The present invention relates to substituted quinazoline compounds, methods for their preparation, as well as their use as intermediates for the preparation of active biomolecules.
The present invention relates to substituted quinazoline compounds, methods for their preparation, as well as their use as intermediates for the preparation of active biomolecules.

Quinazolins are compounds of high interest due to the activity of the compounds which could be prepared starting from them including e.g. saxitoxin.

Saxitoxin is—according to the Merck Index on CD Version 12:—a mussel poison; clam poison; paralytic shellfish poison; gonyaulax toxin. This powerful neurotoxin is produced by the dinoflagellates *Gonyaulax catenella*, or *G. tamarensis*, the consumption of which causes the California sea mussel *Mytilus californianus*, the Alaskan butterclam Saxidomus giganteus and the scallop to become poisonous: Sommer et al., Arch. Pathol. 24, 537, 560 (1937); Schantz et al., Can. J. Chem. 39, 2117 (1961); Ghazarossian et al., Biochem. Biophys. Res. Commun. 59, 1219 (1974). These poisonous shellfish have been connected to instances of toxic “red-tides” where the high concentrations of algae discoloring the water were of the Gonyaulax genus. Isox and partial characterization: Schantz et al., J. Am. Chem. Soc. 79, 5230 (1957); Mold et al., ibid. 5235. Saxitoxin is a very popular tool in neurochemical research and as a sodium channel blocker is recently being described in a number of therapeutic uses.

Thus, in one of its aspects the present invention relates to substituted quinazoline compound of general formula I,

$$\text{Formula I}$$

wherein

$$\text{[0005]}$$

$$R^1$$ and $$R^2$$ independently of one another represent hydrogen; $$C_{1-4-\text{alkyl}},$$ with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; or an appropriate protective group;

$$\text{[0006]}$$

or $$R^1$$ and $$R^2$$ together with the Nitrogen they both bind to form a heterocyclic ring or an appropriate protective group;

$$\text{[0007]}$$

or $$R^3$$ represents halogen, OH or $$O—C_{1-4-\text{alkyl}},$$ with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; or $$O—P,$$ with $$P$$ being an appropriate protective group;

$$\text{[0008]}$$

at least one of $$R^1$$ and $$R^2$$ represents halogen; $$OH; O—C_{1-4-\text{alkyl}},$$ with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; or $$O—P,$$ with $$P$$ being an appropriate protective group; while the other represents hydrogen; $$OH;$$ halogen; $$O—C_{1-4-\text{alkyl}},$$ with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; or $$O—P,$$ with $$P$$ being an appropriate protective group;

$$\text{[0009]}$$

$$R^3$$ represents hydrogen or $$C(O)—NR^5 R^6;$$

$$\text{[0010]}$$

$$R^4$$ and $$R^5$$ independently of one another represent hydrogen; $$C_{1-4-\text{alkyl}},$$ with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; or an appropriate protective group;

$$\text{[0011]}$$

or $$R^7$$ and $$R^8$$ together with the Nitrogen they both bind to form a heterocyclic ring or an appropriate protective group;

$$\text{[0012]}$$

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding N-oxide thereof, or a corresponding salt thereof, or a corresponding solvate thereof.

$$\text{[0013]}$$

These compounds are very useful as intermediates for the synthesis of biomolecules and in addition seem to have a quite surprising effect as sodium channel blockers themselves.

$$\text{[0014]}$$

As a general remark the claim to the compounds will cover as well any prodrg of the claimed and invented compounds as well as any use thereof especially including their esters and others. Examples of well known methods of producing a prodrg of a given acting compound are known to those skilled in the art and can be found e.g. in Krogsgaard-Larsen et al., Textbook of Drugdesign and Discovery, Taylor & Francis (April 2002).

$$\text{[0015]}$$

The expression “an appropriate protective group” is defined as a chemical group blocking a reactive site, e.g. hydroxy groups or amino groups, from taking part in a chemical reaction. The appropriate protective groups are known to the skilled chemist and can be found in literature. Especially, in this application this relates to the protective groups described in Greene and Wuts “Protective Groups in Organic Synthesis”, Third Edition, 1999, John Wiley & Sons Inc. included hereby in its entirety by reference. Preferred protective groups include tert-butoxycarbonyl (Boc), benzyloxy carbonyl (Cbz), trifluoroacetyl (TFA) or 9-fluorenylmethoxycarbonyl (Fmoc), phthaloyl (phthalimide), N-1,1,4,4-Tetramethylisidilazaepyclopentane adduct (STABASE), 1,1,3,3-Tetramethyl-1,3-disilazane (Benzio-STABASE, BSB), N-2,5-bis(trisopropylsilox)pyrrol (BIPSOP), Dithi asuccinimide (Dts), tert-butyl, acetyl or benzoyl including in all cases their structurally related analogs.
In the context of this invention, alkyl and cycloalkyl radicals are understood as meaning saturated and unsaturated (but not aromatic), branched, unbranched and cyclic hydrocarbons, which can be unsubstituted or mono- or polysubstituted. In these radicals, C\(_1\)-alkyl represents C\(_1\)- or C\(_2\)-alkyl, C\(_3\)-alkyl represents C\(_1\)-, C\(_2\)-, or C\(_3\)-alkyl, C\(_4\)-alkyl represents C\(_1\)-, C\(_2\)-, C\(_3\)-, or C\(_4\)-alkyl, C\(_5\)-alkyl represents C\(_1\)-, C\(_2\)-, C\(_3\)-, C\(_4\)-, or C\(_5\)-alkyl, C\(_6\)-alkyl represents C\(_1\)-, C\(_2\)-, C\(_3\)-, C\(_4\)-, C\(_5\)-, or C\(_6\)-alkyl, C\(_7\)-alkyl represents C\(_1\)-, C\(_2\)-, C\(_3\)-, C\(_4\)-, C\(_5\)-, C\(_6\)-, or C\(_7\)-alkyl, C\(_8\)-alkyl represents C\(_1\)-, C\(_2\)-, C\(_3\)-, C\(_4\)-, C\(_5\)-, C\(_6\)-, C\(_7\)-, C\(_8\)-alkyl, C\(_9\)-alkyl represents C\(_1\)-, C\(_2\)-, C\(_3\)-, C\(_4\)-, C\(_5\)-, C\(_6\)-, C\(_7\)-, C\(_8\)-, or C\(_9\)-alkyl and C\(_1\)-alkyl represents C\(_1\)-, C\(_2\)-, C\(_3\)-, C\(_4\)-, C\(_5\)-, C\(_6\)-, C\(_7\)-, or C\(_8\)-alkyl. Furthermore, C\(_3\)_, C\(_4\)_cycoalkyl represents C\(_3\)- or C\(_4\)-cycloalkyl, C\(_5\)_, C\(_6\)_cycloalkyl represents C\(_5\)- or C\(_6\)-cycloalkyl, C\(_7\)_, C\(_8\)_cycloalkyl represents C\(_7\)- or C\(_8\)-cycloalkyl, C\(_9\)_cycloalkyl represents C\(_9\)-cycloalkyl, C\(_10\)_cycloalkyl represents C\(_10\)-cycloalkyl, etc. An aryl radical is understood as meaning a ring system with at least one aromatic ring but without heteroatoms from the group consisting of nitrogen, oxygen and/or sulfur and can also be mono- or polysubstituted. The heterocyclic ring systems may consist of condensed rings and may be fully or just in a part of the condensed rings saturated or unsaturated or even aromatic. A subgroup of the heterocyclic radicals/heteroarenes are the heteroaryl/heteroaromatic radicals which contain at least one aromatic ringsystem. Included examples from the group of heterocyclic radicals are pyrroline, pyrazolidine, triazolidine, piperidine, dithianole, tetrahydrothiophene, tetrahydrofuran, dioxolane, dioxane, tetrahydropyran. Examples from the group of heteroaryl radicals/heteroarenes are furan, benzoferan, thiophene, benzothiophene, pyrrole, pyridine, pyrimidine, pyrazine, quinoline, isoquinoline, phthalazine, benzo-1,2,5-oxadiazole, benzothiazole, indole, benzoazazole, benzothiazole, benzoazidine, carbazole and quinazoline.

A radical defined as a C(O)—NR\(_7\)R\(_8\) group means

\[
\begin{align*}
\text{O} & \quad \text{R}^7 \\
\text{N} & \quad \text{R}^8
\end{align*}
\]

Here, in connection with aryl and heterocyclic, substituted is understood as meaning substitution of the aryl or heteroaryl by R, OR, a halogen, preferably F and/or Cl, a CF\(_3\), a CN, an NO\(_2\), an NRR, a C\(_1\)-alkyl (saturated), a C\(_1\)-alkoxy, a C\(_3\)-cycloalkoxy, a C\(_5\)-cycloalkyl or a C\(_7\)-alkyl.

The term “salt” is to be understood as meaning any form of the active compound used according to the invention in which it assumes an ionic form or is charged and is coupled with a counter-ion (a cation or anion) or is in solution. This are also be understood complexes of the active compound with other molecules and ions, in particular complexes which are complexed via ionic interactions.

The term “physiologically acceptable salt” means in the context of this invention any salt that is physiologically tolerated (most of the time meaning not being toxic especially not caused by the counter-ion) if used appropriately for a treatment especially if used on or applied to humans and/or mammals.

These physiologically acceptable salts can be formed with cations or bases and in the context of this invention is understood as meaning salts of at least one of the compounds used according to the invention—usually a (deprotonated) acid—as an anion with at least one, preferably inorganic, cation which is physiologically tolerated—especially if used on humans and/or mammals. The salts of the alkali metals and alkaline earth metals are particularly preferred, and also those with NH\(_4\) in but particular (mono-) or (di)sodium, (mono-) or (di)potassium, magnesium or calcium salts.

These physiologically acceptable salts can also be formed with anions or acids in the context of this invention is
understood as meaning salts of at least one of the compounds used according to the invention—usually protonated, for example on the nitrogen—as the cation with at least one anion which are physiologically tolerated—especially if used on humans and/or mammals. By this is understood in particular, in the context of this invention, the salt formed with a physiologically tolerated acid, that is to say salts of the particular active compound with inorganic or organic acids which are physiologically tolerated—especially if used on humans and/or mammals. Examples of physiologically tolerated salts of particular acids are salts of: hydrochloric acid, hydrobromic acid, sulfuric acid, methanesulfonic acid, formic acid, acetic acid, oxalic acid, succinic acid, malic acid, tartaric acid, mandelic acid, fumaric acid, lactic acid or citric acid.

[0028] The term “solute” according to this invention is to be understood as meaning any form of the active compound according to the invention in which this compound has attached to it via non-covalent binding another molecule (most likely a polar solvent) especially including hydrates and alcoholates, e.g. methanolate. Solvates, preferably hydrates, of the compounds according to the invention may also be obtained by standard procedures known to those skilled in the art.

[0029] Unless otherwise stated, the compounds of the invention are also meant to include compounds which differ only in the presence of one or more isotopically enriched atoms. For example, compounds having the present structures except for the replacement of a hydrogen by a deuterium or tritium, or the replacement of a carbon by $^{13}$C- or $^{14}$C-enriched carbon or $^{15}$N-enriched nitrogen are within the scope of this invention.

[0030] N-oxides of the compounds according to the invention may also be obtained by standard procedures known to those skilled in the art.

[0031] The purification and isolation of the compounds according to the invention, of a corresponding stereoisomer, or salt, or solvate or any intermediate thereof may, if required, be carried out by conventional methods known to those skilled in the art, e.g. chromatographic methods or recrystallization.

[0032] In a preferred embodiment of the invention for the compound according to the invention according to formula 1

[0033] R$^1$ and R$^2$ independently of one another represent hydrogen; C$_{1-4}$-alkyl, with alkyl being linear or branched, saturated or unsaturated, unsubstituted or substituted by F, Cl, Br, I, NH$_2$, SH or OH; or an appropriate protective group selected from tert-butoxycarbonyl (Boc), benzyloxycarbonyl (Cbz), trityloxyacetyl (TFA) or 9-fluorenylalkoxycarbonyl (Fmoc);

[0034] or R$^1$ and R$^2$ together with the Nitrogen they both bind to form a heterocyclic ring of the following formula:

\[ \text{CH}_2 \text{O} \]

[0035] with n being 1, 2, 3 or 4, m being 1, 2, 3 or 4 and (n + m) being $\leq$6 and X being selected from S, O, NR$^8$ or CHR$^9$ with R$^9$ being selected from hydrogen or C$_{1-4}$-alkyl, with alkyl being linear or branched, saturated or unsaturated, unsubstituted or substituted by F, Cl, Br, I, NH$_2$, SH or OH;

[0036] or an appropriate protective group, selected from phthaloyl (phthalimide), N-1,1,4,4-Tetramethylsilisidazacyclcopentane aduct (STABASE), 1,1,3,3-Tetramethyl-1,3-disiloxanodiolne (Benzo-STABASE, BSB), N-2,5-bis(tribisopropylsilyl)pyrrol (BIPSOP);

[0037] R$^3$ represents halogen, OH or O—C$_{1-4}$-alkyl, with alkyl being linear or branched, saturated or unsaturated, unsubstituted or substituted by F, Cl, Br, I, NH$_2$, SH or OH; or O—P, with P being an appropriate protective group selected from tert-butyl, acetyl or benzoyl;

[0038] at least one of R$^4$ and R$^5$ represents halogen; OH; O—C$_{1-4}$-alkyl, with alkyl being linear or branched, saturated or unsaturated, unsubstituted or substituted by F, Cl, Br, I, NH$_2$, SH or OH; or O—P, with P being an appropriate protective group selected from tert-butyl, acetyl or benzoyl.

[0039] R$^6$ represents hydrogen or C(O)—NR$^7$R$^8$;

[0040] R$^7$ and R$^8$ independently of one another represent hydrogen; C$_{1-4}$-alkyl, with alkyl being linear or branched, saturated or unsaturated, unsubstituted or substituted by F, Cl, Br, I, NH$_2$, SH or OH; or an appropriate protective group selected from tert-butoxycarbonyl (Boc), benzyloxycarbonyl (Cbz), trityloxyacetyl (TFA) or 9-fluorenylalkoxycarbonyl (Fmoc);

[0041] or R$^7$ and R$^8$ together with the Nitrogen they both bind to form a heterocyclic ring of the following formula:

\[ \text{CH}_2 \text{O} \]

[0042] with o being 1, 2, 3 or 4, p being 1, 2, 3 or 4 and (o + p) being $\leq$6 and Y being selected from S, O, NR$^{10}$ or CHR$^{10}$ with R$^{10}$ being selected from hydrogen or C$_{1-4}$-alkyl, with alkyl being linear or branched, saturated or unsaturated, unsubstituted or substituted by F, Cl, Br, I, NH$_2$, SH or OH;

[0043] or an appropriate protective group, selected from phthaloyl (phthalimide), N-1,1,4,4-Tetramethylsilisidazacyclcopentane aduct (STABASE), 1,1,3,3-Tetramethyl-1,3-disiloxanodiolne (Benzo-STABASE, BSB), N-2,5-bis(tribisopropylsilyl)pyrrol (BIPSOP);

[0044] In another preferred embodiment of the invention for the compound according to the invention according to formula 1

[0045] R$^1$ and R$^2$ independently of one another represent hydrogen; C$_{1-4}$-alkyl, with alkyl being linear or branched, saturated or unsaturated, unsubstituted or substituted;

[0046] R$^3$ represents halogen, OH or O—C$_{1-4}$-alkyl, with alkyl being linear or branched, saturated or unsaturated, unsubstituted or substituted;
[0047] at least one of $R^4$ and $R^5$ represents halogen; OH; O—C$_{1-4}$-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; 

[0048] while the other represents hydrogen; OH; halogen; O—C$_{1-4}$-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; 

[0049] $R^2$ represents hydrogen or CO₂—NR$^5$R$^8$; 

[0050] $R^4$ and $R^5$ independently of one another represent hydrogen; C$_{1-4}$-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted.

[0051] In another preferred embodiment of the invention for the compound according to the invention according to formula I 

[0052] $R^1$ and $R^2$ independently of one another represent hydrogen; C$_{1-4}$-alkyl, with alkyl being linear or branched, saturated and unsubstituted; and/or 

[0053] $R^2$ represents halogen, OH or O—C$_{1-4}$-alkyl, with alkyl being linear or branched, saturated and unsubstituted; and/or 

[0054] at least one of $R^4$ and $R^5$ represents halogen; OH; O—C$_{1-4}$-alkyl, with alkyl being linear or branched, saturated and unsubstituted; while the other represents hydrogen; halogen; O—C$_{1-4}$-alkyl, with alkyl being linear or branched, saturated and unsubstituted; and/or 

[0055] $R^4$ represents hydrogen or CO₂—NR$^5$R$^8$; 

[0056] $R^4$ and $R^5$ independently of one another represent hydrogen; C$_{1-4}$-alkyl, with alkyl being linear or branched, saturated and unsubstituted. 

[0057] In another preferred embodiment of the invention for the compound according to the invention according to formula I halogen means Cl or F. 

[0058] In another preferred embodiment of the invention for the compound according to the invention according to formula I neither of $R^3$, $R^4$ or $R^5$ represent OH. 

[0059] In a very preferred embodiment of the invention the compound according to the invention is a compound according to formula II 

\[ \text{Formula II} \]

wherein 

[0060] $R^{11}$ and $R^{12}$ independently of one another represent hydrogen; C$_{1-4}$-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; or an appropriate protective group; 

[0061] or $R^{11}$ and $R^{12}$ together with the Nitrogen they both bind to form a heterocyclic ring or an appropriate protective group; 

[0062] $R^{13}$, $R^{14}$ and $R^{15}$ independently of one another represent hydrogen; C$_{1-4}$-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; or an appropriate protective group; 

[0063] $R^{16}$ represents hydrogen or CO₂—NR$^{17}$R$^{18}$; 

[0064] $R^{17}$ and $R^{18}$ independently of one another represent hydrogen; C$_{1-4}$-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; or an appropriate protective group; 

[0065] or $R^{17}$ and $R^{18}$ together with the Nitrogen they both bind to form a heterocyclic ring or an appropriate protective group; 

[0066] optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding N-oxide thereof, or a corresponding salt thereof, or a corresponding solvate thereof. 

[0067] In a preferred embodiment of the invention for the compound according to the invention according to formula II . 

[0068] $R^{11}$ and $R^{12}$ independently of one another represent hydrogen; C$_{1-4}$-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or substituted by F, Cl, Br, I, NH$_2$, SH or OH; or an appropriate protective group selected from tert-butoxycarbonyl (Boc), benzylxycarbonyl (Cbz), trifluoroacetyl (TFA) or 9-fluorenylmethoxycarbonyl (Fmoc); 

[0069] or $R^{11}$ and $R^{12}$ together with the Nitrogen they both bind to form a heterocyclic ring of the following formula: 

\[ \text{Formula II} \]

\[ \text{with n being 1, 2, 3 or 4, m being 1, 2, 3 or 4 and (n+m) being } \leq 6 \text{ and X being selected from S, O, NR or CHR} \text{.} \]

[0070] with n being 1, 2, 3 or 4, m being 1, 2, 3 or 4 and (n+m) being } \leq 6 \text{ and X being selected from S, O, NR or CHR}^{19} \text{ with } R^{16} \text{ being selected from hydrogen or C$_{1-4}$-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or substituted by F, Cl, Br, I, NH$_2$, SH or OH; or an appropriate protective group selected from tert-butoxycarbonyl (Boc), benzylxycarbonyl (Cbz), trifluoroacetyl (TFA) or 9-fluorenylmethoxycarbonyl (Fmoc);} 

[0071] or an appropriate protective group, selected from phthaloyl (phthalimide), N-1,1,4,4-Tetramethyldisilazacyclopentane adduct (STABASE), 1,1,3,3-Tetramethyldisilazacyclopentane adduct (STABASE), BSB, N-2,5-bis(trisopropylsiloxy)pyrrol (BPSOP); 

[0072] $R^{13}$, $R^{14}$ and $R^{15}$ independently of one another represent hydrogen or C$_{1-4}$-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or substituted by F, Cl, Br, I, NH$_2$, SH or OH; or an appropriate protective group selected from tert-butoxycarbonyl (Boc), benzylxycarbonyl (Cbz), trifluoroacetyl (TFA) or 9-fluorenylmethoxycarbonyl (Fmoc); 

[0073] $R^{16}$ represents hydrogen or CO₂—NR$^{17}$R$^{18}$; 

[0074] $R^{17}$ and $R^{18}$ independently of one another represent hydrogen; C$_{1-4}$-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or substituted by F, Cl, Br, I, NH$_2$, SH or OH; or an appropriate protective group selected from tert-butoxycarbonyl (Boc), benzylxycarbonyl (Cbz), trifluoroacetyl (TFA) or 9-fluorenylmethoxycarbonyl (Fmoc);
or R₁⁷ and R₁⁸ together with the Nitrogen they both bind to form a heterocyclic ring of the following formula:

$$\text{R} \quad \text{H} \quad \text{N} \quad \text{R} \quad \text{H}$$

with or being 1, 2, 3 or 4, p being 1, 2, 3 or 4 and (o + p) being ≥6 and Y being selected from S, O, NR²⁰ or C¼H²⁰ with R²⁰ being selected from hydrogen or C₁₋₆-alkyl, with alkyl being linear or branched, saturated or unsaturated, unsubstituted or substituted by F, Cl, Br, I, NH₂, SH or OH;

or an appropriate protective group, selected from phthalimid (phthalimide), N-1,1,4,4-Tetramethyldisilylazacycloheptane adduct (STABASE), 1,1,3,3-Tetramethyl-1,3-disilaisoindoline (Denzo-STABASE, DSD), N-2,5-bistrisopropylsiloxyperyl (BIPSOP).

In another preferred embodiment of the compound for the compound according to the invention, according to formula II:

R¹ and R¹² independently of one another represent hydrogen; C₁₋₆-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted;

R¹³, R¹⁴ and R¹⁵ independently of one another represent hydrogen; C₁₋₆-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted;

R¹⁶ represents hydrogen or C(O)—NR¹⁷R¹⁸;

R¹⁷ and R¹⁸ independently of one another represent hydrogen; C₁₋₆-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted.

In another preferred embodiment of the invention for the compound according to the invention according to formula II:

R¹³ and R¹² independently of one another represent hydrogen; C₁₋₆-alkyl, with alkyl being linear or branched, saturated and unsubstituted; and/or

R¹³, R¹⁴ and R¹⁵ independently of one another represent hydrogen; C₁₋₆-alkyl, with alkyl being linear or branched, saturated and unsubstituted; and/or

R¹⁶ represents hydrogen or C(O)—NR¹⁷R¹⁸;

with R¹⁷ and R¹⁸ independently of one another represent hydrogen; C₁₋₆-alkyl, with alkyl being linear or branched, saturated and unsubstituted.

In another preferred embodiment of the invention for the compound according to the invention according to formula II:

R¹³, R¹⁴ and R¹⁵ independently of one another represent hydrogen or methyl, preferably

R¹³, R¹⁴ and R¹⁵ all represent hydrogen, or

R¹³, R¹⁴ and R¹⁵ all represent methyl.

In another preferred embodiment of the invention the compound according to the invention according to formula II is selected from

2-amino-6,7,8-trimethoxyquinazolin-4(3H)-one;

6,7,8-Trimethoxy-2-morpholinoquinazolin-4(3H)-one;

2-(4-methylpiperazin)-6,7,8-trimethoxyquinazolin-4(3H)-one;

tert-Butyl 6,7,8-trimethoxy-4-oxo-3,4-dihydroquinazolin-2-ylcarbamate;

2-(disopropylamino)-6,7,8-trimethoxyquinazolin-4(3H)-one;

2-(dimethylamino)-6,7,8-trimethoxyquinazolin-4(3H)-one;

2-(di-tert-butylamino)-6,7,8-trimethoxyquinazolin-4(3H)-one;

2-(diethylamino)-6,7,8-trimethoxyquinazolin-4(3H)-one;

2-amino-6,7,8-trimethoxyquinazolin-4(3H)-one;

6,7,8-trimethoxy-4-oxo-3,4-dihydroquinazolin-5-carboxamide;

2-(disopropylamino)-6,7,8-trimethoxy-4-oxo-3,4-dihydroquinazolin-5-carboxamide;

2-(dimethylamino)-6,7,8-trimethoxy-4-oxo-3,4-dihydroquinazolin-5-carboxamide;

2-(di-tert-butylamino)-6,7,8-trimethoxyquinazolin-4(3H)-one;

2-amino-6,7,8-trimethoxyquinazolin-4(3H)-one;

6,7,8-trihydroxy-2-morpholinoquinazolin-4(3H)-one;

6,7,8-trihydroxy-2-(4-methylpiperazin-1-yl)quinazolin-4(3H)-one;

tert-Butyl 6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazolin-2-ylcarbamate;

2-(disopropylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one;

2-(dimethylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one;

2-(di-tert-butylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one;

2-(diethylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one;

2-amino-6,7,8-trihydroxyquinazolin-4(3H)-one;

6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazolin-5-carboxamide;

2-(disopropylamino)-6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazolin-5-carboxamide;

2-(dimethylamino)-6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazolin-5-carboxamide;

2-(di-tert-butylamino)-6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazolin-5-carboxamide;

2-(diethylamino)-6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazolin-5-carboxamide;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomer and/or diastereomers, in any mixing ratio, or a corresponding N-oxide thereof, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention for the compound according to the invention according to formula II:

R¹⁶ represents hydrogen.

In a very preferred embodiment of the invention the compound according to the invention is a compound according to formula III.
[0123] wherein

[0124] R²¹ and R²² independently of one another represent hydrogen; C₁₋₄-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; or an appropriate protective group;

[0125] or R²¹ and R²² together with the nitrogen they both bind to form a heterocyclic ring or an appropriate protective group;

[0126] R²⁶ represents hydrogen or C(O)—NR²²R²₈;

[0127] R²⁷ and R²⁸ independently of one another represent hydrogen; C₁₋₄-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; or an appropriate protective group;

[0128] or R²⁷ and R²⁸ together with the nitrogen they both bind to form a heterocyclic ring or an appropriate protective group;

[0129] optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding N-oxide thereof, or a corresponding salt thereof, or a corresponding solvate thereof.

[0130] In a preferred embodiment of the invention for the compound according to the invention according to formula III

[0131] R²¹ and R²² independently of one another represent hydrogen; C₁₋₄-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted by F, Cl, Br, I, NH₂, SH or OH; or an appropriate protective group selected from tert-butoxycarbonyl (Boc), benzyloxycarbonyl (Cbz), trifluoroacetyl (TFA) or 9-fluorenylmethoxycarbonyl (Fmoc);

[0132] or R²¹ and R²² together with the nitrogen they both bind to form a heterocyclic ring of the following formula:

[0133] with n being 1, 2, 3 or 4, m being 1, 2, 3 or 4 and (n+m) being ≤6 and X being selected from S, O, NR or CHR with R²⁶ being selected from hydrogen or C₁₋₄-alkyl, with alkyl being linear or branched, saturated or unsaturated, unsubstituted or substituted by F, Cl, Br, I, NH₂, SH or OH;

[0134] or an appropriate protective group, selected from phthaloyl (phthalimide), N-1,1,4,4-Tetramethyldiisylazacycloheptane adduct (STABASE), 1,1,3,3-Tetramethyl-1,3-disilaisoindoline (Benzo-STABASE, BSB), N-2,5-bis(trisopropylsilox)pyrrol (BIPSOP);

[0135] R²⁶ represents hydrogen or C(O)—NR²²R²₈;

[0136] R²⁷ and R²⁸ independently of one another represent hydrogen; C₁₋₄-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted by F, Cl, Br, I, NH₂, SH or OH; or an appropriate protective group selected from tert-butoxycarbonyl (Boc), benzyloxycarbonyl (Cbz), trifluoroacetyl (TFA) or 9-fluorenylmethoxycarbonyl (Fmoc);

[0137] or R²¹ and R²² together with the nitrogen they both bind to form a heterocyclic ring of the following formula:

[0138] with o being 1, 2, 3 or 4, p being 1, 2, 3 or 4 and (o+p) being ≤6 and Y being selected from S, O, NR or CHR with R²⁶ being selected from hydrogen or C₁₋₄-alkyl, with alkyl being linear or branched, saturated or unsaturated, unsubstituted or substituted by F, Cl, Br, I, NH₂, SH or OH;

[0139] or an appropriate protective group, selected from phthaloyl (phthalimide), N-1,1,4,4-Tetramethyldiisylazacycloheptane adduct (STABASE), 1,1,3,3-Tetramethyl-1,3-disilaisoindoline (Benzo-STABASE, BSB), N-2,5-bis(trisopropylsilox)pyrrol (BIPSOP).

[0140] In another preferred embodiment of the invention for the compound according to the invention according to formula III

[0141] R²¹ and R²² independently of one another represent hydrogen; C₁₋₄-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted;

[0142] R²⁶ represents hydrogen or C(O)—NR²²R²₈;

[0143] R²⁷ and R²⁸ independently of one another represent hydrogen; C₁₋₄-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted;

[0144] In another preferred embodiment of the invention for the compound according to the invention according to formula III

[0145] R²¹ and R²² independently of one another represent hydrogen; C₁₋₄-alkyl, with alkyl being linear or branched, saturated and unsubstituted; and/or

[0146] R²⁶ represents hydrogen or C(O)—NR²²R²₈;

[0147] R²⁷ and R²⁸ independently of one another represent hydrogen; C₁₋₄-alkyl, with alkyl being linear or branched, saturated and unsubstituted;

[0148] In another preferred embodiment of the invention for the compound according to the invention according to formula III

[0149] 2-aminoo-6,7,8-trimethoxyquinazolin-4(3H)-one,

[0150] 6,7,8-Trimethoxy-2-morpholinoquinazolin-4(3H)-one,
[0151] 2-(4-methylpiperazin)-6,7,8-trimethoxyquinazolin-4(3H)-one,
[0152] tert-Butyl 6,7,8-trimethoxy-4-oxo-3,4 dihydroquinazolin-2-ylcarbamate,
[0153] 2-(diisopropylamino)-6,7,8-trimethoxyquinazolin-4(3H)-one,
[0154] 2-(dimethylamino)-6,7,8-trimethoxyquinazolin-4(3H)-one,
[0155] 2-(di-tert-butylamino)-6,7,8-trimethoxyquinazolin-4(3H)-one,
[0156] 2-(diethylamino)-6,7,8-trimethoxyquinazolin-4(3H)-one,
[0157] 2-amino-6,7,8-trimethoxy-4-oxo-3,4 dihydroquinazoline-5-carboxamide,
[0158] 2-(diisopropylamino)-6,7,8-trimethoxy-4-oxo-3,4 dihydroquinazoline-5-carboxamide,
[0159] 2-(dimethylamino)-6,7,8-trimethoxy-4-oxo-3,4 dihydroquinazoline-5-carboxamide,
[0160] 2-(di-tert-butylamino)-6,7,8-trimethoxy-4-oxo-3,4 dihydroquinazoline-5-carboxamide or
[0161] 2-(diethylamino)-6,7,8-trimethoxy-4-oxo-3,4 dihydroquinazoline-5-carboxamide,
[0162] optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding N-oxide thereof, or a corresponding salt thereof, or a corresponding solvate thereof.
[0163] In another preferred embodiment of the invention for the compound according to the invention according to formula III R²³ represents hydrogen.
[0164] In a very preferred embodiment of the invention the compound according to the invention according to formula III is selected from
[0165] 2-amino-6,7,8-trimethoxyquinazolin-4(3H)-one,
[0166] 6,7,8-Trimethoxy-2-morpholinoquinazolin-4(3H)-one,
[0167] 2-(4-methylpiperazin)-6,7,8-trimethoxyquinazolin-4(3H)-one,
[0168] tert-Butyl 6,7,8-trimethoxy-4-oxo-3,4 dihydroquinazolin-2-ylcarbamate,
[0169] 2-(diisopropylamino)-6,7,8-trimethoxyquinazolin-4(3H)-one,
[0170] 2-(dimethylamino)-6,7,8-trimethoxyquinazolin-4(3H)-one,
[0171] 2-(di-tert-butylamino)-6,7,8-trimethoxyquinazolin-4(3H)-one or
[0172] 2-(diethylamino)-6,7,8-trimethoxyquinazolin-4(3H)-one;
[0173] optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding N-oxide thereof, or a corresponding salt thereof, or a corresponding solvate thereof.
[0174] In a very preferred embodiment of the invention the compound according to the invention is a compound according to formula IIIa
[0175] Wherein
[0176] R²¹ and R²² independently of oneanother represent hydrogen; C₁₄₋₅-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; or an appropriate protective group;
[0177] R²⁶ represents hydrogen or C(O)—NR²⁷R²⁸,
[0178] R²⁷ and R²⁸ independently of oneanother represent hydrogen; C₁₋₅-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; or an appropriate protective group;
[0179] optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding N-oxide thereof, or a corresponding salt thereof, or a corresponding solvate thereof.
[0180] In a preferred embodiment of the invention for the compound according to the invention according to formula IIIa
[0181] R²¹ and R²² independently of oneanother represent hydrogen; C₁₋₅-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted or substituted by F, Cl, Br, I, NH₂, SH or OH; or an appropriate protective group selected from tert-butoxy carbonyl (Boc), benzoylcarbonyl (Cbz), trifluoroacetyl (TFA) or 9-fluorenylmethoxycarbonyl (Fmoc);
[0182] R²⁶ represents hydrogen or C(O)—NR²⁷R²⁸;
[0183] R²⁷ and R²⁸ independently of oneanother represent hydrogen; C₁₋₅-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or substituted by F, Cl, Br, I, NH₂, SH or OH; or an appropriate protective group selected from tert-butoxy carbonyl (Boc), benzoylcarbonyl (Cbz), trifluoroacetyl (TFA) or 9-fluorenylmethoxycarbonyl (Fmoc).
[0184] In another preferred embodiment of the invention for the compound according to the invention according to formula IIIa
[0185] R²¹ and R²² independently of oneanother represent hydrogen; C₁₋₅-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted;
[0186] R²⁶ represents hydrogen or C(O)—NR²⁷R²⁸;
[0187] R²⁷ and R²⁸ independently of oneanother represent hydrogen; C₁₋₅-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted.
[0188] In another preferred embodiment of the invention for the compound according to the invention according to formula IIIa
[0189] R²¹ and R²² independently of one another represent hydrogen; C₁₋₄-alkyl, with alkyl being linear or branched, saturated and unsubstituted; and/or
[0190] R²³ represents hydrogen or C(O)—NR²⁷R²⁸;
[0191] R²⁴ and R²⁵ independently of one another represent hydrogen; C₁₋₄-alkyl, with alkyl being linear or branched, saturated and unsubstituted.
[0192] In a further preferred embodiment of the invention the compound according to the invention according to formula IIIa is selected from

- 2-amino-6,7,8-trihydroxyquinazolin-4(3H)-one
- 6,7,8-trihydroxy-2-morpholinoquinazolin-4(3H)-one
- 6,7,8-trihydroxy-2-(4-methylpiperazin-1-yl) quinazolin-4(3H)-one
- tert-Butyl 6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazolin-2-ylcarbamate
- 2-(diisopropylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one
- 2-(dimethylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one
- 2-(di-tert-butylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one
- 2-(diethylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one
- 2-amino-6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazoline-5-carboxamide
- 2-(diisopropylamino)-6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazoline-5-carboxamide
- 2-(dimethylamino)-6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazoline-5-carboxamide
- 2-(di-tert-butylamino)-6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazoline-5-carboxamide
- 2-(diethylamino)-6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazoline-5-carboxamide

[0218] optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding N-oxide thereof, or a corresponding salt thereof, or a corresponding solvate thereof.
[0219] Another preferred aspect of the invention are chemical process especially processes for the production of compounds according to the invention or intermediates thereof.

[0220] A part of these processes can be seen in the overall process according to Scheme I leading to compounds according to formula I:

```
R5 R4 R6 Cyanate —> O R3 NH O 2 \ IVa
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```
R5 R4 R6 Base —> O R3 H N NH O 2 \H/ \ 0 Va
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R5 R4 R6 Chlorinating Agent —> O R3 HN \n/ NH O VIa R5 R4 R6
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R5 R4 R6 Cl R3 I N Y N Cl VIIa
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R4 R6
\ R4 R6 O
\ H2 N A M
```

```[0208] R²³ represents hydrogen.
[0209] In a very preferred embodiment of the invention the compound according to the invention according to formula IIIa is selected from

- 2-amino-6,7,8-trihydroxyquinazolin-4(3H)-one,
- 6,7,8-trihydroxy-2-morpholinoquinazolin-4(3H)-one,
- 6,7,8-trihydroxy-2-(4-methylpiperazin-1-yl) quinazolin-4(3H)-one,
- tert-Butyl 6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazolin-2-ylcarbamate
- 2-(diisopropylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one,
- 2-(dimethylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one,
- 2-(di-tert-butylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one or
- 2-(diethylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one;```
In this overall Scheme I the reactions are carried out in a suitable solvent or reaction medium and R1, R2, R3, R4, R5 and R6 have the meaning mentioned above.

It is preferred that the Cyanate (salt of the cyanic acid) in Scheme I is selected from KOCN or NaOCN, more preferably KOCN.

It is further preferred that the Base in Scheme I is an anorganic base, preferably a hydroxide, especially NaOH or KOH, most preferably NaOH.

It is further preferred that the chlorinating agent in Scheme I is an organic compound, most preferably POCl3.

In a majority of the cases R5 in Va in Scheme I is hydrogen with—if applicable—the Amid C(O)NR2R6 being introduced at some later stage according to reactions well known in the art.

In a preferred embodiment of the invention a compound according to the invention according to formula I is prepared by reacting a compound of formula VIIIa with a secondary amine HNR2R2 in a suitable solvent or reaction medium and R1, R2, R3, R4, R5 and R6 having the meaning mentioned above.

In a preferred embodiment of this process to obtain a compound according to formula I to prepare the abovementioned compound according to formula VIIIa a compound of formula VIIIa is reacted with a base in a suitable solvent or reaction medium and R1, R2, R3, R4, R5 and R6 having the meaning mentioned above.

Here it is preferred that the Base is an anorganic base, preferably a hydroxide, especially NaOH or KOH, most preferably NaOH.

In a preferred embodiment of this process to obtain a compound according to formula I to prepare the abovementioned compound according to formula VIIIa a compound of formula VIIIa is reacted with a chlorinating agent in a suitable solvent or reaction medium and R5, R4, R3 and R6 having the meaning mentioned above.

Here it is preferred that the chlorinating agent is an anorganic compound, most preferably POCl3.

In a preferred embodiment of this process to obtain a compound according to formula I to prepare the abovementioned compound according to formula VIIIa a compound of formula Va is reacted with a base in a suitable solvent or reaction medium and R3, R4, R5 and R6 having the meaning mentioned above.

Here it is preferred that the Base is an anorganic base, preferably a hydroxide, especially NaOH or KOH, most preferably NaOH.

In a preferred embodiment of this process to obtain a compound according to formula I to prepare the abovementioned compound according to formula Va a compound of formula Va is reacted with a base in a suitable solvent or reaction medium and R3, R4, R5 and R6 having the meaning mentioned above.
is reacted with a cyanate/salt of cyanic acid in a suitable solvent or reaction medium and R³, R⁴, R⁵ and R⁶ having the meaning mentioned above.

[0234] Here it is preferred that the cyanate (salt of the cyanic acid) is selected from KOCN or NaOCN, more preferably KOCN.

[0235] A selected part of these processes can be seen in the overall process according to Scheme II leading to compounds according to formula II:

[0236] In this overall Scheme II the reactions are carried out in a suitable solvent or reaction medium and R¹³, R¹⁴, R¹⁵, R¹⁶ and R¹⁷ have the meaning mentioned above.

[0237] It is preferred that the Cyanate (salt of the cyanic acid) in Scheme II is selected from KOCN or NaOCN, more preferably KOCN.

[0238] It is further preferred that the Base in Scheme II is an anorganic base, preferably a hydroxide, especially NaOH or KOH, most preferably NaOH.

[0239] It is further preferred that the chlorinating agent in Scheme II is anorganic compound, most preferably POCl₃.

[0240] In a majority of the cases R¹⁶ in IV⁻ in Scheme II is hydrogen with—if applicable—the Amid C(O)NR¹⁷R¹⁸ being introduced at some later stage according to reactions well known in the art.

[0241] In a preferred embodiment of the invention a compound according to the invention according to formula II is prepared by reacting a compound of formula VIIIb with a secondary amine HNR¹¹R¹² in a suitable solvent or reaction medium and R¹¹, R¹², R¹³, R¹⁴, R¹⁵ and R¹⁶ having the meaning mentioned above.

[0242] In a preferred embodiment of this process to obtain a compound according to formula II to prepare the above-mentioned compound according to formula VIIIb a compound of formula VIIb

[0243] Base
is reacted with a base in a suitable solvent or reaction medium and R¹¹, R¹², R¹³, R¹⁴, R¹⁵ and R¹⁶ having the meaning mentioned above.

[0243] Here it is preferred that the base is an anorganic base, preferably a hydroxide, especially NaOH or KOH, most preferably NaOH.

[0244] In a preferred embodiment of this process to obtain a compound according to formula II to prepare the above-mentioned compound according to formula VIIa a compound of formula VIb

is reacted with a chlorinating agent in a suitable solvent or reaction medium and R¹³, R¹⁴, R¹⁵ and R¹⁶ having the meaning mentioned above.

[0249] Here it is preferred that the cyanate (salt of the cyanic acid) is selected from KOCN or NaOCN, more preferably KOCN.

[0250] A further selected part of these processes can be seen in the overall process according to Scheme III leading to compounds according to formula III:

is reacted with a cyanate/salt of cyanic acid in a suitable solvent or reaction medium and R¹³, R¹⁴, R¹⁵ and R¹⁶ having the meaning mentioned above.

[0249] Here it is preferred that the cyanate (salt of the cyanic acid) is selected from KOCN or NaOCN, more preferably KOCN.

[0250] A further selected part of these processes can be seen in the overall process according to Scheme III leading to compounds according to formula III:

is reacted with a chlorinating agent in a suitable solvent or reaction medium and R¹³, R¹⁴, R¹⁵ and R¹⁶ having the meaning mentioned above.

[0247] Here it is preferred that the base is an anorganic base, preferably a hydroxide, especially NaOH or KOH, most preferably NaOH.

[0248] In a preferred embodiment of this process to obtain a compound according to formula II to prepare the above-mentioned compound according to formula IVb a compound of formula IVb
In this overall Scheme III the reactions are carried out in a suitable solvent or reaction medium and R\textsuperscript{21}, R\textsuperscript{22} and R\textsuperscript{26} have the meaning mentioned above.

It is preferred that the Cyanate (salt of the cyanic acid) in Scheme III is selected from KOCN or NaOCN, more preferably KOCN.

It is further preferred that the Base in Scheme III is an inorganic base, preferably a hydroxide, especially NaOH or KOH, most preferably NaOH.

It is further preferred that the chlorinating agent in Scheme III is an organic compound, most preferably POCl\textsubscript{3}.

In a majority of the cases R\textsuperscript{26} in IVc in Scheme III is hydrogen with—if applicable—the Amid C(O)NR\textsuperscript{21}R\textsuperscript{22} being introduced at some later stage according to reactions well known in the art.

In a preferred embodiment of the invention a compound according to the invention according to formula III is prepared by reacting a compound of formula VIIIc with a secondary amine HNR\textsuperscript{21}R\textsuperscript{22} in a suitable solvent or reaction medium and R\textsuperscript{26} having the meaning mentioned above.

In a preferred embodiment of this process to obtain a compound according to formula III to prepare the above-mentioned compound according to formula VIIc a compound of formula VIIc is reacted with a base in a suitable solvent or reaction medium and R\textsuperscript{26} having the meaning mentioned above.

Here it is preferred that the base is a hydroxide, especially NaOH or KOH, most preferably NaOH.

In a preferred embodiment of this process to obtain a compound according to formula III to prepare the above-mentioned compound according to formula VIIc a compound of formula VIIc is reacted with a chlorinating agent in a suitable solvent or reaction medium and R\textsuperscript{26} having the meaning mentioned above.

Here it is preferred that the chlorinating agent is an inorganic compound, most preferably POCl\textsubscript{3}.

In a preferred embodiment of this process to obtain a compound according to formula III to prepare the above-mentioned compound according to formula VIIc a compound of formula VIIc is reacted with a base in a suitable solvent or reaction medium and R\textsuperscript{26} having the meaning mentioned above.

Here it is preferred that the base is the hemihydrate of the cyanic acid, especially NaOH or KOH, most preferably NaOH.

In a preferred embodiment of this process to obtain a compound according to formula III to prepare the above-mentioned compound according to formula VIIc a compound of formula VIIc is reacted with a chlorinating agent in a suitable solvent or reaction medium and R\textsuperscript{26} having the meaning mentioned above.

Here it is preferred that the chlorinating agent is an organic compound, most preferably POCl\textsubscript{3}.
is reacted with a cyanate/salt of cyanic acid in a suitable solvent or reaction medium and \( R^{26} \) having the meaning mentioned above.

[0264] Here it is preferred that the cyanate (salt of the cyanic acid) is selected from KO\( \text{CN} \) or NaO\( \text{CN} \), more preferably KO\( \text{CN} \).

[0265] A further selected part of these processes can be seen in the overall process according to Scheme IIIa leading to compounds according to formula IIIa, based on Scheme III:

\[ \text{IVc} \]

\[ \text{Vlc} \]
[0266] In this overall Scheme IIIa the reactions are carried out in a suitable solvent or reaction medium and R^{21}, R^{22} and R^{26} have the meaning mentioned above.

[0267] It is preferred that the Cyanate (salt of the cyanic acid) in Scheme IIIa is selected from KOCN or NaO CN, more preferably KOCN.

[0268] It is further preferred that the Base in Scheme IIIa is an anorganic base, preferably a hydroxide, especially NaOH or KOH, most preferably NaOH.

[0269] It is further preferred that the chlorinating agent in Scheme IIIa is anorganic compound, most preferably POCl$_3$.

[0270] It is further preferred that the demethylating agent in Scheme IIIa is BCl$_3$.

[0271] In a majority of the cases R^{26} in IVe in Scheme IIIa is hydrogen with—if applicable—the Amid C(O)NR$_2$R$_2$ being introduced at some later stage according to reactions well known in the art.

[0272] In a preferred embodiment of the invention a compound according to the invention according to formula IIIa is prepared by reacting a compound of formula III with a demethylating agent in a suitable solvent or reaction medium and R^{26} having the meaning mentioned above.

[0273] Here it is preferred that the demethylating agent is BCl$_3$.

[0274] Another preferred aspect of the invention is the use of at least one compound according to the invention as an intermediate in the synthesis of active biomolecules.

[0275] It further seems that the compounds according to the invention surprisingly are sodium channel blockers or blockers and thus seem to have pharmaceutical activity (see e.g., Anger et al., J MedChem. Vol 44, No. 2, (2001) 115-137).

[0276] Thus as the compounds according to the invention are toxicologically acceptable they are therefore suitable as pharmaceutical active substances for the preparation of medicaments.

[0277] Thus, another aspect of the present invention relates to a Medicament comprising at least one compound according to the invention and optionally one or more pharmaceutically acceptable excipients.

[0278] In this application the term medicament should be considered as equal to the term pharmaceutical composition.

[0279] The medicament according to the present invention may be in any form suitable for the application to humans and/or animals, preferably humans including infants, children and adults and can be produced by standard procedures known to those skilled in the art. The composition of the medicament may vary depending on the route of administration.

[0280] The medicament of the present invention may for example be administered parentally in combination with conventional injectable liquid carriers, such as water or suitable alcohols. Conventional pharmaceutical excipients for injection, such as stabilizing agents, solubilizing agents, and buffers, may be included in such injectable compositions. These medicaments may for example be injected intramuscularly, intraperitoneally, or intravenously.

[0281] Solid oral compositions (which are preferred as are liquid ones) may be prepared by conventional methods of blending, filling or tabletting. Repeated blending operations may be used to distribute the active agent throughout these compositions employing large quantities of fillers. Such operations are conventional in the art. The tablets may for example be prepared by wet or dry granulation and optionally coated according to the methods well known in normal pharmaceutical practice, in particular with an enteric coating.

[0282] The mentioned formulations will be prepared using standard methods such as those described or referred to in the Spanish and US Pharmacopoeias and similar reference texts.

[0283] Medicaments according to the present invention may also be formulated into orally administrable compositions containing one or more physiologically compatible carriers or excipients, in solid or liquid form. These compositions may contain conventional ingredients such as binding agents, fillers, lubricants, and acceptable wetting agents. The compositions may take any convenient form, such as tablets, pellets, capsules, lozenges, aqueous or oily solutions, suspensions, emulsions, or dry powdered forms suitable for reconstitution with water or other suitable liquid medium before use, for immediate or retarded release.

[0284] The liquid oral forms for administration may also contain certain additives such as sweeteners, flavoring, preservatives, and emulsifying agents. Non-aqueous liquid compositions for oral administration may also be formulated, containing edible oils. Such liquid compositions may be conveniently encapsulated in e.g., gelatin capsules in a unit dosage amount.

[0285] The compositions of the present invention may also be administered topically or via a suppository.

[0286] The daily dosage for humans and animals may vary depending on factors that have their basis in the respective species or other factors, such as age, sex, weight or degree of illness and so forth. The daily dosage for humans may preferably be in the range from 1 to 2000, preferably 1 to 1500, more preferably 1 to 1000 milligrams of active substance to be administered during one or several intakes per day.

[0287] Another preferred aspect of the invention is the use of at least one compound according to the invention (and optionally one or more pharmaceutically acceptable excipients), for the preparation/manufacture of a medicament for the treatment of CNS Disorders.

[0288] Another preferred aspect of the invention is the use of at least one compound according to the invention (and optionally one or more pharmaceutically acceptable excipients), for the preparation of a medicament for the treatment of pain, especially neuropathic pain, stroke, addiction and epilepsy.

[0289] The present invention is illustrated below with the aid of examples and figures. These illustrations are given solely by way of example and do not limit the general spirit of the present invention.
EXPERIMENTAL PART

Examples


[0291] All reactions described below were carried out under argon atmosphere unless otherwise noted. The solvents used were distilled and dried under argon atmosphere before use. All starting materials were purchased commercially (Aldrich, Fluka and Merck) and used without further purification. Flash Chromatography was executed on columns loaded with 230-400 mesh silica gel Merck. TLC was carried out on silica gel Merck (Kieselgel 60F-254).

[0292] Melting points (mp) were determined on a Reichert Microscopic Hot-Stage. 1H and 13C NMR spectra were measured on a Varian Gemini-200 and a Varian Inova-300 spectrometer with (CH3)4Si as an internal reference and CDCl3 as solvent unless otherwise noted. Both 1H and 13C NMR spectral data are reported in parts per million (δ) relative to residual sign of the solvent (CDCl3, 7.26 ppm and 77.0 ppm for 1H and 13C NMR, respectively). 1H and 13C NMR designations are: s (singlet); d (doublet); t (triplet); q (quartet); m (multiplet). Infrared (IR) spectra were record on a Perkin-Elmer FT-IR spectrometer. UV spectra were record on a Perkin-Elmer 402 spectrometer. Low-resolution mass (LRMS) spectra were obtained on a Hewlett Packard 5973 MSD spectrometer with a direct inlet system (EI) at 70 eV.

[0293] The compounds of general formula I were nominated, in general, as derivatives of quinazolin-4(3H)-one and were numerated following the numeration described below.

Formula I

Example 1

2-(diisopropylamino)-6,7,8-trimethoxyquinazolin-4 (3H)-one

[0294] Example 1 was produced according to the following reaction scheme. The NMR spectrum of the resulting compound is shown in FIG. 1.

[0295] Compound Vlc is obtained (white solid, quantitative yield) by the sequence: a) reaction of Compound IVc (Methyl 3,4,5-trimethoxanthranilate or Benzoic acid, 2-amino-3,4,5-trimethoxy-, methyl ester, commercially available from companies like Merck, Apen or Maybride) and potassium cyanoate in acetic acid (aqueous solution), and b) treatment of the crude suspension with NaOH (50%).

[0296] Compound VIIIc is obtained (white solid, quantitative yield) by the sequence: a) reaction of Compound Vlc and phosphorus (III) oxychloride in presence of N,N-dimethylaminine, and b) hydrolysis with NaOH (1N) using THF as solvent.
In a Kimble, to a mixture of 2-chloro-6,7,8-trimethoxyquinazolin-4(3H)-one (70 mg, 0.259 mmol) in EtOH (2.5 ml) was added diisopropylamine (0.4 ml, 2.845 mmol). The resulting mixture was stirred at reflux for 24 h and then concentrated under reduced pressure. The residue was triturated with EtO to give 2-(diisopropylamino)-6,7,8-trimethoxy-2-morpholinooquinazolin-4(3H)-one (63 mg, 73%) as a white solid.

As an alternative analog 2-(dimethylamino)-6,7,8-trimethoxyquinazolin-4(3H)-one will be produced analogously to example 1 above if HN(CH₃)₂ is added in the last step instead of HN(C₃H₇)₂.

To a solution of methyl 3,4,5-trimethoxy-anthranilate (410 mg, 1.7 mmol) in a mixture 5:1 MeOH/HOAc (30 ml) was added N,N-bis-(tert-butoxycarbonyl)-2-methyl-2-thiopseudourea (610 mg, 2.1 mmol). The resulting mixture was stirred under argon at room temperature for one day. Then, the mixture was stirred at reflux for another day. To the mixture was added N,N-bis-(tert-butoxycarbonyl)-2-methyl-2-thiopseudourea (508 mg, 1.7 mmol) and was stirred to reflux for another day. Then it was concentrated under reduced pressure. The residue was purified by silica gel column (Hex:AcOEt 3:1) to give tert-Butyl 6,7,8-trimethoxy-4-oxo-3,4-dihydroquinazolin-2-ylcarbamate as a white solid (90 mg, 15%) and methyl 3,4,5-trimethoxy-anthranilate (308 mg, 75%).
Example 3
2-amino-6,7,8-trimethoxyquinazolin-4(3H)-one

\[
\text{HCl 3M, AcOEt r.t.}
\]

Example 4
6,7,8-Trimethoxy-2-morpholinoquinazolin-4(3H)-one

\[
\text{morpholine, Na}_2\text{CO}_3 \quad \text{EtO}, \text{reflux}
\]

tert-Butyl 6,7,8-trimethoxy-4-oxo-3,4-dihydroquinazolin-2-ylicarbamate (40 mg, 0.114 mmol) as produced according to example 2 was treated with 0.5 ml of a mixture of HCl (3M) and AcOEt (1:1). The mixture was stirred at room temperature for 3.5 h. The solvent was evaporated under reduced pressure. The residue was triturated with Et₂O to give 2-amino-6,7,8-trimethoxyquinazolin-4(3H)-one as a white solid (21 mg, 73%).

Example 4
6,7,8-Trimethoxy-2-morpholinoquinazolin-4(3H)-one

\[
\text{morpholine, Na}_2\text{CO}_3 \quad \text{EtO}, \text{reflux}
\]

To a mixture of 2-chloro-6,7,8-trimethoxyquinazolin-4(3H)-one (70 mg, 0.259 mmol) (VIII produced according to the reaction scheme for example 1) and Na₂CO₃ anhydrous (110 mg, 1.036 mmol) in EtOH (2.6 ml) was added morpholine (0.34 ml, 3.885 mmol). The resulting mixture was stirred at reflux for 3 h and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography (AcOEt) to give 6,7,8-trimethoxy-2-morpholinoquinazolin-4(3H)-one as a white solid (76 mg, 92%).

Yield, 73%; white solid; ¹H-NMR (300 MHz, CD₂OD): δ 7.38 (1H, s, H-5), 4.05 (3H, s, OCH₃), 4.00 (3H, s, OCH₃), 3.92 (3H, s, OCH₃); ¹³C-NMR (75 MHz, CD₂OD): δ 160.3, 153.3, 152.5, 149.6, 142.1, 128.3, 111.9, 104.2, 62.4, 61.8, 56.8; IR (KBr): v 3404, 3210, 2949, 1684, 1553, 1500, 1484, 1432, 1277, 1125, 1084, 974 cm⁻¹; LRMS (API-ES⁺): m/z 525 (2M+Na)+, 274 (M+Na)+, 252 (M+H)+.

Alternatively example 3 may also be produced completely analogous to example 1, with the exception that in the last step preferably HN(Protec)₂ is used with "Protec" meaning a protective group according to e.g. Greene and Wats "Protective Groups in Organic Synthesis" 3rd edition, John Wiley & Sons, Inc., p. 573 (1999) (with "Protec" later being removed) instead of HN(C₃H₅)₂ as in example 1.

Rₗ,0.19 (TLC, AcOEt); yield, 92%; white solid; ¹H-NMR (200 MHz, CDCl₃): δ 11.66 (1H, br s, NH), 7.22 (1H, s, H-5), 4.02 (3H, s, OCH₃), 4.01 (3H, s, OCH₃), 3.90 (3H, s, OCH₃), 3.85 (2H, m, OCH₂CH₂N), 3.76 (2H, m, OCH₂CH₂N); ¹³C-NMR (50 MHz, CDCl₃): δ 164.9, 149.8, 149.2, 148.6, 145.9, 141.0, 112.3, 100.1, 66.4, 61.5, 55.9, 45.5; IR (KBr): v 3427, 3130, 3086, 2960, 2840, 1664, 1602, 1472, 1421, 1390, 1307, 1254, 1134, 1114, 1074, 989, 934, 903, 875, 793 cm⁻¹; LRMS (EI): m/z 321 (M⁺, 100), 306 (34), 290 (35), 276 (26), 264 (58), 246 (16), 231 (10), 219 (10), 205 (8), 192 (14); LRMS (API-ES⁺): m/z 665 (2M+Na)+, 344 (M+Na)+, 322 (M+H)+.
Example 5
2-(4-methylpiperazin)-6,7,8-trimethoxyquinazolin-4(3H)-one

[0310]

[0319] 6,7,8-trihydroxy-2-(4-methylpiperazin-1-yl) quinazolin-4(3H)-one from example 5

1. Substituted quinazoline compound of general formula I,

\[ R^1 \text{ and } R^2 \text{ independently of one another represent hydrogen; } C_{1-4}\text{-alkyl, with alkyl being linear or branched; saturated or unsaturated; substituted or unsubstituted; or an appropriate protective group;}

\text{or } R^1 \text{ and } R^2 \text{ together with the Nitrogen they both bind to a heterocyclic ring or an appropriate protective group;}

\text{R}^2 \text{ represents halogen, } O-H \text{ or } O-C_{1-4}\text{-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; or } O-P \text{ with } P \text{ being an appropriate protective group;}

\text{at least one of } R^4 \text{ and } R^8 \text{ represents halogen; } O-H; O-C_{1-4}\text{-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; or } O-P \text{ with } P \text{ being an appropriate protective group;}

\text{R}^4 \text{ represents hydrogen or } C(O)-NR^2R^4; \text{ or R}^4 \text{ and } R^8 \text{ independently of one another represent hydrogen;}

C_{1-4}\text{-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; or an appropriate protective group;}

\text{or } R^4 \text{ and } R^8 \text{ together with the Nitrogen they both bind to a heterocyclic ring or an appropriate protective group;}

\text{optionally in form of one of the stereo-isomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereo-isomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding N-oxide thereof, or a corresponding salt thereof, or a corresponding solvate thereof.}

2. Compound according to claim 1, characterized in that

\text{R}^4 \text{ and } R^8 \text{ independently of one another represent hydrogen; } C_{1-4}\text{-alkyl, with alkyl being linear or branched; saturated or unsaturated, substituted or unsubstituted by } F, \text{Cl, Br, I, NH}_2, \text{SH or OH; or an appropriate protective group selected from tert-butoxycarbonyl (Boc), benzylxycarbonyl (Cbz), trifluoroacetyl (TFA) or 9-fluorenylethoxycarbonyl (Fmoc);}

[0311] To a stirred solution of 2-chloro-6,7,8-trimethoxyquinazolin-4(3H)-one (120 mg, 0.443 mmol) (VIIIc produced according to the reaction scheme for example I) and Na$_2$CO$_3$ anhydrous (188 mg, 1.772 mmol) in EtOH (4.5 ml) 1-methylpiperazine (0.74 ml, 6.650 mmol) was added. The mixture was heated under reflux during 6.5 hours. After this time, the solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (AcOEt) to give 2-(4-methylpiperazin)-6,7,8-trimethoxyquinazolin-4(3H)-one as a white solid (130 mg, 88%).

[0312] \( R^1 = 0.32 \) (TLC, MeOH); yield, 88%; white solid; \( ^1H\)-NMR (200 MHz, CDCl$_3$): \delta 10.35 (1H, s, NH), 7.25 (1H, s, H-5); 4.02 (3H, s, OCH$_3$), 4.01 (3H, s, OCH$_3$), 3.90 (3H, s, OCH$_3$), 3.73 (4H, t, CH$_2$), 4.9 Hz), 2.54 (4H, t, CH$_2$, J=4.9 Hz), 2.35 (3H, s, NCH$_3$); \( ^13C\)-NMR (75 MHz, CDCl$_3$): \delta 164.8, 150.0, 149.3, 149.0, 146.4, 141.8, 112.7, 101.8, 62.0, 61.8, 56.4, 55.0, 46.5, 45.5; IR (KBr): v 3435, 2931, 1669, 1600, 1474, 1417, 1252, 1133, 1079, 1005 cm$^{-1}$; LMMS (API-ES$^+$): m/z 691 (2M+Na)$^+$, 357 (M+Na)$^+$, 335 (M+H)$^+$.

[0313] As a follow-up step tryhydroxylated compounds may be produced (by treatment with BCl$_3$) like:

[0314] 2-(diisopropylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one from example 1

[0315] 2-(dimethylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one from 2-(dimethylamino)-6,7,8-trimethoxyquinazolin-4(3H)-one (see example 1)

[0316] tert-Butyl 6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazolin-2-ylcarbamate from example 2

[0317] 2-amino-6,7,8-trihydroxyquinazolin-4(3H)-one from example 3, preferably with an appropriate protective group still attached

[0318] 6,7,8-trihydroxy-2-morpholinoquinazolin-4(3H)-one from example 4,
or R¹ and R² together with the Nitrogen they both bind to form a heterocyclic ring of the following formula:

\[
\begin{align*}
\text{R}^1 & \quad \text{R}^2 \\
\text{H}_2C & \quad \text{N} \\
\text{H}_2C & \quad \text{OR}^3 \\
\text{H}_2C & \quad \text{OR}^4 \\
\text{H}_2C & \quad \text{OR}^5 \\
\text{H}_2C & \quad \text{OR}^6 \\
\end{align*}
\]

with n being 1, 2, 3 or 4, m being 1, 2, 3 or 4 and (n+m) being ≤ 6 and X being selected from S, O, NR² or CHR with R⁸ being selected from hydrogen or C₁₋₄-alkyl, with alkyl being linear or branched, saturated or unsubstituted, unsubstituted or substituted by F, Cl, Br, I, NH₂, SH or OH; or an appropriate protective group, selected from phthaloyl (phthalimide), N-1,1,4,4-Tetramethyl-disilylazacyclopentane adduct (STABASE), 1,1,3,3-Tetramethyl-1,3-disilaisoisindoline (Bnzo-STABASE, BSB), N-2,5-bis (trisopropylsilox)pyrrol (BIPSOP); R² represents halogen, OH or O—C₁₋₄-alkyl, with alkyl being linear or branched, saturated or unsubstituted, unsubstituted or substituted by F, Cl, Br, I, NH₂, SH or OH; or O—P, with P being an appropriate protective group selected from tert-butyl, acetyl or benzoyl; at least one of R⁴ and R⁵ represents halogen; OH; O—C₁₋₄-alkyl, with alkyl being linear or branched, saturated or unsubstituted, unsubstituted or substituted by F, Cl, Br, I, NH₂, SH or OH; or O—P, with P being an appropriate protective group selected from tert-butyl, acetyl or benzoyl.

R⁶ represents hydrogen or C(O)—NR¹ R⁴.

R¹ and R² independently of one another represent hydrogen; C₁₋₄-alkyl, with alkyl being linear or branched, saturated or unsubstituted, unsubstituted or substituted by F, Cl, Br, I, NH₂, SH or OH; or an appropriate protective group selected from tert-butoxycarbonyl (Boc), benzylloxycarbonyl (Cbz), trifluoroacetyl (TFA) or 9-fluorenylmethoxycarbonyl (Fmoc); or R¹ and R² together with the Nitrogen they both bind to form a heterocyclic ring of the following formula:

\[
\begin{align*}
\text{R}^1 & \quad \text{R}^2 \\
\text{H}_2C & \quad \text{N} \\
\text{H}_2C & \quad \text{OR}^3 \\
\text{H}_2C & \quad \text{OR}^4 \\
\text{H}_2C & \quad \text{OR}^5 \\
\text{H}_2C & \quad \text{OR}^6 \\
\end{align*}
\]

with o being 1, 2, 3 or 4, p being 1, 2, 3 or 4 and (o+p) being ≤ 6 and Y being selected from S, O, NR¹⁰ or CHR with R¹⁰ being selected from hydrogen or C₁₋₄-alkyl, with alkyl being linear or branched, saturated or unsubstituted, unsubstituted or substituted by F, Cl, Br, I, NH₂, SH or OH; or an appropriate protective group, selected from phthaloyl (phthalimide), N-1,1,4,4-Tetramethyl-disilylazacyclopentane adduct (STABASE), 1,1,3,3-Tetramethyl-1,3-disilaisoisindoline (Bnzo-STABASE, BSB), N-2,5-bis (trisopropylsilox)pyrrol (BIPSOP).

3. Compound according to claim 1, characterized in that R¹ and R² independently of one another represent hydrogen; C₁₋₄-alkyl, with alkyl being linear or branched, saturated or unsubstituted, substituted or unsubstituted; R³ represents halogen, OH or O—C₁₋₄-alkyl, with alkyl being linear or branched, saturated or unsubstituted, substituted or unsubstituted; at least one of R⁴ and R⁵ represents halogen; OH; O—C₁₋₄-alkyl, with alkyl being linear or branched, saturated or unsubstituted, substituted or unsubstituted; while the other represents hydrogen; OH; halogen; O—C₁₋₄-alkyl, with alkyl being linear or branched, saturated or unsubstituted, substituted or unsubstituted; R⁶ represents hydrogen or C(O)—NR¹ R⁴.

R⁷ and R⁸ independently of one another represent hydrogen; C₁₋₄-alkyl, with alkyl being linear or branched, saturated or unsubstituted, substituted or unsubstituted; and/or R⁹ represents halogen; OH or O—C₁₋₄-alkyl, with alkyl being linear or branched, saturated and unsubstituted; and/or at least one of R⁴ and R⁵ represents halogen; OH; O—C₁₋₄-alkyl, with alkyl being linear or branched, saturated and unsubstituted; while the other represents hydrogen; OH; halogen; O—C₁₋₄-alkyl, with alkyl being linear or branched, saturated and unsubstituted; and/or R⁶ represents hydrogen or C(O)—NR¹ R⁴.

R⁸ and R⁹ independently of one another represent hydrogen; C₁₋₄-alkyl, with alkyl being linear or branched, saturated and unsubstituted.

5. Compound according to claim 1, characterized in that halogen is Cl or F.

6. Compound according to claim 1 according to formula II

\[
\text{R}^{11} \quad \text{R}^{12} \quad \text{R}^{13} \quad \text{R}^{14} \quad \text{R}^{15} \quad \text{R}^{16}
\]

wherein R¹ and R¹² independently of one another represent hydrogen; C₁₋₄-alkyl, with alkyl being linear or branched, saturated or unsubstituted, substituted or unsubstituted; or an appropriate protective group; or R¹ and R¹² together with the Nitrogen they both bind to form a heterocyclic ring or an appropriate protective group;
R^{12}, R^{14} and R^{15} independently of one another represent hydrogen; C_{1-a}-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; or an appropriate protective group; R^{16} represents hydrogen or C(O)—NR^{17}R^{18}; R^{17} and R^{18} independently of one another represent hydrogen; C_{1-a}-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; or an appropriate protective group; or R^{17} and R^{18} together with the Nitrogen they both bind to form a heterocyclic ring or an appropriate protective group; optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding N-oxide thereof, or a corresponding salt thereof, or a corresponding solvate thereof.

7. Compound according to claim 6, characterized in that R^{11} and R^{12} independently of one another represent hydrogen; C_{1-a}-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted by F, Cl, Br, I, NH_{2}, SH or OH; or an appropriate protective group selected from tert-butylcarbonyl (Boc), benzyloxy carbonyl (Cbz), trifluoroacetyl (TFA) or 9-fluorenylmethoxycarbonyl (Fmoc); or R^{11} and R^{12} together with the Nitrogen they both bind to form a heterocyclic ring of the following formula:

```
+H_2C         (CH_2)_m
|      |     |
|      |     |
```

with m being 1, 2, 3 or 4, n being 1, 2, 3 or 4 and (n+m) being ≤6 and X being selected from S, O, NR, CH or with R^{19} being selected from hydrogen or C_{1-a}-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted by F, Cl, Br, I, NH_{2}, SH or OH; or an appropriate protective group, selected from phthaloyl (phtalimide), N-1,1,4,4-Tetramethyldisilazyclopecentane adduct (STABASE), 1,1,3,3-Tetramethyl-1,3-disilaisioindoline (Benza-STABASE, BSF), N-2,5-bis(trisopropylsilyl)pyrrol (BIPSO)

R^{13}, R^{14} and R^{15} independently of one another represent hydrogen or C_{1-a}-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted by F, Cl, Br, I, NH_{2}, SH or OH; or an appropriate protective group selected from tert-butyl, acetyl or benzyol.

R^{16} represents hydrogen or C(O)—NR^{17}R^{18}; R^{17} and R^{18} independently of one another represent hydrogen; C_{1-a}-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted or substituted by F, Cl, Br, I, NH_{2}, SH or OH; or an appropriate protective group selected from tert-butoxycarbonyl (Boc), benzyloxy carbonyl (Cbz), trifluoroacetyl (TFA) or 9-fluorenylmethoxycarbonyl (Fmoc); or R^{17} and R^{18} together with the Nitrogen they both bind to form a heterocyclic ring of the following formula:

```
+H_2C         (CH_2)_p
|      |     |
|      |     |
```

with p being 1, 2, 3 or 4, p being 1, 2, 3 or 4 and (o+p) being ≤6 and Y being selected from S, O, NR, or CHR with R^{20} being selected from hydrogen or C_{1-a}-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted by F, Cl, Br, I, NH_{2}, SH or OH; or an appropriate protective group, selected from phthaloyl (phtalimide), N-1,1,4,4-Tetramethyldisilazyclopecentane adduct (STABASE), 1,1,3,3-Tetramethyl-1,3-disilaisioindoline (Benza-STABASE, BSF), N-2,5-bis(trisopropylsilyl)pyrrol (BIPSO).

8. Compound according to claim 6, characterized in that R^{11} and R^{12} independently of one another represent hydrogen; C_{1-a}-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; R^{13}, R^{14} and R^{15} independently of one another represent hydrogen; C_{1-a}-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; or R^{16} represents hydrogen or C(O)—NR^{17}R^{18}; R^{17} and R^{18} independently of one another represent hydrogen; C_{1-a}-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; and/or R^{13}, R^{14} and R^{15} independently of one another represent hydrogen; C_{1-a}-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; and/or R^{16} represents hydrogen or C(O)—NR^{17}R^{18}; with R^{17} and R^{18} independently of one another represent hydrogen; C_{1-a}-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted.

9. Compound according to claim 6, characterized in that R^{11} and R^{12} independently of one another represent hydrogen; C_{1-a}-alkyl, with alkyl being linear or branched, saturated or unsaturated; and/or R^{13}, R^{14} and R^{15} independently of one another represent hydrogen; C_{1-a}-alkyl, with alkyl being linear or branched, saturated or unsaturated; and/or R^{16} represents hydrogen or C(O)—NR^{17}R^{18}; with R^{17} and R^{18} independently of one another represent hydrogen; C_{1-a}-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted.

10. Compound according to claim 6, characterized in that R^{13}, R^{14} and R^{15} independently of one another represent hydrogen or methyl, preferably that R^{13}, R^{14} and R^{15} all represent hydrogen, or R^{13}, R^{14} and R^{15} all represent methyl.

11. Compound according to claim 6, selected from 2-amino-6,7,8-trimethoxyquinazolin-4(3H)-one, 6,7,8-Trimethoxy-2-morpholinquinazolin-4(3H)-one, 2-(4-methylpiperazin)-6,7,8-trimethoxyquinazolin-4(3H)-one tert-Butyl 6,7,8- trimethoxy-4-oxo-3,4-dihydroquinazolin-2-ylcarboxate 2-(diisopropylamino)-6,7,8-trimethoxyquinazolin-4(3H)-one, 2-(dimethylamino)-6,7,8-trimethoxyquinazolin-4(3H)-one, 2-(di-tert-butylamino)-6,7,8-trimethoxyquinazolin-4(3H)-one, 2-(diethylamino)-6,7,8-trimethoxyquinazolin-4(3H)-one,
2-amino-6,7,8-trimethoxy-4-oxo-3,4-dihydroquinazoline-5-carboxamide,
2-(diisopropylamino)-6,7,8-trimethoxy-4-oxo-3,4-dihydroquinazoline-5-carboxamide,
2-(dimethylamino)-6,7,8-trimethoxy-4-oxo-3,4-dihydroquinazoline-5-carboxamide,
2-(di-tert-butylamino)-6,7,8-trimethoxy-4-oxo-3,4-dihydroquinazoline-5-carboxamide,
2-(diethylamino)-6,7,8-trimethoxy-4-oxo-3,4-dihydroquinazoline-5-carboxamide,
2-amino-6,7,8-trihydroxyquinazolin-4(3H)-one,
6,7,8-trihydroxy-2-morpholinoquinazolin-4(3H)-one
6,7,8-trihydroxy-2-(4-methylpiprazin-1-yl)quinazolin-4(3H)-one
2-tert-Butyl,6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazolin-2-yl-carbonate
2-(diisopropylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one,
2-(dimethylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one,
2-(di-tert-butylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one,
2-(diethylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one,
2-amino-6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazoline-5-carboxamide,
2-(diisopropylamino)-6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazoline-5-carboxamide,
2-(dimethylamino)-6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazoline-5-carboxamide,
2-(di-tert-butylamino)-6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazoline-5-carboxamide,
2-(diethylamino)-6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazoline-5-carboxamide

or R\textsuperscript{21} and R\textsuperscript{22} together with the Nitrogen they both bind to form a heterocyclic ring or an appropriate protective group;
R\textsuperscript{26} represents hydrogen or C(O)—NR\textsuperscript{27}R\textsuperscript{28};
R\textsuperscript{27} and R\textsuperscript{28} independently of one another represent hydrogen; C\textsubscript{1-4}-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; or an appropriate protective group;
or R\textsuperscript{27} and R\textsuperscript{28} together with the Nitrogen they both bind to form a heterocyclic ring or an appropriate protective group;
optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding N-oxide thereof, or a corresponding salt thereof, or a corresponding solvate thereof.

14. Compound according to claim 13, characterized in that R\textsuperscript{16} represents hydrogen; C\textsubscript{1-4}-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted by F, Cl, Br, I, NH\textsubscript{2}, SH or OH; or an appropriate protective group selected from tert-butoxycarbonyl (Boc), benzylloxycarbonyl (Cbz), trithiocacetyl (TFA) or 9-fluorenylmethyloxycarbonyl (Fmoc);
or R\textsuperscript{21} and R\textsuperscript{22} together with the Nitrogen they both bind to form a heterocyclic ring of the following formula:

\[
\begin{align*}
\text{(H}_2\text{C})_n & \text{N} \quad \text{(CH}_3)_m \\
\text{O} & \quad \text{O}
\end{align*}
\]

with n being 1, 2, 3 or 4, m being 1, 2, 3 or 4 and (n + m) being \( \leq 6 \) and X being selected from S, O, NR\textsuperscript{27} or CHR\textsuperscript{27} with R\textsuperscript{29} being selected from hydrogen or C\textsubscript{1-4}-alkyl, with alkyl being linear or branched, saturated or unsaturated, unsubstituted or substituted by F, Cl, Br, I, NH\textsubscript{2}, SH or OH;
or an appropriate protective group, selected from phthaloyl (phthalimide), N\textsubscript{1,1,4,4}-Tetramethyldisilazacyclohexacyclooctane adduct (STABASE), 1,1,3,3-Tetramethyl-1,3-disilazacyclooctane (Benzo-STABASE, BSB), N\textsubscript{2,5}-bis(trisopropylsilox)pyrrol (BIPSOP);
R\textsuperscript{26} represents hydrogen or C(O)—NR\textsuperscript{27}R\textsuperscript{28};
R\textsuperscript{27} and R\textsuperscript{28} independently of one another represent hydrogen; C\textsubscript{1-4}-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted by F, Cl, Br, I, NH\textsubscript{2}, SH or OH; or an appropriate protective group selected from tert-butoxycarbonyl (Boc), benzylloxycarbonyl (Cbz), trithiocacetyl (TFA) or 9-fluorenylmethyloxycarbonyl (Fmoc);
or R\textsuperscript{27} and R\textsuperscript{28} together with the Nitrogen they both bind to form a heterocyclic ring of the following formula:

![Chemical Structure](image)

with o being 1, 2, 3 or 4, p being 1, 2, 3 or 4 and (o + p) being \( \geq 6 \) and Y being selected from S, O, NR\textsuperscript{30} or CHR\textsuperscript{17} with R\textsuperscript{30} being selected from hydrogen or C\textsubscript{1}-alkyl, with alkyl being linear or branched, saturated or unsaturated, unsubstituted or substituted by F, Cl, Br, I, NH\textsubscript{2}, SH or OH; or an appropriate protective group, selected from phthaloyl (phthalimide), N-1,1,4,4-Tetramethylidisilazacyclopentane adduct (STABASE), 1,1,3,3-Tetramethyl-1,3-disilaisoindoline (Benzo-STABASE, BSB), N-2,5-bis (trisopropylsilox)pyrrol (BIPOSEP).

15. Compound according to claim 13, characterized in that R\textsuperscript{21} and R\textsuperscript{22} independently of one another represent hydrogen; C\textsubscript{1}-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; R\textsuperscript{26} represents hydrogen or C(O)—NR\textsuperscript{30}R\textsuperscript{28}; R\textsuperscript{27} and R\textsuperscript{28} independently of one another represent hydrogen; C\textsubscript{1}-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted.

16. Compound according to claim 13, characterized in that R\textsuperscript{21} and R\textsuperscript{22} independently of one another represent hydrogen; C\textsubscript{1}-alkyl, with alkyl being linear or branched, saturated and unsubstituted; and/or R\textsuperscript{26} represents hydrogen or C(O)—NR\textsuperscript{30}R\textsuperscript{28}; R\textsuperscript{27} and R\textsuperscript{28} independently of one another represent hydrogen; C\textsubscript{1}-alkyl, with alkyl being linear or branched, saturated and unsubstituted.

17. (canceled)

18. Compound according to claim 13, characterized in that R\textsuperscript{2} represents hydrogen.

19. Compound according to claim 18 selected from 2-amino-6,7,8-trimethoxyquinazolin-4(3H)-one, 6,7,8-trimethoxy-2-morpholinooxazin-4(3H)-one, 2-(4-methylpiperazin)-6,7,8-trimethoxyquinazolin-4(3H)-one, tert-Butyl 6,7,8-trimethoxy-4-oxo-3,4-dihydroquinazolin-2-ylcarbomate, 2-(diisopropylamino)-6,7,8-trimethoxyquinazolin-4(3H)-one, 2-(dimethylamino)-6,7,8-trimethoxyquinazolin-4(3H)-one, 2-(di-tert-butylamino)-6,7,8-trimethoxyquinazolin-4(3H)-one or 2-(dichlorylamino)-6,7,8-trimethoxyquinazolin-4(3H)-one, optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding N-oxide thereof, or a corresponding salt thereof, or a corresponding solvate thereof.

20. Compound according to claim 1 according to formula IIIa

wherein R\textsuperscript{21} and R\textsuperscript{22} independently of one another represent hydrogen; C\textsubscript{1}-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; or an appropriate protective group; R\textsuperscript{26} represents hydrogen or C(O)—NR\textsuperscript{30}R\textsuperscript{28}; R\textsuperscript{27} and R\textsuperscript{28} independently of one another represent hydrogen; C\textsubscript{1}-alkyl, with alkyl being linear or branched, saturated or unsaturated, substituted or unsubstituted; or an appropriate protective group; optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding N-oxide thereof, or a corresponding salt thereof, or a corresponding solvate thereof.

21. Compound according to claim 20, characterized in that R\textsuperscript{21} and R\textsuperscript{22} independently of one another represent hydrogen; C\textsubscript{1}-alkyl, with alkyl being linear or branched, saturated or unsaturated, unsubstituted or substituted by F, Cl, Br, I, NH\textsubscript{2}, SH or OH; or an appropriate protective group selected from tert-butoxycarbonyl (Boc), benzoylcarbonyl (Cbz), trifluoroacetyl (TFA) or 9-fluorenylmethoxycarbonyl (Fmoc).

22. Compound according to claim 20, characterized in that R\textsuperscript{21} and R\textsuperscript{22} independently of one another represent hydrogen; C\textsubscript{1}-alkyl, with alkyl being linear or branched, saturated or unsaturated, unsubstituted or substituted by F, Cl, Br, I, NH\textsubscript{2}, SH or OH; or an appropriate protective group selected from tert-butoxycarbonyl (Boc), benzoylcarbonyl (Cbz), trifluoroacetyl (TFA) or 9-fluorenylmethoxycarbonyl (Fmoc).

23. Compound according to claim 20, characterized in that R\textsuperscript{21} and R\textsuperscript{22} independently of one another represent hydrogen; C\textsubscript{1}-alkyl, with alkyl being linear or branched, saturated and unsubstituted; and/or R\textsuperscript{26} represents hydrogen or C(O)—NR\textsuperscript{30}R\textsuperscript{28}; R\textsuperscript{27} and R\textsuperscript{28} independently of one another represent hydrogen; C\textsubscript{1}-alkyl, with alkyl being linear or branched, saturated and unsubstituted.
24. Compound according to claim 20, selected from
2-amino-6,7,8-trihydroxyquinazolin-4(3H)-one
6,7,8-trihydroxy-2-morpholinoquinazolin-4(3H)-one
6,7,8-trihydroxy-2-(4-methylpiperazin-1-yl)quinazolin-4 (3H)-one
tert-Butyl6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazolin-2-yl carbonate
2-(diisopropylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one
2-(dimethylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one
2-(di-tert-butylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one
2-(diethylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one
2-amino-6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazoline-5-carboxamide
2-(diisopropylamino)-6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazoline-5-carboxamide
2-(dimethylamino)-6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazoline-5-carboxamide
2-(di-tert-butylamino)-6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazoline-5-carboxamide
2-(diethylamino)-6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazoline-5-carboxamide
optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding N-oxide thereof, or a corresponding salt thereof, or a corresponding solvate thereof.

25. Compound according to claim 20, characterized in that R^2 represents hydrogen.

26. Compound according to claim 25, selected from
2-amino-6,7,8-trihydroxyquinazolin-4(3H)-one
6,7,8-trihydroxy-2-morpholinoquinazolin-4(3H)-one
6,7,8-trihydroxy-2-(4-methylpiperazin-1-yl)quinazolin-4 (3H)-one
tert-Butyl6,7,8-trihydroxy-4-oxo-3,4-dihydroquinazolin-2-yl carbonate
2-(diisopropylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one
2-(dimethylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one
2-(di-tert-butylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one
2-(diethylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one
2-(dimethylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one
2-(di-tert-butylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one or
2-(diethylamino)-6,7,8-trihydroxyquinazolin-4(3H)-one;
optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding N-oxide thereof, or a corresponding salt thereof, or a corresponding solvate thereof.

27. Process for the production of a compound according to claim 1 comprising reacting a compound of formula VIIIa

![VIIIa](image)

with a secondary amine HNR^1R^2 in a suitable solvent or reaction medium and R^1, R^2, R^3, R^4, R^5 and R^6 having the meaning according to any of claims 1 to 4.

28-56. (canceled)

57. Medicament comprising at least one compound according to claim 1 and one or more pharmaceutically acceptable excipients.

58. Use of a compound according to claim 1 for the preparation of a medicament for the treatment of CNS disorders.

59. Use of a compound according to claim 1 for the preparation of a medicament for the treatment of pain, stroke, addiction or epilepsy.

* * * * *