



INDENO-, NAPHTHO-, AND BENZOCYCLOHEPTADIHYDROTHIAZOLE
DERIVATIVES, THEIR PREPARATION AND THEIR USE AS ANORECTIC
PHARMACEUTICALS

Description

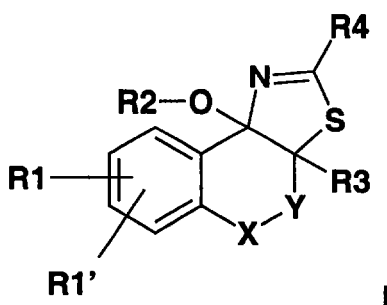
Polycyclic dihydrothiazoles having substituted alkyl radicals in the two-
position, process for their preparation, and their use as pharmaceuticals

The invention relates to polycyclic dihydrothiazoles and their physiologically
acceptable salts and physiologically functional derivatives.

Thiazolidine derivatives having anorectic action have already been
described in the prior art (Austrian Patent No. 365181).

The invention is based on the object of making available further
compounds which display a therapeutically utilizable anorectic action.

The invention therefore relates to compounds of the formula I



in which

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Y is a direct bond, -CH₂-, -CH₂-CH₂-;

X is CH₂, CH(CH₃), CH(C₂H₅), CH(C₃H₇), CH(C₆H₅);

30 R₁, R₁' independently of one another are H, F, Cl, Br, I, CF₃, NO₂,
CN, COOH, COO(C₁-C₆)alkyl, CONH₂, CONH(C₁-C₆)alkyl,
CON[(C₁-C₆)alkyl]₂, (C₁-C₆)-alkyl, (C₂-C₆)-alkenyl, (C₂-C₆)-
alkynyl, O-(C₁-C₆)-alkyl, it being possible in the alkyl radicals



- for one or more, or all hydrogens to be replaced by fluorine, or a hydrogen to be replaced by OH, OC(O)CH₃, OC(O)H, O-CH₂-Ph, NH₂, NH-CO-CH₃ or N(COOCH₂Ph)₂;
- 5 SO₂-NH₂, SO₂NH(C₁-C₆)-alkyl, SO₂N[(C₁-C₆)-alkyl]₂, S-(C₁-C₆)-alkyl, S-(CH₂)_n-phenyl, SO-(C₁-C₆)-alkyl, SO-(CH₂)_n-phenyl, SO₂-(C₁-C₆)-alkyl, SO₂-(CH₂)_n-phenyl, where n can be 0 – 6 and the phenyl radical can be substituted up to two times by F, Cl, Br, OH, CF₃, NO₂, CN, OCF₃, O-(C₁-C₆)-alkyl, (C₁-C₆)-alkyl, NH₂; NH₂, NH-(C₁-C₆)-alkyl, N((C₁-C₆)-alkyl)₂, NH(C₁-C₇)-acyl, phenyl, biphenyl, O-(CH₂)_n-phenyl, where n can be 0 – 6, 1- or 2-naphthyl, 2-, 3- or 4-pyridyl, 2- or 3-furanyl or 2- or 3-thienyl, where the phenyl, biphenyl, naphthyl, pyridyl, furanyl or thienyl rings can each be substituted one to 3 times by F, Cl, Br, I, OH, CF₃, NO₂, CN, OCF₃, O-(C₁-C₆)-alkyl, (C₁-C₆)-alkyl, NH₂, NH(C₁-C₆)-alkyl, N((C₁-C₆)-alkyl)₂, SO₂-CH₃, COOH, COO-(C₁-C₆)-alkyl, CONH₂;
- 10 1,2,3-triazol-5-yl, where the triazole ring can be substituted in the 1-, 2- or 3-position by methyl or benzyl;
- 15 tetrazol-5-yl, where the tetrazole ring can be substituted in the 1- or 2-position by methyl or benzyl;
- 20
- R2 is H, (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl, (CH₂)_n-phenyl, (CH₂)_n-thienyl, (CH₂)_n-pyridyl, (CH₂)_n-furyl, C(O)-(C₁-C₆)-alkyl, C(O)-(C₃-C₆)-cycloalkyl, C(O)-(CH₂)_n-phenyl, C(O)-(CH₂)_n-thienyl, C(O)-(CH₂)_n-pyridyl, C(O)-(CH₂)_n-furyl, where n can be 0 - 5 and in which phenyl, thienyl, pyridyl, furyl can each be substituted up to two times by Cl, F, CN, CF₃, (C₁-C₃)-alkyl, OH, O-(C₁-C₆)-alkyl;
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- 30 R3 is H, (C₁-C₆)-alkyl, F, CN, N₃, O-(C₁-C₆)-alkyl, (CH₂)_n-phenyl, (CH₂)_n-thienyl, (CH₂)_n-pyridyl, (CH₂)_n-furyl, where n can be 0 - 5 and in which phenyl, thienyl, pyridyl, furyl can each be substituted up to two times by Cl, F, CN, CF₃, (C₁-C₃)-alkyl, OH or O-(C₁-C₆)-alkyl, (C₂-C₆)-alkynyl, (C₂-C₆)-alkenyl, C(O)OCH₃, C(O)OCH₂CH₃, C(O)OH, C(O)NH₂, C(O)NHCH₃, C(O)N(CH₃)₂, OC(O)CH₃;
- 35

- R4 is (C₈-C₁₆)-cycloalkyl, it being possible in the alkyl radicals for one or more hydrogens to be replaced by fluorine or a hydrogen to be replaced by OH, OC(O)CH₃, OC(O)H, O-CH₂-Ph or O-(C₁-C₄)-alkyl;
 5 (CH₂)_n-A-R8, where n can be 1-6, except for the group -CH₂-O-CH₂-phenyl in which phenyl is unsubstituted;
 (CH₂)_r-B-R9, where r can be 1-6;
 10
 A is O, S, SO, SO₂;
 B is NH, N-(C₁-C₆)-alkyl, NCHO, N(CO-CH₃);
 15 R8 is (C₅-C₂₄)-alkyl, (C₃-C₁₀)-cycloalkyl, it being possible in the alkyl radicals for one or more hydrogens to be replaced by fluorine or a hydrogen to be replaced by OH, OC(O)CH₃, OC(O)H, O-CH₂-Ph or O-(C₁-C₄)-alkyl;
 20 (CH₂)_m-aryl, where m can be 0-6 and aryl can be phenyl, naphthyl, biphenyl, thienyl or pyridyl;
 and the aryl moiety can be substituted up to two times by F, Cl, Br, OH, CF₃, NO₂, CN, OCF₃, O-(C₁-C₆)-alkyl, S-(C₁-C₆)-alkyl, SO-(C₁-C₆)-alkyl, SO₂-(C₁-C₆)-alkyl, SO₂-NH₂, SO₂-NH(C₁-C₈-alkyl), SO₂-N(C₁-C₈-alkyl)₂, SO₂-NH(C₃-C₈-cycloalkyl), SO₂-N(C₃-C₈-cycloalkyl)₂, (CH₂)_m-SO₂-NH₂, (CH₂)_m-SO₂-NH-(C₁-C₆)-alkyl, (CH₂)_m-SO₂-N((C₁-C₆)-alkyl)₂, where m can be 1-6, SO₂-N(=CH-N(CH₃)₂), (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl, COOH, COO(C₁-C₆)-alkyl, COO(C₃-C₆)-cycloalkyl, CONH₂, CONH(C₁-C₆)-alkyl, CON[(C₁-C₆)-alkyl]₂, CONH(C₃-C₆)-cycloalkyl, NH₂, NH(C₁-C₆)-alkyl, N(C₁-C₆)-alkyl)₂, NH-CO-(C₁-C₆)-alkyl, NH-CO-phenyl, NH-SO₂-(C₁-C₈-alkyl), N(C₁-C₆-alkyl)-SO₂-(C₁-C₈-alkyl), NH-SO₂-phenyl, where the phenyl ring can be substituted up to two times by F, Cl, CN, OH, (C₁-C₆)-alkyl, O-(C₁-C₆)-alkyl, CF₃, COOH, COO(C₁-C₆)-alkyl or CONH₂, pyrrolidin-1-yl, morpholin-1-yl, piperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-
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- 1-yl, (CH₂)_p-phenyl, O-(CH₂)_p-phenyl, S-(CH₂)_p-phenyl or SO₂-(CH₂)_p-phenyl, where p can be 0-3;
- R9 (CH₂)_m-aryl, where m can be 0-6 and aryl can be phenyl, naphthyl, biphenyl, thienyl or pyridyl;
- 5 and the aryl moiety can be substituted up to two times by F, Cl, Br, OH, CF₃, NO₂, CN, OCF₃, O-(C₁-C₆)-alkyl, S-(C₁-C₆)-alkyl, SO-(C₁-C₆)-alkyl, SO₂-(C₁-C₆)-alkyl, SO₂-NH₂, SO₂-NH(C₁-C₈-alkyl), SO₂-N(C₁-C₈-alkyl)₂, SO₂-NH(C₃-C₈-cycloalkyl), SO₂-N(C₃-C₈-cycloalkyl)₂, (CH₂)_m-SO₂-NH₂, (CH₂)_m-SO₂-NH-(C₁-C₆)-alkyl, (CH₂)_m-SO₂-N((C₁-C₆)-alkyl)₂, where m can be 1-6, SO₂-N(=CH-N(CH₃)₂), (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl, COOH, COO(C₁-C₆)-alkyl, COO(C₃-C₆)-cycloalkyl, CONH₂, CONH(C₁-C₆)-alkyl, CON[(C₁-C₆)-alkyl]₂, CONH(C₃-C₆)-cycloalkyl, NH₂, NH(C₁-C₆)-alkyl, N(C₁-C₆)-alkyl)₂, NH-CO-(C₁-C₆)-alkyl, NH-CO-phenyl, NH-SO₂-(C₁-C₈-alkyl), N(C₁-C₆-alkyl)-SO₂-(C₁-C₈-alkyl), NH-SO₂-phenyl, where the phenyl ring can be substituted up to two times by F, Cl, CN, OH, (C₁-C₆)-alkyl, O-(C₁-C₆)-alkyl, CF₃, COOH, COO(C₁-C₆)-alkyl or CONH₂, pyrrolidin-1-yl, morpholin-1-yl, piperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-1-yl, (CH₂)_p-phenyl, O-(CH₂)_p-phenyl, S-(CH₂)_p-phenyl or SO₂-(CH₂)_p-phenyl, where p can be 0-3;

and their physiologically acceptable salts.

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Preference is given to compounds of the formula I in which

- Y is a direct bond;
- 30 X is CH₂;
- R1, R1' independently of one another are H, F, Cl, Br, I, CF₃, NO₂, CN, COOH, COO(C₁-C₆)-alkyl, CONH₂, CONH(C₁-C₆)-alkyl, CON[(C₁-C₆)-alkyl]₂, (C₁-C₆)-alkyl, (C₂-C₆)-alkenyl, (C₂-C₆)-alkynyl, O-(C₁-C₆)-alkyl, it being possible in the alkyl radicals for one or more, or all hydrogens to be replaced by fluorine, or
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- a hydrogen to be replaced by OH, OC(O)CH₃, OC(O)H, O-CH₂-Ph, NH₂, NH-CO-CH₃ or N(COOCH₂Ph)₂;
 SO₂-NH₂, SO₂NH(C₁-C₆)-alkyl, SO₂N[(C₁-C₆)-alkyl]₂,
 S-(C₁-C₆)-alkyl, S-(CH₂)_n-phenyl, SO-(C₁-C₆)-alkyl,
 SO-(CH₂)_n-phenyl, SO₂-(C₁-C₆)-alkyl, SO₂-(CH₂)_n-phenyl,
 where n can be 0–6 and the phenyl radical can be substituted
 up to two times by F, Cl, Br, OH, CF₃, NO₂, CN, OCF₃, O-(C₁-
 C₆)-alkyl, (C₁-C₆)-alkyl, NH₂; NH₂, NH-(C₁-C₆)-alkyl, N((C₁-
 C₆)-alkyl)₂, NH(C₁-C₇)-acyl, phenyl, biphenyl, O-(CH₂)_n-
 phenyl, where n can be 0–6, 1- or 2-naphthyl, 2-, 3- or 4-
 pyridyl, 2- or 3-furanyl or 2- or 3-thienyl, where the phenyl,
 biphenyl, naphthyl, pyridyl, furanyl or thienyl rings can each be
 substituted one to 3 times by F, Cl, Br, I, OH, CF₃, NO₂, CN,
 OCF₃, O-(C₁-C₆)-alkyl, (C₁-C₆)-alkyl, NH₂, NH(C₁-C₆)-alkyl,
 N((C₁-C₆)-alkyl)₂, SO₂-CH₃, COOH, COO-(C₁-C₆)-alkyl,
 CONH₂;
 1,2,3-triazol-5-yl, where the triazole ring can be substituted in
 the 1-, 2- or 3-position by methyl or benzyl;
 tetrazol-5-yl, where the tetrazole ring can be substituted in the
 1- or 2-position by methyl or benzyl;
- R2 is H, (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl, (CH₂)_n-phenyl, (CH₂)_n-
 thienyl, (CH₂)_n-pyridyl, (CH₂)_n-furyl, C(O)-(C₁-C₆)-alkyl, C(O)-
 (C₃-C₆)-cycloalkyl, C(O)-(CH₂)_n-phenyl, C(O)-(CH₂)_n-thienyl,
 C(O)-(CH₂)_n-pyridyl, C(O)-(CH₂)_n-furyl, where n can be 0-5
 and in which phenyl, thienyl, pyridyl, furyl can each be
 substituted up to two times by Cl, F, CN, CF₃, (C₁-C₃)-alkyl,
 OH, O-(C₁-C₆)-alkyl;
- R3 is H, (C₁-C₆)-alkyl, F, CN, N₃, O-(C₁-C₆)-alkyl, (CH₂)_n-phenyl,
 (CH₂)_n-thienyl, (CH₂)_n-pyridyl, (CH₂)_n-furyl, where n can be
 0-5 and in which phenyl, thienyl, pyridyl, furyl can each be
 substituted up to two times by Cl, F, CN, CF₃, (C₁-C₃)-alkyl,
 OH, O-(C₁-C₆)-alkyl;
 (C₂-C₆)-alkynyl, (C₂-C₆)-alkenyl, C(O)OCH₃, C(O)OCH₂CH₃,
 C(O)OH, C(O)NH₂, C(O)NHCH₃, C(O)N(CH₃)₂, OC(O)CH₃;

- R4 is (C₈-C₁₆)-cycloalkyl, it being possible in the alkyl radicals for one or more hydrogens to be replaced by fluorine or a hydrogen to be replaced by OH, OC(O)CH₃, OC(O)H, O-CH₂-Ph or O-(C₁-C₄)-alkyl;
- 5 (CH₂)_n-A-R8, where n can be 1-6, except for the group -CH₂-O-CH₂-phenyl in which phenyl is unsubstituted; (CH₂)_r-B-R9, where r can be 1-6;
- 10 A is O, S, SO, SO₂;
- B is NH, N-(C₁-C₆)-alkyl, NCHO, N(CO-CH₃);
- R8 is (C₅-C₂₄)-alkyl, (C₃-C₁₀)-cycloalkyl, it being possible in the
 15 alkyl radicals for one or more hydrogens to be replaced by fluorine or a hydrogen to be replaced by OH, OC(O)CH₃, OC(O)H, O-CH₂-Ph or O-(C₁-C₄)-alkyl; (CH₂)_m-aryl, where m can be 0-6 and aryl can be phenyl, naphthyl, biphenyl, thienyl or pyridyl
 20 and the aryl moiety can be substituted up to two times by F, Cl, Br, OH, CF₃, NO₂, CN, OCF₃, O-(C₁-C₆)-alkyl, S-(C₁-C₆)-alkyl, SO-(C₁-C₆)-alkyl, SO₂-(C₁-C₆)-alkyl, SO₂-NH₂, SO₂-NH(C₁-C₈-alkyl), SO₂-N(C₁-C₈-alkyl)₂, SO₂-NH(C₃-C₈-cycloalkyl), SO₂-N(C₃-C₈-cycloalkyl)₂, (CH₂)_m-SO₂-NH₂,
 25 (CH₂)_m-SO₂-NH-(C₁-C₆)-alkyl, (CH₂)_m-SO₂-N((C₁-C₆)-alkyl)₂, where m can be 1-6, SO₂-N(=CH-N(CH₃)₂), (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl, COOH, COO(C₁-C₆)-alkyl, COO(C₃-C₆)-cycloalkyl, CONH₂, CONH(C₁-C₆)-alkyl, CON[(C₁-C₆)-alkyl]₂, CONH(C₃-C₆)-cycloalkyl, NH₂, NH(C₁-C₆)-alkyl,
 30 N(C₁-C₆)-alkyl)₂, NH-CO-(C₁-C₆)-alkyl, NH-CO-phenyl, NH-SO₂-(C₁-C₈-alkyl), N(C₁-C₆-alkyl)-SO₂-(C₁-C₈-alkyl), NH-SO₂-phenyl, where the phenyl ring can be substituted up to two times by F, Cl, CN, OH, (C₁-C₆)-alkyl, O-(C₁-C₆)-alkyl, CF₃, COOH, COO(C₁-C₆)-alkyl or CONH₂;
- 35 pyrrolidin-1-yl, morpholin-1-yl, piperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-1-yl, (CH₂)_p-phenyl, O-(CH₂)_p-phenyl, S-(CH₂)_p-phenyl or SO₂-(CH₂)_p-phenyl, where p can be 0-3;

- R9 is $(\text{CH}_2)_m$ -aryl, where m can be 0-6 and aryl can be phenyl, naphthyl, biphenyl, thienyl or pyridyl
 and the aryl moiety can be substituted up to two times by F, Cl,
 5 Br, OH, CF_3 , NO_2 , CN, OCF_3 , O-(C₁-C₆)-alkyl, S-(C₁-C₆)-alkyl, SO-(C₁-C₆)-alkyl, SO_2 -(C₁-C₆)-alkyl, SO_2 -NH₂, SO_2 -NH(C₁-C₈-alkyl), SO_2 -N(C₁-C₈-alkyl)₂, SO_2 -NH(C₃-C₈-cycloalkyl), SO_2 -N(C₃-C₈-cycloalkyl)₂, $(\text{CH}_2)_m$ - SO_2 -NH₂, $(\text{CH}_2)_m$ - SO_2 -NH-(C₁-C₆)-alkyl, $(\text{CH}_2)_m$ - SO_2 -N((C₁-C₆)-alkyl)₂,
 10 where m can be 1-6, SO_2 -N(=CH-N(CH₃)₂), (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl, COOH, COO(C₁-C₆)-alkyl, COO(C₃-C₆)-cycloalkyl, CONH₂, CONH(C₁-C₆)-alkyl, CON[(C₁-C₆)-alkyl]₂, CONH(C₃-C₆)-cycloalkyl, NH₂, NH(C₁-C₆)-alkyl, N(C₁-C₆)-alkyl)₂, NH-CO-(C₁-C₆)-alkyl, NH-CO-phenyl, NH- SO_2 -(C₁-C₈)-alkyl, N(C₁-C₆)-alkyl)- SO_2 -(C₁-C₈)-alkyl, NH- SO_2 -phenyl, where the phenyl ring can be substituted up to two times by F, Cl, CN, OH, (C₁-C₆)-alkyl, O-(C₁-C₆)-alkyl, CF_3 , COOH, COO(C₁-C₆)-alkyl or CONH₂;
 15 pyrrolidin-1-yl, morpholin-1-yl, piperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-1-yl, $(\text{CH}_2)_p$ -phenyl, O- $(\text{CH}_2)_p$ -phenyl, S- $(\text{CH}_2)_p$ -phenyl or SO_2 -(CH_2)_p-phenyl, where p can be 0-3;
 20

and their physiologically acceptable salts.

- 25 Particular preference is given to compounds of the formula I in which

Y is a direct bond;

X is CH_2 ;

30

- R1, R1' independently of one another are H, F, Cl, Br, I, CF_3 , NO_2 , CN, COOH, COO(C₁-C₆)-alkyl, CONH₂, CONH(C₁-C₆)-alkyl, CON[(C₁-C₆)-alkyl]₂, (C₁-C₆)-alkyl, (C₂-C₆)-alkenyl, (C₂-C₆)-alkynyl, O-(C₁-C₆)-alkyl, it being possible in the alkyl radicals
 35 for one or more, or all hydrogens to be replaced by fluorine, or a hydrogen to be replaced by OH, OC(O)CH₃, OC(O)H, O-CH₂-Ph, NH₂, NH-CO-CH₃ or N(COOCH₂Ph)₂;

- 5 SO₂-NH₂, SO₂NH(C₁-C₆)-alkyl, SO₂N[(C₁-C₆)-alkyl]₂,
S-(C₁-C₆)-alkyl, S-(CH₂)_n-phenyl, SO-(C₁-C₆)-alkyl,
SO-(CH₂)_n-phenyl, SO₂-(C₁-C₆)-alkyl, SO₂-(CH₂)_n-phenyl,
where n can be 0–6 and the phenyl radical can be substituted
up to two times by F, Cl, Br, OH, CF₃, NO₂, CN, OCF₃, O-(C₁-
C₆)-alkyl, (C₁-C₆)-alkyl, NH₂;
- 10 NH₂, NH-(C₁-C₆)-alkyl, N((C₁-C₆)-alkyl)₂, NH(C₁-C₇)-acyl,
phenyl, biphenyl, O-(CH₂)_n-phenyl, where n can be 0–6, 1- or
2-naphthyl, 2-, 3- or 4-pyridyl, 2- or 3-furanyl or 2- or 3-thienyl,
where the phenyl, biphenyl, naphthyl, pyridyl, furanyl or thienyl
rings can each be substituted one to 3 times by F, Cl, Br, I,
OH, CF₃, NO₂, CN, OCF₃, O-(C₁-C₆)-alkyl, (C₁-C₆)-alkyl,
NH₂, NH(C₁-C₆)-alkyl, N((C₁-C₆)-alkyl)₂, SO₂-CH₃, COOH,
15 COO-(C₁-C₆)-alkyl, CONH₂;
1,2,3-triazol-5-yl, where the triazole ring can be substituted in
the 1-, 2- or 3-position by methyl or benzyl;
tetrazol-5-yl, where the tetrazole ring can be substituted in the
1- or 2-position by methyl or benzyl;
- 20 R2 is H, (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl, (CH₂)_n-phenyl, (CH₂)_n-
thienyl, (CH₂)_n-pyridyl, (CH₂)_n-furyl, C(O)-(C₁-C₆)-alkyl, C(O)-
(C₃-C₆)-cycloalkyl, C(O)-(CH₂)_n-phenyl, C(O)-(CH₂)_n-thienyl,
C(O)-(CH₂)_n-pyridyl, C(O)-(CH₂)_n-furyl, where n can be 0-5
25 and in which phenyl, thienyl, pyridyl, furyl can each be
substituted up to two times by Cl, F, CN, CF₃, (C₁-C₃)-alkyl,
OH, O-(C₁-C₆)-alkyl;
- 30 R3 is H, F;
- R4 (C₈-C₁₆)-cycloalkyl, it being possible in the alkyl radicals for
one or more hydrogens to be replaced by fluorine or a
hydrogen to be replaced by OH, OC(O)CH₃, OC(O)H, O-CH₂-
Ph or O-(C₁-C₄)-alkyl;
35 (CH₂)_n-A-R8, where n can be 1-6,
except for the group -CH₂-O-CH₂-phenyl in which phenyl is
unsubstituted;

(CH₂)_r-B-R9, where r can be 1-6;

- A is O, S;
- 5 B is NH, N-(C₁-C₆)-alkyl, NCHO, N(CO-CH₃);
- R8 is (C₅-C₂₄)-alkyl, (C₃-C₁₀)-cycloalkyl, it being possible in the alkyl radicals for one or more hydrogens to be replaced by fluorine or a hydrogen to be replaced by OH, OC(O)CH₃,
 10 OC(O)H, O-CH₂-Ph or O-(C₁-C₄)-alkyl;
 (CH₂)_m-aryl, where m can be 0-6 and aryl can be phenyl, naphthyl, biphenyl, thienyl or pyridyl
 and the aryl moiety can be substituted up to two times by F, Cl, Br, OH, CF₃, NO₂, CN, OCF₃, O-(C₁-C₆)-alkyl, S-(C₁-C₆)-
 15 alkyl, SO-(C₁-C₆)-alkyl, SO₂-(C₁-C₆)-alkyl, SO₂-NH₂, SO₂-NH(C₁-C₈-alkyl), SO₂-N(C₁-C₈-alkyl)₂, SO₂-NH(C₃-C₈-cycloalkyl), SO₂-N(C₃-C₈-cycloalkyl)₂, (CH₂)_m-SO₂-NH₂, (CH₂)_m-SO₂-NH-(C₁-C₆)-alkyl, (CH₂)_m-SO₂-N((C₁-C₆)-alkyl)₂, where m can be 1-6, SO₂-N(=CH-N(CH₃)₂), (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl, COOH, COO(C₁-C₆)-alkyl, COO(C₃-C₆)-cycloalkyl, CONH₂, CONH(C₁-C₆)-alkyl, CON[(C₁-C₆)-alkyl]₂, CONH(C₃-C₆)-cycloalkyl, NH₂, NH(C₁-C₆)-alkyl, N(C₁-C₆-alkyl)₂, NH-CO-(C₁-C₆)-alkyl, NH-CO-phenyl, NH-SO₂-(C₁-C₈-alkyl), N(C₁-C₆-alkyl)-SO₂-(C₁-C₈-alkyl), NH-SO₂-phenyl, where the phenyl ring can be substituted up to two times by F, Cl, CN, OH, (C₁-C₆)-alkyl, O-(C₁-C₆)-alkyl, CF₃, COOH, COO(C₁-C₆)-alkyl or CONH₂;
 20 pyrrolidin-1-yl, morpholin-1-yl, piperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-1-yl, (CH₂)_p-phenyl, O-(CH₂)_p-phenyl, S-(CH₂)_p-phenyl or SO₂-(CH₂)_p-phenyl, where p can be 0-3;
- 30
- R9 is (CH₂)_m-aryl, where m can be 0-6 and aryl can be phenyl, naphthyl, biphenyl, thienyl or pyridyl
 and the aryl moiety can be substituted up to two times by F, Cl, Br, OH, CF₃, NO₂, CN, OCF₃, O-(C₁-C₆)-alkyl, S-(C₁-C₆)-alkyl, SO-(C₁-C₆)-alkyl, SO₂-(C₁-C₆)-alkyl, SO₂-NH₂, SO₂-NH(C₁-C₈-alkyl), SO₂-N(C₁-C₈-alkyl)₂, SO₂-NH(C₃-C₈-
- 35

cycloalkyl), $\text{SO}_2\text{-N}(\text{C}_3\text{-C}_8\text{-cycloalkyl})_2$, $(\text{CH}_2)_m\text{-SO}_2\text{-NH}_2$, $(\text{CH}_2)_m\text{-SO}_2\text{-NH}(\text{C}_1\text{-C}_6)\text{-alkyl}$, $(\text{CH}_2)_m\text{-SO}_2\text{-N}((\text{C}_1\text{-C}_6)\text{-alkyl})_2$, where m can be 1-6, $\text{SO}_2\text{-N}(\text{=CH-N}(\text{CH}_3)_2)$, $(\text{C}_1\text{-C}_6)\text{-alkyl}$, $(\text{C}_3\text{-C}_6)\text{-cycloalkyl}$, COOH , $\text{COO}(\text{C}_1\text{-C}_6)\text{alkyl}$, $\text{COO}(\text{C}_3\text{-C}_6)\text{cycloalkyl}$, CONH_2 , $\text{CONH}(\text{C}_1\text{-C}_6)\text{alkyl}$, $\text{CON}[(\text{C}_1\text{-C}_6)\text{alkyl}]_2$, $\text{CONH}(\text{C}_3\text{-C}_6)\text{cycloalkyl}$, NH_2 , $\text{NH}(\text{C}_1\text{-C}_6)\text{-alkyl}$, $\text{N}(\text{C}_1\text{-C}_6\text{-alkyl})_2$, $\text{NH-CO}(\text{C}_1\text{-C}_6)\text{-alkyl}$, NH-CO-phenyl , $\text{NH-SO}_2(\text{C}_1\text{-C}_8\text{-alkyl})$, $\text{N}(\text{C}_1\text{-C}_6\text{-alkyl})\text{-SO}_2(\text{C}_1\text{-C}_8\text{-alkyl})$, $\text{NH-SO}_2\text{-phenyl}$, where the phenyl ring can be substituted up to two times by F, Cl, CN, OH, $(\text{C}_1\text{-C}_6)\text{-alkyl}$, $\text{O}(\text{C}_1\text{-C}_6)\text{-alkyl}$, CF_3 , COOH , $\text{COO}(\text{C}_1\text{-C}_6)\text{-alkyl}$ or CONH_2 ;

pyrrolidin-1-yl, morpholin-1-yl, piperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-1-yl, $(\text{CH}_2)_p\text{-phenyl}$, $\text{O}(\text{CH}_2)_p\text{-phenyl}$, $\text{S}(\text{CH}_2)_p\text{-phenyl}$ or $\text{SO}_2(\text{CH}_2)_p\text{-phenyl}$, where p can be 0-3;

and their physiologically acceptable salts.

Very particular preference is given to compounds of the formula I in which

Y is a direct bond;

X is CH_2 ;

R1, R1' independently of one another are H, F, Cl, Br, I, $(\text{C}_1\text{-C}_6)\text{-alkyl}$;

R2 is H, $(\text{C}_1\text{-C}_6)\text{-alkyl}$;

R3 is H, F;

R4 is $(\text{C}_8\text{-C}_{16})\text{-cycloalkyl}$ or $(\text{CH}_2)_n\text{-A-R}_8$, where n can be 1-6, except for the group $\text{-CH}_2\text{-O-CH}_2\text{-phenyl}$ in which phenyl is unsubstituted;

A is O, S;

R8 is $(\text{C}_5\text{-C}_{24})\text{-alkyl}$, or $(\text{CH}_2)_m\text{-aryl}$, where m can be 0-6 and aryl can be phenyl

and the aryl moiety can be substituted up to two times by F, Cl, Br, OH, CF₃, NO₂, CN, OCF₃, O-(C₁-C₆)-alkyl, S-(C₁-C₆)-alkyl, SO-(C₁-C₆)-alkyl, SO₂-(C₁-C₆)-alkyl, SO₂-NH₂, SO₂-NH(C₁-C₈-alkyl), SO₂-N(C₁-C₈-alkyl)₂, SO₂-NH(C₃-C₈-cycloalkyl), SO₂-N(C₃-C₈-cycloalkyl)₂, (CH₂)_m-SO₂-NH₂, (CH₂)_m-SO₂-NH-(C₁-C₆)-alkyl, (CH₂)_m-SO₂-N((C₁-C₆)-alkyl)₂, where m can be 1-6, SO₂-N(=CH-N(CH₃)₂), (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl, COOH, COO(C₁-C₆)-alkyl, COO(C₃-C₆)-cycloalkyl, CONH₂, CONH(C₁-C₆)-alkyl, CON[(C₁-C₆)-alkyl]₂, CONH(C₃-C₆)-cycloalkyl, NH₂, NH(C₁-C₆)-alkyl, N(C₁-C₆-alkyl)₂, NH-CO-(C₁-C₆)-alkyl, NH-CO-phenyl, NH-SO₂-(C₁-C₈-alkyl), N(C₁-C₆-alkyl)-SO₂-(C₁-C₈-alkyl), NH-SO₂-phenyl, where the phenyl ring can be substituted up to two times by F, Cl, CN, OH, (C₁-C₆)-alkyl, O-(C₁-C₆)-alkyl, CF₃, COOH, COO(C₁-C₆)-alkyl or CONH₂;

pyrrolidin-1-yl, morpholin-1-yl, piperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-1-yl, (CH₂)_p-phenyl, O-(CH₂)_p-phenyl, S-(CH₂)_p-phenyl or SO₂-(CH₂)_p-phenyl, where p can be 0-3;

and their physiologically acceptable salts.

The invention relates to compounds of the formula I, in the form of their racemates, racemic mixtures and pure enantiomers, and to their diastereomers and mixtures thereof.

25

The alkyl, alkenyl and alkynyl radicals in the substituents R₁, R₁', R₂, R₃, R₄, R₈ and A can be either straight-chain or branched.

On account of their higher water solubility, pharmaceutically tolerable salts are particularly suitable for medicinal applications compared with the starting or base compounds. These salts must have a pharmaceutically tolerable anion or cation. Suitable pharmaceutically tolerable acid addition salts of the compounds according to the invention are salts of inorganic acids, such as hydrochloric acid, hydrobromic, phosphoric, metaphosphoric, nitric, sulfonic and sulfuric acid and organic acids, such as, for example, acetic acid, benzenesulfonic, benzoic, citric, ethanesulfonic, fumaric, gluconic, glycolic, isethionic, lactic, lactobionic, maleic, malic, methanesulfonic, succinic, p-toluenesulfonic, tartaric and

trifluoroacetic acid. For medicinal purposes, the chlorine salt is particularly preferably used. Suitable pharmaceutically tolerable basic salts are ammonium salts, alkali metal salts (such as sodium and potassium salts) and alkaline earth metal salts (such as magnesium and calcium salts).

5

Salts with a nonpharmaceutically tolerable anion are likewise included in the scope of the invention as useful intermediates for the production or purification of pharmaceutically tolerable salts and/or for use in nontherapeutic, for example in-vitro, applications.

10

The expression "physiologically functional derivative" used here relates to any physiologically tolerable derivative of a compound of the formula I according to the invention, e.g. an ester, which on administration to a mammal, such as, for example, man, is able (directly or indirectly) to form a compound of the formula I or an active metabolite thereof.

15

The physiologically functional derivatives also include prodrugs of the compounds according to the invention. Such prodrugs can be metabolized in vivo to a compound according to the invention. These prodrugs can themselves be active or inactive.

20

The compounds according to the invention can also be present in various polymorphic forms, e.g. as amorphous and crystalline polymorphic forms. All polymorphic forms of the compounds according to the invention are included in the scope of the invention and are a further aspect of the invention.

25

Below, all references to "compound(s) according to formula (I)" refer to compound(s) of the formula (I) as described above, and their salts, solvates and physiologically functional derivatives as described herein.

30

The amount of a compound according to formula (I) which is necessary in order to achieve the desired biological effect is dependent on a number of factors, e.g. the specific compound selected, the intended use, the manner of administration and the clinical condition of the patient. In general, the daily dose is in the range from 0.3 mg to 100 mg (typically from 3 mg to 50 mg) per day per kilogram of body weight, e.g. 3-10 mg/kg/day. An intravenous dose can be, for example, in the range from 0.3 mg to

35

1.0 mg/kg, which can be suitably administered as an infusion of 10 ng to 100 ng per kilogram per minute. Suitable infusion solutions for these purposes can contain, for example, from 0.1 ng to 10 mg, typically from 1 ng to 10 mg per milliliter. Individual doses can contain, for example, from 1 mg to 10 g of the active compound. Thus, ampoules for injections can contain, for example, from 1 to 100 mg and orally administrable individual dose formulations, such as, for example, tablets or capsules, can contain, for example, from 1.0 to 1000 mg, typically from 10 to 600 mg. In the case of pharmaceutically tolerable salts, the abovementioned weight details relate to the weight of the dihydrothiazolium ion derived from the salt. For the prophylaxis or therapy of the abovementioned conditions, the compounds according to formula (I) itself can be used as the compound, but they are preferably present in the form of a pharmaceutical composition with a tolerable vehicle. The vehicle must of course be tolerable, in the sense that it is compatible with the other constituents of the composition and is not harmful to the patient's health. The vehicle can be a solid or a liquid or both and is preferably formulated with the compound as an individual dose, for example as a tablet which can contain from 0.05% to 95% by weight of the active compound. Further pharmaceutically active substances can also be present, including further compounds according to formula (I). The pharmaceutical compositions according to the invention can be prepared by one of the known pharmaceutical methods, which essentially consist in mixing the constituents with pharmacologically tolerable excipients and/or auxiliaries.

Pharmaceutical compositions according to the invention are those which are suitable for oral, rectal, topical, peroral (e.g. sublingual) and parenteral (e.g. subcutaneous, intramuscular, intradermal or intravenous) administration, although the most suitable manner of administration in each individual case is dependent on the nature and severity of the condition to be treated and on the nature of the compound according to formula (I) used in each case. Sugar-coated formulations and sugar-coated delayed release formulations are also included in the scope of the invention. Acid-resistant and enteric formulations are preferred. Suitable enteric coatings include cellulose acetate phthalate, polyvinyl acetate phthalate, hydroxypropylmethylcellulose phthalate and anionic polymers of methacrylic acid and methyl methacrylate.

Suitable pharmaceutical compounds for oral administration can be present in separate units, such as, for example, capsules, cachets, lozenges or tablets which in each case contain a certain amount of the compound according to formula (I); as powder or granules; as a solution or suspension in an aqueous or nonaqueous liquid; or as an oil-in-water or water-in-oil emulsion. As already mentioned, these compositions can be prepared by any suitable pharmaceutical method which includes a step in which the active compound and the vehicle (which can consist of one or more additional constituents) are brought into contact. In general, the compositions are prepared by uniform and homogeneous mixing of the active compound with a liquid and/or finely divided solid vehicle, after which the product, if necessary, is shaped. Thus a tablet, for example, can be prepared by pressing or shaping a powder or granules of the compound, if appropriate with one or more additional constituents. Pressed tablets can be prepared by tableting the compound in free-flowing form, such as, for example, a powder or granules, if appropriate mixed with a binder, lubricant, inert diluent and/or one (a number of) surface-active/dispersing agents in a suitable machine. Shaped tablets can be prepared by shaping the pulverulent compound, moistened with an inert liquid diluent, in a suitable machine.

Pharmaceutical compositions which are suitable for peroral (sublingual) administration include lozenges which contain a compound according to formula (I) with a flavoring, customarily sucrose and gum arabic or tragacanth, and pastilles which include the compound in an inert base such as gelatin and glycerol or sucrose and gum arabic.

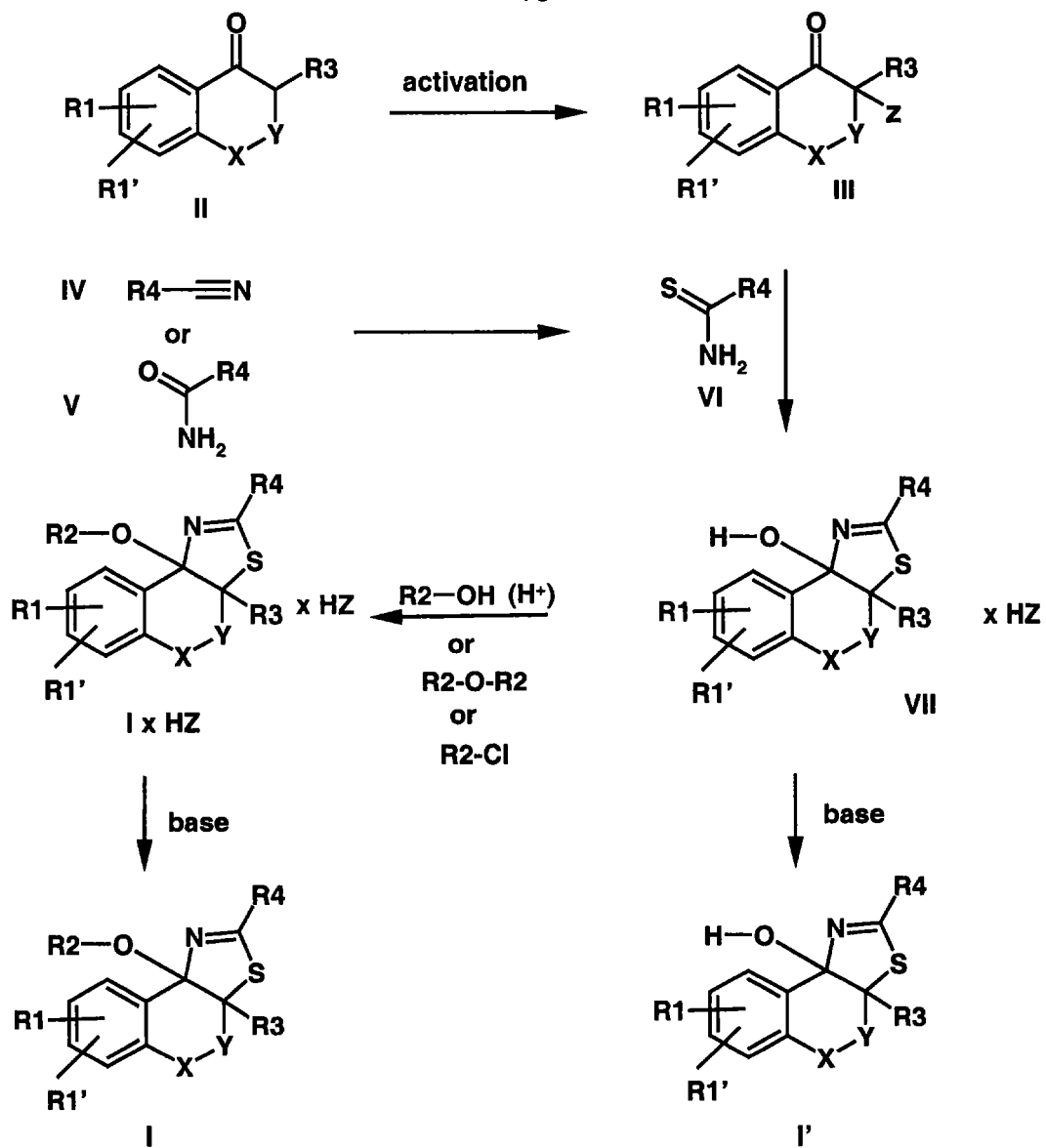
Suitable pharmaceutical compositions for parenteral administration preferably include sterile aqueous preparations of a compound according to formula (I), which are preferably isotonic with the blood of the intended recipient. These preparations are preferably administered intravenously although the administration can also take place subcutaneously, intramuscularly or intradermally as an injection. These preparations can preferably be prepared by mixing the compound with water and rendering the obtained solution sterile and isotonic with the blood. Injectable compositions according to the invention in general contain from 0.1 to 5% by weight of the active compound.

Suitable pharmaceutical compositions for rectal administration are preferably present as individual dose suppositories. These can be prepared by mixing a compound according to formula (I) with one or more conventional solid vehicles, for example cocoa butter, and shaping the resulting mixture.

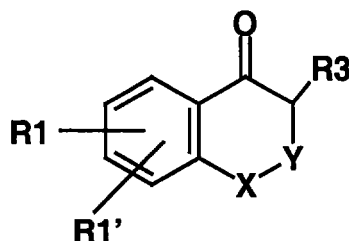
Suitable pharmaceutical compositions for topical application to the skin are preferably present as an ointment, cream, lotion, paste, spray, aerosol or oil. Vehicles which can be used are petroleum jelly, lanolin, polyethylene glycols, alcohols and combinations of two or more of these substances. The active compound is in general present in a concentration of 0.1 to 15% by weight of the composition, for example of 0.5 to 2%.

Transdermal administration is also possible. Suitable pharmaceutical compositions for transdermal administration can be present as individual patches which are suitable for long-term close contact with the epidermis of the patient. Such patches suitably contain the active compound in an optionally buffered aqueous solution, dissolved and/or dispersed in an adhesive or dispersed in a polymer. A suitable active compound concentration is about 1% to 35%, preferably about 3% to 15%. As a particular possibility, the active compound can be released by electrotransport or iontophoresis, as described, for example, in *Pharmaceutical Research*, 2(6): 318 (1986).

The invention furthermore relates to a process for the preparation of the compounds of the formula I, which comprises obtaining the compounds of the formula I in such a way that the procedure is according to the following reaction scheme:



For this, compounds of the formula II

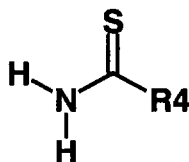


Formula II

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in which R1, R1', R3 and X and Y have the meaning indicated, are activated and converted into a compound of the formula III, in which Z is the radical of an activated ester of an inorganic or organic acid.

- 10 The compounds of the formula III are reacted further with thioamides of the formula VI



VI

- 15 in which R4 has the meaning indicated, to give compounds of the formula VII or I', where, if appropriate, the compounds of the formula I' are converted into their acid addition salts of the formula VII using organic or inorganic acids or salts of the formula VII obtained are converted into the free basic compounds of the formula I' using organic or inorganic bases.

20

Suitable inorganic acids are, for example:

hydrohalic acids such as hydrochloric acid and hydrobromic acid, as well as sulfuric acid, phosphoric acid and amidosulfonic acid.

- 25 Organic acids which may be mentioned are, for example: formic acid, acetic acid, benzoic acid, p-toluenesulfonic acid, benzenesulfonic acid, succinic acid, fumaric acid, maleic acid, lactic acid, tartaric acid, citric acid, L-ascorbic acid, salicylic acid, isethionic acid, methanesulfonic acid, trifluoromethanesulfonic acid, 1,2-benzisothiazol-3(2H)-one, 6-methyl-
30 1,2,3-oxathiazine-4(3H)-one-2,2-dioxide.

- The procedure described above is advantageously carried out such that the compounds III are reacted with the thioamides VI in the molar ratio from 1:1 to 1:1.5. The reaction is advantageously carried out in an inert solvent, e.g. in polar organic solvents such as dimethylformamide, dimethylacetamide, N-methyl-2-pyrrolidone, dioxane, tetrahydrofuran, acetonitrile, nitromethane or diethylene glycol dimethyl ether. Particularly advantageous solvents, however, have proved to be methyl acetate and ethyl acetate, short-chain alcohols such as methanol, ethanol, propanol, isopropanol, and lower dialkyl ketones, such as, for example, acetone, butan-2-one or hexan-2-one. Mixtures of the reaction media mentioned can also be used; and mixtures of the solvents mentioned can also be used with solvents which taken per se are less suitable, such as, for example, mixtures of methanol with benzene, ethanol with toluene, methanol with diethyl ether or with tert-butyl methyl ether, ethanol with tetrachloromethane, acetone with chloroform, dichloromethane or 1,2-dichloroethane, where the more polar solvent in each case should expediently be used in an excess. The reaction components can be suspended or dissolved in the respective reaction medium. Fundamentally, the reaction components can also be reacted without solvent, in particular if the respective thioamide has a melting point which is as low as possible. The reaction proceeds in an only slightly exothermic manner and can be carried out between -10°C and 150°C , preferably between 30°C and 100°C . A temperature range between 50°C and 90°C as a rule proves to be particularly favorable.
- The reaction time is largely dependent on the reaction temperature and is between 2 minutes and 3 days at relatively high and relatively low temperatures respectively. In the favorable temperature range, the reaction time is in general between 5 minutes and 48 hours.
- Frequently, the compounds VII separate in the form of their poorly soluble acid addition salts in the course of the reaction, expediently a suitable precipitating agent is additionally subsequently added. Those used are, for example, hydrocarbons such as benzene, toluene, cyclohexane or heptane or tetrachloromethane; in particular, alkyl acetates such as ethyl acetate or n-butyl acetate or dialkyl ethers such as diethyl ether, diisopropyl ether, di-n-butyl ether or tert-butyl methyl ether prove particularly suitable. If the reaction mixture remains in solution after the end of the reaction, the salts of the compounds VII can be precipitated using one of the precipitating

agents mentioned, if appropriate after concentration of the reaction solution. Furthermore, the solution of the reaction mixture can also be advantageously filtered into the solution of one of the precipitating agents mentioned with stirring. Since the reaction of the compounds III with the thioamides VI proceeds virtually quantitatively, the crude products obtained are usually already analytically pure. The working-up of the reaction mixture can also be carried out such that the reaction mixture is rendered alkaline with addition of an organic base, such as, for example, triethylamine or diisobutylamine or ammonia or morpholine or piperidine or 1,8-diazabicyclo[5.4.0]undec-7-ene, and the crude reaction product is purified chromatographically, e.g. on a silica gel column, after concentration. Suitable elution media for this prove to be, for example, mixtures of ethyl acetate with methanol, mixtures of dichloromethane with methanol, mixtures of toluene with methanol or ethyl acetate or mixtures of ethyl acetate with hydrocarbons such as heptane. If the purification of the crude product is carried out in the manner last described, an acid addition product of the formula VII can be obtained from the pure base of the formula I' thus obtained by dissolving or suspending the base in an organic protic solvent such as methanol, ethanol, propanol or isopropanol or in an organic aprotic solvent such as ethyl acetate, diethyl ether, diisopropyl ether, tert-butyl methyl ether, dioxane, tetrahydrofuran, acetone or butan-2-one and then treating this mixture with an at least equimolar amount of an inorganic acid such as, for example, hydrochloric acid, dissolved in an inert solvent such as, for example, diethyl ether or ethanol, or another of the inorganic or organic acids mentioned further above.

The compounds of the formula I' can be recrystallized from an inert, suitable solvent such as, for example, acetone, butan-2-one, acetonitrile, nitromethane. Particularly advantageous, however, is reprecipitation from a solvent such as, for example, dimethylformamide, dimethylacetamide, nitromethane, acetonitrile, preferably methanol or ethanol.

The reaction of the compounds of the formula II with the thioamides of the formula VI can also be carried out such that an at least equimolar amount of a base, such as, for example, triethylamine, is added to the reaction mixture and the compounds I' thus obtained are then optionally converted into their acid addition products VII.

A possible radical of an activated ester Z in the compounds of the formula III is, for example: Cl, Br, I, O-C(O)-(C₆H₄)-4-NO₂, O-SO₂-CH₃, O-SO₂-CF₃, O-SO₂-(C₆H₄)-4-CH₃, O-SO₂-C₆H₄.

- 5 The acid addition products VII and I x HZ can be reacted to give the compounds of the formulae I and I' by treatment with bases. Possible bases are, for example, solutions of inorganic hydroxides, such as lithium, sodium, potassium, calcium or barium hydroxide, carbonates or hydrogencarbonates, such as sodium or potassium carbonate, sodium or
10 potassium hydrogencarbonate, ammonia and amines, such as triethylamine, diisopropylamine, dicyclohexylamine, piperidine, morpholine, methyldicyclohexylamine.

- Thioamides of the formula VI are either commercially obtainable or can be
15 obtained, for example, by reaction of the corresponding carboxamide V with phosphorus pentasulfide in pyridine (R. N. Hurd, G. Delameter, Chem. Rev. 61, 45 (1961)), or with Lawesson's reagent in toluene, pyridine, hexamethylphosphoric triamide [Scheibye, Pedersen und Lawesson: Bull. Soc. Chim. Belges 87, 229 (1978)], preferably in a mixture of
20 tetrahydrofuran with 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone or 1,3-dimethyl-2-imidazolidinone. Hydroxyl, amino or additional carbonyl functions are in this case expediently protected using a removable protective function, such as, for example, a benzyl, tert-butyloxycarbonyl or benzyloxycarbonyl radical or converted into an optionally cyclic acetal.
25 Methods for this are described, for example, in Th. W. Greene and P. G. M. Wuts, Protective Groups in Organic Synthesis, Second Edition, 1991, John Wiley & Sons, New York.

- Thioamides of the formula VI are also obtainable by reacting nitriles of the
30 formula IV



Formula IV

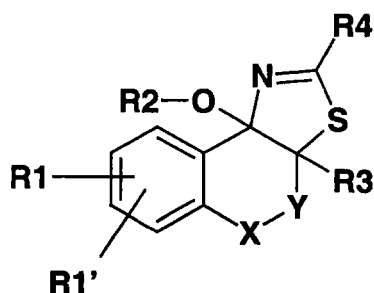
- 35 with hydrogen sulfide (Houben-Weyl IX, 762) or thioacetamide (E. C. Taylor, J. A. Zoltewicz, J. Am. Chem. Soc. 82, 2656 (1960)) or O,O-diethyl-dithiophosphoric acid. The reactions with hydrogen sulfide are preferably carried out in an organic solvent such as methanol or ethanol,

those with thioacetamide in a solvent such as dimethylformamide with addition of hydrochloric acid, and those with O,O-diethyldithiophosphoric acid in a solvent such as ethyl acetate under acidic, e.g. HCl, conditions at room temperature or with warming.

5

The examples listed below serve to illustrate the invention, but without restricting it. The measured melting or decomposition points (m.p.) were not corrected and are generally dependent on the heating rate.

10 Table 1: Examples



Formula I

Example	R1; R1'	R2	R3	R4	Y	X	Salt	m.p. [°C]
1	6-Cl; H	H	H	CH ₂ -O-phenyl	-	CH ₂	-	121
2	6-Cl; H	H	H	CH ₂ -O-(C ₆ H ₄ -4-OCH ₃)	-	CH ₂	-	110
3	6-Cl; H	H	H	CH ₂ -O-(C ₆ H ₄ -2-Cl)	-	CH ₂	-	178
4	6-Cl; H	H	H	CH ₂ -O-(C ₆ H ₄ -3-Cl)	-	CH ₂	-	121
5	6-Cl; H	H	H	CH ₂ -O-(C ₆ H ₄ -4-Cl)	-	CH ₂	-	123
6	6-Cl; H	H	H	CH ₂ -O-phenyl-2,4-di-Cl	-	CH ₂	HBr	170
7	6-Cl; H	H	H	adamant-1-yl	-	CH ₂	-	173
8	6-Cl; H	H	H	CH ₂ -O-(phenyl-3,5-di-Cl)	-	CH ₂	-	125
9	6-Cl; H	H	H	CH ₂ -O-(phenyl-4-tBu)	-	CH ₂	-	123
10	6-Cl; H	H	H	CH ₂ -O-CH ₂ -CH ₂ -C ₆ H ₅	-	CH ₂	-	94
11	6-Cl; H	H	H	CH ₂ -O-(CH ₂) ₅ -CH ₃	-	CH ₂	-	78
12	6-Cl; H	H	H	CH ₂ -S-CH ₂ -C ₆ H ₅	-	CH ₂	-	102

15

The compounds of the formula I are distinguished by favorable effects on the lipid metabolism; in particular, they are suitable as anorectics. The compounds can be employed on their own or in combination with further

anorectics (such as are described, for example, in Chapter 01 of the Roten Liste, under slimming preparations/appetite suppressants). The compounds are suitable for the prophylaxis and in particular for the treatment of obesity. The compounds are furthermore suitable for the prophylaxis and in particular for the treatment of type II diabetes.

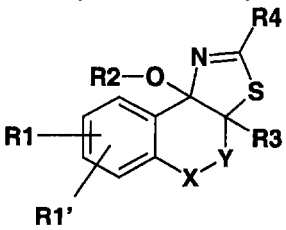
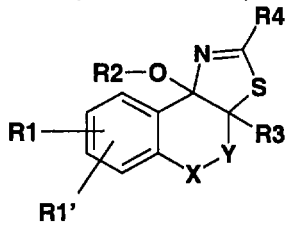
The efficacy of the compounds was tested as follows:

Biological test model:

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The anorectic action was tested on male or female NMRI mice. After withdrawal of feed for 24 hours, the test preparation was administered via a stomach tube. Kept individually and with free access to drinking water, the animals were offered evaporated milk 30 minutes after giving the preparation. The consumption of evaporated milk was determined half-hourly for 7 hours and the general condition of the animals was observed. The measured milk consumption was compared with that of the untreated control animals.

Table 2: Anorectic action, measured as the reduction of the cumulated milk consumption of treated animals in comparison to that of untreated animals.

Compound/Example  Formula I	Oral dose [mg/kg]	Number of animals/ cumulated milk consumption of the treated animals (male) N / [ml]	Number of animals/ cumulated milk consumption of the untreated control animals (male) N / [ml]	Reduction of the cumulated milk consumption in % of the control
Example 1	50	5 / 0.42	5 / 2.90	86
Example 2	50	5 / 0.34	5 / 2.90	88
Example 3	50	5 / 0.78	5 / 2.90	73
Example 5	50	5 / 0.42	5 / 4.18	90
Example 6	50	5 / 0.22	5 / 4.20	95
Example 8	50	5 / 0.28	5 / 4.20	93
Example 9	50	5 / 0.26	5 / 3.46	93
Compound/Example  Formula I	Oral dose [mg/kg]	Number of animals/ cumulated milk consumption of the treated animals (female) N / [ml]	Number of animals/ cumulated milk consumption of the untreated control animals (female) N / [ml]	Reduction of the cumulated milk consumption in % of the control
Example 10	50	5 / 1.04	5 / 4.64	78
Example 11	50	5 / 1.34	5 / 4.64	71
Example 12	50	5 / 1.36	5 / 4.64	71

5

It can be inferred from the table that the compounds of the formula 1 exhibit very good anorectic action.

The preparation of some examples is described in detail below; the other
10 compounds of the formula I were obtained analogously:

Example 1 (Compound 1):

6-chloro-2-phenoxyethyl-8,8a-dihydroindeno[1,2-d]thiazol-3a-ol:

5 a) 2-bromo-5-chloroindan-1-one:

At room temperature, 10 g (0.06 Mol) of 5-chloroindan-1-one are dissolved with stirring in 120 ml of glacial acetic acid. 0.05 ml of a 48% strength solution of HBr in water and then 3.074 ml (0.06 mol) of bromine, dissolved in 25 ml of glacial acetic acid, are added dropwise. After 2 h of stirring at room temperature, the reaction is ended (monitored by TLC). The solution of the crude product is slowly added dropwise, with stirring, to 300 ml of ice-water. The precipitated crude product is filtered off with suction and washed thoroughly with water. The moist residue is removed from the filter using ethyl acetate, and the phases of the filtrate are separated. The organic phase is dried over sodium sulfate, filtered and concentrated under reduced pressure. The residue is dissolved in 120 ml of hot n-heptane; the hot solution is filtered through a pleated filter and the solution is then left to crystallize at 0°C. The crystalline product is filtered off with suction and dried under reduced pressure.
m.p.: 94-96°C

b) 6-chloro-2-phenoxyethyl-8,8a-dihydroindeno[1,2-d]thiazol-3a-ol:

At room temperature, 0.49 g of 2-bromo-5-chloroindan-1-one are dissolved in 10 ml of dry acetone and mixed with 335 mg of 2-phenoxy-thioacetamide. The mixture is stirred at room temperature for 6 h, the crystallized hydrobromide of the product is filtered off with suction and the residue is washed with acetone and dried under reduced pressure. The free base is obtained by introducing the salt into a mixture of 30 ml of ethyl acetate and 20 ml of saturated sodium bicarbonate solution and stirring for 20 mins. The organic phase is separated off, washed with saturated sodium fluoride solution and dried over magnesium sulfate. The mixture is filtered and the filtrate is concentrated under reduced pressure. This gives 6-chloro-2-phenoxyethyl-8,8a-dihydroindeno[1,2-d]thiazol-3a-ol of melting point 121°C.

Example 2 (Compound 6):

6-chloro-2-(2,4-dichlorophenoxy)methyl)-8,8a-dihydroindeno[1,2-d]thiazol-3a-ol hydrobromide:

5

At room temperature, 0.25 g of 2-bromo-5-chloroindan-1-one and 0.24 g of 2-(2,4-dichlorophenoxy)-thioacetamide are dissolved in 5 ml of dry acetone, and the mixture is stirred at room temperature for 12 h. The resulting precipitate is filtered off with suction, washed with acetone and dried under high vacuum. This gives the hydrobromide of 6-chloro-2-(2,4-dichlorophenoxy)methyl)-8,8a-dihydroindeno[1,2-d]thiazol-3a-ol of melting point 170°C (decomposition).

15

Example 3 (Compound 9):

2-(4-tert-butylphenoxy)methyl)-6-chloro-8,8a-dihydroindeno[1,2-d]thiazol-3a-ol:

20

At room temperature, 0.49 g of 2-bromo-5-chloroindan-1-one and 0.45 g of 2-(4-tert-butylphenoxy)-thioacetamide are dissolved in 10 ml of dry acetone, and the mixture is stirred at room temperature for 12 h. The precipitated hydrobromide is filtered off with suction and washed with acetone. The residue is suspended in a little ethyl acetate and treated with saturated sodium bicarbonate solution. The organic phase is separated off, dried over magnesium sulfate, filtered and concentrated under reduced pressure. This gives 2-(4-tert-butylphenoxy)methyl)-6-chloro-8,8a-dihydroindeno[1,2-d]thiazol-3a-ol of melting point 122-124°C.

25

Example 4 (Compound 12):

30

2-benzylsulfanylmethyl)-6-chloro-8,8a-dihydroindeno[1,2-d]thiazol-3a-ol:

a) 2-benzylsulfanyl-thioacetamide:

35

At room temperature, 1.2 g of benzylsulfanyl-acetonitrile are dissolved in 10 ml of dry ethanol and mixed with 1.25 ml of diethyl dithiophosphate, and the mixture is stirred at reflux for 6 h. The cooled reaction solution is concentrated under reduced pressure and

purified chromatographically over silica gel using ethyl acetate/n-heptane 1/2. The resulting 2-benzylsulfanyl-thioacetamide is used for the next step.

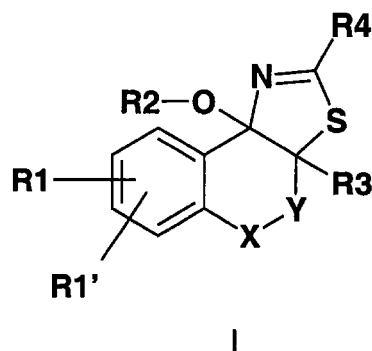
- 5 b) 2-benzylsulfanylmethyl-6-chloro-8,8a-dihydroindeno[1,2-d]thiazol-3a-ol:

10 At room temperature, 0.54 g of 2-benzylsulfanyl-thioacetamide are dissolved in 10 ml of dry acetone and mixed with 0.67 g of 2-bromo-5-chlorindan-1-on, and the mixture is stirred at room temperature for 4 h. The resulting precipitate is filtered off with suction, washed with acetone, taken up in ethyl acetate, mixed with saturated sodium bicarbonate solution and extracted twice. The organic phase is dried over magnesium sulfate, filtered and concentrated under reduced pressure. This gives 2-benzylsulfanylmethyl-6-chloro-8,8a-dihydroindeno[1,2-d]thiazol-3a-ol of melting point 102-104°C.

15

Patent claims:

- 5 1. A compound of the formula I,



in which

10

Y is a direct bond, $-\text{CH}_2-$, $-\text{CH}_2\text{-CH}_2-$;

X is CH_2 , $\text{CH}(\text{CH}_3)$, $\text{CH}(\text{C}_2\text{H}_5)$, $\text{CH}(\text{C}_3\text{H}_7)$, $\text{CH}(\text{C}_6\text{H}_5)$;

15

R1, R1' independently of one another are H, F, Cl, Br, I, CF_3 , NO_2 , CN, COOH , $\text{COO}(\text{C}_1\text{-C}_6)\text{alkyl}$, CONH_2 , $\text{CONH}(\text{C}_1\text{-C}_6)\text{alkyl}$, $\text{CON}[(\text{C}_1\text{-C}_6)\text{alkyl}]_2$, $(\text{C}_1\text{-C}_6)\text{-alkyl}$, $(\text{C}_2\text{-C}_6)\text{-alkenyl}$, $(\text{C}_2\text{-C}_6)\text{-alkynyl}$, $\text{O}(\text{C}_1\text{-C}_6)\text{-alkyl}$, it being possible in the alkyl radicals for one or more, or all hydrogens to be replaced by fluorine, or a hydrogen to be replaced by OH, $\text{OC}(\text{O})\text{CH}_3$, $\text{OC}(\text{O})\text{H}$, $\text{O-CH}_2\text{-Ph}$, NH_2 , NH-CO-CH_3 or $\text{N}(\text{COOCH}_2\text{Ph})_2$;

20

$\text{SO}_2\text{-NH}_2$, $\text{SO}_2\text{NH}(\text{C}_1\text{-C}_6)\text{-alkyl}$, $\text{SO}_2\text{N}[(\text{C}_1\text{-C}_6)\text{-alkyl}]_2$, $\text{S}(\text{C}_1\text{-C}_6)\text{-alkyl}$, $\text{S}(\text{CH}_2)_n\text{-phenyl}$, $\text{SO}(\text{C}_1\text{-C}_6)\text{-alkyl}$, $\text{SO}(\text{CH}_2)_n\text{-phenyl}$, $\text{SO}_2(\text{C}_1\text{-C}_6)\text{-alkyl}$, $\text{SO}_2(\text{CH}_2)_n\text{-phenyl}$,

25

where n can be 0 – 6 and the phenyl radical can be substituted up to two times by F, Cl, Br, OH, CF_3 , NO_2 , CN, OCF_3 , $\text{O}(\text{C}_1\text{-C}_6)\text{-alkyl}$, $(\text{C}_1\text{-C}_6)\text{-alkyl}$, NH_2 ; NH_2 , $\text{NH}(\text{C}_1\text{-C}_6)\text{-alkyl}$, $\text{N}[(\text{C}_1\text{-C}_6)\text{-alkyl}]_2$, $\text{NH}(\text{C}_1\text{-C}_7)\text{-acyl}$, phenyl, biphenyl, $\text{O}(\text{CH}_2)_n\text{-phenyl}$, where n can be 0 – 6, 1- or 2-naphthyl, 2-, 3- or 4-pyridyl, 2- or 3-furanyl or 2- or 3-thienyl, where the phenyl, biphenyl, naphthyl, pyridyl, furanyl or thienyl rings can each be substituted one to 3 times by F, Cl, Br, I, OH, CF_3 ,

30

NO₂, CN, OCF₃, O-(C₁-C₆)-alkyl, (C₁-C₆)-alkyl, NH₂, NH(C₁-C₆)-alkyl, N((C₁-C₆)-alkyl)₂, SO₂-CH₃, COOH, COO-(C₁-C₆)-alkyl, CONH₂;

5 1,2,3-triazol-5-yl, where the triazole ring can be substituted in the 1-, 2- or 3-position by methyl or benzyl;
tetrazol-5-yl, where the tetrazole ring can be substituted in the 1- or 2-position by methyl or benzyl;

10 R2 is H, (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl, (CH₂)_n-phenyl, (CH₂)_n-thienyl, (CH₂)_n-pyridyl, (CH₂)_n-furyl, C(O)-(C₁-C₆)-alkyl, C(O)-(C₃-C₆)-cycloalkyl, C(O)-(CH₂)_n-phenyl, C(O)-(CH₂)_n-thienyl, C(O)-(CH₂)_n-pyridyl, C(O)-(CH₂)_n-furyl, where n can be 0 - 5 and in which phenyl, thienyl, pyridyl, furyl can each be substituted up to two times by Cl, F, CN, CF₃, (C₁-C₃)-alkyl, OH, O-(C₁-C₆)-alkyl;

20 R3 is H, (C₁-C₆)-alkyl, F, CN, N₃, O-(C₁-C₆)-alkyl, (CH₂)_n-phenyl, (CH₂)_n-thienyl, (CH₂)_n-pyridyl, (CH₂)_n-furyl, where n can be 0 - 5 and in which phenyl, thienyl, pyridyl, furyl can each be substituted up to two times by Cl, F, CN, CF₃, (C₁-C₃)-alkyl, OH or O-(C₁-C₆)-alkyl, (C₂-C₆)-alkynyl, (C₂-C₆)-alkenyl, C(O)OCH₃, C(O)OCH₂CH₃, C(O)OH, C(O)NH₂, C(O)NHCH₃, C(O)N(CH₃)₂, OC(O)CH₃;

25 R4 is (C₈-C₁₆)-cycloalkyl, it being possible in the alkyl radicals for one or more hydrogens to be replaced by fluorine or a hydrogen to be replaced by OH, OC(O)CH₃, OC(O)H, O-CH₂-Ph or O-(C₁-C₄)-alkyl;
(CH₂)_n-A-R8, where n can be 1-6,
30 except for the group -CH₂-O-CH₂-phenyl in which phenyl is unsubstituted;
(CH₂)_r-B-R9, where r can be 1-6;

35 A is O, S, SO, SO₂;

B is NH, N-(C₁-C₆)-alkyl, NCHO, N(CO-CH₃);

- R8 is (C₅-C₂₄)-alkyl, (C₃-C₁₀)-cycloalkyl, it being possible in the alkyl radicals for one or more hydrogens to be replaced by fluorine or a hydrogen to be replaced by OH, OC(O)CH₃, OC(O)H, O-CH₂-Ph or O-(C₁-C₄)-alkyl;
- 5 (CH₂)_m-aryl, where m can be 0-6 and aryl can be phenyl, naphthyl, biphenyl, thienyl or pyridyl;
and the aryl moiety can be substituted up to two times by F, Cl, Br, OH, CF₃, NO₂, CN, OCF₃, O-(C₁-C₆)-alkyl, S-(C₁-C₆)-alkyl, SO-(C₁-C₆)-alkyl, SO₂-(C₁-C₆)-alkyl, SO₂-NH₂, SO₂-NH(C₁-C₈-alkyl), SO₂-N(C₁-C₈-alkyl)₂, SO₂-NH(C₃-C₈-cycloalkyl), SO₂-N(C₃-C₈-cycloalkyl)₂, (CH₂)_m-SO₂-NH₂, (CH₂)_m-SO₂-NH-(C₁-C₆)-alkyl, (CH₂)_m-SO₂-N((C₁-C₆)-alkyl)₂, where m can be 1-6, SO₂-N(=CH-N(CH₃)₂), (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl, COOH, COO(C₁-C₆)-alkyl, COO(C₃-C₆)-cycloalkyl, CONH₂, CONH(C₁-C₆)-alkyl, CON[(C₁-C₆)-alkyl]₂, CONH(C₃-C₆)-cycloalkyl, NH₂, NH(C₁-C₆)-alkyl, N(C₁-C₆)-alkyl)₂, NH-CO-(C₁-C₆)-alkyl, NH-CO-phenyl, NH-SO₂-(C₁-C₈-alkyl), N(C₁-C₆-alkyl)-SO₂-(C₁-C₈-alkyl), NH-SO₂-phenyl, where the phenyl ring can be substituted up to two times by F, Cl, CN, OH, (C₁-C₆)-alkyl, O-(C₁-C₆)-alkyl, CF₃, COOH, COO(C₁-C₆)-alkyl or CONH₂, pyrrolidin-1-yl, morpholin-1-yl, piperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-1-yl, (CH₂)_p-phenyl, O-(CH₂)_p-phenyl, S-(CH₂)_p-phenyl or SO₂-(CH₂)_p-phenyl, where p can be 0-3;
- 25
- R9 (CH₂)_m-aryl, where m can be 0-6 and aryl can be phenyl, naphthyl, biphenyl, thienyl or pyridyl;
and the aryl moiety can be substituted up to two times by F, Cl, Br, OH, CF₃, NO₂, CN, OCF₃, O-(C₁-C₆)-alkyl, S-(C₁-C₆)-alkyl, SO-(C₁-C₆)-alkyl, SO₂-(C₁-C₆)-alkyl, SO₂-NH₂, SO₂-NH(C₁-C₈-alkyl), SO₂-N(C₁-C₈-alkyl)₂, SO₂-NH(C₃-C₈-cycloalkyl), SO₂-N(C₃-C₈-cycloalkyl)₂, (CH₂)_m-SO₂-NH₂, (CH₂)_m-SO₂-NH-(C₁-C₆)-alkyl, (CH₂)_m-SO₂-N((C₁-C₆)-alkyl)₂, where m can be 1-6, SO₂-N(=CH-N(CH₃)₂), (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl, COOH, COO(C₁-C₆)-alkyl, COO(C₃-C₆)-cycloalkyl, CONH₂, CONH(C₁-C₆)-alkyl, CON[(C₁-C₆)-alkyl]₂, CONH(C₃-C₆)-cycloalkyl, NH₂, NH(C₁-C₆)-alkyl,
- 30
- 35

N(C₁-C₆-alkyl)₂, NH-CO-(C₁-C₆)-alkyl, NH-CO-phenyl, NH-SO₂-(C₁-C₈-alkyl), N(C₁-C₆-alkyl)-SO₂-(C₁-C₈-alkyl), NH-SO₂-phenyl, where the phenyl ring can be substituted up to two times by F, Cl, CN, OH, (C₁-C₆)-alkyl, O-(C₁-C₆)-alkyl, CF₃,
 5 COOH, COO(C₁-C₆)-alkyl or CONH₂, pyrrolidin-1-yl, morpholin-1-yl, piperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-1-yl, (CH₂)_p-phenyl, O-(CH₂)_p-phenyl, S-(CH₂)_p-phenyl or SO₂-(CH₂)_p-phenyl, where p can be 0-3;

10 and its physiologically acceptable salts.

2. A compound of the formula I as claimed in claim 1, wherein

Y is a direct bond;

15

X is CH₂;

R₁, R₁' independently of one another are H, F, Cl, Br, I, CF₃, NO₂, CN, COOH, COO(C₁-C₆)alkyl, CONH₂, CONH(C₁-C₆)alkyl,
 20 CON[(C₁-C₆)alkyl]₂, (C₁-C₆)-alkyl, (C₂-C₆)-alkenyl, (C₂-C₆)-alkynyl, O-(C₁-C₆)-alkyl, it being possible in the alkyl radicals for one or more, or all hydrogens to be replaced by fluorine, or a hydrogen to be replaced by OH, OC(O)CH₃, OC(O)H, O-CH₂-Ph, NH₂, NH-CO-CH₃ or N(COOCH₂Ph)₂;
 25 SO₂-NH₂, SO₂NH(C₁-C₆)-alkyl, SO₂N[(C₁-C₆)-alkyl]₂, S-(C₁-C₆)-alkyl, S-(CH₂)_n-phenyl, SO-(C₁-C₆)-alkyl, SO-(CH₂)_n-phenyl, SO₂-(C₁-C₆)-alkyl, SO₂-(CH₂)_n-phenyl, where n can be 0-6 and the phenyl radical can be substituted up to two times by F, Cl, Br, OH, CF₃, NO₂, CN, OCF₃, O-(C₁-C₆)-alkyl, (C₁-C₆)-alkyl, NH₂; NH₂, NH-(C₁-C₆)-alkyl, N((C₁-C₆)-alkyl)₂, NH(C₁-C₇)-acyl, phenyl, biphenyl, O-(CH₂)_n-phenyl, where n can be 0-6, 1- or 2-naphthyl, 2-, 3- or 4-pyridyl, 2- or 3-furanyl or 2- or 3-thienyl, where the phenyl, biphenyl, naphthyl, pyridyl, furanyl or thienyl rings can each be
 30 substituted one to 3 times by F, Cl, Br, I, OH, CF₃, NO₂, CN, OCF₃, O-(C₁-C₆)-alkyl, (C₁-C₆)-alkyl, NH₂, NH(C₁-C₆)-alkyl,
 35

- $N((C_1-C_6)\text{-alkyl})_2$, $SO_2\text{-CH}_3$, $COOH$, $COO\text{-(}C_1\text{-}C_6\text{)-alkyl}$, $CONH_2$;
 1,2,3-triazol-5-yl, where the triazole ring can be substituted in the 1-, 2- or 3-position by methyl or benzyl;
 5 tetrazol-5-yl, where the tetrazole ring can be substituted in the 1- or 2-position by methyl or benzyl;
- 10 R2 is H, $(C_1-C_6)\text{-alkyl}$, $(C_3-C_6)\text{-cycloalkyl}$, $(CH_2)_n\text{-phenyl}$, $(CH_2)_n\text{-thienyl}$, $(CH_2)_n\text{-pyridyl}$, $(CH_2)_n\text{-furyl}$, $C(O)\text{-(}C_1\text{-}C_6\text{)-alkyl}$, $C(O)\text{-(}C_3\text{-}C_6\text{)-cycloalkyl}$, $C(O)\text{-(}CH_2)_n\text{-phenyl}$, $C(O)\text{-(}CH_2)_n\text{-thienyl}$, $C(O)\text{-(}CH_2)_n\text{-pyridyl}$, $C(O)\text{-(}CH_2)_n\text{-furyl}$, where n can be 0-5 and in which phenyl, thienyl, pyridyl, furyl can each be substituted up to two times by Cl, F, CN, CF_3 , $(C_1-C_3)\text{-alkyl}$, OH, $O\text{-(}C_1\text{-}C_6\text{)-alkyl}$;
 15
- 20 R3 is H, $(C_1-C_6)\text{-alkyl}$, F, CN, N_3 , $O\text{-(}C_1\text{-}C_6\text{)-alkyl}$, $(CH_2)_n\text{-phenyl}$, $(CH_2)_n\text{-thienyl}$, $(CH_2)_n\text{-pyridyl}$, $(CH_2)_n\text{-furyl}$, where n can be 0-5 and in which phenyl, thienyl, pyridyl, furyl can each be substituted up to two times by Cl, F, CN, CF_3 , $(C_1-C_3)\text{-alkyl}$, OH, $O\text{-(}C_1\text{-}C_6\text{)-alkyl}$;
 $(C_2-C_6)\text{-alkynyl}$, $(C_2-C_6)\text{-alkenyl}$, $C(O)OCH_3$, $C(O)OCH_2CH_3$, $C(O)OH$, $C(O)NH_2$, $C(O)NHCH_3$, $C(O)N(CH_3)_2$, $OC(O)CH_3$;
- 25 R4 is $(C_8-C_{16})\text{-cycloalkyl}$, it being possible in the alkyl radicals for one or more hydrogens to be replaced by fluorine or a hydrogen to be replaced by OH, $OC(O)CH_3$, $OC(O)H$, $O\text{-CH}_2\text{-Ph}$ or $O\text{-(}C_1\text{-}C_4\text{)-alkyl}$;
 $(CH_2)_n\text{-A-R8}$, where n can be 1-6,
 except for the group $\text{-CH}_2\text{-O-CH}_2\text{-phenyl}$ in which phenyl is unsubstituted;
 30 $(CH_2)_r\text{-B-R9}$, where r can be 1-6;
- A is O, S, SO, SO_2 ;
- 35 B is NH, $N\text{-(}C_1\text{-}C_6\text{)-alkyl}$, NCHO, $N(CO\text{-CH}_3)$;

- R8 is (C₅-C₂₄)-alkyl, (C₃-C₁₀)-cycloalkyl, it being possible in the alkyl radicals for one or more hydrogens to be replaced by fluorine or a hydrogen to be replaced by OH, OC(O)CH₃, OC(O)H, O-CH₂-Ph or O-(C₁-C₄)-alkyl;
- 5 (CH₂)_m-aryl, where m can be 0-6 and aryl can be phenyl, naphthyl, biphenyl, thienyl or pyridyl
and the aryl moiety can be substituted up to two times by F, Cl, Br, OH, CF₃, NO₂, CN, OCF₃, O-(C₁-C₆)-alkyl, S-(C₁-C₆)-alkyl, SO-(C₁-C₆)-alkyl, SO₂-(C₁-C₆)-alkyl, SO₂-NH₂, SO₂-NH(C₁-C₈-alkyl), SO₂-N(C₁-C₈-alkyl)₂, SO₂-NH(C₃-C₈-cycloalkyl), SO₂-N(C₃-C₈-cycloalkyl)₂, (CH₂)_m-SO₂-NH₂, (CH₂)_m-SO₂-NH-(C₁-C₆)-alkyl, (CH₂)_m-SO₂-N((C₁-C₆)-alkyl)₂, where m can be 1-6, SO₂-N(=CH-N(CH₃)₂), (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl, COOH, COO(C₁-C₆)-alkyl, COO(C₃-C₆)-cycloalkyl, CONH₂, CONH(C₁-C₆)-alkyl, CON[(C₁-C₆)-alkyl]₂, CONH(C₃-C₆)-cycloalkyl, NH₂, NH(C₁-C₆)-alkyl, N(C₁-C₆)-alkyl)₂, NH-CO-(C₁-C₆)-alkyl, NH-CO-phenyl, NH-SO₂-(C₁-C₈-alkyl), N(C₁-C₆-alkyl)-SO₂-(C₁-C₈-alkyl), NH-SO₂-phenyl, where the phenyl ring can be substituted up to two times by F, Cl, CN, OH, (C₁-C₆)-alkyl, O-(C₁-C₆)-alkyl, CF₃, COOH, COO(C₁-C₆)-alkyl or CONH₂;
- 10 pyrrolidin-1-yl, morpholin-1-yl, piperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-1-yl, (CH₂)_p-phenyl, O-(CH₂)_p-phenyl, S-(CH₂)_p-phenyl or SO₂-(CH₂)_p-phenyl, where p can be 0-3;
- 15
- 20
- 25
- R9 is (CH₂)_m-aryl, where m can be 0-6 and aryl can be phenyl, naphthyl, biphenyl, thienyl or pyridyl
and the aryl moiety can be substituted up to two times by F, Cl, Br, OH, CF₃, NO₂, CN, OCF₃, O-(C₁-C₆)-alkyl, S-(C₁-C₆)-alkyl, SO-(C₁-C₆)-alkyl, SO₂-(C₁-C₆)-alkyl, SO₂-NH₂, SO₂-NH(C₁-C₈-alkyl), SO₂-N(C₁-C₈-alkyl)₂, SO₂-NH(C₃-C₈-cycloalkyl), SO₂-N(C₃-C₈-cycloalkyl)₂, (CH₂)_m-SO₂-NH₂, (CH₂)_m-SO₂-NH-(C₁-C₆)-alkyl, (CH₂)_m-SO₂-N((C₁-C₆)-alkyl)₂, where m can be 1-6, SO₂-N(=CH-N(CH₃)₂), (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl, COOH, COO(C₁-C₆)-alkyl, COO(C₃-C₆)-cycloalkyl, CONH₂, CONH(C₁-C₆)-alkyl, CON[(C₁-C₆)-alkyl]₂, CONH(C₃-C₆)-cycloalkyl, NH₂, NH(C₁-C₆)-alkyl,
- 30
- 35

N(C₁-C₆-alkyl)₂, NH-CO-(C₁-C₆)-alkyl, NH-CO-phenyl, NH-SO₂-(C₁-C₈-alkyl), N(C₁-C₆-alkyl)-SO₂-(C₁-C₈-alkyl), NH-SO₂-phenyl, where the phenyl ring can be substituted up to two times by F, Cl, CN, OH, (C₁-C₆)-alkyl, O-(C₁-C₆)-alkyl, CF₃, COOH, COO(C₁-C₆)-alkyl or CONH₂;
 pyrrolidin-1-yl, morpholin-1-yl, piperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-1-yl, (CH₂)_p-phenyl, O-(CH₂)_p-phenyl, S-(CH₂)_p-phenyl or SO₂-(CH₂)_p-phenyl, where p can be 0-3;

and its physiologically acceptable salts.

3. A compound of the formula I, as claimed in claim 1 or 2, wherein

Y is a direct bond;

X is CH₂;

R₁, R₁' independently of one another are H, F, Cl, Br, I, CF₃, NO₂, CN, COOH, COO(C₁-C₆)alkyl, CONH₂, CONH(C₁-C₆)alkyl, CON[(C₁-C₆)alkyl]₂, (C₁-C₆)-alkyl, (C₂-C₆)-alkenyl, (C₂-C₆)-alkynyl, O-(C₁-C₆)-alkyl, it being possible in the alkyl radicals for one or more, or all hydrogens to be replaced by fluorine, or a hydrogen to be replaced by OH, OC(O)CH₃, OC(O)H, O-CH₂-Ph, NH₂, NH-CO-CH₃ or N(COOCH₂Ph)₂;
 SO₂-NH₂, SO₂NH(C₁-C₆)-alkyl, SO₂N[(C₁-C₆)-alkyl]₂, S-(C₁-C₆)-alkyl, S-(CH₂)_n-phenyl, SO-(C₁-C₆)-alkyl, SO-(CH₂)_n-phenyl, SO₂-(C₁-C₆)-alkyl, SO₂-(CH₂)_n-phenyl, where n can be 0-6 and the phenyl radical can be substituted up to two times by F, Cl, Br, OH, CF₃, NO₂, CN, OCF₃, O-(C₁-C₆)-alkyl, (C₁-C₆)-alkyl, NH₂;

NH₂, NH-(C₁-C₆)-alkyl, N((C₁-C₆)-alkyl)₂, NH(C₁-C₇)-acyl, phenyl, biphenyl, O-(CH₂)_n-phenyl, where n can be 0-6, 1- or 2-naphthyl, 2-, 3- or 4-pyridyl, 2- or 3-furanyl or 2- or 3-thienyl, where the phenyl, biphenyl, naphthyl, pyridyl, furanyl or thienyl rings can each be substituted one to 3 times by F, Cl, Br, I, OH, CF₃, NO₂, CN, OCF₃, O-(C₁-C₆)-alkyl, (C₁-C₆)-alkyl,

- NH₂, NH(C₁-C₆)-alkyl, N((C₁-C₆)-alkyl)₂, SO₂-CH₃, COOH, COO-(C₁-C₆)-alkyl, CONH₂;
 1,2,3-triazol-5-yl, where the triazole ring can be substituted in the 1-, 2- or 3-position by methyl or benzyl;
 5 tetrazol-5-yl, where the tetrazole ring can be substituted in the 1- or 2-position by methyl or benzyl;
- R2 is H, (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl, (CH₂)_n-phenyl, (CH₂)_n-thienyl, (CH₂)_n-pyridyl, (CH₂)_n-furyl, C(O)-(C₁-C₆)-alkyl, C(O)-(C₃-C₆)-cycloalkyl, C(O)-(CH₂)_n-phenyl, C(O)-(CH₂)_n-thienyl, C(O)-(CH₂)_n-pyridyl, C(O)-(CH₂)_n-furyl, where n can be 0-5 and in which phenyl, thienyl, pyridyl, furyl can each be substituted up to two times by Cl, F, CN, CF₃, (C₁-C₃)-alkyl, OH, O-(C₁-C₆)-alkyl;
 10
- R3 is H, F;
 15
- R4 (C₈-C₁₆)-cycloalkyl, it being possible in the alkyl radicals for one or more hydrogens to be replaced by fluorine or a hydrogen to be replaced by OH, OC(O)CH₃, OC(O)H, O-CH₂-Ph or O-(C₁-C₄)-alkyl;
 20 (CH₂)_n-A-R8, where n can be 1-6, except for the group -CH₂-O-CH₂-phenyl in which phenyl is unsubstituted;
 25 (CH₂)_r-B-R9, where r can be 1-6;
- A is O, S;
- B is NH, N-(C₁-C₆)-alkyl, NCHO, N(CO-CH₃);
 30
- R8 is (C₅-C₂₄)-alkyl, (C₃-C₁₀)-cycloalkyl, it being possible in the alkyl radicals for one or more hydrogens to be replaced by fluorine or a hydrogen to be replaced by OH, OC(O)CH₃, OC(O)H, O-CH₂-Ph or O-(C₁-C₄)-alkyl;
 35 (CH₂)_m-aryl, where m can be 0-6 and aryl can be phenyl, naphthyl, biphenyl, thienyl or pyridyl

- and the aryl moiety can be substituted up to two times by F, Cl, Br, OH, CF₃, NO₂, CN, OCF₃, O-(C₁-C₆)-alkyl, S-(C₁-C₆)-alkyl, SO-(C₁-C₆)-alkyl, SO₂-(C₁-C₆)-alkyl, SO₂-NH₂, SO₂-NH(C₁-C₈-alkyl), SO₂-N(C₁-C₈-alkyl)₂, SO₂-NH(C₃-C₈-cycloalkyl), SO₂-N(C₃-C₈-cycloalkyl)₂, (CH₂)_m-SO₂-NH₂, (CH₂)_m-SO₂-NH-(C₁-C₆)-alkyl, (CH₂)_m-SO₂-N((C₁-C₆)-alkyl)₂, where m can be 1-6, SO₂-N(=CH-N(CH₃)₂), (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl, COOH, COO(C₁-C₆)-alkyl, COO(C₃-C₆)-cycloalkyl, CONH₂, CONH(C₁-C₆)-alkyl, CON[(C₁-C₆)-alkyl]₂, CONH(C₃-C₆)-cycloalkyl, NH₂, NH(C₁-C₆)-alkyl, N(C₁-C₆)-alkyl)₂, NH-CO-(C₁-C₆)-alkyl, NH-CO-phenyl, NH-SO₂-(C₁-C₈-alkyl), N(C₁-C₆-alkyl)-SO₂-(C₁-C₈-alkyl), NH-SO₂-phenyl, where the phenyl ring can be substituted up to two times by F, Cl, CN, OH, (C₁-C₆)-alkyl, O-(C₁-C₆)-alkyl, CF₃, COOH, COO(C₁-C₆)-alkyl or CONH₂;
- pyrrolidin-1-yl, morpholin-1-yl, piperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-1-yl, (CH₂)_p-phenyl, O-(CH₂)_p-phenyl, S-(CH₂)_p-phenyl or SO₂-(CH₂)_p-phenyl, where p can be 0-3;
- R9 is (CH₂)_m-aryl, where m can be 0-6 and aryl can be phenyl, naphthyl, biphenyl, thienyl or pyridyl and the aryl moiety can be substituted up to two times by F, Cl, Br, OH, CF₃, NO₂, CN, OCF₃, O-(C₁-C₆)-alkyl, S-(C₁-C₆)-alkyl, SO-(C₁-C₆)-alkyl, SO₂-(C₁-C₆)-alkyl, SO₂-NH₂, SO₂-NH(C₁-C₈-alkyl), SO₂-N(C₁-C₈-alkyl)₂, SO₂-NH(C₃-C₈-cycloalkyl), SO₂-N(C₃-C₈-cycloalkyl)₂, (CH₂)_m-SO₂-NH₂, (CH₂)_m-SO₂-NH-(C₁-C₆)-alkyl, (CH₂)_m-SO₂-N((C₁-C₆)-alkyl)₂, where m can be 1-6, SO₂-N(=CH-N(CH₃)₂), (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl, COOH, COO(C₁-C₆)-alkyl, COO(C₃-C₆)-cycloalkyl, CONH₂, CONH(C₁-C₆)-alkyl, CON[(C₁-C₆)-alkyl]₂, CONH(C₃-C₆)-cycloalkyl, NH₂, NH(C₁-C₆)-alkyl, N(C₁-C₆-alkyl)₂, NH-CO-(C₁-C₆)-alkyl, NH-CO-phenyl, NH-SO₂-(C₁-C₈-alkyl), N(C₁-C₆-alkyl)-SO₂-(C₁-C₈-alkyl), NH-SO₂-phenyl, where the phenyl ring can be substituted up to two times by F, Cl, CN, OH, (C₁-C₆)-alkyl, O-(C₁-C₆)-alkyl, CF₃, COOH, COO(C₁-C₆)-alkyl or CONH₂;

pyrrolidin-1-yl, morpholin-1-yl, piperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-1-yl, (CH₂)_p-phenyl, O-(CH₂)_p-phenyl, S-(CH₂)_p-phenyl or SO₂-(CH₂)_p-phenyl, where p can be 0-3;

5 and its physiologically acceptable salts.

4. A compound of the formula I, as claimed in one or more of claims 1 to 3, wherein

10 Y is a direct bond;

X is CH₂;

15 R₁, R_{1'} independently of one another are H, F, Cl, Br, I, (C₁-C₆)-alkyl;

R₂ is H, (C₁-C₆)-alkyl;

R₃ is H, F;

20 R₄ is (C₈-C₁₆)-cycloalkyl or (CH₂)_n-A-R₈, where n can be 1-6, except for the group -CH₂-O-CH₂-phenyl in which phenyl is unsubstituted;

25 A is O, S;

30 R₈ is (C₅-C₂₄)-alkyl, or (CH₂)_m-aryl, where m can be 0-6 and aryl can be phenyl and the aryl moiety can be substituted up to two times by F, Cl, Br, OH, CF₃, NO₂, CN, OCF₃, O-(C₁-C₆)-alkyl, S-(C₁-C₆)-alkyl, SO-(C₁-C₆)-alkyl, SO₂-(C₁-C₆)-alkyl, SO₂-NH₂, SO₂-NH(C₁-C₈-alkyl), SO₂-N(C₁-C₈-alkyl)₂, SO₂-NH(C₃-C₈-cycloalkyl), SO₂-N(C₃-C₈-cycloalkyl)₂, (CH₂)_m-SO₂-NH₂, (CH₂)_m-SO₂-NH-(C₁-C₆)-alkyl, (CH₂)_m-SO₂-N((C₁-C₆)-alkyl)₂, where m can be 1-6, SO₂-N(=CH-N(CH₃)₂), (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl, COOH, COO(C₁-C₆)-alkyl, COO(C₃-C₆)-cycloalkyl, CONH₂, CONH(C₁-C₆)-alkyl, CON[(C₁-C₆)-alkyl]₂, CONH(C₃-C₆)-cycloalkyl, NH₂, NH(C₁-C₆)-alkyl,

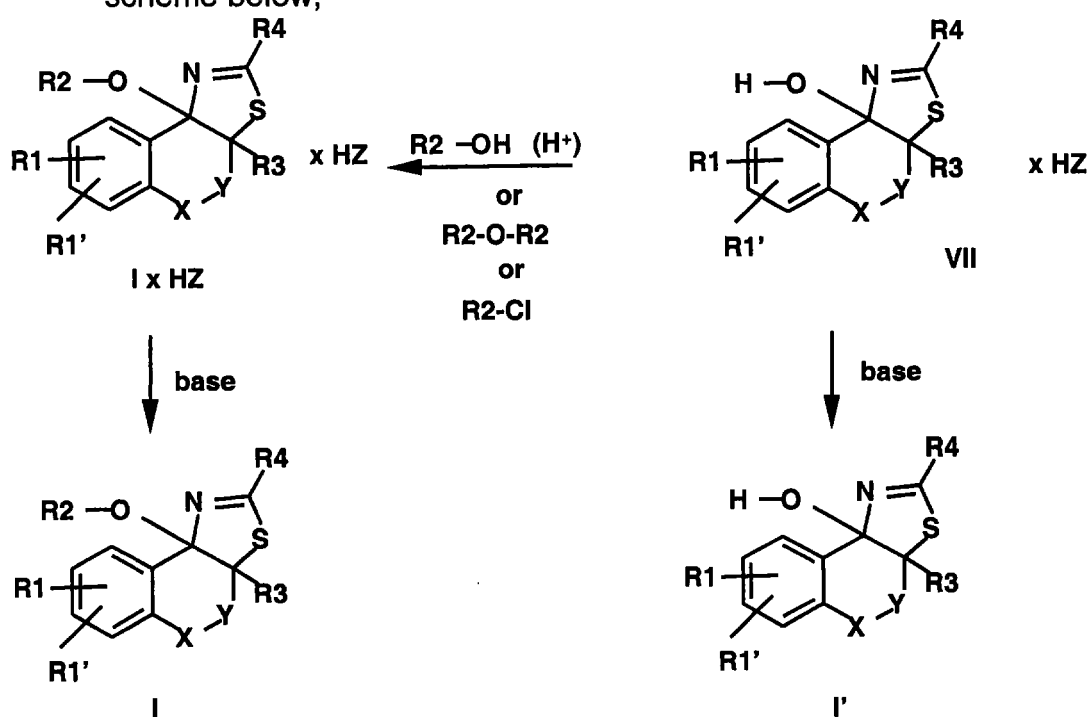
35

5 N(C₁-C₆-alkyl)₂, NH-CO-(C₁-C₆)-alkyl, NH-CO-phenyl, NH-SO₂-(C₁-C₈-alkyl), N(C₁-C₆-alkyl)-SO₂-(C₁-C₈-alkyl), NH-SO₂-phenyl, where the phenyl ring can be substituted up to two times by F, Cl, CN, OH, (C₁-C₆)-alkyl, O-(C₁-C₆)-alkyl, CF₃, COOH, COO(C₁-C₆)-alkyl or CONH₂;
pyrrolidin-1-yl, morpholin-1-yl, piperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-1-yl, (CH₂)_p-phenyl, O-(CH₂)_p-phenyl, S-(CH₂)_p-phenyl or SO₂-(CH₂)_p-phenyl, where p can be 0-3;

10 and its physiologically acceptable salts.

5. A pharmaceutical comprising one or more of the compounds as claimed in one or more of claims 1 to 4.
- 15 6. A pharmaceutical comprising one or more of the compounds as claimed in one or more of claims 1 to 4 and one or more anorectic active preparations.
7. A compound as claimed in one or more of claims 1 to 4 for use as a
20 medicament for the prophylaxis or treatment of obesity.
8. A compound as claimed in one or more of claims 1 to 4 for use as a medicament for the prophylaxis or treatment of type II diabetes.
- 25 9. A compound as claimed in one or more of claims 1 to 4 in combination with at least one further anorectic active compound for use as a medicament for the prophylaxis or treatment of obesity.
- 30 10. A compound as claimed in one or more of claims 1 to 4 in combination with at least one further anorectic active compound for use as a medicament for the prophylaxis or treatment of type II diabetes.
- 35 11. A process for preparing a pharmaceutical comprising one or more compounds as claimed in one or more of claims 1 to 4, which comprises mixing the active compound with a pharmaceutically suitable vehicle and bringing this mixture into a form suitable for administration.

12. The use of the compounds as claimed in one or more of claims 1 to 4 for preparing a medicament for the prophylaxis or treatment of obesity.
- 5 13. The use of the compounds as claimed in one or more of claims 1 to 4 for preparing a medicament for the prophylaxis or treatment of type II diabetes.
- 10 14. A process for preparing the compounds as claimed in one or more of claims 1 to 4, which comprises reacting, according to the formula scheme below,



- 15 a compound of the formula VII in which X, Y, R1, R1', R3 and R4 are as defined under formula I either with a base to give compound I' in which R2 is hydrogen or with one of the compounds R2-OH, R2-O-R2 or R2-Cl in which R2 is as defined under formula I to give a compound of the formula I x HZ, which is then reacted further with a base to give the compound of the formula I.