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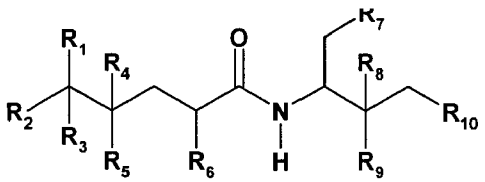
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(54) Title: SUBSTITUTED CYCLOHEXANECARBOXAMIDES USEFUL AS BACE INHIBITORS



(I)

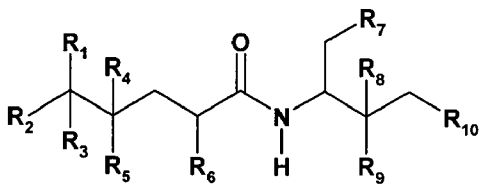
(57) Abstract: The invention relates to novel amide compounds of the formula (I) in which all of the variables are as defined in the specification, in free form or in salt form, to their preparation, to their use as medicaments and to medicaments comprising them.

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Substituted cyclohexanecarboxamides useful as BACE inhibitors

The present invention relates to novel amide compounds, to their preparation, to their use as medicaments and to medicaments comprising them.

More particularly, the invention relates to a compound of the formula



(I),

in which

R_1 is a group of the formula $N(R_a)$-$C(=O)R_b$ (Ia); $N(R_a)$-$S(=O)R_b$ (Ib); $N(R_a)$-$S(=O)_2R_b$ (Ic); $C(=O)$-$N(R_a)R_b$ (Id); $S(=O)$-$N(R_a)R_b$ (Ie); or $S(=O)_2$-$N(R_a)R_b$ (If),

in which formulae Ia, Ib and Ic

either R_a is hydrogen; C_1-C_8-alkyl; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl; or heterocyclyl-C_1-C_4-alkyl; and

R_b is hydrogen; C_1-C_8-alkyl; trifluoromethyl; C_1-C_8-alkoxy; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_8-alkylthio; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl; heterocyclyl-C_1-C_4-alkyl; amino; C_1-C_8-alkylamino; or di-(C_1-C_8-alkyl)amino with two identical or different C_1-C_8-alkyl moieties, which two C_1-C_8-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_8-alkyl moieties of the di-(C_1-C_8-alkyl)amino group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member,

or R_a and R_b, taken together, complete, together with the 2 atoms, to which they are attached, a saturated or unsaturated ring, which ring is in the case of

the formulae Ia and Ib monosubstituted by oxo and in the case of the formula Ic disubstituted by oxo, the said ring being optionally further substituted by 1 or 2 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in the case of the formula Ia, the nitrogen ring member depicted in the formula Ia and optionally 1 or 2 further ring members being hetero ring members and any other ring member being present being a carbon ring member and, in the case of the formulae Ib and Ic, the nitrogen and the sulfur ring members depicted in the formulae Ib and Ic and optionally 1 further ring member being hetero ring members and any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, and

in which formulae Id, Ie and If

either R_a is hydrogen; C_1-C_8-alkyl; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl attached via one of its carbon ring members to the nitrogen atom depicted in the formulae Id, Ie and If; or heterocyclyl-C_1-C_4-alkyl; and

R_b is hydrogen; C_1-C_8-alkyl; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl; or heterocyclyl-C_1-C_4-alkyl

or R_a and R_b, taken together, complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is in the case of the formulae Id and Ie monosubstituted by oxo and in the case of the formula If disubstituted by oxo, the said ring being optionally further substituted by 1 or 2 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in the case of the formula Id, the nitrogen ring member depicted in the formula Id and optionally 1 or 2 further ring members being hetero ring members and any other ring member being present being a carbon ring member and, in the case of the formulae Ie and If, the nitrogen and the sulfur ring members depicted in the formulae Ie and If and optionally 1 further ring member being hetero ring members and any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, con-

sisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member;

R_2 and R_3 are

either, independently from each other, hydrogen; C_1-C_8-alkyl; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_4-alkylthio-C_1-C_4-alkyl; or an aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl group, which aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl group is optionally ring-substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkyl-carbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)-amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)-amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino,

or, taken together, complete, together with the carbon atom, to which they are attached, a C_3-C_8-cycloalkyl ring, in which C_3-C_8-cycloalkyl ring 1 or 2 of its 2 to 7 methylene ring members optionally are hetero ring members independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member;

R_4 is hydrogen; hydroxy; or C_1-C_6-alkoxy;

R_5 and R_6, taken together, complete, together with the 2 carbon atoms, to which they are attached, and together with the methylene group, to which the said 2 carbon atoms are attached, a saturated ring, which ring is, in addition to the substitution by the substituents $(R_1)(R_2)(R_3)C$ and R_4 and the N-substituted aminocarbonyl group depicted in the formula I, optionally further substituted by 1 or 2 substituents independently selected from the group, consisting of C_1-C_8-alkyl, oxo, hydroxy, C_1-C_8-alkoxy, C_1-C_4-alkoxy- C_1-C_4-alkyl, C_1-C_8-alkylthio, C_1-C_4-alkylthio-C_1-C_4-alkyl, formyl, C_1-C_8-alkylcarbonyl, C_1-C_8-alkoxycarbonyl, carbamyl, N-C_1-C_8-alkylcarbamyl, N,N-di-(C_1-C_8-alkyl)carbamyl with two identical or different C_1-C_8-alkyl moieties, which two C_1-C_8-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio,

and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_8-alkyl moieties of the N,N-di- (C_1-C_8-alkyl)carbamyl group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, C_1-C_8-alkylsulfonyl, C_1-C_8-alkoxysulfonyl, aminosulfonyl, N-C_1-C_8-alkylaminosulfonyl, N,N-di-(C_1-C_8-alkyl)aminosulfonyl with two identical or different C_1-C_8-alkyl moieties, which two C_1-C_8-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_8-alkyl moieties of the N,N-di-(C_1-C_8-alkyl)aminosulfonyl group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, C_1-C_8-alkylsulfinyl, C_1-C_8-alkoxysulfinyl, aminosulfinyl, N-C_1-C_8-alkylaminosulfinyl, N,N-di-(C_1-C_8-alkyl)aminosulfinyl with two identical or different C_1-C_8-alkyl moieties, which two C_1-C_8-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_8-alkyl moieties of the N,N-di-(C_1-C_8-alkyl)aminosulfinyl group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, C_1-C_8-alkylsulfonylamino, C_1-C_8-alkoxysulfonylamino, aminosulfonylamino, N-C_1-C_8-alkylaminosulfonylamino, N,N-di-(C_1-C_8-alkyl)aminosulfonylamino with two identical or different C_1-C_8-alkyl moieties, formylamino, C_1-C_8-alkylcarbonylamino, C_1-C_8-alkoxycarbonylamino, carbamylamino, N-C_1-C_8-alkylcarbamylamino, N,N-di-(C_1-C_8-alkyl)carbamylamino with two identical or different C_1-C_8-alkyl moieties and a heterocyclyl or heteroaryl group, the said heterocyclyl or heteroaryl group being optionally substituted by 1 or 2 substituents indepen-

dently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 5 to 7 ring members, of which ring members 1 or 2 ring members optionally being hetero ring members and any other ring member being a carbon ring member, the said hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member;

R_7 is a C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, cyano, C_3-C_8-cycloalkyl, heterocyclyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl and an aryl or heteroaryl group, which aryl or heteroaryl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, which two C_1-C_4-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_4-alkyl moieties of the N,N-di-(C_1-C_4-alkyl)amino group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino; an aryl or heteroaryl group, which aryl or heteroaryl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, aryl, heteroaryl,

C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, fluoromethyl, difluoromethyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, N,N-di-(C_1-C_4-alkyl)aminosulfonyl with two identical or different C_1-C_4-alkyl moieties, which two C_1-C_4-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_4-alkyl moieties of the N,N-di-(C_1-C_4-alkyl)aminosulfonyl group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, which two C_1-C_4-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_4-alkyl moieties of the N,N-di-(C_1-C_4-alkyl)amino group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino; or an aryl group, which aryl group is optionally substituted at two of its carbon ring members, which two carbon ring members are adjacent to each other, by two substituents, which two substituents form, together with the two adjacent carbon ring members, to which they are attached, a heteroaryl ring, which heteroaryl ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkyl-

carbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkylcarbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino;

either

R_8 is hydrogen; and

R_9 is hydroxy

or

R_8 and R_9, taken together, are oxo; and

R_{10} is a group of the formula $CH(R_c)C(=O)N(R_d)R_e$ (Ig); or $(CH_2)_kN(H)R_f$ (Ih),

in which formula Ig

R_c is a C_1-C_8-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl; and

R_d and R_e

either are, independently from each other, hydrogen; a C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl; or an aryl, aryl-C_1-C_4-alkyl, heteroaryl or heteroaryl-C_1-C_4-alkyl group, which aryl, aryl-C_1-C_4-alkyl, heteroaryl or heteroaryl-C_1-C_4-alkyl group is optionally ring-substituted by 1 to 3 substituents independently selected from the

group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkylcarbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino,

or, taken together, complete, together with the nitrogen atom, to which they are attached, an azepanyl, morpholinyl, piperazinyl, piperidyl or pyrrolidyl ring, which azepanyl, morpholinyl, piperazinyl, piperidyl or pyrrolidyl ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl, and in which azepanyl, morpholinyl, piperazinyl, piperidyl or pyrrolidyl ring 1 or 2 of its methylene ring members can be replaced by a hetero ring member independently selected from the group, consisting of -S(=O)- and -S(=O)$_2$-, and

in which formula Ih

k is 0; 1; or 2; and

R_f is hydrogen; a C_1-C_8-alkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, fluoromethyl, difluoromethyl, trifluoromethyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl; an aryl, aryl-C_1-C_4-alkyl, heteroaryl, heteroaryl-C_1-C_4-alkyl, chroman-4-yl, isochroman-4-yl, thiochroman-4-yl, isothiochroman-4-yl, 1,1-dioxo-1lambda*6*-thiochroman-4-yl, 2,2-dioxo-2lambda*6*-isothiochroman-4-yl, 1,2,3,4-tetrahydro-quinol-4-yl, 1,2,3,4-tetrahydro-

isoquinol-4-yl, 1,2,3,4-tetrahydro-naphth-1-yl, 1,1-dioxo-1,2,3,4-tetrahydro-1lambda*6*-benzo[e][1,2]thiazin-4-yl, 2,2-dioxo-1,2,3,4-tetrahydro-2lambda*6*-benzo-[c][1,2]thiazin-4-yl, 1,1-dioxo-3,4-dihydro-1H-1lambda*6*-benzo[c][1,2]oxathiin-4-yl, 2,2-dioxo-3,4-dihydro-2H-2lambda*6*-benzo[e][1,2]oxathiin-4-yl, 2,3,4,5-tetrahydro-benzo[b]oxepin-5-yl or 1,3,4,5-tetrahydro-benzo[c]oxepin-5-yl group, which aryl, aryl-C_1-C_4-alkyl, heteroaryl, heteroaryl-C_1-C_4-alkyl, chroman-4-yl, isochroman-4-yl, thiochroman-4-yl, isothiochroman-4-yl, 1,1-dioxo-1lambda*6*-thiochroman-4-yl, 2,2-dioxo-2lambda*6*-isothiochroman-4-yl, 1,2,3,4-tetrahydro-quinol-4-yl, 1,2,3,4-tetrahydro-isoquinol-4-yl, 1,2,3,4-tetrahydro-naphth-1-yl, 1,1-dioxo-1,2,3,4-tetrahydro-1lambda*6*-benzo[e][1,2]thiazin-4-yl, 2,2-dioxo-1,2,3,4-tetrahydro-2lambda*6*-benzo[c][1,2]thiazin-4-yl, 1,1-dioxo-3,4-dihydro-1H-1lambda*6*-benzo-[c][1,2]oxathiin-4-yl, 2,2-dioxo-3,4-dihydro-2H-2lambda*6*-benzo[e][1,2]oxathiin-4-yl, 2,3,4,5-tetrahydro-benzo[b]oxepin-5-yl or 1,3,4,5-tetrahydro-benzo[c]oxepin-5-yl group is optionally ring-substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkylcarbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino, and in which aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl group the C_1-C_4-alkyl moiety is optionally substituted by 1 or 2 substituents independently selected from the group, consisting of fluoromethyl, difluoromethyl and trifluoromethyl; or a C_4-C_8-cycloalkyl group, in which C_4-C_8-cycloalkyl group

(a) one of the carbon ring members of the C_4-C_8-cycloalkyl moiety, which carbon ring members are different from the carbon ring member of the C_4-C_8-cycloalkyl moiety, to which the nitrogen atom depicted in the formula Ih is attached, is optionally replaced by a hetero ring member independently selected from the group, consisting of -O-, -S-, -S(=O)-, -S(=O)$_2$- and -N(R_g)-,

R_g being hydrogen; a C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl; or an aryl, aryl-C_1-C_4-alkyl, heteroaryl or heteroaryl-C_1-C_4-alkyl group, which aryl, aryl-C_1-C_4-alkyl, heteroaryl or heteroaryl-C_1-C_4-alkyl group is optionally ring-substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkylcarbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino,

(b) the C_4-C_8-cycloalkyl moiety, which C_4-C_8-cycloalkyl moiety is optionally modified as defined under (a) hereinbefore to contain one hetero ring member, is optionally substituted by 1 to 4 substituents independently selected from the group, consisting of halogen, cyano, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkoxycarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, a C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl, and an aryl, aryl-C_1-C_4-alkyl, heteroaryl, heteroaryl-C_1-C_4-alkyl, heterocyclyl or heterocyclyl-C_1-C_4-alkyl group, which

aryl, aryl-C_1-C_4-alkyl, heteroaryl, heteroaryl-C_1-C_4-alkyl, heterocyclyl or heterocyclyl-C_1-C_4-alkyl group is optionally ring-substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkylcarbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino, and

(c) the C_4-C_8-cycloalkyl moiety, which C_4-C_8-cycloalkyl moiety is optionally modified as defined under (a) hereinbefore to contain one hetero ring member, is optionally substituted at two of its carbon ring members, which two carbon ring members are adjacent to each other, by two substituents, which two substituents form, together with the two adjacent carbon ring members, to which they are attached, a C_3-C_8-cycloalkyl ring, in which C_3-C_8-cycloalkyl ring

(i) one of the carbon ring members of the C_3-C_8-cycloalkyl ring thus formed, which carbon ring members are different from the said two adjacent carbon ring members of the C_3-C_8-cycloalkyl ring thus formed, to which the said two substituents are optionally attached, is optionally replaced by a hetero ring member independently selected from the group, consisting of -O-, -S-, -S(=O)-, -$S(=O)_2$- and -$N(R_h)$-,

R_h being hydrogen; a C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl; or an aryl, aryl-C_1-C_4-alkyl, heteroaryl or heteroaryl-C_1-C_4-alkyl group, which aryl, aryl-C_1-C_4-alkyl, heteroaryl or heteroaryl-C_1-C_4-alkyl group is optionally ring-substituted by 1 to 3 substituents

independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkylcarbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino, and

(ii) the C_3-C_8-cycloalkyl ring thus formed, which C_3-C_8-cycloalkyl ring is optionally modified as defined under (i) hereinbefore to contain one hetero ring member, is optionally substituted by 1 to 4 substituents independently selected from the group, consisting of halogen, cyano, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkoxycarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, a C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl, and an aryl, aryl-C_1-C_4-alkyl, heteroaryl, heteroaryl-C_1-C_4-alkyl, heterocyclyl or heterocyclyl-C_1-C_4-alkyl group, which aryl, aryl-C_1-C_4-alkyl, heteroaryl, heteroaryl-C_1-C_4-alkyl, heterocyclyl or heterocyclyl-C_1-C_4-alkyl group is optionally ring-substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkylcarbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkyl-

carbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl- C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino,

in free form or in salt form.

E. g. on account of one or more than one asymmetrical carbon atom, which may be present in a compound of the formula I, a corresponding compound of the formula I may exist in pure optically active form or in the form of a mixture of optical isomers, e. g. in the form of a racemic mixture. All of such pure optical isomers and all of their mixtures, including the racemic mixtures, are part of the present invention.

A compound of the formula I may exist in free form or in salt form, e. g. a basic compound in acid addition salt form or an acidic compound in the form of a salt with a base. All of such free compounds and salts are part of the present invention.

A compound of the formula I may exist in tautomeric form. All of such tautomers are part of the present invention.

Halogen denotes fluorine, chlorine, bromine or iodine.

An aryl group, ring or moiety is a naphthyl or, preferably, phenyl group, ring or moiety.

A heteroaryl group, ring or moiety is an aromatic 5- or 6-membered structure, in which structure 1, 2, 3 or 4 ring members are hetero ring members independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, such as furyl, pyrrolyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, triazolyl, tetrazolyl, pyridazinyl, pyrimidyl or pyridyl, and which structure can also be anellated with a phenyl ring, such as benzothiazolyl, benzoxazolyl or quinolyl.

A heterocyclyl group, ring or moiety is a non-aromatic 5- or 6-membered cyclic structure, in which cyclic structure 1, 2 or 3 ring members are hetero ring members independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a

sulfur ring member, such as pyrrolinyl, pyrrolidyl, tetrahydrofuryl, tetrahydrothienyl, piperidyl, piperazinyl, tetrahydropyranyl or morpholinyl.

Any non-cyclic carbon containing group or moiety with more than 1 carbon atom is straight-chain or branched.

Unless defined otherwise, carbon containing groups, moieties or molecules contain 1 to 8, preferably 1 to 6, preferably 1 to 4, preferably 1 or 2, carbon atoms.

In preferred embodiments, the invention relates to a compound of the formula I, in free form or in salt form, in which

(1) R_1 is a group of the formula $N(R_a)$-$C(=O)R_b$ (Ia); $N(R_a)$-$S(=O)R_b$ (Ib); $N(R_a)$-$S(=O)_2R_b$ (Ic); $C(=O)$-$N(R_a)R_b$ (Id); $S(=O)$-$N(R_a)R_b$ (Ie); or $S(=O)_2$-$N(R_a)R_b$ (If),

in which formulae Ia, Ib and Ic

either R_a is hydrogen; C_1-C_8-alkyl; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl; or heterocyclyl-C_1-C_4-alkyl; and

R_b is hydrogen; C_1-C_8-alkyl; trifluoromethyl; C_1-C_8-alkoxy; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_8-alkylthio; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl; heterocyclyl-C_1-C_4-alkyl; amino; C_1-C_8-alkylamino; or di-(C_1-C_8-alkyl)amino with two identical or different C_1-C_8-alkyl moieties, which two C_1-C_8-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_8-alkyl moieties of the di-(C_1-C_8-alkyl)amino group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member,

or R_a and R_b, taken together, complete, together with the 2 atoms, to which they are attached, a saturated or unsaturated ring, which ring is in the case of

the formulae Ia and Ib monosubstituted by oxo and in the case of the formula Ic disubstituted by oxo, the said ring being optionally further substituted by 1 or 2 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in the case of the formula Ia, the nitrogen ring member depicted in the formula Ia and optionally 1 or 2 further ring members being hetero ring members and any other ring member being present being a carbon ring member and, in the case of the formulae Ib and Ic, the nitrogen and the sulfur ring members depicted in the formulae Ib and Ic and optionally 1 further ring member being hetero ring members and any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, and

in which formulae Id, Ie and If

either R_a is hydrogen; C_1-C_8-alkyl; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl attached via one of its carbon ring members to the nitrogen atom depicted in the formulae Id, Ie and If; or heterocyclyl-C_1-C_4-alkyl; and

R_b is hydrogen; C_1-C_8-alkyl; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl; or heterocyclyl-C_1-C_4-alkyl

or R_a and R_b, taken together, complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is in the case of the formulae Id and Ie monosubstituted by oxo and in the case of the formula If disubstituted by oxo, the said ring being optionally further substituted by 1 or 2 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in the case of the formula Id, the nitrogen ring member depicted in the formula Id and optionally 1 or 2 further ring members being hetero ring members and any other ring member being present being a carbon ring member and, in the case of the formulae Ie and If, the nitrogen and the sulfur ring members depicted in the formulae Ie and If and optionally 1 further ring member being hetero ring members and any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, con-

sisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member;

preferably is a group of the formula $N(R_a)$-$C(=O)R_b$ (Ia); or $C(=O)$-$N(R_a)R_b$ (Id);

in which formula Ia

either R_a is hydrogen; C_1-C_8-alkyl; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl; or heterocyclyl-C_1-C_4-alkyl; and

R_b is hydrogen; C_1-C_8-alkyl; trifluoromethyl; C_1-C_8-alkoxy; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_8-alkylthio; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl; heterocyclyl-C_1-C_4-alkyl; amino; C_1-C_8-alkylamino; or di-(C_1-C_8-alkyl)amino with two identical or different C_1-C_8-alkyl moieties, which two C_1-C_8-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_8-alkyl moieties of the di-(C_1-C_8-alkyl)amino group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member,

or R_a and R_b, taken together, complete, together with the 2 atoms, to which they are attached, a saturated or unsaturated ring, which ring is in the case of the formulae Ia and Ib monosubstituted by oxo and in the case of the formula Ic disubstituted by oxo, the said ring being optionally further substituted by 1 or 2 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in the case of the formula Ia, the nitrogen ring member depicted in the formula Ia and optionally 1 or 2 further ring members being hetero ring members and any other ring member being present being a carbon ring member and, in the case of the formulae Ib and Ic, the nitrogen and the sulfur ring members depicted in the formulae Ib and Ic and optionally 1 further ring member being hetero ring members and any other ring member being present being a carbon ring member, the said further hetero

ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, and

in which formula Id

either R_a is hydrogen; C_1-C_8-alkyl; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl attached via one of its carbon ring members to the nitrogen atom depicted in the formulae Id, Ie and If; or heterocyclyl-C_1-C_4-alkyl; and

R_b is hydrogen; C_1-C_8-alkyl; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl; or heterocyclyl-C_1-C_4-alkyl

or R_a and R_b, taken together, complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is in the case of the formulae Id and Ie monosubstituted by oxo and in the case of the formula If disubstituted by oxo, the said ring being optionally further substituted by 1 or 2 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in the case of the formula Id, the nitrogen ring member depicted in the formula Id and optionally 1 or 2 further ring members being hetero ring members and any other ring member being present being a carbon ring member and, in the case of the formulae Ie and If, the nitrogen and the sulfur ring members depicted in the formulae Ie and If and optionally 1 further ring member being hetero ring members and any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member;

preferably is a group of the formula $N(R_a)$-$C(=O)R_b$ (Ia); or $C(=O)$-$N(R_a)R_b$ (Id);

in which formula Ia

either R_a is hydrogen; or C_1-C_8-alkyl; and

R_b is C_1-C_8-alkyl; C_1-C_8-alkoxy; or trifluoromethyl

or R_a and R_b, taken together, are straight-chain C_1-C_5-alkylene and

in which formula Id

R_a is hydrogen; and

R_b is C_1-C_8-alkyl;

preferably is a group of the formula $N(R_a)$-$C(=O)R_b$ (Ia); or $C(=O)$-$N(R_a)R_b$ (Id);

in which formula Ia

either R_a is hydrogen; or C_1-C_6-alkyl; and

R_b is C_1-C_6-alkyl; C_1-C_8-alkoxy; or trifluoromethyl

or R_a and R_b, taken together, are straight-chain C_1-C_5-alkylene and

in which formula Id

R_a is hydrogen; and

R_b is C_1-C_6-alkyl;

preferably is a group of the formula $N(R_a)$-$C(=O)R_b$ (Ia);

in which formula Ia

either R_a is hydrogen; or C_1-C_6-alkyl; and

R_b is C_1-C_6-alkyl; C_1-C_8-alkoxy; or trifluoromethyl

or R_a and R_b, taken together, are straight-chain C_1-C_5-alkylene;

preferably is a group of the formula $N(R_a)$-$C(=O)R_b$ (Ia);

in which formula Ia

R_a and R_b, taken together, are straight-chain C_1-C_5-alkylene;

(2) R_2 and R_3 are

either, independently from each other, hydrogen; C_1-C_8-alkyl; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_4-alkylthio-C_1-C_4-alkyl; or an aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl group, which aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl group is optionally ring-substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkyl-carbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)-amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)-amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino,

or, taken together, complete, together with the carbon atom, to which they are attached, a C_3-C_8-cycloalkyl ring, in which C_3-C_8-cycloalkyl ring 1 or 2 of its 2 to 7 methylene ring

members optionally are hetero ring members independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member;

preferably are

either, independently from each other, hydrogen; or C_1-C_8-alkyl

or, taken together, complete, together with the carbon atom, to which they are attached, a C_3-C_8-cycloalkyl ring;

preferably are

either, independently from each other, hydrogen; or C_1-C_6-alkyl

or, taken together, complete, together with the carbon atom, to which they are attached, a C_3-C_6-cycloalkyl ring;

preferably are,

independently from each other, hydrogen; or C_1-C_6-alkyl;

preferably are,

independently from each other, C_1-C_6-alkyl;

(3) R_4 is hydrogen; hydroxy; or C_1-C_6-alkoxy;

preferably hydrogen; or hydroxy;

preferably hydrogen;

(4) R_5 and R_6, taken together, complete, together with the 2 carbon atoms, to which they are attached, and together with the methylene group, to which the said 2 carbon atoms are attached, a saturated ring, which ring is, in addition to the substitution by the substituents $(R_1)(R_2)(R_3)C$ and R_4 and the N-substituted aminocarbonyl group depicted in the formula I, optionally further substituted by 1 or 2 substituents independently selected from the group, consisting of C_1-C_8-alkyl, oxo, hydroxy, C_1-C_8-alkoxy, C_1-C_4-alkoxy- C_1-C_4-alkyl, C_1-C_8-alkylthio, C_1-C_4-alkylthio-C_1-C_4-alkyl, formyl, C_1-C_8-alkylcarbonyl, C_1-C_8-alkoxycarbonyl, carbamyl, N-C_1-C_8-alkylcarbamyl, N,N-di-(C_1-C_8-alkyl)carbamyl with two identical or different C_1-C_8-alkyl moieties, which two C_1-C_8-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_8-alkyl moieties of the N,N-di- (C_1-C_8-alkyl)carbamyl group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said

further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, C_1-C_8-alkylsulfonyl, C_1-C_8-alkoxysulfonyl, aminosulfonyl, N-C_1-C_8-alkylaminosulfonyl, N,N-di-(C_1-C_8-alkyl)aminosulfonyl with two identical or different C_1-C_8-alkyl moieties, which two C_1-C_8-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_8-alkyl moieties of the N,N-di-(C_1-C_8-alkyl)aminosulfonyl group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, C_1-C_8-alkylsulfinyl, C_1-C_8-alkoxysulfinyl, aminosulfinyl, N-C_1-C_8-alkylaminosulfinyl, N,N-di-(C_1-C_8-alkyl)aminosulfinyl with two identical or different C_1-C_8-alkyl moieties, which two C_1-C_8-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_8-alkyl moieties of the N,N-di-(C_1-C_8-alkyl)aminosulfinyl group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, C_1-C_8-alkylsulfonylamino, C_1-C_8-alkoxysulfonylamino, aminosulfonylamino, N-C_1-C_8-alkylaminosulfonylamino, N,N-di-(C_1-C_8-alkyl)aminosulfonylamino with two identical or different C_1-C_8-alkyl moieties, formylamino, C_1-C_8-alkylcarbonylamino, C_1-C_8-alkoxycarbonylamino, carbamylamino, N-C_1-C_8-alkylcarbamylamino, N,N-di-(C_1-C_8-alkyl)carbamylamino with two identical or different C_1-C_8-alkyl moieties and a heterocyclyl or heteroaryl group, the said heterocyclyl or heteroaryl group being optionally substituted by 1 or 2 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 5 to 7 ring members, of which ring members 1 or 2 ring members optionally being hetero ring members and any other ring member being a carbon ring member, the said hetero ring member(s) being independently selected from

the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member;

preferably, taken together, are straight-chain C_2-C_4-alkylene;

(5) R_7 is a C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, cyano, C_3-C_8-cycloalkyl, heterocyclyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl and an aryl or heteroaryl group, which aryl or heteroaryl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, which two C_1-C_4-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_4-alkyl moieties of the N,N-di-(C_1-C_4-alkyl)amino group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino; an aryl or heteroaryl group, which aryl or heteroaryl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, fluoromethyl, difluoromethyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, benzyloxy, phenoxy,

formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, N,N-di-(C_1-C_4-alkyl)aminosulfonyl with two identical or different C_1-C_4-alkyl moieties, which two C_1-C_4-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_4-alkyl moieties of the N,N-di-(C_1-C_4-alkyl)aminosulfonyl group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, which two C_1-C_4-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_4-alkyl moieties of the N,N-di-(C_1-C_4-alkyl)amino group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino; or an aryl group, which aryl group is optionally substituted at two of its carbon ring members, which two carbon ring members are adjacent to each other, by two substituents, which two substituents form, together with the two adjacent carbon ring members, to which they are attached, a heteroaryl ring, which heteroaryl ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyl-

oxy, carbamyloxy, N-C_1-C_4-alkylcarbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino;

preferably an aryl group, which aryl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, fluoromethyl, difluoromethyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, N,N-di-(C_1-C_4-alkyl)aminosulfonyl with two identical or different C_1-C_4-alkyl moieties, which two C_1-C_4-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_4-alkyl moieties of the N,N-di-(C_1-C_4-alkyl)aminosulfonyl group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, which two C_1-C_4-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_4-alkyl moieties of the N,N-di-(C_1-C_4-alkyl)amino group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, N-(C_1-C_4-alkoxy-C_1-C_4-

alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino;

preferably an unsubstituted aryl group;

preferably unsubstituted phenyl;

(6) either

R_8 is hydrogen; and

R_9 is hydroxy

or

R_8 and R_9, taken together, are oxo;

preferably R_8 is hydrogen; and R_9 is hydroxy;

(7) R_{10} is a group of the formula $CH(R_c)C(=O)N(R_d)R_e$ (Ig); or $(CH_2)_kN(H)R_f$ (Ih),

in which formula Ig

R_c is a C_1-C_8-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl; and

R_d and R_e

either are, independently from each other, hydrogen; a C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl; or an aryl, aryl-C_1-C_4-alkyl, heteroaryl or heteroaryl-C_1-C_4-alkyl group, which aryl, aryl-C_1-C_4-alkyl, heteroaryl or heteroaryl-C_1-C_4-alkyl group is optionally ring-substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-

alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkylcarbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino,

or, taken together, complete, together with the nitrogen atom, to which they are attached, an azepanyl, morpholinyl, piperazinyl, piperidyl or pyrrolidyl ring, which azepanyl, morpholinyl, piperazinyl, piperidyl or pyrrolidyl ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl, and in which azepanyl, morpholinyl, piperazinyl, piperidyl or pyrrolidyl ring 1 or 2 of its methylene ring members can be replaced by a hetero ring member independently selected from the group, consisting of -S(=O)- and -$S(=O)_2$-, and

in which formula Ih

k is 0; 1; or 2; and

R_f is hydrogen; a C_1-C_8-alkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, fluoromethyl, difluoromethyl, trifluoromethyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl; an aryl, aryl-C_1-C_4-alkyl, heteroaryl, heteroaryl-C_1-C_4-alkyl, chroman-4-yl, isochroman-4-yl, thiochroman-4-yl, isothiochroman-4-yl, 1,1-dioxo-1lambda*6*-thiochroman-4-yl, 2,2-dioxo-2lambda*6*-isothiochroman-4-yl, 1,2,3,4-tetrahydro-quinol-4-yl, 1,2,3,4-tetrahydro-isoquinol-4-yl, 1,2,3,4-tetrahydro-naphth-1-yl, 1,1-dioxo-1,2,3,4-tetrahydro-1lamb-

da*6*-benzo[e][1,2]thiazin-4-yl, 2,2-dioxo-1,2,3,4-tetrahydro-2lambda*6*-benzo-[c][1,2]thiazin-4-yl, 1,1-dioxo-3,4-dihydro-1H-1lambda*6*-benzo[c][1,2]oxathiin-4-yl, 2,2-dioxo-3,4-dihydro-2H-2lambda*6*-benzo[e][1,2]oxathiin-4-yl, 2,3,4,5-tetrahydro-benzo[b]oxepin-5-yl or 1,3,4,5-tetrahydro-benzo[c]oxepin-5-yl group, which aryl, aryl-C_1-C_4-alkyl, heteroaryl, heteroaryl-C_1-C_4-alkyl, chroman-4-yl, isochroman-4-yl, thiochroman-4-yl, isothiochroman-4-yl, 1,1-dioxo-1lambda*6*-thiochroman-4-yl, 2,2-dioxo-2lambda*6*-isothiochroman-4-yl, 1,2,3,4-tetrahydro-quinol-4-yl, 1,2,3,4-tetrahydro-isoquinol-4-yl, 1,2,3,4-tetrahydro-naphth-1-yl, 1,1-dioxo-1,2,3,4-tetrahydro-1lambda*6*-benzo[e][1,2]thiazin-4-yl, 2,2-dioxo-1,2,3,4-tetrahydro-2lambda*6*-benzo[c][1,2]thiazin-4-yl, 1,1-dioxo-3,4-dihydro-1H-1lambda*6*-benzo-[c][1,2]oxathiin-4-yl, 2,2-dioxo-3,4-dihydro-2H-2lambda*6*-benzo[e][1,2]oxathiin-4-yl, 2,3,4,5-tetrahydro-benzo[b]oxepin-5-yl or 1,3,4,5-tetrahydro-benzo[c]oxepin-5-yl group is optionally ring-substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkylcarbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino, and in which aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl group the C_1-C_4-alkyl moiety is optionally substituted by 1 or 2 substituents independently selected from the group, consisting of fluoromethyl, difluoromethyl and trifluoromethyl; or a C_4-C_8-cycloalkyl group, in which C_4-C_8-cycloalkyl group

(a) one of the carbon ring members of the C_4-C_8-cycloalkyl moiety, which carbon ring members are different from the carbon ring member of the C_4-C_8-cycloalkyl moiety, to which the nitrogen atom depicted in the formula Ih is attached, is optionally replaced by a hetero ring member independently selected from the group, consisting of -O-, -S-, -S(=O)-, -S(=O)$_2$- and -N(R_g)-,

R_g being hydrogen; a C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl; or an aryl, aryl-C_1-C_4-alkyl, heteroaryl or heteroaryl-C_1-C_4-alkyl group, which aryl, aryl-C_1-C_4-alkyl, heteroaryl or heteroaryl-C_1-C_4-alkyl group is optionally ring-substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkylcarbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino,

(b) the C_4-C_8-cycloalkyl moiety, which C_4-C_8-cycloalkyl moiety is optionally modified as defined under (a) hereinbefore to contain one hetero ring member, is optionally substituted by 1 to 4 substituents independently selected from the group, consisting of halogen, cyano, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkoxycarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, a C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl, and an aryl, aryl-C_1-C_4-alkyl, heteroaryl, heteroaryl-C_1-C_4-alkyl, heterocyclyl or heterocyclyl-C_1-C_4-alkyl group, which

aryl, aryl-C_1-C_4-alkyl, heteroaryl, heteroaryl-C_1-C_4-alkyl, heterocyclyl or heterocyclyl-C_1-C_4-alkyl group is optionally ring-substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkylcarbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino, and

(c) the C_4-C_8-cycloalkyl moiety, which C_4-C_8-cycloalkyl moiety is optionally modified as defined under (a) hereinbefore to contain one hetero ring member, is optionally substituted at two of its carbon ring members, which two carbon ring members are adjacent to each other, by two substituents, which two substituents form, together with the two adjacent carbon ring members, to which they are attached, a C_3-C_8-cycloalkyl ring, in which C_3-C_8-cycloalkyl ring

(i) one of the carbon ring members of the C_3-C_8-cycloalkyl ring thus formed, which carbon ring members are different from the said two adjacent carbon ring members of the C_3-C_8-cycloalkyl ring thus formed, to which the said two substituents are optionally attached, is optionally replaced by a hetero ring member independently selected from the group, consisting of -O-, -S-, -S(=O)-, -S(=O)$_2$- and -N(R_h)-,

R_h being hydrogen; a C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl; or an aryl, aryl-C_1-C_4-alkyl, heteroaryl or heteroaryl-C_1-C_4-alkyl group, which aryl, aryl-C_1-C_4-alkyl, heteroaryl or heteroaryl-C_1-C_4-alkyl group is optionally ring-substituted by 1 to 3 substituents

independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkylcarbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino, and

(ii) the C_3-C_8-cycloalkyl ring thus formed, which C_3-C_8-cycloalkyl ring is optionally modified as defined under (i) hereinbefore to contain one hetero ring member, is optionally substituted by 1 to 4 substituents independently selected from the group, consisting of halogen, cyano, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkoxycarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, a C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl, and an aryl, aryl-C_1-C_4-alkyl, heteroaryl, heteroaryl-C_1-C_4-alkyl, heterocyclyl or heterocyclyl-C_1-C_4-alkyl group, which aryl, aryl-C_1-C_4-alkyl, heteroaryl, heteroaryl-C_1-C_4-alkyl, heterocyclyl or heterocyclyl-C_1-C_4-alkyl group is optionally ring-substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkylcarbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkyl-

carbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino;

preferably R_{10} is a group of the formula $CH(R_c)C(=O)N(R_d)R_e$ (Ig); or $(CH_2)_kN(H)R_f$ (Ih),

in which formula Ig

R_c is C_1-C_8-alkyl; and

R_d and R_e are, independently from each other, hydrogen; or C_1-C_8-alkyl; and

in which formula Ih

k is 0; and

R_f is an aryl-C_1-C_4-alkyl group, which aryl-C_1-C_4-alkyl group is optionally ring-substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkylcarbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)-amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)-amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino, and in which aryl-C_1-C_4-alkyl group the C_1-C_4-alkyl moiety is optionally substituted by 1 or 2 substituents independently selected from the group, consisting of fluoromethyl, difluoromethyl and trifluoromethyl;

preferably R_{10} is a group of the formula $CH(R_c)C(=O)N(R_d)R_e$ (Ig); or $(CH_2)_kN(H)R_f$ (Ih),

in which formula Ig

R_c is C_1-C_6-alkyl; and

R_d and R_e are, independently from each other, hydrogen; or C_1-C_8-alkyl; and

in which formula Ih

k is 0; and

R_f is an aryl-C_1-C_4-alkyl group, which aryl-C_1-C_4-alkyl group is optionally ring-substituted by 1 or 2 substituents independently selected from the group, consisting of C_1-C_6-alkyl;

preferably R_{10} is a group of the formula $CH(R_c)C(=O)N(R_d)R_e$ (Ig); or $(CH_2)_kN(H)R_f$ (Ih),

in which formula Ig

R_c is C_1-C_6-alkyl; and

R_d and R_e are, independently from each other, hydrogen; or C_1-C_8-alkyl; and

in which formula Ih

k is 0; and

R_f is an aryl-C_1-C_4-alkyl group ring-substituted by 1 or 2 substituents independently selected from the group, consisting of C_1-C_6-alkyl;

preferably R_{10} is a group of the formula $(CH_2)_kN(H)R_f$ (Ih),

in which formula Ih

k is 0; and

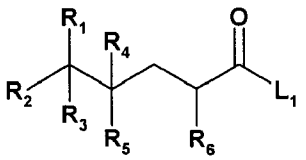
R_f is an aryl-C_1-C_4-alkyl group ring-substituted by 1 or 2 substituents independently selected from the group, consisting of C_1-C_6-alkyl.

The preferred embodiments (1) to (7) are preferred independently, collectively or in any combination or sub-combination.

In especially preferred embodiments, the invention relates to one or more than one of the compounds of the formula I mentioned in the Examples hereinafter, in free form or in salt form.

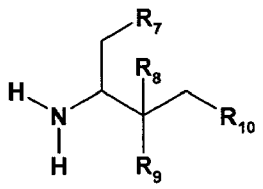
In a further aspect, the invention relates to a process for the preparation of a compound of the formula I, in free form or in salt form, comprising the steps of

a) reaction of a compound of the formula



(II),

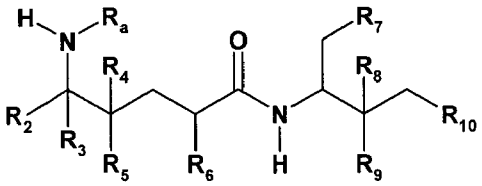
in which R_1, R_2, R_3, R_4, R_5 and R_6 are as defined for the formula I and L_1 is a leaving group, in free form or in salt form, with a compound of the formula



(III),

in which R_7, R_8, R_9 and R_{10} are as defined for the formula I, in free form or in salt form, or

b) for the preparation of a compound of the formula I, in free form or in salt form, in which R_1 is a group of the formula $N(R_a)$-C(=O)R_b (Ia); $N(R_a)$-S(=O)R_b (Ib); or $N(R_a)$-S(=O)$_2R_b$ (Ic), in which formulae Ia, Ib and Ic R_a is hydrogen; C_1-C_8-alkyl; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl; or heterocyclyl-C_1-C_4-alkyl; and R_b is hydrogen; C_1-C_8-alkyl; trifluoromethyl; C_1-C_8-alkoxy; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_8-alkylthio; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl; heterocyclyl-C_1-C_4-alkyl; amino; C_1-C_8-alkylamino; or di-(C_1-C_8-alkyl)amino with two identical or different C_1-C_8-alkyl moieties, which two C_1-C_8-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_8-alkyl moieties of the di-(C_1-C_8-alkyl)amino group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, reaction of a compound of the formula



(IV),

in which R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9 and R_{10} are as defined for the formula I and R_a is hydrogen; C_1-C_8-alkyl; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl; or heterocyclyl-C_1-C_4-alkyl, in free form or in salt form, with a compound of the formula R_b-C(=O)-L_2 (V); R_b-S(=O)-L_3 (VI); or R_b-S(=O)$_2$-L_4 (VII), in which formulae V, VI and VII R_b is hydrogen; C_1-C_8-alkyl; trifluoromethyl; C_1-C_8-alkoxy; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_8-alkylthio; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl; heterocyclyl-C_1-C_4-alkyl; amino; C_1-C_8-alkylamino;

or di-(C_1-C_8-alkyl)amino with two identical or different C_1-C_8-alkyl moieties, which two C_1-C_8-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_8-alkyl moieties of the di-(C_1-C_8-alkyl)amino group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, L_2 is a leaving group, L_3 is a leaving group and L_4 is a leaving group, in free form or in salt form,

in each case optionally followed by reduction, oxidation or other functionalisation of the resulting compound and/or by cleavage of any protecting group(s) optionally present,

and of recovering the so obtainable compound of the formula I in free form or in salt form.

A leaving group L_1, L_2, L_3 or L_4 is, e. g., halogen, such as F, Cl or Br, hydroxy or C_1-C_8-alkoxy, such as methoxy, preferably Cl or hydroxy.

The reactions can be effected according to conventional methods, for example as described in the Examples.

The working-up of the reaction mixtures and the purification of the compounds thus obtainable may be carried out in accordance with known procedures.

Salts may be prepared from free compounds in known manner, and vice-versa.

Compounds of the formula I can also be prepared by further conventional processes, which processes are further aspects of the invention, e. g. as described in the Examples.

The starting materials of the formulae II, III, IV, V, VI and VII are known or may be prepared according to conventional procedures starting from known compounds, for example as described in the Examples.

Compounds of the formula I, in free form or in pharmaceutically acceptable salt form, hereinafter often referred to as "agents of the invention", exhibit valuable pharmacological properties, when tested in vitro or in vivo, and are, therefore, useful in medicaments.

E. g., agents of the invention are inhibitors of aspartic proteases and can be used for the treatment of a condition, disease or disorder involving processing by such enzymes. Particularly, agents of the invention inhibit beta-secretase and, thus, the generation of beta-amyloid and the subsequent aggregation into oligomers and fibrils.

The inhibiting properties of an agent of the invention towards proteases can be evaluated, e. g., in a test as described hereinafter.

Test 1: Inhibition of human BACE

Recombinant BACE (extracellular domain, expressed in baculovirus and purified using standard methods) at 0.1 to 10 nM concentrations is incubated with the test compound at various concentrations for 1 hour at room temperature in 10 to 100 mM acetate buffer, pH 4.5, containing 0.1 % CHAPS. Synthetic fluorescence-quenched peptide substrate, derived from the sequence of APP and containing a suitable fluorophore-quencher pair, is added to a final concentration of 1 to 5 µM, and the increase in fluorescence is recorded at a suitable excitation / emission wavelength in a microplate spectro-fluorimeter for 5 to 30 minutes in 1-minute intervals. IC_{50} values are calculated from percentage of inhibition of BACE-activity as a function of the test compound concentration.

Test 2: Inhibition of human BACE-2

Recombinant BACE-2 (extracellular domain, expressed in baculovirus and purified using standard methods) at 0.1 to 10 nM concentrations is incubated with the test compound at various concentrations for 1 hour at room temperature in 10 to 100 mM acetate buffer, pH 4.5, containing 0.1 % CHAPS. Synthetic peptide substrate, derived from the sequence of APP and containing a suitable fluorophore-quencher pair, is added to a final concentration of 1 to 5 µM, and the increase in fluorescence is recorded at a suitable excitation / emission wavelength in a microplate spectro-fluorimeter for 5 to 30 minutes in 1-minute intervals. IC_{50} values are calculated from percentage of inhibition of BACE-2-activity as a function of the test compound concentration.

Test 3: Inhibition of human cathepsin D

Recombinant cathepsin D (expressed as procathepsin D in baculovirus, purified using standard methods and activated by incubation in sodium formate buffer pH 3.7) is incubated with the test compound at various concentrations for 1 hour at room temperature in sodium formate or sodium acetate buffer at a suitable pH within the range of pH 3.0 to 5.0. Synthetic peptide substrate Mca-Gly-Lys-Pro-Ile-Leu-Phe-Phe-Arg-Leu-Lys(DNP)-D-Arg-NH_2 is added to a final concentration of 1 to 5 µM, and the increase in fluorescence is recorded at excitation of 325 nm and emission at 400 nm in a microplate spectro-fluorimeter for 5 to 30 minutes in 1-minute intervals. IC_{50} values are calculated from the percentage of inhibition of cathepsin D-activity as a function of the test compound concentration.

Test 4: Inhibition of cellular release of amyloid peptide 1-40

Chinese hamster ovary cells are transfected with the gene for amyloid precursor protein. The cells are plated at a density of 8000 cells/well into 96-well microtiter plates and cultivated for 24 hours in DMEM cell culture medium containing 10 % FCS. The test compound is added to the cells at various concentrations, and the cells are cultivated for 24 hours in the presence of the test compound. The supernatants are collected, and the concentration of amyloid peptide 1-40 is determined using sandwich ELISA. The potency of the compound is calculated from the percentage of inhibition of amyloid peptide release as a function of the test compound concentration.

In at least one of the above-described tests, agents of the invention show activity at concentrations below 50 µM.

Specifically, the agent of the invention described in Example 6 shows an IC_{50} value of 4.22 µM in Test 1.

Due to their inhibiting properties towards proteases, agents of the invention are useful, e. g., in the treatment or prevention of a neurological or vascular condition, disease or disorder, in which beta-amyloid generation or aggregation plays a role, such as a neurodegenerative condition, disease or disorder, e. g. Alzheimer's disease, Down's syndrome, memory impairment, cognitive impairment, dementia, amyloid neuropathies, brain inflammation, nerve trauma, brain trauma, vascular amyloidosis or cerebral haemorrhage with amyloidosis, or, based on the inhibition of BACE-2 (beta-site APP-cleaving enzyme 2) or cathepsin D, which are close homologues of the pepsin-type aspartyl proteases and beta-secretase, and the corre-

lation of the BACE-2 or cathepsin D expression with a more tumorigenic or metastatic potential of tumor cells, in the suppression of the metastasis process associated with tumor cells.

For the above-mentioned indications, the appropriate dosage will vary depending on, e. g., the compound employed as active pharmaceutical ingredient, the host, the mode of administration, the nature and severity of the condition, disease or disorder or the effect desired. However, in general, satisfactory results in animals are indicated to be obtained at a daily dosage of from about 0.1 to about 100, preferably from about 1 to about 50, mg/kg of animal body weight. In larger mammals, for example humans, an indicated daily dosage is in the range of from about 0.5 to about 2000, preferably from about 2 to about 200, mg of an agent of the invention conveniently administered, for example, in divided doses up to four times a day or in sustained release form.

An agent of the invention may be administered by any conventional route, in particular enterally, preferably orally, e. g. in the form of a tablet or capsule, or parenterally, e. g. in the form of an injectable solution or suspension.

In accordance with the foregoing, in a further aspect, the invention relates to an agent of the invention for use as a medicament, e. g. for the treatment or prevention of a neurological or vascular condition, disease or disorder, in which beta-amyloid generation or aggregation plays a role, or for the suppression of the metastasis process associated with tumor cells.

In a further aspect, the invention relates to the use of an agent of the invention as active pharmaceutical ingredient in a medicament, e. g. for the treatment or prevention of a neurological or vascular condition, disease or disorder, in which beta-amyloid generation or aggregation plays a role, or for the suppression of the metastasis process associated with tumor cells.

In a further aspect, the invention relates to a pharmaceutical composition comprising an agent of the invention as active pharmaceutical ingredient in association with at least one pharmaceutically acceptable carrier or diluent. Such a composition may be manufactured in conventional manner, e. g. by mixing its components. Unit dosage forms contain, e. g., from about 0.1 to about 1000, preferably from about 1 to about 500, mg of an agent of the invention.

An agent of the invention can be administered as sole active pharmaceutical ingredient or as a combination with at least one other active pharmaceutical ingredient effective, e. g., in the treatment or prevention of a neurological or vascular condition, disease or disorder, in which beta-amyloid generation or aggregation plays a role, or in the suppression of the metastasis process associated with tumor cells. Such a pharmaceutical combination may be in the form of a unit dosage form, which unit dosage form comprises a predetermined quantity of each of the at least two active components in association with at least one pharmaceutically acceptable carrier or diluent. Alternatively, the pharmaceutical combination may be in the form of a package comprising the at least two active components separately, e. g. a pack or dispenser-device adapted for the concomitant or separate administration of the at least two active components, in which these active components are separately arranged. In a further aspect, the invention relates to such pharmaceutical combinations.

In a further aspect, the invention relates to the use of an agent of the invention for the manufacture of a medicament for the treatment or prevention of a neurological or vascular condition, disease or disorder, in which beta-amyloid generation or aggregation plays a role, or for the suppression of the metastasis process associated with tumor cells.

In a further aspect, the invention relates to a method for the treatment or prevention of a neurological or vascular condition, disease or disorder, in which beta-amyloid generation or aggregation plays a role, or for the suppression of the metastasis process associated with tumor cells, in a subject in need of such treatment, prevention or suppression, which method comprises administering to such subject an effective amount of an agent of the invention.

The following Examples illustrate the invention, but do not limit it.

Examples

Abbreviations

BOC	tert-butoxycarbonyl
DCC	dicyclohexylcarbodiimide
DCM	dichloromethane
DIAD	diisopropyl azodicarboxylate
DIBALH	diisobutylaluminum hydride

DIEA	diisopropyl-ethyl-amine
DMAP	4-(N,N-dimethylamino)-pyridine
DMF	dimethylformamide
DMSO	dimethylsulfoxide
DPPA	diphenylphosphoryl azide
EDCI	1-ethyl-3-[3-(dimethylamino)propyl]-carbodiimide hydrochloride
ESI	electrospray ionization
EtOAc	ethyl acetate
Grubbs' first generation catalyst	bis(tricyclohexylphosphine)benzylideneruthenium dichloride
Grubbs' second generation catalyst	benzylidene(1,3-dimesitylimidazolidin-2-ylidene)(tricyclohexylphosphine) ruthenium dichloride
h	hour(s)
HRMS	high resolution mass spectrometry
IR	infrared
KHMDS	potassium hexamethyldisilazide
LDA	lithium diisopropylamide
min	minute(s)
MS	mass spectrometry
NMR	nuclear magnetic resonance spectrometry
PyBOP	(benzotriazole-1-yloxy)-tripyrrolidinophosponium-hexafluorophosphate
rt	room temperature
TBAF	tetrabutylammonium fluoride
TBD	1,5,7-triazabicyclo[4.4.0]dec-5-ene
TEMPO	2,2,6,6-tetramethyl-1-piperidinooxy, free radical
THF	tetrahydrofuran
TLC	thin-layer chromatography
TMSCl	trimethylsilylchloride
TMSI	trimethylsilyliodide

Building block A1: (1R,3S)-3-(1-Acetylamino-1-methyl-ethyl)-cyclohexanecarboxylic acid methyl ester

a) 2-[(S)-3-(1-Methyl-1-nitro-ethyl)-cyclohexylidene]-[1,3]dithiane

To a solution of [1,3]dithian-2-yl-phosphonic acid diethyl ester (0.768 g, 3.0 mmol) in THF (10 ml) is added at -78°C over a period of 15 min n-butyllithium (1.4 ml, 2.24 mmol, 1.6 M in hexanes). The mixture is stirred for 1 h, and a solution of (S)-3-(1-methyl-1-nitro-ethyl)-cyclohexanone (0.361 g, 1.95 mmol) in THF (5 ml) is added. The mixture is stirred for further 15 min at -78°C, allowed to warm to rt, treated with saturated aqueous ammonium chloride solution (3 ml) and extracted with EtOAc (2 x 20 ml). The organic layer is washed with brine, dried over sodium sulfate and evaporated. The residue is purified by chromatography (5% EtOAc in hexanes) to yield a colorless oil.

IR ($CHCl_3$): 1348, 1536 cm^{-1}.

b) (1R,3S)-3-(1-Methyl-1-nitro-ethyl)-cyclohexanecarboxylic acid methyl ester

A solution of building block A1a) (0.125 g, 0.438 mmol), mercuric chloride (0.476 g, 1.753 mmol) and perchloric acid (0.18 ml of a 70% aqueous solution, 1.31 mmol) in methanol (5 ml) is heated to reflux for 2 h. After cooling and filtration, the reaction mixture is neutralized with saturated aqueous bicarbonate solution and extracted with DCM. The combined organic layers are washed with brine, dried over sodium sulfate and concentrated to yield a diastereomeric mixture of the ester as a thick gum. This product is, together with sodium methoxide in methanol (0.5 M, 5 ml), heated to reflux for 48 h. The reaction mixture is cooled to rt, neutralized with Amberlite IR-120 (H^+) resin and filtered. The filtrate is concentrated, and the residue is purified by column chromatography (EtOAc:hexanes 1:4) to yield a colorless oil.

IR ($CHCl_3$): 1534, 1730 cm^{-1}.

c) (1R,3S)-3-(1-Acetylamino-1-methyl-ethyl)-cyclohexanecarboxylic acid methyl ester

Building block A1b) (40 mg, 0.174 mmol) is dissolved in CH_3OH (2 ml) in a thick-walled tube. Raney-Ni (50% in water, 0.3 ml) is added, followed by a catalytic amount of H_2PtCl_6. The mixture is stirred under H_2 (60 psi) for 14 h. The catalyst is filtered off, and the filtrate is evaporated to yield the crude amine, which is dissolved in DCM. Acetic anhydride (35 µl, 0.32 mmol), triethylamine (64 µl, 0.460 mmol) and DMAP (catalytic amount) are added. The reaction mixture is stirred at rt for 3 h and treated with aqueous ammonium chloride solution and EtOAc (10ml). The organic layer is washed with hydrochloric acid (1 N) and sodium bicarbonate solution, dried and evaporated. The residue is purified by chromatography (EtOAc:hexanes 1:1) to yield a colorless solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.4 (s, 1H), 3.64 (s, 3H), 2.34-2.29 (m, 1H), 2.17-2.11 (m, 1H), 1.94-1.85 (m, 5H), 1.83 (m, 1H), 1.72-1.69 (m, 1H), 1.31-1.16 (m, 9H), 1.10 (m, 1H).

Building block A2: (1R,3S)-3-(1-Methyl-1-propionylamino-ethyl)-cyclohexanecarboxylic acid methyl ester

To a solution of building block A1b) (46 mg, 0.2 mmol) in CH_3OH (4 ml) are added Raney-Ni (80 mg) and a catalytic amount of H_2PtCl_6. The mixture is stirred at rt under a hydrogen atmosphere for 14 h and filtered through Celite. The filter cake is washed with CH_3OH (3 x 8 ml). The combined filtrates are evaporated to yield a colorless oil, which is dissolved in DCM (2 ml). To this solution are added pyridine (48.5 µl, 0.6 mmol), $(CH_3CH_2CO)_2O$ (78 mg, 0.6 mmol) and a catalytic amount of DMAP. The mixture is stirred at rt for 4 h and then quenched by adding 1 N aqueous hydrochloric acid. The organic layer is diluted with EtOAc, washed with brine and saturated sodium bicarbonate solution, dried and evaporated. The purification of the residue by column chromatography yields a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.13 (br s, 1H), 3.66 (s, 3H), 2.34 (m, 1H), 2.17 (q, J = 7.6 Hz, 2H), 1.93 (m, 2H), 1.85 (m, 2H), 1.71 (m, 2H), 1.34-1.29 (m, 2H), 1.28 (s, 3H), 1.26 (s, 3H), 1.12 (t, J = 7.6 Hz, 3H), 0.98-0.88 (m, 1H).

Building block A3: (1R,3S)-3-[1-Methyl-1-(2-oxo-2,5-dihydro-pyrrol-1-yl)-ethyl]-cyclo-hexanecarboxylic acid methyl ester

a) (1R,3S)-3-(1-Allylamino-1-methyl-ethyl)-cyclohexanecarboxylic acid methyl ester

To a solution of building block A1b) (30 mg, 0.13 mmol) in CH_3OH (2 ml) are added Raney-Ni (45 mg) and a catalytic amount of H_2PtCl_6. The mixture is stirred at rt under a hydrogen atmosphere for 12 h and filtered through Celite. The filter cake is washed with CH_3OH (3 x 5 ml). The combined filtrates are evaporated to yield a colorless oil, which is dissolved in acetonitrile (5 ml). Sodium bicarbonate (32.9 mg, 0.39 mmol) and allyl bromide (11 µl, 0.13 mmol) are added to the solution. The mixture is stirred for 5 h and, after the addition of water (5 ml), extracted with DCM (3 x 10 ml). The combined organic layers are dried over sodium sulfate and evaporated. The purification of the residue by column chromatography yields a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.98-5.91 (m, 1H), 5.21 (dd, J = 1.6, 1.5 Hz, 1H), 5.07 (dd, J = 1.6, 1.5 Hz, 1H), 3.69 (s, 3H), 3.16 (d, J = 6.0 Hz, 2H), 2.31 (m, 1H), 1.99-1.89 (m, 3H), 1.78-1.75 (m, 1H), 1.42-1.14 (m, 5H), 1.05 (s, 6H), 1.03-0.99 (m. 1H).

b) (1R,3S)-3-[1-(Acryloyl-allyl-amino)-1-methyl-ethyl]-cyclohexanecarboxylic acid methyl ester

To a solution of building block A3a) (10 mg, 0.042 mmol) in DCM (1.5 ml) are added under argon at 0°C pyridine (34.0 µl, 0.42 mmol) and $CH_2CHCOCl$ (17.1 µl, 0.21 mmol). The mixture is stirred for 30 min, quenched with aqueous 1 N hydrochloric acid (0.5 ml) and extracted with DCM. The organic layer is washed with water, dried over sodium sulfate and evaporated. The purification of the residue by column chromatography yields a colorless oil.
^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.47 (dd, J = 10.2, 10.1 Hz, 1H), 6.25 (dd, J = 1.5, 1.6 Hz, 1H), 5.87 (m, 1H), 5.57 (dd, J = 1.5, 1.6 Hz, 1H), 5.27 (m, 2H), 3.93 (m, 2H), 3.65 (s, 3H), 2.77 (m, 1H), 2.34 (m, 1H), 1.94 (m, 1H), 1.89-1.77 (m, 2H), 1.71-1.55 (m, 2H), 1.42 (s, 6H), 1.37-1.12 (m, 3H).

c) (1R,3S)-3-[1-Methyl-1-(2-oxo-2,5-dihydro-pyrrol-1-yl)-ethyl]-cyclohexanecarboxylic acid methyl ester

To a solution of building block A3b) (10 mg, 0.034mmol) in DCM (10 ml) is added under argon at reflux temperature Grubbs' first generation catalyst (1.4 mg, 0.0017 mmol). The mixture is stirred for 3 h and then filtered through Florisil/silica. The filter cake is washed with DCM, and the combined filtrates are evaporated. The residue is purified by column chromatography to yield a colorless oil.
^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.97 (dd, J = 1.7, 4.1 Hz, 1H), 6.09 (dd, J = 1.7, 4.0 Hz, 1H), 4.05 (br s, 2H), 3.64 (s, 3H), 2.65 (m, 1H), 2.36 (m, 1H), 1.93 (m, 1H), 1.84-1.76 (m, 2H), 1.58-1.56 (m, 2H), 1.40 (s, 6H), 1.32-1.16 (m, 3H).

<u>Building block A4:</u> (1R,3S)-3-[1-Methyl-1-(2,2,2-trifluoro-acetylamino)-ethyl]-cyclohexanecarboxylic acid methyl ester

Building block A1b) (40 mg, 0.174 mmol) is dissolved in CH_3OH (2 ml) in a thick-walled tube. Raney-Ni (50% in water, 0.3 ml) is added, followed by a catalytic amount of H_2PtCl_6. The mixture is stirred under H_2 (60 psi) for 14 h. The catalyst is filtered off, and the filtrate is evaporated to yield the crude amine, which is dissolved in dry DCM. Trifluoroacetic anhydride (71 µl, 0.51 mmol) is added, followed by triethylamine (71 µl, 0.51 mmol) and DMAP (catalytic amount). The reaction mixture is stirred at rt for 3 h and then quenched by adding aqueous ammonium chloride solution. The organic layer is diluted with EtOAc, washed with hy-

drochloric acid (1 N) and sodium bicarbonate solution, dried and concentrated. The residue is purified by chromatography (EtOAc:hexanes 1:1) to yield a colorless oil.
^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.92 (m, 1H), 3.70 (s, 3H), 2.38 (m, 1H), 2.13-1.89 (m, 4H), 1.75-1.67 (m, 2H), 1.39-1.14 (m, 9H).

Building block A5: (1R,3S)-3-(1-Acetylamino-cyclopentyl)-cyclohexanecarboxylic acid methyl ester

a) (S)-1-(Bis-methylsulfanyl-methylene)-3-(1-nitro-cyclopentyl)-cyclohexane
To a stirred solution of bis(methylmercapto)methyl-phosphonic acid diethyl ester (0.41 g, 1.88 mmol) in THF (10 ml) is added at -78°C over a period of 15 min n-butyllithium (1.3 ml, 2.08 mmol, 1.6 M in hexanes). The mixture is stirred for 1 h, and a solution of (S)-3-(1-nitro-cyclopentyl)-cyclohexanone (0.39 g, 2.10 mmol) in THF (5 ml) is added. The mixture is stirred for further 15 min at -78°C, allowed to warm to rt, treated after 1 h with saturated aqueous ammonium chloride solution (3 ml) and extracted with EtOAc (40 ml). The organic layer is washed with brine, dried over sodium sulfate and concentrated. The residue is purified by column chromatography (5% EtOAc in hexanes) to yield a colorless oil.
IR ($CHCl_3$): 1537, 1710 cm^{-1}.

b) (1R,3S)-3-(1-Nitro-cyclopentyl)-cyclohexanecarboxylic acid methyl ester
A solution of building block A5a) (0.437 g, 1.44 mmol), mercuric chloride (1.57 g, 5.82 mmol) and perchloric acid (0.62 ml of a 70% aqueous solution, 4.35 mmol) in methanol (35 ml) is heated to reflux for 2 h. After cooling and filtration, the reaction mixture is neutralized with saturated aqueous bicarbonate solution and extracted with DCM. The combined organic layers are washed with brine, dried over sodium sulfate and concentrated to yield a diastereomeric mixture of the ester as a thick gum. This product is, together with sodium methoxide in methanol (0.5 M, 5 ml), heated to reflux for 48 h. The reaction mixture is cooled to rt, neutralized with Amberlite IR-120 (H^+) resin and filtered. The filtrate is concentrated, and the residue is purified by column chromatography (EtOAc:hexanes 1:4) to yield a colorless oil.
IR ($CHCl_3$): 1535, 1735 cm^{-1}.

c) (1R,3S)-3-(1-Acetylamino-cyclopentyl)-cyclohexanecarboxylic acid methyl ester
Building block A5b) (56 mg, 0.22 mmol) is dissolved in CH_3OH (2 ml) in a thick-walled tube. Raney-Ni (50% in water, 0.3 ml) is added, followed by a catalytic amount of H_2PtCl_6. The

mixture is stirred under H_2 (60 psi) for 14 h. The catalyst is filtered off, and the filtrate is evaporated to yield the crude amine, which is dissolved in DCM (2 ml). Acetic anhydride (62 µl, 0.66 mmol) is added, followed by triethylamine (92 µl, 0.66 mmol) and DMAP (catalytic amount). The reaction mixture is stirred at rt for 3 h and then quenched with aqueous ammonium chloride solution. The organic layer is diluted with EtOAc, washed with hydrochloric acid (1 N) and sodium bicarbonate solution, dried and concentrated. The residue is purified by chromatography (EtOAc:hexanes 1:1) to yield a colorless oil.
^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.20 (s, 1H), 3.60 (s, 3H), 2.36-2.22 (m, 1H), 2.20-2.00 (m, 1H), 1.97-1.84 (m, 8H), 1.79-1.63 (m, 8H), 1.33-1.27 (m, 3H).

<u>Building block A6:</u> (1R,3S)-3-[1-Methyl-1-(methyl-propionyl-amino)-ethyl]-cyclohexanecarboxylic acid

a) (1R,3S)-3-(1-Ethoxycarbonylamino-1-methyl-ethyl)-cyclohexanecarboxylic acid methyl ester

Building block A1b) (200 mg, 0.86 mmol) is dissolved in CH_3OH (10 ml) in a thick-walled tube. Raney-Ni (50% in water, 1.5 ml) is added, followed by a catalytic amount of H_2PtCl_6. The mixture is stirred under H_2 (60 psi) for 14 h (until TLC shows the full consumption of the starting material). The catalyst is filtered off, and the filtrate is evaporated to yield the crude amine, which is dissolved in DCM (3.3 ml) and water (1.6 ml). Sodium carbonate (159 mg, 1.4 mmol) is added, and the mixture is stirred for 10 min. Ethyl chloroformate (0.1 ml, 1.05 mmol) is added dropwise. The mixture is stirred at rt for 30 min, then quenched by adding aqueous ammonium chloride solution and extracted with DCM. The combined organic extracts are washed with brine, dried over sodium sulfate and concentrated. The residue is purified by column chromatography to yield a colorless solid.
MS (ESI): 272 $(M + 1)^+$.

b) N-[1-((1S,3R)-3-Hydroxymethyl-cyclohexyl)-1-methyl-ethyl]-N-methyl-propionamide

To a solution of building block A6a) (190 mg, 0.7 mmol) in THF (5 ml) is added lithium aluminium hydride (80 mg, 2.1 mmol) portionwise at 0°C during 15 min. The mixture is heated to 60°C and stirred for 4 h. After cooling to 0°C, saturated aqueous $KHSO_4$ solution (2 ml) is added carefully, and the mixture is stirred for 30 min at a temperature between 0°C and rt, diluted with DCM and water and filtered through a pad of Celite. The filtrate is washed with saturated sodium bicarbonate solution and brine, dried over sodium sulfate and concentrated

to yield the methylamine. To a solution of this amine (28 mg, 0.15 mmol) in DCM (1 ml) and water (0.5 ml) is added sodium carbonate (35 mg, 0.31 mmol), and the mixture is stirred for 10 min. Propionyl chloride (26 µl, 0.3 mmol) is added dropwise. The mixture is stirred at rt for 40 min, then quenched by adding aqueous ammonium chloride solution and extracted with DCM. The combined organic extracts are washed with brine, dried over sodium sulfate and concentrated. The residue is purified by column chromatography to yield the title compound.
^{1}H-NMR (400 MHz, $CDCl_3$): δ 3.42 (m, 5H), 2.88 (s, 3H), 2.60 (tt, J = 12.2, 3.0 Hz, 1H), 2.33 (m, 3H), 1.80-1.47 (m, 4H), 1.35 (s, 3H), 1.32 (s, 3H), 1.29 (m, 1H), 1.08 (t, J = 7.3 Hz, 3H), 0.94 (qd, J = 12.4, 3.5 Hz, 1H), 0.80 (qd, J = 12.4, 3.5 Hz, 1H), 0.71 (q, J = 12.0 Hz, 1H).

c) (1R,3S)-3-[1-Methyl-1-(methyl-propionyl-amino)-ethyl]-cyclohexanecarboxylic acid
To a solution of building block A6b) (38 mg, 0.16 mmol) in acetone (2 ml) and saturated sodium bicarbonate solution (0.5 ml) are added at 0°C under stirring sodium bromide (4 mg, 0.04 mmol), TEMPO (1 mg) and trichloroisocyanuric acid (73 mg, 0.32 mmol). The mixture is stirred overnight at a temperature between 0°C and rt. Isopropanol (1 ml) is added. The mixture is filtered through a pad of Celite, and the filter cake is washed with EtOAc. The combined filtrates are washed with 1 N aqueous hydrochloric acid (2 ml) and brine, dried over sodium sulfate and concentrated to yield the title compound.
^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.00 (b, 1H), 2.89 (s, 3H), 2.69 (t, J = 12.0 Hz, 1H), 2.32 (m, 3H), 1.95 (m, 1H), 1.80 (m, 2H), 1.57 (m, 1H), 1.35 (s, 3H), 1.32 (s, 3H), 1.29-1.12 (m, 3H), 1.08 (t, J = 7.3 Hz, 3H), 0.94 (m, 1H).

<u>Building block A7:</u> (1R,3S)-3-[1-Methyl-1-(6-oxo-3,6-dihydro-2H-pyridin-1-yl)-ethyl]-cyclohexanecarboxylic acid methyl ester

a) (1R,3S)-3-[1-(Allyl-but-3-enoyl-amino)-1-methyl-ethyl]-cyclohexanecarboxylic acid methyl ester
To a solution of building block A3a) (14 mg, 0.059 mmol) in DCM (1 ml) are added under argon at rt but-3-enoic acid (7.5 µl, 0.088 mmol), DCC (16.9 mg, 0.082 mmol), DIEA (20.4 µl, 0.12 mmol) and DMAP (catalytic amount). The mixture is stirred for 30 min, then quenched with 1 N hydrochloric acid (0.2 ml) and extracted with DCM. The combined organic extracts are washed with water, dried over sodium sulfate and evaporated. The residue is purified by column chromatography to yield the title compound.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.01-5.83 (m, 2H), 5.26-5.05 (m, 4H), 3.91 (m, 2H), 3.66 (s, 3H), 3.10 (m, 2H), 2.75-2.69 (m, 1H), 2.34-2.31 (m, 1H), 1.98-1.55 (m, 8H), 1.39 (s, 6H).

b) (1R,3S)-3-[1-Methyl-1-(6-oxo-3,6-dihydro-2H-pyridin-1-yl)-ethyl]-cyclohexane-carboxylic acid methyl ester

To a solution of building block A7a) (10 mg, 0.034 mmol) in DCM (6 ml) is added under argon at reflux temperature a catalytic amount of Grubbs' first generation catalyst. The mixture is heated under reflux for 3 h, filtered through a pad of Florisil/silica and evaporated. The residue is purified by column chromatography to yield the title compound.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.77-5.73 (m, 1H), 5.68-5.64 (m, 1H), 3.94 (m, 1H), 3.65 (s, 3H), 2.96-2.85 (m, 3H), 2.38-2.32 (m, 1H), 1.94-1.86 (m, 1H), 1.85-1.80 (m, 2H), 1.64-1.61 (m, 1H), 1.41 (s, 3H), 1.40 (s, 3H).

<u>Building block A8:</u> (1R,3S)-3-((S)-1-Acetylamino-2-methyl-propyl)-cyclohexane-carboxylic acid methyl ester

a) (3R,4R)-4-Benzyloxymethoxy-5-methyl-3-vinyl-hexanoic acid methyl ester

To a suspension of copper(I)iodide (5.71 g, 30 mmol) in THF (100 ml) is added at -78°C over 20 min vinylmagnesium bromide (60 ml, 1 M in THF). The mixture is stirred for 45 min. (E)-(R)-4-Benzyloxymethoxy-5-methyl-hex-2-enoic acid methyl ester (1.39 g, 5 mmol) in THF (20 ml) and TMSCl (11.4 ml, 90 mmol) are added, and the mixture is stirred at -78°C for 4 h, then quenched with aqueous NH_4OH/NH_4Cl solution (1:1, 100 ml) and allowed to warm to rt. The organic layer is washed with aqueous saturated ammonium chloride solution and brine, dried over sodium sulfate and evaporated. The residue is purified by column chromatography (5% EtOAc in hexanes) to yield a colorless oil.

IR ($CHCl_3$): 1740 cm^{-1}.

b) (3R,4R)-4-Benzyloxymethoxy-5-methyl-3-vinyl-hexan-1-ol

To a solution of building block A8a) (0.612 g, 2 mmol) in THF (20 ml) is added at 0°C DIBALH (3 ml, 1.5 M in toluene, 4.5 mmol). The mixture is stirred for 2 h, then quenched with CH_3OH (5 ml), followed by *Rochelle salt* (sodium potassium tartrate tetrahydrate) solution (15 ml) and EtOAc (50 ml), and stirred for further 2 h. The organic layer is washed with brine, dried over sodium sulfate and concentrated. The residue is filtered through a short pad of

silica gel (the filter cake being washed with 15% EtOAC in hexanes) to yield a colorless viscous oil.
IR ($CHCl_3$): 3416 cm^{-1}.

c) ((3R,4R)-4-Benzyloxymethoxy-5-methyl-3-vinyl-hexyloxy)-tert-butyl-dimethyl-silane
To a solution of building block A8b) (2.2 g, 7.91 mmol) in DCM (80 ml) are added DMAP (2.89 g, 23.73 mmol) and tert-butyl-dimethylsilylchloride (1.31 g, 8.7 mmol). The mixture is stirred at rt for 30 min, diluted with DCM (100 ml), washed with 1 N hydrochloric acid and brine, dried over sodium sulfate and concentrated. The residue is filtered through a short pad of silica gel to yield a transparent oil.
MS (ESI): 393.3 $(M + 1)^+$.

d) (3R,4R)-4-[2-(tert-Butyl-dimethyl-silanyloxy)-ethyl]-2-methyl-hex-5-en-3-ol
Building block A8c) (1 g, 2.55 mmol) in THF (7 ml) is added at -78°C to a solution of sodium (0.704 g, 30.6 mmol) in liquid ammonia (250 ml). The mixture is stirred at -78°C for 1 h. Then, the cooling bath is removed, and the ammonia is refluxed at rt for 2 h. The mixture is quenched by careful addition of solid ammonium chloride, until it turns colorless. The excess ammonia is removed by a stream of nitrogen. The mixture is extracted with diethylether (3 x 75 ml). The combined extracts are evaporated, and the residue is purified by column chromatography (4% EtOAc in hexanes) to yield a colorless oil.
IR ($CHCl_3$): 3437 cm^{-1}.

e) ((3R,4S)-4-Azido-5-methyl-3-vinyl-hexyloxy)-tert-butyl-dimethyl-silane
To a solution of building block A8d) (0.51 g, 1.87 mmol) in THF (19 ml) is added at 0°C triphenyl phosphine (2.454 g, 9.37 mmol). The mixture is stirred, until a homogeneous solution is obtained. DIAD (1.85 ml, 9.37 mmol) is added with stirring over 5 min (a white precipitate is formed). DPPA (2.018 ml, 9.37 mmol) is added dropwise at 0°C. The mixture is stirred at rt for 24 h and concentrated. The residue is purified by chromatography (5% EtOAc in hexanes) to yield a colorless transparent oil.
IR (neat): 2099 cm^{-1}.

f) (3R,4S)-4-Azido-5-methyl-3-vinyl-hexan-1-ol
To a solution of building block A8e) (0.4 g, 1.35 mmol) in THF (15 ml) is added tetrabutylammonium fluoride (1.35 ml, 1 M in THF, 1.35 mmol). The mixture is stirred at rt for 2 h and

concentrated. The residue is purified by chromatography (20% EtOAc in hexanes) to yield a colorless oil.
IR (neat): 3341, 2097 cm^{-1}.

g) (3R,4S)-4-Azido-5-methyl-3-vinyl-hexanal

To a solution of oxalyl chloride (138 µl, 1.5 mmol) in DCM (10 ml) is added dropwise at -78°C DMSO (289 µl, 4.08 mmol). The mixture is stirred for 15 min. Building block A8f) (0.250 g, 1.36 mmol) in DCM (5 ml) is added, followed after 30 min by DIEA (945 µl, 5.44 mmol). The mixture is stirred for 30 min, then allowed to warm to rt over 30 min, quenched with water (5 ml) and extracted with DCM (50 ml). The organic extract is washed with citric acid solution and brine, dried over sodium sulphate and concentrated. The residue is purified by column chromatography (4% EtOAc in hexanes) to yield a transparent viscous oil.
IR (neat): 2100, 1726 cm^{-1}.

h) 2-((3R,4S)-4-Azido-5-methyl-3-vinyl-hexylidene)-[1,3]dithiane

To a solution of 2-phosphoryl-1,3-dithiane (0.371 g, 1.45 mmol) in THF (15 ml) is added at -78°C n-butyllithium (0.9 ml, 1.6 M in hexane, 1.45 mmol). The mixture is stirred for 1 h. Building block A8g) (0.24 g, 1.32 mmol) in THF (5 ml) is added. The mixture is stirred at -78°C for 15 min and after the removal of the cooling bath for further 30 min, quenched with aqueous ammonium chloride solution (5 ml) and extracted with diethylether (50 ml). The organic extract is concentrated, and the residue is purified by column chromatography (2% EtOAc in hexanes) to yield a pale yellow oil.
IR (neat): 2099 cm^{-1}.

i) (4R,5S)-5-Azido-6-methyl-4-vinyl-heptanoic acid methyl ester

Building block A8h) (0.22 g, 0.77 mmol) is dissolved in a methanolic solution of $CuSO_4$ (30 ml, 0.2 M). The mixture is stirred at 65°C for 2.5 h, cooled to rt and concentrated. The residue is diluted with EtOAc (40 ml) and water (5 ml). The organic layer is concentrated, and the residue is purified by column chromatography (3% EtOAc in hexanes) to yield a colorless viscous oil.
IR (neat): 2100, 1740 cm^{-1}.

j) (4R,5S)-2-Allyl-5-azido-6-methyl-4-vinyl-heptanoic acid methyl ester

To a solution of building block A8i) (0.15 g, 0.66 mmol) in THF (30 ml) are added at -78°C KHMDS (3.3 ml, 0.5 M in toluene, 1.65 mmol) and allyl bromide (285 µl, 3.3 mmol). The mixture is stirred for 5 min, quenched with water (7 ml) and allowed to warm to rt. The organic layer is extracted with EtOAc (50 ml), dried over sodium sulfate and concentrated. The residue is purified by column chromatography (2% EtOAc in hexanes) to yield a colorless oil.
IR (neat): 2100, 1737 cm^{-1}.

k) (1R,5R)-5-((S)-1-Azido-2-methyl-propyl)-cyclohex-3-enecarboxylic acid methyl ester

To a solution of building block A8j) (0.029 g, 0.11 mmol) in DCM (20 ml) is added Grubbs' second generation catalyst (13 mg, 0.0153 mmol). The mixture is stirred at rt for 3 h and then concentrated. The residue is purified by chromatography (3% EtOAc in hexanes) to yield a colorless gum (mixture of epimers). This gum is taken up in a methanolic solution of $NaOCH_3$ (0.5 M, 3 ml). The mixture is heated under reflux for 48 h, cooled to rt, neutralized with Amberlite resin, diluted with chloroform (15 ml) and filtered. The organic filtrate is concentrated, the residue is dissolved in CH_3OH (5 ml), the solution is treated at 0°C with an excess of diazomethane, and the mixture is allowed to warm to rt over 1 h and concentrated. The residue is filtered through a small pad of silica gel to yield the title compound.
IR ($CHCl_3$): 2099, 1737 cm^{-1}.

l) (1R,3S)-3-((S)-1-Acetylamino-2-methyl-propyl)-cyclohexanecarboxylic acid methyl ester

To a solution of building block A8k) (0.04 g, 0.168 mmol) in CH_3OH (12 ml) is added $Pd(OH)_2$/carbon (0.080 g, 20% by weight). The mixture is stirred under a hydrogen atmosphere (1 atm) for 3 h and then filtered through Celite. The organic filtrate is concentrated, and the residue is taken up in DCM (2 ml). Pyridine (41 µl, 0.504 mmol) and acetic anhydride (48 µl, 0.504 mmol) are added, and the mixture is stirred at rt for 12 h, diluted with DCM (12 ml), washed with aqueous HCl and brine, dried over sodium sulfate and evaporated. The residue is purified by chromatography (80% EtOAc in hexanes) to yield a colorless solid.
^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.10 (d, J = 6.5 Hz, 1H), 3.66 (s, 3H), 2.36 (tt, J = 3.5 Hz, 1H), 2.02 (s, 3H), 1.98-1.81 (m, 2H), 1.75-1.72 (m, 2H), 1.70-1.67 (m, 3H), 1.60-1.40 (m, 1H), 1.40-1.20 (m, 3H), 0.93 (d, J = 6.7 Hz, 3H), 0.85 (d, J = 6.7 Hz, 3H).

Building block A9: **(1R,3R)-3-((R)-1-tert-Butoxycarbonylamino-butyl)-3-hydroxy-cyclohexanecarboxylic acid 2-trimethylsilanyl-ethyl ester** (assignment of stereochemistry of amino substituent arbitrary)

a) (R)-3-Oxo-cyclohexanecarboxylic acid 2-trimethylsilanyl-ethyl ester
(R)-3-Oxo-cyclohexanecarboxylic acid (184 mg, 1.29 mmol) is dissolved in DCM (12 ml). 2-Trimethylsilanyl-ethanol (0.37 ml, 2.58 mmol, 2 equivalents) and EDCI (298 mg, 1.2 equivalents) are added. The mixture is stirred at a temperature between 0°C and 5°C for 24 h, quenched with aqueous ammonium chloride solution and diluted with EtOAc. The organic layer is dried over sodium sulfate and evaporated to yield a colorless oil, which is used in the next reaction step without further purification.

b) (1R,3R)-3-Hydroxy-3-((R)-1-nitro-butyl)-cyclohexanecarboxylic acid 2-trimethylsilanyl-ethyl ester (assignment of stereochemistry of nitro substituent arbitrary)
To a solution of building block A9a) (124 mg, 0.51 mmol) in DCM (10 ml) are added at 0°C 1-nitrobutane (1 ml), 4 Å molecular sieve (50 mg) and TBD (53 mg). The mixture is stirred at 0°C for 72 h, quenched with aqueous ammonium chloride solution and diluted with EtOAc. The organic layer is dried over sodium sulfate and evaporated to yield an oil (1:1 mixture of epimers). Chromatography of the oil on silica gel (EtOAc : hexanes = 1 : 6) yields the title compound (less polar epimer).
$[\alpha]_D^{20}$ (c = 1.0, $CHCl_3$): + 5.0.

c) (1R,3R)-3-((R)-1-tert-Butoxycarbonylamino-butyl)-3-hydroxy-cyclohexanecarboxylic acid 2-trimethylsilanyl-ethyl ester (assignment of stereochemistry of amino substituent arbitrary)
A solution of building block A9b) in CH_3OH (10 ml) is overnight subjected to reduction in the presence of Raney-Ni (20 mg) and H_2PtCl_6 (5 mg) under a hydrogen atmosphere (60 psi). The mixture is filtered, and to the filtrate is added BOC_2O in dioxane and aqueous 1 N NaOH. The mixture is stirred for 12 h, neutralized with 0.1 N aqueous hydrochloric acid and extracted with EtOAc. The extract is dried over sodium sulfate and evaporated. The residue is purified by chromatography on silica gel (EtOAc : hexanes = 1 : 3) to yield the title compound.
$[\alpha]_D^{20}$ (c = 0.8, $CHCl_3$): + 3.0.

Building block A10: (1R,3R)-3-((S)-1-tert-Butoxycarbonylamino-butyl)-3-hydroxy-cyclohexanecarboxylic acid 2-trimethylsilanyl-ethyl ester (assignment of stereochemistry of amino substituent arbitrary)

a) (1R,3R)-3-Hydroxy-3-((S)-1-nitro-butyl)-cyclohexanecarboxylic acid 2-trimethylsilanyl-ethyl ester (assignment of stereochemistry of nitro substituent arbitrary)
The title compound is obtained as the more polar epimer in the final chromatography step of the synthesis of building block A9b).
$[\alpha]_D^{20}$ (c = 1.7, $CHCl_3$): - 10.4.

b) (1R,3R)-3-((S)-1-tert-Butoxycarbonylamino-butyl)-3-hydroxy-cyclohexanecarboxylic acid 2-trimethylsilanyl-ethyl ester (assignment of stereochemistry of amino substituent arbitrary)
A solution of building block A10a) in CH_3OH (10 ml) is overnight subjected to reduction in the presence of Raney-Ni (20 mg) and H_2PtCl_6 (5 mg) under a hydrogen atmosphere (60 psi). The mixture is filtered, and to the filtrate is added BOC_2O in dioxane and aqueous 1 N NaOH. The mixture is stirred for 12 h, neutralized with 0.1 N aqueous hydrochloric acid and extracted with EtOAc. The extract is dried over sodium sulfate and evaporated. The residue is purified by chromatography on silica gel (EtOAc : hexanes = 1 : 3) to yield the title compound.
$[\alpha]_D^{20}$ (c = 1.2, $CHCl_3$): - 19.94.

Building block A11: (1R,3R)-3-Hydroxy-3-(1-methylcarbamoyl-butyl)-cyclohexanecarboxylic acid 2-trimethylsilanyl-ethyl ester

a) (1R,3R)-3-(1-Benzyloxycarbonyl-butyl)-3-hydroxy-cyclohexanecarboxylic acid 2-trimethylsilanyl-ethyl ester
To a solution of benzyl pentanoate (480 mg, 2.5 mmol) in THF (4 ml) are added at rt LDA (2.5 mmol) and $CeCl_3$ (3 mmol). To this mixture is added at -78°C building block A9a) (242 mg, 1 mmol) in THF (10 ml). The mixture is stirred for 5 h, quenched with aqueous ammonium chloride solution and extracted with EtOAc. The organic extract is dried over sodium sulfate and evaporated to yield the title compound (mixture of epimers).

b) (1R,3R)-3-Hydroxy-3-(1-methylcarbamoyl-butyl)-cyclohexanecarboxylic acid 2-trimethylsilanyl-ethyl ester

A solution of building block A11a) (34 mg) in EtOAc is hydrogenated at rt in the presence of 10% Pd/carbon. The mixture is filtered, the filtrate is evaporated, and the residue is dissolved in DCM (10 ml). PyBOP (78 mg), DIEA (207 mg) and methylamine (27 mg) are added at 0°C. The mixture is stirred for 3 h, neutralized with 0.1 N aqueous hydrochloric acid and extracted with EtOAc. The organic extract is evaporated, and the residue is purified by chromatography on silica gel (EtOAc : hexanes = 1 : 3) to yield the title compound (mixture of epimers).
$[\alpha]_D^{20}$ (c = 1, $CHCl_3$): + 5.2.

Example 1: (1R,3S)-3-(1-Acetylamino-1-methyl-ethyl)-cyclohexanecarboxylic acid ((1S,2S,4R)-1-benzyl-4-butylcarbamoyl-2-hydroxy-pentyl)-amide

A solution of building block A1 (25.4 mg, 0.105 mmol) and LiOH (1 N, 0.26 ml) in CH_3OH (0.5 ml) is stirred at rt for 14 h, neutralized with 1 N hydrochloric acid and extracted with EtOAc (3 x 5 ml). The combined extracts are dried and concentrated to yield the crude acid, which is added to a solution of (2R,4S,5S)-5-amino-4-hydroxy-2-methyl-6-phenyl-hexanoic acid butylamide (building block B1, 12 mg, 0.042 mmol) in DCM/DMF (5:1, 1 ml). At 0°C PyBOP (21.8 mg, 0.042 mmol) and DIEA (14.6 µl, 0.084 mmol) are added. The mixture is stirred at 5°C for 14 h, diluted with EtOAc (5 ml), washed with 1 N hydrochloric acid and saturated aqueous sodium bicarbonate solution, dried and concentrated. The residue is purified by chromatography (EtOAc/CH_3OH 9:1) to yield a colorless solid.
^{1}H-NMR (400 MHz, CD_3OD): δ 7.28-7.14 (m, 5H), 6.18-6.15 (m, 2H), 5.20 (s, 1H), 4.52 (s, 1H), 4.07-4.04 (m, 1H), 3.65 (dd, J = 13.0, 6.8 Hz, 1H), 3.22-3.12 (m, 3H), 2.94 (m, 2H), 2.52 (dd, J = 13.0, 6.8 Hz, 1H), 2.16-2.02 (m, 3H), 1.90-1.53 (m, 4H), 1.46-1.32 (m, 8H), 1.29-1.24 (m, 5H), 1.12-1.02 (m, 7H), 0.92 (t, J =7.2 Hz, 3H).

Example 2: (1R,3S)-3-(1-Methyl-1-propionylamino-ethyl)-cyclohexanecarboxylic acid ((1S,2S,4R)-1-benzyl-4-butylcarbamoyl-2-hydroxy-pentyl)-amide

The title compound is prepared as a colorless solid in a manner analogous to that described in Example 1 starting from building block A2 and building block B1.
^{1}H-NMR (400 MHz, CD_3OD): δ 7.24-7.13 (m, 5H), 4.07 (m, 1H), 3.58 (m, 1H), 3.33 (m, 2H), 3.15 (t, J = 6.9 Hz, 2H), 2.91 (m, 1H), 2.90-2.78 (m, 1H), 2.58 (m, 1H), 2.18-2.12 (m, 4H), 1.83 (m, 1H), 1.75-1.64 (m, 3H), 1.49-1.26 (m, 8H), 1.22 (s, 3H), 1.20 (s, 3H), 1.12-1.01 (m, 6H), 0.98-0.93 (m, 4H).

Example 3: (1R,3S)-3-[1-Methyl-1-(2-oxo-pyrrolidin-1-yl)-ethyl]-cyclohexanecarboxylic acid ((1S,2S,4R)-1-benzyl-4-butylcarbamoyl-2-hydroxy-pentyl)-amide

To a solution of building block A3 (20 mg, 0.075 mmol) in CH_3OH (5 ml) is added 10% Pd/-carbon (catalytic amount). The mixture is stirred at rt under a hydrogen atmosphere for 14 h and then filtered through Celite. The filter cake is rinsed with CH_3OH (3 x 5 ml). The combined filtrates are evaporated to yield a colorless oil, which is treated with a solution of lithium hydroxide monohydrate (9.4 mg, 0.22 mmol) in CH_3OH/water (2:1, 0.66 ml). The mixture is stirred for 12 h, neutralized with aqueous 1 N hydrochloric acid and extracted with EtOAc (3 x 5 ml). The combined extracts are dried over sodium sulfate and concentrated to yield the crude acid, which is dissolved in DCM (1.5 ml). At 0°C are added building block B1 (21.9 mg, 0.075 mmol), PyBOP (78.0 mg, 0.15 mmol) and DIEA (52.3 µl, 0.30 mmol). The mixture is stirred at 0°C for 14 h, then diluted with EtOAc to a volume of 15 ml, washed with aqueous 1 N hydrochloric acid and saturated aqueous sodium bicarbonate solution, dried and evaporated. The residue is purified by column chromatography to yield the title compound.

^{1}H-NMR (400 MHz, CD_3OD): δ 7.26-7.24 (m, 5H), 4.10 (m, 1H), 3.61-3.45 (m, 3H), 3.15 (t, J = 6.9 Hz, 2H), 2.92 (m, 1H), 2.78 (m, 1H), 2.60 (m, 1H), 2.51 (m, 1H), 2.34 (m, 2H), 2.16 (m, 1H), 1.96 (m, 2H), 1.86 (m, 1H), 1.79-1.68 (m, 2H), 1.60 (m, 1H), 1.47-1.45 (m, 3H), 1.37-1.29 (m, 12H), 1.11 (d, J = 7.0 Hz, 3H), 1.03 (m, 2H), 0.95 (t, J = 7.3 Hz, 3H).

Example 4:

(1R,3S)-3-[1-Methyl-1-(2,2,2-trifluoro-acetylamino)-ethyl]-cyclohexanecarboxylic acid ((1S,2S,4R)-1-benzyl-4-butylcarbamoyl-2-hydroxy-pentyl)-amide

The title compound is prepared in a manner analogous to that described in Example 1 starting from building block A4 and building block B1.

^{1}H-NMR (400 MHz, CD_3OD): δ 7.31-7.18 (m, 5H), 5.92-5.84 (m, 3H), 4.04 (dd, J = 15.9, 8.2 Hz, 1H), 3.77-3.69 (m, 1H), 3.29-3.16 (m, 2H), 2.95 (d, J = 7.4 Hz, 2H), 2.54 (dd, J = 12.9, 6.7 Hz, 1H), 2.09-1.86 (m, 2H), 1.78-1.45 (m, 8H), 1.43-1.33 (m, 10H), 1.27-1.13 (m, 5H), 0.90 (t, J = 7.3 Hz, 3H).

Example 5: (1R,3S)-3-(1-Acetylamino-cyclopentyl)-cyclohexanecarboxylic acid ((1S,2S,4R)-1-benzyl-4-butylcarbamoyl-2-hydroxy-pentyl)-amide

The title compound is prepared in a manner analogous to that described in Example 1 starting from building block A5 and building block B1.

^{1}H-NMR (400 MHz, CD_3OD): δ 7.29-7.11 (m, 5H), 4.05 (m, 1H), 3.56 (m, 1H), 3.12 (t, J = 6.8 Hz, 2H), 2.90 (dd, J = 13.8, 5.3 Hz, 1H), 2.73 (dd, J = 13.8, 6.9 Hz, 1H), 2.55 (m, 1H), 2.11 (m, 2H), 1.97 (m, 1H), 1.88 (s, 3H), 1.86 (m, 2H), 1.74 (m, 4H), 1.69 (m, 5H), 1.51-1.12 (m, 9H), 1.08 (d, J = 6.9 Hz, 3H), 1.01 (m, 1H), 0.92 (t, J = 7.2 Hz, 3H).

Example 6: (1R,3S)-3-(1-Acetylamino-1-methyl-ethyl)-cyclohexanecarboxylic acid [(1S,2R)-1-benzyl-2-hydroxy-3-(3-isopropyl-benzylamino)-propyl]-amide

A solution of building block A1 (8.1 mg, 0.033 mmol) and lithium hydroxide monohydrate (4.2 mg, 0.099 mmol) in CH_3OH/water (2:1, 0.66 ml) is stirred for 12 h. The mixture is then carefully neutralized with 1 N hydrochloric acid and extracted with EtOAc (3 x 5 ml). The combined extracts are dried over sodium sulfate and concentrated to yield the crude acid, which is dissolved in DCM (1.5 ml). At 0°C are added (2R,3S)-3-amino-1-(3-isopropyl-benzylamino)-4-phenyl-butan-2-ol (building block B2, 14.0 mg, 0.036 mmol), PyBOP (34.3 mg, 0.066 mmol) and DIEA (34.8 µl, 0.2 mmol). The mixture is stirred at 0°C for 14 h, then diluted with EtOAc to a volume of 10 ml, dried and concentrated. The residue is purified by column chromatography to yield a colorless solid.

^{1}H-NMR (400 MHz, CD_3OD): δ 7.41-7.17 (m, 9H), 4.21 (s, 2H), 4.00 (m, 1H), 3.78 (m, 1H), 3.10 (dd, J = 3.0, 2.9 Hz, 1H), 2.99-2.94 (m, 2H), 2.60 (t, J = 11.4 Hz, 1H), 2.11 (m, 1H), 2.01 (m, 1H), 1.89 (s, 3H), 1.80 (m, 1H), 1.65 (m, 1H), 1.50 (m, 1H), 1.30 (d, J = 6.9 Hz, 6H), 1.28 (s, 6H), 1.18-1.14 (m, 6H), 0.94-0.84 (m, 2H).

Example 7: (1R,3S)-3-(1-Methyl-1-propionylamino-ethyl)-cyclohexanecarboxylic acid [(1S,2R)-1-benzyl-2-hydroxy-3-(3-isopropyl-benzylamino)-propyl]-amide

The title compound is prepared in a manner analogous to that described in Example 6 starting from building block A2 and building block B2.

^{1}H-NMR (400 MHz, CD_3OD): δ 7.41-7.18 (m, 9H), 4.21 (s, 2H), 4.00 (m, 1H), 3.80 (m, 1H), 3.10 (d, J = 2.9 Hz, 1H), 2.99-2.94 (m, 2H), 2.59 (m, 1H), 2.17-2.10 (m, 3H), 2.01 (m, 1H), 1.85 (m, 1H), 1.66 (d, J = 7.0 Hz, 1H), 1.49 (d, J = 7.0 Hz, 1H), 1.30 (s, 3H), 1.28 (s, 3H), 1.26 (m, 1H), 1.20 (d, J = 6.1 Hz, 6H), 1.18-1.10 (m, 3H), 1.09 (t, J = 7.6 Hz, 3H), 0.97-0.80 (m, 2H).

Example 8: (1R,3S)-3-[1-Methyl-1-(methyl-propionyl-amino)-ethyl]-cyclohexanecarboxylic acid [(1S,2R)-1-benzyl-2-hydroxy-3-(3-isopropyl-benzylamino)-propyl]-amide

The title compound is prepared in a manner analogous to that described in Example 6 starting from building block A6 and building block B2.
^{1}H-NMR (CD_3OD): δ 7.39-7.18 (m, 9H), 4.2 (s, 2H), 4.03 (m, 1H), 3.75 (m, 1H), 3.07 (m, 1H), 2.96 (m, 2H), 2.88 (s, 3H), 2.58 (m, 2H), 2.34 (m, 2H), 1.97 (m, 1H), 1.78 (m, 1H), 1.49 (m, 2H), 1.37 (m, 1H), 1.29 (s, 3H), 1.27 (s, 3H), 1.26 (d, J = 13.7 Hz, 6H), 1.22-1.10 (m, 3H), 1.05 (t, J = 7.4 Hz, 3H), 1.02-0.88 (m, 2H).

Example 9: (1R,3S)-3-[1-Methyl-1-(2-oxo-pyrrolidin-1-yl)-ethyl]-cyclohexanecarboxylic acid [(1S,2R)-1-benzyl-2-hydroxy-3-(3-isopropyl-benzylamino)-propyl]-amide
To a solution of building block A3 (20 mg, 0.075 mmol) in CH_3OH (5 ml) is added 10% Pd/-carbon (catalytic amount). The mixture is stirred at rt under a hydrogen atmosphere for 14 h and then filtered through Celite. The filter cake is rinsed with CH_3OH (3 x 5 ml). The combined filtrates are evaporated to yield a colorless oil, which is treated with a solution of lithium hydroxide monohydrate (9.4 mg, 0.22 mmol) in CH_3OH/water (2:1, 0.66 ml). The mixture is stirred for 12 h, neutralized with aqueous 1 N hydrochloric acid and extracted with EtOAc (3 x 5 ml). The combined extracts are dried over sodium sulfate and concentrated to yield the crude acid, which is dissolved in DCM (1.5 ml). At 0°C are added building block B2 (31.6 mg, 0.082 mmol), PyBOP (78.1 mg, 0.15 mmol) and DIEA (78.4 µl, 0.45 mmol). The mixture is stirred at 0°C for 14 h, then diluted with EtOAc to a volume of 15 ml, washed with aqueous 1 N hydrochloric acid and saturated aqueous sodium bicarbonate solution, dried and concentrated. The residue is purified by column chromatography to yield the title compound.
^{1}H-NMR (400 MHz, CD_3OD): δ 7.39-7.18 (m, 9H), 4.20 (s, 2H), 4.05 (m, 1H), 3.76 (m, 1H), 3.45 (m, 2H), 3.08 (m, 1H), 2.96 (m, 2H), 2.60 (m, 1H), 2.44 (m, 1H), 2.30 (m, 2H), 2.05-1.86 (m, 4H), 1.79 (m, 1H), 1.57 (d, J = 12.6 Hz, 1H), 1.49 (d, J = 12.6 Hz, 1H), 1.29 (s, 3H), 1.27 (s, 3H), 1.23 (d, J = 7.9 Hz, 6H), 1.17-1.05 (m, 3H), 1.03-0.86 (m, 2H).

Example 10: (1R,3S)-3-[1-Methyl-1-(2-oxo-piperidin-1-yl)-ethyl]-cyclohexanecarboxylic acid [(1S,2R)-1-benzyl-2-hydroxy-3-(3-isopropyl-benzylamino)-propyl]-amide
To a solution of building block A7 (10 mg, 0.036 mmol) in CH_3OH (2 ml) is added 10% Pd/-carbon (catalytic amount). The mixture is stirred at rt under a hydrogen atmosphere for 14 h and then filtered through Celite. The filter cake is rinsed with CH_3OH (3 x 5 ml). The combined filtrates are evaporated to yield a colorless oil, which is treated with a solution of lithium hydroxide monohydrate (4.6 mg, 0.11 mmol) in THF/water (2:1, 0.66 ml). The mixture is stirred for 10 h, carefully neutralized with aqueous 1 N hydrochloric acid and extracted with

EtOAc (3 x 5 ml). The combined extracts are dried over sodium sulfate and concentrated to yield a colorless solid, which is dissolved in DCM (0.8 ml). At 0°C are added building block B2 (13.9 mg, 0.036 mmol), PyBOP (31.2 mg, 0.06 mmol) and DIEA (31.3 µl, 0.18 mmol). The mixture is stirred at 0°C for 7 h, then diluted with EtOAc to a volume of 10 ml, washed with aqueous 1 N hydrochloric acid and saturated aqueous sodium bicarbonate solution, dried and concentrated. The residue is purified by column chromatography to yield the title compound.

^{1}H-NMR (400 MHz, CD_3OD): δ 7.39-7.16 (m, 9H), 4.20 (s, 2H), 4.05-3.99 (m, 1H), 3.79-3.75 (m, 1H), 3.32 (m, 2H), 3.30-3.26 (m, 2H), 3.16 (q, J = 6.7 Hz, 1H), 3.09 (dd, J = 3.0, 2.9 Hz, 1H), 2.98-2.92 (m, 2H), 2.64-2.55 (m, 2H), 2.29 (m, 2H), 1.99-1.94 (m, 1H), 1.87 (m, 2H), 1.79 (m, 1H), 1.71-1.63 (m, 4H), 1.29 (d, J = 7.0 Hz, 6H), 1.24 (s, 3H), 1.21 (s, 3H), 1.18-1.11 (m, 3H).

Example 11: (1R,3S)-3-((S)-1-Acetylamino-2-methyl-propyl)-cyclohexanecarboxylic acid ((1S,2S,4R)-1-benzyl-4-butylcarbamoyl-2-hydroxy-pentyl)-amide

The title compound is prepared in a manner analogous to that described in Example 1 starting from building block A8 and building block B1.

^{1}H-NMR (400 MHz, CD_3OD): δ 7.59 (d, J = 10.1 Hz, 1H), 7.28-7.22 (m, 3H), 7.19-7.15 (m, 1H), 4.09-4.04 (br s, 1H), 3.57-3.55 (m, 1H), 3.48-3.47 (m, 1H), 3.33-3.32 (4H, exchangable), 3.14 (t, J = 7.1 Hz, 2H), 2.92 (dd, J = 5.4, 5.5 Hz, 1H), 2.74 (dd, J = 9.8, 9.8 Hz, 1H), 2.59-2.54 (m, 1H), 2.20-2.18 (m, 1H), 1.98 (s, 3H), 1.84-1.70 (m, 5H), 1.51-1.28 (m, 10H), 1.10 (d, J = 7.0 Hz, 3H), 0.94 (t, J = 7.2 Hz, 4H), 0.91 (d, J = 6.7 Hz, 3H), 0.86 (d, J = 6.7 Hz, 3H).

Example 12: {(S)-1-[(1R,3R)-3-((1S,2S,4R)-1-Benzyl-4-butylcarbamoyl-2-hydroxy-pentylcarbamoyl)-1-hydroxy-cyclohexyl]-butyl}-carbamic acid tert-butyl ester (assignment of stereochemistry of amino substituent arbitrary)

Building block A10 is treated with TBAF in 10 ml of THF. The solvent is evaporated to yield as residue the carboxylic acid. This carboxylic acid (0.033 mmol) is dissolved in DCM (1 ml). The solution is treated with building block B1 (0.040 mmol), PyBOP (22 mg), DIEA (17.6 µl) and DMF (0.25 ml). The mixture is stirred overnight at 0°C, then neutralized with 0.1 N aqueous hydrochloric acid and extracted with EtOAc. The organic extract is evaporated, and the residue is purified by column chromatography (EtOAc : hexanes = 20 : 1) to yield a colorless solid.

HRMS: $(M + 1)^+$ 590.4174; calculated M^+ 589.4090.

Example 13: (1R,3R)-3-((S)-1-Acetylamino-butyl)-3-hydroxy-cyclohexanecarboxylic acid ((1S,2S,4R)-1-benzyl-4-butylcarbamoyl-2-hydroxy-pentyl)-amide (assignment of stereochemistry of amino substituent arbitrary)

The title compound of Example 12 (10 mg) is treated with TMSI (15 µl) in 0.5 ml of DCM. The mixture is stirred at 0°C for 30 min and then evaporated. The residue is dissolved in DCM. To the solution are added solid sodium bicarbonate and acetyl chloride (10 µl, 10 eqivalents). The mixture is diluted with EtOAc, washed with aqueous sodium carbonate solution, dried over sodium sulfate and evaporated to yield the title compound.

HRMS: $(M + 1)^+$ 532.3442; calculated M^+ 531.3672.

Example 14: {(R)-1-[(1R,3R)-3-((1S,2S,4R)-1-Benzyl-4-butylcarbamoyl-2-hydroxy-pentylcarbamoyl)-1-hydroxy-cyclohexyl]-butyl}-carbamic acid tert-butyl ester (assignment of stereochemistry of amino substituent arbitrary)

The title compound is prepared in a manner analogous to that described in Example 12 starting from building block A9 and building block B1.

HRMS: $(M + 1)^+$ 590.4162; calculated M^+ 589.4090.

Example 15: (1R,3R)-3-((R)-1-Acetylamino-butyl)-3-hydroxy-cyclohexanecarboxylic acid ((1S,2S,4R)-1-benzyl-4-butylcarbamoyl-2-hydroxy-pentyl)-amide (assignment of stereochemistry of amino substituent arbitrary)

The title compound is prepared in a manner analogous to that described in Example 13 starting from the title compound of Example 14.

^{13}C-NMR (CD_3OD): δ 177.96, 157.95, 139.16, 129.32, 128.3, 126.22, 78.85, 73.58, 69.84, 59.68, 54.95, 40.78, 39.02, 38.14, 37.67, 37.04, 35.09, 33.17, 31.59, 29.32, 27.84, 20.70, 20.09, 19.92, 17.61, 13.34, 13.13.

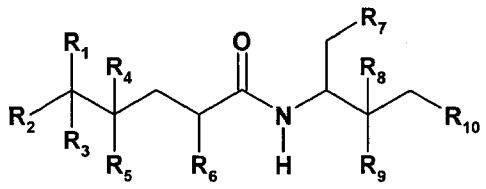
Example 16: (1R,3R)-3-Hydroxy-3-(1-methylcarbamoyl-butyl)-cyclohexanecarboxylic acid ((1S,2S,4R)-1-benzyl-4-butylcarbamoyl-2-hydroxy-pentyl)-amide

The title compound is prepared in a manner analogous to that described in Example 12 starting from building block A11 and building block B1.

HRMS: $(M + 1)^+$ 532.10; calculated M^+ 531.37.

Claims

1. A compound of the formula



(I),

in which

R_1 is a group of the formula $N(R_a)$-$C(=O)R_b$ (Ia); $N(R_a)$-$S(=O)R_b$ (Ib); $N(R_a)$-$S(=O)_2R_b$ (Ic); $C(=O)$-$N(R_a)R_b$ (Id); $S(=O)$-$N(R_a)R_b$ (Ie); or $S(=O)_2$-$N(R_a)R_b$ (If),

in which formulae Ia, Ib and Ic

either R_a is hydrogen; C_1-C_8-alkyl; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl; or heterocyclyl-C_1-C_4-alkyl; and

R_b is hydrogen; C_1-C_8-alkyl; trifluoromethyl; C_1-C_8-alkoxy; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_8-alkylthio; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl; heterocyclyl-C_1-C_4-alkyl; amino; C_1-C_8-alkylamino; or di-(C_1-C_8-alkyl)amino with two identical or different C_1-C_8-alkyl moieties, which two C_1-C_8-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_8-alkyl moieties of the di-(C_1-C_8-alkyl)amino group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member,

or R_a and R_b, taken together, complete, together with the 2 atoms, to which they are attached, a saturated or unsaturated ring, which ring is in the case of the formulae Ia and Ib monosubstituted by oxo and in the case of the formula Ic disubstituted by oxo, the said ring being optionally further substituted by 1 or 2 substituents independently selected from the group, consisting of oxo, C_1-

C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in the case of the formula Ia, the nitrogen ring member depicted in the formula Ia and optionally 1 or 2 further ring members being hetero ring members and any other ring member being present being a carbon ring member and, in the case of the formulae Ib and Ic, the nitrogen and the sulfur ring members depicted in the formulae Ib and Ic and optionally 1 further ring member being hetero ring members and any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, and

in which formulae Id, Ie and If

either R_a is hydrogen; C_1-C_8-alkyl; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl attached via one of its carbon ring members to the nitrogen atom depicted in the formulae Id, Ie and If; or heterocyclyl-C_1-C_4-alkyl; and

R_b is hydrogen; C_1-C_8-alkyl; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl; or heterocyclyl-C_1-C_4-alkyl

or R_a and R_b, taken together, complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is in the case of the formulae Id and Ie monosubstituted by oxo and in the case of the formula If disubstituted by oxo, the said ring being optionally further substituted by 1 or 2 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in the case of the formula Id, the nitrogen ring member depicted in the formula Id and optionally 1 or 2 further ring members being hetero ring members and any other ring member being present being a carbon ring member and, in the case of the formulae Ie and If, the nitrogen and the sulfur ring members depicted in the formulae Ie and If and optionally 1 further ring member being hetero ring members and any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member;

R_2 and R_3 are

either, independently from each other, hydrogen; C_1-C_8-alkyl; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_4-alkylthio-C_1-C_4-alkyl; or an aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl group, which aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl group is optionally ring-substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkyl-carbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)-amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)-amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino,

or, taken together, complete, together with the carbon atom, to which they are attached, a C_3-C_8-cycloalkyl ring, in which C_3-C_8-cycloalkyl ring 1 or 2 of its 2 to 7 methylene ring members optionally are hetero ring members independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member;

R_4 is hydrogen; hydroxy; or C_1-C_6-alkoxy;

R_5 and R_6, taken together, complete, together with the 2 carbon atoms, to which they are attached, and together with the methylene group, to which the said 2 carbon atoms are attached, a saturated ring, which ring is, in addition to the substitution by the substituents $(R_1)(R_2)(R_3)C$ and R_4 and the N-substituted aminocarbonyl group depicted in the formula I, optionally further substituted by 1 or 2 substituents independently selected from the group, consisting of C_1-C_8-alkyl, oxo, hydroxy, C_1-C_8-alkoxy, C_1-C_4-alkoxy- C_1-C_4-alkyl, C_1-C_8-alkylthio, C_1-C_4-alkylthio-C_1-C_4-alkyl, formyl, C_1-C_8-alkylcarbonyl, C_1-C_8-alkoxycarbonyl, carbamyl, N-C_1-C_8-alkylcarbamyl, N,N-di-(C_1-C_8-alkyl)carbamyl with two identical or different C_1-C_8-alkyl moieties, which two C_1-C_8-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_8-alkyl moieties of the N,N-di- (C_1-C_8-alkyl)carbamyl group are attached, optionally 1 or 2 further ring members are hetero ring

members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, C_1-C_8-alkylsulfonyl, C_1-C_8-alkoxysulfonyl, aminosulfonyl, N-C_1-C_8-alkylaminosulfonyl, N,N-di-(C_1-C_8-alkyl)aminosulfonyl with two identical or different C_1-C_8-alkyl moieties, which two C_1-C_8-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_8-alkyl moieties of the N,N-di-(C_1-C_8-alkyl)aminosulfonyl group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, C_1-C_8-alkylsulfinyl, C_1-C_8-alkoxysulfinyl, aminosulfinyl, N-C_1-C_8-alkylaminosulfinyl, N,N-di-(C_1-C_8-alkyl)aminosulfinyl with two identical or different C_1-C_8-alkyl moieties, which two C_1-C_8-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_8-alkyl moieties of the N,N-di-(C_1-C_8-alkyl)aminosulfinyl group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, C_1-C_8-alkylsulfonylamino, C_1-C_8-alkoxysulfonylamino, aminosulfonylamino, N-C_1-C_8-alkylaminosulfonylamino, N,N-di-(C_1-C_8-alkyl)aminosulfonylamino with two identical or different C_1-C_8-alkyl moieties, formylamino, C_1-C_8-alkylcarbonylamino, C_1-C_8-alkoxycarbonylamino, carbamylamino, N-C_1-C_8-alkylcarbamylamino, N,N-di-(C_1-C_8-alkyl)carbamylamino with two identical or different C_1-C_8-alkyl moieties and a heterocyclyl or heteroaryl group, the said heterocyclyl or heteroaryl group being optionally substituted by 1 or 2 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 5 to 7 ring members, of which ring members 1 or 2 ring members optionally being hetero ring members and any other ring member being a

carbon ring member, the said hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member;

R_7 is a C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, cyano, C_3-C_8-cycloalkyl, heterocyclyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl and an aryl or heteroaryl group, which aryl or heteroaryl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, which two C_1-C_4-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_4-alkyl moieties of the N,N-di-(C_1-C_4-alkyl)amino group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino; an aryl or heteroaryl group, which aryl or heteroaryl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, fluoromethyl, difluoromethyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfo-

nyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, N,N-di-(C_1-C_4-alkyl)aminosulfonyl with two identical or different C_1-C_4-alkyl moieties, which two C_1-C_4-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_4-alkyl moieties of the N,N-di-(C_1-C_4-alkyl)aminosulfonyl group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, which two C_1-C_4-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_4-alkyl moieties of the N,N-di-(C_1-C_4-alkyl)amino group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino; or an aryl group, which aryl group is optionally substituted at two of its carbon ring members, which two carbon ring members are adjacent to each other, by two substituents, which two substituents form, together with the two adjacent carbon ring members, to which they are attached, a heteroaryl ring, which heteroaryl ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkylcarbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-

alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino;

either

R_8 is hydrogen; and

R_9 is hydroxy

or

R_8 and R_9, taken together, are oxo; and

R_{10} is a group of the formula $CH(R_c)C(=O)N(R_d)R_e$ (Ig); or $(CH_2)_kN(H)R_f$ (Ih),

in which formula Ig

R_c is a C_1-C_8-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl; and

R_d and R_e

either are, independently from each other, hydrogen; a C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl; or an aryl, aryl-C_1-C_4-alkyl, heteroaryl or heteroaryl-C_1-C_4-alkyl group, which aryl, aryl-C_1-C_4-alkyl, heteroaryl or heteroaryl-C_1-C_4-alkyl group is optionally ring-substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-

alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkylcarbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino,

or, taken together, complete, together with the nitrogen atom, to which they are attached, an azepanyl, morpholinyl, piperazinyl, piperidyl or pyrrolidyl ring, which azepanyl, morpholinyl, piperazinyl, piperidyl or pyrrolidyl ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl, and in which azepanyl, morpholinyl, piperazinyl, piperidyl or pyrrolidyl ring 1 or 2 of its methylene ring members can be replaced by a hetero ring member independently selected from the group, consisting of -S(=O)- and -$S(=O)_2$-, and

in which formula Ih

k is 0; 1; or 2; and

R_f is hydrogen; a C_1-C_8-alkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, fluoromethyl, difluoromethyl, trifluoromethyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl; an aryl, aryl-C_1-C_4-alkyl, heteroaryl, heteroaryl-C_1-C_4-alkyl, chroman-4-yl, isochroman-4-yl, thiochroman-4-yl, isothiochroman-4-yl, 1,1-dioxo-1lambda*6*-thiochroman-4-yl, 2,2-dioxo-2lambda*6*-isothiochroman-4-yl, 1,2,3,4-tetrahydro-quinol-4-yl, 1,2,3,4-tetrahydro-isoquinol-4-yl, 1,2,3,4-tetrahydro-naphth-1-yl, 1,1-dioxo-1,2,3,4-tetrahydro-1lambda*6*-benzo[e][1,2]thiazin-4-yl, 2,2-dioxo-1,2,3,4-tetrahydro-2lambda*6*-benzo-[c][1,2]thiazin-4-yl, 1,1-dioxo-3,4-dihydro-1H-1lambda*6*-benzo[c][1,2]oxathiin-4-yl,

2,2-dioxo-3,4-dihydro-2H-2lambda*6*-benzo[e][1,2]oxathiin-4-yl, 2,3,4,5-tetrahydro-benzo[b]oxepin-5-yl or 1,3,4,5-tetrahydro-benzo[c]oxepin-5-yl group, which aryl, aryl-C_1-C_4-alkyl, heteroaryl, heteroaryl-C_1-C_4-alkyl, chroman-4-yl, isochroman-4-yl, thiochroman-4-yl, isothiochroman-4-yl, 1,1-dioxo-1lambda*6*-thiochroman-4-yl, 2,2-dioxo-2lambda*6*-isothiochroman-4-yl, 1,2,3,4-tetrahydro-quinol-4-yl, 1,2,3,4-tetrahydro-isoquinol-4-yl, 1,2,3,4-tetrahydro-naphth-1-yl, 1,1-dioxo-1,2,3,4-tetrahydro-1lambda*6*-benzo[e][1,2]thiazin-4-yl, 2,2-dioxo-1,2,3,4-tetrahydro-2lambda*6*-benzo[c][1,2]thiazin-4-yl, 1,1-dioxo-3,4-dihydro-1H-1lambda*6*-benzo-[c][1,2]oxathiin-4-yl, 2,2-dioxo-3,4-dihydro-2H-2lambda*6*-benzo[e][1,2]oxathiin-4-yl, 2,3,4,5-tetrahydro-benzo[b]oxepin-5-yl or 1,3,4,5-tetrahydro-benzo[c]oxepin-5-yl group is optionally ring-substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkylcarbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino, and in which aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl group the C_1-C_4-alkyl moiety is optionally substituted by 1 or 2 substituents independently selected from the group, consisting of fluoromethyl, difluoromethyl and trifluoromethyl; or a C_4-C_8-cycloalkyl group, in which C_4-C_8-cycloalkyl group

(a) one of the carbon ring members of the C_4-C_8-cycloalkyl moiety, which carbon ring members are different from the carbon ring member of the C_4-C_8-cycloalkyl moiety, to which the nitrogen atom depicted in the formula Ih is attached, is optionally replaced by a hetero ring member independently selected from the group, consisting of -O-, -S-, -S(=O)-, -S(=O)$_2$- and -N(R_g)-,

R_g being hydrogen; a C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group,

consisting of cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl; or an aryl, aryl-C_1-C_4-alkyl, heteroaryl or heteroaryl-C_1-C_4-alkyl group, which aryl, aryl-C_1-C_4-alkyl, heteroaryl or heteroaryl-C_1-C_4-alkyl group is optionally ring-substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkylcarbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino,

(b) the C_4-C_8-cycloalkyl moiety, which C_4-C_8-cycloalkyl moiety is optionally modified as defined under (a) hereinbefore to contain one hetero ring member, is optionally substituted by 1 to 4 substituents independently selected from the group, consisting of halogen, cyano, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkoxycarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, a C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl, and an aryl, aryl-C_1-C_4-alkyl, heteroaryl, heteroaryl-C_1-C_4-alkyl, heterocyclyl or heterocyclyl-C_1-C_4-alkyl group, which aryl, aryl-C_1-C_4-alkyl, heteroaryl, heteroaryl-C_1-C_4-alkyl, heterocyclyl or heterocyclyl-C_1-C_4-alkyl group is optionally ring-substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloal-

kyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkylcarbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino, and

(c) the C_4-C_8-cycloalkyl moiety, which C_4-C_8-cycloalkyl moiety is optionally modified as defined under (a) hereinbefore to contain one hetero ring member, is optionally substituted at two of its carbon ring members, which two carbon ring members are adjacent to each other, by two substituents, which two substituents form, together with the two adjacent carbon ring members, to which they are attached, a C_3-C_8-cycloalkyl ring, in which C_3-C_8-cycloalkyl ring

(i) one of the carbon ring members of the C_3-C_8-cycloalkyl ring thus formed, which carbon ring members are different from the said two adjacent carbon ring members of the C_3-C_8-cycloalkyl ring thus formed, to which the said two substituents are optionally attached, is optionally replaced by a hetero ring member independently selected from the group, consisting of -O-, -S-, -S(=O)-, -S(=O)$_2$- and -N(R_h)-,

R_h being hydrogen; a C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl; or an aryl, aryl-C_1-C_4-alkyl, heteroaryl or heteroaryl-C_1-C_4-alkyl group, which aryl, aryl-C_1-C_4-alkyl, heteroaryl or heteroaryl-C_1-C_4-alkyl group is optionally ring-substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hy-

droxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkylcarbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formylamino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl-C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino, and

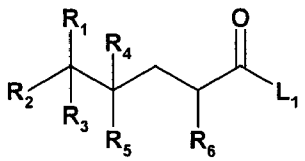
(ii) the C_3-C_8-cycloalkyl ring thus formed, which C_3-C_8-cycloalkyl ring is optionally modified as defined under (i) hereinbefore to contain one hetero ring member, is optionally substituted by 1 to 4 substituents independently selected from the group, consisting of halogen, cyano, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkoxycarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, a C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group, which C_1-C_8-alkyl, C_3-C_8-cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl group is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, cyano, C_3-C_8-cycloalkyl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, oxo, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, formyl, C_1-C_4-alkylcarbonyl and C_1-C_4-alkoxycarbonyl, and an aryl, aryl-C_1-C_4-alkyl, heteroaryl, heteroaryl-C_1-C_4-alkyl, heterocyclyl or heterocyclyl-C_1-C_4-alkyl group, which aryl, aryl-C_1-C_4-alkyl, heteroaryl, heteroaryl-C_1-C_4-alkyl, heterocyclyl or heterocyclyl-C_1-C_4-alkyl group is optionally ring-substituted by 1 to 3 substituents independently selected from the group, consisting of halogen, nitro, cyano, C_3-C_8-cycloalkyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, aryl, heteroaryl, C_1-C_6-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylcarbonyl-C_1-C_4-alkyl, trifluoromethyl, hydroxy, C_1-C_6-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkoxy, C_1-C_4-alkylcarbonyl-C_1-C_4-alkoxy, benzyloxy, phenoxy, formyloxy, C_1-C_4-alkylcarbonyloxy, carbamyloxy, N-C_1-C_4-alkylcarbamyloxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, aminosulfonyl, N-C_1-C_4-alkylaminosulfonyl, carboxy, carbamyl, N-C_1-C_4-alkylcarbamyl, formyl, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, N-C_1-C_4-alkylamino, N,N-di-(C_1-C_4-alkyl)amino with two identical or different C_1-C_4-alkyl moieties, N-(C_1-C_4-alkoxy-C_1-C_4-alkyl)amino, N-(C_1-C_4-alkylsulfonyl)amino, N-formyl-

amino, N-(C_1-C_4-alkylcarbonyl)amino, N-(C_1-C_4-alkoxycarbonyl)amino, N-(aryl- C_1-C_4-alkoxycarbonyl)amino and N-(heteroaryl-C_1-C_4-alkoxycarbonyl)amino,

in free form or in salt form.

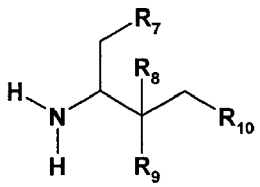
2. A process for the preparation of a compound as defined in claim 1 of the formula I, in free form or in salt form, comprising the steps of

a) reaction of a compound of the formula



(II),

in which R_1, R_2, R_3, R_4, R_5 and R_6 are as defined for the formula I and L_1 is a leaving group, in free form or in salt form, with a compound of the formula

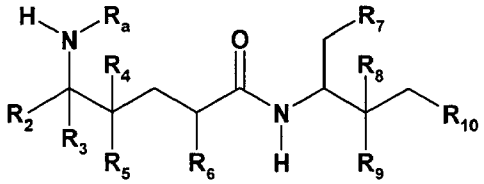


(III),

in which R_7, R_8, R_9 and R_{10} are as defined for the formula I, in free form or in salt form, or

b) for the preparation of a compound of the formula I, in free form or in salt form, in which R_1 is a group of the formula $N(R_a)$-C(=O)R_b (Ia); $N(R_a)$-S(=O)R_b (Ib); or $N(R_a)$-$S(=O)_2R_b$ (Ic), in which formulae Ia, Ib and Ic R_a is hydrogen; C_1-C_8-alkyl; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl; or heterocyclyl-C_1-C_4-alkyl; and R_b is hydrogen; C_1-C_8-alkyl; trifluoromethyl; C_1-C_8-alkoxy; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_8-alkylthio; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl; heterocyclyl-C_1-C_4-alkyl; amino; C_1-C_8-alkylamino; or di-(C_1-C_8-alkyl)amino with two identical or different C_1-C_8-alkyl moieties, which two C_1-C_8-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_8-alkyl moieties of the di-(C_1-C_8-alkyl)amino group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring

member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, reaction of a compound of the formula



(IV),

in which R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9 and R_{10} are as defined for the formula I and R_a is hydrogen; C_1-C_8-alkyl; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl; or heterocyclyl-C_1-C_4-alkyl, in free form or in salt form, with a compound of the formula R_b-C(=O)-L_2 (V); R_b-S(=O)-L_3 (VI); or R_b-S(=O)$_2$-L_4 (VII), in which formulae V, VI and VII R_b is hydrogen; C_1-C_8-alkyl; trifluoromethyl; C_1-C_8-alkoxy; C_1-C_4-alkoxy-C_1-C_4-alkyl; C_1-C_8-alkylthio; C_1-C_4-alkylthio-C_1-C_4-alkyl; C_3-C_8-cycloalkyl; C_3-C_8-cycloalkyl-C_1-C_4-alkyl; heterocyclyl; heterocyclyl-C_1-C_4-alkyl; amino; C_1-C_8-alkylamino; or di-(C_1-C_8-alkyl)amino with two identical or different C_1-C_8-alkyl moieties, which two C_1-C_8-alkyl moieties, taken together, can complete, together with the nitrogen atom, to which they are attached, a saturated or unsaturated ring, which ring is optionally substituted by 1 to 3 substituents independently selected from the group, consisting of oxo, C_1-C_6-alkyl, C_1-C_6-alkoxy and C_1-C_6-alkylthio, and which ring has 3 to 7 ring members, of which ring members, in addition to the nitrogen ring member, to which the two C_1-C_8-alkyl moieties of the di-(C_1-C_8-alkyl)amino group are attached, optionally 1 or 2 further ring members are hetero ring members, any other ring member being present being a carbon ring member, the said further hetero ring member(s) being independently selected from the group, consisting of a nitrogen ring member, an oxygen ring member and a sulfur ring member, L_2 is a leaving group, L_3 is a leaving group and L_4 is a leaving group, in free form or in salt form,

in each case optionally followed by reduction, oxidation or other functionalisation of the resulting compound and/or by cleavage of any protecting group(s) optionally present,

and of recovering the so obtainable compound of the formula I in free form or in salt form.

3. A compound as defined in claim 1, in free form or in pharmaceutically acceptable salt form, for use as a medicament.

4. A compound as defined in claim 1, in free form or in pharmaceutically acceptable salt form, for use in the treatment of neurological or vascular disorders related to beta-amyloid generation and/or aggregation.

5. A pharmaceutical composition comprising a compound as defined in claim 1, in free form or in pharmaceutically acceptable salt form, as active ingredient and a pharmaceutical carrier or diluent.

6. The use of a compound as defined in claim 1, in free form or in pharmaceutically acceptable salt form, as a medicament for the treatment of neurological or vascular disorders related to beta-amyloid generation and/or aggregation.

7. The use of a compound as defined in claim 1, in free form or in pharmaceutically acceptable salt form, for the manufacture of a medicament for the treatment of neurological or vascular disorders related to beta-amyloid generation and/or aggregation.

8. A method for the treatment of neurological or vascular disorders related to beta-amyloid generation and/or aggregation in a subject in need of such treatment, which comprises administering to such subject a therapeutically effective amount of a compound as defined in claim 1, in free form or in pharmaceutically acceptable salt form.

9. A combination comprising a therapeutically effective amount of a compound as defined in claim 1, in free form or in pharmaceutically acceptable salt form, and a second drug substance, for simultaneous or sequential administration.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2008/059606

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07C233/62 C07C235/34 C07C235/40 C07D211/76 C07D207/267
A61K31/16 A61K31/4015 A61K31/4412 A61P25/28

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07C C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, CHEM ABS Data, BEILSTEIN Data, WPI Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2004/121947 A1 (GHOSH ARUN K [US] ET AL) 24 June 2004 (2004-06-24) paragraphs [0040], [0048] page 171	1
A	US 2003/125257 A1 (BROCKHAUS MANFRED [CH] ET AL) 3 July 2003 (2003-07-03) examples 3,4	1
A	WO 01/21600 A (LG CHEMICAL LTD [KR]; KIM EUNICE EUN KYEONG [KR]; PARK MI JEONG [KR];) 29 March 2001 (2001-03-29) claim 1	1

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
20 October 2008	28/10/2008

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Götz, Gerhard

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2008/059606

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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