (TRK71, Amersham Biosciences) to a final concentration of 200 for initiation of glycine uptake. The plates were placed in a Wallac Microbeta (PerkinElmer) and continuously counted by solid phase scintillation spectrometry during up to 3 hours. Nonspecific uptake was determined in the presence of 10 µM Org24598. IC_{50} calculations were made by four-parametric logistic nonlinear regression analysis (GraphPad Prism) using determinations within the range of linear increase of [^{3}H]-glycine incorporation between 60 and 120 min.

2. [^{3}H]-(R)-NPTS radioligand binding assays using recombinant hGlyT1 expressing cell membranes:
Radioligand binding to human GlyT1c transporter-expressing membranes was measured in duplicate in a total volume of 200 µl in 96-well plates. To 100 µl of membrane suspension (yielding a final membrane protein concentration of 50 µg/ml) in assay buffer (120 mM NaCl, 2 mM KCl, 10 mM Hepes, 1 mM MgCl2, 1 mM CaCl2, pH 7.5) 80 µl of [^{3}H]-(R)-NPTS (0.5 nM final) were added in assay buffer. For competition experiments 10 µl of buffer or unlabeled compound solution obtained from dilution series of test compounds in DMSO followed. An intermediate 1:10 dilution in assay buffer yielded a final DMSO concentration of 1%. Non-specific binding was determined in the presence of 10 µM Org24598 (or its racemate Org24461) for [^{3}H]-(R)-NPTS. After incubation at room temperature for 1h, the incubation mixture was harvested (Tomtec Mach III U Harvester) through 96-well GF/B filter plates (PerkinElmer), presoaked for 1 h with 40 µl per well of 0.1% polyethylene-imine (PEI). After washing twice with ice-cold 50 mM Tris-HCl pH 7.4 buffer, drying and addition of 35 µl scintillator (BetaplateScint, PerkinElmer) per well followed. The radioactivity was determined by liquid scintillation spectrometry in a MicroBeta (PerkinElmer) plate counter.

Data analysis: For binding of [^{3}H]-(R)-NPTS to cell membranes, the calculation of Kd and Bmax values from the saturation binding assays and the IC_{50} values from the displacement binding was performed by iterative non-linear regression analysis adapted from the 'Ligand' program (Munson and Rodbard, 1980). Radioligand displacement curves in absence or in presence of increasing concentrations of tested compounds were fitted using

a one-site fit and the apparent Ki values were calculated from the IC_{50} values using the Cheng-Prusoff equation (Cheng and Prusoff 1973).

The following results were obtained with the compounds of examples 1 to 96:

Table 1:

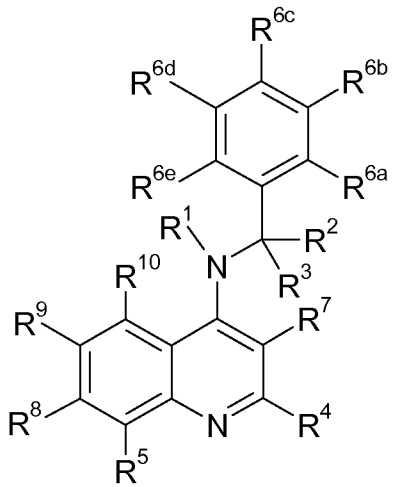
	[3H]-(R)-NPTS bindung	Glycine uptake
Example	Ki [µmol]	IC_{50} [µmol]
1	≤ 1	≤ 10
2	≤ 1	≤ 1000
3	≤ 1	≤ 10
4	≤ 1	≤ 100
5	≤ 0.1	≤ 0.1
6	≤ 0.1	≤ 1
7	≤ 1	≤ 1
8	≤ 1	≤ 10
9	≤ 0.1	≤ 1
10	≤ 1	≤ 100
11	≤ 10	≤ 100
12	≤ 1	≤ 10
13	≤ 1	≤ 1
14	≤ 10	≤ 10
15	≤ 0.1	≤ 1
16	≤ 0.1	≤ 1
17	≤ 1	≤ 10
18	≤ 0.1	≤ 1
19	≤ 0.1	≤ 0.1
20	≤ 0.01	≤ 1
21	≤ 0.01	≤ 0.1
22	≤ 0.01	≤ 0.1
23	≤ 0.01	≤ 1
24	≤ 0.1	≤ 1
26	≤ 1	≤ 1
27	≤ 0.01	≤ 0.01
28	≤ 0.1	≤ 1
29	≤ 0.1	≤ 0.1
30	≤ 0.01	≤ 0.1
31	≤ 0.01	≤ 0.1

32	≤ 0.1	≤ 1
33	≤ 10	≤ 10
34	≤ 10	≤ 100
35	≤ 10	≤ 10
36	≤ 0,1	≤ 10
37	≤ 0.1	≤ 1
38	≤ 0.1	≤ 1
39	≤ 0.1	≤ 1
40	≤ 0.1	≤ 10
41	≤ 0.1	≤ 1
42	≤ 0.1	≤ 0.1
43	≤ 0.1	≤ 1
44	≤ 1	≤ 1
45	≤ 10	≤ 10
46	≤ 0.1	≤ 1
47	≤ 0.1	≤ 1
48	≤ 0.1	≤ 0.1
49	≤ 0.1	≤ 0.1
50	≤ 0.1	≤ 1
51	≤ 1	≤ 1
52	≤ 0.1	≤ 1
53	≤ 10	≤ 100
54	≤ 1	≤ 1
55	≤ 1	≤ 10
56	≤ 1	≤ 0.1
57	≤ 10	≤ 100
58	≤ 0.1	≤ 1
59	≤ 10	≤ 100
60	≤ 1	≤ 1
61	≤ 10	≤ 10
62	≤ 10	≤ 10
63	≤ 10	≤ 100
64	≤ 10	≤ 10
65	≤ 10	≤ 10
66	≤ 10	≤ 10
67	≤ 1	≤ 10
68	≤ 0.01	≤ 0.1
69	≤ 10	≤ 10

70	≤ 10	≤ 100
71	≤ 0.1	≤ 1
72	≤ 1	≤ 10
73	≤ 1	≤ 1
74	≤ 10	≤ 1000
75	≤ 1	≤ 1
76	≤ 0.001	≤ 0.1
77	≤ 1	≤ 10
78	≤ 1	≤ 10
79	≤ 10	≤ 10
80	≤ 1	≤ 1
81	≤ 0.1	≤ 1
82	≤ 1	≤ 1
83	≤ 1	≤ 1
84	≤ 1	≤ 1
85	≤ 1	≤ 1
86	≤ 1	≤ 1
87	≤ 0.1	≤ 0.1
88	≤ 0.1	≤ 0.1
89	≤ 0.1	≤ 1
90	≤ 1	≤ 1
91	≤ 10	≤ 10
92	≤ 1	≤ 1
93	≤ 1	≤ 10
94	≤ 10	≤ 100
95	≤ 0.1	≤ 0.1
96	≤ 1	≤ 10

We claim:

1. 4-Benzylaminoquinoline of the formula (I)



(I)

wherein

R^1 is hydrogen, C_1-C_6-alkyl or C_6-C_{12}-aryl;

R^2, R^3
are independently hydrogen, C_1-C_6-alkyl, substituted C_1-C_4-alkyl, C_3-C_{12}-cycloalkyl, C_6-C_{12}-aryl, aminocarbonyl, amino or optionally substituted C_3-C_{12}-heterocyclyl;

R^4 is C_1-C_6-alkyl, halogenated C_1-C_6-alkyl, C_1-C_6-alkoxy, di-(C_1-C_6-alkyl)amino, C_6-C_{12}-arylamino or sulfonylamino;

R^5 is hydrogen, halogen, C_1-C_6-alkyl, hydroxy, C_1-C_6-alkoxy, substituted C_1-C_4-alkoxy, C_6-C_{12}-aryloxy, C_6-C_{12}-heteroaryloxy, C_1-C_6-alkylthio, C_1-C_6-alkylsulfinyl, C_1-C_6-alkylsulfonyl, aminosulfonyl, C_1-C_6-alkylaminosulfonyl, di-C_1-C_6-alkylaminosulfonyl, (optionally substituted C_6-C_{12}-aryl)aminosulfonyl, amino, substituted amino or optionally substituted C_3-C_{12}-heterocyclyl;

R^{6a}, R^{6b}, R^{6c}, R^{6d}, R^{6e}
are independently hydrogen, halogen, C_1-C_6-alkyl, halogenated C_1-C_4-alkyl, C_1-C_4-hydroxyalkyl, C_1-C_6-alkoxycarbonyl, (halogenated C_1-C_4-alkoxy)carbonyl, cyano, C_1-C_6-alkoxy, halogenated C_1-C_4-alkoxy, optionally substituted C_6-C_{12}-aryl, C_1-C_4-alkylthio, (halogenated C_1-C_4-alkyl)thio, nitro, amino, C_1-C_6-alkylamino, (halogenated C_1-C_6-alkyl)amino, di-C_1-C_6-alkylamino, di-(halogenated C_1-C_6-

alkyl)amino, C_1-C_6-alkylcarbonylamino, (halogenated C_1-C_4-alkyl)carbonylamino, C_1-C_6-alkylsulfonylamino, (halogenated C_1-C_4-alkyl)sulfonylamino or C_6-C_{12}-arylsulfonylamino; or

R^{6a}, R^2
together are optionally substituted C_1-C_4-alkylene; or

R^{6a} and R^{6b} or R^{6b} and R^{6c}
together with the carbon atoms to which they are attached form an anellated aryl ring; or
together are C_1-C_2-alkylenedioxo; and

R^7, R^8, R^9, R^{10}
are independently hydrogen, halogen, C_1-C_6-alkyl or C_1-C_6-alkoxy,

or a physiologically tolerated salt thereof,

provided that the following compounds and the physiologically tolerated salts thereof are excluded:

a) 4'-[[(2-methyl-4-quinolinyl)amino]methyl]-[1,1'-biphenyl]-2-carboxylic acid, 1,1-dimethylethyl ester
b) 2-methyl-N-[[2'-[1-(triphenylmethyl)-1H-tetrazol-5-yl][1,1'-biphenyl]-4-yl]methyl]-4-quinolinamine,
c) 2-methyl-N-[[3'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-4-quinolinamine,
d) 4'-[[(2-methyl-4-quinolinyl)amino]methyl]-[1,1'-biphenyl]-2-carboxylic acid,
e) 4'-[[(2-methyl-4-quinolinyl)amino]methyl]-[1,1'-biphenyl]-3-carboxylic acid, 1,1-dimethylethyl ester
f) 2-methyl-N-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-4-quinolinamine,
g) 4'-[[(8-methoxy-2-methyl-4-quinolinyl)amino]methyl]-[1,1'-biphenyl]-2-carboxylic acid,
h) 8-methoxy-2-methyl-N-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-4-quinolinamine,
i) 4'-[[(2-methyl-4-quinolinyl)amino]methyl]-N-(methylsulfonyl)-[1,1'-biphenyl]-2-carboxamide,
j) 4'-[[(2-methyl-4-quinolinyl)amino]methyl]-[1,1'-biphenyl]-2-carboxylic acid,
k) 4'-[[(2-methyl-4-quinolinyl)amino]methyl]-[1,1'-biphenyl]-2-carboxylic acid, methyl ester
l) N-[(2-methylphenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
m) N-[(2-methoxyphenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
n) N-[(2-ethylphenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,

o) N-[(2-bromophenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
p) N-[(2,6-dichlorophenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
q) N-[(2,6-dimethoxyphenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
r) N-[(2,6-dimethylphenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
s) N-[(2,3-dimethylphenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
t) N-[(2,4-dimethylphenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
u) N-[(2,5-dimethylphenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
v) N-[(2-chlorophenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
w) N-[(2-fluorophenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
x) N-[(2-chloro-6-fluorophenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
y) N-[(2,6-difluorophenyl)methyl]-8-methoxy-2-methyl-4-quinolinamine,
z) N-[[2-(trifluoromethyl)phenyl]methyl]-8-methoxy-2-methyl-4-quinolinamine,
aa) 4-[[(8-methoxy-2-methyl-4-quinolinyl)amino]methyl]-3-methyl-phenol,
ab) 4-[(p-chlorobenzyl)amino]-quinaldine,
ac) N-[(1S)-1-phenylethyl]-2-methyl-4-quinolinamine,
ad) N-(phenylmethyl)-2-methyl-4-quinolinamine,
ae) 4-[[1-(3,4-dimethoxyphenyl)hexyl]amino]-2-methyl-8-quinolinol,
af) 4-[[1-(2-hexyl-4,5-dimethoxyphenyl)ethyl]amino]-2-methyl-8-quinolinol,
ag) 4-[[1-(3,4-dimethoxyphenyl)hexyl]amino]-2-methyl-8-quinolinol,
ah) 4-[[1-(2-hexyl-4,5-dimethoxyphenyl)ethyl]amino]-2-methyl-4-quinolinol,
ai) N-[1-(3,4-dimethoxyphenyl)hexyl]-8-methoxy-2-methyl-4-quinolinamine,
aj) N-[1-(2-hexyl-4,5-dimethoxyphenyl)ethyl]-8-methoxy-2-methyl-4-quinolinamine.

2. Compound as claimed in claim 1, wherein R^1 is hydrogen.

3. Compound as claimed in claim 1 or 2, wherein R^2 and R^3 are independently hydrogen, C_1-C_6-alkyl, C_1-C_4-alkyl substituted with C_1-C_6-alkoxy, amino, C_1-C_6-alkylamino, di-C_1-C_6-alkylamino, (C_6-C_{12}-aryl-C_1-C_4-alkyl)amino, C_1-C_6-alkylcarbonylamino, C_1-C_6-alkylsulfonylamino or C_3-C_{12}-heterocyclyl, or C_3-C_{12}-cycloalkyl, aminocarbonyl or optionally substituted C_3-C_{12}-heterocyclyl.

4. Compound as claimed in claim 3, wherein R^2 and R^3 are independently hydrogen, C_1-C_6-alkyl, C_1-C_4-alkyl substituted with amino, C_1-C_6-alkylamino, di-C_1-C_6-alkylamino, (C_6-C_{12}-aryl-C_1-C_4-alkyl)amino or C_3-C_{12}-heterocyclyl, or C_3-C_{12}-cycloalkyl, aminocarbonyl or optionally substituted C_3-C_{12}-heterocyclyl.

5. Compound as claimed in any one of claims 1 to 4, wherein R^2 is hydrogen or C_1-C_3-alkyl and R^3 is defined as in any one of claims 1 to 4.

6. Compound as claimed in any one of claims 1 to 5, wherein R^2 is hydrogen.

7. Compound as claimed in claim 5 or 6, wherein R^3 is C_1-C_2-alkyl substituted with amino, C_1-C_4-alkylamino, di-C_1-C_4-alkylamino, (C_6-C_{12}-aryl-C_1-C_2-alkyl)amino or C_3-C_{12}-heterocyclyl.

8. Compound as claimed in claim 7, wherein R^3 is aminomethyl, C_1-C_4-alkylaminomethyl, di-C_1-C_4-alkylaminomethyl, (C_6-C_{12}-aryl-C_1-C_2-alkyl)aminomethyl or C_3-C_{12}-heterocyclylmethyl.

9. Compound as claimed in claim 5 or 6, wherein R^3 is optionally substituted C_3-C_{12}-heterocyclyl.

10. Compound as claimed in claim 9, wherein R^3 is piperidinyl or piperidinyl substituted with C_1-C_4-alkyl or C_2-C_4-allyl.

11. Compound as claimed in any one of claims 1 to 10, wherein R^4 is methyl or dimethyl-amino.

12. Compound as claimed in any one of claims 1 to 11, wherein R^5 is hydrogen or halogen.

13. Compound as claimed in claim 12, wherein R^5 is hydrogen.

14. Compound as claimed in any one of claims 1 to 11, wherein R^5 is hydroxy, C_1-C_6-alkoxy, halogenated C_1-C_4-alkoxy, C_6-C_{12}-aryloxy or C_6-C_{12}-heteroaryloxy.

15. Compound as claimed in claim 14, wherein R^5 is C_1-C_2-alkoxy.

16. Compound as claimed in any one of claims 1 to 11, wherein R^5 is a group of the formula (II):

$$—A^1—A^2—A^3—R^{5a} \qquad (II)$$

wherein

A^1 is O, NR^{5b};

A^2 is optionally substituted C_1-C_4-alkylene;

A^3 is O, NR^{5b};

R^{5a} is hydrogen, C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl, C_6-C_{12}-arylcarbonyl, C_1-C_6-alkoxycarbonyl, halogenated C_1-C_4-alkoxycarbonyl, C_6-C_{12}-aryloxycarbonyl, C_1-C_6-alkylaminocarbonyl, (halogenated C_1-C_4-alkyl)aminocarbonyl, C_6-C_{12}-arylaminocarbonyl, C_1-C_6-alkylsulfonyl, (halogenated C_1-C_6-alkyl)sulfonyl, C_6-C_{12}-arylsulfonyl, (C_6-C_{12}-aryl-C_1-C_4-alkyl)sulfonyl, C_3-C_{12}-heterocyclylsulfonyl or C_6-C_{12}-aryl; and

R^{5b} is hydrogen or C_1-C_4-alkyl; or

R^{5a} and R^{5b}
together with the nitrogen atom to which they are attached are C_3-C_{12}-heterocyclyl.

17. Compound as claimed in claim 16, wherein substituted C_1-C_4-alkylene is C_1-C_4-alkylene substituted with halogen, C_1-C_4-alkyl or C_1-C_3-alkoxy.

18. Compound as claimed in claim 16, wherein A^1 is O, A^2 is C_1-C_2-alkylene, A^3 is NR^{5b}, and R^{5a} and R^{5b} are as defined in claim 16.

19. Compound as claimed in any one of claims 16 to 18, wherein R^{5a} is C_1-C_4-alkylsulfonyl and R^{5b} is hydrogen.

20. Compound as claimed in any one of claims 1 to 11, wherein R^5 is C_1-C_4-alkoxy substituted with C_1-C_6-alkoxy, amino, di-C_1-C_6-alkylamino, C_1-C_6-alkylcarbonylamino, C_6-C_{12}-arylcarbonylamino, C_1-C_6-alkoxycarbonylamino, C_3-C_{12}-heterocyclyl, C_1-C_6-alkylsulfonylamino, (halogenated C_1-C_4-alkyl)sulfonylamino, C_6-C_{12}-arylsulfonylamino, (C_6-C_{12}-aryl-C_1-C_4-alkyl)sulfonylamino, C_3-C_{12}-heterocyclylsulfonylamino or C_6-C_{12}-aryl.

21. Compound as claimed in claim 20, wherein R^5 is C_1-C_2-alkoxy substituted with C_1-C_4-alkoxy, amino, di-C_1-C_4-alkylamino, C_1-C_4-alkylcarbonylamino, C_6-C_{12}-arylcarbonylamino, C_1-C_4-alkoxycarbonylamino, C_3-C_{12}-heterocyclyl, C_1-C_4-alkylsulfonylamino, (halogenated C_1-C_4-alkyl)sulfonylamino, C_6-C_{12}-arylsulfonylamino, (C_6-C_{12}-aryl-C_1-C_2-alkyl)sulfonylamino, C_3-C_{12}-heterocyclylsulfonylamino or C_6-C_{12}-aryl.

22. Compound as claimed in claim 21, wherein R^5 is C_1-C_6-alkoxy-ethoxy, amino-ethoxy, di-C_1-C_6-alkylamino-ethoxy, C_1-C_6-alkylcarbonylamino-ethoxy, C_6-C_{12}-arylcarbonylamino-ethoxy, C_1-C_6-alkoxycarbonylamino-ethoxy, C_3-C_{12}-heterocyclyl-ethoxy, C_1-C_6-alkylsulfonylamino-ethoxy, (halogenated C_1-C_4-alkyl)sulfonylamino-ethoxy, C_6-C_{12}-arylsulfonylamino-ethoxy, (C_6-C_{12}-aryl-C_1-C_4-alkyl)sulfonylamino-ethoxy or C_3-C_{12}-heterocyclylsulfonylamino-ethoxy.

23. Compound as claimed in any one of claims 1 to 11, wherein R^5 is C_1-C_6-alkylthio, C_1-C_6-alkylsulfinyl, C_1-C_6-alkylsulfonyl, aminosulfonyl, C_1-C_6-alkylaminosulfonyl, di-C_1-C_6-alkylaminosulfonyl or (optionally substituted C_6-C_{12}-aryl)aminosulfonyl.

24. Compound as claimed in any one of claims 1 to 11, wherein R^5 is amino.

25. Compound as claimed in any one of claims 1 to 11, wherein R^5 is C_1-C_6-alkylamino, di-C_1-C_6-alkylamino, C_1-C_6-alkylcarbonylamino, C_6-C_{12}-arylcarbonylamino, C_1-C_6-alkylsulfonylamino, C_6-C_{12}-arylsulfonylamino, di-(C_1-C_6-alkylsulfonyl)amino or optionally substituted C_3-C_{12}-heterocyclyl.

26. Compound as claimed in any one of claims 1 to 25, wherein R^{6a} is hydrogen, halogen, C_1-C_6-alkyl, halogenated C_1-C_4-alkyl, C_1-C_4-hydroxyalkyl, cyano, C_1-C_6-alkoxy, optionally substituted C_6-C_{12}-aryl, amino, C_1-C_6-alkylamino, (halogenated C_1-C_6-alkyl)amino, di-C_1-C_6-alkylamino, di-(halogenated C_1-C_6-alkyl)amino, C_1-C_6-alkylcarbonylamino, (halogenated C_1-C_4-alkyl)carbonylamino, C_1-C_6-alkylsulfonylamino, (halogenated C_1-C_4-alkyl)sulfonylamino or C_6-C_{12}-arylsulfonylamino.

27. Compound as claimed in claim 26, wherein R^{6a} is hydrogen, halogen, C_1-C_6-alkyl, halogenated C_1-C_4-alkyl, C_1-C_6-alkoxy or optionally substituted C_6-C_{12}-aryl.

28. Compound as claimed in any one of claims 1 to 27, wherein R^{6b} is hydrogen, halogen, C_1-C_6-alkyl, halogenated C_1-C_4-alkyl, C_1-C_4-hydroxyalkyl, cyano, C_1-C_6-alkoxy, nitro, amino, C_1-C_6-alkylamino, (halogenated C_1-C_6-alkyl)amino, di-C_1-C_6-alkylamino, di-(halogenated C_1-C_6-alkyl)amino, C_1-C_6-alkylcarbonylamino, (halogenated C_1-C_4-alkyl)carbonylamino, C_1-C_6-alkylsulfonylamino, (halogenated C_1-C_4-alkyl)sulfonylamino or C_6-C_{12}-arylsulfonylamino.

29. Compound as claimed in claim 28, wherein R^{6b} is hydrogen, halogen, C_1-C_6-alkyl, halogenated C_1-C_4-alkyl, C_1-C_6-alkoxy or nitro.

30. Compound as claimed in any one of claims 1 to 29, wherein R^{6c} is hydrogen, halogen, C_1-C_6-alkyl, halogenated C_1-C_4-alkyl, C_1-C_4-hydroxyalkyl, C_1-C_6-alkoxycarbonyl, cyano, C_1-C_6-alkoxy, halogenated C_1-C_4-alkoxy, halogenated C_1-C_4-alkylthio, nitro, amino, C_1-C_6-alkylamino, (halogenated C_1-C_6-alkyl)amino, di-C_1-C_6-alkylamino, di-(halogenated C_1-C_6-alkyl)amino, C_1-C_6-alkylcarbonylamino, (halogenated C_1-C_4-alkyl)carbonylamino, C_1-C_6-alkylsulfonylamino, (halogenated C_1-C_4-alkyl)sulfonylamino or C_6-C_{12}-arylsulfonylamino.

31. Compound as claimed in claim 30, wherein R^{6c} is hydrogen, halogen, C_1-C_6-alkyl, halogenated C_1-C_4-alkyl, C_1-C_6-alkoxycarbonyl, C_1-C_6-alkoxy, halogenated C_1-C_4-alkoxy, halogenated C_1-C_4-alkylthio or nitro.

32. Compound as claimed in any one of claims 1 to 31, wherein R^{6d} is hydrogen, halogen, C_1-C_6-alkyl, halogenated C_1-C_4-alkyl, C_1-C_4-hydroxyalkyl, cyano, C_1-C_6-alkoxy, nitro, amino, C_1-C_6-alkylamino, (halogenated C_1-C_6-alkyl)amino, di-C_1-C_6-alkylamino, di-(halogenated C_1-C_6-alkyl)amino, C_1-C_6-alkylcarbonylamino, (halogenated C_1-C_4-alkyl)carbonylamino, C_1-C_6-alkylsulfonylamino, (halogenated C_1-C_4-alkyl)sulfonylamino or C_6-C_{12}-arylsulfonylamino.

33. Compound as claimed in claim 32, wherein R^{6d} is hydrogen, halogen, C_1-C_6-alkyl or C_1-C_6-alkoxy.

34. Compound as claimed in any one of claims 1 to 33, wherein R^{6e} is hydrogen, halogen, C_1-C_6-alkyl, halogenated C_1-C_4-alkyl, C_1-C_4-hydroxyalkyl, cyano, C_1-C_6-alkoxy, optionally substituted C_6-C_{12}-aryl, amino, C_1-C_6-alkylamino, (halogenated C_1-C_6-alkyl)amino, di-C_1-C_6-alkylamino, di-(halogenated C_1-C_6-alkyl)amino, C_1-C_6-alkylcarbonylamino, (halogenated C_1-C_4-alkyl)carbonylamino, C_1-C_6-alkylsulfonylamino, (halogenated C_1-C_4-alkyl)sulfonylamino or C_6-C_{12}-arylsulfonylamino.

35. Compound as claimed in claim 34, wherein R^{6e} is hydrogen.

36. Compound as claimed in any one of claims 1 to 25, wherein R^{6a} and R^2 together are C_1-C_4-alkylene.

37. Compound as claimed in any one of claims 1 to 25, wherein R^{6a} and R^{6b} together with the carbon atoms to which they are attached form an anellated C_5-C_{10}-aryl ring.

38. Compound as claimed in any one of claims 1 to 25, wherein R^{6b} and R^{6c} together are C_1-C_2-alkylenedioxo.

39. Compound as claimed in any one of claims 1 to 35, wherein at least one of R^{6a}, R^{6b}, R^{6c}, R^{6d}, R^{6e} is different from hydrogen.

40. Compound as claimed in claim 39, wherein at least one of R^{6a}, R^{6b}, R^{6c}, R^{6d}, R^{6e} is halogen, C_1-C_4-hydroxyalkyl, cyano or nitro.

41. Compound as claimed in claim 40, wherein at least one of R^{6a}, R^{6b}, R^{6c}, R^{6d}, R^{6e} is halogen or nitro.

42. Compound as claimed in any one of claims 1 to 35, wherein at least one of R^{6a}, R^{6c} is different from hydrogen.

43. Compound as claimed in claim 42, wherein at least one of R^{6a}, R^{6c} is halogen, C_1-C_4-hydroxyalkyl, cyano or nitro.

44. Compound as claimed in claim 43, wherein at least one of R^{6a}, R^{6c} is halogen or nitro.

45. Compound as claimed in any one of claims 1 to 35, wherein at least one of R^{6b}, R^{6c}, R^{6d} is different from hydrogen.

46. Compound as claimed in claim 45, wherein at least one of R^{6b}, R^{6c}, R^{6d} is halogen, C_1-C_4-hydroxyalkyl, cyano or nitro.

47. Compound as claimed in claim 46, wherein at least one of R^{6b}, R^{6c}, R^{6d} is halogen or nitro.

48. Compound as claimed in any one of claims 1 to 35, wherein at least one of R^{6b}, R^{6c} is different from hydrogen.

49. Compound as claimed in claim 48, wherein at least one of R^{6b}, R^{6c} is halogen, C_1-C_4-hydroxyalkyl, cyano or nitro.

50. Compound as claimed in claim 49, wherein at least one of R^{6b}, R^{6c} is halogen or nitro.

51. Compound as claimed in any one of claims 1 to 35, wherein R^{6c} is different from hydrogen.

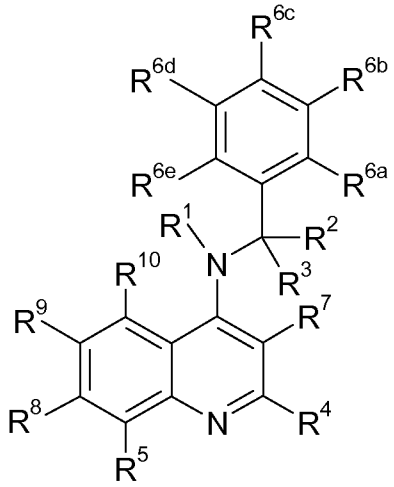
52. Compound as claimed in claim 51, wherein R^{6c} is halogen, C_1-C_4-hydroxyalkyl, cyano or nitro.

53. Compound as claimed in claim 52, wherein R^{6c} is halogen or nitro.

54. Compound as claimed in any one of claims 1 to 35, wherein R^{6a}, R^{6e} are both hydrogen.

55. Compound as claimed in any one of claims 1 to 54, wherein R^7, R^8, R^9, R^{10} are all hydrogen.

56. 4-Benzylaminoquinoline of the formula (I)



(I)

wherein

R^1 is hydrogen;

R^2 is hydrogen, C_1-C_4-alkyl, amino-C_1-C_4-alkyl, C_1-C_6-alkylamino-C_1-C_4-alkyl, di-C_1-C_6-alkylamino-C_1-C_4-alkyl, (C_6-C_{12}-aryl-C_1-C_4-alkyl)amino-C_1-C_4-alkyl, C_3-C_{12}-heterocyclyl-C_1-C_4-alkyl, C_3-C_{12}-cycloalkyl, C_6-C_{12}-aryl, aminocarbonyl or C_3-C_{12}-heterocyclyl;

R^3 is hydrogen;

R^4 is methyl or dimethylamino;

R^5 is hydrogen, halogen, C_1-C_6-alkyl, hydroxy, C_1-C_6-alkoxy, halogenated C_1-C_4-alkoxy, C_1-C_6-alkoxy-C_1-C_4-alkoxy, amino-C_1-C_4-alkoxy, di-C_1-C_6-alkylamino-C_1-C_4-alkoxy, C_1-C_6-alkylcarbonylamino-C_1-C_4-alkoxy, C_6-C_{12}-arylcarbonylamino-C_1-C_4-alkoxy, C_1-C_6-alkoxycarbonylamino-C_1-C_4-alkoxy, C_3-C_{12}-heterocyclyl-C_1-C_4-alkoxy, C_1-C_6-alkylsulfonylamino-C_1-C_4-alkoxy, (halogenated C_1-C_4-alkyl)sulfonylamino-C_1-C_4-alkoxy, C_6-C_{12}-arylsulfonylamino-C_1-C_4-alkoxy, (C_6-C_{12}-aryl-C_1-C_4-alkyl)sulfonylamino-C_1-C_4-alkoxy, C_3-C_{12}-heterocyclylsulfonylamino-C_1-C_4-alkoxy, C_6-C_{12}-aryl-C_1-C_4-alkoxy, C_6-C_{12}-aryloxy, C_6-C_{12}-heteroaryloxy, C_1-C_6-alkylthio, C_1-C_6-alkylsulfinyl, C_1-C_6-alkylsulfonyl, aminosulfonyl, C_1-C_6-alkylaminosulfonyl, di-C_1-C_6-alkylaminosulfonyl, (optionally substituted C_6-C_{12}-aryl)aminosulfonyl, amino, C_1-C_6-alkylamino, di-C_1-C_6-alkylamino, C_1-C_6-alkylcarbonylamino, C_6-C_{12}-arylcarbonylamino, C_1-C_6-alkylsulfonylamino, C_6-C_{12}-arylsulfonylamino, di-(C_1-C_6-alkylsulfonyl)amino or optionally substituted C_3-C_{12}-heterocyclyl;

R^{6a}, R^{6e}
are hydrogen;

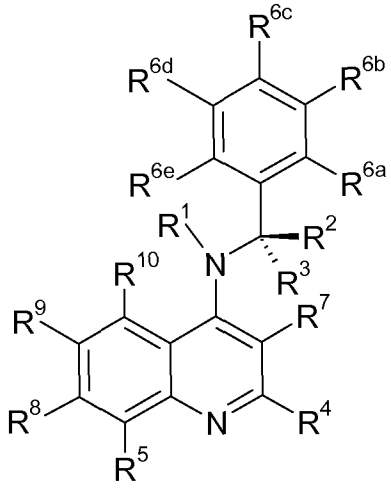
R^{6b}, R^{6c}, R^{6d}
are indpendently hydrogen, halogen, C_1-C_6-alkyl, halogenated C_1-C_4-alkyl, C_1-C_6-alkoxycarbonyl, C_1-C_6-alkoxy, halogenated C_1-C_4-alkoxy, halogenated C_1-C_4-alkylthio, nitro, at least one of R^{6b}, R^{6c}, R^{6d} being different from hydrogen; and

R^7, R^8, R^9, R^{10}
are all hydrogen,

or a physiologically tolerated acid addition salt thereof,

provided that 4-[(p-chlorobenzyl)amino]-quinaldine is excluded.

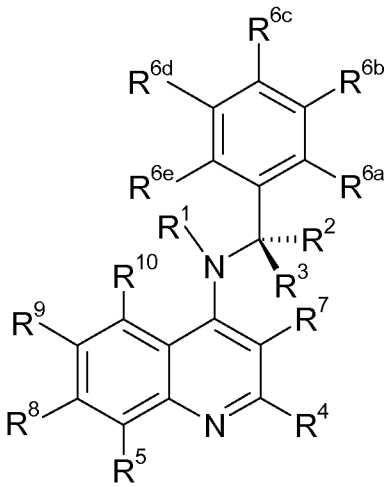
57. Compound as claimed in any one of claims 1 to 56, having the following formula (Ia):



(Ia)

wherein R^1, R^2, R^3, R^4, R^5, R^{6a}, R^{6b}, R^{6c}, R^{6d}, R^{6e}, R^7, R^8, R^9, R^{10} are as defined as in any one of claims 1 to 56.

58. Compound as claimed in any one of claims 1 to 56, having the following formula (Ib):



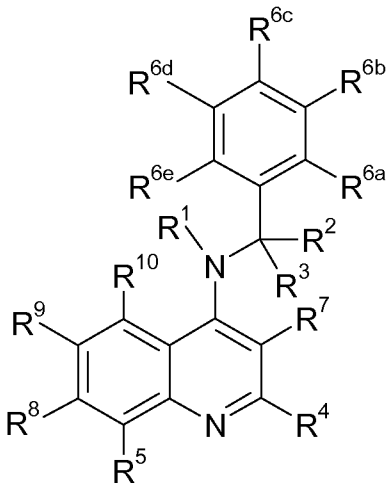
(Ib)

wherein R^1, R^2, R^3, R^4, R^5, R^{6a}, R^{6b}, R^{6c}, R^{6d}, R^{6e}, R^7, R^8, R^9, R^{10} are as defined as in any one of claims 1 to 56.

59. The compound as claimed in any one of claims 1 to 58 for use in therapy.

60. Pharmaceutical composition which comprises an carrier and a compound of any one of claims 1 to 58.

61. A method for inhibiting the glycine transporter GlyT1 in a mammal in need thereof which comprises the administration of an effective amount of a 4-benzylaminoquinoline of the formula (I)



(I)

wherein

R^1 is hydrogen, C_1-C_6-alkyl or C_6-C_{12}-aryl;

R^2, R^3
are independently hydrogen, C_1-C_6-alkyl, substituted C_1-C_4-alkyl, C_3-C_{12}-cycloalkyl, C_6-C_{12}-aryl, aminocarbonyl, amino or optionally substituted C_3-C_{12}-heterocyclyl;

R^4 is C_1-C_6-alkyl, halogenated C_1-C_6-alkyl, C_1-C_6-alkoxy, di-(C_1-C_6-alkyl)amino, C_6-C_{12}-arylamino or sulfonylamino;

R^5 is hydrogen, halogen, C_1-C_6-alkyl, hydroxy, C_1-C_6-alkoxy, substituted C_1-C_4-alkoxy, C_6-C_{12}-aryloxy, C_6-C_{12}-heteroaryloxy, C_1-C_6-alkylthio, C_1-C_6-alkylsulfinyl, C_1-C_6-alkylsulfonyl, aminosulfonyl, C_1-C_6-alkylaminosulfonyl, di-C_1-C_6-alkylaminosulfonyl, (optionally substituted C_6-C_{12}-aryl)aminosulfonyl, amino, substituted amino or optionally substituted C_3-C_{12}-heterocyclyl;

R^{6a}, R^{6b}, R^{6c}, R^{6d}, R^{6e}
are independently hydrogen, halogen, C_1-C_6-alkyl, halogenated C_1-C_4-alkyl, C_1-C_4-hydroxyalkyl, C_1-C_6-alkoxycarbonyl, (halogenated C_1-C_4-alkoxy)carbonyl, cyano, C_1-C_6-alkoxy, halogenated C_1-C_4-alkoxy, optionally substituted C_6-C_{12}-aryl, C_1-C_4-alkylthio, (halogenated C_1-C_4-alkyl)thio, nitro, amino, C_1-C_6-alkylamino, (halogenated C_1-C_6-alkyl)amino, di-C_1-C_6-alkylamino, di-(halogenated C_1-C_6-alkyl)amino, C_1-C_6-alkylcarbonylamino, (halogenated C_1-C_4-alkyl)carbonylamino, C_1-C_6-alkylsulfonylamino, (halogenated C_1-C_4-alkyl)sulfonylamino or C_6-C_{12}-arylsulfonylamino; or

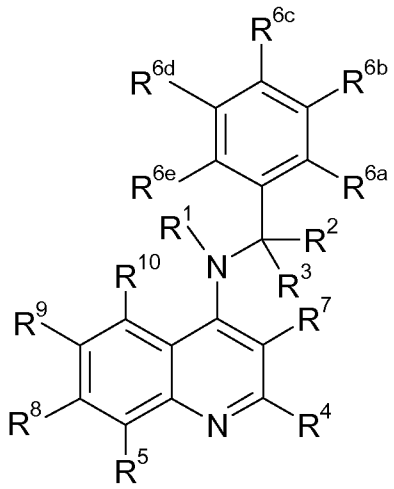
R^{6a}, R^2
together are optionally substituted C_1-C_4-alkylene; or

R^{6a} and R^{6b} or R^{6b} and R^{6c}
together with the carbon atoms to which they are attached form an anellated aryl ring; or
together are C_1-C_2-alkylenedioxo; and

R^7, R^8, R^9, R^{10}
are independently hydrogen, halogen, C_1-C_6-alkyl or C_1-C_6-alkoxy,

or a physiologically tolerated salt thereof.

62. The use of a 4-benzylaminoquinoline of the formula (I)



(I)

wherein

R^1 is hydrogen, C_1-C_6-alkyl or C_6-C_{12}-aryl;

R^2, R^3
are independently hydrogen, C_1-C_6-alkyl, substituted C_1-C_4-alkyl, C_3-C_{12}-cycloalkyl, C_6-C_{12}-aryl, aminocarbonyl, amino or optionally substituted C_3-C_{12}-heterocyclyl;

R^4 is C_1-C_6-alkyl, halogenated C_1-C_6-alkyl, C_1-C_6-alkoxy, di-(C_1-C_6-alkyl)amino, C_6-C_{12}-arylamino or sulfonylamino;

R^5 is hydrogen, halogen, C_1-C_6-alkyl, hydroxy, C_1-C_6-alkoxy, substituted C_1-C_4-alkoxy, C_6-C_{12}-aryloxy, C_6-C_{12}-heteroaryloxy, C_1-C_6-alkylthio, C_1-C_6-alkylsulfinyl, C_1-C_6-alkylsulfonyl, aminosulfonyl, C_1-C_6-alkylaminosulfonyl, di-C_1-C_6-alkylaminosulfonyl, (optionally substituted C_6-C_{12}-aryl)aminosulfonyl, amino, substituted amino or optionally substituted C_3-C_{12}-heterocyclyl;

R^{6a}, R^{6b}, R^{6c}, R^{6d}, R^{6e}
are independently hydrogen, halogen, C_1-C_6-alkyl, halogenated C_1-C_4-alkyl, C_1-C_4-hydroxyalkyl, C_1-C_6-alkoxycarbonyl, (halogenated C_1-C_4-alkoxy)carbonyl, cyano, C_1-C_6-alkoxy, halogenated C_1-C_4-alkoxy, optionally substituted C_6-C_{12}-aryl, C_1-C_4-alkylthio, (halogenated C_1-C_4-alkyl)thio, nitro, amino, C_1-C_6-alkylamino, (halogenated C_1-C_6-alkyl)amino, di-C_1-C_6-alkylamino, di-(halogenated C_1-C_6-alkyl)amino, C_1-C_6-alkylcarbonylamino, (halogenated C_1-C_4-alkyl)carbonylamino, C_1-C_6-alkylsulfonylamino, (halogenated C_1-C_4-alkyl)sulfonylamino or C_6-C_{12}-arylsulfonylamino; or

R^{6a}, R^2
together are optionally substituted C_1-C_4-alkylene; or

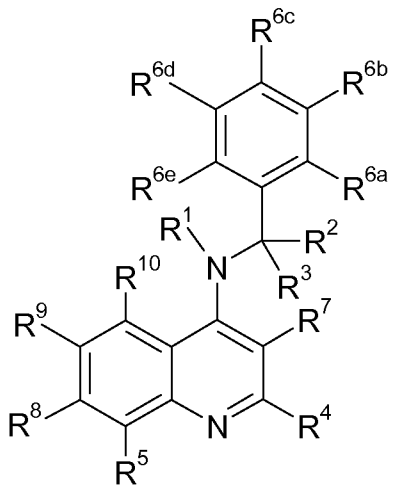
R^{6a} and R^{6b} or R^{6b} and R^{6c}
together with the carbon atoms to which they are attached form an anellated aryl ring; or
together are C_1-C_2-alkylenedioxo; and

R^7, R^8, R^9, R^{10}
are independently hydrogen, halogen, C_1-C_6-alkyl or C_1-C_6-alkoxy,

or a physiologically tolerated salt thereof,

in the manufacture of a medicament for inhibiting the glycine transporter GlyT1.

63. A method for treating a neurologic or psychiatric disorder in a mammalian patient in need thereof which comprises administering to the patient a therapeutically effective amount of a 4-benzylaminoquinoline of the formula (I)



(I)

wherein

R^1 is hydrogen, C_1-C_6-alkyl or C_6-C_{12}-aryl;

R^2, R^3
are independently hydrogen, C_1-C_6-alkyl, substituted C_1-C_4-alkyl, C_3-C_{12}-cycloalkyl, C_6-C_{12}-aryl, aminocarbonyl, amino or optionally substituted C_3-C_{12}-heterocyclyl;

R^4 is C_1-C_6-alkyl, halogenated C_1-C_6-alkyl, C_1-C_6-alkoxy, di-(C_1-C_6-alkyl)amino, C_6-C_{12}-arylamino or sulfonylamino;

R^5 is hydrogen, halogen, C_1-C_6-alkyl, hydroxy, C_1-C_6-alkoxy, substituted C_1-C_4-alkoxy, C_6-C_{12}-aryloxy, C_6-C_{12}-heteroaryloxy, C_1-C_6-alkylthio, C_1-C_6-alkylsulfinyl, C_1-C_6-alkylsulfonyl, aminosulfonyl, C_1-C_6-alkylaminosulfonyl, di-C_1-C_6-alkylaminosulfonyl, (optionally substituted C_6-C_{12}-aryl)aminosulfonyl, amino, substituted amino or optionally substituted C_3-C_{12}-heterocyclyl;

R^{6a}, R^{6b}, R^{6c}, R^{6d}, R^{6e}
are independently hydrogen, halogen, C_1-C_6-alkyl, halogenated C_1-C_4-alkyl, C_1-C_4-hydroxyalkyl, C_1-C_6-alkoxycarbonyl, (halogenated C_1-C_4-alkoxy)carbonyl, cyano, C_1-C_6-alkoxy, halogenated C_1-C_4-alkoxy, optionally substituted C_6-C_{12}-aryl, C_1-C_4-alkylthio, (halogenated C_1-C_4-alkyl)thio, nitro, amino, C_1-C_6-alkylamino, (halogenated C_1-C_6-alkyl)amino, di-C_1-C_6-alkylamino, di-(halogenated C_1-C_6-alkyl)amino, C_1-C_6-alkylcarbonylamino, (halogenated C_1-C_4-alkyl)carbonylamino, C_1-C_6-alkylsulfonylamino, (halogenated C_1-C_4-alkyl)sulfonylamino or C_6-C_{12}-arylsulfonylamino; or

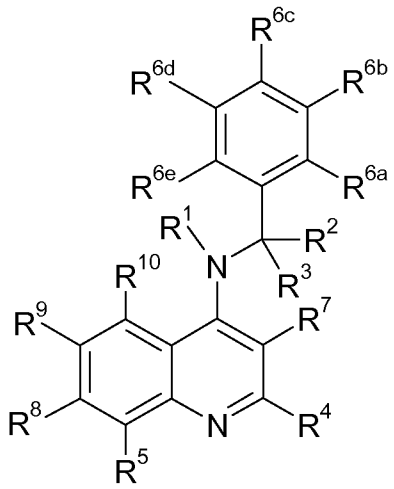
R^{6a}, R^2
together are optionally substituted C_1-C_4-alkylene; or

R^{6a} and R^{6b} or R^{6b} and R^{6c}
together with the carbon atoms to which they are attached form an anellated aryl ring; or
together are C_1-C_2-alkylenedioxo; and

R^7, R^8, R^9, R^{10}
are independently hydrogen, halogen, C_1-C_6-alkyl or C_1-C_6-alkoxy,

or a physiologically tolerated salt thereof.

64. The use of a 4-benzylaminoquinoline of the formula (I)



(I)

wherein

R^1 is hydrogen, C_1-C_6-alkyl or C_6-C_{12}-aryl;

R^2, R^3
are independently hydrogen, C_1-C_6-alkyl, substituted C_1-C_4-alkyl, C_3-C_{12}-cycloalkyl, C_6-C_{12}-aryl, aminocarbonyl, amino or optionally substituted C_3-C_{12}-heterocyclyl;

R^4 is C_1-C_6-alkyl, halogenated C_1-C_6-alkyl, C_1-C_6-alkoxy, di-(C_1-C_6-alkyl)amino, C_6-C_{12}-arylamino or sulfonylamino;

R^5 is hydrogen, halogen, C_1-C_6-alkyl, hydroxy, C_1-C_6-alkoxy, substituted C_1-C_4-alkoxy, C_6-C_{12}-aryloxy, C_6-C_{12}-heteroaryloxy, C_1-C_6-alkylthio, C_1-C_6-alkylsulfinyl, C_1-C_6-alkylsulfonyl, aminosulfonyl, C_1-C_6-alkylaminosulfonyl, di-C_1-C_6-alkylaminosulfonyl, (optionally substituted C_6-C_{12}-aryl)aminosulfonyl, amino, substituted amino or optionally substituted C_3-C_{12}-heterocyclyl;

R^{6a}, R^{6b}, R^{6c}, R^{6d}, R^{6e}
are independently hydrogen, halogen, C_1-C_6-alkyl, halogenated C_1-C_4-alkyl, C_1-C_4-hydroxyalkyl, C_1-C_6-alkoxycarbonyl, (halogenated C_1-C_4-alkoxy)carbonyl, cyano, C_1-C_6-alkoxy, halogenated C_1-C_4-alkoxy, optionally substituted C_6-C_{12}-aryl, C_1-C_4-alkylthio, (halogenated C_1-C_4-alkyl)thio, nitro, amino, C_1-C_6-alkylamino, (halogenated C_1-C_6-alkyl)amino, di-C_1-C_6-alkylamino, di-(halogenated C_1-C_6-alkyl)amino, C_1-C_6-alkylcarbonylamino, (halogenated C_1-C_4-alkyl)carbonylamino, C_1-C_6-alkylsulfonylamino, (halogenated C_1-C_4-alkyl)sulfonylamino or C_6-C_{12}-arylsulfonylamino; or

R^{6a}, R^2
together are optionally substituted C_1-C_4-alkylene; or

R^{6a} and R^{6b} or R^{6b} and R^{6c}
together with the carbon atoms to which they are attached form an anellated aryl ring; or
together are C_1-C_2-alkylenedioxo; and

R^7, R^8, R^9, R^{10}
are independently hydrogen, halogen, C_1-C_6-alkyl or C_1-C_6-alkoxy,

or a physiologically tolerated salt thereof,

in the manufacture of a medicament for treating a neurologic or psychiatric disorder.

65. The method or use as claimed in claim 61 to 64, wherein the 4-benzylaminoquinoline is a 4-benzylaminoquinoline of formula (I), (Ia) or (Ib), wherein R^1, R^2, R^3, R^4, R^5, R^{6a}, R^{6b}, R^{6c}, R^{6d}, R^{6e}, R^7, R^8, R^9, R^{10} is defined as in any one of claims 1 to 56.

66. The method or use as claimed in any one of claims 63 to 65, wherein the disorder is associated with glycinergic or glutamatergic neurotransmission dysfunction.

67. The method or use as claimed in any one of claims 63 to 65, wherein the neurologic disorder is a cognitive disorder such as dementia, cognitive impairment, attention deficit disorder.

68. The method or use as claimed in claim 67, wherein the attention deficit disorder is a the attention deficit disorder with hyperactivity.

69. The method or use as claimed in any one of claims 63 to 65, wherein the psychiatric disorder is an anxiety disorder, a mood disorder such as depression, a bipolar disorder, schizophrenia, or a psychotic disorder.