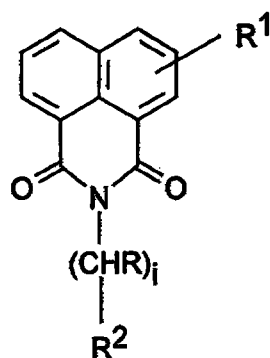


- 1 -

Substituted benzo[de]isoquinoline-1,3-diones

This application is a continuation-in-part of
Serial No. 09/199,409, the entirety of which is
5 incorporated by reference herein.

The invention relates to substituted benzo[de]-
isoquinoline-1,3-diones of the formula I



10

in which

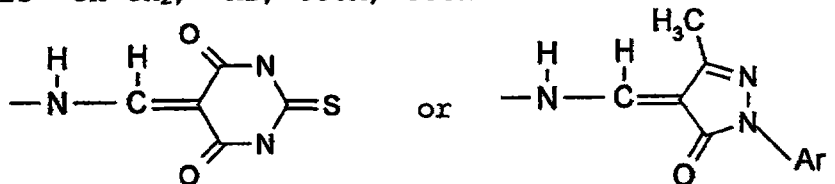
R is H, A or CH₂-Ph,

R¹ is -Het, -N-[(CH₂)_s-OH]₂, -N-[(CH₂)_s-OA]₂,
-NA-(CH₂)_s-Ar, -NA-(CH₂)_m-R⁵, -Y-(CH₂)_m-R⁵,
15 -Y-(CH₂)₂-NHA, -Y-(CH₂)₂-NH-(CH₂)_s-OH, -Y-(CH₂)₂-NA₂,
-Y-(CH₂)_m-OH, -Y-(CH₂)_n-(CHR⁴)-R³, -Y-(CH₂)_n-R⁴, R⁴,
-Y-(CH₂)_n-Het-(CH₂)_o-R⁶, -Y-(CH₂)_n-Ar'-(CH₂)_o-R⁶,
-Het-(CH₂)_n-Ar, -Het-Het, -Y-(CH₂)_s-Ar'-(CH₂)_o-R¹¹,
-Y-[X-O]_t-[X¹-O]_u-X²-R⁵ or -Y-(CH₂)_n-NA-(CH₂)_o-R⁵,

20 R² is H, OH, OA, COOH, COOA, CH(Ph)-Ph, Ar, Het¹, R⁵,
R⁷ or R⁸

R³ is CH₃,

R⁴ is -CH=CH₂, -Ar, COOA, COOH



25 R⁵ is NH₂, NHA, NA₂, NHA_r, -NH-(CH₂)_n-OH or
-NH-(CH₂)_n-OA,

R⁶ is H or R⁵

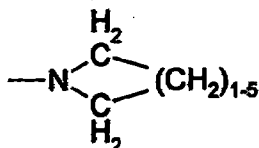
R⁷ is -Ar'-(CH₂)_n-R⁸ or -Ar'-(CH₂)_n-R⁵

- 2 -

- R^8 is CONH_2 , CONHA , CONA_2 , $\text{CONH}-(\text{CH}_2)_o\text{-Ar}$,
 $\text{CONH}-(\text{CH}_2)_o\text{-Het}$, $\text{CONH}-(\text{CH}_2)_o\text{-R}^5$, $\text{CONH}-(\text{CH}_2)_o\text{-CH}(\text{Ar}^1)\text{-}$
 Ar^2 , $\text{CONH}-(\text{CH}_2)_o\text{-CH}(\text{A})\text{-Ph}$, $\text{CONH}-(\text{CH}_2)_o\text{-Ar}'\text{-NH-CO-Ar}$,
 $\text{CONH-Ar}'\text{-Het}$ or CHA-CONH_2 ,
 5 R^{11} is -NH-(C=NH)-NH_2 , -NH-(C=NH)-NHA , -NH-(C=NH)-NA_2 ,
 -NA-(C=NH)-NH_2 , -NA-(C=NH)-NHA or -NA-(C=NH)-NA_2 ,
 Ar' is phenylene, cycloalkylene or biphenylene, which is
 unsubstituted or mono- or disubstituted by A, OH, OA,
 Hal, CN, NH_2 , NHA, NA_2 , NO_2 , CF_3 , CO-A, SO_2NH_2 , SO_2NAH ,
 10 SO_2NA_2 ,
 Ar is phenyl, cycloalkyl, naphthyl, cyclohex-1-enyl,
 biphenyl, bicyclohexyl, 4-cyclohexyl-phenyl,
 benzo[1,3]dioxol-5-yl, or indanyl, which is
 unsubstituted or mono-, di- or trisubstituted by
 15 A, OH, OA, O-Ph, O- $\text{CH}_2\text{-Ph}$, O-Ph- CH_3 , O(cycloalkyl),
 Hal, CN, NH_2 , NHA, NA_2 , NH-C(O)A , $(\text{CH}_2)_n\text{-NH}_2$, $(\text{CH}_2)_n\text{-}$
 NHA , $(\text{CH}_2)_n\text{-NA}_2$, NO_2 , CF_3 , C(O)A , $\text{SO}_2\text{-Ph}$, SO_2NH_2 ,
 SO_2NAH , SO_2NA_2 or $\text{SO}_2\text{NA-Ph}$,
 Ar^1 and Ar^2
 20 are each independently phenyl,
 Het is a saturated, partially or completely unsatura-
 ted mono- or bicyclic heterocyclic radical having
 5 to 10 ring members, where 1 or 2 N and/or 1 or
 2 S or O atoms can be present and the heterocyclic
 25 radical can be mono- or disubstituted by CN, Hal,
 OH, OA, CF_3 , A, NO_2 , CO, CO-A or R^5 ,
 Het^1 is an unsaturated mono- or bicyclic heterocyclic
 radical having 5 to 10 ring members, where 1 or
 2 N and/or 1 or 2 S or O atoms can be present
 30 and/or can be mono- or disubstituted by Hal, OH,
 OA,
 A is unbranched or branched alkyl having 1-6 C
 atoms,
 Hal is F, Cl, Br or I,
 35 X,
 X^1, X^2 in each case independently of one another are
 alkylene having 1 to 12 C atoms,
 Y is O, S or NH
 i is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12,

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m is 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12,
 n, o in each case independently of one another are 0,
 1, 2, 3 or 4,
 s is 1, 2, 3 or 4,
 5 t is 0, 1 or 2,
 u is 1 or 2,
 where if R² is Ar or H, R¹ is not



and their pharmaceutically tolerable salts and
 10 solvates.

Similar compounds having a benzo[de]iso-
 quinoline-1,3-dione parent structure as dyes are
 disclosed in US 4,200,752, FR 2 271 216 A and Chemical
 Abstracts, Vol. 111, No. 20, November 1989.

15 US 3,821,383 describes benzó[de]isoquinoline-
 acetic acid derivatives as active compounds in a
 pharmaceutical preparation against diabetes mellitus.
 Similar benzo[de]isoquinolines are also disclosed in
 EP 0 243 841 A and DE 37 07 652 A, which carry
 20 alkylamino groups mainly in the 2-position. These
 derivatives are suitable for the treatment of solid
 tumours and certain forms of leukemia, as well as for
 the control of viral disorders. The benzo[de]iso-
 quinoline derivatives from US 5,235,045 are mainly
 25 present alkylated or alternatively fluoroalkylated in
 the 2-position and cause a chemical change to the lipid
 membrane of viruses or other target cells.

The invention is based on the object of finding
 novel compounds having valuable properties, in parti-
 30 cular those which can be used for the production of
 medicaments.

It has been found that the compounds of the
 formula I and their salts or solvates have very
 valuable pharmacological properties together with good
 35 tolerability. They act especially as GPIbIX inhibitors,
 in particular inhibiting the interaction of this

- 4 -

receptor with the ligand von Willebrand factor (vWF). This action can be demonstrated, for example, by a method which is described by S. Meyer et al. in J. Biol. Chem. 1993, 268, 20555-20562. The GPIbIX
5 alpha-thrombin receptor (N.J. Greco, Biochemistry 1996, 35, 915-921) can also be blocked by the compounds mentioned.

The significance of GPIbIX as an adhesion receptor on platelets, which mediates the primary interaction of
10 platelets with an arteriosclerotically modified vascular wall via binding to the vWF expressed there, has been described by many authors (e.g. Z.M. Ruggeri in Thromb. Hemost. 1997, 78, 611-616). The activation of another platelet adhesion receptor, GPIIbIIIa,
15 following the GPIbIX-vWF interaction, leads to platelet aggregation and thus to thrombotic vascular occlusion.

A GPIbIX antagonist can thus prevent the start of thrombus formation and thus also release of active substances from the platelets which, for example,
20 promote thrombus growth and have an additional trophic action on the vascular wall. This has been shown with inhibitory peptides or antibodies in various experimental models (e.g. H Yamamoto et al., Thromb. Hemost. 1998, 79, 202-210).

25 In the case of higher shear forces, the blocking action of GPIbIX inhibitors exerts its maximum effect, as described by J.J. Sixma et al. in Arteriosclerosis, Thrombosis, and Vascular Biology 1996, 16, 64-71. According to the flow chamber method
30 used there, the compounds of the formula I can be characterized as GPIbIX inhibitors in whole blood.

The inhibition of thrombus formation of the GPIbIX inhibitors can be measured by a modified Born method (Nature 1962, 4832, 927-929) using botrocetin or
35 ristocetin as an aggregation stimulant.

The compounds of the formula I according to the invention can therefore be employed as pharmaceutical active compounds in human and veterinary medicine. They act as adhesion receptor antagonists, in particular as

- 5 -

glycoprotein IbIX antagonists, and are suitable for the prophylaxis and/or therapy of thrombotic disorders and sequelae deriving therefrom. The preferentially best action is to be expected in the case of thrombotic disorders in the arterial vascular system, but GPIbIX inhibitors also have an effect in the case of thrombotic disorders in the venous vascular bed. The disorders are acute coronary syndromes, angina pectoris, myocardial infarct, peripheral circulatory disorders, stroke, transient ischaemic attacks, arteriosclerosis, reocclusion/restenosis after angioplasty/stent implantation. The compounds can furthermore be employed as anti-adhesive substances where the body comes into contact with foreign surfaces such as implants, catheters or cardiac pacemakers.

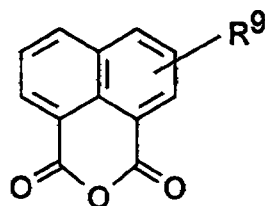
Comparison medication introduced onto the market which may be mentioned are aspirin and GPIIbIIIa antagonists.

The invention relates to the compounds of the formula I and their salts or solvates, and to a process for the preparation of these compounds and their salts or solvates, characterized in that

a) a compound of the formula I is liberated from one of its functional derivatives by treating with a solvolysing or hydrogenolysing agent,

or

b) a compound of the formula II



II

30

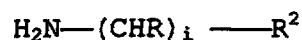
in which

R⁹ is Cl, Br, NO₂ or R¹, and

R¹ has the meaning indicated in Claim 1

is reacted with a compound of the formula III

35



III

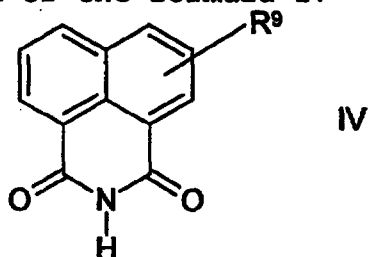
- 6 -

in which R, R² and i have the meanings indicated in Claim 1,

and, if necessary, the radical R⁹ is converted into a radical R¹,

5 or

(c) a compound of the formula IV

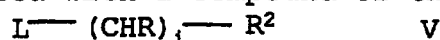


in which

R⁹ is Cl, Br, NO₂ or R¹, where

10 R¹ has the meaning indicated in Claim 1

is reacted with a compound of the formula V



in which L is Cl, Br, or I, OH or a reactive esterified OH group and R, R² and i have the meanings indicated in Claim 1

15

and, if appropriate, the radical R⁹ is converted into a radical R¹,

or

(d) a radical R and/or R² and/or R⁹ is converted into another radical R and/or R² and/or R⁹ by, for example

20

- converting an amino group into a guanidino group by reaction with an amidinating agent,

25

- reacting an aryl bromide or iodide to give the corresponding coupling products by means of a Suzuki coupling with boronic acids,

- reducing a nitro group, sulfonyl group or sulfoxyl group,

30

- etherifying an OH group or subjecting an OA group to ether cleavage,

- alkylating a primary or secondary amino group,

- partially or completely hydrolysing a CN group,

- cleaving an ester group or esterifying a carboxylic acid radical,

- 7 -

- or carrying out a nucleophilic or electrophilic substitution,

and/or

- (e) a base or acid of the formula I is converted into
5 one of its salts or solvates.

The compounds of the formula I can have a chiral centre and therefore occur in a number of stereoisomeric forms. All these forms (e.g. R and S forms) and their mixtures (e.g. the RS forms) are
10 included in the formula I.

The compounds according to the invention also include so-called prodrug derivatives, i.e. compounds of the formula I modified with, for example, alkyl or acyl groups, sugars or oligopeptides and which are rapidly
15 cleaved in the body to give the active compounds according to the invention.

Furthermore, free amino groups as substituents of compounds of the formula I can be provided with appropriate conventional protective groups.

20 Solvates of the compounds of the formula I are understood as meaning adducts of inert solvent molecules to the compounds of the formula I which are formed on account of their mutual power of attraction. Solvates are, for example, mono- or dihydrates or
25 alcoholates.

The abbreviations used have the following meanings:

	BOC	tert-butoxycarbonyl
	CBZ	benzyloxycarbonyl
30	DCC	dicyclohexylcarbodiimide
	DMF	dimethylformamide
	Et	ethyl
	Fmoc	fluorenylmethoxycarbonyl
	Me	methyl
35	Mtr	4-methoxy-2,3,6-trimethylphenylsulfonyl
	OBu	tert-butyl ester
	OMe	methyl ester
	OEt	ethyl ester
	POA	phenoxyacetyl

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Ph phenyl

TFA trifluoroacetic acid

In the above formulae, A is alkyl and has 1 to 6, preferably 1, 2, 3 or 4 C atoms. Alkyl is preferably methyl, furthermore ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl or tert-butyl, additionally also pentyl, 1-, 2- or 3-methylbutyl, 1,1-, 1,2- or 2,2-dimethylpropyl, 1-ethylpropyl, hexyl, 1-, 2-, 3- or 4-methylpentyl, 1,1-, 1,2-, 1,3-, 2,2-, 2,3- or 3,3-dimethylbutyl, 1- or 2-ethylbutyl, 1-ethyl-1-methylpropyl, 1-ethyl-2-methylpropyl, 1,1,2- or 1,2,2-trimethylpropyl,.

Ar is preferentially phenyl, preferably - as indicated - monosubstituted phenyl, specifically preferentially phenyl, o-, m- or p-methylphenyl, o-, m- or p-ethylphenyl, o-, m- or p-propylphenyl, o-, m- or p-isopropylphenyl, o-, m- or p-tert-butylphenyl, o-, m- or p-aminophenyl, o-, m- or p-(N,N-dimethylamino)phenyl, o-, m- or p-sulfonamoylphenyl, o-, m- or p-nitrophenyl, o-, m- or p-hydroxyphenyl, o-, m- or p-methoxyphenyl, o-, m- or p-ethoxyphenyl, o-, m- or p-phenoxyphenyl, o-, m- or p-(phenylmethoxy)phenyl, o-, m- or p-(trifluoromethyl)phenyl, o-, m- or p-(trifluoromethoxy)phenyl, o-, m- or p-fluorophenyl, o-, m- or p-chlorophenyl, o-, m- or p-bromophenyl, o-, m- or p-iodophenyl, 4-benzenesulfonyl-phenyl, 4-(4-chloro-phenoxy)-phenyl, furthermore preferentially 2,3-, 2,4-, 2,5-, 2,6-, 3,4- or 3,5-dimethylphenyl, 2,3-, 2,4-, 2,5-, 2,6-, 3,4- or 3,5-dimethoxyphenyl, 2,3-, 2,4-, 2,5-, 2,6-, 3,4- or 3,5-dihydroxyphenyl, 2,3-, 2,4-, 2,5-, 2,6-, 3,4- or 3,5-difluorophenyl, 2,3-, 2,4-, 2,5-, 2,6-, 3,4- or 3,5-dichlorophenyl, 2,3-, 2,4-, 2,5-, 2,6-, 3,4- or 3,5-dibromophenyl, 2-chloro-3-methyl-, 2-chloro-4-methyl-, 2-chloro-5-methyl-, 2-chloro-6-methyl-, 3-chloro-2-methyl-, 4-chloro-2-methyl-, 5-chloro-2-methyl-, 3-chloro-4-methyl-, 3-chloro-5-methyl-, 4-chloro-3-methylphenyl, 2-bromo-3-methyl-, 2-bromo-4-methyl-, 2-bromo-5-

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- methyl-, 2-bromo-6-methyl-, 3-bromo-2-methyl-, 4-bromo-2-methyl-, 5-bromo-2-methyl-, 3-bromo-4-methyl-, 3-bromo-5-methyl-, 4-bromo-3-methylphenyl, 2-iodo-3-methyl-, 2-iodo-4-methyl-, 2-iodo-5-methyl-, 2-iodo-6-methyl-, 3-iodo-2-methyl-, 4-iodo-2-methyl-, 5-iodo-2-methyl-, 3-iodo-4-methyl-, 3-iodo-5-methyl-, 4-iodo-3-methylphenyl, 2-chloro-3-methoxy-, 2-chloro-4-methoxy-, 2-chloro-5-methoxy-, 2-chloro-6-methoxy-, 3-chloro-2-methoxy-, 4-chloro-2-methoxy-, 5-chloro-2-methoxy-, 3-chloro-4-methoxy-, 3-chloro-5-methoxy-, 4-chloro-3-methoxyphenyl, 2-chloro-3-hydroxy-, 2-chloro-4-hydroxy-, 2-chloro-5-hydroxy-, 2-chloro-6-hydroxy-, 3-chloro-2-hydroxy-, 4-chloro-2-hydroxy-, 5-chloro-2-hydroxy-, 3-chloro-4-hydroxy-, 3-chloro-5-hydroxy-, 4-chloro-3-hydroxyphenyl, 3-fluoro-4-methoxy-, 4-fluoro-3-methoxyphenyl, 2-chloro-3-fluoro-, 2-chloro-4-fluoro-, 2-chloro-5-fluoro-, 2-chloro-6-fluoro-, 3-chloro-2-fluoro-, 4-chloro-2-fluoro-, 5-chloro-2-fluoro-, 3-chloro-4-fluoro-, 3-chloro-5-fluoro-, 4-chloro-3-fluorophenyl, 2-fluoro-3-methyl-, 2-fluoro-4-methyl-, 2-fluoro-5-methyl-, 2-fluoro-6-methyl-, 3-fluoro-2-methyl-, 4-fluoro-2-methyl-, 5-fluoro-2-methyl-, 3-fluoro-4-methyl-, 3-fluoro-5-methyl-, 4-fluoro-3-methylphenyl, 2,5- or 3,4-dimethoxyphenyl, 3-diethylaminomethyl-4-hydroxy-phenyl, 1-dimethylamino-2-(toluene-4-sulfonyl)-phenyl-4-yl, N-ethyl-2-methyl-N-phenyl-5-yl-benzenesulfonamoyl, 3-cyclopentyloxy-4-methoxy-phenyl, 3,4-bis-benzyloxy-phenyl, 2-cyano-4,5-dimethoxyphenyl, 5-chloro-2,4-dimethoxy-phenyl, 2-cyano-3,4-dimethoxyphenyl or 3,4,5-trimethoxy-phenyl, furthermore, however, also preferentially unsubstituted naphthyl, cyclohex-1-enyl, benzo[1,3]-dioxol-5-yl, 4-cyclohexyl-phenyl, bicyclohexyl or indanyl.
- Furthermore, however, Ar is also preferentially unsubstituted biphenyl - as indicated - or alternatively monosubstituted biphenyl, specifically preferentially biphenyl-4-yl or biphenyl-3-yl, 2'-methylbiphenyl-4-yl, 3'-methylbiphenyl-4-yl,

- 10 -

- 4'-methylbiphenyl-4-yl, 2'-methylbiphenyl-3-yl,
3'-methylbiphenyl-3-yl, 4'-methylbiphenyl-3-yl,
2-methylbiphenyl-4-yl, 3-methylbiphenyl-4-yl,
2-methylbiphenyl-3-yl, 4-methylbiphenyl-3-yl, 2'-tert-
5 butylbiphenyl-4-yl, 3'-tert-butylbiphenyl-4-yl,
4'-tert-butylbiphenyl-4-yl, 2'-tert-butylbiphenyl-3-yl,
3'-tert-butylbiphenyl-3-yl, 4'-tert-butylbiphenyl-3-yl,
2-tert-butylbiphenyl-4-yl, 3-tert-butylbiphenyl-4-yl,
2-tertbutylbiphenyl-3-yl, 4-tert-butylbiphenyl-3-yl,
10 2'-isopropylbiphenyl-4-yl, 3'-isopropylbiphenyl-4-yl,
4'-isopropylbiphenyl-4-yl, 2'-isopropylbiphenyl-3-yl,
3'-isopropylbiphenyl-3-yl, 4'-isopropylbiphenyl-3-yl,
2-isopropylbiphenyl-4-yl, 3-isopropylbiphenyl-4-yl,
2-isopropylbiphenyl), 4-isopropylbiphenyl-3-yl,
15 2'-fluorobiphenyl-4-yl, 3'-fluorobiphenyl-4-yl,
4'-fluorobiphenyl-4-yl, 2'-fluorobiphenyl-3-yl,
3'-fluorobiphenyl-3-yl, 4'-fluorobiphenyl-3-yl,
2-fluorobiphenyl-4-yl, 3-fluorobiphenyl-4-yl,
2-fluorobiphenyl-3-yl, 4-fluorobiphenyl-3-yl,
20 2'-methoxybiphenyl-4-yl, 3'-methoxybiphenyl-4-yl,
4'-methoxybiphenyl-4-yl, 2'-methoxybiphenyl-3-yl,
3'-methoxybiphenyl-3-yl, 4'-methoxybiphenyl-3-yl, 2-
methoxybiphenyl-4-yl, 3-methoxybiphenyl-4-yl,
2-methoxybiphenyl-3-yl, 4-methoxybiphenyl-3-yl,
25 2'-nitrobiphenyl-4-yl, 3'-nitrobiphenyl-4-yl,
4'-nitrobiphenyl-4-yl, 2'-nitrobiphenyl-3-yl,
3'-nitrobiphenyl-3-yl, 4'-nitrobiphenyl-3-yl,
2-nitrobiphenyl-4-yl, 3-nitrobiphenyl-4-yl, 2-nitro-
biphenyl-3-yl, 4-nitrobiphenyl-3-yl,
30 2'-trifluoromethylbiphenyl-4-yl,
3'-trifluoromethylbiphenyl-4-yl, 4'-trifluoromethyl-
biphenyl-4-yl, 2'-trifluoromethylbiphenyl-3-yl,
3'-trifluoromethylbiphenyl-3-yl, 4'-trifluoromethyl-
biphenyl-3-yl, 2-trifluoromethylbiphenyl-4-yl, 3-tri-
35 fluoromethylbiphenyl-4-yl, 2-trifluoromethylbiphenyl-3-
yl, 4-trifluoromethylbiphenyl-3-yl,
2'-trifluoromethoxybiphenyl-4-yl, 3'-trifluoromethoxy-
biphenyl-4-yl, 4'-trifluoromethoxybiphenyl-4-yl,
2'-trifluoromethoxybiphenyl-3-yl,

- 3'-trifluoromethoxybiphenyl-3-yl, 4'-tri-
fluoromethoxybiphenyl-3-yl, 2-trifluoromethoxybiphenyl-
4-yl, 3-trifluoromethoxybiphenyl-4-yl,
2-trifluoromethoxybiphenyl-3-yl,
5 4-trifluoromethoxybiphenyl-3-yl, furthermore
preferentially disubstituted biphenyls, such as
2'-methyl-3'-nitrobiphenyl-4-yl, 2'-methyl-4'-nitro-
biphenyl-4-yl, 2'-methyl-5'-nitrobiphenyl-4-yl, 2'-
methyl-6'-nitrobiphenyl-4-yl, 3'-methyl-2'-
10 nitrobiphenyl-4-yl, 3'-methyl-4'-nitrobiphenyl-4-yl,
3'-methyl-5'-nitrobiphenyl-4-yl, 3'-methyl-6'-
nitrobiphenyl-4-yl, 4'-methyl-2'-nitrobiphenyl-4-yl,
4'-methyl-3'-nitrobiphenyl-4-yl, 2'-methyl-3'-
nitrobiphenyl-3-yl, 2'-methyl-4'-nitrobiphenyl-3-yl,
15 2'-methyl-5'-nitrobiphenyl-3-yl, 2'-methyl-6'-nitro-
biphenyl-3-yl, 3'-methyl-2'-nitrobiphenyl-3-yl,
3'-methyl-4'-nitrobiphenyl-3-yl, 3'-methyl-5'-
nitrobiphenyl-3-yl, 3'-methyl-6'-nitrobiphenyl-3-yl,
4'-methyl-2'-nitrobiphenyl-3-yl, 4'-methyl-3'-
20 nitrobiphenyl-3-yl, 2'-methoxy-2-methylbiphenyl-4-yl,
3'-methoxy-2-methylbiphenyl-4-yl, 4'-methoxy-2-
methylbiphenyl-4-yl, 4'-methoxy-3-nitrobiphenyl-4-yl,
2'-chloro-3'-fluorobiphenyl-4-yl, 2'-chloro-4'-
fluorobiphenyl-4-yl, 2'-chloro-5'-fluorobiphenyl-4-yl,
25 2'-chloro-6'-fluorobiphenyl-4-yl, 3'-chloro-2'-
fluorobiphenyl-4-yl, 3'-chloro-4'-fluorobiphenyl-4-yl,
3'-chloro-5'-fluorobiphenyl-4-yl, 3'-chloro-6'-
fluorobiphenyl-4-yl, 4'-chloro-2'-fluorobiphenyl-4-yl,
4'-chloro-3'-fluorobiphenyl-4-yl, 2'-chloro-3'-
30 fluorobiphenyl-3-yl, 2'-chloro-4'-fluorobiphenyl-3-yl,
2'-chloro-5'-fluorobiphenyl-3-yl, 2'-chloro-6'-
fluorobiphenyl-3-yl, 3'-chloro-2'-fluorobiphenyl-3-yl,
3'-chloro-4'-fluorobiphenyl-3-yl, 3'-chloro-5'-
fluorobiphenyl-3-yl, 3'-chloro-6'-fluorobiphenyl-3-yl,
35 4'-chloro-2'-fluorobiphenyl-3-yl, 4'-chloro-3'-
fluorobiphenyl-3-yl, (2',3'-dimethoxy)biphenyl-4-yl,
2',4'-dimethoxy)biphenyl-4-yl,
(2',5'-dimethoxy)biphenyl-4-yl, (2',6'-dimethoxy)-
biphenyl-4-yl, (3',4'-dimethoxy)biphenyl-4-yl,

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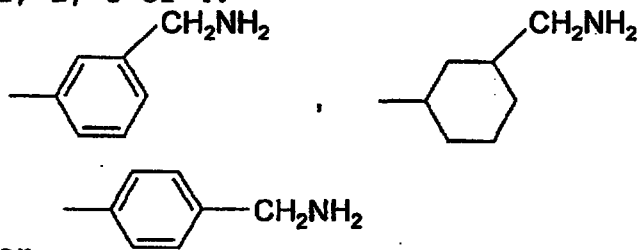
- (3',5'-dimethoxy)biphenyl-4-yl, (2',3'-dimethoxy)-
 biphenyl-3-yl, (2',4'-dimethoxy)biphenyl-3-yl,
 (2',5'-dimethoxy)biphenyl-3-yl, (2',6'-dimethoxy)-
 biphenyl-3-yl, (3',4'-dimethoxy)biphenyl-3-yl,
 5 (3',5'-dimethoxy)biphenyl-3-yl,
 (2',3'-di(trifluoromethyl))biphenyl-4-yl,
 (2',4'-di(trifluoromethyl))biphenyl-4-yl,
 (2',5'-di(trifluoromethyl))biphenyl-4-yl,
 (2',6'-di(trifluoromethyl))biphenyl-4-yl,
 10 (3',4'-di(trifluoromethyl))biphenyl-4-yl, (3',5'-
 di(trifluoromethyl))biphenyl-4-yl,
 (2',3'-di(trifluoromethyl))biphenyl-3-yl,
 (2',4'-di(trifluoromethyl))biphenyl-3-yl, (2',5'-
 di(trifluoromethyl))biphenyl-3-yl,
 15 (2',6'-di(trifluoromethyl))biphenyl-3-yl,
 (3',4'-di(trifluoromethyl))biphenyl-3-yl, (3',5'-
 di(trifluoromethyl))biphenyl-3-yl,
 (2,2'-dimethyl)biphenyl-4-yl, (2,3'-dimethyl)biphenyl-
 4-yl, (2,4'-dimethyl)biphenyl-4-yl,
 20 (2,2'-dimethyl)biphenyl-3-yl, (2,3'-dimethyl)biphenyl-
 3-yl or (2,4'-dimethyl)biphenyl-3-yl.

Furthermore, Ar is preferably cycloalkyl, particularly preferred cyclohexyl or cyclopentyl.

Ar¹ and Ar² are each independently phenyl.

- 25 Ar' preferentially is phenylene, cyclohexylene or biphenylene, which is unsubstituted or monosubstituted by Hal or CN.

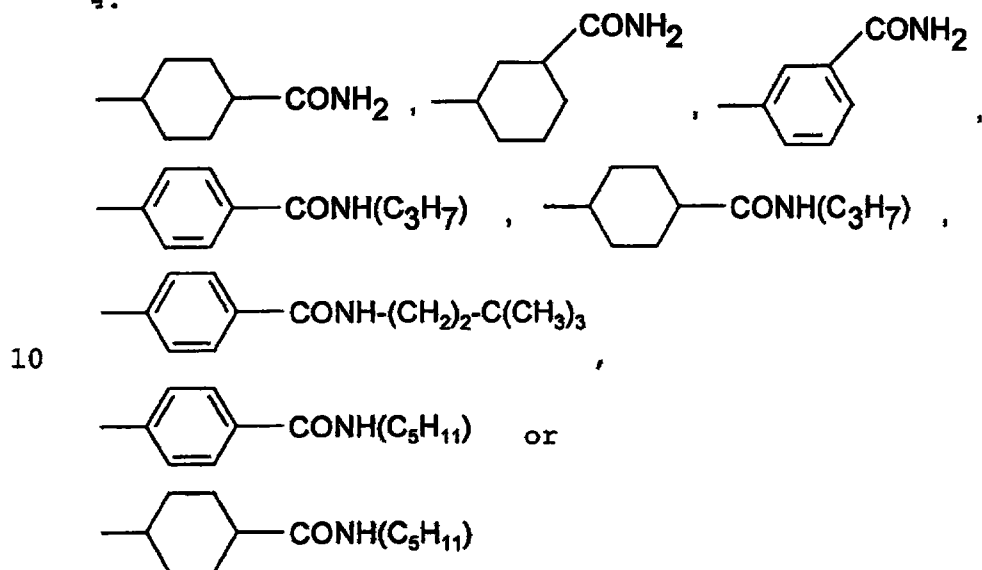
- In -Ar'-(CH₂)_n-R⁵, Ar' is preferentially unsubstituted or substituted phenylene or
 30 cycloalkylene, where R⁵ is preferentially an amino, alkylamino or dialkylamino group and where n can be 0, 1, 2, 3 or 4.



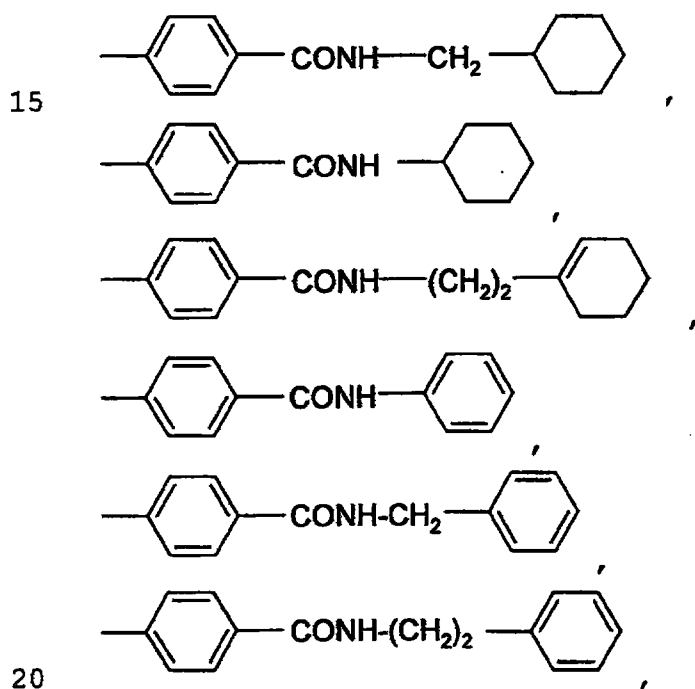
- 35 is particularly preferred for -Ar'-(CH₂)_n-R⁵.

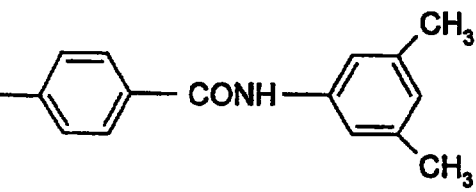
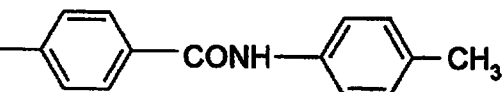
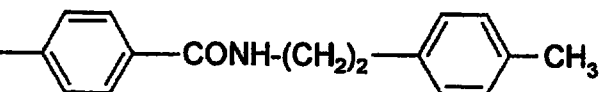
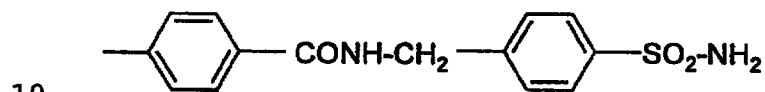
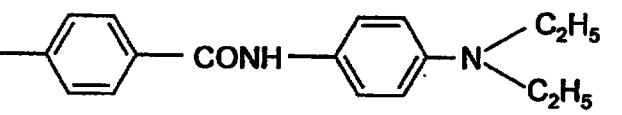
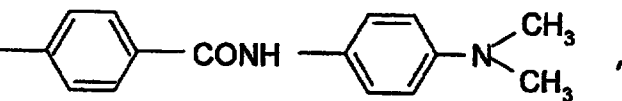
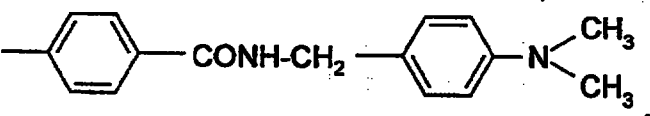
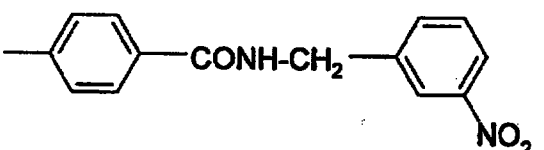
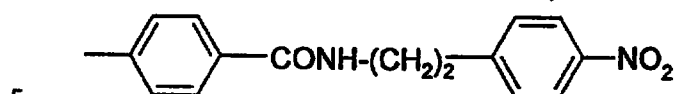
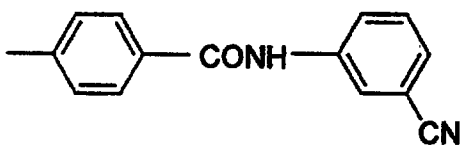
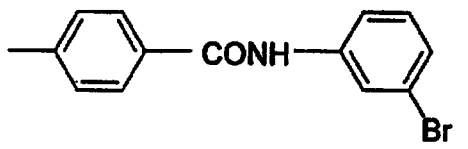
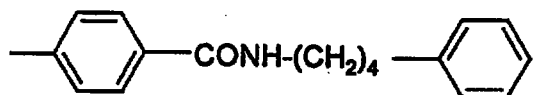
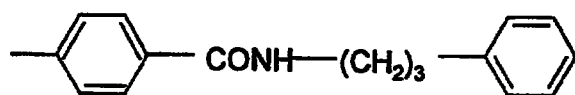
- 13 -

In $-\text{Ar}'-(\text{CH}_2)_n-\text{R}^8$, Ar' is preferably unsubstituted or substituted phenylene or cycloalkylene, where R^8 is preferentially an amido, an alkylamido or dialkylamido group or $-\text{CONH}-(\text{CH}_2)_o-\text{Ar}$,
 5 $-\text{CONH}-(\text{CH}_2)_o-\text{Het}$, $-\text{CONH}-(\text{CH}_2)_o-\text{CH}(\text{Ar}^1)-\text{Ar}^2$, $-\text{CONH}-(\text{CH}_2)_o-\text{CH}(\text{A})-\text{Ph}$ or $-\text{CONH}-(\text{CH}_2)_o-\text{R}^5$ and where n is 0, 1, 2, 3 or 4.

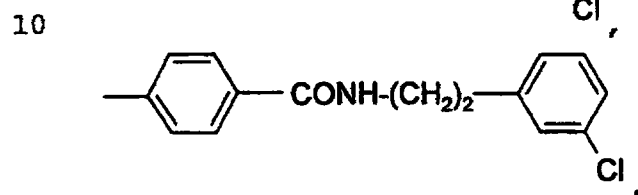
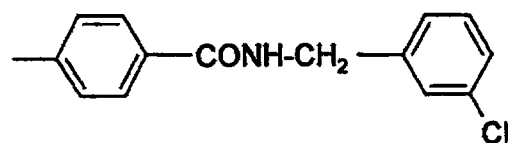
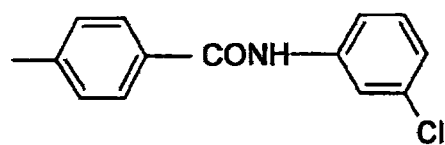
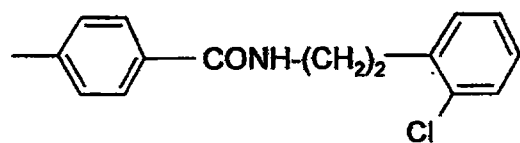
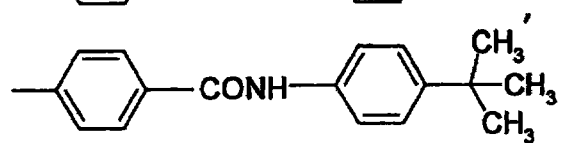
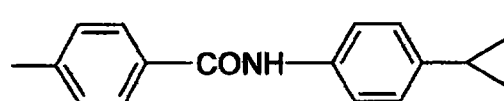
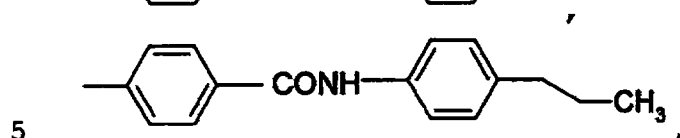
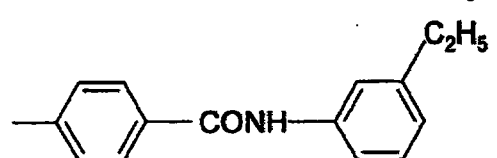
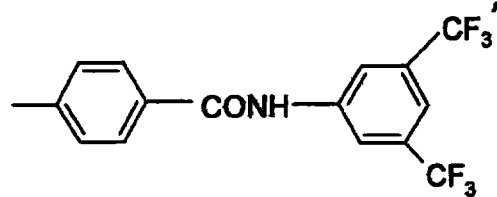
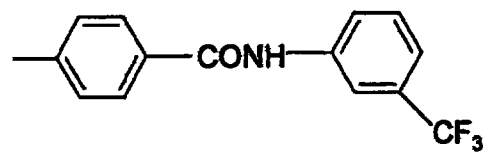
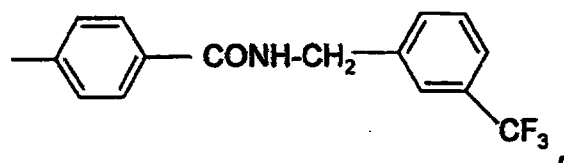


is particularly preferred for $-\text{Ar}'-(\text{CH}_2)_n-\text{R}^8$.

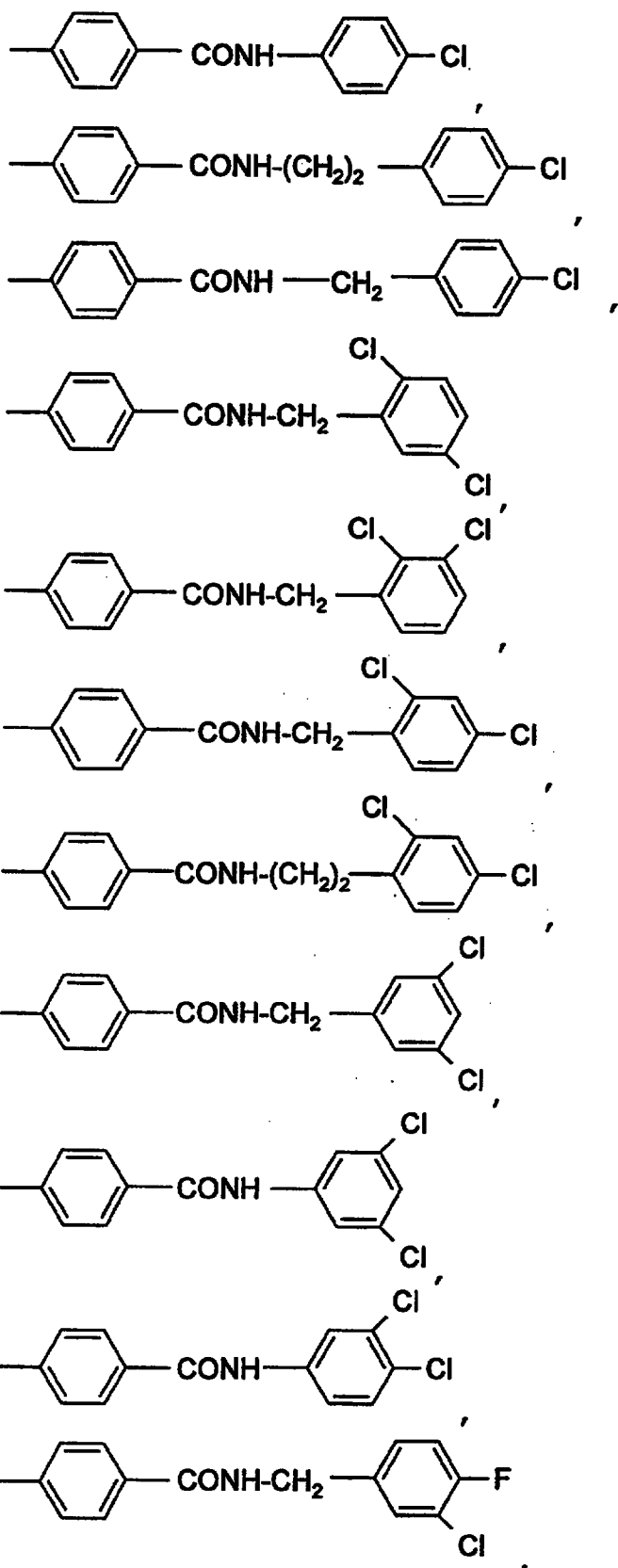




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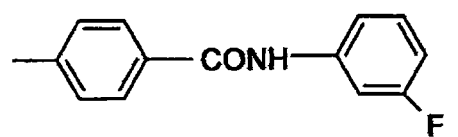
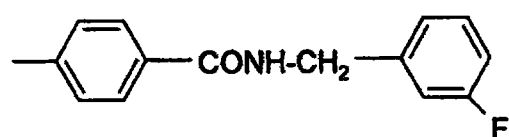
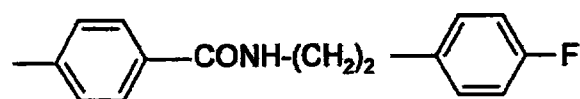
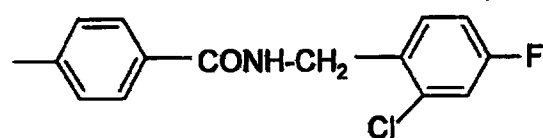
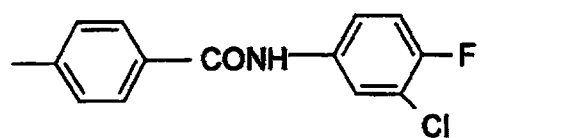
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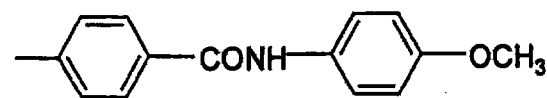
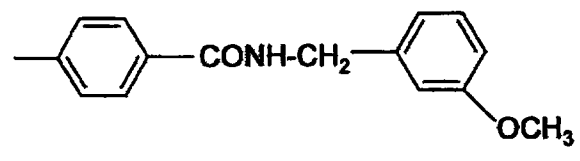
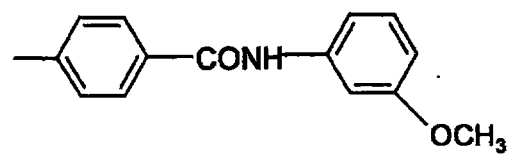
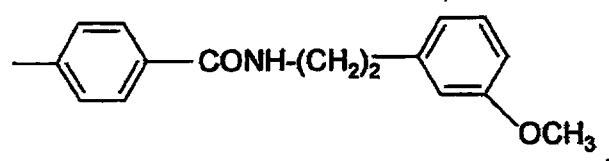
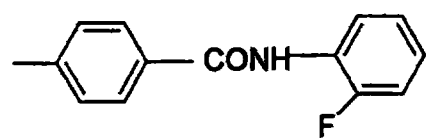
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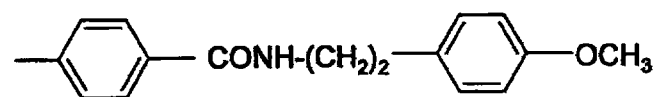
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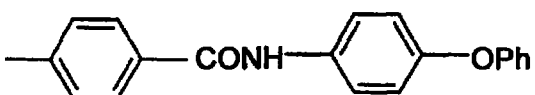
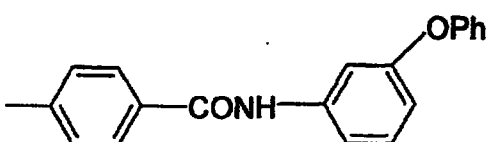
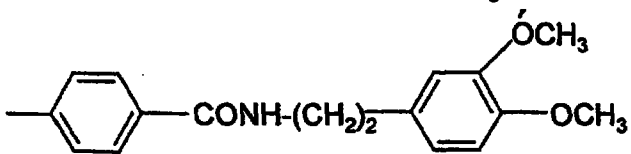
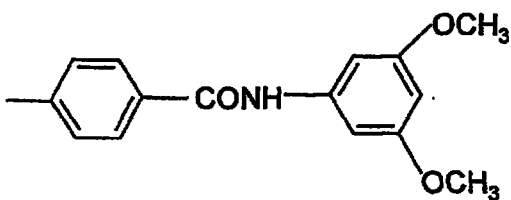
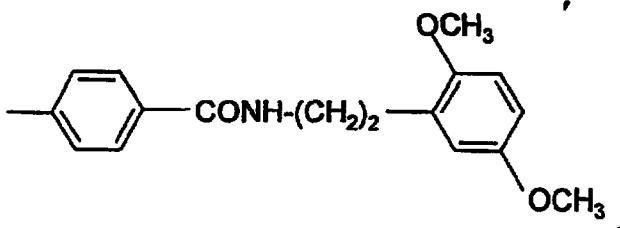
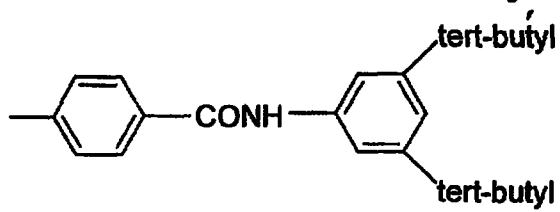
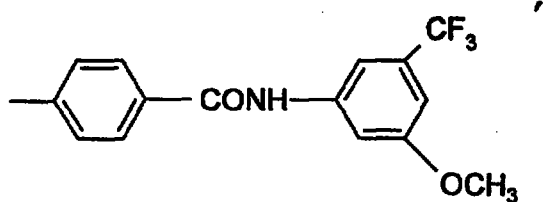
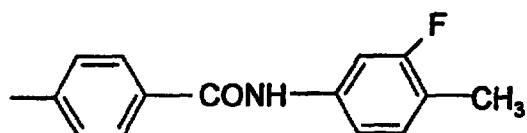
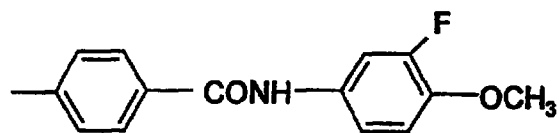
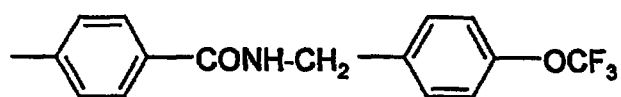
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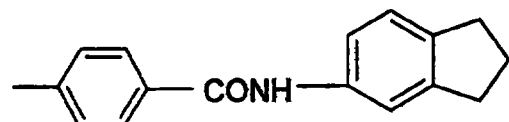
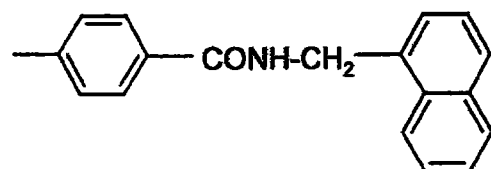
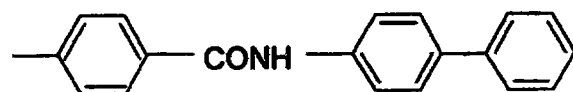
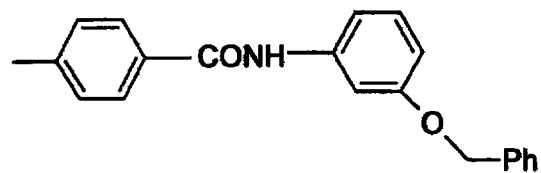
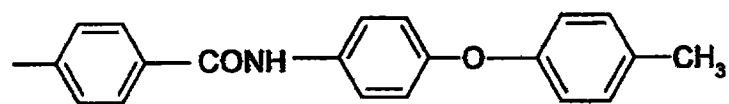


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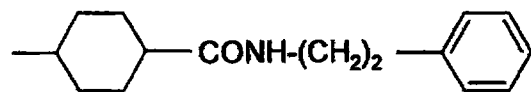
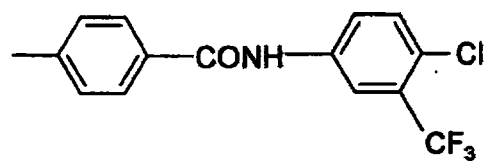
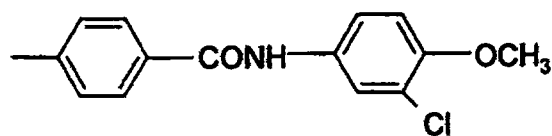


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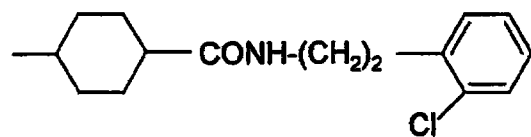


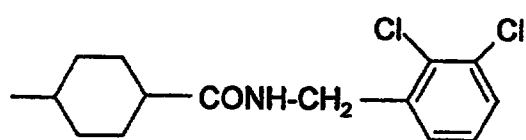
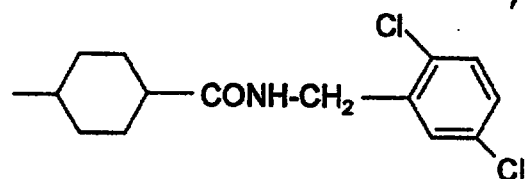


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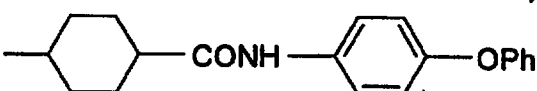
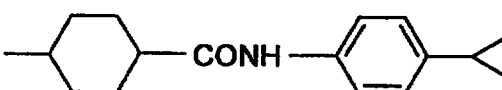
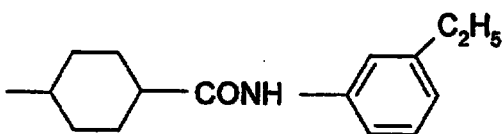
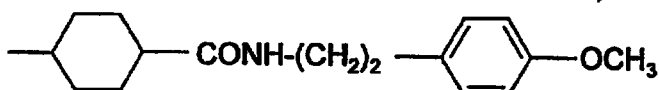
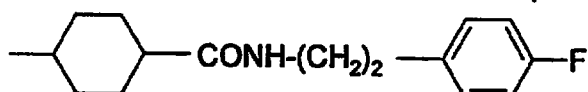


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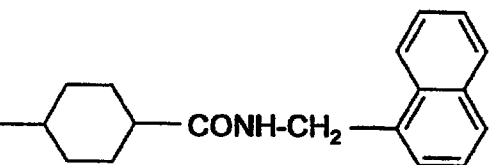
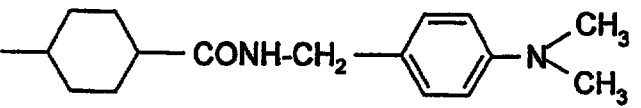
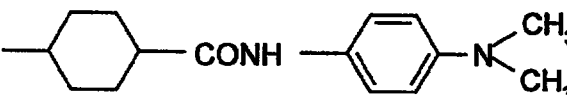
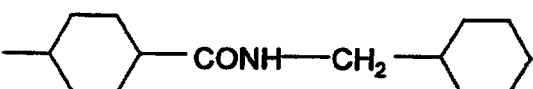




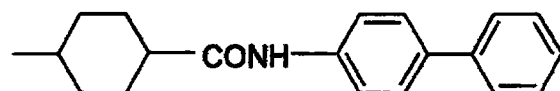
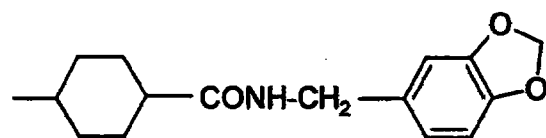
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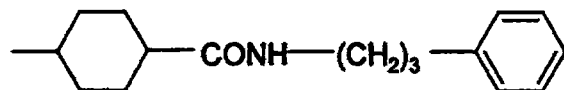
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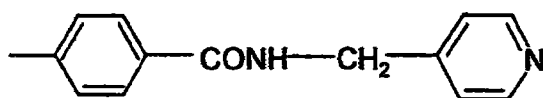
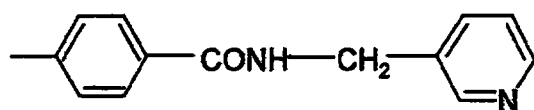
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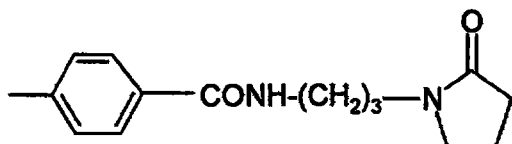
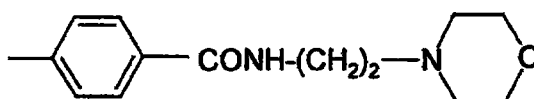
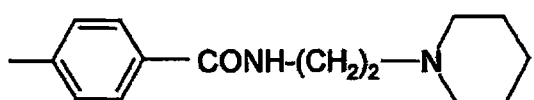
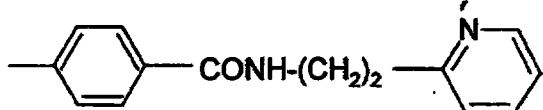
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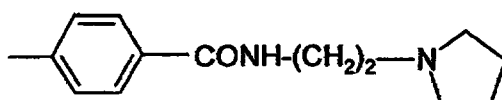
5 are furthermore particularly preferred for
 $-\text{Ar}'-(\text{CH}_2)_n-\text{R}^8$ where R^8 is $-\text{CONH}-(\text{CH}_2)_6-\text{Ar}$.



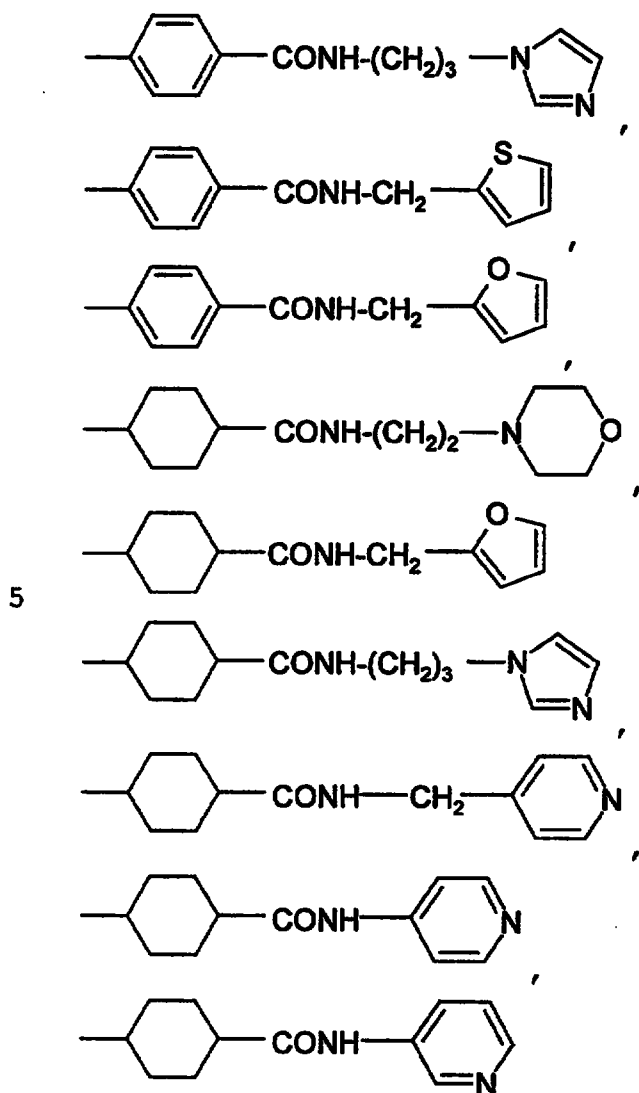
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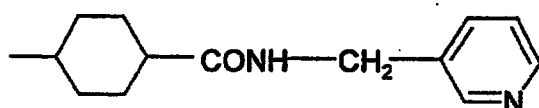
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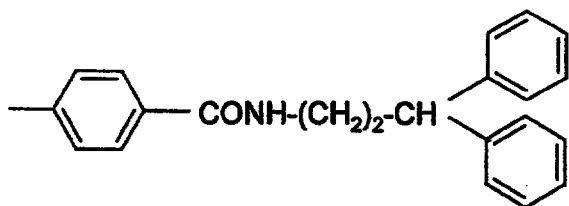
- 22 -



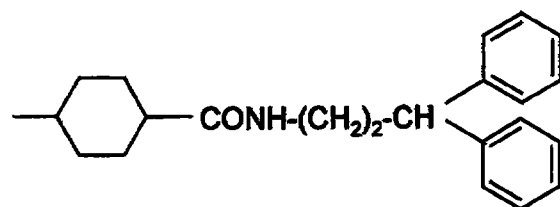
10 or



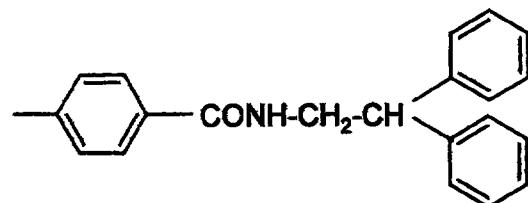
is particularly preferred for $-\text{Ar}'-(\text{CH}_2)_n-\text{R}^8$ where R^8 is $-\text{CONH}-(\text{CH}_2)_o-\text{Het}$.



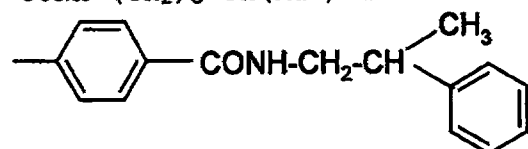
- 23 -



or

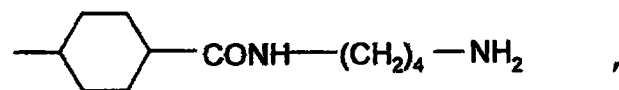


is particularly preferred for $-\text{Ar}'-(\text{CH}_2)_n-\text{R}^8$ where R^8 is
 5 $-\text{CONH}-(\text{CH}_2)_o-\text{CH}(\text{Ar}^1)-\text{Ar}^2$.

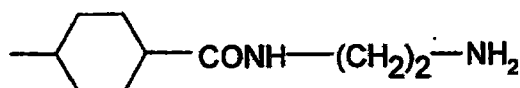


is particularly preferred for $-\text{Ar}'-(\text{CH}_2)_n-\text{R}^8$ where R^8 is
 $-\text{CONH}-(\text{CH}_2)_o-\text{CH}(\text{A})-\text{Ph}$.

Furthermore,



10



or

is particularly preferred for $-\text{Ar}'-(\text{CH}_2)_n-\text{R}^8$ where R^8 is
 15 $-\text{CONH}-(\text{CH}_2)_o-\text{R}^5$.

Cycloalkyl having 3 to 8 carbon atoms is preferentially cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl; particularly preferred cyclohexyl or cyclopentyl.

20 Cycloalkylene having 3 to 8 carbon atoms is preferentially cyclobutylene, cyclopentylene,

- 24 -

cyclohexylene, or cycloheptylene; particularly preferred cyclohexylene.

O(cycloalkyl) having 3 to 8 carbon atoms is preferentially cyclobutyloxy, cyclopentyloxy, 5 cyclohexyloxy or cycloheptyloxy; particularly preferred cyclopentyloxy.

Hal is preferably F, Cl, Br or iodine.

Het¹ is preferentially substituted or unsubstituted 2-, 3-, or 4-pyridyl, 2- or 10 3-benzo[b]thiophenyl, 1H-indol-2-yl, 1H-indol-3-yl, 4-, 5-, 6-, 7-fluoro-1H-indol-2-yl, 4-, 5-, 6-, 7-fluoro-1H-indol-3-yl, 4-, 5-, 6-, 7-methyl-1H-indol-2-yl, 4-, 5-, 6-, 7-methyl-1H-indol-3-yl, 4-, 5-, 6-, methoxy-1H-indol-2-yl or 4-, 5-, 6-, 7-methoxy-1H-indol-3-yl, 15 4-Pyridyl, 3-benzo[b]thiophenyl, 1H-indol-3-yl, 5-fluoro-1H-indol-3-yl, 5-methyl-1H-indol-3-yl, 5- or 6-methoxy-1H-indol-3-yl are furthermore particularly preferred.

Het is preferably substituted or unsubstituted 20 2- or 3-furyl, 2- or 3-thienyl, 2-chloro-thienyl-5-yl, 2-acetyl-thienyl-5-yl, 1-, 2- or 3-pyrrolyl, 1-, 2-, 4- or 5-imidazolyl, 1-, 3-, 4- or 5-pyrazolyl, 2-, 4- or 5-oxazolyl, 3-, 4- or 5-isoxazolyl, 2-, 4- or 5-thiazolyl, 3-, 4- or 5-isothiazolyl, 2-, 3- or 25 4-pyridyl, 2-, 4-, 5- or 6-pyrimidinyl, furthermore preferably 1,2,3-triazol-1-, -4- or -5-yl, 1,2,4-triazol-1-, -4- or -5-yl, 1- or 5-tetrazolyl, 1,2,3-oxadiazol-4- or -5-yl, 1,2,4-oxadiazol-3- or -5-yl, 1,3,4-thiadiazol-2- or -5-yl, 30 1,2,4-thiadiazol-3- or -5-yl, 1,2,3-thiadiazol-4- or -5-yl, 2-, 3-, 4-, 5- or 6-2H-thiopyranyl, 2-, 3- or 4-4H-thiopyranyl, 3- or 4-pyridazinyl, pyrazinyl, 2-, 3-, 4-, 5-, 6- or 7-benzofuryl, 2-, 3-, 4-, 5-, 6- or 7-benzothienyl, 1-, 2-, 3-, 4-, 5-, 6- or 7-1H-indolyl, 35 1-, 2-, 4- or 5-benzimidazolyl, 1-, 3-, 4-, 5-, 6- or 7-benzopyrazolyl, 2-, 4-, 5-, 6- or 7-benzoxazolyl, 3-, 4-, 5-, 6- or 7-benzisoxazolyl, 2-, 4-, 5-, 6- or 7-benzothiazolyl, 2-, 4-, 5-, 6- or 7-benzisothiazolyl, 4-, 5-, 6- or 7-benz-2,1,3-

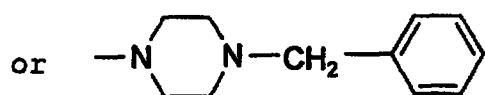
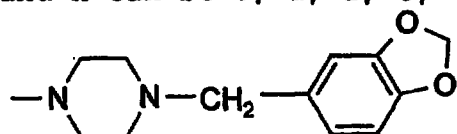
- 25 -

oxadiazolyl, 1-, 2-, 3-, 4-, 5-, 6-, 7- or
 8-quinolinyl, 1-, 3-, 4-, 5-, 6-, 7- or
 8-isoquinolinyl, 1-, 2-, 3-, 4- or 9-carbazolyl, 1-,
 2-, 3-, 4-, 5-, 6-, 7-, 8- or 9-acridinyl, 3-, 4-, 5-,
 5 6-, 7- or 8-cinnolinyl, 2-, 4-, 5-, 6-, 7- or
 8-quinazolinyl, 1,1-dioxo-1H-1 λ ⁶-benzo[b]thiophen-5-yl
 or 2,2-dioxo-2,3-dihydro-1H-2 λ ⁶-benzo[c]thiophen-5-yl.
 The heterocyclic radicals can also be partially or
 completely hydrogenated. Het can thus also be
 10 2,3-dihydro-2-, -3-, -4- or -5-furyl, 2,5-dihydro-2-,
 -3-, -4- or -5-furyl, tetrahydro-2- or -3-furyl,
 1,3-dioxolan-4-yl, tetrahydro-2- or -3-thienyl,
 2,3-dihydro-1-, -2-, -3-, -4- or -5-pyrrolyl,
 2,5-dihydro-1-, -2-, -3-, -4- or -5-pyrrolyl, 1-, 2- or
 15 3-pyrrolidinyl, pyrrolidine-2-on-1-yl, tetrahydro-1-,
 -2- or -3-pyrrolyl, tetrahydro-1-, -2- or 4-imidazolyl,
 2,3-dihydro-1-, -2-, -3-, -4-, -5-, -6-, -7-1H-indolyl,
 2,3-dihydro-1-, -2-, -3-, -4- or -5-pyrazolyl,
 tetrahydro-1-, -3- or -4-pyrazolyl, 1,4-dihydro-1-,
 20 -2-, -3- or -4-pyridyl, 1,2,3,4-tetrahydro-1-, -2-,
 -3-, -4-, -5- or -6-pyridyl, 1,2,3,6-tetrahydro-1-,
 -2-, -3-, -4-, -5- or -6-pyridyl, 1-, 2-, 3- or
 4-piperidinyl, 1-, 2-, 3- or 4-azepanyl, 2-, 3- or
 4-morpholinyl, tetrahydro-2-, -3- or -4-pyranyl,
 25 1,4-dioxanyl, 1,3-dioxan-2-, -4- or -5-yl, hexahydro-
 1-, -3- or -4-pyridazinyl, hexahydro-1-, -2-, -4- or
 -5-pyrimidinyl, 1-, 2- or 3-piperazinyl,
 1,2,3,4-tetrahydro-1-, -2-, -3-, -4-, -5-, -6-, -7- or
 -8-quinolinyl, 1,2,3,4-tetrahydro-1-, -2-, -3-, -4-,
 30 -5-, -6-, -7- or -8-isoquinolinyl.
 2-, 3- or 4-pyridyl, 1-imidazolyl,
 2-methyl-1-imidazolyl, 2-pyrimidinyl, 5-fluoro-1H-
 indol-2-yl, 2, 3-dihydro-1-, -2-, -3-, -4-, -5-,
 -6-, -7-1H-indolyl, 1-quinolinyl, 1-isoquinolinyl,
 35 1,2,3,4-tetrahydroisoquinoline-1-yl, tetrahydro-
 1-pyrrolyl, 1-piperidinyl, 2,6-tetramethyl-
 piperidine-4-yl, 1-azepanyl, 4-morpholinyl, 1-
 piperazinyl, 4-methyl-piperazin-1-yl, 4-phenyl-

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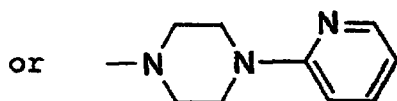
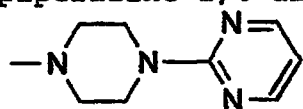
piperazin-1-yl or 4-phenylmethylpiperazin-1-yl is particularly preferred.

In $\text{-Het-(CH}_2\text{)}_n\text{-Ar}$, Het and Ar have one of the preferred meanings indicated above, where Het is preferably piperidine-1,4-diyl or piperazine-1,4-diyl and n can be 0, 1, 2, 3, or 4.



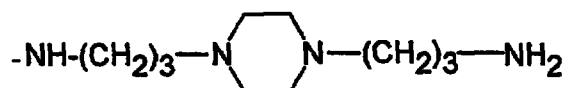
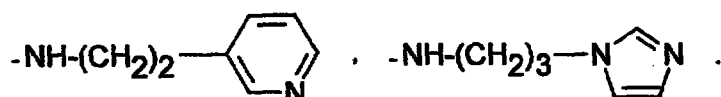
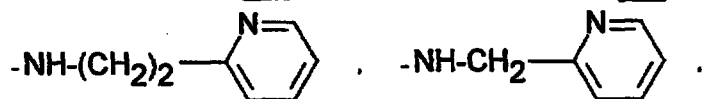
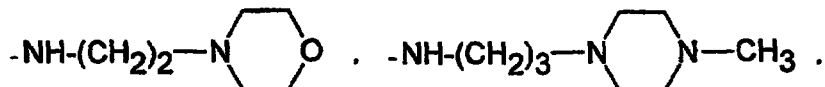
is particularly preferred for $\text{-Het-(CH}_2\text{)}_n\text{-Ar}$.

In -Het-Het , Het has one of the preferred meanings indicated above, where in -Het-Het the first heterocycle is preferably piperidine-1,4-diyl or piperazine-1,4-diyl.

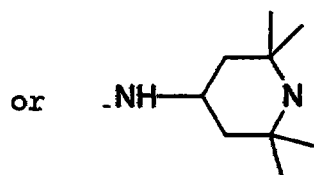


is particularly preferred for -Het-Het .

In $\text{-Y-(CH}_2\text{)}_n\text{-Het-(CH}_2\text{)}_o\text{-R}^6$, Y is preferably O, S or NH, where Het has one of the preferred meanings indicated above and R^6 is preferentially H, amino or alkylamino. Furthermore, n and o independently of one another are preferably 0, 1, 2, 3 or 4.

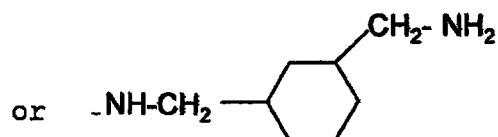
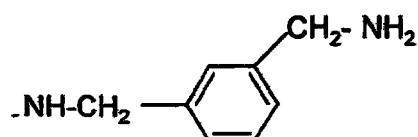
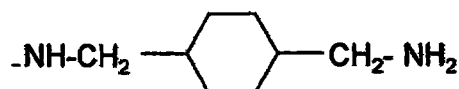
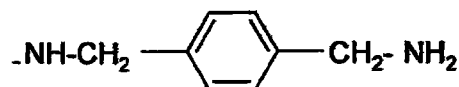
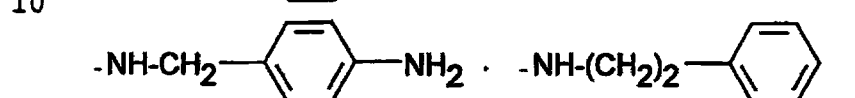
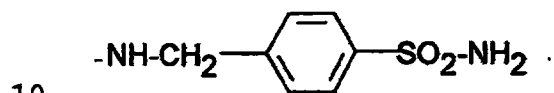
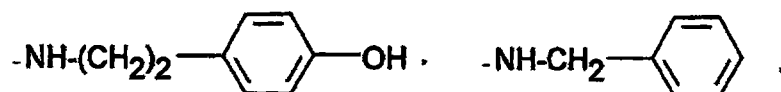
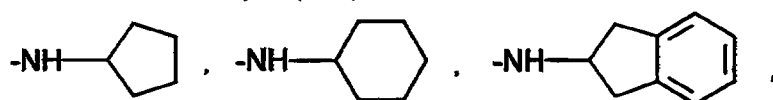


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are particularly preferred for $-Y-(CH_2)_n-Het(CH_2)_o-R^6$.

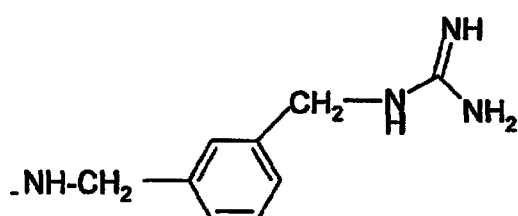
Furthermore, in $-Y-(CH_2)_n-Ar'-(CH_2)_o-R^6$, Y is preferentially O, S, or NH, where Ar' has a preferred meaning indicated beforehand and R⁶ is preferably H, amino or alkylamino and n and o independently of one another are 0, 1, 2, 3 or 4.



is particularly preferred for $-Y-(CH_2)_n-Ar'-(CH_2)_o-R^6$.

Furthermore, in $-Y-(CH_2)_s-Ar'-(CH_2)_o-R^{11}$, Y is preferentially O, S, or NH, where Ar' has a preferred meaning indicated beforehand and R¹¹ is preferably $-NH-(C=NH)-NH_2$ and s and o independently of one another are 0, 1, 2, 3 or 4.

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is particularly preferred for $\text{-Y-(CH}_2\text{)}_s\text{-Ar'-(CH}_2\text{)}_o\text{-R}^{11}$.

X and/or X^1 and/or X^2 is alkylene and is preferably methylene, ethylene, propylene, butylene, furthermore also pentylene or hexylene.

In $\text{-Y-[X-O]}_t\text{-[X}^1\text{-O]}_u\text{-X}^2\text{-R}^5$, Y is preferentially O, S or NH, where X, X^1 and X^2 have a preferred meaning indicated beforehand. Furthermore, R^5 is preferably amino, alkylamino or dialkylamino, t is 0, 1 or 2 and u is 1 or 2. $\text{-NH-(CH}_2\text{)}_3\text{-O-(CH}_2\text{)}_4\text{-O-(CH}_2\text{)}_3\text{-NH}_2$ is particularly preferred for $\text{-Y-[X-O]}_t\text{-[X}^1\text{-O]}_u\text{-X}^2\text{-R}^5$.

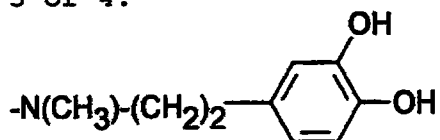
Y is preferentially O, S or NH, particularly preferentially NH.

R is preferably H, A, or $\text{CH}_2\text{-Ph}$, where A has a preferred meaning indicated above. H, sec-butyl or $\text{CH}_2\text{-Ph}$ is particularly preferred.

R^1 is preferably -Het , $\text{-N-[(CH}_2\text{)}_s\text{-OH]}_2$, $\text{-N-[(CH}_2\text{)}_s\text{-OA]}_2$, $\text{-NA-(CH}_2\text{)}_s\text{-Ar}$, $\text{-NA-(CH}_2\text{)}_m\text{-R}^5$, $\text{-Y-(CH}_2\text{)}_m\text{-R}^5$, $\text{-Y-(CH}_2\text{)}_2\text{-NHA}$, $\text{-Y-(CH}_2\text{)}_2\text{-NA}_2$, $\text{-Y-(CH}_2\text{)}_2\text{-NH-(CH}_2\text{)}_s\text{-OH}$, $\text{-Y-(CH}_2\text{)}_m\text{-OH}$, $\text{-Y-(CH}_2\text{)}_n\text{-(CHR}^4\text{)-R}^3$, $\text{-Y-(CH}_2\text{)}_n\text{-R}^4$, R^4 , $\text{-Y-(CH}_2\text{)}_n\text{-Het-(CH}_2\text{)}_o\text{-R}^6$, $\text{-Y-(CH}_2\text{)}_n\text{-Ar'-(CH}_2\text{)}_o\text{-R}^6$, $\text{-Het-(CH}_2\text{)}_n\text{-Ar}$, -Het-Het , $\text{-Y-[X-O]}_t\text{-[X}^1\text{-O]}_u\text{-X}^2\text{-R}^5$ or $\text{-Y-(CH}_2\text{)}_n\text{-NA-(CH}_2\text{)}_o\text{-R}^5$, where -Het , $\text{-Y-(CH}_2\text{)}_n\text{-Het-(CH}_2\text{)}_o\text{-R}^6$, $\text{-Y-(CH}_2\text{)}_n\text{-Ar'-(CH}_2\text{)}_o\text{-R}^6$, $\text{-Y-(CH}_2\text{)}_s\text{-Ar'-(CH}_2\text{)}_o\text{-R}^{11}$, $\text{-Het-(CH}_2\text{)}_n\text{-Ar}$, -Het-Het and $\text{-Y-[X-O]}_t\text{-[X}^1\text{-O]}_u\text{-X}^2\text{-R}^5$ in particular have the preferred meanings indicated beforehand. Furthermore, s in $\text{-N-[(CH}_2\text{)}_s\text{-OH]}_2$ and $\text{-N-[(CH}_2\text{)}_s\text{-OA]}_2$ is preferably 1, 2, 3 or 4 and A has the preferred meaning indicated beforehand. $\text{-N-[(CH}_2\text{)}_2\text{-OH]}_2$ is particularly preferred for $\text{-N-[(CH}_2\text{)}_s\text{-OH]}_2$.

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In $-\text{NA}-(\text{CH}_2)_s-\text{Ar}$, A and Ar have a preferred meaning indicated beforehand and s is preferably 1, 2, 3 or 4.



5 is particularly preferred for $-\text{NA}-(\text{CH}_2)_s-\text{Ar}$.

Furthermore, A in $-\text{NA}-(\text{CH}_2)_s-\text{R}^5$ as a substituent for R^1 has a preferred meaning indicated beforehand, where R^5 is preferably amino, alkylamino or dialkylamino and s is 1, 2, 3 or 4. $-\text{N}(\text{CH}_3)-(\text{CH}_2)_3-\text{NH}(\text{CH}_3)$ and
 10 $-\text{N}(\text{CH}_3)-(\text{CH}_2)_2-\text{N}(\text{C}_2\text{H}_5)_2$ are particularly preferred for $-\text{NA}-(\text{CH}_2)_s-\text{R}^5$.

In $-\text{Y}-(\text{CH}_2)_m-\text{R}^5$ Y is preferentially O, S or NH, where R^5 is preferably amino, alkylamino or dialkylamino and m is 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12. $-\text{NH}-(\text{CH}_2)_3-\text{NH}_2$,
 15 $-\text{NH}-(\text{CH}_2)_3-\text{NH}(\text{CH}_3)$, $-\text{NH}-(\text{CH}_2)_3-\text{N}(\text{CH}_3)_2$,
 $-\text{NH}-(\text{CH}_2)_3-\text{NH}[\text{CH}(\text{CH}_3)_2]$, $-\text{NH}-(\text{CH}_2)_3-\text{NH}(\text{C}_6\text{H}_{11})$,
 $-\text{NH}-(\text{CH}_2)_4-\text{NH}_2$, $-\text{NH}-(\text{CH}_2)_5-\text{NH}_2$, $-\text{NH}-(\text{CH}_2)_7-\text{NH}_2$ and
 $-\text{NH}-(\text{CH}_2)_8-\text{NH}_2$ are particularly preferred for $-\text{Y}-(\text{CH}_2)_m-\text{R}^5$.

20 In $-\text{Y}-(\text{CH}_2)_2-\text{NHA}$ and $-\text{Y}-(\text{CH}_2)_2-\text{NA}_2$, Y is preferably O, S or NH, where A has a preferred meaning indicated beforehand. $-\text{NH}-(\text{CH}_2)_2-\text{NH}(\text{C}_2\text{H}_5)$, $-\text{NH}-(\text{CH}_2)_2-\text{NH}(\text{C}_3\text{H}_7)$ and $-\text{NH}-(\text{CH}_2)_2-\text{NH}[\text{CH}(\text{CH}_3)_2]$ are particularly preferred for $-\text{Y}-(\text{CH}_2)_2-\text{NHA}$.

25 In $-\text{Y}-(\text{CH}_2)_2-\text{NH}-(\text{CH}_2)_s-\text{OH}$, Y is preferably O, S or NH, where s is 1, 2, 3 or 4. $-\text{NH}-(\text{CH}_2)_2-\text{NH}(\text{CH}_2)_2-\text{OH}$ is particularly preferred for $-\text{Y}-(\text{CH}_2)_2-\text{NH}-(\text{CH}_2)_s-\text{OH}$.

In $-\text{Y}-(\text{CH}_2)_m-\text{OH}$, Y is preferably O, S or NH, where m is 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12. $-\text{NH}-(\text{CH}_2)_5-\text{OH}$ is
 30 particularly preferred for $-\text{Y}-(\text{CH}_2)_m-\text{OH}$.

In $-\text{Y}-(\text{CH}_2)_n-(\text{CHR}^4)-\text{R}^3$, Y is preferably O, S or NH, where R^3 is preferably methyl, R^4 is preferentially Ar and n is 0, 1, 2, 3 or 4. $-\text{NH}-(\text{CHPh})-\text{CH}_3$ is particularly preferred for $-\text{Y}-(\text{CH}_2)_n-(\text{CHR}^4)-\text{R}^3$.

35 In $-\text{Y}-(\text{CH}_2)_n-\text{R}^4$, Y is preferentially O, S or NH, where in this formula R^4 is preferably COOH or COOA, A has a

- 30 -

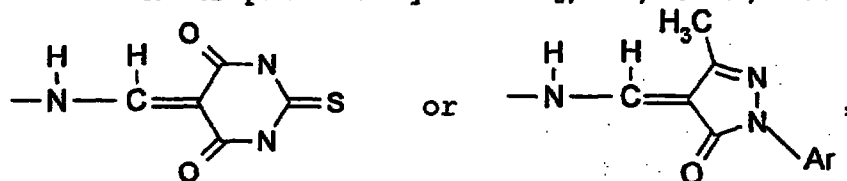
preferred meaning indicated beforehand and n is 0, 1, 2, 3 or 4. $-\text{NH}-(\text{CH}_2)_2-\text{COOMe}$ is particularly preferred. In $-\text{Y}-(\text{CH}_2)_n-\text{NA}-(\text{CH}_2)_o-\text{R}^5$, Y is preferentially O, S, NH, where A has a preferred meaning indicated beforehand, R^5 is preferably amino, alkylamino or dialkylamino and n and o in each case independently of one another are 0, 1, 2, 3 or 4. $-\text{NH}-(\text{CH}_2)_3-\text{N}(\text{CH}_3)-(\text{CH}_2)_3-\text{NH}_2$ is particularly preferred for $-\text{Y}-(\text{CH}_2)_n-\text{NA}-(\text{CH}_2)_o-\text{R}^5$.

i is preferentially 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12, particularly preferentially 1, 2, 3, 5, 7, 10 or 11.

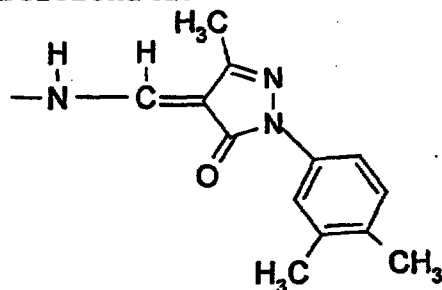
R^2 is preferably H, OH, OA, COOH, COOA, Ar, $\text{CH}(\text{Ph})-\text{Ph}$, Het^1 , R^5 , R^7 or R^8 , where A, Ar and Het^1 have a preferred meaning indicated beforehand.

R^3 is preferentially CH_3 .

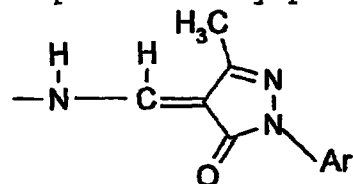
R^4 is preferably $-\text{CH}=\text{CH}_2$, Ar, COOA, COOH



where Ar and A have a preferred meaning indicated beforehand.



is particularly preferred for



R^5 is preferentially amino, alkylamino, dialkylamino, $\text{NHA}r$, $-\text{NH}-(\text{CH}_2)_n-\text{OH}$ or $-\text{NH}-(\text{CH}_2)_n-\text{OA}$, where A and Ar have a preferred meaning indicated beforehand

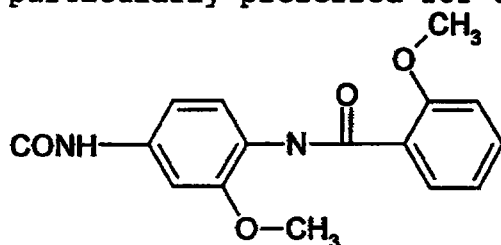
- 31 -

and n is 0, 1, 2, 3, or 4. $\text{-NH-(CH}_2\text{)}_2\text{-OH}$ is particularly preferred for $\text{-NH-(CH}_2\text{)}_n\text{-OH}$.

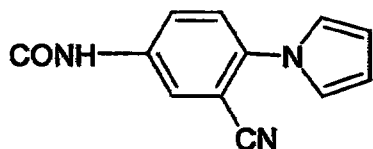
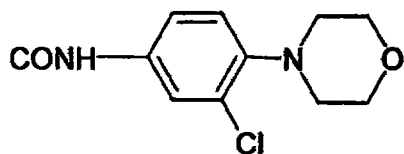
R^6 is H or R^5 , where R^5 has a preferred meaning indicated beforehand.

- 5 R^7 is preferentially $\text{-Ar'-(CH}_2\text{)}_n\text{-R}^8$ or $\text{-Ar'-(CH}_2\text{)}_n\text{-R}^5$, where $\text{-Ar'-(CH}_2\text{)}_n\text{-R}^8$ and $\text{-Ar'-(CH}_2\text{)}_n\text{-R}^5$ have a preferred or particularly preferred meaning indicated beforehand.

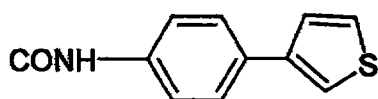
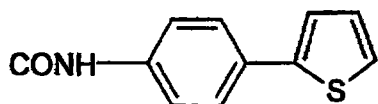
- R^8 is preferably CONH_2 , CONHA , CONA_2 ,
 10 $\text{CONH-(CH}_2\text{)}_o\text{-Ar}$, $\text{CONH-(CH}_2\text{)}_o\text{-Het}$, $\text{CONH-(CH}_2\text{)}_o\text{-CH(Ar}^1\text{)-Ar}^2$,
 CONH-Ar'-NH-CO-Ar , CONH-Ar'-Het , $\text{CONH-(CH}_2\text{)}_o\text{-R}^5$ or
 CHA-CONH_2 , where A, $\text{CONH-(CH}_2\text{)}_o\text{-Ar}$, $\text{CONH-(CH}_2\text{)}_o\text{-Het}$,
 $\text{CONH-(CH}_2\text{)}_o\text{-CH(Ar}^1\text{)-Ar}^2$, and $\text{CONH-(CH}_2\text{)}_o\text{-R}^5$ have a
 15 preferred or particularly preferred meaning indicated
 beforehand in $\text{-Ar'-(CH}_2\text{)}_n\text{-R}^8$. $\text{CH(CH}_3\text{)-CONH}_2$ is
 particularly preferred for CHA-CONH_2 .



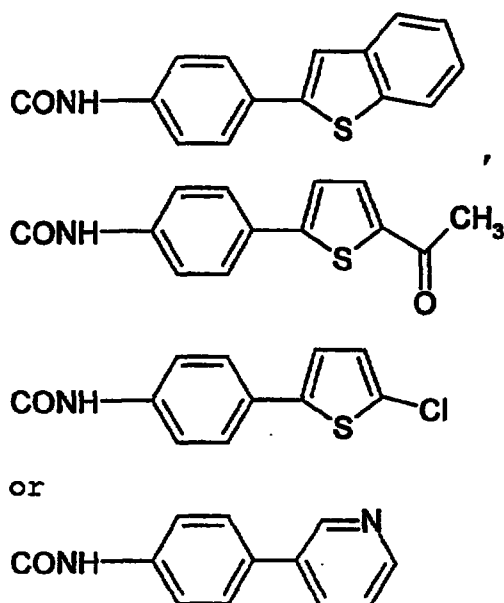
is particularly preferred for CONH-Ar'-NH-CO-Ar .



20



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5

is particularly preferred for CONH-Ar'-Het.

R^{11} is $-NH-(C=NH)-NH_2$, $-NH-(C=NH)-NHA$,
 $-NH-(C=NH)-NA_2$, $-NA-(C=NH)-NH_2$, $-NA-(C=NH)-NHA$ or
 $-NA-(C=NH)-NA_2$, where A has a meaning indicated
 10 beforehand. $-NH-(C=NH)-NH_2$ is particularly preferred for
 R^{11} .

i is preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, 10,
 11 or 12, particularly preferred 1, 2, 3, 4, 5 or 6.

15 m is preferably 3, 4, 5, 6, 7, 8, 9, 10, 11 or
 12, particularly preferred 3, 4, 5, 6, 7 or 8.

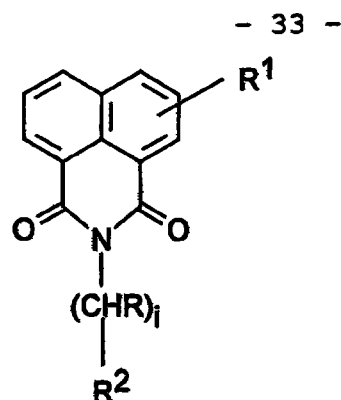
n and o are in each case independently of one
 another preferably 0, 1, 2, 3 or 4.

s is preferably 1, 2, 3 or 4.

t is preferably 0, 1 or 2.

20 u is preferably 1 or 2.

Some preferred groups of compounds can be
 expressed by the following subformulae Ia to Iv, which
 correspond to the formula I



and in which the radicals not designated in greater
 detail have the meanings indicated in formula I, but in
 5 which:

in Ia R is H,
 R² is H,
 R¹ is -Het, -N-[(CH₂)_s-OH]₂, -Y-(CH₂)_n-R⁴ or R⁴
 10 and
 i is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

in Ib R is H,
 R² is OH
 15 R¹ is -Het or -Y-(CH₂)_n-(CHR⁴)-R³ and
 i is 2;

in Ic R is H,
 20 R² is COOA,
 R¹ is -Het, -Y-(CH₂)_n-(CHR⁴)-R³,
 -Y-(CH₂)_n-Ar'-(CH₂)_o-R⁶, -Het-(CH₂)_n-Ar or
 -NA-(CH₂)_s-Ar and
 i is 2;

25 in Id R is H,
 R² is Ar,
 R¹ is -Het, -NA-(CH₂)_s-Ar, -Y-(CH₂)_m-R⁵,
 -Y-(CH₂)_m-OH, -Y-(CH₂)_n-(CHR⁴)-R³,
 30 -Y-(CH₂)_n-R⁴, -Y-(CH₂)_n-Het-(CH₂)_o-R⁶,
 -Y-(CH₂)_n-Ar'-(CH₂)_o-R⁶ or -Het-(CH₂)_n-Ar and
 i is 1 or 2;

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- in Ie R is H,
 R² is Het¹,
 R¹ is -Het, -NA-(CH₂)_s-Ar, -Y-(CH₂)_m-R⁵,
 -Y-(CH₂)_m-OH, -Y-(CH₂)_n-(CHR⁴)-R³,
 -Y-(CH₂)_n-R⁴, -Y-(CH₂)_n-Ar'-(CH₂)_o-R⁶ or
 -Het-(CH₂)_n-Ar and
 i is 1 or 2;
- in If R is H,
 R² is R⁵,
 R¹ is -Het, -Y-(CH₂)_m-R⁵, -Y-(CH₂)_m-OH,
 -Y-(CH₂)_n-(CHR⁴)-R³, -Y-(CH₂)_n-R⁴,
 -Y-(CH₂)_n-Het-(CH₂)_o-R⁶,
 -Y-(CH₂)_n-Ar'-(CH₂)_o-R⁶ or -Het-(CH₂)_n-Ar and
 i is 3 or 5;
- in Ig R is H,
 R² is R⁸,
 R¹ is -Het, -NA-(CH₂)_m-R⁵, -Y-(CH₂)_m-R⁵,
 -Y-(CH₂)₂-NH-(CH₂)_s-OH, -Y-(CH₂)_m-OH,
 -Y-(CH₂)_n-(CHR⁴)-R³, -Y-(CH₂)_n-R⁴,
 -Y-(CH₂)_n-Het-(CH₂)_o-R⁶,
 -Y-(CH₂)_n-Ar'-(CH₂)_o-R⁶, -Het-(CH₂)_n-Ar,
 -Het-Het, -Y-[X-O]_t-[X¹-O]_u-X²-R⁵ or
 -Y-(CH₂)_n-NA-(CH₂)_o-R⁵ and
 i is 1, 2, 7, 10 or 11;
- in Ih R is H,
 R² is R⁷,
 R¹ is -Het, -NA-(CH₂)_m-R⁵, -Y-(CH₂)_m-R⁵,
 -Y-(CH₂)₂-NHA, -Y-(CH₂)₂-NH-(CH₂)_s-OH,
 -Y-(CH₂)_m-OH, -Y-(CH₂)_n-(CHR⁴)-R³,
 -Y-(CH₂)_n-R⁴, -Y-(CH₂)_n-Het-(CH₂)_o-R⁶,
 -Y-(CH₂)_n-Ar'-(CH₂)_o-R⁶,
 -Y-(CH₂)_s-Ar'-(CH₂)_o-R¹¹, -Het-(CH₂)_n-Ar,
 -Het-Het, -Y-[X-O]_t-[X¹-O]_u-X²-R⁵ or
 -Y-(CH₂)_n-NA-(CH₂)_o-R⁵ and
 i is 1 or 2;

- 35 -

- in Ik R is A or CH₂-Ph,
 R² is R⁸,
 R¹ is -Het, -Y-(CH₂)_m-R⁵, -Y-(CH₂)_n-Het-(CH₂)_o-R⁶
 or -Y-(CH₂)_n-Ar'-(CH₂)_o-R⁶ and
 5 i is 1;
- in Im R is H,
 R² is CONH₂,
 R¹ is -Het, -NA-(CH₂)_m-R⁵, -Y-(CH₂)_m-R⁵,
 10 -Y-(CH₂)₂-NH-(CH₂)_s-OH, -Y-(CH₂)_m-OH,
 -Y-(CH₂)_n-(CHR⁴)-R³, -Y-(CH₂)_n-R⁴,
 -Y-(CH₂)_n-Het-(CH₂)_o-R⁶,
 -Y-(CH₂)_n-Ar'-(CH₂)_o-R⁶, -Het-(CH₂)_n-Ar,
 -Het-Het, -Y-[X-O]_t-[X¹-O]_u-X²-R⁵ or
 15 -Y-(CH₂)_n-NA-(CH₂)_o-R⁵ and
 i is 1, 2, 7, 10 or 11;
- in In R is H,
 R² is CONHA,
 R¹ is -Y-(CH₂)_m-R⁵ or -Y-(CH₂)_n-Ar'-(CH₂)_o-R⁶ and
 20 i is 2;
- in Io R is H,
 R² is CONH-(CH₂)_o-Ar,
 R¹ is -Y-(CH₂)_m-R⁵, -Y-(CH₂)_n-Het-(CH₂)_o-R⁶ or
 -Y-(CH₂)_n-Ar'-(CH₂)_o-R⁶ and
 i is 1 or 2;
- 30 in Ip R is H,
 R² is CONH-(CH₂)_o-Het,
 R¹ is -Y-(CH₂)_m-R⁵, or -Y-(CH₂)_n-Ar'-(CH₂)_o-R⁶ and
 i is 2;
- 35 in Iq R is H,
 R² is CONH-(CH₂)_o-CH(Ar¹)-Ar²,
 R¹ is -Y-(CH₂)_n-Ar'-(CH₂)_o-R⁶ and
 i is 2;

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in Ir R is H,
 R^2 is CONH-Ar'-NH-CO-Ar,
 R^1 is $-Y-(CH_2)_n-Ar'-(CH_2)_o-R^6$ and
 i is 2;

5

in Is R is H,
 R^2 is CONH-Ar'-Het,
 R^1 is $-Y-(CH_2)_n-Ar'-(CH_2)_o-R^6$ and
 i is 2;

10

in It R is H,
 R^2 is CH(Ph)-Ph,
 R^1 is $-Y-(CH_2)_m-R^5$, or $-Y-(CH_2)_n-Ar'-(CH_2)_o-R^6$ and
 i is 2;

15

in Iu R is H,
 R^2 is $Ar'-(CH_2)_n-R^8$,
 R^1 is $-Y-(CH_2)_m-R^5$, $-Y-(CH_2)_n-Ar'-(CH_2)_o-R^6$ or
 $-Y-(CH_2)_n-Ar'-(CH_2)_o-R^{11}$ and
 i is 1 or 2;

20

in Iv R is H,
 R^2 is Ar, R^8 or $Ar'-(CH_2)_n-R^8$,
 R^1 is $-Y-(CH_2)_m-R^5$, or $-Y-(CH_2)_n-Ar'-(CH_2)_o-R^6$ and
 i is 1 or 2.

25

The compounds of the formula I and also the starting substances for their preparation are otherwise prepared by methods known per se, such as are described in the literature (e.g. in the standard works such as Houben-Weyl, Methoden der organischen Chemie [Methods of Organic Chemistry], Georg-Thieme-Verlag, Stuttgart), namely under reaction conditions which are known and suitable for the reactions mentioned. In this case, use can also be made of variants which are known per se, but not mentioned here in greater detail.

35

The starting substances, if desired, can also be formed in situ such that they are not isolated from

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the reaction mixture, but immediately reacted further to give the compounds of the formula I.

The compounds of the formula I can be obtained by liberating them from their functional derivatives by
5 solvolysis, in particular hydrolysis or by hydrogenolysis.

Preferred starting substances for the solvolysis or hydrogenolysis are those which otherwise correspond to the formula I, but instead of one or more
10 free amino and/or hydroxyl groups contain corresponding protected amino and/or hydroxyl groups, in particular those which instead of an H-N- group carry an R'-N-group, in which R' is an amino protective group and/or those which instead of the H atom of a hydroxyl group
15 carry a hydroxyl protective group, e.g. those which correspond to the formula I, but instead of a group -COOH carry a group -COOR'', in which R'' is a hydroxyl protective group.

A number of - identical or different -
20 protected amino and/or hydroxyl groups can also be present in the molecule of the starting substance. If the protective groups present are different from one another, in many cases they can be removed selectively.

The expression "amino protective group" is
25 generally known and relates to groups which are suitable for protecting (for blocking) an amino group against chemical reactions, but which are easily removable after the desired chemical reaction has been carried out at other positions in the molecule. Typical
30 groups of this type are, in particular, unsubstituted or substituted acyl, aryl, aralkoxymethyl or aralkyl groups. Since the amino protective groups are removed after the desired reaction (or reaction sequence), their nature and size is otherwise not critical;
35 however, those having 1-20, in particular 1-8, C atoms are preferred. The expression "acyl group" is to be interpreted in the widest sense in connection with the present process. It includes acyl groups derived from aliphatic, araliphatic, aromatic or heterocyclic

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carboxylic acids or sulfonic acids and, in particular, alkoxy carbonyl groups, aryloxy carbonyl groups and especially aralkoxy carbonyl groups. Examples of acyl groups of this type are alkanoyl such as acetyl, 5 propionyl, butyryl; aralkanoyl such as phenylacetyl; aroyl such as benzoyl or toluylyl; aryloxyalkanoyl such as POA; alkoxy carbonyl such as methoxy carbonyl, ethoxy carbonyl, 2,2,2-trichloroethoxy carbonyl, BOC, 2-iodoethoxy carbonyl; aralkyloxy carbonyl such as CBZ 10 ("carbobenzoxy"), 4-methoxybenzyloxy carbonyl, Fmoc; arylsulfonyl such as Mtr. Preferred amino protective groups are BOC, furthermore CBZ, Fmoc, benzyl and acetyl.

The expression "hydroxyl protective group" is 15 also generally known and relates to groups which are suitable for protecting a hydroxyl group against chemical reactions, but which are easily removable after the desired chemical reaction has been carried out at other positions in the molecule. Typical groups 20 of this type are the abovementioned unsubstituted or substituted aryl, aralkyl or acyl groups, furthermore also alkyl groups. The nature and size of the hydroxyl protective groups is not critical, since they are removed again after the desired chemical reaction or 25 reaction sequence; groups having 1-20, in particular 1-10 C atoms, are preferred. Examples of hydroxyl protective groups are, inter alia, benzyl, p-nitrobenzoyl, p-toluolsulfonyl, tert-butyl and acetyl, benzyl and tert-butyl being particularly 30 preferred.

The liberation of the compounds of the formula I from their functional derivatives is carried out - depending on the protective group used - for example using strong acids, expediently using TFA or 35 perchloric acid, but also using other strong inorganic acids such as hydrochloric acid or sulfuric acid, strong organic carboxylic acids such as trichloroacetic acid or sulfonic acids such as benzene- or p-toluene-sulfonic acid. The presence of an additional inert

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solvent is possible, but not always necessary. Suitable inert solvents are preferably organic, for example carboxylic acids such as acetic acid, ethers such as tetrahydrofuran or dioxane, amides such as DMF, 5 halogenated hydrocarbons such as dichloromethane, furthermore also alcohols such as methanol, ethanol or isopropanol, and also water. Furthermore, mixtures of the abovementioned solvents are possible. TFA is preferably used in an excess without addition of a 10 further solvent, perchloric acid in the form of a mixture of acetic acid and 70% perchloric acid in the ratio 9:1. The reaction temperatures for the cleavage are expediently between approximately 0 and approximately 50°C; the reaction is preferably carried 15 out between 15 and 30°C (room temperature).

The groups BOC and Obutyl can preferably be removed, for example, using TFA in dichloromethane or using approximately 3 to 5N HCl in dioxane at 15-30°C, the Fmoc group using an approximately 5 to 50% solution 20 of dimethylamine, diethylamine or piperidine in DMF at 15-30°C.

Hydrogenolytically removable protective groups (e.g. CBZ or benzyl) can be removed, for example, by treating with hydrogen in the presence of a catalyst 25 (e.g. of a noble metal catalyst such as palladium, expediently on a support such as carbon). Suitable solvents in this case are those indicated above, in particular, for example, alcohols such as methanol or ethanol or amides such as DMF. As a rule, the 30 hydrogenolysis is carried out at temperatures between approximately 0 and 100°C and pressures between approximately 1 and 200 bar, preferentially at 20-30°C and 1-10 bar. Hydrogenolysis of the CBZ group takes place readily, for example, on 5 to 10% Pd/C in 35 methanol or ammonium formate (instead of hydrogen) on Pd/C in methanol/DMF at 20-30°C.

Compounds of the formula I can also preferably be obtained by reacting compounds of the formula II with compounds of the formula III. As a rule, the

- 40 -

starting compounds of the formulae II and III are known or commercially available. The unknown compounds, however, can be prepared by methods known per se. The compounds of the formula II are naphthalene-
5 1,8-dicarboxylic anhydride derivatives. They can be prepared in a conventional manner from appropriately substituted 1,8-naphthalenedicarboxylic acids or corresponding derivatives. It is furthermore possible to introduce appropriate substituents into the aromatic
10 by conventional electrophilic or alternatively nucleophilic substitutions.

The compounds of the formula III are primary amines, which, as a rule, are also commercially available. Furthermore, syntheses for the preparation
15 of primary amines, such as, for example, the Gabriel synthesis, can be used.

As a rule, the reaction is carried out in an inert solvent. Depending on the conditions used, the reaction time is between a few minutes and a number of
20 days, the reaction temperature between approximately 0° and 150°C, normally between 20° and 130°C. The reactions can be carried out in analogy to the methods indicated in Eur. J. Chem. Chim. Ther. 1981, 16, 207-212 and in J. Med. Chem. 1982, 25, 714-719.

Suitable inert solvents are, for example, hydrocarbons such as hexane, petroleum ether, benzene, toluene or xylene; chlorinated hydrocarbons such as trichloroethylene, 1,2-dichloroethane, carbon tetrachloride, chloroform or dichloromethane; alcohols
30 such as methanol, ethanol, isopropanol, n-propanol, n-butanol or tert-butanol; ethers such as diethyl ether, diisopropyl ether, tetrahydrofuran (THF) or dioxane; glycol ethers such as ethylene glycol monomethyl or monoethyl ether (methyl glycol or ethyl glycol), ethylene glycol dimethyl ether (diglyme);
35 ketones such as acetone or butanone; amides such as acetamide, N-methylpyrrolidone (NMP), dimethylacetamide or dimethylformamide (DMF); nitriles such as acetonitrile; sulfoxides such as dimethyl sulfoxide

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(DMSO); carbon disulfide; carboxylic acids such as formic acid or acetic acid; nitro compounds such as nitromethane or nitrobenzene; esters such as ethyl acetate or mixtures of the solvents mentioned.

5 For the preparation of compounds of the formula I in which R^{11} is $H_2N-C(=NH)-NH-$, an appropriate amino-substituted compound can be treated with an amidinating agent. The preferred amidinating agent is 1-amidino-3,5-dimethylpyrazole (DPFN), which is
10 employed, in particular, in the form of its nitrate, or pyrazole-1-carboxamidine. The reaction is expediently carried out with addition of a base such as triethylamine or ethyldiisopropylamine in an inert solvent or solvent mixture, e.g. DMF at temperatures
15 between 0° and $150^\circ C$, preferably between 60° and $120^\circ C$.

For the preparation of compounds of the formula I in which R^2 is unsubstituted or substituted biphenyl, $-Ar'-Het$ and/or $-CONH-(CH_2)_n-Ar$, an appropriate compound of the formula I in which R^2 is
20 aryl bromide or aryl iodide can be reacted with the appropriate boronic acid derivatives in a Suzuki reaction. The Suzuki reaction is expediently carried out in palladium-mediated form, preferably by addition of $Pd(PPh_3)_4$, in the presence of a base such as
25 potassium carbonate in an inert solvent or solvent mixture, e.g. DMF at temperatures between 0° and 150° , preferably between 60° and 120° . Depending on the conditions used, the reaction time is between a few minutes and a number of days. The boronic acid
30 derivatives can be prepared by conventional methods or are commercially available. The reactions can be carried out in analogy to the methods indicated in Suzuki et al., J. Am. Chem. Soc. 1989, 111, 314ff. and Suzuki et al., Chem. Rev. 1995, 95, 2457ff.

35 The compounds of the formula IV are derived from the anhydrides of the formula II and can be prepared from these by reaction with ammonia under conditions known per se. As a rule, the imides of the formula IV, however, are known and commercially

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available. The substituent R^1 can preferably be introduced into the aromatic by substitution. In many cases, it is expedient to introduce this substituent before the reaction with ammonia.

5 As a rule, the alcohols, activated alcohols or halides of the formula V are known and their preparation is familiar to the person skilled in the art, so that a description of the syntheses is unnecessary here.

10 The reaction of the compounds of the formula IV with compounds of the formula V is preferably carried out in an inert solvent, with addition of a base and at temperatures and with reaction times as indicated beforehand. Suitable acid-binding agents are preferably
15 alkali metal or alkaline earth metal hydroxides, carbonates or bicarbonates or other salts of a weak acid of the alkali or alkaline earth metals, preferably of potassium, sodium, calcium or caesium. The addition of an organic base such as triethylamine,
20 dimethylaniline, pyridine or quinoline or an excess of the amine component of the formula IV may also be favourable.

Derivatives having a free primary or an additional secondary amino group are expediently
25 employed in protected form. Possible protective groups are those mentioned beforehand.

For the esterification, an acid of the formula I ($R^1 = \text{COOH}$ or $-\text{Y}-(\text{CH}_2)_n-\text{COOH}$ and/or $R^2 = \text{COOH}$) can be treated with an excess of an alcohol,
30 expediently in the presence of a strong acid such as hydrochloric acid or sulfuric acid at temperatures between 0° and 100°C , preferably between 20° and 50°C . Conversely, an ester of the formula I ($R^1 = \text{COOA}$ or $-\text{Y}-(\text{CH}_2)_n-\text{COOA}$ and/or $R^2 = \text{COOA}$) can be converted into
35 the corresponding acid of the formula I, expediently by solvolysis according to one of the methods indicated above, e.g. using NaOH or KOH in water-dioxane at temperatures between 0° and 40°C , preferably between 10° and 30°C .

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Furthermore, free amino groups can be acylated in a customary manner using an acid chloride or anhydride, expediently in an inert solvent such as dichloromethane or THF and/or in the presence of a base
5 such as triethylamine or pyridine at temperatures between -60°C and +30°C.

A base of the formula I can be converted into the associated acid addition salt using an acid, for example by reaction of equivalent amounts of the base
10 and of the acid in an inert solvent such as ethanol and subsequent evaporation. Acids which give physiologically acceptable salts are particularly suitable for this reaction. Thus inorganic acids can be used, e.g. sulfuric acid, nitric acid, hydrohalic acids such as
15 hydrochloric acid or hydrobromic acid, phosphoric acids such as orthophosphoric acid, sulfamic acid, furthermore organic acids, in particular aliphatic, alicyclic, araliphatic, aromatic or heterocyclic mono- or polybasic carboxylic, sulfonic or sulfuric acids, e.g.
20 formic acid, acetic acid, propionic acid, pivalic acid, diethylacetic acid, malonic acid, succinic acid, pimelic acid, fumaric acid, maleic acid, lactic acid, tartaric acid, malic acid, citric acid, gluconic acid, ascorbic acid, nicotinic acid, isonicotinic acid,
25 methane- or ethanesulfonic acid, p-toluenesulfonic acid, naphthalenemono- and disulfonic acids or laurylsulfuric acid. Salts with physiologically unacceptable acids, e.g. picrates, can be used for the isolation and/or purification of the compounds of the
30 formula I.

On the other hand, compounds of the formula I with bases (e.g. sodium or potassium hydroxide or carbonate) can be converted into the corresponding metal salts, in particular alkali metal or alkaline
35 earth metal salts, or into the corresponding ammonium salts.

All synthesis methods indicated here and all other suitable processes for the preparation of compounds of the formula I can also be carried out by

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means of the novel methods of combinatorial chemistry, i.e. by robot- and computer-assisted syntheses, and subjected to mass screening (for this see: US 5,463,564; M. A. Gallop et al., J. Med. Chem. 1994, 37, 1233-1251 and 1385-1401 and M.J. Sofia, Drugs Discovery Today 1996, 1, 27-34).

The invention furthermore relates to pharmaceutical preparations comprising at least one compound of the formula I and/or one of its physiologically acceptable salts, which are prepared, in particular, in a non-chemical way. In this case, the compounds of the formula I can be brought into a suitable dose form together with at least one solid, liquid and/or semi-liquid excipient or auxiliary and, if appropriate, in combination with one or more other active compounds.

These preparations can be used as medicaments in human or veterinary medicine. Possible excipients are organic or inorganic substances which are suitable for enteral (e.g. oral) or parenteral administration or topical application and do not react with the novel compounds, for example water, vegetable oils, benzyl alcohols, alkylene glycols, polyethylene glycols, glyceryl triacetate, gelatin, carbohydrates such as lactose or starch, magnesium stearate, talc and petroleum jelly. Tablets, pills, coated tablets, capsules, powders, granules, syrups, juices or drops are used, in particular, for oral administration, suppositories are used for rectal administration, solutions, preferably oily or aqueous solutions, furthermore suspensions, emulsions or implants, are used for parenteral administration, and ointments, creams or powders are used for topical application. The novel compounds can also be lyophilized and the lyophilizates obtained used, for example, for the production of injection preparations. The preparations indicated can be sterilized and/or can contain auxiliaries such as lubricants, preservatives, stabilizers and/or wetting agents, emulsifiers, salts

for affecting the osmotic pressure, buffer substances, colourants, flavourings and/or one or more other active compounds, e.g. one or more vitamins.

The compounds of the formula I and their
5 physiologically acceptable salts act as adhesion
receptor antagonists, in particular glycoprotein IbIX
antagonists, and can be employed for the prophylaxis
and/or therapy of thrombotic disorders and sequelae
deriving therefrom. The disorders are acute coronary
10 syndromes, angina pectoris, myocardial infarct,
peripheral circulatory disorders, stroke, transient
ischaemic attacks, arteriosclerosis and
reocclusion/restenosis after angioplasty/stent
implantation.

15 In this case, the substances according to the
invention are as a rule administered in the dose of the
glycoprotein IIbIIIa antagonist ReoPro® of preferably
between approximately 1 and 500 mg, in particular
between 5 and 100 mg, per dose unit. The daily dose is
20 preferably between approximately 0.02 and 10 mg/kg of
body weight. The specific dose for each patient
depends, however, on all sorts of factors, for example
on the efficacy of the specific compound employed, on
the age, body weight, general state of health and sex,
25 on the diet, on the time and route of administration,
and on the excretion rate, pharmaceutical combination
and severity of the particular disorder to which the
therapy applies. Oral administration is preferred.

Above and below, all temperatures are indicated
30 in °C. In the following examples, "customary working-
up" means: if necessary, water is added, if necessary,
depending on the constitution of the final product, the
mixture is adjusted to pHs between 2 and 10 and
extracted with ethyl acetate or dichloromethane, the
35 organic phase is separated off, dried over sodium
sulfate and evaporated, and the residue is purified by
chromatography on silica gel and/or by crystallization.
Mass spectrometry (MS) apparatuses Kratos Maldi III and
Finnigan LCQ. (M+H)⁺ values are determined.

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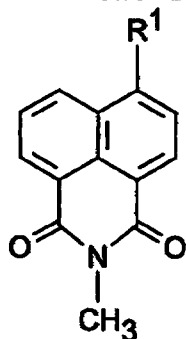
In the foregoing and in the following examples, all temperatures are set forth uncorrected in degrees Celsius; and, unless otherwise indicated, all parts and percentages are by weight.

The entire disclosure of all applications, patents and publications, cited above and below, is hereby incorporated by reference.

EXAMPLESExample 1

A suspension of 4 g of 6-chlorobenzo[de]iso-
chromene-1,3-dione in 100 ml of toluene is treated with
5 0.8 g of methylamine and heated under reflux. After
reaction is complete, the reaction mixture is allowed
to cool and is worked up as is customary. 6-Chloro-
2-methylbenzo[de]isoquinoline-1,3-dione is obtained.
This compound is then heated in morpholine until
10 conversion is complete. After cooling the reaction
mixture, it is worked up as is customary and 2-methyl-
6-morpholin-4-ylbenzo[de]isoquinoline-1,3-dione is
obtained.

Analogously, by reaction of 6-chloro-2-
15 methylbenzo[de]isoquinoline-1,3-dione with R^1-H , the
following compounds of the formula Ia are obtained:

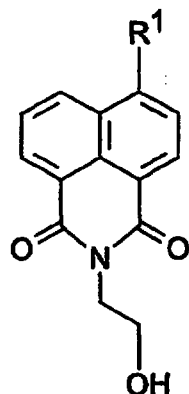


R^1 in R^1-H and Ia
$-N[(CH_2)_2-OH]_2$
$-NH-CH_2-CH=CH_2$

Example 2

A suspension of 4 g of 6-chlorobenzo[de]iso-
 chromene-1,3-dione in 100 ml of dichloromethane is
 5 treated with 3.2 g of 2-aminoethanol and heated under
 reflux. After reaction is complete, the reaction
 mixture is allowed to cool and is worked up as is
 customary. 6-Chloro-2-(2-hydroxyethyl)benzo[de]iso-
 quinoline-1,3-dione is obtained. This compound is then
 10 heated in morpholine until conversion is complete.
 After cooling the reaction mixture, it is worked up as
 is customary and 2-(2-hydroxyethyl)-6-morpholin-4-yl-
 benzo[de]isoquinoline-1,3-dione is obtained.

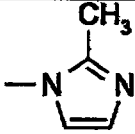
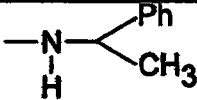
Analogously, by reaction of 6-chloro-
 15 2-(2-hydroxyethyl)benzo[de]isoquinoline-1,3-dione with
 R^1 -H, the following compounds of the formula Ib are
 obtained



Ib

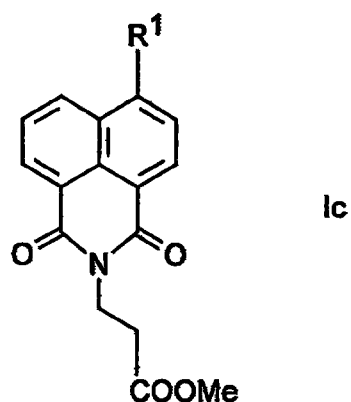
R^1 in R^1 -H and in Ib

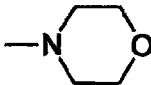
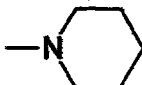
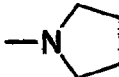
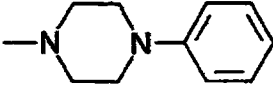
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R^1 in R^1 -H and in Ib



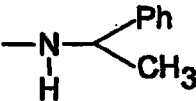
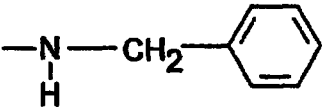
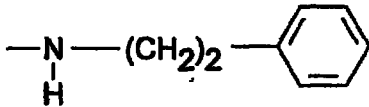
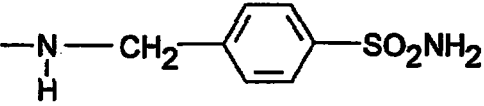
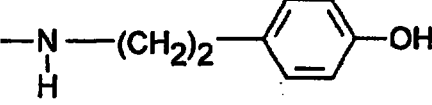
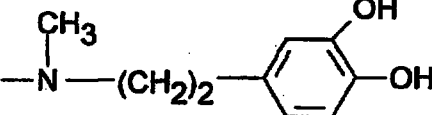
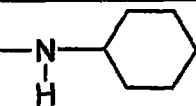
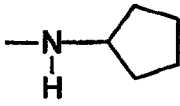
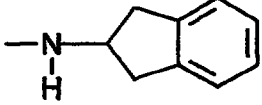
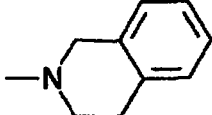
Example 3

Analogously to Example 2, 6-chloro-
 5 benzo[de]isochromene-1,3-dione is reacted with methyl
 3-aminopropionate and then with R^1 -H. The following
 compounds of the formula Ic are obtained:



R^1 in R^1 -H and in Ic	MS	
	calculated	found
	368	369
	366	367
	352	353
	443	444

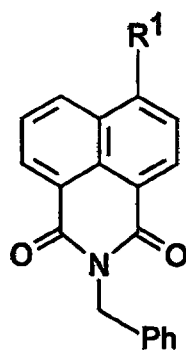
- 50 -

R ¹ in R ¹ -H and in Ic	MS	
	calculated	found
		
	388	389
	402	403
		
		
		
	380	381
	366	367
		
	414	415

Example 4

Analogously to Example 2, 6-chloro-benzo[de]isochromene-1,3-dione is reacted with
 5 benzylamine and then with R¹-H. The following compounds of the formula Ida are obtained:

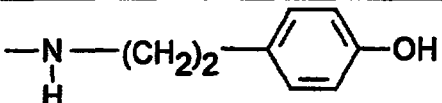
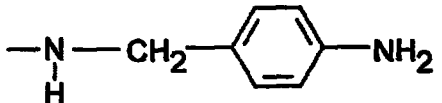
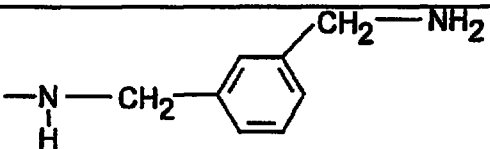
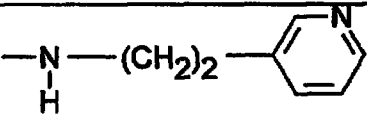
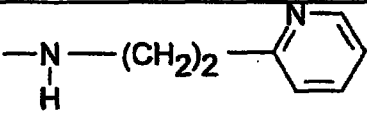
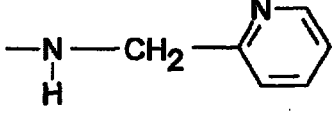
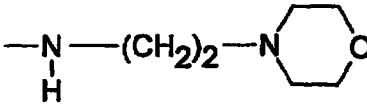
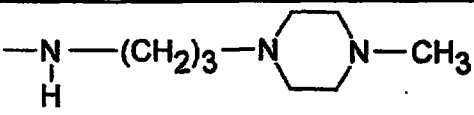
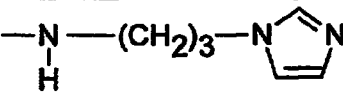
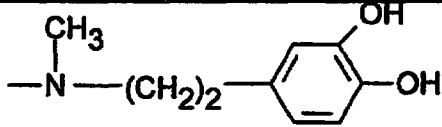
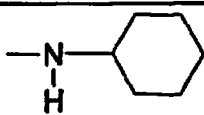
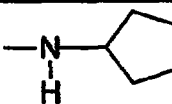
- 51 -

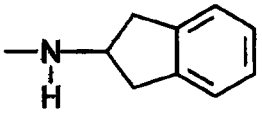
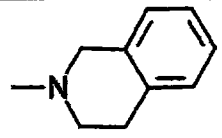


Ida

R ¹ in R ¹ -H and in Ida	MS	
	calculated	found
	372	373
	370	371
	356	357
	447	448
	406	407
-NH-(CH ₂) ₅ -OH	388	389
-NH-(CH ₂) ₂ -COOMe	388	389
-NH-(CH ₂) ₃ -N(CH ₃) ₂		
	392	393
	406	407

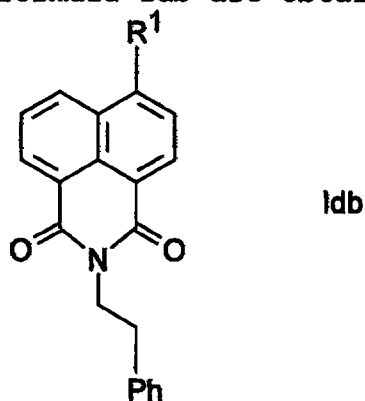
- 52 -

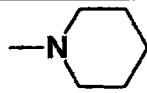
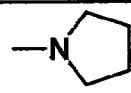
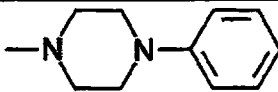
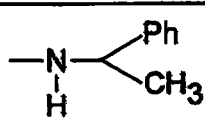
R ¹ in R ¹ -H and in Ida	MS	
	calculated	found
	422	423
		
	421	422
	407	408
	407	408
	393	394
	415	416
		
	410	411
		
	384	385
	370	371

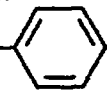
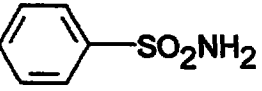
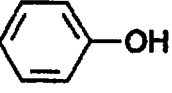
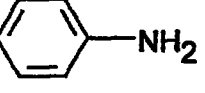
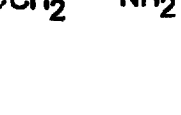
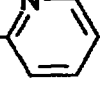
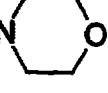
R ¹ in R ¹ -H and in Ida	MS	
	calculated	found
	418	419
	418	419

Example 5

Analogously to Example 2, 6-chlorobenzo-
 5 [de]isochromene-1,3-dione is reacted with
 phenylethylamine and then with R¹-H. The following
 compounds of the formula Idb are obtained:



R ¹ in R ¹ -H and in Idb	MS	
	calculated	found
	384	385
	370	371
	461	462
	420	421
-NH-(CH ₂) ₅ -OH	402	403

R ¹ in R ¹ -H and in Idb	MS	
	calculated	found
$\text{-NH- (CH}_2\text{)}_2\text{-COOMe}$	402	403
$\text{-NH- (CH}_2\text{)}_3\text{-N (CH}_3\text{)}_2$	401	402
$\text{-N-CH}_2\text{-}$ 	406	407
$\text{-N- (CH}_2\text{)}_2\text{-}$ 	420	421
$\text{-N-CH}_2\text{-}$ 		
$\text{-N- (CH}_2\text{)}_2\text{-}$ 		
$\text{-N-CH}_2\text{-}$ 	421	422
$\text{-N-CH}_2\text{-}$ 	435	436
$\text{-N- (CH}_2\text{)}_2\text{-}$ 	421	422
$\text{-N- (CH}_2\text{)}_2\text{-}$ 	421	422
$\text{-N-CH}_2\text{-}$ 	407	408
$\text{-N- (CH}_2\text{)}_2\text{-}$ 	429	430

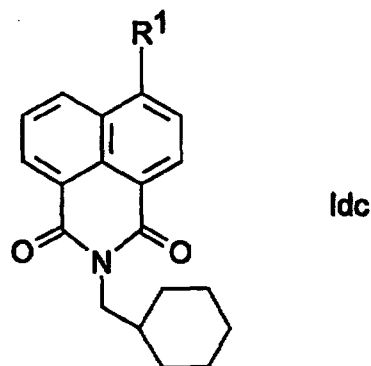
R ¹ in R ¹ -H and in Idb	MS	
	calculated	found
	424	425
	398	399
	384	385

Example 6

A suspension of 4 g of 6-chlorobenzo[de]iso-
 5 quinoline-1,3-dione and 7 g of K₂CO₃ in 100 ml of DMF is
 heated under reflux with 6 g of phenylethyl chloride.
 After conversion is complete, the mixture is allowed to
 cool, and is filtered and worked up as is customary.
 6-Chloro-2-(2-phenylethyl)benzo[de]isoquinoline-1,3-dione
 10 is then heated in morpholine until conversion is
 complete. After cooling of the reaction mixture, it is
 worked up as is customary and 2-(2-phenylethyl-
 6-morpholin-4-ylbenzo[de]isoquinoline-1,3-dione is
 obtained. MS: calculated: 386; found: 387.

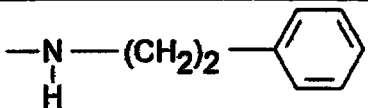
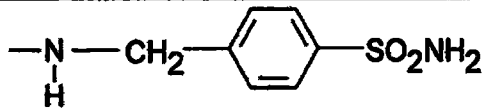
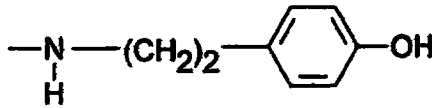
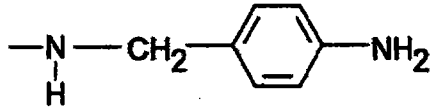
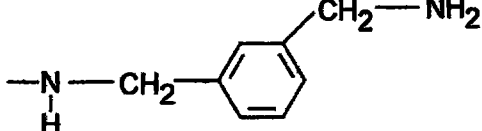
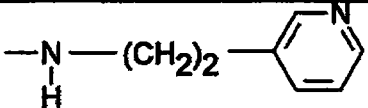
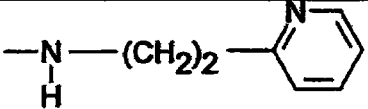
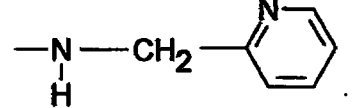
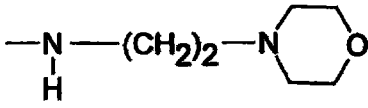
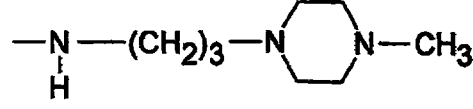
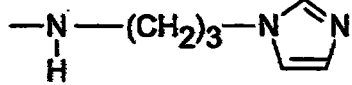
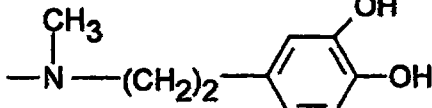
Example 7

Analogously to Example 2, 6-chlorobenzo-[de]isochromene-1,3-dione is reacted with C-cyclohexylmethylamine and then with R¹-H. The following 5 compounds of the formula Idc are obtained:

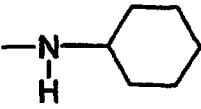
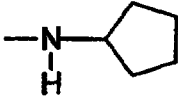
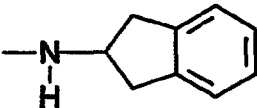
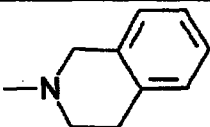


R ¹ in R ¹ -H and in Idc	MS	
	calculated	found
	378	379
	376	377
	362	363
	453	454
	330	331
-NH-(CH ₂) ₅ -OH	394	395
-NH-(CH ₂) ₂ -COOMe	394	395
-NH-(CH ₂) ₃ -N(CH ₃) ₂	393	394
	398	399

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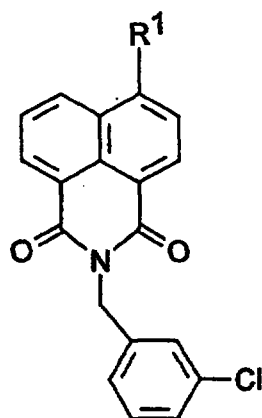
R ¹ in R ¹ -H and in Idc	MS	
	calculated	found
	412	413
		
	428	429
		
		
	413	414
	413	414
	399	400
	421	422
		
	416	417
		

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R ¹ in R ¹ -H and in Idc	MS	
	calculated	found
	390	391
	376	377
	424	425
	424	425

Example 8

- 5 Analogously to Example 2, 6-chlorobenzo-[de]isochromene-1,3-dione is reacted with (3-chlorophenyl)methylamine and then with R¹-H. The following compounds of the formula Idd are obtained:

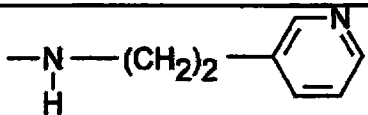
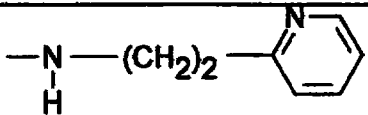
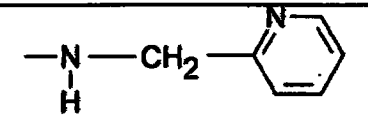
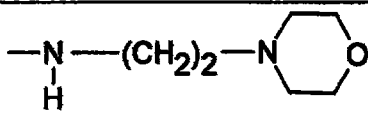
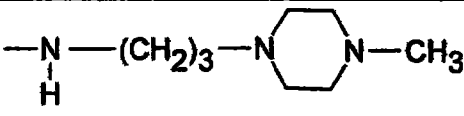
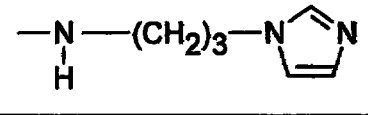
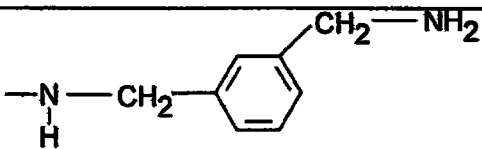


Idd

10

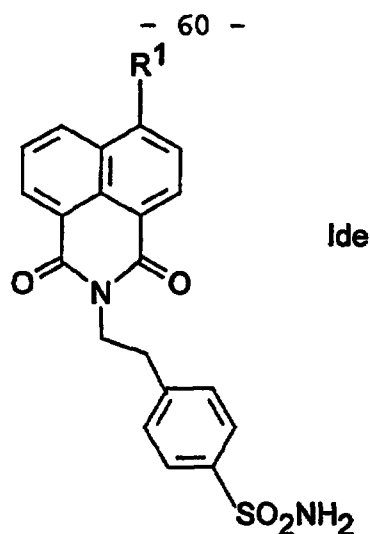
R ¹ in R ¹ -H and in Idd	MS	
	calculated	found
-NH-(CH ₂) ₃ -N(CH ₃) ₂	421	422

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R ¹ in R ¹ -H and in Idd	MS	
	calculated	found
	441	442
	441	442
	427	428
	449	450
	476	477
	444	445
$\text{-NH-(CH}_2\text{)}_5\text{-OH}$	422	423
		

Example 9

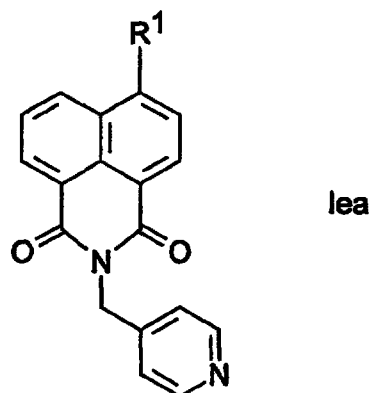
5 Analogously to Example 2, 6-chlorobenzo-[de]isochromene-1,3-dione is reacted with 4-(2-aminoethyl)benzenesulfonamide and then with R¹-H. The following compounds of the formula Ide are obtained:

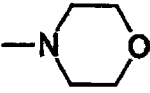
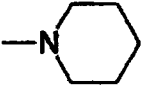
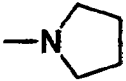
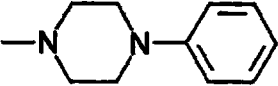
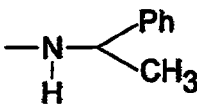
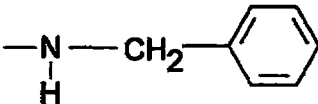
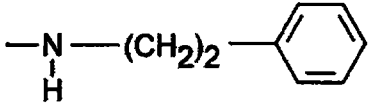
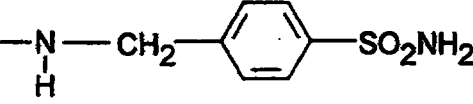
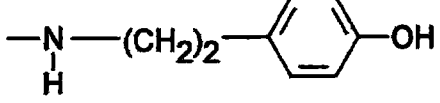
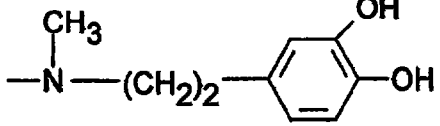
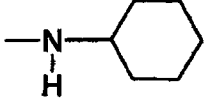


R¹ in R¹-H and in Ide	MS	
	calculated	found
-NH-(CH₂)₇-NH₂	508	509
-NH-(CH₂)₅-NH₂	480	481
-NH-(CH₂)₃-NH₂	452	453
	514	515

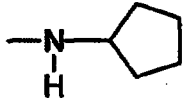
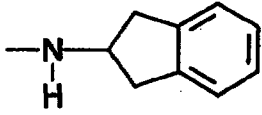
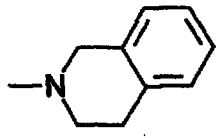
Example 10

- 5 Analogously to Example 2, 6-chlorobenzo-[de]isochromene-1,3-dione is reacted with C-pyridin-4-ylmethylamine and then with R¹-H. The following compounds of the formula Iea are obtained:



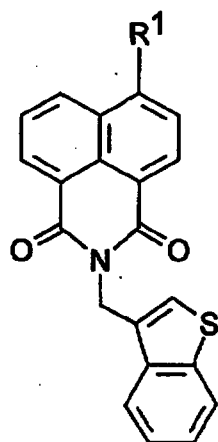
R ¹ in R ¹ -H and in Iea	MS	
	calculated	found
	373	374
	371	372
	357	358
	448	449
	407	408
$\text{-NH-(CH}_2\text{)}_2\text{-COOMe}$		
	393	394
	407	408
	472	473
		
		
	385	386

- 62 -

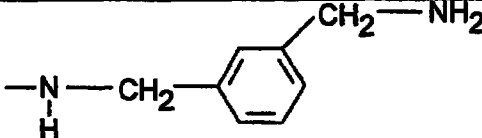
R ¹ in R ¹ -H and in Iea	MS	
	calculated	found
	371	372
	419	420
		

Example 11

Analogously to Example 2, 6-chlorobenzo-
 5 [de]isochromene-1,3-dione is reacted with C-
 benzo[b]thiophen-3-ylmethylamine and then with R¹-H. The
 following compounds of the formula Ieb are obtained:



Ieb

R ¹ in R ¹ -H and in Ieb	MS	
	calculated	found
-NH-(CH ₂) ₅ -NH ₂	443	444
-NH-(CH ₂) ₇ -NH ₂	471	472
	477	478

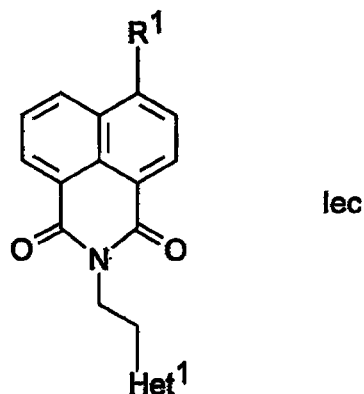
Example 12

10 ml of TFA are added at room temperature to a
 5 solution of 2 g of tert-butyl [3-(2-benzo[b]thiophen-
 3-ylmethyl-1,3-dioxo-2,3-dihydro-1H-benzo[de]iso-
 quinolin-6-ylamino)propyl]carbamate in 40 ml of
 dichloromethane [obtainable by reaction of
 6-chlorobenzo[de]isochromene-1,3-dione with C-benzo[b]-
 10 thiophen-3-ylmethylamine and $\text{H}_2\text{N}-(\text{CH}_2)_3-\text{NH}-\text{BOC}$] and the
 reaction mixture is stirred until removal is complete.
 After customary work-up 6-(3-aminopropylamino)-
 2-benzo[b]thiophen-3-ylmethylbenzo[de]isoquinoline-
 1,3-dione is obtained. MS: calculated: 415; found: 416.

15

Example 13

Analogously to Example 2, 6-chlorobenzo[de]iso-
 chromene-1,3-dione is reacted with $\text{H}_2\text{N}-(\text{CH}_2)_2-\text{Het}^1$ and
 then with R^1-H . The following compounds of the formula
 20 Iec are obtained:



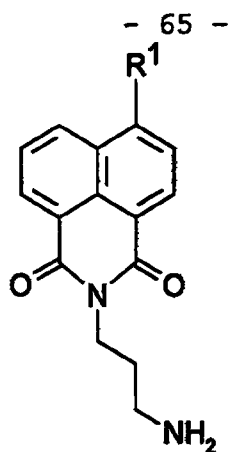
Het ¹	R ¹ in R ¹ -H and in Iec
	$-\text{NH}-(\text{CH}_2)_3-\text{NH}_2$
	$-\text{NH}-(\text{CH}_2)_5-\text{NH}_2$
	$-\text{NH}-(\text{CH}_2)_7-\text{NH}_2$

- 64 -

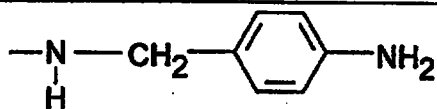
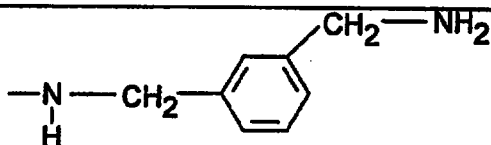
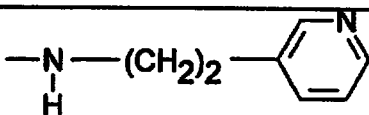
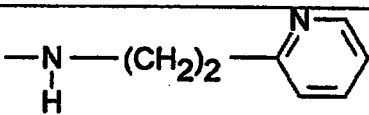
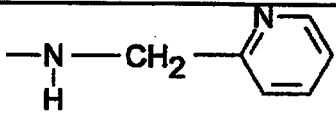
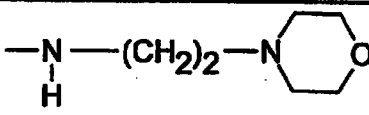
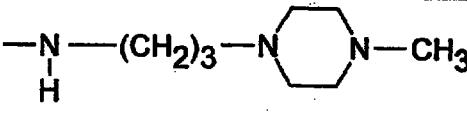
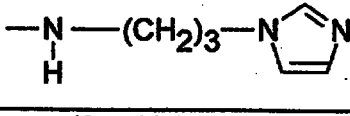
Het ¹	R ¹ in R ¹ -H and in Iec
	$\text{-NH-(CH}_2\text{)}_3\text{-NH}_2$ $\text{-NH-(CH}_2\text{)}_5\text{-NH}_2$ $\text{-NH-(CH}_2\text{)}_7\text{-NH}_2$
	$\text{-NH-(CH}_2\text{)}_3\text{-NH}_2$ $\text{-NH-(CH}_2\text{)}_5\text{-NH}_2$ $\text{-NH-(CH}_2\text{)}_7\text{-NH}_2$
	$\text{-NH-(CH}_2\text{)}_3\text{-NH}_2$ $\text{-NH-(CH}_2\text{)}_5\text{-NH}_2$ $\text{-NH-(CH}_2\text{)}_7\text{-NH}_2$
	$\text{-NH-(CH}_2\text{)}_3\text{-NH}_2$ $\text{-NH-(CH}_2\text{)}_5\text{-NH}_2$ $\text{-NH-(CH}_2\text{)}_7\text{-NH}_2$

Example 14

Analogously to Example 2, 6-chlorobenzo[de]isochromene-1,3-dione is reacted with 1,3-propanediamine and then with R¹-H. The following compounds of the formula If are obtained:

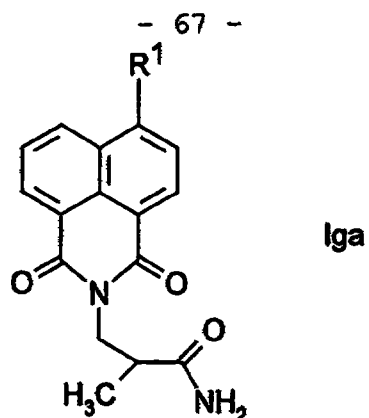


R^1 in R^1-H and in If
$-NH-(CH_2)_2-COOMe$
$-NH-(CH_2)_5-OH$
$-NH-(CH_2)_3-N(CH_3)_2$

R^1 in R^1-H and in If








$-NH-(CH_2)_5-NH_2$
$-NH-(CH_2)_7-NH_2$

Example 15

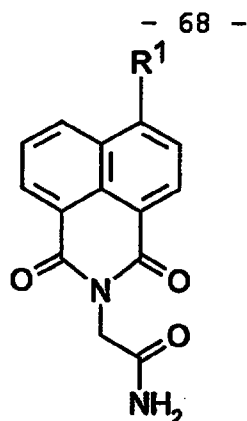
5 Analogously to Example 2, 6-chlorobenzo[de]iso-chromene-1,3-dione is reacted with 3-amino-2-methylpropionamide and then with R^1-H . The following compounds of the formula Iga are obtained:



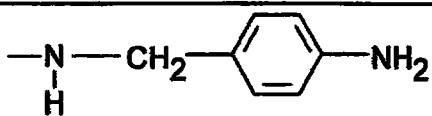
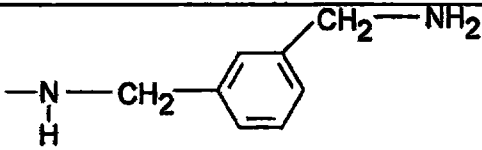
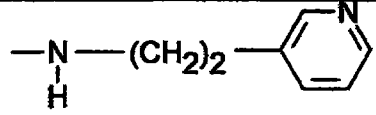
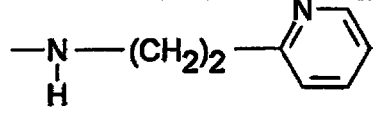
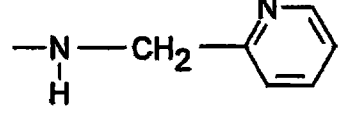
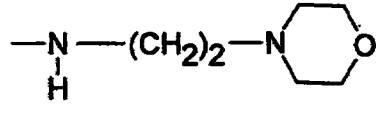
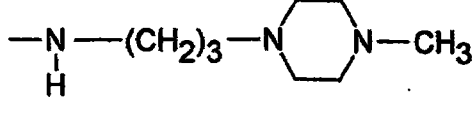
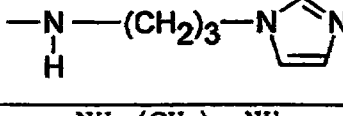
R¹ in R¹-H and in Iga
-NH-(CH₂)₃-N(CH₃)₂
-NH-(CH₂)₄-NH₂
-NH-(CH₂)₇-NH₂
-NH-(CH₂)₈-NH₂

Example 16

- 5 Analogously to Example 2, 6-chlorobenzo[de]isochromene-1,3-dione is reacted with 2-aminoacetamide and then with R¹-H. The following compounds of the formula Igb are obtained:

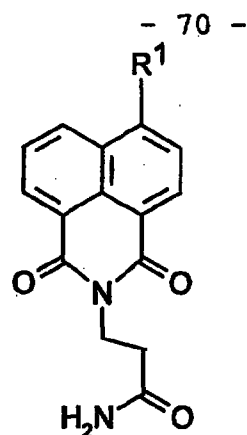


R ¹ in R ¹ -H and in Igb	MS	
	calculated	found
	337	338
	323	324
-NH-(CH ₂) ₂ -COOMe		
-NH-(CH ₂) ₅ -OH		

R ¹ in R ¹ -H and in Igb	MS	
	calculated	found
$-\text{NH}-(\text{CH}_2)_3-\text{N}(\text{CH}_3)_2$	354	355
		
		
		
	374	375
		
		
		
	379	380
$-\text{NH}-(\text{CH}_2)_5-\text{NH}_2$		
$-\text{NH}-(\text{CH}_2)_7-\text{NH}_2$		

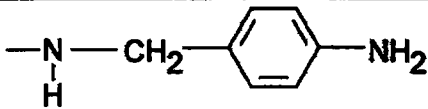
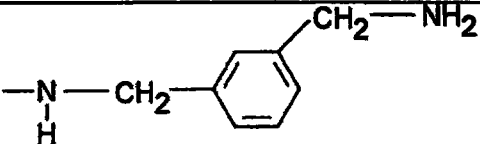
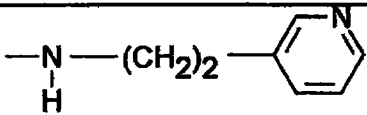
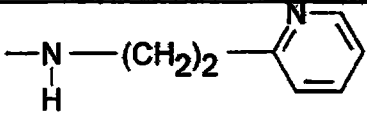
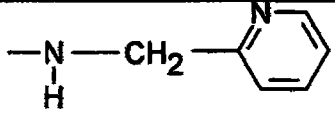
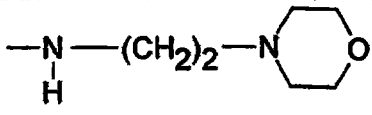
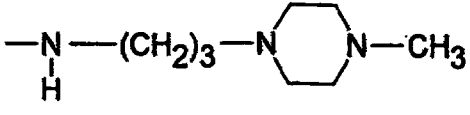
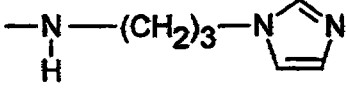
Example 17

5 Analogously to Example 2, 6-chlorobenzo[de]iso-chromene-1,3-dione is reacted with 3-aminopropionamide and then with R¹-H. The following compounds of the formula Igc are obtained:



Igc

R ¹ in R ¹ -H and in Igc	MS	
	calculated	found
	351	352
	337	338
-NH-(CH ₂) ₂ -COOMe		

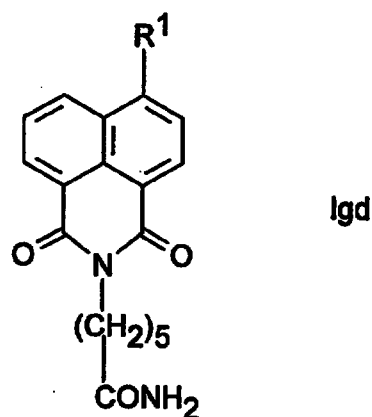
R ¹ in R ¹ -H and in Ig _c	MS	
	calculated	found
-NH-(CH ₂) ₅ -OH	369	370
-NH-(CH ₂) ₃ -N(CH ₃) ₂		
		
		
		
		
		
		
		
		
-NH-(CH ₂) ₅ -NH ₂		
-NH-(CH ₂) ₇ -NH ₂	396	397

Example 18

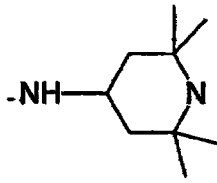
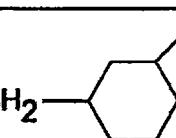
- 5 Analogously to Example 2, 6-chlorobenzo[de]isochromene-1,3-dione is reacted with 6-amino-hexanoamide

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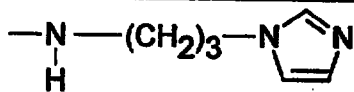
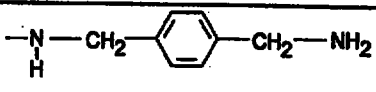
and then with R^1-H . The following compounds of the formula Igd are obtained:



R^1 in R^1-H and in Igd	MS calc. fnd.	R^1 in R^1-H und in Igd	MS calc. fnd.
		$-NH-(CH_2)_3-NH(CH_3)$	396 397
		$-N(CH_3)-(CH_2)_3-NH(CH_3)$	410 411
	379 380	$-N(CH_3)-(CH_2)_2-N(C_2H_5)_2$	438 439
	470 471		410 411
$-NH-(CH_2)_2-COOMe$			484 485
			471 472

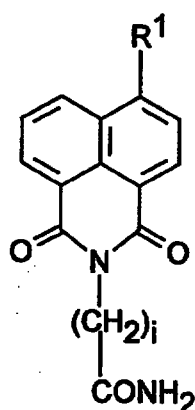
R^1 in R^1-H and in Igd	MS calc. fnd.	R^1 in R^1-H and in Igd	MS calc. fnd.
$-N(H)-CH_2-C_6H_4-SO_2NH_2$		$-NH-(CH_2)_3-N(CH_2)_3-NH_2$	508 509
$-N(H)-(CH_2)_2-C_6H_5$		$-NH-$ 	
$-NH-(CH_2)_5-OH$		$-NH-(CH_2)_2-NH-(CH_2)_2-OH$	412 413
$-NH-(CH_2)_3-N(CH_3)_2$		$-NH-(CH_2)_2-NH(C_3H_7)$	410 411
$-N(H)-CH_2-C_6H_4-NH_2$		$-NH-(CH_2)_3-O-(CH_2)_4-O-(CH_2)_3-NH_2$	512 513
$-N(H)-CH_2-C_6H_4-CH_2-NH_2$		$-NH-(CH_2)_3-N(H)-C_6H_{11}$	464 465
$-N(H)-(CH_2)_2-C_5H_4N$		$-NH-CH_2-$  $-CH_2NH_2$	450 451
$-N(H)-(CH_2)_2-C_5H_4N$	430 431	$-NH-(CH_2)_3-N(CH_3)-(CH_2)_3-NH_2$	453 454
$-N(H)-CH_2-C_5H_4N$	416 417	$-NH-(CH_2)_2-NH(C_2H_5)$	396 397
$-N(H)-(CH_2)_2-N(CH_2)_4O$		$-NH-(CH_2)_5-NH_2$	
$-N(H)-(CH_2)_3-N(CH_2)_4-N-CH_3$	462 463	$-NH-(CH_2)_7-NH_2$	

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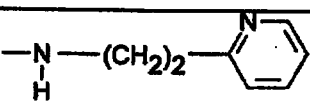
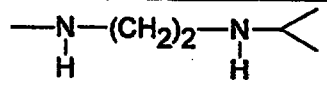
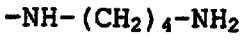
R ¹ in R ¹ -H and in Igd	MS calc. fnd.	R ¹ in R ¹ -H und in Igd	MS calc. fnd.
			

Example 19

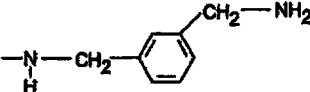
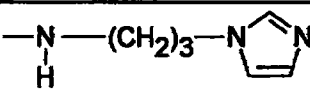
Analogously to Example 2, 6-chlorobenzo[de]iso-chromene-1,3-dione is reacted with H₂N-(CH₂)_i-CONH₂ and then with R¹-H. The following compounds of the formula Ige are obtained:



Ige

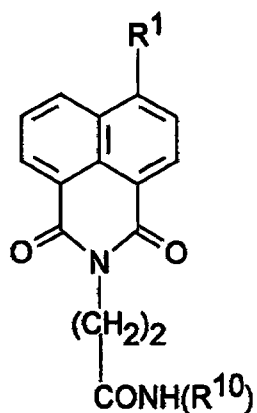
R ¹ in R ¹ -H and in Ige	i	MS calculated	found
	7	458	459
	10	500	501
	11		
	7	452	453
	10	494	495
	11	508	509
	7		
	10	466	467
	11		

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R ¹ in R ¹ -H and in Ige	i	MS	
		calculated	found
-NH-(CH ₂) ₃ -N(CH ₃) ₂	7	438	439
	10		
	11	494	495
-NH-(CH ₂) ₇ -NH ₂	7		
	10		
	11		
-NH-(CH ₂) ₈ -NH ₂	7	480	481
	10	522	523
	11	536	537
	7	472	473
	10		
	11	528	529
	7	463	464
	10	505	506
	11	519	520

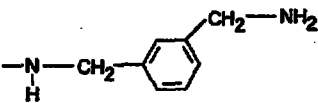
Example 20

Analogously to Example 2, 6-chlorobenzo[de]iso-chromene-1,3-dione is reacted with H₂N-(CH₂)₂-CONH(R¹⁰) and then with R¹-H. The following compounds of the formula Igf are obtained:



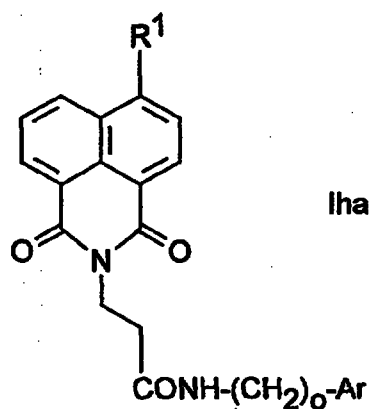
Igf.

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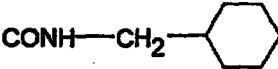
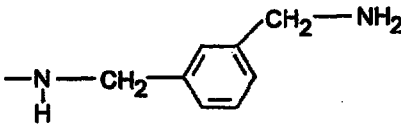
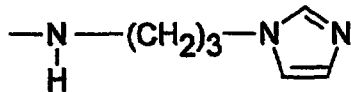
R ¹ in R ¹ -H and in Igf	R ¹⁰	MS	
		calculated	found
-NH-(CH ₂) ₇ -NH ₂	C ₃ H ₇	438	439
	C ₅ H ₁₁	466	467
	C ₃ H ₇	444	445
	C ₅ H ₁₁	472	473

Example 21

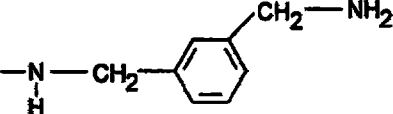
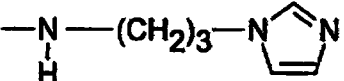
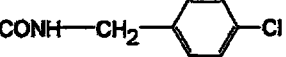
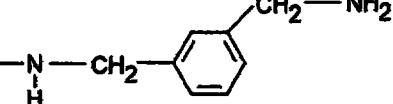
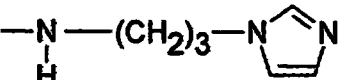
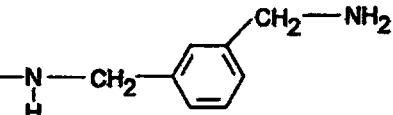
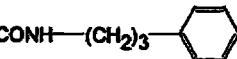
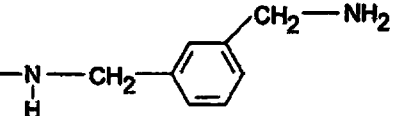
- 5 Analogously to Example 2, 6-chlorobenzo[de]isochromene-1,3-dione is reacted with H₂N-(CH₂)₂-CONH-(CH₂)_o-Ar and then with R¹-H. The following compounds of the formula Iha are obtained:



10

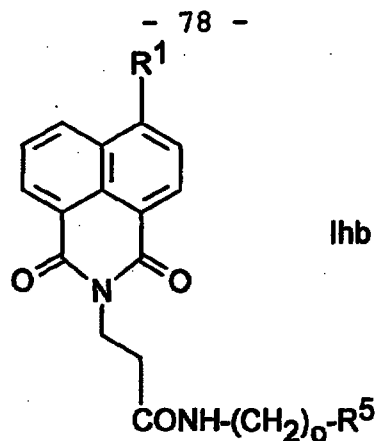
CONH-(CH ₂) _o -Ar	R ¹ in R ¹ -H and in Iha	MS	
		calc.	find.
	-NH-(CH ₂) ₇ -NH ₂		
		499	500
		489	490

- 77 -

CONH-(CH ₂) _o -Ar	R ¹ in R ¹ -H and in Iha	MS	
		calc.	find.
	-NH-(CH ₂) ₇ -NH ₂	515	516
		521	522
			
	-NH-(CH ₂) ₇ -NH ₂	520	521
		526	527
			
	-NH-(CH ₂) ₇ -NH ₂	548	549
		517	518
	-NH-(CH ₂) ₇ -NH ₂	514	515
		511	512

Example 22

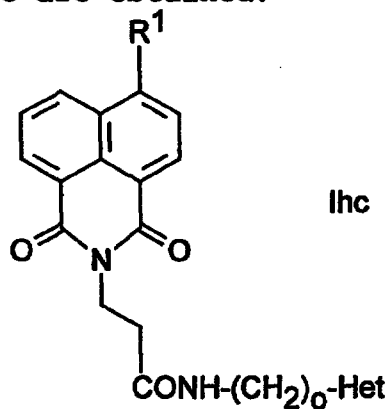
5 Analogously to Example 2, 6-chlorobenzo[de]isochromene-1,3-dione is reacted with H₂N-(CH₂)₂-CONH-(CH₂)_o-R⁵ and then with R¹-H. The following compounds of the formula Ihb are obtained:



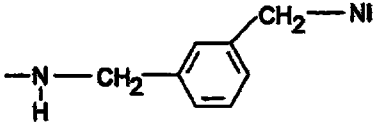
CONH-(CH ₂) ₆ -R ⁵	R ¹ in R ¹ -H and in Ihb	MS	
		calc.	find.
	-NH-(CH ₂) ₇ -NH ₂	467	468
CONH-(CH ₂) ₄ -NH ₂		473	474
	-NH-(CH ₂) ₇ -NH ₂	539	540
CONH-(CH ₂) ₂ -NH ₂		445	446

Example 23

- 5 Analogously to Example 2, 6-chlorobenzo[de]isochromene-1,3-dione is reacted with H₂N-(CH₂)₂-CONH-(CH₂)₆-Het and then with R¹-H. The following compounds of the formula Ihc are obtained:

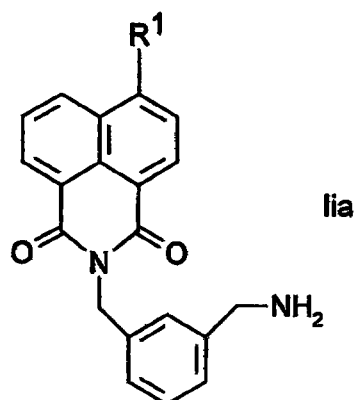


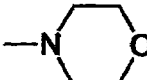
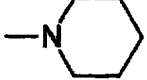
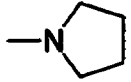
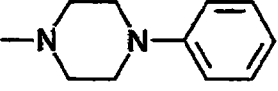
- 79 -

CONH-(CH ₂) ₆ -Het	R ¹ in R ¹ -H and in Ihc	MS	
		calc.	find.
	-NH-(CH ₂) ₇ -NH ₂	487	488
CONH-CH ₂ - 		493	494

Example 24

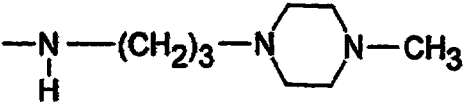
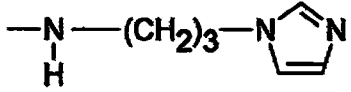
Analogously to Example 2, 6-chlorobenzo[de]isochromene-1,3-dione is reacted with 3-aminomethylbenzylamine and then with R¹-H. The following compounds of the formula Iia are obtained:



R ¹ in R ¹ -H and in Iia





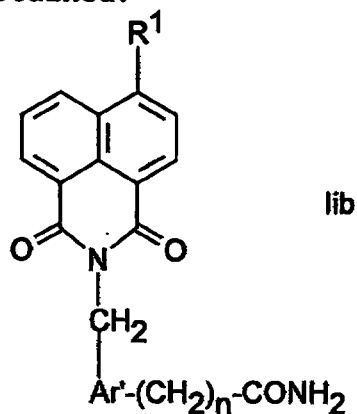
R^1 in R^1-H and in Iia
$-NH-(CH_2)_2-COOMe$
$-NH-(CH_2)_5-OH$
$-NH-(CH_2)_3-N(CH_3)_2$

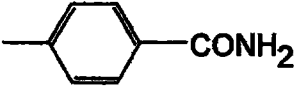
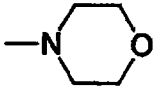
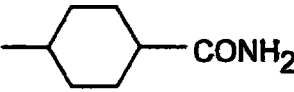
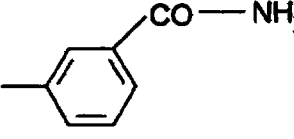
- 81 -

R^1 in R^1 -H and in Iia
$\text{—N—(CH}_2\text{)}_3\text{—N—CH}_3$ 
$\text{—N—(CH}_2\text{)}_3\text{—N—}$ 
$\text{—NH—(CH}_2\text{)}_5\text{—NH}_2$
$\text{—NH—(CH}_2\text{)}_7\text{—NH}_2$

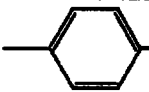
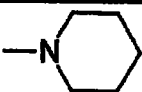
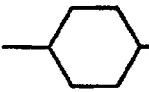
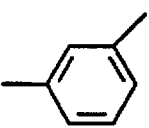
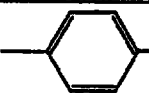
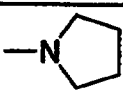
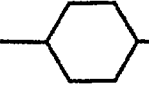
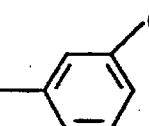
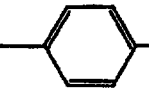
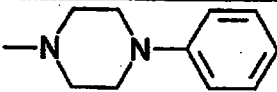
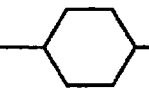
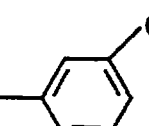
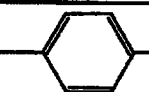
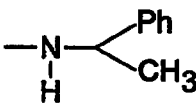
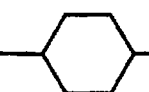
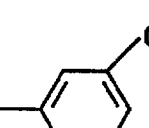
Example 25

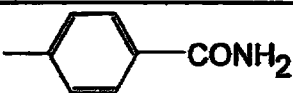
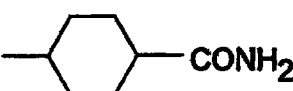
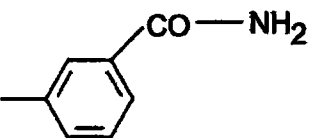
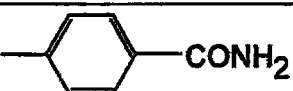
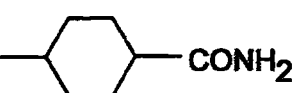
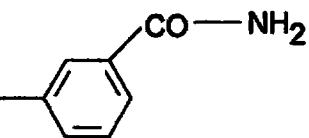
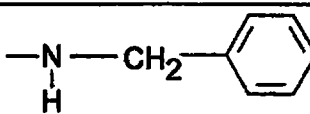
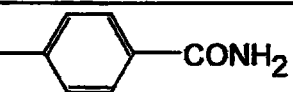
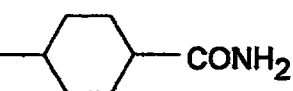
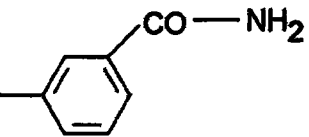
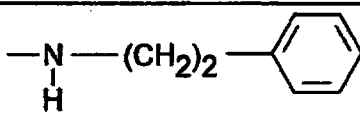
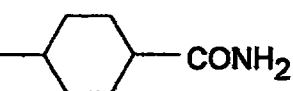
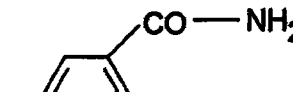
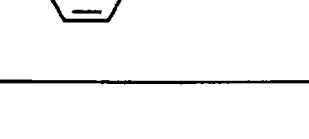
- 5 Analogously to Example 2, 6-chlorobenzo[de]isochromene-1,3-dione is reacted with $\text{H}_2\text{N—CH}_2\text{—Ar'—(CH}_2\text{)}_n\text{—CONH}_2$ and then with $R^1\text{—H}$. The following compounds of the formula Iib are obtained:



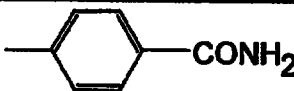
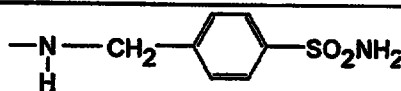
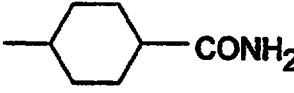
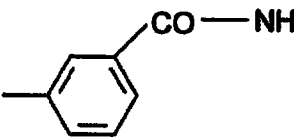
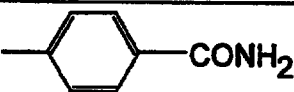
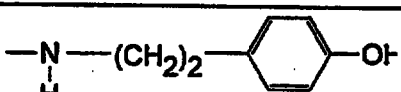
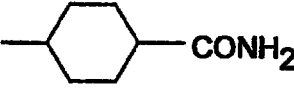
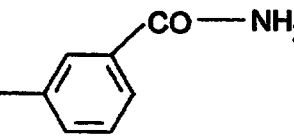
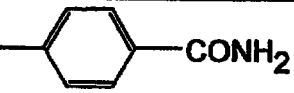
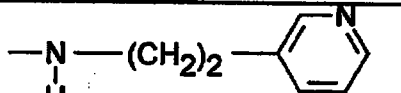
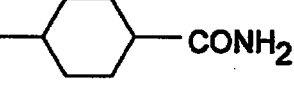
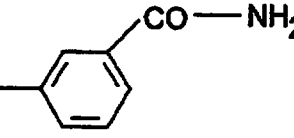
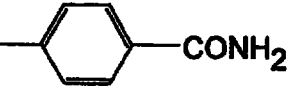
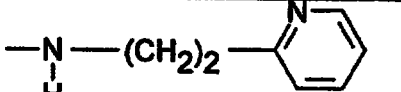
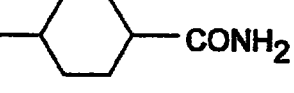
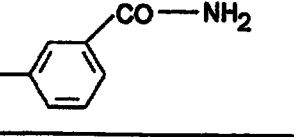
$\text{Ar'—(CH}_2\text{)}_n\text{—CONH}_2$	R^1 in $R^1\text{—H}$ and in Iib	MS	
		calc.	find.
		415	416
			
			

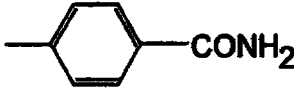
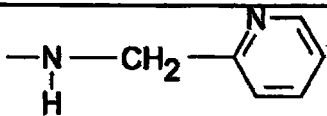
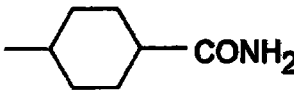
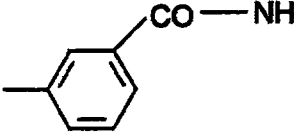
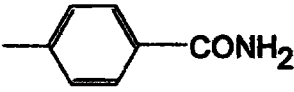
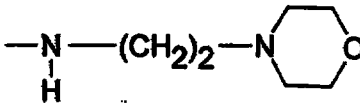
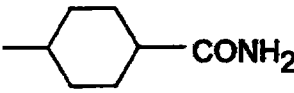
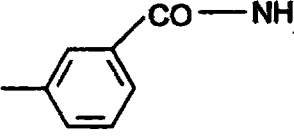
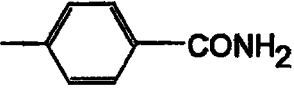
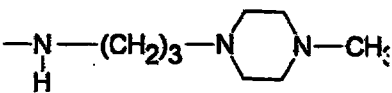
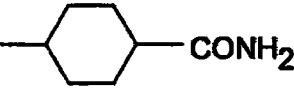
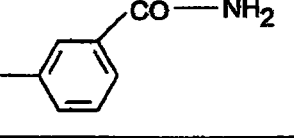
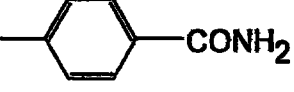
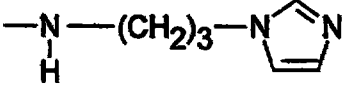
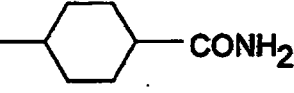
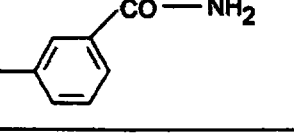
- 82 -

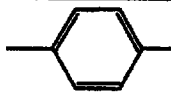
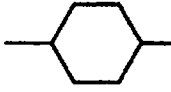
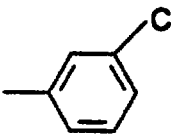
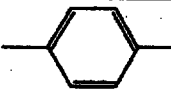
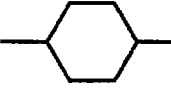
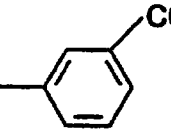
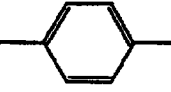
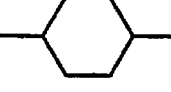
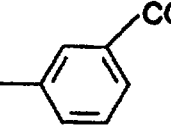
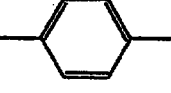
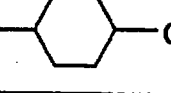
Ar'-(CH ₂) _n -CONH ₂	R ¹ in R ¹ -H and in Iib	MS	
		calc.	fnd.
			
		419	420
		413	414
		399	400
		405	406
		399	400
			
			
		490	491
		449	450
			
			

Ar'-(CH ₂) _n -CONH ₂	R ¹ in R ¹ -H and in Iib	MS	
		calc.	find.
  	-NH-(CH ₂) ₂ -COOMe	431	432
  		441	442
  		449	450
  		455	456

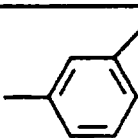
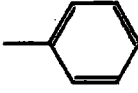
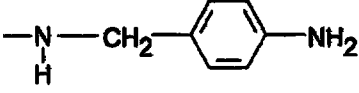
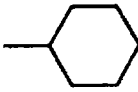
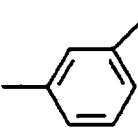
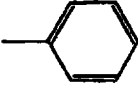
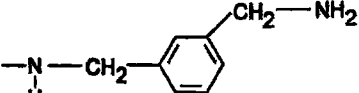
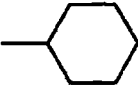
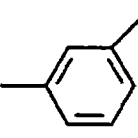
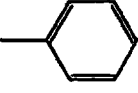
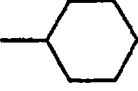
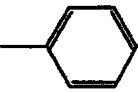
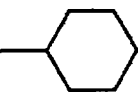
- 84 -

Ar'-(CH ₂) _n -CONH ₂	R ¹ in R ¹ -H and in Iib	MS	
		calc.	find.
			
		520	521
			
		465	466
		471	472
			
		450	451
		457	458
		450	451
		450 451	
		456	
		457	

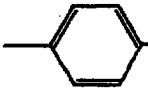
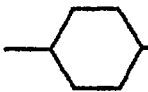
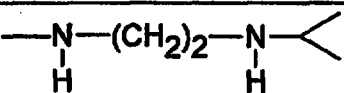
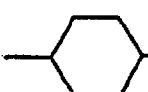
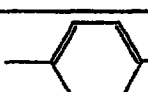
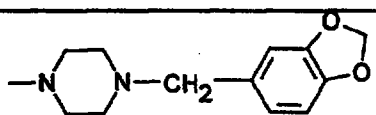
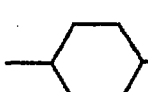
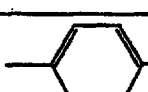
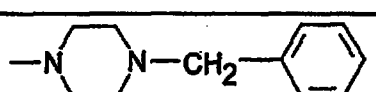
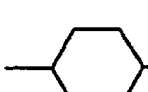
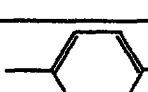
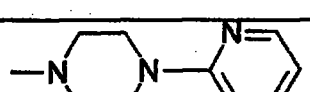
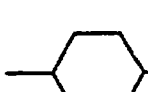
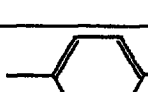
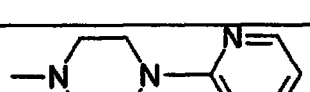
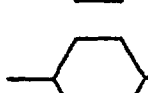
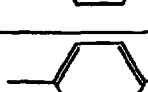
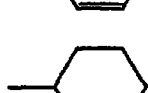
Ar'-(CH ₂) _n -CONH ₂	R ^I in R ^I -H and in Iib	MS	
		calc.	find.
		436	437
		442	443
		436 437	
		458	459
		464	465
		458	459
		485	486
		491	492
		485	486
		455	456
		461	462
			

Ar'-(CH ₂) _n -CONH ₂	R ¹ in R ¹ -H and in Iib	MS	
		calc.	find.
	-NH-(CH ₂) ₅ -NH ₂		
		436	437
		430	431
	-NH-(CH ₂) ₇ -NH ₂	458	459
		464	465
			
	-NH-(CH ₂) ₃ -N(CH ₃) ₂	430	431
		436	437
		430	431
	-NH-(CH ₂) ₅ -OH	431	432
		437	438

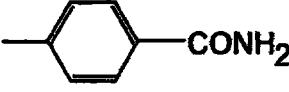
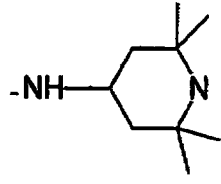
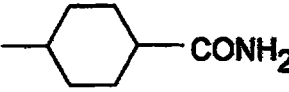
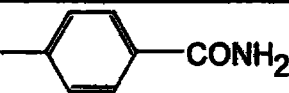
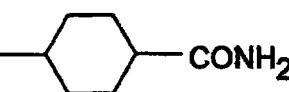
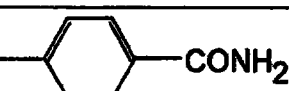
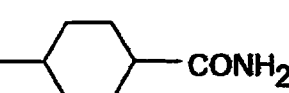
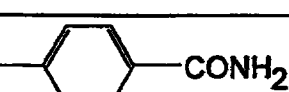
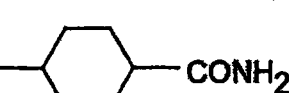
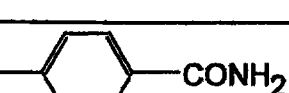
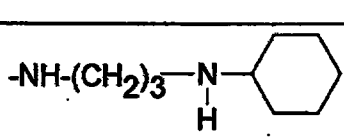
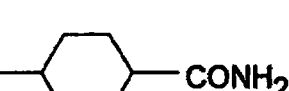
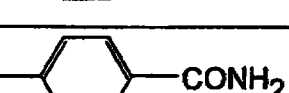
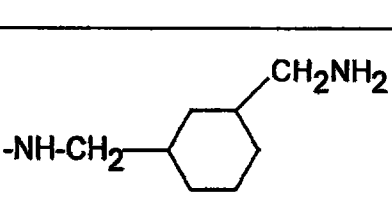
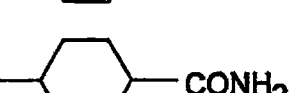
- 87 -

Ar'-(CH ₂) _n -CONH ₂ R ¹ in R ¹ -H and in Iib		MS	
		calc.	find.
	-NH-(CH ₂) ₅ -OH		
			
			
			
		464	465
			
			
	-NH-(CH ₂) ₃ -NH(CH ₃)	416	417
		422	423
	-N(CH ₃)-(CH ₂) ₃ -NH(CH ₃)	430	431
		436	437

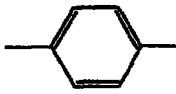
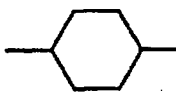
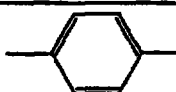
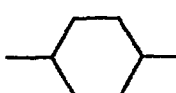
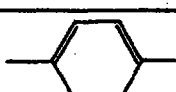
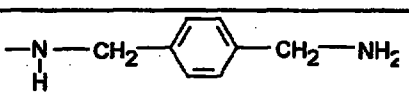
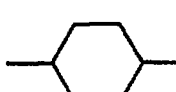
- 88 -

Ar ¹ -(CH ₂) _n -CONH ₂	R ¹ in R ¹ -H and in Iib	MS	
		calc.	find.
 -CONH ₂	-N(CH ₃)-(CH ₂) ₂ -N(C ₂ H ₅) ₂	458	459
 -CONH ₂		464	465
 -CONH ₂		430	431
 -CONH ₂		436	437
 -CONH ₂		548	549
 -CONH ₂		554	555
 -CONH ₂		504	505
 -CONH ₂			
 -CONH ₂		491	492
 -CONH ₂			
 -CONH ₂		492	493
 -CONH ₂			
 -CONH ₂	-NH-(CH ₂) ₃ -N  -(CH ₂) ₃ -NH ₂	528	529
 -CONH ₂			

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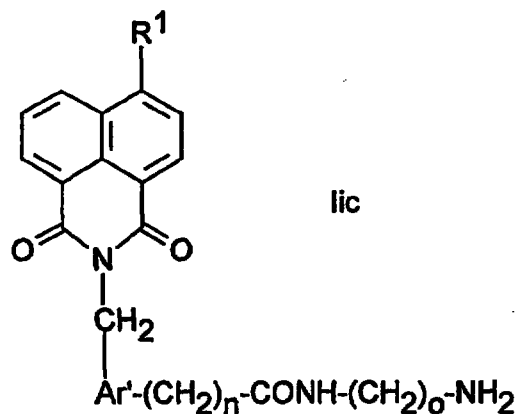
Ar'-(CH ₂) _n -CONH ₂	R ¹ in R ¹ -H and in Iib	MS	
		calc.	find.
		484	485
		490	491
	-NH-(CH ₂) ₂ -NH-(CH ₂) ₂ -OH	432	433
		438	439
	-NH-(CH ₂) ₂ -NH(C ₃ H ₇)	430	431
		436	437
	-NH-(CH ₂) ₃ -O-(CH ₂) ₄ -O-(CH ₂) ₃ -NH ₂	538	539
			
		484	485
		490	491
		476	477
			

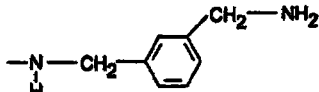
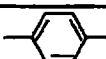
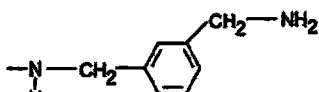
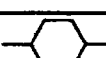
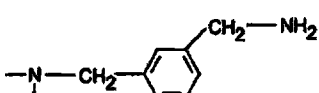
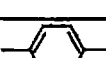
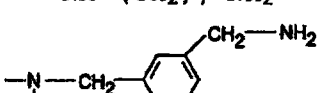
- 90 -

Ar'-(CH ₂) _n -CONH ₂	R ¹ in R ¹ -H and in Iib	MS	
		calc.	find.
 -CONH ₂	-NH-(CH ₂) ₃ -N(CH ₃)-(CH ₂) ₃ -NH ₂	473	474
 -CONH ₂			
 -CONH ₂	-NH-(CH ₂) ₂ -NH(C ₂ H ₅)	416	417
 -CONH ₂			
 -CONH ₂		422	423
 -CONH ₂			

Example 26

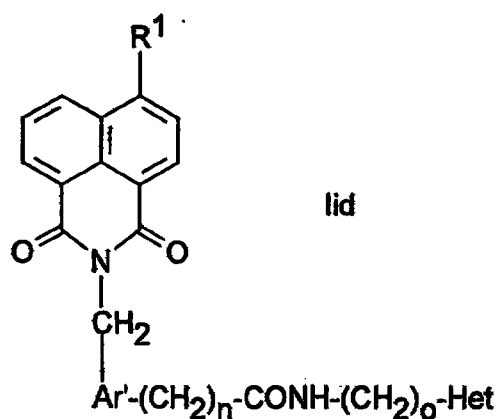
- 5 Analogously to Example 2, 6-nitrobenzo[de]iso-chromene-1,3-dione is reacted with H₂N-CH₂-Ar'-(CH₂)_n-CONH-(CH₂)₆-NH₂ and then with R¹-H. The following compounds of the formula Iic are obtained:



91			
Ar'-(CH ₂) _n -CONH-	R ¹ in R ¹ -H and Iic	MS	
(CH ₂) _o -NH ₂		calc.	find.
 -CONH-(CH ₂) ₄ -NH ₂	-NH-(CH ₂) ₇ -NH ₂ 	541	542
 -CONH-(CH ₂) ₄ -NH ₂	-NH-(CH ₂) ₇ -NH ₂ 	529	530
 -CONH-(CH ₂) ₂ -NH ₂	-NH-(CH ₂) ₇ -NH ₂ 	507	508
 -CONH-(CH ₂) ₂ -NH ₂	-NH-(CH ₂) ₇ -NH ₂ 	501	502

Example 27

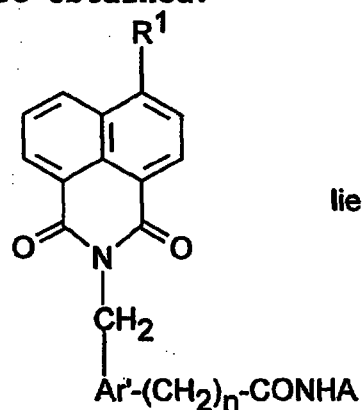
- 5 Analogously to Example 2, 6-chlorobenzo[de]iso-chromene-1,3-dione is reacted with H₂N-CH₂-Ar'-(CH₂)_n-CONH-(CH₂)_o-Het and then with R¹-H. The following compounds of the formula Iid are obtained:



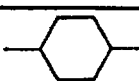
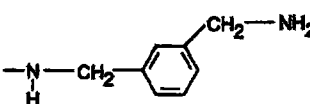
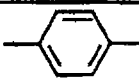
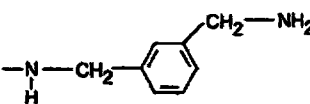
Ar'-(CH ₂) _n -CONH- (CH ₂) _o -Het	R ¹ in R ¹ -H and Iid	MS	
		calc.	find.
	-NH-(CH ₂) ₃ -N(CH ₃) ₂		
	-NH-(CH ₂) ₇ -NH ₂	555	556
		561	562
	-NH-(CH ₂) ₃ -N(CH ₃) ₂	521	522
	-NH-(CH ₂) ₇ -NH ₂		
		555	556

Example 28

Analogously to Example 2, 6-chlorobenzo[de]isochromene-1,3-dione is reacted with H₂N-CH₂-Ar'-(CH₂)_n-CONHA and then with R¹-H. The following compounds of the formula Iie are obtained:

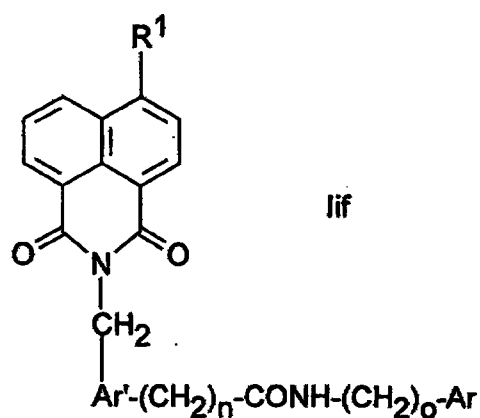


Ar'-(CH ₂) _n -CONHA	R ¹ in R ¹ -H and Iie	MS	
		calc.	find.
	-NH-(CH ₂) ₇ -NH ₂		
		512	513
	-NH-(CH ₂) ₃ -N(CH ₃) ₂	472	473
	-NH-(CH ₂) ₇ -NH ₂		
		506	507

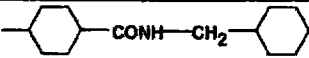
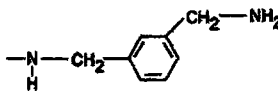
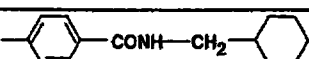
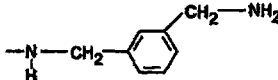
93		MS	
Ar'-(CH ₂) _n -CONHA	R ¹ in R ¹ -H and Iie	calc.	find.
 -CONH(C ₅ H ₁₁)	-NH-(CH ₂) ₇ -NH ₂ 	540	541
 -CONH(C ₅ H ₁₁)	-NH-(CH ₂) ₃ -N(CH ₃) ₂ - NH-(CH ₂) ₇ -NH ₂ 	500	501

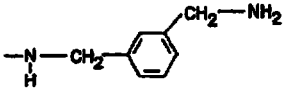
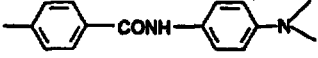
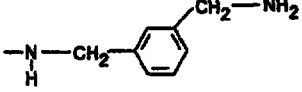
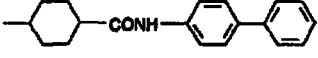
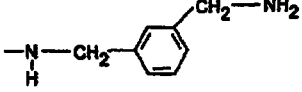
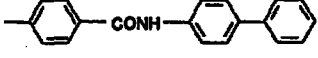
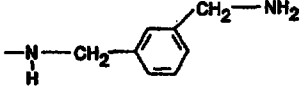
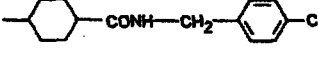
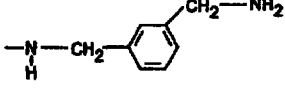
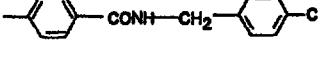
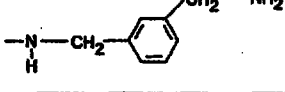
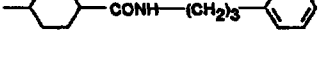
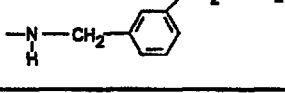
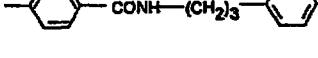
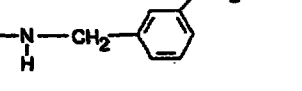
Example 29

- 5 Analogously to Example 2, 6-chlorobenzo[de]isochromene-1,3-dione is reacted with H₂N-CH₂-Ar'-(CH₂)_n-CONH-(CH₂)₆-Ar and then with R¹-H. The following compounds of the formula Iif are obtained:



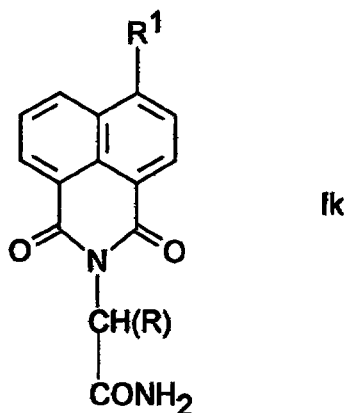
10

Ar'-(CH ₂) _n -CONH- (CH ₂) ₆ -Ar	R ¹ in R ¹ -H and Iif	MS	
		calc.	find.
	-NH-(CH ₂) ₃ -N(CH ₃) ₂ - NH-(CH ₂) ₇ -NH ₂ 	566	567
	-NH-(CH ₂) ₇ -NH ₂ 	554 560	555 561

Ar'-(CH ₂) _n -CONH- (CH ₂) _o -Ar	R ¹ in R ¹ -H and Iif	MS	
		calc.	find.
	-NH-(CH ₂) ₃ -N(CH ₃) ₂		
	-NH-(CH ₂) ₇ -NH ₂	583	584
		589	590
	-NH-(CH ₂) ₇ -NH ₂	577	578
			
	-NH-(CH ₂) ₇ -NH ₂		
			
	-NH-(CH ₂) ₃ -N(CH ₃) ₂		
	-NH-(CH ₂) ₇ -NH ₂		
			
	-NH-(CH ₂) ₃ -N(CH ₃) ₂	560	561
	-NH-(CH ₂) ₇ -NH ₂	588	589
		594	595
	-NH-(CH ₂) ₇ -NH ₂	582	583
		588	589
	-NH-(CH ₂) ₃ -N(CH ₃) ₂	554	555
	-NH-(CH ₂) ₇ -NH ₂	582	583
			
	-NH-(CH ₂) ₇ -NH ₂	576	577
			

Example 30

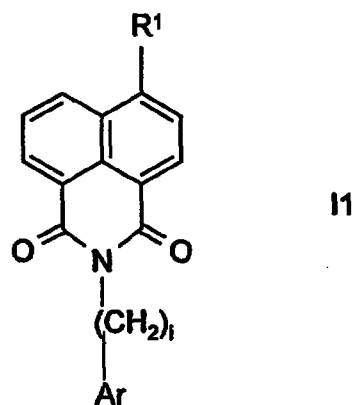
Analogously to Example 2, 6-chlorobenzo[de]isochromene-1,3-dione is reacted with $\text{H}_2\text{N}-\text{CH}(\text{R})-\text{CONH}_2$ and then with R^1-H . The following compounds of the formula 5 Ik are obtained:



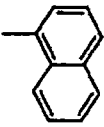
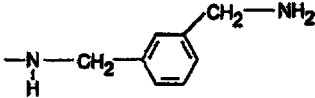
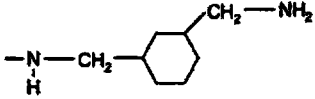
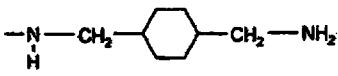
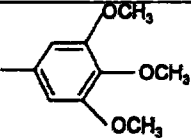
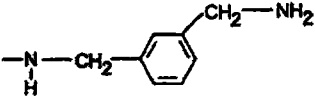
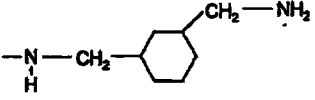
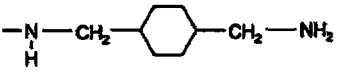
R ¹ in R ¹ -H and Ik	R	MS	
		calc.	find.
	CH ₂ -Ph		
	CH ₂ -CH(CH ₃) ₂		
-NH-(CH ₂) ₃ -N(CH ₃) ₂	CH ₂ -Ph		
	CH ₂ -CH(CH ₃) ₂		
-NH-(CH ₂) ₄ -NH ₂	CH ₂ -Ph		
	CH ₂ -CH(CH ₃) ₂		
-NH-(CH ₂) ₇ -NH ₂	CH ₂ -Ph		
	CH ₂ -CH(CH ₃) ₂		
-NH-(CH ₂) ₈ -NH ₂	CH ₂ -Ph		
	CH ₂ -CH(CH ₃) ₂		
	CH ₂ -Ph	469	470
	CH ₂ -CH(CH ₃) ₂	435	436
	CH ₂ -Ph		
	CH ₂ -CH(CH ₃) ₂		
	CH ₂ -Ph		
	CH ₂ -CH(CH ₃) ₂		

Example 31:

Analogously to Example 2, 6-chlorobenzo-[de]isochromene-1,3-dione is reacted with $\text{H}_2\text{N-Ar}$ and then with $\text{R}^1\text{-H}$. The following compounds of the formula 5 I1 are obtained:



i	Ar	R^1 in $\text{R}^1\text{-H}$ and in I1	
2		$-\text{NH}-(\text{CH}_2)_3-\text{NH}_2$ $-\text{NH}-(\text{CH}_2)_5-\text{NH}_2$ $-\text{NH}-(\text{CH}_2)_7-\text{NH}_2$ 	
2		$-\text{NH}-(\text{CH}_2)_3-\text{NH}_2$ $-\text{NH}-(\text{CH}_2)_5-\text{NH}_2$ $-\text{NH}-(\text{CH}_2)_7-\text{NH}_2$ 	

i	Ar	R ¹ in R ¹ -H and in I1	
1		$\text{-NH-(CH}_2\text{)}_3\text{-NH}_2$ $\text{-NH-(CH}_2\text{)}_5\text{-NH}_2$ $\text{-NH-(CH}_2\text{)}_7\text{-NH}_2$   	
1		$\text{-NH-(CH}_2\text{)}_3\text{-NH}_2$ $\text{-NH-(CH}_2\text{)}_5\text{-NH}_2$ $\text{-NH-(CH}_2\text{)}_7\text{-NH}_2$   	

Example 32:

Equimolar amounts of 6-(3-amino-propylamino)-2-(3,4,5-trimethoxy-benzyl)-benzo[de]isoquinoline-1,3-dione
 5 (according to example 31, page 96, table line 4) and methanesulfonic acid are reacted according to known procedures to give the acid addition salt 6-(3-amino-propylamino)-2-(3,4,5-trimethoxy-benzyl)-benzo[de]isoquinoline-1,3-dione, methane sulfonate.

10

¹H-nmr (DMSO-d₆):

8.74 (dd, J = 0.8 and J = 8.5 Hz, 1H), 8.46 (dd, J = 0.8 and J = 7.3 Hz, 1H), 8.29 (d, J = 8.5 Hz, 1H), 7.81
 (t, J = 5.5 Hz, 1H(NH)), 7.77-7.68 (m, 4H (3xNH)), 6.86
 15 (d, J = 8.7 Hz, 1H), 6.66 (s, 2H), 3.75 (s, 3H), 3.74 (s, 3H), 3.53-3.47 (m, 2H), 3.02-2.94 (m, 2H), 2.31 (s, 3H), 2.04-1.96 (m, 2H).

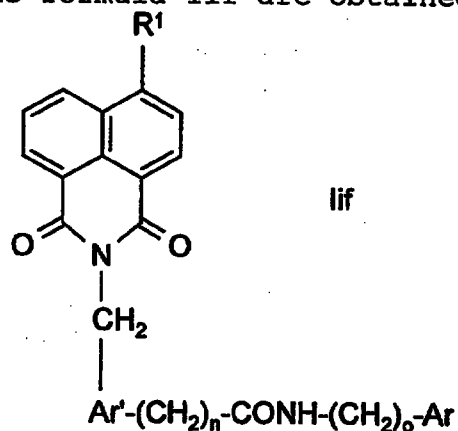
- 98 -

Abbreviations of the nmr-signals (nmr = nuclear magnetic resonance):

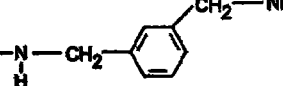
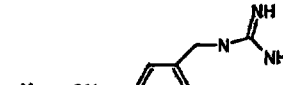
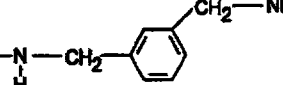
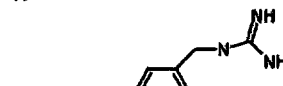
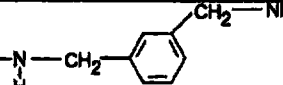
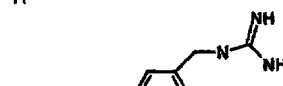
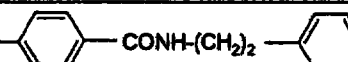
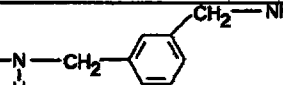
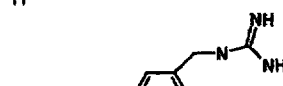
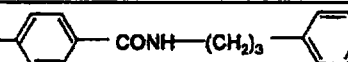
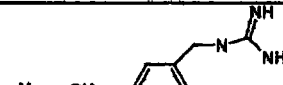
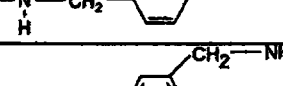
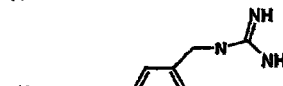
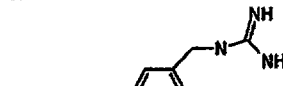
- s singlet,
 d doublet,
 5 dd double doublet,
 t triplet,
 sbr broad singlet,
 m multiplet,
 q quadruplet,
 10 J coupling constant J in Hz

Example 33:

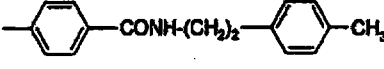
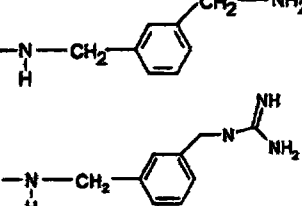
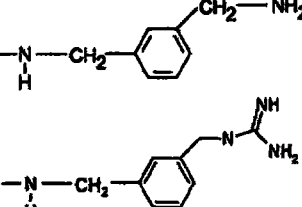
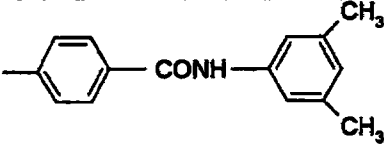
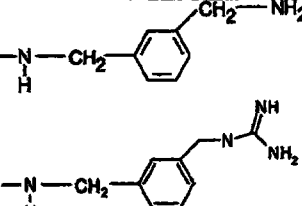
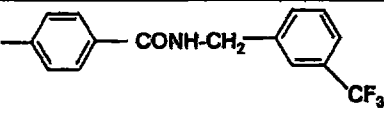
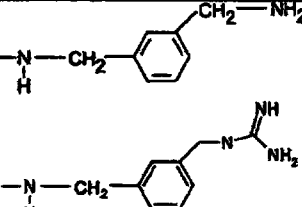
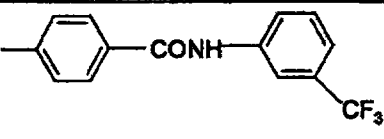
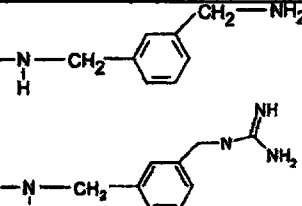
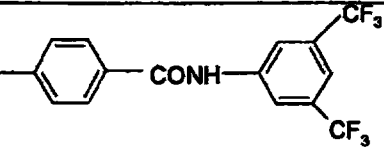
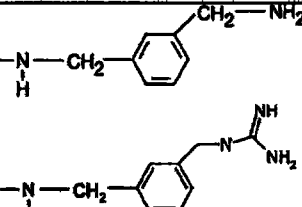
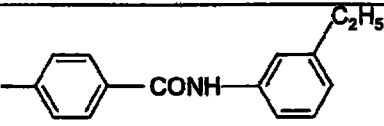
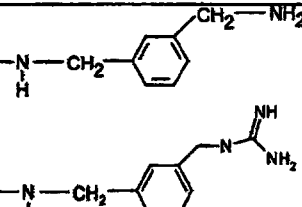
Analogously to Example 2, 6-chlorobenzo-[de]isochromene-1,3-dione is reacted with $\text{H}_2\text{N}-\text{CH}_2-\text{Ar}'-(\text{CH}_2)_n-\text{CONH}-(\text{CH}_2)_o-\text{Ar}$ and then with R^1-H . The following compounds of the formula Iif are obtained:

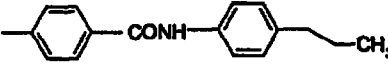
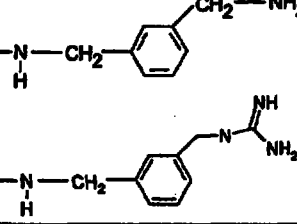
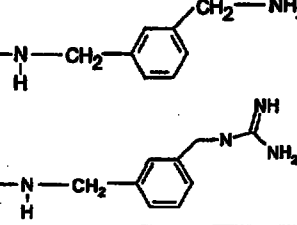
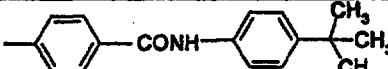
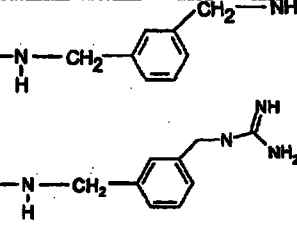
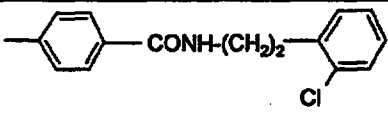
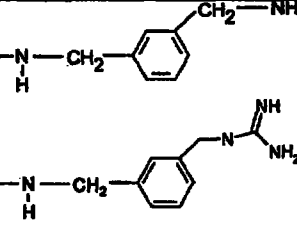
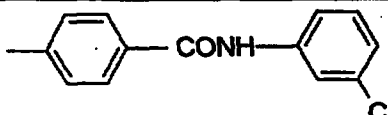
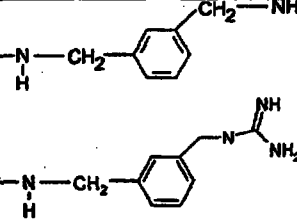
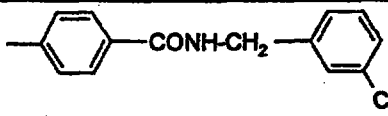
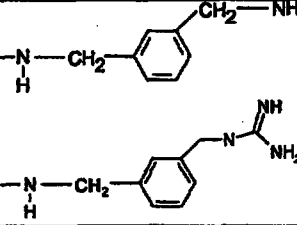
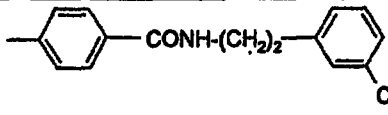
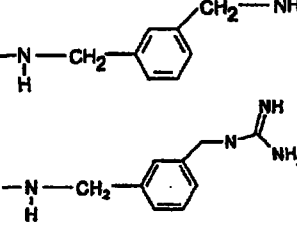


$\text{Ar}'-(\text{CH}_2)_n-\text{CONH}-(\text{CH}_2)_o-\text{Ar}$	R^1 in R^1-H and Iif	

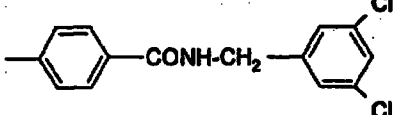
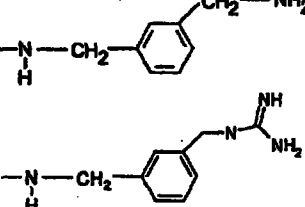
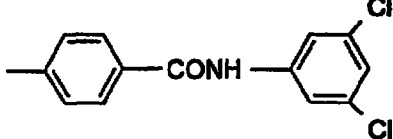
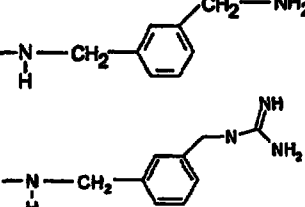
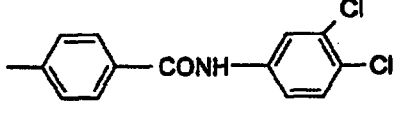
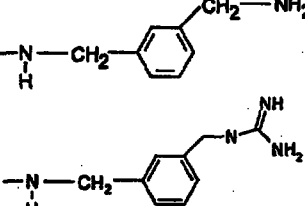
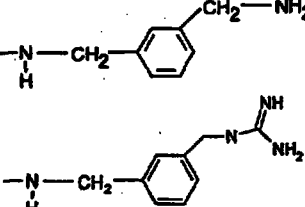
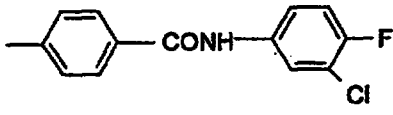
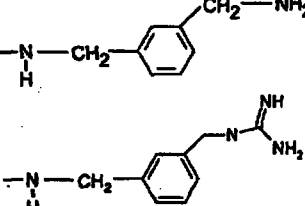
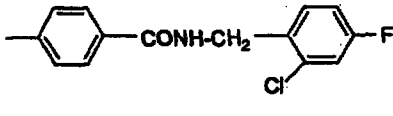
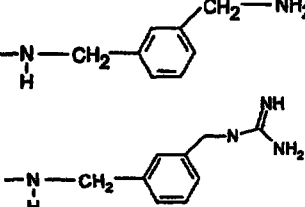
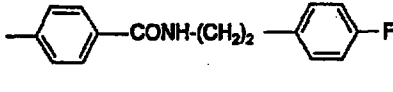
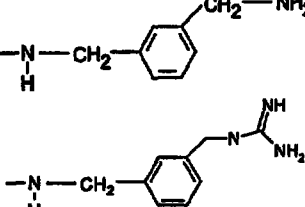
Ar'-(CH ₂) _n -CONH-(CH ₂) _o -Ar	R ¹ in R ¹ -H and Iif	
	 	
	 	
	 	
	 	
	 	
	 	
	 	

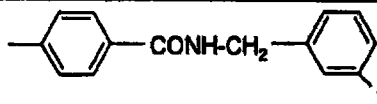
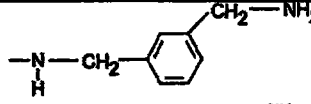
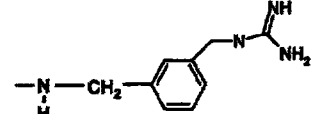
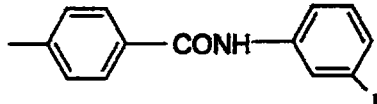
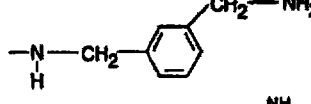
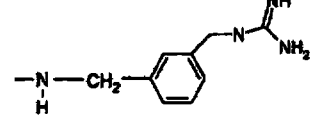
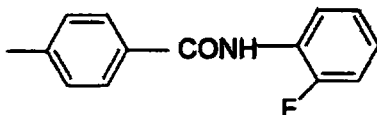
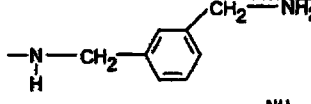
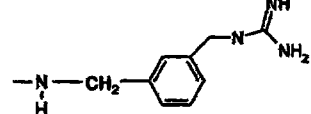
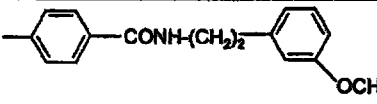
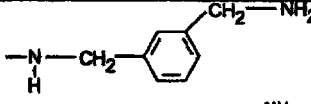
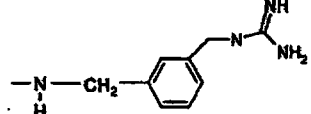
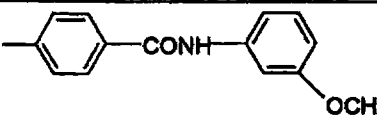
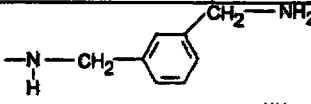
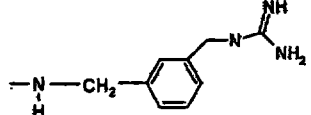
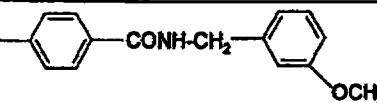
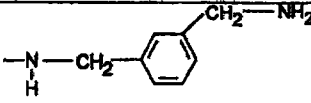
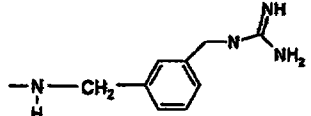
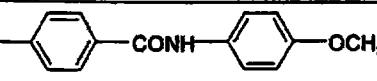
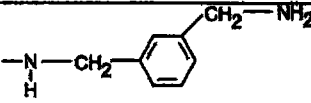
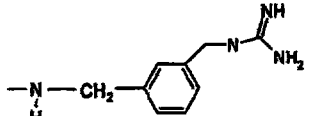
$\text{Ar}'-(\text{CH}_2)_n-\text{CONH}-(\text{CH}_2)_6-\text{Ar}$	R^1 in $\text{R}^1\text{-H}$ and Iif	

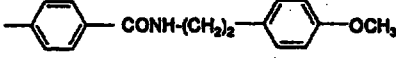
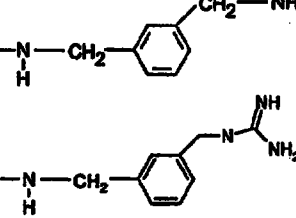
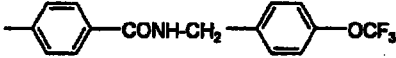
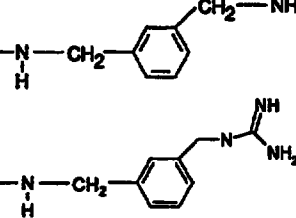
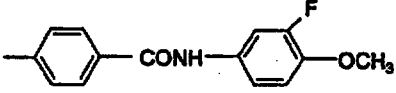
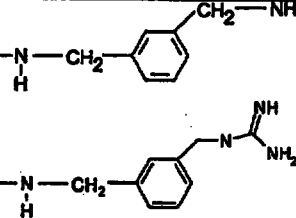
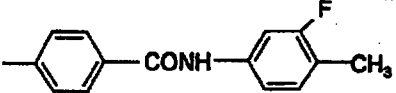
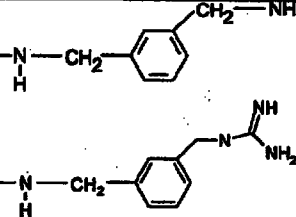
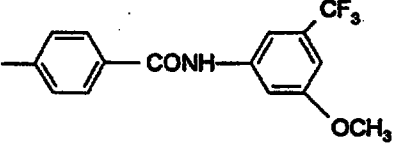
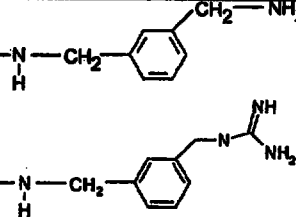
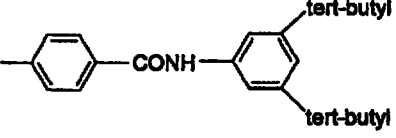
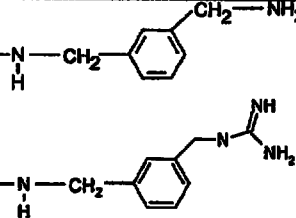
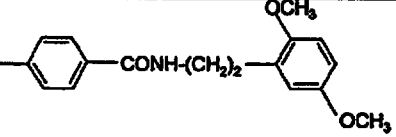
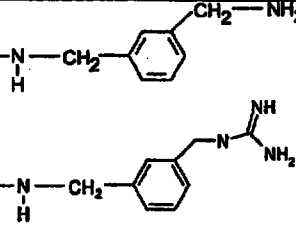
$\text{Ar}'-(\text{CH}_2)_n-\text{CONH}-(\text{CH}_2)_o-\text{Ar}$	R^1 in $\text{R}^1\text{-H}$ and Iif	
		
		
		
		
		
		
		

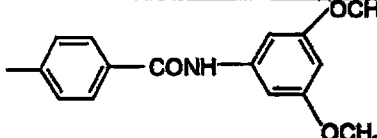
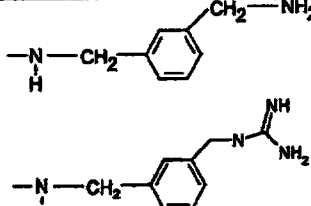
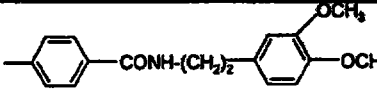
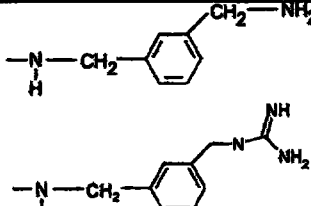
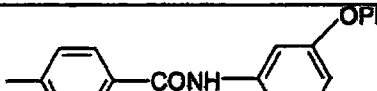
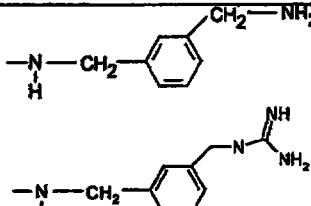
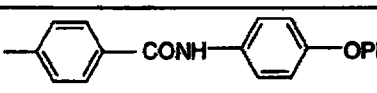
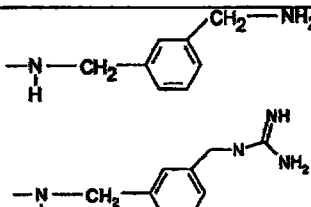
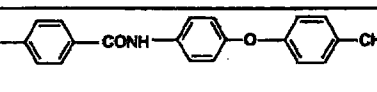
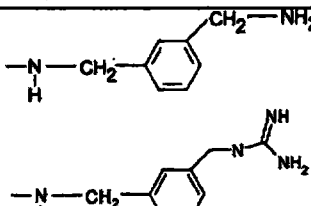
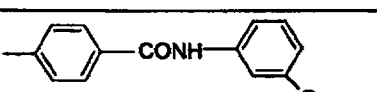
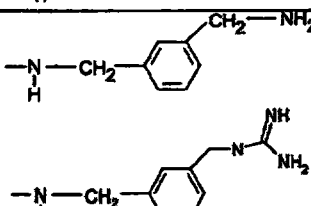
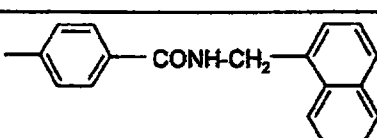
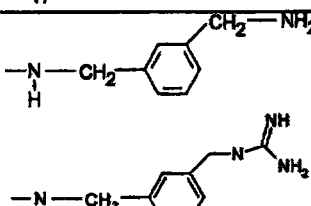
Ar ¹ - (CH ₂) _n - CONH - (CH ₂) _o - Ar	R ¹ in R ¹ -H and Iif	
		
		
		
		
		
		
		

$\text{Ar}' - (\text{CH}_2)_n - \text{CONH} - (\text{CH}_2)_o - \text{Ar}$	R^1 in $\text{R}^1\text{-H}$ and Iif	

$\text{Ar}' - (\text{CH}_2)_n - \text{CONH} - (\text{CH}_2)_o - \text{Ar}$	R^1 in $\text{R}^1\text{-H}$ and Iif	
		
		
		
		
		
		
		

$Ar'-(CH_2)_n-CONH-(CH_2)_o-Ar$	R^1 in R^1-H and Iif	
	 	
	 	
	 	
	 	
	 	
	 	
	 	

$\text{Ar}^1 - (\text{CH}_2)_n - \text{CONH} - (\text{CH}_2)_m - \text{Ar}$	R^1 in $\text{R}^1\text{-H}$ and Iif	
		
		
		
		
		
		
		

Ar'-(CH ₂) _n -CONH-(CH ₂) ₆ -Ar	R ¹ in R ¹ -H and Iif	
		
		
		
		
		
		
		

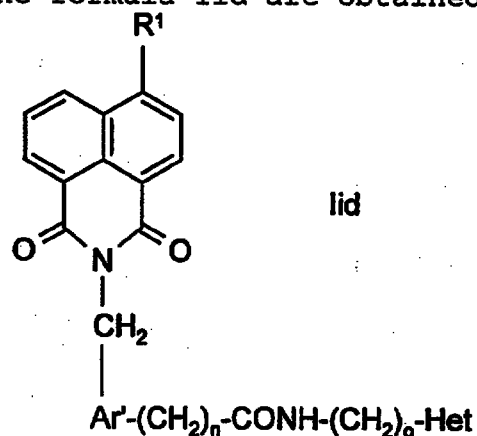
$\text{Ar}' - (\text{CH}_2)_n - \text{CONH} - (\text{CH}_2)_o - \text{Ar}$	R^1 in $\text{R}^1\text{-H}$ and Iif	

$\text{Ar}' - (\text{CH}_2)_n - \text{CONH} - (\text{CH}_2)_6 - \text{Ar}$	R^1 in $\text{R}^1\text{-H}$ and Iif	

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Example 34:

Analogously to Example 2, 6-chlorobenzo-[de]isochromene-1,3-dione is reacted with $\text{H}_2\text{N}-\text{CH}_2-\text{Ar}'-(\text{CH}_2)_n-\text{CONH}-(\text{CH}_2)_6-\text{Het}$ and then with R^1-H . The following 5 compounds of the formula Iid are obtained:



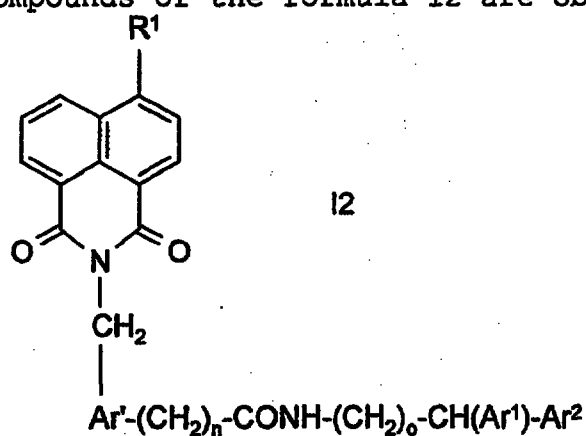
$\text{Ar}'-(\text{CH}_2)_n-\text{CONH}-(\text{CH}_2)_6-\text{Het}$	R^1 in R^1-H and Iid	

$\text{Ar}'-(\text{CH}_2)_n-\text{CONH}-(\text{CH}_2)_o-\text{Het}$	R^1 in $\text{R}^1\text{-H}$ and Id	

$\text{Ar}'-(\text{CH}_2)_n-\text{CONH}-(\text{CH}_2)_o-\text{Het}$	R^1 in $\text{R}^1\text{-H}$ and Iid	

Example 35:

Analogously to Example 2, 6-chlorobenzo-
 5 [de]isochromene-1,3-dione is reacted with $\text{H}_2\text{N}-\text{CH}_2-\text{Ar}'-(\text{CH}_2)_n-\text{CONH}-(\text{CH}_2)_o-\text{CH}(\text{Ar}^1)-\text{Ar}^2$ and then with $\text{R}^1\text{-H}$. The following compounds of the formula I2 are obtained:



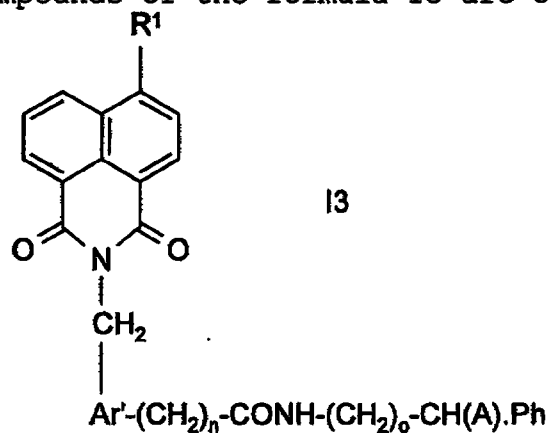
$\text{Ar}'-(\text{CH}_2)_n-\text{CONH}-(\text{CH}_2)_o-\text{CH}(\text{Ar}^1)-\text{Ar}^2$	R^1 in $\text{R}^1\text{-H}$ and I2	

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$\text{Ar}'-(\text{CH}_2)_n-\text{CONH}-(\text{CH}_2)_o-\text{CH}(\text{Ar}^1)-\text{Ar}^2$	R^1 in $\text{R}^1\text{-H}$ and I2	

Example 36:

Analogously to Example 2, 6-chlorobenzo-[de]isochromene-1,3-dione is reacted with $\text{H}_2\text{N}-\text{CH}_2-\text{Ar}'-(\text{CH}_2)_n-\text{CONH}-(\text{CH}_2)_o-\text{CH}(\text{A})-\text{Ph}$ and then with $\text{R}^1\text{-H}$. The following compounds of the formula I3 are obtained:

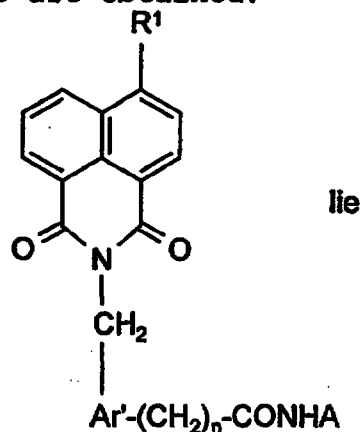


$\text{Ar}'-(\text{CH}_2)_n-\text{CONH}-(\text{CH}_2)_o-\text{CH}(\text{A})-\text{Ph}$	R^1 in $\text{R}^1\text{-H}$ and I3	

Example 37:

Analogously to Example 2, 6-chlorobenzo-[de]isochromene-1,3-dione is reacted with $\text{H}_2\text{N}-\text{CH}_2-\text{Ar}'-(\text{CH}_2)_n-\text{CONHA}$ and then with R^1-H . The following compounds

5 of the formula Iie are obtained:

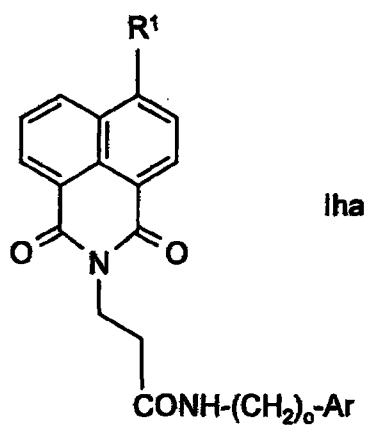


$\text{Ar}'-(\text{CH}_2)_n-\text{CONHA}$	R^1 in R^1-H and Iie	

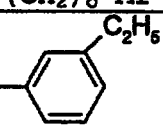
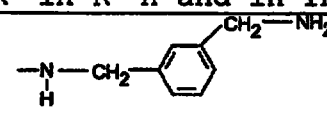
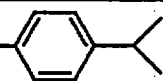
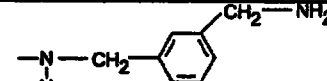
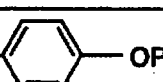
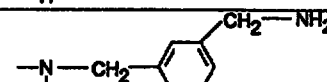
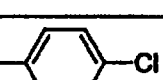
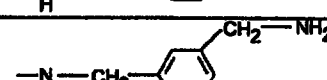
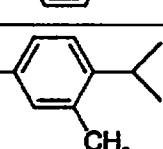
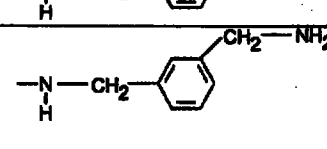
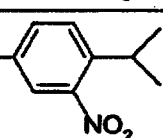
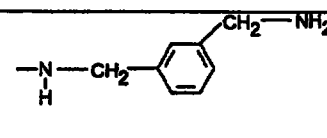
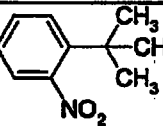
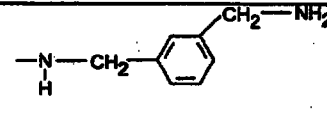
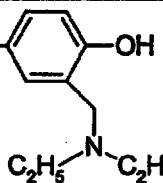
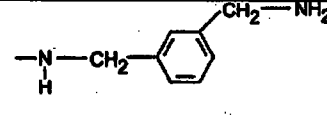
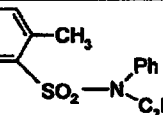
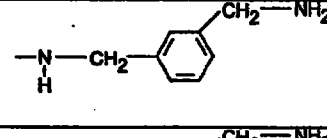
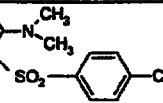
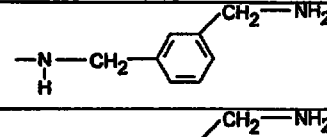
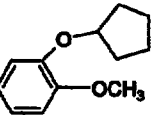
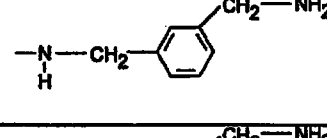
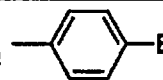
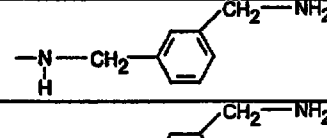
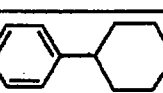
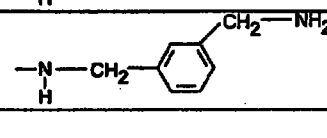
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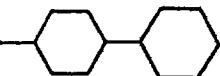
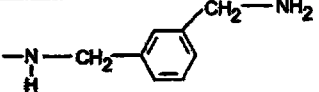
10 Analogously to Example 2, 6-nitrobenzo-[de]isochromene-1,3-dione is reacted with $\text{H}_2\text{N}-(\text{CH}_2)_2-\text{CONH}-(\text{CH}_2)_6-\text{Ar}$ and then with R^1-H . The following compounds of the formula Iha are obtained:

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CONH-(CH ₂) ₆ -Ar	R ¹ in R ¹ -H and in IHa	
CONH-(CH ₂) ₂ -		
CONH-(CH ₂) ₂ -		
CONH-(CH ₂) ₂ -		
CONH-(CH ₂) ₂ -		
CONH-CH ₂ -		
CONH-CH ₂ -		
CONH-CH ₂ -		
CONH-CH ₂ -		
CONH-CH ₂ -		
CONH-CH ₂ -		

CONH-(CH ₂) ₀ -Ar	R ¹ in R ¹ -H and in IHa	
CONH- 		
CONH- 		
CONH- 		
CONH- 		
CONH- 		
CONH- 		
CONH- 		
CONH- 		
CONH- 		
CONH- 		
CONH- 		
CONH-CH ₂ - 		
CONH- 		

CONH-(CH ₂) _o -Ar	R ¹ in R ¹ -H and in IHa	
CONH- 		

Example 39:

A suspension of 4 g of 6-nitrobenzo[de]iso-
chromene-1,3-dione in 100 ml of toluene is treated with
5 3.1 g of 2-amino-N-(4-iodo-phenyl)-acetamide and the
mixture is heated under reflux. After reaction is
complete, the reaction mixture is allowed to cool and
is worked up as is customary. N-(4-Iodo-phenyl)-2-(6-
nitro-1,3-dioxo-1H,3H-benzo[de]isoquinolin-2-yl)-
10 acetamide is obtained. 1.2 Equivalents of K₂CO₃, 1.2
equivalents of Ph-B-(OH)₂ and 10 mol% of Pd((PPh)₃)₄ are
added to a solution of this compound in 80 ml of DMF
and it is heated at 80°C until conversion is complete.
After filtering off the catalyst and customary working
15 up, N-biphenyl-4-yl-2-(6-nitro-1,3-dioxo-1H,3H-
benzo[de]isoquinolin-2-yl)-acetamide is heated with 3-
aminomethyl-benzylamine until conversion is complete.
After cooling the reaction mixture, it is worked up as
is customary and 2-[6-(3-aminomethyl-benzylamino)-1,3-
20 dioxo-1H,3H-benzo[de]isoquinolin-2-yl]-N-biphenyl-4-yl-
acetamide is obtained.

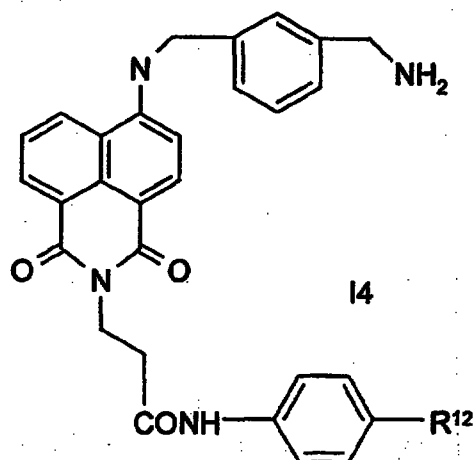
Analogously, by reaction of N-(4-iodo-3-
methoxyphenyl)-2-(6-nitro-1,3-dioxo-1H,3H-
25 benzo[de]isoquinolin-2-yl)-propionamide with Ph-B-(OH)₂
and 3-aminomethyl-benzylamine, 3-[6-(3-aminomethyl-
benzylamino)-1,3-dioxo-1H,3H-benzo[de]isoquinolin-2-
yl]-N-(2-methoxy-biphenyl-4-yl)-propionamide is
obtained.

30

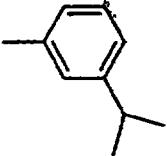
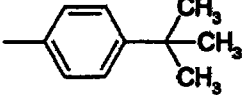
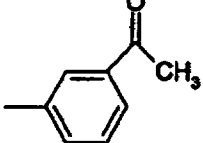
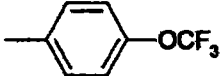
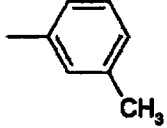
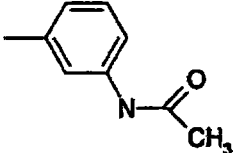
Analogously, by reaction of N-(4-iodo-benzyl)-
3-(6-nitro-1,3-dioxo-1H,3H-benzo[de]isoquinolin-2-yl)-
propionamide with Ph-B-(OH)₂ and 3-aminomethyl-
benzylamine, 3-[6-(3-aminomethyl-benzylamino)-1,3-
35 dioxo-1H,3H-benzo[de]isoquinolin-2-yl]-N-biphenyl-4-
ylmethyl-propionamide is obtained.

Example 40:

Analogously to example 39, by reaction of 6-nitro-2-(4-iodophenyl)benzo[de]isoquinoline-1,3-dione with R^{12} -B-(OH)₂ and 3-aminomethyl-benzylamine, the following compounds of the formula I4 are obtained:

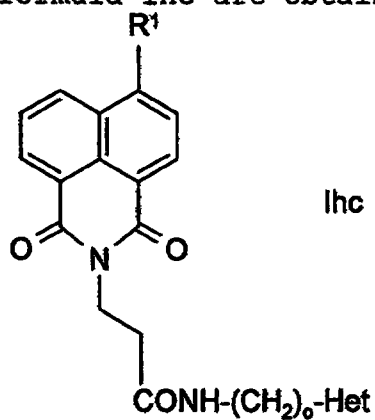


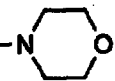
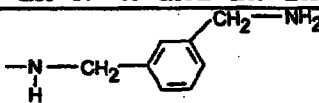
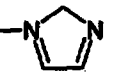
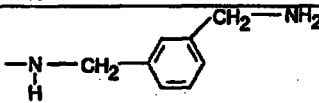
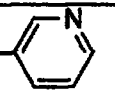
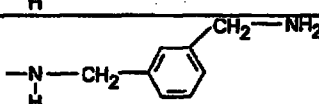
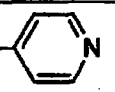
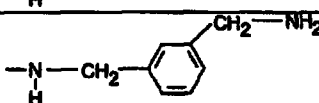
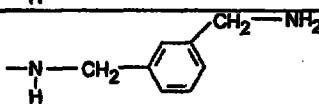
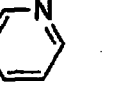
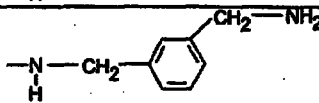
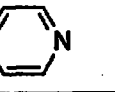
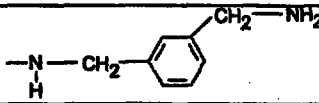
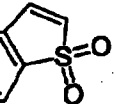
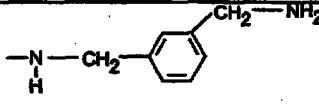
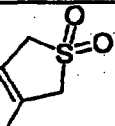
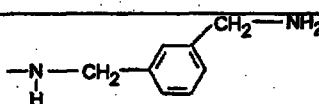
R^{12} in I4	

R^{12} in I4	
	
	
	
	
	
	

Example 41:

Analogously to Example 2, 6-nitrobenzo-
[de]isochromene-1,3-dione is reacted with $H_2N-(CH_2)_2-$
5 $CONH-(CH_2)_6-Het$ and then with R^1-H . The following
compounds of the formula Ihc are obtained:



CONH-(CH ₂) _o -Het	R ¹ in R ¹ -H and in Ihca	
CONH-(CH ₂) ₂ -N 		
CONH-(CH ₂) ₃ -N 		
CONH-CH ₂ - 		
CONH-CH ₂ - 		
CONH-CH ₂ - 		
CONH- 		
CONH- 		
CONH- 		
CONH- 		

Example 42:

Analogously to example 2, by reaction of 6-nitro-benzo[de]isochromene-1,3-dione with 3-amino-N-(3,3-diphenyl-propyl)-propionamide and 3-aminomethyl-benzylamine, 3-[6-(3-aminomethyl-benzylamino)-1,3-dioxo-1H,3H-benzo[de]isoquinolin-2-yl]-N-(3,3-diphenyl-propyl)-propionamide is obtained.

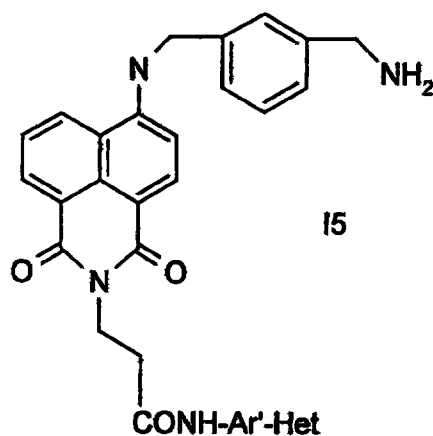
10 Example 43:

Analogously to example 2, by reaction of 6-nitro-benzo[de]isochromene-1,3-dione with N-[4-(3-amino-propionylamino)-2-methoxy-phenyl]-2-methoxy-benzamide and 3-aminomethyl-benzylamine, N-(4-{3-[6-(3-aminomethyl-benzylamino)-1,3-dioxo-1H,3H-

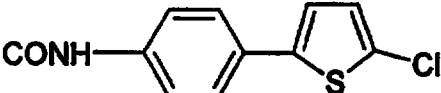
benzo[de]isoquinolin-2-yl]-propionylamino}-2-methoxy-phenyl)-2-methoxy-benzamide is obtained.

Example 44:

- 5 Analogously to example 2, 6-nitrobenzo-[de]isochromene-1,3-dione is reacted with $\text{H}_2\text{N}-(\text{CH}_2)_2-\text{CONH}-\text{Ar}'-\text{Het}$ and then with 3-aminomethyl-benzylamine. The following compounds of the formula I5 are obtained:

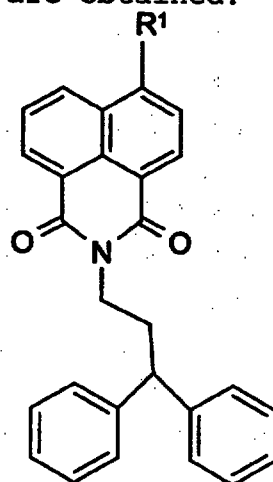


CONH-Ar'-Het in I5	

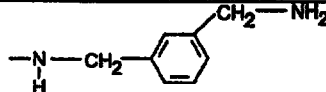
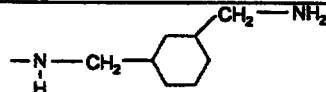
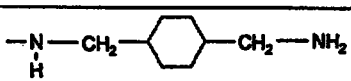
CONH-Ar'-Het in I5	
	
	

Example 45:

Analogously to example 2, 6-nitrobenzo-
 5 [de]isochromene-1,3-dione is reacted with 3,3-diphenyl-
 propylamine and then with R¹-H. The following compounds
 of the formula I6 are obtained:



I6

R ¹ in R ¹ -H and I6	
-NH-(CH ₂) ₃ -NH ₂	
-NH-(CH ₂) ₅ -NH ₂	
-NH-(CH ₂) ₇ -NH ₂	
	
	
	

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The following examples relate to pharmaceutical preparations:

Example A: Injection vials

5 A solution of 100 g of an active compound of the formula I and 5 g of disodium hydrogenphosphate is adjusted to pH 6.5 in 3 l of double-distilled water using 2N hydrochloric acid, sterile-filtered, dispensed into injection vials, lyophilized under sterile
10 conditions and aseptically sealed. Each injection vial contains 5 mg of active compound.

Example B: Suppositories

15 A mixture of 20 g of an active compound of the formula I is melted with 100 g of soya lecithin and 1400 g of cocoa butter, poured into moulds and allowed to cool. Each suppository contains 20 mg of active compound.

Example C: Solution

20 A solution is prepared from 1 g of an active compound of the formula I, 9.38 g of $\text{NaH}_2\text{PO}_4 \cdot 2\text{H}_2\text{O}$, 28.48 g of $\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$ and 0.1 g of benzalkonium chloride in 940 ml of double-distilled water. The
25 mixture is adjusted to pH 6.8, made up to 1 l and sterilized by irradiation. This solution can be used in the form of eye drops.

Example D: Ointment

30 500 mg of an active compound of the formula I is mixed with 99.5 g of petroleum jelly under aseptic conditions.

Example E: Tablets

35 A mixture of 1 kg of active compound of the formula I, 4 kg of lactose, 1.2 kg of potato starch, 0.2 g of talc and 0.1 kg of magnesium stearate is compressed in a customary manner to give tablets such that each tablet contains 10 mg of active compound.

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Example F: Coated tablets

Analogously to Example E, tablets are pressed which are then coated with a coating of sucrose, potato
5 starch, talc, tragacanth and colourant in a customary manner.

Example G: Capsules

2 kg of active compound of the formula I are
10 dispensed into hard gelatin capsules in a customary manner such that each capsule contains 20 mg of the active compound.

Example H: Ampoules

15 A solution of 1 kg of active compound of the formula I in 60 ml of double-distilled water is sterile-filtered, dispensed into ampoules, lyophilized under sterile conditions and aseptically sealed. Each
20 ampoule contains 10 mg of active compound.

The preceding examples can be repeated with similar success by substituting the generically or specifically described reactants and/or operating conditions of this invention for those used in the
25 preceding examples.

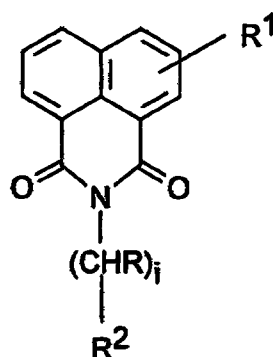
From the foregoing description, one skilled in the art can easily ascertain the essential characteristics of this invention and, without departing from the spirit and scope thereof, can make
30 various changes and modifications of the invention to adapt it to various usages and conditions.



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What is claimed is:

1. Compounds of the formula I



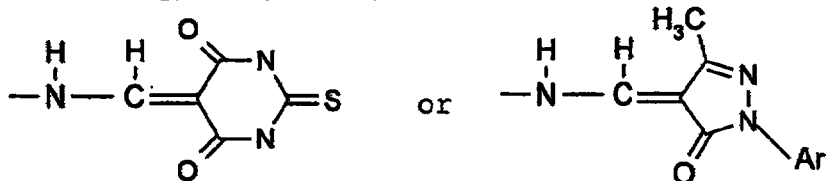
5

in which

R is H, A or CH₂-Ph,

10 R¹ is -Het, -N-[(CH₂)_s-OH]₂, -N-[(CH₂)_s-OA]₂,
 -NA-(CH₂)_s-Ar, -NA-(CH₂)_m-R⁵, -Y-(CH₂)_m-R⁵,
 -Y-(CH₂)₂-NHA, -Y-(CH₂)₂-NH-(CH₂)_s-OH, -Y-(CH₂)₂-NA₂,
 -Y-(CH₂)_m-OH, -Y-(CH₂)_n-(CHR⁴)-R³, -Y-(CH₂)_n-R⁴, R⁴,
 -Y-(CH₂)_n-Het-(CH₂)_o-R⁶, -Y-(CH₂)_n-Ar'-(CH₂)_o-R⁶,
 -Het-(CH₂)_n-Ar, -Het-Het, -Y-(CH₂)_s-Ar'-(CH₂)_o-R¹¹,
 15 -Y-[X-O]_t-[X¹-O]_u-X²-R⁵ or -Y-(CH₂)_n-NA-(CH₂)_o-R⁵,

R² is H, OH, OA, COOH, COOA, CH(Ph)-Ph, Ar, Het¹, R⁵,
 R⁷ or R⁸

R³ is CH₃,R⁴ is -CH=CH₂, -Ar, COOA, COOH

20

R⁵ is NH₂, NHA, NA₂, NHA_r, -NH-(CH₂)_n-OH or
 -NH-(CH₂)_n-OA,

R⁶ is H or R⁵R⁷ is -Ar'-(CH₂)_n-R⁸ or -Ar'-(CH₂)_n-R⁵

25 R⁸ is CONH₂, CONHA, CONA₂, CONH-(CH₂)_o-Ar,
 CONH-(CH₂)_o-Het, CONH-(CH₂)_o-R⁵, CONH-(CH₂)_o-CH(Ar¹)-
 Ar², CONH-(CH₂)_o-CH(A)-Ph, CONH-(CH₂)_o-Ar'-NH-CO-Ar,
 CONH-Ar'-Het or CHA-CONH₂,



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- R^{11} is $-NH-(C=NH)-NH_2$, $-NH-(C=NH)-NHA$, $-NH-(C=NH)-NA_2$,
 $-NA-(C=NH)-NH_2$, $-NA-(C=NH)-NHA$ or $-NA-(C=NH)-NA_2$,
- 5 Ar' is phenylene, cycloalkylene or biphenylene, which is
unsubstituted or mono- or disubstituted by A, OH, OA,
Hal, CN, NH_2 , NHA, NA_2 , NO_2 , CF_3 , CO-A, SO_2NH_2 , SO_2NAH or
 SO_2NA_2 ,
- 10 Ar is phenyl, cycloalkyl, naphthyl, cyclohex-1-enyl,
biphenyl, bicyclohexyl, 4-cyclohexyl-phenyl,
benzo[1,3]dioxol-5-yl or indanyl, which is
unsubstituted or mono-, di- or trisubstituted by
A, OH, OA, O-Ph, O- CH_2 -Ph, O-PH- CH_3 , O(cycloalkyl),
Hal, CN, NH_2 , NHA, NA_2 , $NH-C(O)A$, $(CH_2)_n-NH_2$,
 $(CH_2)_n-NHA$, $(CH_2)_n-NA_2$, NO_2 , CF_3 , C(O)A, SO_2 -Ph,
 SO_2NH_2 , SO_2NAH , SO_2NA_2 or SO_2NA -Ph,
- 15 Ar^1 and Ar^2
are each independently phenyl,
- Het is a saturated, partially or completely unsatura-
ted mono- or bicyclic heterocyclic radical having
5 to 10 ring members, where 1 or 2 N and/or 1 or
20 2 S or O atoms can be present and the heterocyclic
radical can be mono- or disubstituted by CN, Hal,
OH, OA, CF_3 , A, NO_2 , CO, CO-A or R^5 ,
- Het¹ is an unsaturated mono- or bicyclic heterocyclic
radical having 5 to 10 ring members, where 1 or
25 2 N and/or 1 or 2 S or O atoms can be present
and/or can be mono- or disubstituted by Hal, OH,
OA,
- A is unbranched or branched alkyl having 1-6 C
atoms,
- 30 Hal is F, Cl, Br or I,
X,
 X^1, X^2 in each case independently of one another are
alkylene having 1 to 12 C atoms,
- Y is O, S or NH,
- 35 i is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12,
m is 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12,
n, o in each case independently of one another are 0,
1, 2, 3 or 4,
s is 1, 2, 3 or 4,

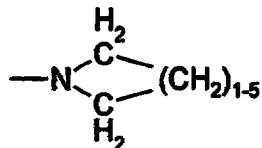


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t is 0, 1 or 2,

u is 1 or 2,

where if R^2 is Ar or H, R^1 is not



5 and their pharmaceutically tolerable salts and solvates.

2. Compound of the formula I according to Claim 1

a) methyl 3-(1,3-dioxo-6-piperidin-1-yl-3a,9b-dihydro-1H-3H-benzo[de]isoquinolin-2-yl)propionate;

b) 6-(3-amino-propylamino)-2-(3,4,5-trimethoxy-benzyl)-benzo[de]isoquinoline-1,3-dione;

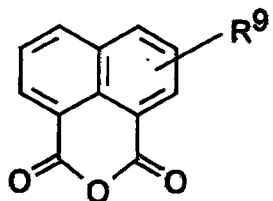
and its physiologically acceptable salts and solvates.

3. Process for the preparation of the compounds of the formula I according to Claim 1 and their salts or solvates, characterized in that

a) a compound of the formula I is liberated from one of its functional derivatives by treating with a solvolysing or hydrogenolysing agent,

or

b) a compound of the formula II



II

25 in which

R^9 is Cl, Br, NO_2 or R^1 , where

R^1 has the meaning indicated in Claim 1

is reacted with a compound of the formula III



30 in which R, R^2 and i have the meanings indicated in Claim 1,

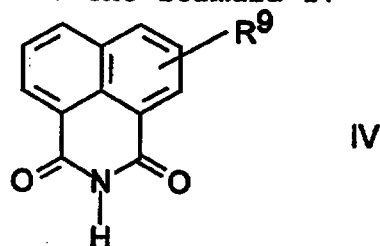
and, if necessary, the radical R^9 is converted into a radical R^1 ,



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or

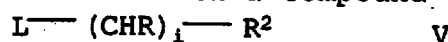
(c) a compound of the formula IV



5 in which

 R^9 is Cl, Br, NO_2 or R^1 , where R^1 has the meaning indicated in Claim 1

is reacted with a compound of the formula V



10 in which L is Cl, Br, or I, OH or a reactive esterified OH group and R, R^2 and i have the meanings indicated in Claim 1

and, if appropriate, the radical R^9 is converted into a radical R^1 ,

15 or

(d) a radical R and/or R^2 and/or R^9 is converted into another radical R and/or R^2 and/or R^9 by, for example

- converting an amino group into a guanidino group by reaction with an amidinating agent,
- reacting an aryl bromide or iodide to give the corresponding coupling products by means of a Suzuki coupling with boronic acids,
- reducing a nitro group, sulfonyl group or sulfoxyl group,
- etherifying an OH group or subjecting an OA group to ether cleavage,
- alkylating a primary or secondary amino group,
- partially or completely hydrolysing a CN group,
- cleaving an ester group or esterifying a carboxylic acid radical,
- or carrying out a nucleophilic or electrophilic substitution,

and/or



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(e) a base or acid of the formula I is converted into one of its salts or solvates.

4. A pharmaceutical composition comprising an effective amount of a compound of formula I of claim 1
5 or a physiologically acceptable salt or solvate thereof, and a pharmaceutically acceptable excipient.

5. A pharmaceutical composition of claim 4 which is effective as a glycoprotein IbIX antagonist.

6. A pharmaceutical composition of claim 5,
10 wherein said glycoprotein IbIX antagonist is effective for the control of thrombotic disorders and sequelae deriving therefrom.

7. A compound of formula I of claim 1, or a physiologically acceptable salt or solvate thereof as
15 pharmaceutical active compound.

8. A compound of formula I of claim 1, or a physiologically acceptable salt or solvate thereof as a glycoprotein IbIX antagonist.

9. Use of compounds of the formula I according to
20 Claim 1 and/or their physiologically acceptable salts or solvates for the production of a medicament for the control of thrombotic disorders and sequelae deriving therefrom or for use as anti-adhesive substances.

10. Use of compounds of the formula I according to
25 Claim 1 and/or their physiologically acceptable salts or solvates in the treatment of illnesses, such as for the prophylaxis and/or therapy of thrombotic disorders, as well as sequelae such as, for example, myocardial infarct, arteriosclerosis, angina pectoris, acute
30 coronary syndromes, peripheral circulatory disorders, stroke, transient ischaemic attacks, reocclusion/restenosis after angioplasty/stent implantations or as anti-adhesive substances for implants, catheters or heart pacemakers.