23 AUG 2004

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

WIPO

PCT

(43) International publication date
30 August 2001 (30.08.2001)

(10) International publication number
WO 01/62745 A1

(51) International patent classification[7]: C07D 277/60, A61K 31/425

(21) International application number: PCT/EP01/01498

(22) International filing date: 12 February 2001 (12.02.2001)

(25) Language of filing: German

(26) Language of publication: German

(30) Data relating to the priority:
100 08 274.2 23 February 2000 (23.02.2000) DE

(71) Applicant: AVENTIS PHARMA DEUTSCHLAND GMBH [DE/DE]; Brüningstrasse 50, 65929 Frankfurt (DE).

(72) Inventors: JAEHNE, Gerhard; Seebachstrasse 22, 65929 Frankfurt (DE). LANG, Hans-Jochen; Rüdesheimer Strasse 7, 65719 Hofheim (DE). GOSSEL, Matthias; Im Lorsbachtal 17a, 65719 Hofheim (DE). BICKEL, Martin; Mittelstedter Weg 3, 61348 Bad Homburg (DE).

(81) Designated states *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated states *(regional)*: ARIPO Patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian Patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European Patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI Patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
- *With the International Search Report.*

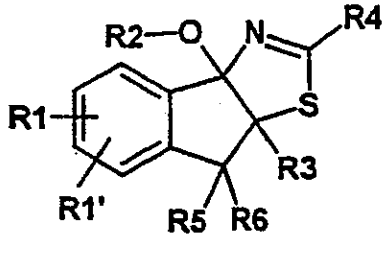
For an explanation of the two-letter codes and the other abbreviations, reference is made to the explanations ("Guidance Notes on Codes and Abbreviations") at the beginning of each regular edition of the PCT Gazette.

As printed

(54) Title: SUBSTITUTED 8, 8A-DIHYDRO-3AH-INDENO[1,2-D]THIAZOLES, A METHOD FOR THEIR PRODUCTION AND THEIR USE AS MEDICAMENTS

(54) Bezeichnung: SUBSTITUIERTE 8,8a-DIHYDRO-3aH-INDENO[1,2-d]THIAZOLE, VERFAHREN ZU IHRER HERSTELLUNG UND IHRE VERWENDUNG ALS ARZNEIMITTEL

WO 01/62745 A1



(I)

(57) Abstract: The invention relates to substituted 8, 8a-dihydro-3aH-indeno[1,2-d]thiazoles and to their physiologically compatible salts and physiologically functional derivatives. The invention relates to compounds of formula (I), wherein the groups have the given meanings, to their physiologically compatible salts and to a method for their production. The compounds are, for example, suitable for use as anorectic agents.

(57) Zusammenfassung: Die Erfindung betrifft substituierte 8,8a-Dihydro-3aH-indeno[1,2-d]thiazole sowie deren physiologisch verträgliche Salze und physiologisch funktionelle Derivate. Es werden Verbindungen der Formel (I), worin die Reste die angegebenen Bedeutungen haben, sowie deren physiologisch verträglichen Salze und Verfahren zu deren Herstellung beschrieben. Die Verbindungen eignen sich z.B. als Anorektika.

Description

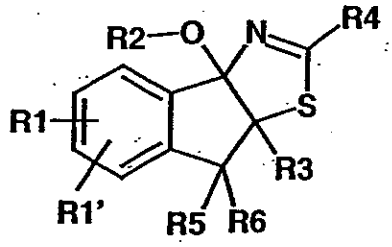
Substituted 8,8a-dihydro-3aH-indeno[1,2-d]thiazoles, processes for their preparation and their use as medicaments

The invention relates to substituted 8,8a-dihydro-3aH-indeno[1,2-d]thiazoles and to 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 object of the invention was to provide further compounds having a therapeutically useful anorectic action.

Accordingly, a first aspect of the present invention provides compounds of the formula I,



I

in which

R1, R1' independently of one another are H, F, Cl, Br, I, CF_3, NO_2, CN, COOH, $COO(C_1-C_6)$-alkyl, $CONH_2$, $CONH(C_1-C_6)$-alkyl, $CON[(C_1-C_6)\text{-alkyl}]_2$, (C_1-C_6)-alkyl, (C_2-C_6)-alkenyl, (C_2-C_6)-alkynyl, $O-(C_1-C_6)$-alkyl, where in the alkyl, alkenyl, or alkynyl radicals one or more, or all hydrogens may be replaced by fluorine, or one hydrogen may be replaced by OH, $OC(O)CH_3$, OC(O)H, $O-CH_2-Ph$, NH_2, $NH-CO-CH_3$ or $N(COOCH_2Ph)_2$;

are SO_2-NH_2, $SO_2NH(C_1$-$C_6)$-alkyl, $SO_2N[(C_1$-$C_6)$-alkyl$]_2$, S-$(C_1$-$C_6)$-alkyl, S-$(CH_2)_n$-phenyl, SO-$(C_1$-$C_6)$-alkyl, SO-$(CH_2)_n$-phenyl, SO_2-$(C_1$-$C_6)$-alkyl, SO_2-$(CH_2)_n$-phenyl, 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, O-$(C_1$-$C_6)$-alkyl, $(C_1$-$C_6)$-alkyl, NH_2;

are NH_2, NH-$(C_1$-$C_6)$-alkyl, $N[(C_1$-$C_6)$-alkyl$]_2$, $NH(C_1$-$C_7)$-acyl, phenyl, biphenylyl, O-$(CH_2)_n$-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 in each case be substituted one to 3 times by F, Cl, Br, I, OH, CF_3, NO_2, CN, OCF_3, O-$(C_1$-$C_6)$-alkyl, $(C_1$-$C_6)$-alkyl, NH_2, $NH(C_1$-$C_6)$-alkyl, $N[(C_1$-$C_6)$-alkyl$]_2$, SO_2-CH_3, COOH, COO-$(C_1$-$C_6)$-alkyl, $CONH_2$;

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

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

are 1,3,4-oxadiazol-2-yl; 2-amino-1,3,4-oxadiazol-5-yl, where the amino function can be mono- or disubstituted by $(C_1$-$C_6)$-alkyl, –C(O)-$(C_1$-$C_6)$-alkyl, -C(O)-(cyclo-C_3-$C_7)$-alkyl, -C(O)-phenyl, -C(O)-NH-$(C_1$-$C_6)$-alkyl, -C(O)-NH-(cyclo-C_3-$C_7)$-alkyl, or -C(O)-NH-aryl, aryl being phenyl, 2-,3- or 4-pyridyl, 2- or 3-thienyl or 2- or 3-furanyl, -C(O)-morpholin-4-yl, -C(O)-piperidin-1-yl, -C(O)-piperazin-4-yl, -C(O)-1-methyl-, 1-benzyl-piperazin-4-yl, $–SO_2$-$(C_1$-$C_6)$-alkyl or $–SO_2$-phenyl, where the phenyl ring can be substituted up to two times by F, Cl, Br, CN, CF_3, OH, OCF_3, $(C_1$-$C_6)$-alkyl, O-$(C_1$-$C_6)$-alkyl, $(CH_2)_n$-phenyl or O-$(CH_2)_n$-phenyl, where n can be 0-6, NH_2, $NH(C_1$-$C_6)$-alkyl, $N[(C_1$-$C_6)$-alkyl$]_2$, SO_2-CH_3, COOH, COO-$(C_1$-$C_6)$-alkyl, $CONH_2$;

R2 is H, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-cycloalkyl, $(CH_2)_n$-phenyl, $(CH_2)_n$-thienyl, $(CH_2)_n$-pyridyl, $(CH_2)_n$-furyl, C(O)-$(C_1$-$C_6)$-alkyl, C(O)-$(C_3$-$C_6)$-cycloalkyl, C(O)-$(CH_2)_n$-phenyl, C(O)-$(CH_2)_n$-thienyl, C(O)-$(CH_2)_n$-pyridyl, C(O)-$(CH_2)_n$-furyl, where n can be 0-5 and in which phenyl,

thienyl, pyridyl and furyl can in each case be substituted up to two times by Cl, F, CN, CF_3, $(C_1$-$C_3)$-alkyl, OH, O-$(C_1$-$C_6)$-alkyl;

R3 is H, $(C_1$-$C_6)$-alkyl, F, Cl, Br, CN, N_3, O-$(C_1$-$C_6)$-alkyl, $(CH_2)_n$-phenyl, $(CH_2)_n$-thienyl, $(CH_2)_n$-pyridyl, $(CH_2)_n$-furyl, where n can be 0-5 and in which phenyl, thienyl, pyridyl and furyl can in each case be substituted up to two times by Cl, F, CN, CF_3, $(C_1$-$C_3)$-alkyl, OH, O-$(C_1$-$C_6)$-alkyl,
is $(C_2$-$C_6)$-alkynyl, $(C_2$-$C_6)$-alkenyl, $OC(O)CH_3$, $(CH_2)_n$-$C(O)O(C_1$-$C_6)$-alkyl, $(CH_2)_n$-C(O)OH, $(CH_2)_n$-$C(O)NH_2$, $(CH_2)_n$-$C(O)NHCH_3$, $(CH_2)_n$-$C(O)N(CH_3)_2$, where n can be 0–3;

R4 is $(C_1$-$C_8)$-alkyl, $(C_3$-$C_7)$-cycloalkyl, $(C_2$-$C_6)$-alkenyl, $(C_2$-$C_6)$-alkynyl, $(C_4$-$C_7)$-cycloalkenyl, where in the alkyl radicals one or more, or all hydrogens can be replaced by fluorine or one hydrogen can be replaced by OH, $OC(O)CH_3$, OC(O)H, O-CH_2-Ph or O-$(C_1$-$C_4)$-alkyl;
is $(CH_2)_n$-pyrrolidin-1-yl, $(CH_2)_n$-piperidin-1-yl, $(CH_2)_n$-morpholin-4-yl, $(CH_2)_n$-piperazin-1-yl, $(CH_2)_n$-N-4-methylpiperazin-1-yl, $(CH_2)_n$-N-4-benzylpiperazin-1-yl, $(CH_2)_n$-phthalimidoyl, where n can be 1-6;
is $(CH_2)_n$-aryl, where n can be 0–6 and aryl is phenyl, biphenylyl, 1- or 2-naphthyl, 2-, 3- or 4-pyridyl, 2- or 3-thienyl, 2- or 3-furyl, 2-, 4- or 5-thiazolyl, 2-, 4- or 5-oxazolyl, 1-pyrazolyl, 3- or 5-isoxazolyl, 2- or 3-pyrrolyl, 2- or 3-pyridazinyl, 2-, 4- or 5-pyrimidinyl, 2-pyrazinyl, 2-(1,3,5-triazinyl), 2- or 5-benzimidazolyl, 2-benzothiazolyl, 1,2,4-triazol-3-yl, 1,2,4-triazol-5-yl, tetrazol-5-yl, indol-3-yl, indol-5-yl or N-methylimidazol-2-, -4- or -5-yl and the aryl radical or heteroaryl radical can be substituted up to two times by F, Cl, Br, OH, CF_3, NO_2, CN, OCF_3, O-$(C_1$-$C_6)$-alkyl, S-$(C_1$-$C_6)$-alkyl, SO-$(C_1$-$C_6)$-alkyl, $(CH_2)_n$-SO_2-$(C_1$-$C_6)$-alkyl, $(CH_2)_n$-SO_2-NH_2, $(CH_2)_n$-SO_2-N(=CH-$N(CH_3)_2$), where n can be 0-6; $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-cycloalkyl, COOH, $COO(C_1$-$C_6)$-alkyl, $COO(C_3$-$C_6)$-cycloalkyl, $CONH_2$, $CONH(C_1$-$C_6)$-alkyl, $CON[(C_1$-$C_6)$-alkyl$]_2$, $CONH(C_3$-$C_6)$-cycloalkyl, NH_2, NH-CO-$(C_1$-$C_6)$-alkyl, NH-CO-phenyl, NH-SO_2-$(C_1$-$C_6)$-alkyl, NH-SO_2-phenyl,

where the phenyl ring can be substituted up to two times by F, Cl, CN, OH, (C_1-C_6)-alkyl, O-(C_1-C_6)-alkyl, CF_3, COOH, COO(C_1-C_6)-alkyl or $CONH_2$; pyrrolidin-1-yl, morpholin-1-yl, piperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-1-yl, $(CH_2)_n$-phenyl, O-$(CH_2)_n$-phenyl, S-$(CH_2)_n$-phenyl, SO_2-$(CH_2)_n$-phenyl, where n can be 0-3;

is $(CH_2)_n$-A-R8, where n can be 1-6;

A is O, NH, N-(C_1-C_6)-alkyl, NCHO, N(CO-CH_3), S, SO, SO_2;

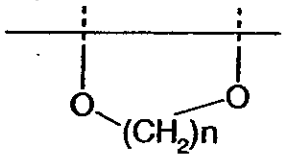
R8 is (C_1-C_8)-alkyl, (C_3-C_8)-cycloalkyl, where in the alkyl radicals one or more hydrogens can be replaced by fluorine or one hydrogen can be replaced by OH, $OC(O)CH_3$, OC(O)H, O-CH_2-Ph or O-(C_1-C_4)-alkyl; is $(CH_2)_m$-aryl, where m can be 0-6 and aryl can be phenyl, thienyl or pyridyl and the aryl moiety can be substituted up to two times by F, Cl, Br, OH, CF_3, NO_2, CN, OCF_3, O-(C_1-C_6)-alkyl, S-(C_1-C_6)-alkyl, SO-(C_1-C_6)-alkyl, $(CH_2)_n$ -SO_2-(C_1-C_6)-alkyl, $(CH_2)_n$-SO_2-NH_2, $(CH_2)_n$-SO_2-N(=CH-N$(CH_3)_2$), $(CH_2)_n$-SO_2-NH(C_1-C_8)-alkyl, $(CH_2)_n$-SO_2-N[(C_1-C_8)-alkyl]$_2$, $(CH_2)_n$-SO_2-NH(C_3-C_8)-cycloalkyl, $(CH_2)_n$-SO_2-N[(C_3-C_8)-cycloalkyl$_2$], where n can be 0-6; (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl, COOH, COO(C_1-C_6)-alkyl, COO(C_3-C_6)-cycloalkyl, $CONH_2$, CONH(C_1-C_6)-alkyl, CON[(C_1-C_6)-alkyl]$_2$, CONH(C_3-C_6)-cycloalkyl, NH_2, NH(C_1-C_6)-alkyl, N[(C_1-C_6)-alkyl]$_2$, NH-CO-(C_1-C_6)-alkyl, NH-CO-phenyl, NH-SO_2-phenyl, where the phenyl ring can be substituted up to two times by F, Cl, CN, OH, (C_1-C_6)-alkyl, O-(C_1-C_6)-alkyl, CF_3, COOH, COO(C_1-C_6)-alkyl or $CONH_2$; NH-SO_2-(C_1-C_8)-alkyl, N(C_1-C_6)-alkyl-SO_2-(C_1-C_8)-alkyl, pyrrolidin-1-yl, morpholin-1-yl, piperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-1-yl, $(CH_2)_p$-phenyl, O-$(CH_2)_p$-phenyl, S-$(CH_2)_p$-phenyl or SO_2-$(CH_2)_p$-phenyl, where p can be 0-3;

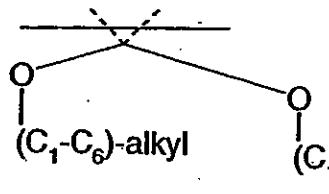
R5 is H;

23 AUG 2004

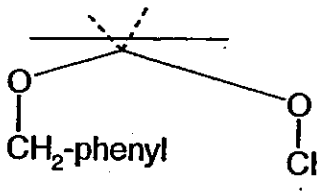
R6 is Cl, Br, OH, O-(C_1-C_6)-alkyl, O-(CH_2)$_n$-aryl, where n can be 0-6 and aryl can be phenyl, 2-,3- or 4-pyridyl or 2- or 3-thienyl; O-C(O)-H, O-C(O)-(C_1-C_6)-alkyl, O-C(O)-(C_3-C_8)-cycloalkyl, O-C(O)-aryl, where aryl can be phenyl, pyridyl, thienyl or furanyl; O-alpha- or -beta-glucuronic acid, SH, S-(C_1-C_6)-alkyl, S-(CH_2)$_n$-phenyl, where n is 0-6; S-C(O)-(C_1-C_6)-alkyl, S-C(O)-(C_3-C_8)-cycloalkyl, S-C(O)-phenyl; SO-(C_1-C_6)-alkyl, SO-(CH_2)$_n$-phenyl, where n can be 0-6; SO_2-(C_1-C_6)-alkyl, SO_2-(CH_2)$_n$-phenyl, where n can be 0-6; NH_2, NH-(C_1-C_6)-alkyl, NH-(C_3-C_7)-cycloalkyl, N[(C_1-C_6)-alkyl]$_2$, morpholin-4-yl, pyrrolidin-1-yl, piperidin-1-yl, piperazin-1-yl, 1-methylpiperazin-4-yl, 1-benzylpiperazin-4-yl, NH-phenyl, NH-CH_2-phenyl, NH-C(O)-(C_1-C_6)-alkyl, NH-C(O)-phenyl

or

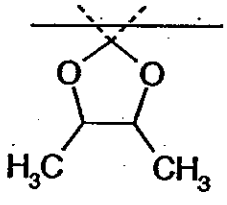
R5 and R6 together form =O, , where n is 2-6,



,



,



; =NOH

and their physiologically acceptable salts and physiologically functional derivatives.

Preference may be given to compounds of the formula in which

R1, R1' independently of one another may be H, F, Cl, Br, I CF_3 NO_2 CN, COOH, $COO(C_1-C_6)$-alkyl, $CONH_2$, $CONH(C_1-C_6)$-alkyl, $CON[(C_1-C_6)\text{-alkyl}]_2$, (C_1-C_6)-alkyl, (C_2-C_6)-alkenyl, (C_2-C_6)-alkynyl, $O-(C_1-C_6)$-alkyl, where in the alkyl radicals one or more, or all hydrogens can be replaced by fluorine, or one hydrogen can be replaced by OH, $OC(O)CH_3$, OC(O)H, $O-CH_2-Ph$, NH_2, $NH-CO-CH_3$ or $N(COOCH_2Ph)_2$;

are SO_2-NH_2, $SO_2NH(C_1-C_6)$-alkyl, $SO_2N[(C_1-C_6)\text{-alkyl}]_2$, $S-(C_1-C_6)$-alkyl, $S-(CH_2)_n$-phenyl, $SO-(C_1-C_6)$-alkyl, $SO-(CH_2)_n$-phenyl, $SO_2-(C_1-C_6)$-alkyl, $SO_2-(CH_2)_n$-phenyl, 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, $O-(C_1-C_6)$-alkyl, (C_1-C_6)-alkyl, NH_2;

may be NH_2 $NH-(C_1-C_6)$-alkyl, $N[(C_1-C_6)\text{-alkyl}]_2$, $NH(C_1-C_7)$-acyl, phenyl, biphenylyl, $O-(CH_2)_n$-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, biphenylyl, naphthyl, pyridyl, furanyl or thienyl rings can in each case be substituted one to 3 times by F, Cl, Br, I, OH, CF_3, NO_2, CN, OCF_3, $O-(C_1-C_6)$-alkyl, (C_1-C_6)-alkyl, NH_2, $NH(C_1-C_6)$-alkyl, $N[(C_1-C_6)\text{-alkyl}]_2$, SO_2-CH_3, COOH, $COO-(C_1-C_6)$-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;
tetrazol-5-yl, where the tetrazole ring can be substituted in the 1- or 2-position by methyl or benzyl;

R2 may be H, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl, $(CH_2)_n$-phenyl, $(CH_2)_n$-thienyl, $(CH_2)_n$-pyridyl, $(CH_2)_n$-furyl, $C(O)-(C_1-C_6)$-alkyl, $C(O)-(C_3-C_6)$-cycloalkyl, $C(O)-(CH_2)_n$-phenyl, $C(O)-(CH_2)_n$-thienyl, $C(O)-(CH_2)_n$-pyridyl, $C(O)-(CH_2)_n$-furyl, where n can be 0-5 and in which phenyl, thienyl, pyridyl and furyl can in each case be substituted up to two times by Cl, F, CN, CF_3, (C_1-C_3)-alkyl, OH, $O-(C_1-C_6)$-alkyl;

R3 may be H, (C_1-C_6)-alkyl, F, Cl, Br, CN, N_3, O-(C_1-C_6)-alkyl, $(CH_2)_n$-phenyl, $(CH_2)_n$-thienyl, $(CH_2)_n$-pyridyl, $(CH_2)_n$-furyl, where n can be 0-5 and in which phenyl, thienyl, pyridyl and furyl can in each case be substituted up to two times by Cl, F, CN, CF_3, (C_1-C_3)-alkyl, OH, O-(C_1-C_6)-alkyl,
is (C_2-C_6)-alkynyl, (C_2-C_6)-alkenyl, $OC(O)CH_3$, $(CH_2)_n$-$C(O)O(C_1-C_6)$-alkyl, $(CH_2)_n$-C(O)OH, $(CH_2)_n$-$C(O)NH_2$, $(CH_2)_n$-$C(O)NHCH_3$, $(CH_2)_n$-$C(O)N(CH_3)_2$, where n can be 0–3;

R4 may be (C_1-C_8)-alkyl, (C_3-C_7)-cycloalkyl, (C_2-C_6)-alkenyl, (C_2-C_6)-alkynyl, (C_4-C_7)-cycloalkenyl, where in the alkyl radicals one or more, or all hydrogens can be replaced by fluorine or one hydrogen can be replaced by OH, $OC(O)CH_3$, OC(O)H, O-CH_2-Ph or O-(C_1-C_4)-alkyl;
is $(CH_2)_n$-pyrrolidin-1-yl, $(CH_2)_n$-piperidin-1-yl, $(CH_2)_n$-morpholin-4-yl, $(CH_2)_n$-piperazin-1-yl, $(CH_2)_n$-N-4-methylpiperazin-1-yl, $(CH_2)_n$-N-4-benzylpiperazin-1-yl, $(CH_2)_n$-phthalimidoyl, where n can be 1-6;
is $(CH_2)_n$-aryl, where n can be 0–6 and aryl can be phenyl, 1- or 2-naphthyl, 2-, 3- or 4-pyridyl, 2- or 3-thienyl and the aryl radical or heteroaryl radical can be substituted up to two times by F, Cl, Br, OH, CF_3, O-(C_1-C_6)-alkyl, $(CH_2)_n$-SO_2-(C_1-C_6)-alkyl, $(CH_2)_n$-SO_2-NH_2, $(CH_2)_n$-SO_2-N(=CH-$N(CH_3)_2$), where n can be 0-6; NH-SO_2-(C_1-C_6)-alkyl, NH-SO_2-phenyl, where the phenyl ring can be substituted up to two times by F, Cl, CN, OH, (C_1-C_6)-alkyl, O-(C_1-C_6)-alkyl, CF_3, COOH, $COO(C_1-C_6)$-alkyl or $CONH_2$;
(C_1-C_6)-alkyl, COOH, $COO(C_1-C_6)$-alkyl or $CONH_2$;
is $(CH_2)_n$-A-R8, where n can be 1-6;

A may be O, NH, (C_1-C_6)-alkyl, SO_2;

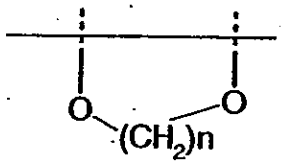
R8 may be (C_1-C_8)-alkyl, (C_3-C_8)-cycloalkyl, where in the alkyl radicals one or more hydrogens can be replaced by fluorine or one hydrogen can be replaced by OH, $OC(O)CH_3$, OC(O)H, O-CH_2-Ph or O-(C_1-C_4)-alkyl;

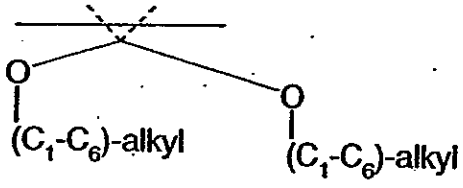
is $(CH_2)_m$-aryl, where m can be 0-6 and aryl can be phenyl, thienyl or pyridyl and the aryl moiety can be substituted up to two times by F, Cl, Br, OH, CF_3, O-$(C_1$-$C_6)$-alkyl, $(CH_2)_n$-SO_2-$(C_1$-$C_6)$-alkyl, $(CH_2)_n$-SO_2-NH_2, $(CH_2)_n$-SO_2-N(=CH-N$(CH_3)_2$), where n can be 0-6; NH-SO_2-$(C_1$-$C_6)$-alkyl, NH-SO_2-phenyl, where the phenyl ring can be substituted up to two times by F, Cl, CN, OH, $(C_1$-$C_6)$-alkyl, O-$(C_1$-$C_6)$-alkyl, CF_3, COOH, COO$(C_1$-$C_6)$-alkyl, $CONH_2$, where n can be 0-6; COOH, COO$(C_1$-$C_6)$-alkyl, or $CONH_2$;

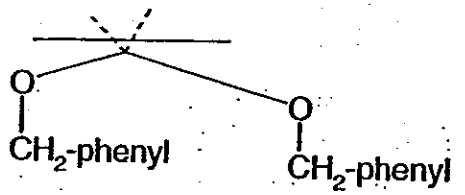
R5 may be H;

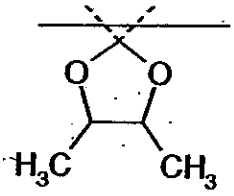
R6 may be Cl, Br, OH, O-$(C_1$-$C_6)$-alkyl, O-$(CH_2)_n$-aryl, where n can be 0-6 and aryl can be phenyl, 2-, 3- or 4-pyridyl or 2- or 3-thienyl; O-C(O)-H, O-C(O)-$(C_1$-$C_6)$-alkyl, O-C(O)-$(C_3$-$C_8)$-cycloalkyl, O-C(O)-aryl, where aryl can be phenyl, pyridyl, thienyl or furanyl; O-alpha- or -beta-glucuronic acid, SH, S-$(C_1$-$C_6)$-alkyl, S-$(CH_2)_n$-phenyl, where n can be 0-6; S-C(O)-$(C_1$-$C_6)$-alkyl, S-C(O)-$(C_3$-$C_8)$-cycloalkyl, S-C(O)-phenyl; SO-$(C_1$-$C_6)$-alkyl, SO-$(CH_2)_n$-phenyl, where n can be 0-6; SO_2-$(C_1$-$C_6)$-alkyl, SO_2-$(CH_2)_n$-phenyl, where n can be 0-6; NH_2, NH-$(C_1$-$C_6)$-alkyl, NH-$(C_3$-$C_7)$-cycloalkyl, N[$(C_1$-$C_6)$-alkyl$]_2$, morpholin-4-yl, pyrrolidin-1-yl, piperidin-1-yl, piperazin-1-yl, 1-methylpiperazin-4-yl, 1-benzylpiperazin-4-yl, NH-phenyl, NH-CH_2-phenyl, NH-C(O)-$(C_1$-$C_6)$-alkyl, NH-C(O)-phenyl

or

R5 and R6 together form =O,  , where n is 2-6,





 ; =NOH

and their physiologically acceptable salts and physiologically functional derivatives.

An embodiment may provide compounds of the formula I in which

R1, R1' independently of one another may be H, F, Cl, Br, -OH, O-(C_1-C_6)-alkyl, (C_1-C_6)-alkyl, where in the alkyl radicals one hydrogen can be replaced by OH;

R2 may be H, (C_1-C_6)-alkyl, C(O)-(C_1-C_6)-alkyl;

R3 may be Cl, Br, $(CH_2)_n$-COO(C_1-C_6)-alkyl, $(CH_2)_n$-COOH, $(CH_2)_n$-$CONH_2$, where n can be 0 or 1;

R4 may be (C_1-C_4)-alkyl or (C_3-C_6)-cycloalkyl, where in the alkyl radicals one hydrogen can be replaced by OH;
$(CH_2)_n$-aryl, where n can be 0–6 and aryl can be phenyl, 1- or 2-naphthyl, 2-, 3- or 4-pyridyl, 2- or 3-thienyl and the aryl radical or

heteroaryl radical can be substituted up to two times by F, Cl, Br, OH, CF_3, O-(C_1-C_6)-alkyl, SO_2-(C_1-C_6)-alkyl, $(CH_2)_n$-SO_2-NH_2, where n can be 0-6; (C_1-C_6)-alkyl, COOH, $COO(C_1$-$C_6)$-alkyl or $CONH_2$;

$(CH_2)_n$-A-R8, where n can be 1-6;

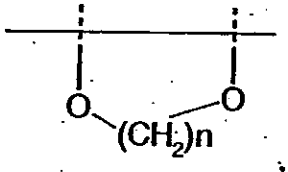
A may be O, SO_2;

R8 may be (C_1-C_8)-alkyl, (C_3-C_8)-cycloalkyl, where in the alkyl radicals one hydrogen can be replaced by OH;
$(CH_2)_m$-aryl, where m can be 0-6 and aryl can be phenyl or thienyl and the aryl moiety can be substituted up to two times by F, Cl, Br, OH, CF_3, O-(C_1-C_6)-alkyl, SO_2-(C_1-C_6)-alkyl, SO_2-NH_2, COOH, $COO(C_1$-$C_6)$-alkyl or $CONH_2$;

R5 may be H;

R6 may be OH, O-(C_1-C_6)-alkyl, where n can be 0-6;
O-C(O)-(C_1-C_6)-alkyl, O-C(O)-aryl, where aryl can be phenyl or thienyl;
O-alpha or -beta-glucuronic acid;
SO_2-(C_1-C_6)-alkyl, SO_2-$(CH_2)_n$-phenyl, where phenyl can be 0-6;
NH_2, morpholin-4-yl, NH-C(O)-(C_1-C_6)-alkyl, NH-C(O)-phenyl

or

R5 and R6 together form =O or , where n can be 2-6,

and their physiologically acceptable salts.

A second aspect of the present invention provides a medicament, comprising one or more compounds as defined above.

A third aspect of the present invention provides a medicament, comprising one or more compounds as defined above and one or more anorectics.

A fourth aspect of the present invention provides a compound defined above for use as a medicament for the prophylaxis or treatment of obesity.

A fifth aspect of the present invention provides a compound as defined above for use as a medicament for the prophylaxis or treatment of type II diabetes.

A sixth aspect of the present invention provides a compound as defined above in combination with at least one further anorectic for use as a medicament for the prophylaxis or treatment of obesity.

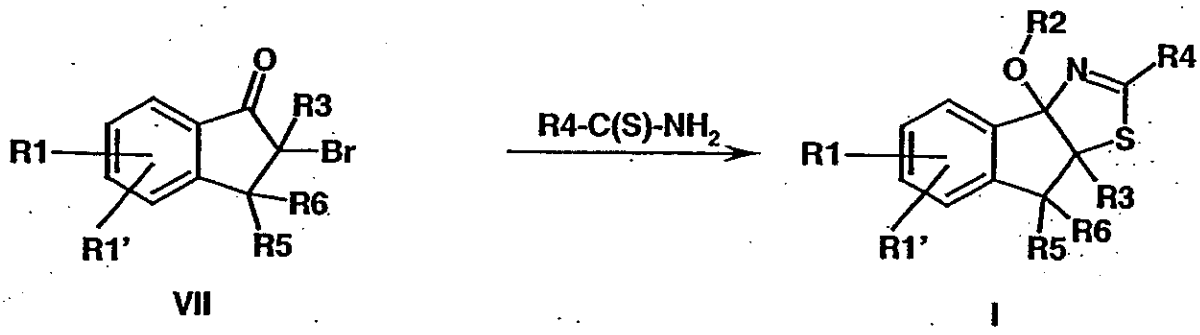
A seventh aspect of the present invention provides a compound as defined above in combination with at least one further anorectic for use as a medicament for the prophylaxis or treatment of type II diabetes.

An eighth aspect of the present invention provides a process for preparing a medicament comprising one or more of the compounds as defined above, which comprises mixing the active compound with a pharmaceutically suitable excipient and bringing this mixture into a form suitable for administration.

A ninth aspect of the present invention provides the use of the compounds as defined above for preparing a medicament for the prophylaxis or treatment of obesity.

A tenth aspect of the present invention provides the use of the compounds as defined above for preparing a medicament for the prophylaxis or treatment of type II diabetes.

An eleventh aspect of the present invention provides a process for preparing compounds as defined above, which comprises reacting, according to the equation below,



VII I

a compound of the formula VII in which the radicals are as defined for formula I with a thioamide of the formula R4-C(S)-NH_2, in which R4 is as defined for formula I to give compounds of the formula I in which R2 is hydrogen and, if appropriate, derivatizing these compounds further at the R2 position such that the other radicals R2 given to formula I are formed.

Embodiments provide compounds of the formula I, in the form of their racemates, racemic mixtures and pure enantiomers, and to their diastereomers and mixtures thereof.

The alkyl, alkenyl and alkynyl radicals in the substituents R1, R1', R2, R3, R4, R6, R8 and A can be either straight-chain or branched.

On account of their higher water solubility, pharmaceutically acceptable salts may be particularly suitable for medicinal applications compared with the starting materials or base compounds. These salts must have a pharmaceutically acceptable anion or cation. Suitable pharmaceutically acceptable acid addition salts of the compounds may be salts of inorganic acids, such as hydrochloric acid, hydrobromic acid, phosphoric acid, metaphosphoric acid, nitric acid, sulfonic acid and sulfuric acid, and of organic acids, such as, for example, acetic acid, benzenesulfonic acid, benzoic acid, citric acid, ethanesulfonic acid, fumaric acid, gluconic acid, glycolic acid, isethionic acid, lactic acid, lactobionic acid, maleic acid, malic acid, methanesulfonic acid, succinic acid, p-toluenesulfonic acid, tartaric acid and trifluoroacetic acid. For medicinal purposes, the chlorine salt may be particularly preferred. Suitable pharmaceutically acceptable basic salts may be ammonium salts, alkali metal salts (such as sodium salts and potassium salts) and alkaline earth metal salts (such as magnesium salts and calcium salts).

Salts having a pharmaceutically unacceptable anion may be likewise included as useful intermediates for the production or purification of pharmaceutically acceptable salts and/or for use in nontherapeutic, for example in-vitro, applications.

The term "physiologically functional derivative" used here may relate to any physiologically acceptable derivative of a compound of the formula I, for example an ester, which on administration to a mammal, such as, for example, man, may be able (directly or indirectly) to form a compound of the formula I or an active metabolite thereof.

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

The compounds can also be present in various polymorphic forms, for example as amorphous and crystalline polymorphic forms. All polymorphic forms of the compounds may be provided.

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

The amount of a compound according to formula (I) which may be necessary in order to achieve the desired biological effect may be dependent on a number of factors, for example the specific compound selected, the intended use, the manner of administration and the clinical condition of the patient. In general, the daily dose may be in the range from 0.3 mg to 100 mg (typically from 3 mg to 50 mg) per day per kilogram of bodyweight, for example 3-10 mg/kg/day. An intravenous dose can be, for example, in the range from 0.3 mg to 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 injection can contain, for example, from 1 mg to 100 mg, and orally administrable individual dose formulations, such as, for example, tablets or capsules, can contain, for example, from 1.0 to 1 000 mg, typically from 10 to 600 mg. In the case of pharmaceutically acceptable salts, the abovementioned weight details may 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) can be used themselves as the compound, but they may be preferably present in the form of a pharmaceutical composition with a tolerable excipient. The excipient

must of course be tolerable, in the sense that it may be compatible with the other constituents of the composition and may not be harmful to the patient's health. The excipient can be a solid or a liquid or both and may be 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 can be prepared by one of the known pharmaceutical methods, which essentially consist in mixing the constituents with pharmacologically acceptable excipients and/or auxiliaries.

Pharmaceutical compositions according to one embodiment may be 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 may also be included in the scope of the invention. Acid-resistant and enteric formulations may be preferred. Suitable enteric coatings may 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 may contain a certain amount of the compound according to formula (I); as powders or granules; as 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 may include a step in which the active compound and the excipient (which can consist of one or more additional constituents) may be brought into contact. In general, the compositions may be prepared by uniform and homogeneous mixing of the active compound compound with a liquid and/or finely divided solid excipient, after which the product , if necessary, may be 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 may be suitable for peroral (sublingual) administration may include lozenges which may contain a compound according to formula (I) with a flavoring, customarily sucrose and gum arabic or tragacanth, and pastilles which may include the compound in an inert base such as gelatin and glycerol or sucrose and gum arabic.

Suitable pharmaceutical compositions for parenteral administration may preferably include sterile aqueous preparations of a compound according to formula (I), which may preferably isotonic with the blood of the intended recipient. These preparations may preferably be 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 may contain from 0.1 to 5% by weight of the active compound.

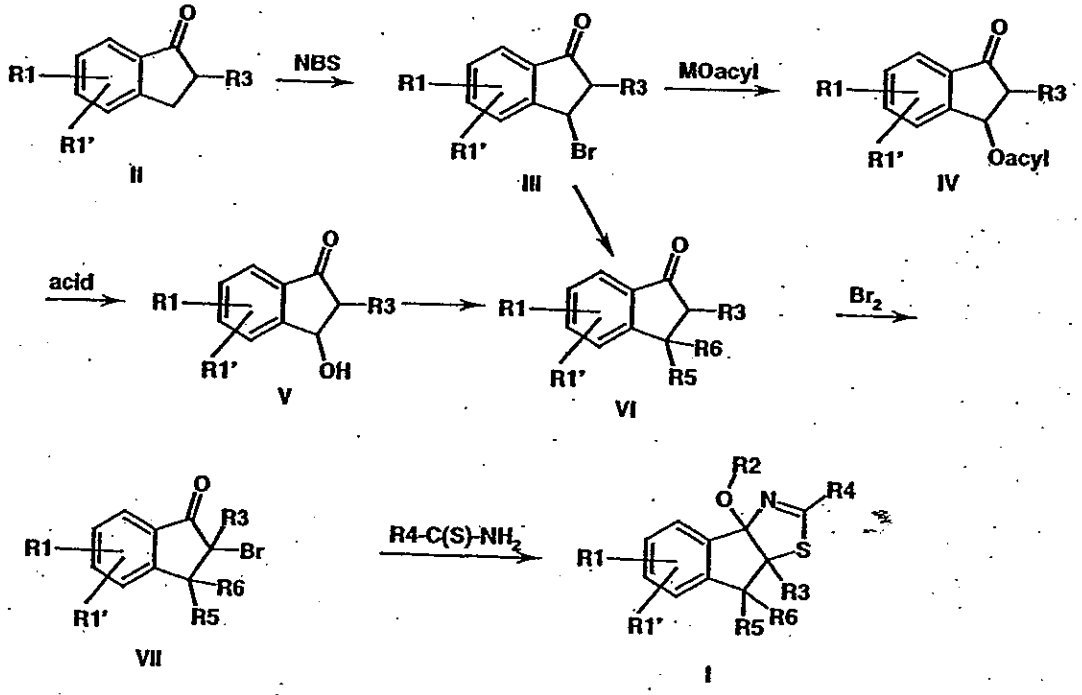
Suitable pharmaceutical compositions for rectal administration may preferably be present as individual dose suppositories. These can be prepared by mixing a compound according to formula (I) with one or more conventional solid excipients, for example cocoa butter, and shaping the resulting mixture.

Suitable pharmaceutical compositions for topical application to the skin may preferably be present as ointment, cream, lotion, paste, spray, aerosol or oil. Excipients which can be used are petroleum jelly, lanolin, polyethylene glycols, alcohols and combinations of two or more of these substances. The active

compound may in general be present in a concentration of from 0.1 to 15% by weight of the composition, for example of from 0.5 to 2%.

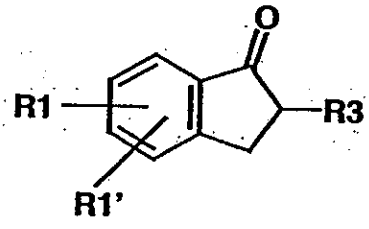
Transdermal administration may also be possible. Suitable pharmaceutical compositions for transdermal administration can be present as individual patches which are suitable for long–term close contact with the epidermis of the patient. Such patches may suitably contain the active compound in an optionally buffered aqueous solution, dissolved and/or dispersed in an adhesive or dispersed in a polymer. A suitable active compound concentration may be from about 1% to 35%, preferably from 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).

Another embodiment may furthermore provide a process for the preparation of the compounds of the formula I, which may comprise obtaining the compounds of the formula I in such a way that the procedure may be according to the following reaction scheme:



To this end, compounds of the formula II,

23 AUG 2004



Formula II

in which R1, R1' and R3' may be defined above, may be converted into a compound of the formula III using N-bromosuccinimide.

The compounds of the formula III may react further with metal salts of organic acids (MOacyl), such as, for example, silver acetate, into compounds of the formula IV.

It may also be possible to convert compounds of the formula III by nucleophilic

R6 may be defined above.

Compounds of the formula IV can be converted into compounds of the formula V, for example by acid hydrolysis.

Under standard conditions, the compounds of the formulae V and VI can be converted by reaction with bromine into the corresponding alpha-bromoketones of the formula VII, in which, for example, R5 can be hydrogen and R6 can be OH.

Reaction of the thioamides of the formula R4-C(S)-NH_2, in which R4 may be as defined above, with compounds of the formula VII which may give compounds of the formula I in which R2 may be hydrogen. Using standard methods, these compounds can be converted into compounds of the formula I in which R2 is as described further above.

Suitable inorganic acids for salt formation may be, for example: hydrohalic acids, such as hydrochloric acid and hydrobromic acid, and also sulfuric acid, phosphoric acid and amidosulfonic acid.

Organic acids which may be suitable for salt formation may be, 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-1,2,3-oxathiazin-4(3H)-one 2,2-dioxide.

The procedure described above may advantageously be carried out such that the compounds of the formula VII may react with the thioamides R4-C(S)-NH_2 in a molar ratio of from 1:1 to 1:1.5. The reaction may be advantageously carried out in an inert solvent, for example in polar organic solvents, such as dimethylformamide, dimethylacetamide, N-methyl-2-pyrrolidone, dimethyl sulfoxide, dioxane, tetrahydrofuran, acetonitrile, nitromethane or diethylene glycol dimethyl ether. Particularly advantageous solvents, however, may have been 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 with solvents which, taken per se, may be 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 carbon tetrachloride, acetone with chloroform, dichloromethane or 1,2-dichloroethane, can also be used, where the more polar solvent in each case should expediently be used in an excess. The reactants can be suspended or dissolved in the respective reaction medium. In principle, the reactants can also be reacted in the absence of a solvent, in particular if the respective thioamide may have a melting point which may be as low as possible. The reaction may proceed 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 may have generally been found to be particularly favorable.

The reaction time may be largely dependent on the reaction temperature and may be between 2 minutes and 3 days at relatively high and relatively low temperatures,

respectively. In the favorable temperature range, the reaction time may be generally between 5 minutes and 48 hours.

In the course of the reaction, the compounds I may frequently form a poorly soluble deposit in the form of their acid addition salts, expediently a suitable precipitating agent may additionally be subsequently added. Those used may be, for example, hydrocarbons such as benzene, toluene, cyclohexane or heptane or carbon tetrachloride; 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 I 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. Work-up of the reaction mixture can also be carried out such that the reaction mixture may be rendered alkaline by 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 may be purified chromatographically, for example on a silica gel column, after concentration. Suitable eluents 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 may be carried out in the manner last described, an acid addition product of the formula I can be obtained from the pure base of the compound 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 or nitromethane. However, particularly advantageous may be reprecipitation from a solvent such as, for example, dimethylformamide, dimethylacetamide, nitromethane, acetonitrile, preferably methanol or ethanol.

The reaction of the compounds of the formula VII with the thioamides R4-C(S)-NH_2 can also be carried out such that an at least equimolar amount of a base, such as, for example, triethylamine, may be added to the reaction mixture and the resulting free bases of the formula I may then be optionally converted into their acid addition products.

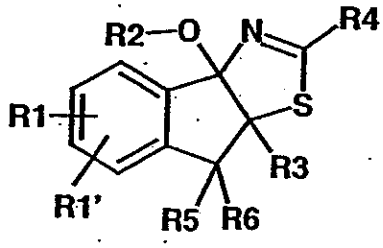
The acid addition products of the compounds of the formula I can be reacted to give the free bases of the formula I by treatment with bases. Suitable bases may be, for example, solutions of inorganic hydroxides, such as lithium hydroxide, sodium hydroxide, potassium hydroxide, calcium hydroxide or barium hydroxide, carbonates or hydrogen carbonates, such as sodium carbonate or potassium carbonate, sodium hydrogen carbonate or potassium hydrogen carbonate, ammonia and amines, such as triethylamine, diisopropylamine, dicyclohexylamine, piperidine, morpholine, methyldicyclohexylamine.

Thioamides of the formula R4-C(S)-NH_2 may be either commercially available or can be obtained, for example, by reaction of the corresponding carboxamide 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 and Lawesson: Bull. Soc. Chim. Belges 87, 229 (1978)], preferably in a mixture of 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 may 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. 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 R4-C(S)-NH_2 can also be obtained by reacting nitriles of the formula R4-CN 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 may be 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-diethyl dithiophosphoric acid in a solvent such as ethyl acetate under acidic, e.g. HCl, conditions at room temperature or with warming.

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

Table 1: Examples



Formula I

Example	R1; R1'	R2	R3	R4	R5	R6	Salt	m.p. [°C]
1	6-Cl; H	H	H	phenyl	H	OH	-	152
2	H; H	H	H	phenyl-2-OH	H	OH	-	110 (decomp.)

The compounds of the formula I may be distinguished by favorable effects on lipid metabolism; in particular, they may be suitable as anorectics. The compounds can be

23 AUG 2004

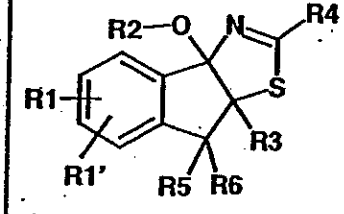
employed on their own or in combination with other anorectically active compounds. Such further anorectically active compounds may be mentioned, for example, in the Rote Liste, chapter 01 under slimming preparations/anorectics. The compounds may be suitable for the prophylaxis and in particular for the treatment of obesity. The compounds may be 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:

The anorectic action was tested on 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 the administration of the preparation. The consumption of evaporated milk was determined half-hourly for 1.5 hours and the general condition of the animals was observed. The measured milk consumption was compared with that of untreated control animals.

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

Compound/Example  Formula	Oral dose [mg/kg]	Number of animals / cumulated milk consumption of the treated animals N / [ml]	Number of animals / cumulated milk consumption of the untreated control animals N / [ml]	Reduction of the cumulated milk consumption in % of the control
Example 1	30	5 / 1.06	5 / 1.54	31%

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

The preparation of some examples is described in detail below; the other compounds of the formula I were obtained in a similar manner:

Example 1 (Compound 1):

6-Chloro-2-phenyl-8,8a-dihydroindeno[1,2-d]thiazole-3a,8-diol:

a) 3-Bromo-5-chloroindan-1-one:

8.33 g (50 mmol) of 5-chloroindan-1-one and 8.9 g (50 mmol) of N-bromosuccinimide were suspended in 175 ml of carbon tetrachloride, admixed with 1 g of benzoyl peroxide and, with stirring, heated under reflux for 3 h. The cooled reaction solution was filtered, extracted 2x with 100 ml of water, dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was dissolved in 120 ml of a hot 1:1 mixture of n-heptane and cyclohexane, boiled with activated carbon and filtered, and the filtrate was concentrated under reduced pressure. This gave 3-bromo-5-chloroindan-1-one of melting point 96-97°C

b) 3-Acetoxy-5-chloroindan-1-one:

4.91 g (20 mmol) of 3-bromo-5-chloroindan-1-one and 3.34 [lacuna] (20 mmol) of silver acetate were suspended in 100 ml of acetic acid and, with stirring, heated under reflux for 5 h. The cooled reaction solution was concentrated under reduced pressure and the residue was purified chromatographically on silica gel using toluene/acetone 10/1. This gave 3-acetoxy-5-chloroindan-1-one of melting point 65-67°C.

c) 5-Chloro-3-hydroxyindan-1-one:

With addition of 50 ml of 3N HCl, 1.98 g (8.8 mmol) of 3-acetoxy-5-chloroindan-1-one were dissolved in 10 ml of acetonitrile. The reaction mixture was stirred at room temperature for 48 h. The solvent acetonitrile was then distilled off under reduced pressure and the precipitated crude product was filtered off and purified chromatographically on silica gel using

toluene/acetone 5/1. The product, 5-chloro-3-hydroxyindan-1-one, had a melting point of 125-128°C.

d) 2-Bromo-5-chloro-3-hydroxyindan-1-one:

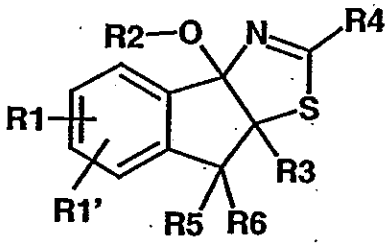
0.69 g (3.78 mmol) of 5-chloro-3-hydroxyindan-1-one was dissolved in 100 ml of diethyl ether. With stirring, 1 drop of bromine was added, and the mixture was stirred until the color had disappeared. The mixture was then cooled to –5°C, and 0.194 ml (3.78 mmol) of bromine in 2 ml of dichloromethane were added dropwise over a period of 30 min. Stirring was then continued for 30 min, 50 ml of water were added and the organic phase was separated off, dried over magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure and the residue was dried under reduced pressure. This gave 2-bromo-5-chloro-3-hydroxyindan-1-one of melting point 118-119°C.

e) 6-Chloro-2-phenyl-8,8a-dihydroindeno[1,2-d]thiazole-3a,8-diol:

0.6 g (2.3 mmol) of 2-bromo-5-chloro-3-hydroxyindan-1-one and 0.473 g (3.45 mmol) of thiobenzamide were dissolved in 5 ml of isopropanol. 0.478 ml (3.45 mmol) of triethylamine was added, and the mixture was then stirred at room temperature for 12 h and subsequently at 50°C for 8 h. The cooled reaction mixture was concentrated under reduced pressure and the residue was purified chromatographically on silica gel using initially n-heptane/ethyl acetate 3/1 and then toluene/acetone 5/1. This gave 6-chloro-2-phenyl-8,8a-dihydroindeno[1,2-d]thiazole-3a,8-diol of melting point 151-153°C (with decomposition).

Patent claims:

1. A compound of the formula I,



I

in which

R1, R1' independently of one another are H, F, Cl, Br, I, CF_3, NO_2, CN, COOH, $COO(C_1-C_6)$-alkyl, $CONH_2$, $CONH(C_1-C_6)$-alkyl, $CON[(C_1-C_6)\text{-alkyl}]_2$, (C_1-C_6)-alkyl, (C_2-C_6)-alkenyl, (C_2-C_6)-alkynyl, $O-(C_1-C_6)$-alkyl, where in the alkyl, alkenyl, or alkynyl radicals one or more, or all hydrogens may be replaced by fluorine, or one hydrogen may be replaced by OH, $OC(O)CH_3$, OC(O)H, $O-CH_2-Ph$, NH_2, $NH-CO-CH_3$ or $N(COOCH_2Ph)_2$;
are SO_2-NH_2, $SO_2NH(C_1-C_6)$-alkyl, $SO_2N[(C_1-C_6)\text{-alkyl}]_2$, $S-(C_1-C_6)$-alkyl, $S-(CH_2)_n$-phenyl, $SO-(C_1-C_6)$-alkyl, $SO-(CH_2)_n$-phenyl, $SO_2-(C_1-C_6)$-alkyl, $SO_2-(CH_2)_n$-phenyl, 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, $O-(C_1-C_6)$-alkyl, (C_1-C_6)-alkyl, NH_2;
are NH_2, $NH-(C_1-C_6)$-alkyl, $N[(C_1-C_6)\text{-alkyl}]_2$, $NH(C_1-C_7)$-acyl, phenyl, biphenylyl, $O-(CH_2)_n$-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 in each case be substituted one to 3 times by F, Cl, Br, I, OH, CF_3, NO_2, CN, OCF_3, $O-(C_1-C_6)$-alkyl, (C_1-C_6)-alkyl, NH_2, $NH(C_1-C_6)$-alkyl, $N[(C_1-C_6)\text{-alkyl}]_2$, SO_2-CH_3, COOH, $COO-(C_1-C_6)$-alkyl, $CONH_2$;

are 1,2,3-triazol-5-yl, where the triazole ring can be substituted in the 1-, 2- or 3-position by methyl or benzyl;
are tetrazol-5-yl, where the tetrazole ring can be substituted in the 1- or 2-position by methyl or benzyl;
are 1,3,4-oxadiazol-2-yl; 2-amino-1,3,4-oxadiazol-5-yl, where the amino function can be mono- or disubstituted by (C_1-C_6)-alkyl, –C(O)-(C_1-C_6)-alkyl, -C(O)-(cyclo-C_3-C_7)-alkyl, -C(O)-phenyl, -C(O)-NH-(C_1-C_6)-alkyl, -C(O)-NH-(cyclo-C_3-C_7)-alkyl, or -C(O)-NH-aryl, aryl being phenyl, 2-,3- or 4-pyridyl, 2- or 3-thienyl or 2- or 3-furanyl, -C(O)-morpholin-4-yl, -C(O)-piperidin-1-yl, -C(O)-piperazin-4-yl, -C(O)-1-methyl-, 1-benzyl-piperazin-4-yl, $–SO_2$-(C_1-C_6)-alkyl or $–SO_2$-phenyl, where the phenyl ring can be substituted up to two times by F, Cl, Br, CN, CF_3, OH, OCF_3, (C_1-C_6)-alkyl, O-(C_1-C_6)-alkyl, $(CH_2)_n$-phenyl or O-$(CH_2)_n$-phenyl, where n can be 0-6, NH_2, NH(C_1-C_6)-alkyl, N[(C_1-C_6)-alkyl]$_2$, SO_2-CH_3, COOH, COO-(C_1-C_6)-alkyl, $CONH_2$;

R2 is H, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl, $(CH_2)_n$-phenyl, $(CH_2)_n$-thienyl, $(CH_2)_n$-pyridyl, $(CH_2)_n$-furyl, C(O)-(C_1-C_6)-alkyl, C(O)-(C_3-C_6)-cycloalkyl, C(O)-$(CH_2)_n$-phenyl, C(O)-$(CH_2)_n$-thienyl, C(O)-$(CH_2)_n$-pyridyl, C(O)-$(CH_2)_n$-furyl, where n can be 0-5 and in which phenyl, thienyl, pyridyl and furyl can in each case be substituted up to two times by Cl, F, CN, CF_3, (C_1-C_3)-alkyl, OH, O-(C_1-C_6)-alkyl;

R3 is H, (C_1-C_6)-alkyl, F, Cl, Br, CN, N_3, O-(C_1-C_6)-alkyl, $(CH_2)_n$-phenyl, $(CH_2)_n$-thienyl, $(CH_2)_n$-pyridyl, $(CH_2)_n$-furyl, where n can be 0-5 and in which phenyl, thienyl, pyridyl and furyl can in each case be substituted up to two times by Cl, F, CN, CF_3, (C_1-C_3)-alkyl, OH, O-(C_1-C_6)-alkyl,
is (C_2-C_6)-alkynyl, (C_2-C_6)-alkenyl, $OC(O)CH_3$, $(CH_2)_n$-C(O)O(C_1-C_6)-alkyl, $(CH_2)_n$-C(O)OH, $(CH_2)_n$-C(O)NH_2, $(CH_2)_n$-C(O)$NHCH_3$, $(CH_2)_n$-C(O)$N(CH_3)_2$, where n can be 0–3;

R4 is (C_1-C_8)-alkyl, (C_3-C_7)-cycloalkyl, (C_2-C_6)-alkenyl, (C_2-C_6)-alkynyl,

$(C_4$-$C_7)$-cycloalkenyl, where in the alkyl radicals one or more, or all hydrogens can be replaced by fluorine or one hydrogen can be replaced by OH, $OC(O)CH_3$, OC(O)H, O-CH_2-Ph or O-$(C_1$-$C_4)$-alkyl;

is $(CH_2)_n$-pyrrolidin-1-yl, $(CH_2)_n$-piperidin-1-yl, $(CH_2)_n$-morpholin-4-yl, $(CH_2)_n$-piperazin-1-yl, $(CH_2)_n$-N-4-methylpiperazin-1-yl, $(CH_2)_n$-N-4-benzylpiperazin-1-yl, $(CH_2)_n$-phthalimidoyl, where n can be 1-6;

is $(CH_2)_n$-aryl, where n can be 0–6 and aryl is phenyl, biphenylyl, 1- or 2-naphthyl, 2-, 3- or 4-pyridyl, 2- or 3-thienyl, 2- or 3-furyl, 2-, 4- or 5-thiazolyl, 2-, 4- or 5-oxazolyl, 1-pyrazolyl, 3- or 5-isoxazolyl, 2- or 3-pyrrolyl, 2- or 3-pyridazinyl, 2-, 4- or 5-pyrimidinyl, 2-pyrazinyl, 2-(1,3,5-triazinyl), 2- or 5-benzimidazolyl, 2-benzothiazolyl, 1,2,4-triazol-3-yl, 1,2,4-triazol-5-yl, tetrazol-5-yl, indol-3-yl, indol-5-yl or N-methylimidazol-2-, -4- or -5-yl and the aryl radical or heteroaryl radical can be substituted up to two times by F, Cl, Br, OH, CF_3, NO_2, CN, OCF_3, O-$(C_1$-$C_6)$-alkyl, S-$(C_1$-$C_6)$-alkyl, SO-$(C_1$-$C_6)$-alkyl, $(CH_2)_n$-SO_2-$(C_1$-$C_6)$-alkyl, $(CH_2)_n$-SO_2-NH_2, $(CH_2)_n$-SO_2-N(=CH-$N(CH_3)_2$), where n can be 0-6; $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-cycloalkyl, COOH, $COO(C_1$-$C_6)$-alkyl, $COO(C_3$-$C_6)$-cycloalkyl, $CONH_2$, $CONH(C_1$-$C_6)$-alkyl, $CON[(C_1$-$C_6)$-alkyl$]_2$, $CONH(C_3$-$C_6)$-cycloalkyl, NH_2, NH-CO-$(C_1$-$C_6)$-alkyl, NH-CO-phenyl, NH-SO_2-$(C_1$-$C_6)$-alkyl, NH-SO_2-phenyl, where the phenyl ring can be substituted up to two times by F, Cl, CN, OH, $(C_1$-$C_6)$-alkyl, O-$(C_1$-$C_6)$-alkyl, CF_3, COOH, $COO(C_1$-$C_6)$-alkyl or $CONH_2$; pyrrolidin-1-yl, morpholin-1-yl, piperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-1-yl, $(CH_2)_n$-phenyl, O-$(CH_2)_n$-phenyl, S-$(CH_2)_n$-phenyl, SO_2-$(CH_2)_n$-phenyl, where n can be 0-3;

is $(CH_2)_n$-A-R8, where n can be 1-6;

A is O, NH, N-$(C_1$-$C_6)$-alkyl, NCHO, N(CO-CH_3), S, SO, SO_2;

R8 is $(C_1$-$C_8)$-alkyl, $(C_3$-$C_8)$-cycloalkyl, where in the alkyl radicals one or more hydrogens can be replaced by fluorine or one hydrogen can be replaced by OH, $OC(O)CH_3$, OC(O)H, O-CH_2-Ph or O-$(C_1$-$C_4)$-alkyl;

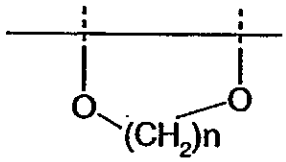
is $(CH_2)_m$-aryl, where m can be 0-6 and aryl can be phenyl, thienyl or pyridyl and the aryl moiety can be substituted up to two times by F, Cl, Br, OH, CF_3, NO_2, CN, OCF_3, O-$(C_1$-$C_6)$-alkyl, S-$(C_1$-$C_6)$-alkyl, SO-$(C_1$-$C_6)$-alkyl, $(CH_2)_n$ -SO_2-$(C_1$-$C_6)$-alkyl, $(CH_2)_n$-SO_2-NH_2, $(CH_2)_n$-SO_2-N(=CH-N$(CH_3)_2$), $(CH_2)_n$-SO_2-NH$(C_1$-$C_8)$-alkyl, $(CH_2)_n$-SO_2-N[$(C_1$-$C_8)$-alkyl]$_2$, $(CH_2)_n$-SO_2-NH$(C_3$-$C_8)$-cycloalkyl, $(CH_2)_n$-SO_2-N[$(C_3$-$C_8)$-cycloalkyl]$_2$, where n can be 0-6; $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-cycloalkyl, COOH, COO$(C_1$-$C_6)$-alkyl, COO$(C_3$-$C_6)$-cycloalkyl, $CONH_2$, CONH$(C_1$-$C_6)$-alkyl, CON[$(C_1$-$C_6)$-alkyl]$_2$, CONH$(C_3$-$C_6)$-cycloalkyl, NH_2, NH$(C_1$-$C_6)$-alkyl, N$(C_1$-$C_6)$-alkyl$_2$, NH-CO-$(C_1$-$C_6)$-alkyl, NH-CO-phenyl, NH-SO_2-phenyl, where the phenyl ring can be substituted up to two times by F, Cl, CN, OH, $(C_1$-$C_6)$-alkyl, O-$(C_1$-$C_6)$-alkyl, CF_3, COOH, COO$(C_1$-$C_6)$-alkyl or $CONH_2$;
NH-SO_2-$(C_1$-$C_8)$-alkyl, N$(C_1$-$C_6)$-alkyl-SO_2-$(C_1$-$C_8)$-alkyl, pyrrolidin-1-yl, morpholin-1-yl, piperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-1-yl, $(CH_2)_p$-phenyl, O-$(CH_2)_p$-phenyl, S-$(CH_2)_p$-phenyl or SO_2-$(CH_2)_p$-phenyl, where p can be 0-3;

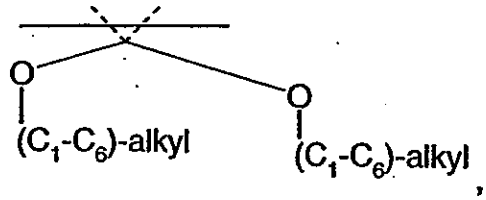
R5 is H;

R6 is Cl, Br, OH, O-$(C_1$-$C_6)$-alkyl, O-$(CH_2)_n$-aryl, where n can be 0-6 and aryl can be phenyl, 2-,3- or 4-pyridyl or 2- or 3-thienyl; O-C(O)-H, O-C(O)-$(C_1$-$C_6)$-alkyl, O-C(O)-$(C_3$-$C_8)$-cycloalkyl, O-C(O)-aryl, where aryl can be phenyl, pyridyl, thienyl or furanyl; O-alpha- or -beta-glucuronic acid, SH, S-$(C_1$-$C_6)$-alkyl, S-$(CH_2)_n$-phenyl, where n is 0-6; S-C(O)-$(C_1$-$C_6)$-alkyl, S-C(O)-$(C_3$-$C_8)$-cycloalkyl, S-C(O)-phenyl; SO-$(C_1$-$C_6)$-alkyl, SO-$(CH_2)_n$-phenyl, where n can be 0-6; SO_2-$(C_1$-$C_6)$-alkyl, SO_2-$(CH_2)_n$-phenyl, where n can be 0-6; NH_2, NH-$(C_1$-$C_6)$-alkyl, NH-$(C_3$-$C_7)$-cycloalkyl, N[$(C_1$-$C_6)$-alkyl]$_2$, morpholin-4-yl, pyrrolidin-1-yl, piperidin-1-yl, piperazin-1-yl, 1-methylpiperazin-4-yl, 1-benzylpiperazin-4-yl, NH-phenyl, NH-CH_2-phenyl, NH-C(O)-$(C_1$-$C_6)$-alkyl, NH-C(O)-phenyl

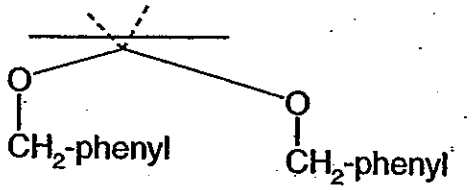
or

23 AUG 2004

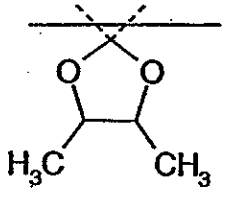
R5 and R6 together form =O,  , where n is 2-6,



,



,



; =NOH

and its physiologically acceptable salts and physiologically functional derivatives.

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

R1, R1' independently of one another are H F, Cl, Br, I CF_3, NO_2, CN, COOH, $COO(C_1-C_6)$-alkyl, $CONH_2$, $CONH(C_1-C_6)$-alkyl, $CON[(C_1-C_6)\text{-alkyl}]_2$, (C_1-C_6)-alkyl, (C_2-C_6)-alkenyl, (C_2-C_6)-alkynyl, $O-(C_1-C_6)$-alkyl, where in the alkyl radicals one or more, or all hydrogens can be replaced by fluorine, or one hydrogen can be replaced by OH, $OC(O)CH_3$, OC(O)H, $O-CH_2-Ph$, NH_2, $NH-CO-CH_3$ or $N(COOCH_2Ph)_2$;
are SO_2-NH_2, $SO_2NH(C_1-C_6)$-alkyl, $SO_2N[(C_1-C_6)\text{-alkyl}]_2$, $S-(C_1-C_6)$-alkyl, $S-(CH_2)_n$-phenyl, $SO-(C_1-C_6)$-alkyl, $SO-(CH_2)_n$-phenyl, $SO_2-(C_1-C_6)$-alkyl, $SO_2-(CH_2)_n$-phenyl, 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, $O-(C_1-C_6)$-alkyl, (C_1-C_6)-alkyl, NH_2;

are NH_2, $NH-(C_1-C_6)$-alkyl, $N[(C_1-C_6)\text{-alkyl}]_2$, $NH(C_1-C_7)$-acyl, phenyl, biphenylyl, $O-(CH_2)_n$-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, biphenylyl, naphthyl, pyridyl, furanyl or thienyl rings can in each case be substituted one to 3 times by F, Cl, Br, I, OH, CF_3, NO_2, CN, OCF_3, O-(C_1-C_6)-alkyl, (C_1-C_6)-alkyl, NH_2, NH(C_1-C_6)-alkyl, N[(C_1-C_6)-alkyl]$_2$, SO_2-CH_3, COOH, COO-(C_1-C_6)-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;
tetrazol-5-yl, where the tetrazole ring can be substituted in the 1- or 2-position by methyl or benzyl;

R2 is H, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl, $(CH_2)_n$-phenyl, $(CH_2)_n$-thienyl, $(CH_2)_n$-pyridyl, $(CH_2)_n$-furyl, C(O)-(C_1-C_6)-alkyl, C(O)-(C_3-C_6)-cycloalkyl, C(O)-$(CH_2)_n$-phenyl, C(O)-$(CH_2)_n$-thienyl, C(O)-$(CH_2)_n$-pyridyl, C(O)-$(CH_2)_n$-furyl, where n can be 0-5 and in which phenyl, thienyl, pyridyl and furyl can in each case be substituted up to two times by Cl, F, CN, CF_3, (C_1-C_3)-alkyl, OH, O-(C_1-C_6)-alkyl;

R3 is H, (C_1-C_6)-alkyl, F, Cl, Br, CN, N_3, O-(C_1-C_6)-alkyl, $(CH_2)_n$-phenyl, $(CH_2)_n$-thienyl, $(CH_2)_n$-pyridyl, $(CH_2)_n$-furyl, where n can be 0-5 and in which phenyl, thienyl, pyridyl and furyl can in each case be substituted up to two times by Cl, F, CN, CF_3, (C_1-C_3)-alkyl, OH, O-(C_1-C_6)-alkyl,
is (C_2-C_6)-alkynyl, (C_2-C_6)-alkenyl, $OC(O)CH_3$, $(CH_2)_n$-C(O)O(C_1-C_6)-alkyl, $(CH_2)_n$-C(O)OH, $(CH_2)_n$-$C(O)NH_2$, $(CH_2)_n$-$C(O)NHCH_3$, $(CH_2)_n$-$C(O)N(CH_3)_2$, where n can be 0–3;

R4 is (C_1-C_8)-alkyl, (C_3-C_7)-cycloalkyl, (C_2-C_6)-alkenyl, (C_2-C_6)-alkynyl, (C_4-C_7)-cycloalkenyl, where in the alkyl radicals one or more, or all hydrogens can be replaced by fluorine or one hydrogen can be replaced by OH, $OC(O)CH_3$, OC(O)H, O-CH_2-Ph or O-(C_1-C_4)-alkyl;
is $(CH_2)_n$-pyrrolidin-1-yl, $(CH_2)_n$-piperidin-1-yl, $(CH_2)_n$-morpholin-4-yl, $(CH_2)_n$-piperazin-1-yl, $(CH_2)_n$-N-4-methylpiperazin-1-yl, $(CH_2)_n$-N-4-benzylpiperazin-1-yl, $(CH_2)_n$-phthalimidoyl, where n can be 1-6;

is $(CH_2)_n$-aryl, where n can be 0–6 and aryl can be phenyl, 1- or 2-naphthyl, 2-, 3- or 4-pyridyl, 2- or 3-thienyl and the aryl radical or heteroaryl radical can be substituted up to two times by F, Cl, Br, OH, CF_3, O-$(C_1$-$C_6)$-alkyl, $(CH_2)_n$-SO_2-$(C_1$-$C_6)$-alkyl, $(CH_2)_n$-SO_2-NH_2, $(CH_2)_n$-SO_2-N(=CH-N$(CH_3)_2$), where n can be 0-6; NH-SO_2-$(C_1$-$C_6)$-alkyl, NH-SO_2-phenyl, where the phenyl ring can be substituted up to two times by F, Cl, CN, OH, $(C_1$-$C_6)$-alkyl, O-$(C_1$-$C_6)$-alkyl, CF_3, COOH, COO$(C_1$-$C_6)$-alkyl or $CONH_2$;
$(C_1$-$C_6)$-alkyl, COOH, COO$(C_1$-$C_6)$-alkyl or $CONH_2$;
is $(CH_2)_n$-A-R8, where n can be 1-6;

A is O, NH, $(C_1$-$C_6)$-alkyl, SO_2;

R8 is $(C_1$-$C_8)$-alkyl, $(C_3$-$C_8)$-cycloalkyl, where in the alkyl radicals one or more hydrogens can be replaced by fluorine or one hydrogen can be replaced by OH, OC(O)CH_3, OC(O)H, O-CH_2-Ph or O-$(C_1$-$C_4)$-alkyl;
is $(CH_2)_m$-aryl, where m can be 0-6 and aryl can be phenyl, thienyl or pyridyl and the aryl moiety can be substituted up to two times by F, Cl, Br, OH, CF_3, O-$(C_1$-$C_6)$-alkyl, $(CH_2)_n$-SO_2-$(C_1$-$C_6)$-alkyl, $(CH_2)_n$-SO_2-NH_2, $(CH_2)_n$-SO_2-N(=CH-N$(CH_3)_2$), where n can be 0-6;
NH-SO_2-$(C_1$-$C_6)$-alkyl, NH-SO_2-phenyl, where the phenyl ring can be substituted up to two times by F, Cl, CN, OH, $(C_1$-$C_6)$-alkyl, O-$(C_1$-$C_6)$-alkyl, CF_3, COOH, COO$(C_1$-$C_6)$-alkyl, $CONH_2$, where n can be 0-6;
COOH, COO$(C_1$-$C_6)$-alkyl, or $CONH_2$;

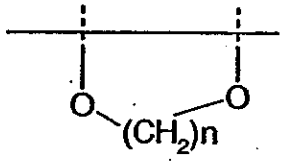
R5 is H;

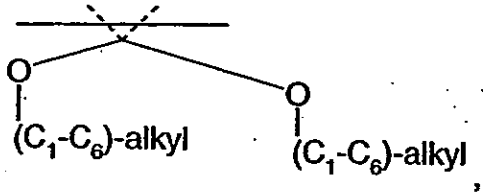
R6 is Cl, Br, OH, O-$(C_1$-$C_6)$-alkyl, O-$(CH_2)_n$-aryl, where n can be 0-6 and aryl can be phenyl, 2-, 3- or 4-pyridyl or 2- or 3-thienyl; O-C(O)-H, O-C(O)-$(C_1$-$C_6)$-alkyl, O-C(O)-$(C_3$-$C_8)$-cycloalkyl, O-C(O)-aryl, where aryl can be phenyl, pyridyl, thienyl or furanyl; O-alpha- or -beta-glucuronic acid, SH, S-$(C_1$-$C_6)$-alkyl, S-$(CH_2)_n$-phenyl, where n can be 0-6; S-C(O)-$(C_1$-$C_6)$-alkyl, S-C(O)-$(C_3$-$C_8)$-cycloalkyl, S-C(O)-phenyl;

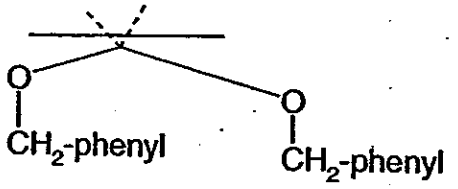
23 AUG 2004

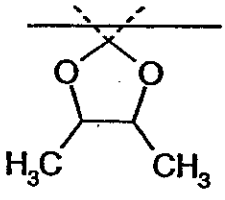
$SO-(C_1-C_6)$-alkyl, $SO-(CH_2)_n$-phenyl, where n can be 0-6; $SO_2-(C_1-C_6)$-alkyl, $SO_2-(CH_2)_n$-phenyl, where n can be 0-6; NH_2, $NH-(C_1-C_6)$-alkyl, $NH-(C_3-C_7)$-cycloalkyl, $N[(C_1-C_6)\text{-alkyl}]_2$, morpholin-4-yl, pyrrolidin-1-yl, piperidin-1-yl, piperazin-1-yl, 1-methylpiperazin-4-yl, 1-benzylpiperazin-4-yl, NH-phenyl, $NH-CH_2$-phenyl, $NH-C(O)-(C_1-C_6)$-alkyl, NH-C(O)-phenyl

or

R5 and R6 together form =O, , where n is 2-6,







; =NOH

and its physiologically acceptable salts and physiologically functional derivatives.

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

R1, R1' independently of one another are H, F, Cl, Br, -OH, $O-(C_1-C_6)$-alkyl, (C_1-C_6)-alkyl, where in the alkyl radicals one hydrogen can be replaced by OH;

R2 is H, (C_1-C_6)-alkyl, $C(O)-(C_1-C_6)$-alkyl;

R3 is Cl, Br, $(CH_2)_n$-$COO(C_1$-$C_6)$-alkyl, $(CH_2)_n$-COOH, $(CH_2)_n$-$CONH_2$, where n can be 0 or 1;

R4 is $(C_1$-$C_4)$-alkyl or $(C_3$-$C_6)$-cycloalkyl, where in the alkyl radicals one hydrogen can be replaced by OH;
$(CH_2)_n$-aryl, where n can be 0–6 and aryl can be phenyl, 1- or 2-naphthyl, 2-, 3- or 4-pyridyl, 2- or 3-thienyl and the aryl radical or heteroaryl radical can be substituted up to two times by F, Cl, Br, OH, CF_3, O-$(C_1$-$C_6)$-alkyl, SO_2-$(C_1$-$C_6)$-alkyl, $(CH_2)_n$-SO_2-NH_2, where n can be 0-6; $(C_1$-$C_6)$-alkyl, COOH, $COO(C_1$-$C_6)$-alkyl or $CONH_2$;

$(CH_2)_n$-A-R8, where n can be 1-6;

A is O, SO_2;

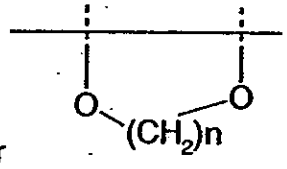
R8 is $(C_1$-$C_8)$-alkyl, $(C_3$-$C_8)$-cycloalkyl, where in the alkyl radicals one hydrogen can be replaced by OH;
$(CH_2)_m$-aryl, where m can be 0-6 and aryl can be phenyl or thienyl and the aryl moiety can be substituted up to two times by F, Cl, Br, OH, CF_3, O-$(C_1$-$C_6)$-alkyl, SO_2-$(C_1$-$C_6)$-alkyl, SO_2-NH_2, COOH, $COO(C_1$-$C_6)$-alkyl or $CONH_2$;

R5 is H;

R6 is OH, O-$(C_1$-$C_6)$-alkyl, where n can be 0-6;
O-C(O)-$(C_1$-$C_6)$-alkyl, O-C(O)-aryl, where aryl can be phenyl or thienyl;
O-alpha or -beta-glucuronic acid;
SO_2-$(C_1$-$C_6)$-alkyl, SO_2-$(CH_2)_n$-phenyl, where phenyl can be 0-6;
NH_2, morpholin-4-yl, NH-C(O)-$(C_1$-$C_6)$-alkyl, NH-C(O)-phenyl

or

23 AUG 2004

R5 and R6 together form =O or  , where n can be 2-6,

and its physiologically acceptable salts.

4. A medicament, comprising one or more compounds as claimed in one or more of claims 1 to 3.

5. A medicament, comprising one or more compounds as claimed in one or more of claims 1 to 3 and one or more anorectics.

6. A compound as claimed in one or more of claims 1 to 3 for use as a medicament for the prophylaxis or treatment of obesity.

7. A compound as claimed in one or more of claims 1 to 3 for use as a medicament for the prophylaxis or treatment of type II diabetes.

8. A compound as claimed in one or more of claims 1 to 3 in combination with at least one further anorectic for use as a medicament for the prophylaxis or treatment of obesity.

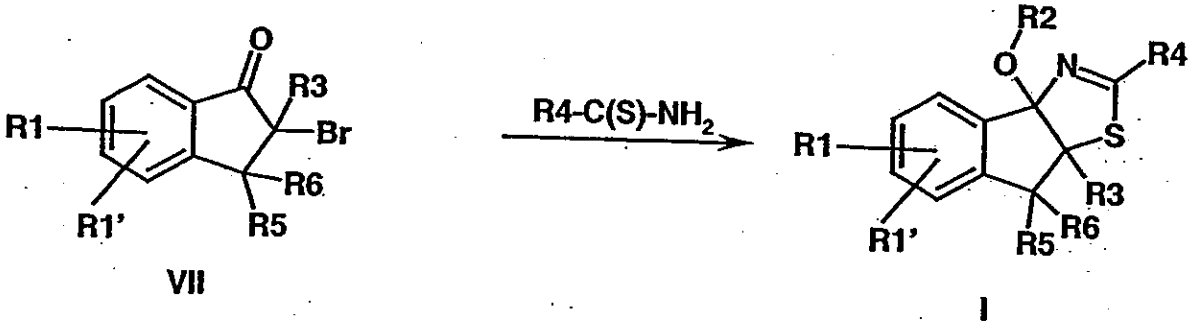
9. A compound as claimed in one or more of claims 1 to 3 in combination with at least one further anorectic for use as a medicament for the prophylaxis or treatment of type II diabetes.

10. A process for preparing a medicament comprising one or more of the compounds as claimed in one or more of claims 1 to 3, which comprises mixing the active compound with a pharmaceutically suitable excipient and bringing this mixture into a form suitable for administration.

11. The use of the compounds as claimed in one or more of claims 1 to 3 for preparing a medicament for the prophylaxis or treatment of obesity.

12. The use of the compounds as claimed in one or more of claims 1 to 3 for preparing a medicament for the prophylaxis or treatment of type II diabetes.

13. A process for preparing compounds as claimed in one or more of claims 1 to 3, which comprises reacting, according to the equation below,



VII I

a compound of the formula VII in which the radicals are as defined for formula I with a thioamide of the formula R4-C(S)-NH_2, in which R4 is as defined for formula I to give compounds of the formula I in which R2 is hydrogen and, if appropriate, derivatizing these compounds further at the R2 position such that the other radicals R2 given to formula I are formed.