



(51) International Patent Classification:

C07C 235/34 (2006.01) A61K 8/42 (2006.01)
C07C 235/36 (2006.01) A61K 8/49 (2006.01)
C07D 295/185 (2006.01) A61K 8/60 (2006.01)
C07C 231/02 (2006.01) A61Q 19/02 (2006.01)

(21) International Application Number:

PCT/EP2016/080911

(22) International Filing Date:

14 December 2016 (14.12.2016)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

1562427 15 December 2015 (15.12.2015) FR

(71) Applicant: L'OREAL [FR/FR]; 14 Rue Royale, 75008 Paris (FR).

(72) Inventors: MARAT, Xavier; 6 impasse Chausson, 75010 Paris (FR). MA, Chunyu; No. 1028 YunQiao Rd. - Pudong New Area, Shanghai, 210206 (CN).

(74) Agent: LE COUPANEC, Pascale; Cabinet NONY, 11 rue Saint-Georges, 75009 Paris (FR).

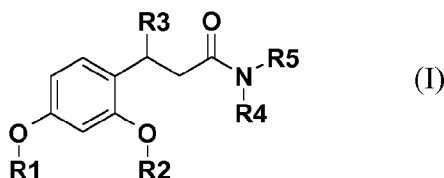
(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))

(54) Title: RESORCINOL DERIVATIVES FOR THEIR COSMETIC USE



(57) Abstract: The present invention relates to a compound of formula (I) for its depigmenting, lightening and/or bleaching the skin in which R¹ and R² independently denote H, an alkyl radical, a radical S* denoting a monosaccharide sugar radical or a polysaccharide sugar radical, a radical COR₆; R₃ denotes a C₁-C₂₀ alkyl radical; R₄ and R₅ independently denote H, a saturated C₁-C₂₀ or unsaturated C₂-C₂₀ or branched C₃-C₂₀, or cyclic C₃-C₈ alkyl radical, which is optionally interrupted and/or optionally substituted; R₇ and R₈, which may be identical or different, being chosen from H, an unsaturated linear C₁-C₁₀ alkyl group, an unsaturated linear C₂-C₁₀ alkyl group, a saturated or unsaturated branched C₃-C₁₀ alkyl group, and a C₃-C₈ cycloalkyl group; a (C₁-C₄)alkyl(hetero)(C₆)aryl group optionally containing a nitrogen atom, especially a benzyl group; an acetyl radical, and also the salts thereof, the solvates thereof and the optical and/or geometrical isomers thereof, and the racemic mixtures thereof, alone or as a mixture. The present invention also relates to novel compounds (II), and also to the process for preparing them and to a cosmetic process for depigmenting the skin using such compounds (I) or (II).



RESORCINOL DERIVATIVES FOR THEIR COSMETIC USE

The present invention relates to the cosmetic use of resorcinol derivatives for depigmenting and/or bleaching the skin, and also to certain novel resorcinol derivatives.

At various periods of their life, some people see the appearance on their skin, and more in particular on the hands and the face, of darker and/or more colored spots, which give the skin heterogeneity. These spots are in particular due to a high concentration of melanin in the keratinocytes located at the surface of the skin.

The use of harmless topical depigmenting substances with good efficacy is most particularly desired for the purpose of treating pigmentation spots.

The mechanism of formation of skin pigmentation, i.e. the formation of melanin, is particularly complex and schematically involves the following main steps:

Tyrosine → Dopa → Dopakinone → Dopachrome → Melanin

Tyrosinase (monophenol dihydroxyl phenylalanine: oxygen oxidoreductase EC 1.14.18.1) is the essential enzyme involved in this sequence of reactions. It in particular catalyzes the reaction for conversion of tyrosine into dopa (dihydroxyphenylalanine) by means of its hydroxylase activity, and the reaction for conversion of dopa into dopakinone by means of its oxidase activity. This tyrosinase acts only when it is in mature form under the action of certain biological factors.

A substance is acknowledged as being depigmenting if it acts directly on the vitality of the epidermal melanocytes where melanogenesis takes place, and/or if it interferes with one of the steps of melanin biosynthesis, either by inhibiting one of the enzymes involved in melanogenesis, or by inserting itself as a structural analogue of one of the chemical compounds of the melanin synthesis chain, which chain can then be blocked, thus ensuring depigmentation.

Arbutin and kojic acid are known as skin depigmenting agents.

Substances with efficient depigmenting action, especially better than that of arbutin and kojic acid, have been sought.

There is still a need for a novel agent for bleaching human skin whose action is as efficient as the known agents, but which does not have their drawbacks, i.e. which is not irritant, not toxic and/or not allergizing for the skin, while at the same time being stable in a composition, or alternatively which has reinforced action so as to be able to be used in lower amounts, which considerably reduces the side effects observed.

In this regard, the Applicant has discovered, surprisingly and unexpectedly, that certain resorcinol compounds have good depigmenting activity, even at low concentration, without showing any cytotoxicity.

5 In this regard, the Applicant has discovered, surprisingly and unexpectedly, that certain resorcinol derivatives have good depigmenting activity, even at low concentration.

Certain resorcinol derivatives are already known in the prior art for their depigmenting activity. In this regard, mention may be made in particular of WO 2005/085
10 169 and WO 2004/017 936.

One subject of the invention is compounds of formula (I) as defined below for their dermatological use for depigmenting the skin.

A subject of the invention is also novel compounds of formula (II) as defined below.

15 A subject of the invention is also a non-therapeutic cosmetic treatment process for depigmenting, lightening and/or bleaching keratin materials, especially the skin, comprising the application to the skin of at least one compound of formula (I) as defined below.

A subject of the invention is also a composition comprising, in a
20 physiologically acceptable medium, at least one compound of formula (II) as defined below.

A subject of the invention is also a non-therapeutic cosmetic process for depigmenting, lightening and/or bleaching keratin materials, especially the skin, comprising the application of the composition described previously.

25 More preferably, it is the process for depigmenting, lightening and/or bleaching the skin.

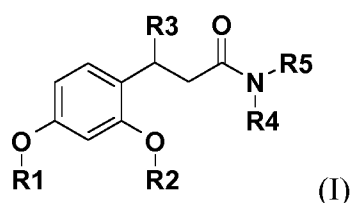
The invention also relates to the non-therapeutic cosmetic use of at least one compound of formula (I) as defined below, as an agent for bleaching, lightening and/or depigmenting keratin materials, especially the skin.

30 The compounds in accordance with the invention, i.e. in particular of formula (I) or of formula (II) as defined below, make it possible to depigment and/or lighten efficiently, or even bleach, human skin. They are in particular intended to be applied to the

skin of individuals bearing brownish pigmentation spots or senescence spots, or to the skin of individuals wishing to combat the appearance of a brownish color caused by melanogenesis.

They may also make it possible to depigment and/or lighten bodily hairs, the eyelashes, head hair, and also the lips and/or the nails.

One subject of the invention is thus compounds of formula (I) as follows, for their use for depigmenting, lightening and/or bleaching the skin:



in which:

R1 and **R2** independently denote:

- a) H,
- b) a saturated C_1-C_{20} or unsaturated C_2-C_{20} , linear or branched C_3-C_{20} , or cyclic C_3-C_8 alkyl radical,
- c) a radical S^* denoting a monosaccharide sugar radical or a polysaccharide sugar radical comprising from 2 to 5 saccharide units, preferably from 2 to 3 saccharide units, preferentially a sugar radical comprising 1 or 2 saccharide units (monosaccharide or disaccharide), said monosaccharide or polysaccharide radical S^* being connected to the rest of the molecule via a bond between the carbon atom C1 of one of the sugars of said monosaccharide or polysaccharide radical, this bond possibly being α or β anomeric,
- d) a radical COR6 in which

R6 denotes a saturated linear C_1-C_{20} alkyl radical, an unsaturated linear C_2-C_{20} alkyl radical, a branched saturated or unsaturated C_3-C_{20} radical or a C_3-C_8 cycloalkyl radical,

R3 denotes a saturated C_1-C_{20} or unsaturated C_2-C_{20} , linear or branched C_3-C_{20} , or cyclic C_3-C_8 alkyl radical,

R4 and **R5** independently denote

a) H;

b) a saturated C₁-C₂₀ or unsaturated C₂-C₂₀ or branched C₃-C₂₀, or cyclic C₃-C₈ alkyl radical, optionally interrupted with one or more non-adjacent heteroatoms or groups, especially one to three, chosen from N, O, -CO- and combinations thereof such as -NHCO-, -NHCONH-, and/or optionally substituted with one or more identical or different groups, especially one to three, chosen from:

i) -OR₇

ii) -SR₇

iii) -NR₇R₈

iv) -CONHR₇

v) -CONR₇R₈

vi) -COOR₇

vii) -NHCONHR₇

viii) -C(O)alkyl(C₁-C₄)

ix) a saturated or unsaturated non-aromatic (hetero)cyclic group, said (hetero)cyclic group being optionally substituted with one or more hydroxyls, especially one to three, and/or with one or more C₁-C₈ alkoxy and/or C₁-C₈ alkyl radicals, especially one to three; one of the chain members of the (hetero)cyclic group possibly being a carbonyl group

x) a C₅-C₁₂ (hetero)aryl group optionally substituted with one or more hydroxyl radicals, especially one to three, and/or with one or more C₁-C₈ alkoxy and/or C₁-C₈ alkyl radicals, especially one to three

xi) -NH-C=NH(NH₂) (guanidine group)

R7 and **R8**, which may be identical or different, being chosen from H, a saturated linear C₁-C₁₀ alkyl group, an unsaturated linear C₂-C₁₀ alkyl group, a saturated or unsaturated branched C₃-C₁₀ alkyl group, and a C₃-C₈ cycloalkyl group; a (C₁-C₄)alkyl(C₆)(hetero)aryl group optionally containing a nitrogen atom, especially a benzyl group; an acetyl radical;

R7 and **R8** possibly forming with the nitrogen that bears them a 5- to 8-membered heterocycle, which may contain one or more heteroatoms or groups chosen

from N, O, -CO-, especially one to three, and/or optionally substituted with a C₁-C₁₀ hydrocarbon-based chain;

c) NR₉R₁₀

with **R₉** and **R₁₀** denoting a radical chosen from

i) -H

ii) a saturated linear C₁-C₁₀ or unsaturated C₂-C₁₀ or branched C₃-C₁₀ or cyclic C₃-C₈ alkyl group, optionally interrupted with one or more heteroatoms or groups chosen from N, O, -CO and combinations thereof such as -NHCO-, -NHCONH-, and/or optionally substituted with one or more identical or different C₁-C₈ alkyl groups, especially one to three

iii) a C₅-C₁₂ (hetero)aryl group, optionally containing one or more heteroatoms chosen from O, N and S, especially one to three, optionally substituted with one or more hydroxyls and/or with one or more C₁-C₈ alkoxy radicals, especially one to three; R₉ and R₁₀ possibly forming with the nitrogen that bears them a 5- to 8-membered heterocycle, which may contain one or more heteroatoms or groups chosen from N, O and -CO-, especially one to three, and/or optionally substituted with a C₁-C₁₀ hydrocarbon-based chain optionally containing one or more radicals chosen from hydroxyl and C₁-C₄ alkoxy, especially one to three;

d) OR₁₁

with **R₁₁** denoting a radical chosen from:

i) -H

ii) a saturated linear C₁-C₁₀ or branched C₃-C₁₀ or cyclic C₃-C₈ alkyl group,

R₄ and **R₅** possibly forming with the nitrogen that bears them a 5- to 8-membered heterocycle, which may contain one or more heteroatoms or groups chosen from N, O, -CO-, especially one to three, and/or optionally substituted with a C₁-C₁₀ hydrocarbon-based chain;

and also the salts thereof, the solvates thereof and the optical and/or geometrical isomers thereof, including enantiomers and diastereoisomers, and the racemic mixtures thereof, alone or as a mixture.

5 In the context of the present invention, it is understood that:

- when the radical S* represents a monosaccharide radical, it may be in pyranose form (the sugar heterocycle which forms it is 6-membered) or furanose form (the sugar heterocycle which forms it is 5-membered); and

10 - when said radical S* represents a polysaccharide radical, it comprises the sequence of 2 to 5 identical or different saccharide units which may be in furanose or pyranose form.

These definitions of the radical S* apply to the compounds of formula (I) and also to the compounds of formula (II) as defined below.

15 Preferably, the polysaccharide is a disaccharide which results from the sequence of a saccharide unit in furanose form and a unit in pyranose form or the sequence of a saccharide unit in pyranose form and a unit in furanose form; whether it is for the monosaccharide or polysaccharide radical, each saccharide unit may be in levorotatory L or dextrorotatory D form, and in α or β anomeric form.

20 Preferably, the monosaccharide is chosen from glucose, galactose, mannose, xylose, lyxose, fucose, arabinose, rhamnose, quinovose, fructose, sorbose, talose, N-acetylglucosamine and N-acetylgalactosamine, and preferably glucose, galactose, mannose, xylose, lyxose, fucose, arabinose, rhamnose and fructose.

25 According to another embodiment, the polysaccharide radical may be formed from 2 to 5 saccharide units, in particular from 2 to 3 and preferably 2 saccharide units, linked together via a 1 $\rightarrow$ 4 (C1 of one saccharide unit $\rightarrow$ C4 of the other saccharide unit) or 1 $\rightarrow$ 3 (C1 of one saccharide unit $\rightarrow$ C3 of the other saccharide unit) or 1 $\rightarrow$ 6 (C1 of one saccharide unit $\rightarrow$ C6 of the other saccharide unit) oxygen atom (oxy) 5, each saccharide
30 unit of which is formed from a heterocycle comprising 4 or 5 carbon atoms.

When the polysaccharide radical is a disaccharide, it may be chosen from: lactose, maltulose, palatinose, lactulose, amygdalose, turanose, cellobiose, isomaltose, rutinose and maltose; and preferably it may be maltose.

5 Still within the context of the present invention, the salts of the compounds of formula (I) and of formula (II) as defined below comprise the conventional non-toxic salts of said compounds such as those formed from acid or base.

As salts of the compound of formula (I) or of formula (II) (when it comprises a quaternizable nitrogen atom),

10 mention may be made of:

a) the salts obtained by addition of the compound of formula (I) or (II) to a mineral acid, chosen especially from hydrochloric, boric, hydrobromic, hydriodic, sulfuric, nitric, carbonic, phosphoric and tetrafluoroboric acids;

15 b) or the salts obtained by addition of the compound of formula (I) or (II) to an organic acid, chosen especially from acetic, propionic, succinic, fumaric, lactic, glycolic, citric, gluconic, salicylic, tartaric, terephthalic, methanesulfonic, ethanesulfonic, benzenesulfonic, toluenesulfonic and triflic acids.

Mention may also be made of the salts obtained by addition of the compound of formula (I) or (II) (when it comprises an acid group) to a mineral base, such as sodium
20 hydroxide, potassium hydroxide, calcium hydroxide, ammonium hydroxide, magnesium hydroxide, lithium hydroxide, and sodium, potassium or calcium carbonate or hydrogen carbonate, for example;

or to an organic base such as a primary, secondary or tertiary alkylamine, for example triethylamine or butylamine. This primary, secondary or tertiary alkylamine may
25 comprise one or more nitrogen and/or oxygen atoms and may thus comprise, for example, one or more alcohol functions; mention may be made in particular of 2-amino-2-methylpropanol, ethanolamine, triethanolamine, 2-dimethylaminopropanol, 2-amino-2-(hydroxymethyl)-1,3-propanediol and 3-(dimethylamino)propylamine.

Mention may also be made of the salts of amino acids, for instance lysine,
30 arginine, guanidine, glutamic acid and aspartic acid. Advantageously, the salts of the compound of formula (I) or (II) (when it comprises an acid group) may be chosen from

alkali metal and alkaline-earth metal salts such as sodium, potassium, calcium or magnesium salts; ammonium salts.

Advantageously, the salts of the compound of formula (I) or (II) (when it comprises a quaternizable nitrogen atom) may be chosen from halides such as chloride or bromide; citrate, acetate, succinate, phosphate, lactate, tartrate.

The acceptable solvates of the compounds described in the present invention comprise conventional solvates such as those formed during the preparation of said compounds owing to the presence of solvents. Mention may be made, by way of example, of the solvates due to the presence of water or of linear or branched alcohols, such as ethanol or isopropanol.

The optical isomers are in particular the enantiomers and the diastereoisomers.

Still in the context of the present invention:

- a "**(C_x-C_y)alkyl group**" denotes an alkyl group comprising from x to y carbon atoms. Such an alkyl group may be linear and saturated and typically contain from 1 to 20 carbon atoms or from 1 to 10 carbon atoms. It may also be linear and typically contain from 2 to 20 carbon atoms or from 2 to 10 carbon atoms. It may also be branched and typically contain from 3 to 20 carbon atoms or from 3 to 10 carbon atoms. An alkyl group may also be cyclic: it is then a cycloalkyl group which may typically contain from 3 to 8 carbon atoms.

Unless otherwise indicated, a "**(C_x-C_y)alkyl group**" denotes a saturated linear alkyl group comprising from x to y carbon atoms.

Preferentially, the linear saturated or branched alkyl groups may be chosen from: methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert-butyl, pentyl, hexyl, heptyl, 2-ethylhexyl, octyl, nonyl, decyl, undecyl, dodecyl, tridecyl, tetradecyl, pentadecyl, hexadecyl, heptadecyl, octadecyl, nonadecyl and eicosyl.

More preferentially, the linear saturated or branched alkyl groups may be chosen from: methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert-butyl, pentyl, hexyl, heptyl, 2-ethylhexyl and octyl.

The cycloalkyl group may be chosen from: cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and cyclooctyl.

- a "**(C_x-C_y)alkoxy group**" denotes a linear and, where appropriate, branched group of formula -O(C_x-C_y)alkyl which may typically contain from 1 to 8 carbon atoms or from 1 to 4 carbon atoms.

5 The alkoxy group may be chosen from methoxy, ethoxy, propoxy and butoxy and may more particularly be a methoxy group.

- a "**saturated or unsaturated nonaromatic (hetero)cyclic group**" denotes a 5- to 12-membered and in particular 5- to 8-membered monocyclic or bicyclic carbocyclic group which may contain one to three heteroatoms or groups chosen from N, O, S and -C(O)-.

10 Such a (hetero)cyclic group may be chosen from cyclohexyl, piperidyl, morpholinyl, piperazinyl, imidazolyl and pyrrolidinyl. Preferentially, it is a piperidyl or morpholinyl ring.

- a "**(hetero)aryl group**" denotes an unsaturated or partially unsaturated monocyclic or bicyclic carbocyclic group containing from 5 to 12 carbon atoms and which
15 may contain one to three heteroatoms chosen from N, O and S.

The aryl radicals may be chosen from phenyl, naphthyl, indenyl, fluorenyl and anthracenyl. Preferentially, it is a phenyl group.

a "**heteroaryl group**" denotes a fused or nonfused, 5- to 22-membered monocyclic or polycyclic group, comprising from 1 to 6 heteroatoms chosen from
20 nitrogen, oxygen and sulfur, and at least one ring of which is aromatic.

The heteroaryl radicals may be chosen from furyl, acridinyl, benzimidazolyl, benzobistriazolyl, benzopyrazolyl, benzopyridazinyl, benzoquinolyl, benzothiazolyl, benzotriazolyl, benzoxazolyl, pyridinyl, tetrazolyl, dihydrothiazolyl, imidazopyridinyl, imidazolyl, indolyl, isoquinolyl, naphthoimidazolyl, naphthooxazolyl, naphthopyrazolyl, oxadiazolyl, oxazolyl, oxazolopyridyl, phenazinyl, phenooxazolyl, pyrazinyl, pyrazolyl, pyrilyl, pyrazoyltriazyl, pyridyl, pyridinoimidazolyl, pyrrolyl, quinolyl, tetrazolyl, thiadiazolyl, thiazolyl, thiazolopyridinyl, thiazoylimidazolyl, thiopyrylyl, triazolyl, xanthyl
25 and the ammonium salt thereof.

30 According to a **first variant**, the compounds of formula (I) are such that **R4 denotes a hydrogen atom**, R1, R2, R3 and R5 having the definitions given previously or hereinbelow, in the preferences.

As examples of compounds of formula (I) according to this variant, mention may be made of compounds **1** to **11**, **14** to **25**, **28** to **37**, **39** to **57** described hereinbelow.

According to a **second variant**, the compounds of formula (I) are such that **R4**
5 **and R5 are identical**, R1, R2 and R3 having the definitions given previously or hereinbelow, in the preferences.

According to this variant, preferably, R4 and R5 are identical and represent a C₁-C₂₀ alkyl radical, preferably a C₁-C₁₀ alkyl radical, optionally substituted with a radical OR7 as defined previously.

10 As examples of compounds of formula (I) according to this second variant, mention may be made of compounds **12**, **13**, **26** described hereinbelow.

According to a **third variant**, the compounds of formula (I) are such that **R4**
and R5 are different and R4 denotes a radical chosen from methyl, ethyl and
15 **hydroxyethyl radicals**, R1, R2, R3 and R5 having the definitions given previously or hereinbelow, in the preferences.

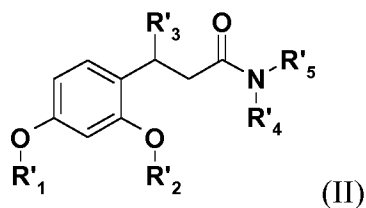
As examples of compounds of formula (I) according to this third variant, mention may be made of compounds **27**, **38** and **58** described hereinbelow.

20 According to a **fourth variant**, the compounds of formula (I) are such that **R4**
and R5 form a 5- to 8-membered saturated or unsaturated non-aromatic heterocycle, which may contain one or more heteroatoms or groups chosen from N, O and -CO-, especially one to three, and/or optionally substituted with a C₁-C₁₀ hydrocarbon-based chain; such a heterocycle possibly being chosen from pyrrolidine, piperidine, morpholine
25 and piperazine, R1, R2 and R3 having the definitions given previously or hereinbelow, in the preferences.

As examples of compounds of formula (I) according to this third variant, mention may be made of compound **59**, described hereinbelow.

According to a further variant, the compound of formula (I) is compound 25 as
30 defined herein after and illustrated in examples 21 and 58.

Among the compounds of formula (I), some are novel and constitute another subject of the invention, as do the compositions, in particular the cosmetic compositions, which contain them; they are the compounds of formula (II) below:



in which:

R'1 and **R'2** independently denote

a) H;

b) a saturated C_1 - C_{20} or unsaturated linear or branched C_3 - C_{20} , or cyclic C_3 - C_8 alkyl radical,

c) a radical S^* denoting a monosaccharide sugar radical or a polysaccharide sugar radical comprising from 2 to 5 saccharide units, preferably from 2 to 3 saccharide units, preferentially a sugar radical comprising 1 or 2 saccharide units (monosaccharide or disaccharide), said monosaccharide or polysaccharide radical S^* being connected to the rest of the molecule via a bond between the carbon atom C1 of one of the sugars of said monosaccharide or polysaccharide radical, this bond possibly being α or β anomeric,

d) a radical COR'6

in which R'6 denotes a saturated linear C_1 - C_{20} alkyl radical, an unsaturated linear C_2 - C_{20} alkyl radical, a branched saturated or unsaturated C_3 - C_{20} radical or a C_3 - C_8 cycloalkyl radical,

it being understood that R'1 and R'2 cannot simultaneously denote a methyl radical,

R'3 denotes a saturated C_1 - C_{20} or unsaturated C_2 - C_{20} , linear or branched C_3 - C_{20} , or cyclic C_3 - C_8 alkyl radical,

R'4 and **R'5** independently denote

a) -H;

b) a saturated C₁-C₂₀ or unsaturated C₂-C₂₀ or branched C₃-C₂₀, or cyclic C₃-C₈ alkyl radical, optionally interrupted with one or more non-adjacent heteroatoms or groups, chosen from N, O, -CO- and combinations thereof such as -NHCO-, -NHCONH-,
 5 especially one to three, and/or optionally substituted with one or more identical or different groups, especially one to three, chosen from:

i) -OR'⁷

ii) -SR'⁷

iii) -NR'⁷R'⁸

10 iv) -CONHR'⁷

v) -CONR'⁷R'⁸

vi) -COOR'⁷

vii) -NHCONHR'⁷

viii) -C(O)(C₁-C₄)alkyl

15 ix) a saturated or unsaturated non-aromatic (hetero)cyclic group, said (hetero)cyclic group being optionally substituted with one or more hydroxyls, especially one to three, and/or with one or more C₁-C₈ alkoxy or C₁-C₈ alkyl radicals, especially one to three; one of the chain members possibly being a carbonyl group;

x) a C₅-C₁₂ (hetero)aryl group optionally substituted with one or more hydroxyl
 20 radicals, especially one to three, and/or with one or more C₁-C₈ alkoxy and/or C₁-C₈ alkyl radicals, especially one to three

xi) -NH-C=NH(NH₂) (guanidine group)

R'⁷ and **R'⁸**, which may be identical or different, being chosen from H, a
 25 saturated linear C₁-C₁₀ alkyl group, an unsaturated linear or branched C₂-C₁₀ alkyl group, a saturated or unsaturated branched C₃-C₁₀ alkyl group, and a C₃-C₈ cycloalkyl group; a (C₁-C₄)alkyl(C₆)(hetero)aryl group optionally containing a nitrogen atom, especially a benzyl group; an acetyl radical;

R'⁷ and R'⁸ possibly forming with the nitrogen that bears them a 5- to 8-
 30 membered heterocycle, which may contain one or more heteroatoms or groups chosen from N, O, -CO-, especially one to three, and/or optionally substituted with a C₁-C₁₀ hydrocarbon-based chain;

c) NR'9R'10

R'9 and R'10 denoting a radical chosen from

i) -H

5 ii) a saturated linear C₁-C₁₀ or unsaturated C₂-C₁₀ or branched C₃-C₁₀ or cyclic C₃-C₈ alkyl group, optionally interrupted with one or more non-adjacent heteroatoms or groups chosen from N, O, -CO and combinations thereof such as -NHCO-, -NHCONH-, especially one to three, and/or optionally substituted with one or more identical or different C₁-C₈ alkyl groups, especially one to three;

10 iii) a C₅-C₁₂ (hetero)aryl group, optionally containing one or more non-adjacent heteroatoms chosen from O, N and S, especially one to three, optionally substituted with one or more hydroxyls and/or with one or more C₁-C₈ alkoxy radicals, especially one to three; R₉ and R₁₀ possibly forming with the nitrogen that bears them a 5- to 8-membered heterocycle, which may contain one or more heteroatoms or groups chosen from N, O
15 and -CO-, especially one to three, and/or optionally substituted with a C₁-C₁₀ hydrocarbon-based chain optionally containing one or more radicals chosen from hydroxyl and C₁-C₄ alkoxy, especially one to three;

d) OR'11

20 with R'11 denoting a radical chosen from:

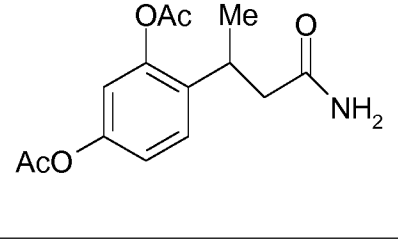
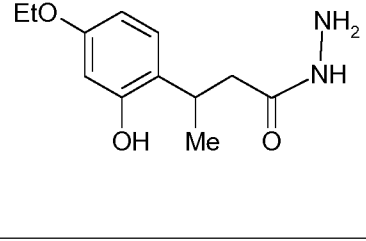
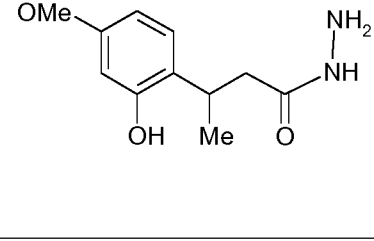
i) -H

ii) a saturated linear C₁-C₁₀ or branched C₃-C₁₀ or cyclic C₃-C₈ alkyl group,

R'4 and R'5 possibly forming with the nitrogen that bears them a 5- to 8-
25 membered heterocycle, which may contain one or more heteroatoms or groups chosen from N, O, -CO-, especially one to three, and/or optionally substituted with a C₁-C₁₀ hydrocarbon-based chain

and also the salts thereof, the solvates thereof and the optical and/or
30 geometrical isomers thereof, including enantiomers and diastereoisomers, and the racemic mixtures thereof,

with the exception of the following 3 compounds:

		
CAS 200056-48-0	CAS = 24535-08-8	CAS = 1020241-68-2

The four variants described above for the compounds of formula (I) may be applied to the compounds of formula (II) and also form part of the invention.

5

It is understood in the context of the present invention that when a first radical is substituted with one or more second radicals, the term "more" may mean two or three.

Similarly, when a first cyclic radical optionally contains one or more heteroatoms or groups, the term "more" may mean two or three.

10

Preferably, the compounds of formula (I) are such that:

R1 and **R2** independently denote

a) H;

15

b) a saturated C₁-C₁₀ or unsaturated C₂-C₁₀, linear or branched C₃-C₁₀, or cyclic C₃-C₆ alkyl radical,

c) a radical S* as defined previously and in particular a glucosyl, xylosyl, mannosyl, fucosyl or maltosyl radical

d) a radical COR₆ in which

20

R₆ denotes a saturated linear C₁-C₁₅ alkyl radical, an unsaturated linear C₂-C₁₅ alkyl radical or a branched saturated or unsaturated C₃-C₁₅ alkyl radical,

R3 denotes a saturated linear C₁-C₁₀ alkyl radical, an unsaturated linear C₂-C₁₀ alkyl radical, a branched saturated or unsaturated C₃-C₁₀ alkyl radical or a C₃-C₆ cycloalkyl radical,

25

R4 and **R5** independently denote

a) -H;

b) a saturated linear C₁-C₁₅ alkyl radical, an unsaturated linear C₂-C₁₅ alkyl radical, a saturated or unsaturated branched C₃-C₁₅ alkyl radical or a C₃-C₈ cycloalkyl radical, optionally interrupted with one or more non-adjacent heteroatoms or groups
5 chosen from N, O and -CO- and combinations thereof such as -NHCO-, -NHCONH-, especially one to three, and/or optionally substituted with one or more identical or different groups, especially one or two, chosen from:

i) -OR₇ -OR₇ such as a methyl or ethyl or isopropyl radical

ii) -SR₇

10 iii) -NR₇R₈

iv) -CONHR₇

v) -CONR₇R₈

vi) -COOR₇

vii) -NHCONHR₇

15 viii) -C(O)(C₁-C₄)alkyl

ix) a saturated or unsaturated non-aromatic (hetero)cyclic group, said (hetero)cyclic group being optionally substituted with one or more hydroxyls and/or with one or more C₁-C₈ alkoxy and/or C₁-C₈ alkyl radicals, especially one to three;

x) a C₅-C₁₂ (hetero)aryl group optionally substituted with one or more hydroxyl
20 radicals, especially one to three, and/or with one or more C₁-C₈ alkoxy and/or C₁-C₈ alkyl radicals, especially one to three

xi) -NH-C=NH(NH₂) (guanidine group)

R₇ and **R₈**, which may be identical or different, being chosen from H, a
25 saturated linear C₁-C₁₀ alkyl group, an unsaturated linear C₂-C₁₀ alkyl group, a saturated or unsaturated branched C₃-C₁₀ alkyl group, and a C₃-C₈ cycloalkyl group; a (C₁-C₄)alkyl(C₆)(hetero)aryl group optionally containing a nitrogen atom, especially a benzyl group; an acetyl radical;

R₇ and **R₈** possibly forming with the nitrogen that bears them a 5- to 8-
30 membered heterocycle, which may contain one or more heteroatoms or groups chosen from N, O, -CO-, and/or optionally substituted with a C₁-C₁₀ hydrocarbon-based chain, especially one to three;

R4 and **R5** possibly forming with the nitrogen that bears them a 5- to 8-membered heterocycle, which may contain one or more heteroatoms or groups chosen from N, O, -CO-, and/or optionally substituted with a C₁-C₁₀ hydrocarbon-based chain
5 such as pyrrolidine, piperidine, morpholine or piperazine.

Preferably, the compounds of formula (II) are such that:

R'1 and **R'2** independently denote

- 10 a) H;
- b) a saturated linear C₁-C₁₀ alkyl radical, an unsaturated linear or branched C₂-C₁₀ alkyl radical, a branched saturated or unsaturated C₃-C₁₀ alkyl group or a C₃-C₆ cycloalkyl group,
- 15 c) a radical S* denoting a monosaccharide sugar radical or a polysaccharide sugar radical comprising from 2 to 5 saccharide units, preferably from 2 to 3 saccharide units, preferentially a sugar radical comprising 1 or 2 saccharide units (monosaccharide or disaccharide), said monosaccharide or polysaccharide radical S* being connected to the rest of the molecule via a bond between the carbon atom C1 of one of the sugars of said
20 monosaccharide or polysaccharide radical, this bond possibly being α or β anomeric; and in particular a glucosyl, xylosyl, mannosyl, fucosyl or maltosyl radical
- d) a group COR'6 in which
R'6 denotes a saturated linear C₁-C₁₅ alkyl group or an unsaturated linear C₂-
25 C₁₅ alkyl group

it being understood that R'1 and R'2 cannot simultaneously denote a methyl radical

30 **R'3** denotes a saturated linear C₁-C₁₀ alkyl radical, an unsaturated linear C₂-C₁₀ alkyl radical, a branched saturated or unsaturated C₃-C₁₀ alkyl radical or a C₃-C₆ cycloalkyl radical,

R'4 and **R'5** independently denote

a) -H;

b) a linear C₁-C₁₅ alkyl radical, an unsaturated linear C₂-C₁₅ alkyl radical, a saturated or unsaturated branched C₃-C₁₅ radical or a C₃-C₈ cycloalkyl radical, optionally interrupted with one or more heteroatoms or groups chosen from N, O and -CO- and a combination thereof such as -NHCO-, -NHCONH-, especially one to three, and/or optionally substituted with one or more identical or different groups, especially one to three, chosen from:

i) -OR'⁷ such as a methyl or ethyl or isopropyl radical

ii) -SR'⁷

iii) -NR'⁷R'⁸

iv) -CONHR'⁷

v) -CONR'⁷R'⁸

vi) -COOR'⁷

vii) -NHCONHR'⁷

viii) -C(O)(C₁-C₄)alkyl

ix) a saturated or unsaturated non-aromatic heterocyclic group, said (hetero)cyclic group being optionally substituted with one or more hydroxyl radicals, especially one to three, and/or with one or more C₁-C₈ alkoxy or C₁-C₈ alkyl radicals, especially one to three; one of the chain members possibly being a carbonyl group;

x) a C₅-C₁₂ (hetero)aryl group optionally substituted with one or more hydroxyl radicals, especially one to three, and/or with one or more C₁-C₈ alkoxy and/or C₁-C₈ alkyl radicals, especially one to three

xi) -NH-C=NH(NH₂) (guanidine group)

R'7 and **R'8**, which may be identical or different, being chosen from H, a saturated linear C₁-C₁₀ alkyl group, an unsaturated linear or branched C₂-C₁₀ alkyl radical, a saturated or unsaturated branched C₃-C₁₀ alkyl radical, and a C₃-C₈ cycloalkyl radical; a (C₁-C₄)alkyl(C₆)(hetero)aryl group optionally containing a nitrogen atom, especially a benzyl group; an acetyl radical;

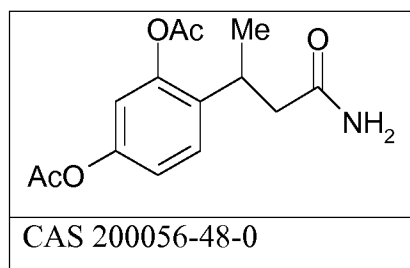
R'7 and **R'8** possibly forming with the nitrogen that bears them a 5- to 8-membered heterocycle, which may contain one or more heteroatoms or groups chosen from N, O, -CO-, especially one to three, and/or optionally substituted with a C₁-C₁₀ hydrocarbon-based chain;

5

R'4 and **R'5** possibly forming with the nitrogen that bears them a 5- to 8-membered heterocycle, which may contain one or more heteroatoms or groups chosen from N, O and -CO-, especially one or two, and/or optionally substituted with a C₁-C₁₀ hydrocarbon-based chain such as pyrrolidine, piperidine, morpholine or piperazine;

10

and with the exception of the following compound:



Even more preferentially, the compounds of formula (I) are such that:

15

R1 and **R2** independently denote

- H;
- a saturated linear C₁-C₆ alkyl radical, an unsaturated linear C₂-C₆ alkyl radical or a branched saturated or unsaturated C₃-C₆ alkyl radical, such as ethyl, isopropyl and n-propyl radicals
- a radical S* denoting a monosaccharide sugar radical or a polysaccharide sugar radical comprising from 2 to 5 saccharide units, preferably from 2 to 3 saccharide units, preferentially a sugar radical comprising 1 or 2 saccharide units (monosaccharide or disaccharide), said monosaccharide or polysaccharide radical S* being connected to the rest of the molecule via a bond between the carbon atom C₁ of one of the sugars of said

25

monosaccharide or polysaccharide radical, this bond possibly being α or β anomeric, S* in particular denoting a glucose radical

d) a radical COR6 in which

R6 denotes a saturated linear C₁-C₁₅ alkyl radical, such as a methyl or hexyl

5 radical

R3 denotes a saturated linear C₁-C₆ alkyl radical, a saturated or unsaturated branched C₃-C₆ alkyl radical or a C₃-C₆ cycloalkyl radical, such as a methyl, ethyl or isopropyl radical

10

R4 and **R5** independently denote

a) -H;

b) a linear C₁-C₁₅ alkyl group, a branched saturated or unsaturated C₃-C₁₅ alkyl group or a C₃-C₈ cycloalkyl group, optionally interrupted with one or more non-adjacent heteroatoms or groups chosen from N, O and -CO- and combinations thereof such as -NHCO-, -NHCONH-, especially one to three, and/or optionally substituted with one or more identical or different groups, especially one to three, chosen from:

15

i) -OR7 such as a methyl or ethyl or isopropyl radical

ii) -SR7 such as SH or SMe

20

iii) -NR7R8 such as NH₂

iv) -CONHR7 such as CONH₂

v) -COOR7 such as CO₂Me, CO₂Et and CO₂iPr

vi) a saturated or unsaturated non-aromatic (hetero)cyclic group such as cyclohexyl, optionally substituted with one or more hydroxyl radicals, especially one to three, and/or with one or more C₁-C₄ alkoxy or C₁-C₄ alkyl radicals, especially one to three; one of the chain members possibly being a carbonyl group

25

vii) a C₅-C₁₂ (hetero)aryl group such as a phenyl, imidazolyl and indolyl radical, optionally substituted with one or more hydroxyl radicals, especially one to three, and/or with one or more C₁-C₈ alkoxy and/or C₁-C₈ alkyl radicals, especially one to three

30

R7 and **R8**, which may be identical or different, being chosen from H, a saturated linear C₁-C₆ alkyl group, a branched saturated or unsaturated C₃-C₆ alkyl group

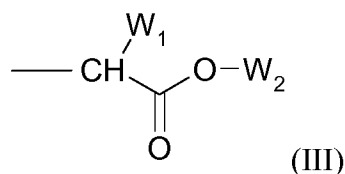
and a (C₁-C₄)alkyl(C₆)(hetero)aryl group optionally containing a nitrogen atom, especially a benzyl group; an acetyl radical;

R7 and **R8** possibly forming with the nitrogen that bears them a 5- to 8-membered heterocycle, which may contain one or more heteroatoms or groups chosen from N, O, -CO-, especially one to three, and/or optionally substituted with a C₁-C₁₀ hydrocarbon-based chain;

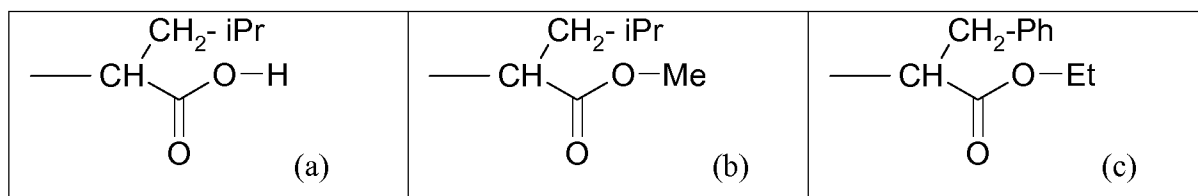
R4 and R5 possibly forming with the nitrogen that bears them a heterocycle chosen from pyrrolidine, piperidine, morpholine and piperazine.

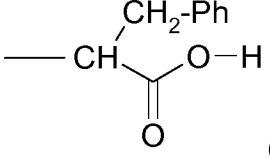
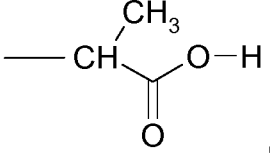
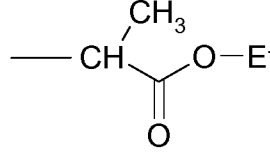
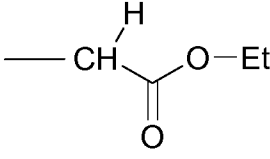
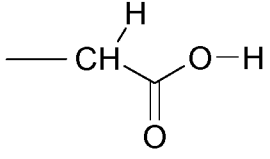
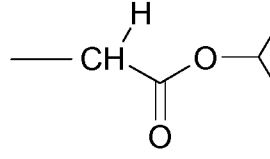
As examples of radicals R4, mention may be made, for example, of H, methyl, ethyl, n-butyl and -(CH₂)_xOMe radicals with x denoting an integer ranging from 1 to 4, limits inclusive, in particular -(CH₂)₂OMe.

As examples of radicals R5, mention may be made, for example, of a hydrogen atom, the radicals: n-butyl; -(CH₂)_xOT with x denoting an integer ranging from 1 to 4, limits inclusive, and T denoting a methyl or ethyl radical, in particular -(CH₂)₃OMe, -(CH₂)₃OEt, -(CH₂)₂OMe, ethyl; n-propyl; n-pentyl; n-hexyl; isopropyl; isobutyl; -(CH₂)_x-iPr, x having the same definition as previously; cyclohexyl; -CH₂-cyclohexyl; a radical of formula (III)

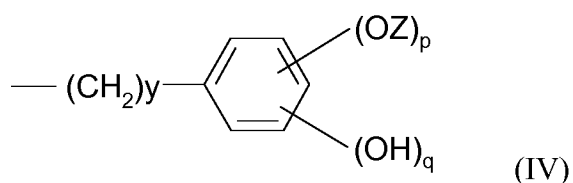


in which W1 denotes a saturated linear or branched C₁-C₆ alkyl radical optionally substituted with a phenyl radical and W2 denotes H or a saturated linear or branched C₁-C₄ alkyl radical, such as the radicals of formulae (a) to (i) below:



 (d)	 (e)	 (f)
 (g)	 (h)	 (i)

or alternatively a radical of formula (IV)



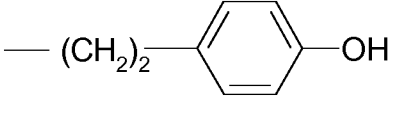
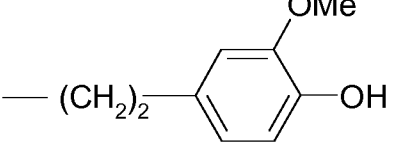
with y denoting an integer between 1 and 4, limits inclusive,

p being equal to 0, 1, 2 or 3,

q being equal to 0, 1, 2 or 3, and p+q < 6

Z denoting a saturated linear C₁-C₄ alkyl radical such as methyl,

such as the radicals (j) and (k) below:

 (j)	 (k)
--	---

Even more preferentially, the compounds of formula (I) denote compounds **1** to **59** as listed in Table 1 below, and also the salts and/or solvates thereof.

More particularly, the compounds of formula (II) denote compounds for which:

R'1 and **R'2** independently denote

a) H;

b) a saturated linear C₁-C₆ alkyl group or an saturated or unsaturated branched C₃-C₆ alkyl group such as ethyl, isopropyl and n-propyl radicals

c) a radical S* denoting a monosaccharide sugar radical or a polysaccharide sugar radical comprising from 2 to 5 saccharide units, preferably from 2 to 3 saccharide units, preferentially a sugar radical comprising 1 or 2 saccharide units (monosaccharide or disaccharide), said monosaccharide or polysaccharide radical S* being connected to the rest of the molecule via a bond between the carbon atom C1 of one of the sugars of said monosaccharide or polysaccharide radical, this bond possibly being α or β anomeric, S* in particular denoting a glucose radical

d) a group COR'6

with R'6 denoting a saturated linear C₁-C₁₅ alkyl radical or an unsaturated linear C₂-C₁₅ group, preferably a saturated linear C₁-C₁₅ alkyl radical, such as a methyl or hexyl radical

it being understood that R'1 and R'2 cannot simultaneously denote a methyl radical

R'3 denotes a saturated linear C₁-C₆ alkyl radical, an unsaturated linear C₂-C₁₀ alkyl radical, a saturated or unsaturated branched C₃-C₆ alkyl radical or a C₃-C₆ cycloalkyl radical, such as a methyl, ethyl or isopropyl radical

R'4 and **R'5** independently denote

a) -H;

b) a saturated linear C₁-C₁₅ alkyl radical, an unsaturated linear C₂-C₁₅ alkyl radical, a saturated or unsaturated branched C₃-C₁₅ radical or a C₃-C₈ cycloalkyl radical, optionally interrupted with one or more non-adjacent heteroatoms or groups chosen from N, O and -CO- and combinations thereof such as -NHCO-, -NHCONH-, especially one to three, and/or optionally substituted with one or more identical or different groups, especially one to three, chosen from:

i) -OR7 such as a methyl or ethyl or isopropyl radical

ii) -SR7 such as SH or SMe

iii) -NR7R8 such as NH₂

iv) $-\text{CONHR}_7$ such as CONH_2

v) $-\text{COOR}_7$ such as CO_2Me , CO_2Et and CO_2iPr

vi) a saturated or unsaturated non-aromatic (hetero)cyclic group such as cyclohexyl, optionally substituted with one or more hydroxyl radicals, especially one to three, and/or with one or more $\text{C}_1\text{-C}_4$ alkoxy or $\text{C}_1\text{-C}_4$ alkyl radicals, especially one to three;

vii) a $\text{C}_5\text{-C}_{12}$ (hetero)aryl group such as a phenyl, imidazolyl and indolyl radical, optionally substituted with one or more hydroxyl radicals, especially one to three, and/or with one or more $\text{C}_1\text{-C}_8$ alkoxy and/or $\text{C}_1\text{-C}_8$ alkyl radicals, especially one to three

viii) $-\text{NH-C}=\text{NH}(\text{NH}_2)$ (guanidine group)

R'7 and **R'8**, which may be identical or different, being chosen from H, a saturated linear $\text{C}_1\text{-C}_{10}$ alkyl group, an unsaturated linear $\text{C}_2\text{-C}_{10}$ alkyl group, a saturated or unsaturated branched $\text{C}_3\text{-C}_{10}$ alkyl group, and a $\text{C}_3\text{-C}_8$ cycloalkyl group; a $(\text{C}_1\text{-C}_4)\text{alkyl}(\text{C}_6)(\text{hetero})\text{aryl}$ group optionally containing a nitrogen atom, especially a benzyl group; an acetyl radical;

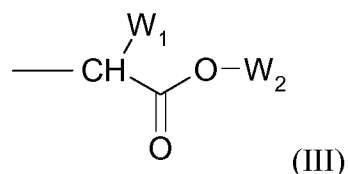
R'7 and **R'8** possibly forming with the nitrogen that bears them a 5- to 8-membered heterocycle, which may contain one or more heteroatoms or groups, especially one or two chosen from N, O, $-\text{CO}-$ and/or optionally substituted with a $\text{C}_1\text{-C}_{10}$ hydrocarbon-based chain;

R'4 and **R'5** possibly forming with the nitrogen that bears them a heterocycle chosen from pyrrolidine, piperidine, morpholine and piperazine.

As examples of radicals **R'4**, mention may be made, for example, of H, methyl, ethyl, n-butyl and $-(\text{CH}_2)_x\text{OMe}$ radicals with x denoting an integer ranging from 1 to 4, limits inclusive, in particular $-(\text{CH}_2)_2\text{OMe}$.

As examples of radicals **R'5**, mention may be made, for example, of the radicals: n-butyl; $-(\text{CH}_2)_x\text{OT}$ with x denoting an integer ranging from 1 to 4, limits inclusive, and T denoting a methyl or ethyl radical, in particular $-(\text{CH}_2)_3\text{OMe}$, $-(\text{CH}_2)_3\text{OEt}$, $-(\text{CH}_2)_2\text{OMe}$,

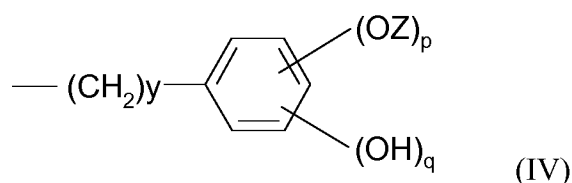
-(CH₂)₂OMe; ethyl; n-propyl; n-pentyl; n-hexyl; isopropyl; isobutyl; -(CH₂)_x-iPr, x having the same definition as previously; cyclohexyl; -CH₂-cyclohexyl; a radical of formula (III)



in which W1 denotes a saturated linear or branched C₁-C₆ alkyl radical optionally substituted with a phenyl radical and W2 denotes H or a saturated linear or branched C₁-C₄ alkyl radical, such as the radicals of formulae (a) to (i) below:

$\begin{array}{c} \text{---CH} \begin{array}{l} \nearrow \text{CH}_2\text{-iPr} \\ \searrow \text{C(=O)O-H} \end{array} \end{array} \quad \text{(a)}$	$\begin{array}{c} \text{---CH} \begin{array}{l} \nearrow \text{CH}_2\text{-iPr} \\ \searrow \text{C(=O)O-Me} \end{array} \end{array} \quad \text{(b)}$	$\begin{array}{c} \text{---CH} \begin{array}{l} \nearrow \text{CH}_2\text{-Ph} \\ \searrow \text{C(=O)O-Et} \end{array} \end{array} \quad \text{(c)}$
$\begin{array}{c} \text{---CH} \begin{array}{l} \nearrow \text{CH}_2\text{-Ph} \\ \searrow \text{C(=O)O-H} \end{array} \end{array} \quad \text{(d)}$	$\begin{array}{c} \text{---CH} \begin{array}{l} \nearrow \text{CH}_3 \\ \searrow \text{C(=O)O-H} \end{array} \end{array} \quad \text{(e)}$	$\begin{array}{c} \text{---CH} \begin{array}{l} \nearrow \text{CH}_3 \\ \searrow \text{C(=O)O-Et} \end{array} \end{array} \quad \text{(f)}$
$\begin{array}{c} \text{---CH} \begin{array}{l} \nearrow \text{H} \\ \searrow \text{C(=O)O-Et} \end{array} \end{array} \quad \text{(g)}$	$\begin{array}{c} \text{---CH} \begin{array}{l} \nearrow \text{H} \\ \searrow \text{C(=O)O-H} \end{array} \end{array} \quad \text{(h)}$	$\begin{array}{c} \text{---CH} \begin{array}{l} \nearrow \text{H} \\ \searrow \text{C(=O)O-} \begin{array}{c} \diagup \quad \diagdown \\ \quad \end{array} \end{array} \end{array} \quad \text{(i)}$

or alternatively a radical of formula (IV)



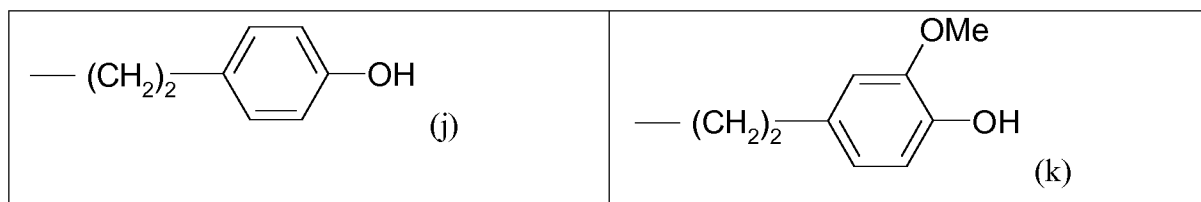
with y denoting an integer between 1 and 4, limits inclusive,

p being equal to 0, 1, 2 or 3,

q being equal to 0, 1, 2 or 3, and p+q < 6

Z denoting a saturated linear C₁-C₄ alkyl radical such as methyl,

such as the radicals (j) and (k) below:



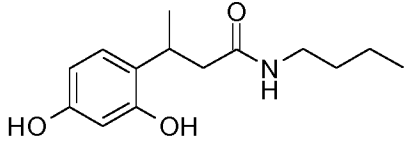
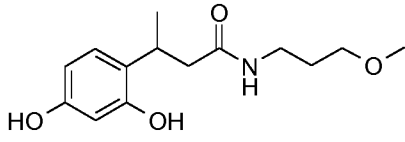
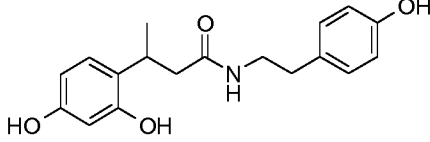
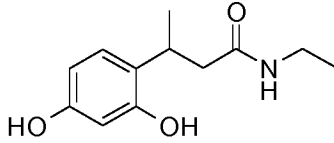
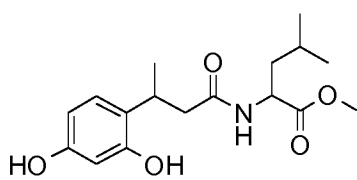
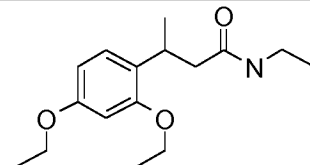
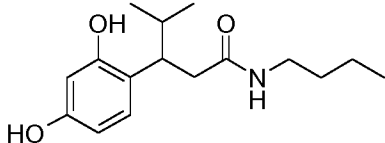
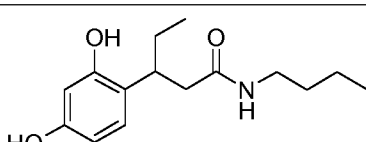
Even more preferentially, the compounds of formula (II) denote compounds **1** to **59** as listed in Table 1 below, and also the salts and/or solvates thereof.

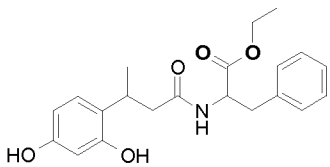
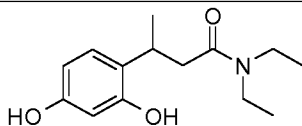
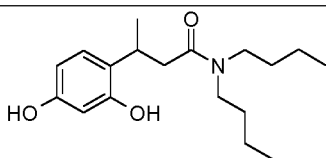
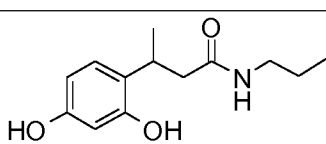
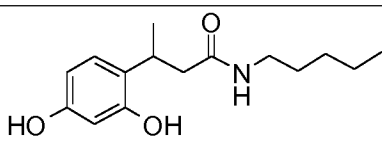
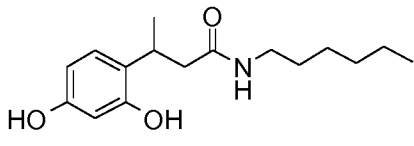
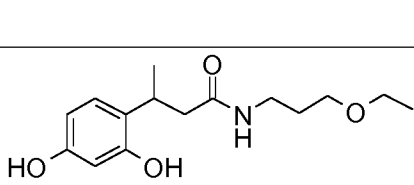
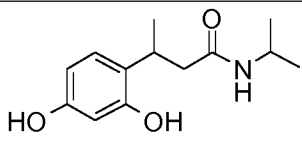
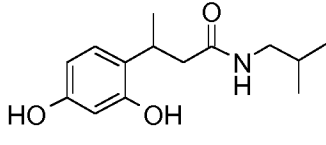
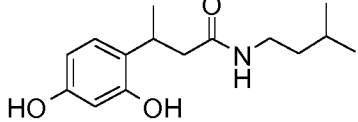
- 5 Examples of compounds of formulae (I) and (II) of the invention are collated in Table 1 below.

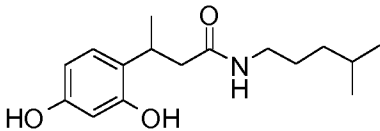
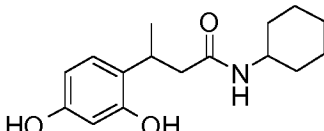
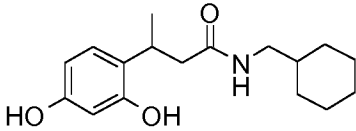
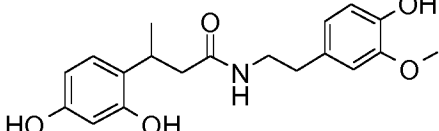
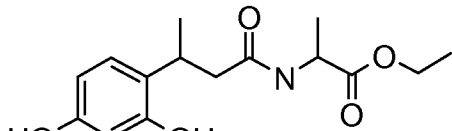
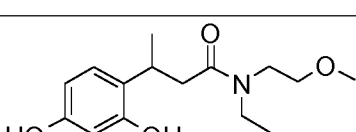
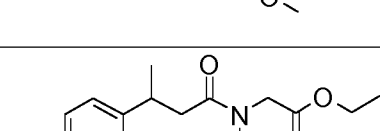
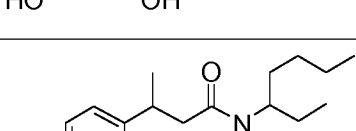
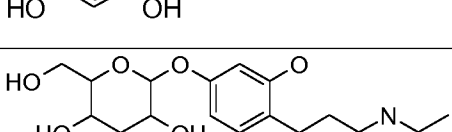
Table 1

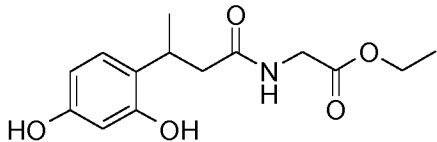
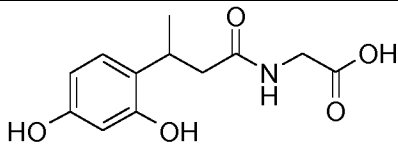
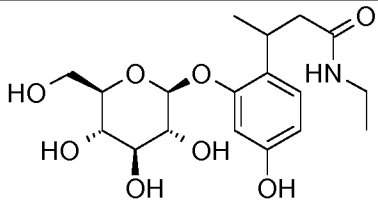
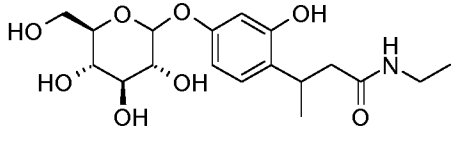
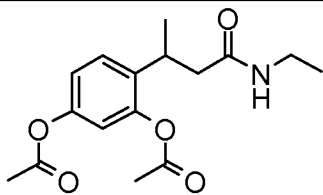
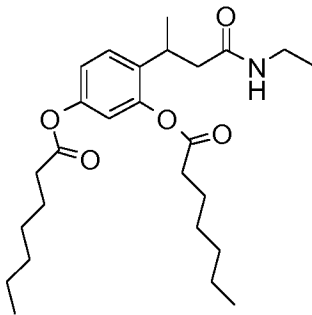
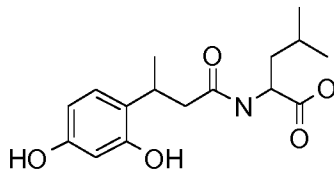
The numbers in the table correspond to the number is used in the examples

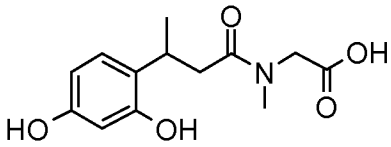
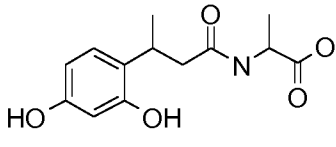
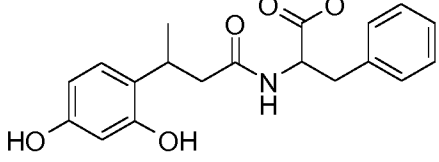
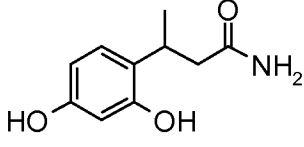
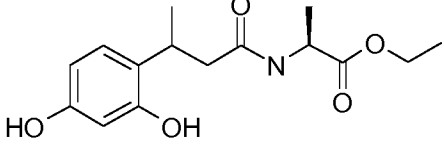
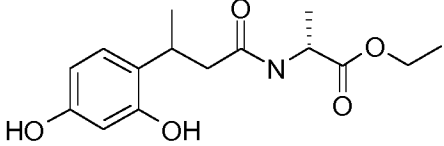
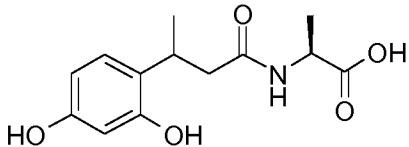
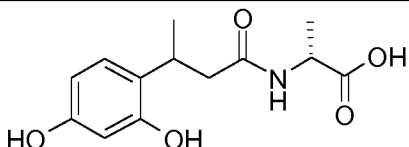
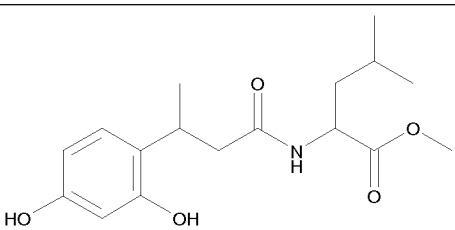
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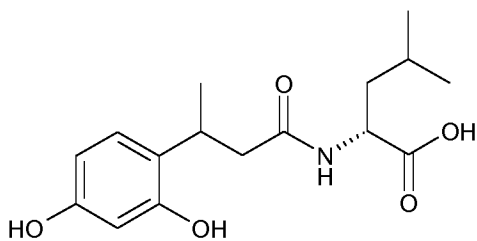
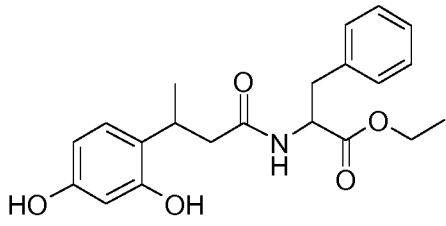
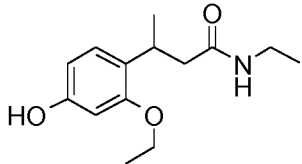
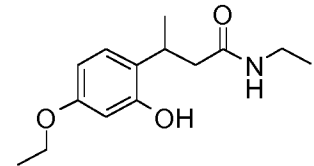
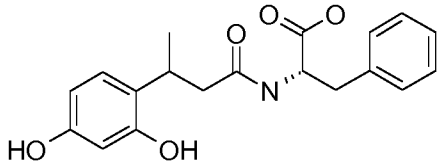
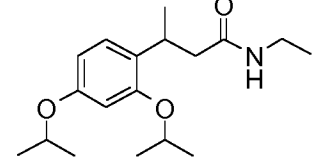
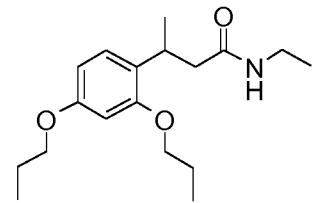
Comp ound No.	Structure	Chemical name
1		N-butyl-3-(2,4-dihydroxyphenyl)butanamide
2		3-(2,4-dihydroxyphenyl)-N-(3-methoxypropyl)butanamide
3		N-(4-hydroxyphenethyl)-3-(2,4-dihydroxyphenyl)butanamide
4		3-(2,4-dihydroxyphenyl)-N-ethylbutanamide
5		methyl 2-(3-(2,4-dihydroxyphenyl)butanamido)-4-methylpentanoate
6		3-(2,4-diethoxyphenyl)-N-ethylbutanamide
9		N-butyl-3-(2,4-dihydroxyphenyl)-4-methylpentanamide
10		N-butyl-3-(2,4-dihydroxyphenyl)pentanamide

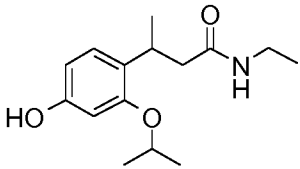
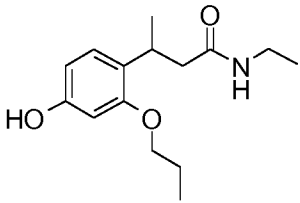
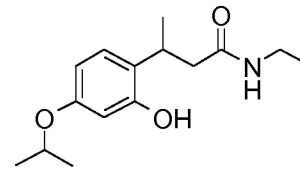
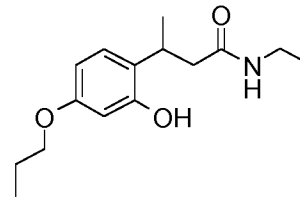
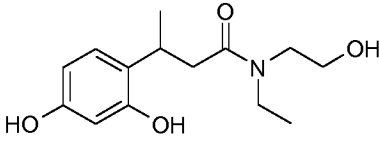
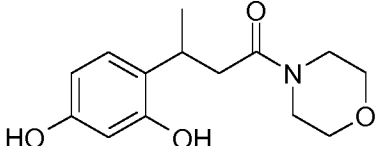
11		ethyl 2-(3-(2,4-dihydroxyphenyl)butanamido)-3-phenylpropanoate
12		3-(2,4-dihydroxyphenyl)-N,N-diethylbutanamide
13		N,N-dibutyl-3-(2,4-dihydroxyphenyl)butanamide
14		3-(2,4-dihydroxyphenyl)-N-propylbutanamide
15		3-(2,4-dihydroxyphenyl)-N-pentylbutanamide
16		3-(2,4-dihydroxyphenyl)-N-hexylbutanamide
17		3-(2,4-dihydroxyphenyl)-N-(3-ethoxypropyl)butanamide
18		3-(2,4-dihydroxyphenyl)-N-isopropylbutanamide
19		3-(2,4-dihydroxyphenyl)-N-isobutylbutanamide
20		3-(2,4-dihydroxyphenyl)-N-isopentylbutanamide

21		3-(2,4-dihydroxyphenyl)-N-(4-methylpentyl)butanamide
22		N-cyclohexyl-3-(2,4-dihydroxyphenyl)butanamide
23		N-(cyclohexylmethyl)-3-(2,4-dihydroxyphenyl)butanamide
24		N-(4-hydroxy-3-methoxyphenethyl)-3-(2,4-dihydroxyphenyl)butanamide
25		ethyl 2-(3-(2,4-dihydroxyphenyl)butanamido)propanoate
26		3-(2,4-dihydroxyphenyl)-N,N-bis(2-methoxyethyl)butanamide
27		ethyl 2-(3-(2,4-dihydroxyphenyl)-N-methylbutanamido)acetate
28		3-(2,4-dihydroxyphenyl)-N-(heptan-3-yl)butanamide
29		N-ethyl-3-(2-hydroxy-4-((2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)-tetrahydro-2H-pyran-2-yloxy)phenyl)butanamide
30		3-(2,4-dihydroxyphenyl)-N-(2-hydroxyethyl)butanamide

31		ethyl 2-(3-(2,4-dihydroxyphenyl)butanamido)acetate
32		2-(3-(2,4-dihydroxyphenyl)butanamido)acetic acid
33		N-ethyl-3-(4-hydroxy-2-((2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)-tetrahydro-2H-pyran-2-yloxy)phenyl)butanamide
34		N-ethyl-3-(2-hydroxy-4-((3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)-tetrahydro-2H-pyran-2-yloxy)phenyl)butanamide
35		4-(4-(ethylamino)-4-oxobutan-2-yl)-1,3-phenylene diacetate
36		4-(4-(ethylamino)-4-oxobutan-2-yl)-1,3-phenylene diheptanoate
37		2-(3-(2,4-dihydroxyphenyl)butanamido)-4-methylpentanoic acid

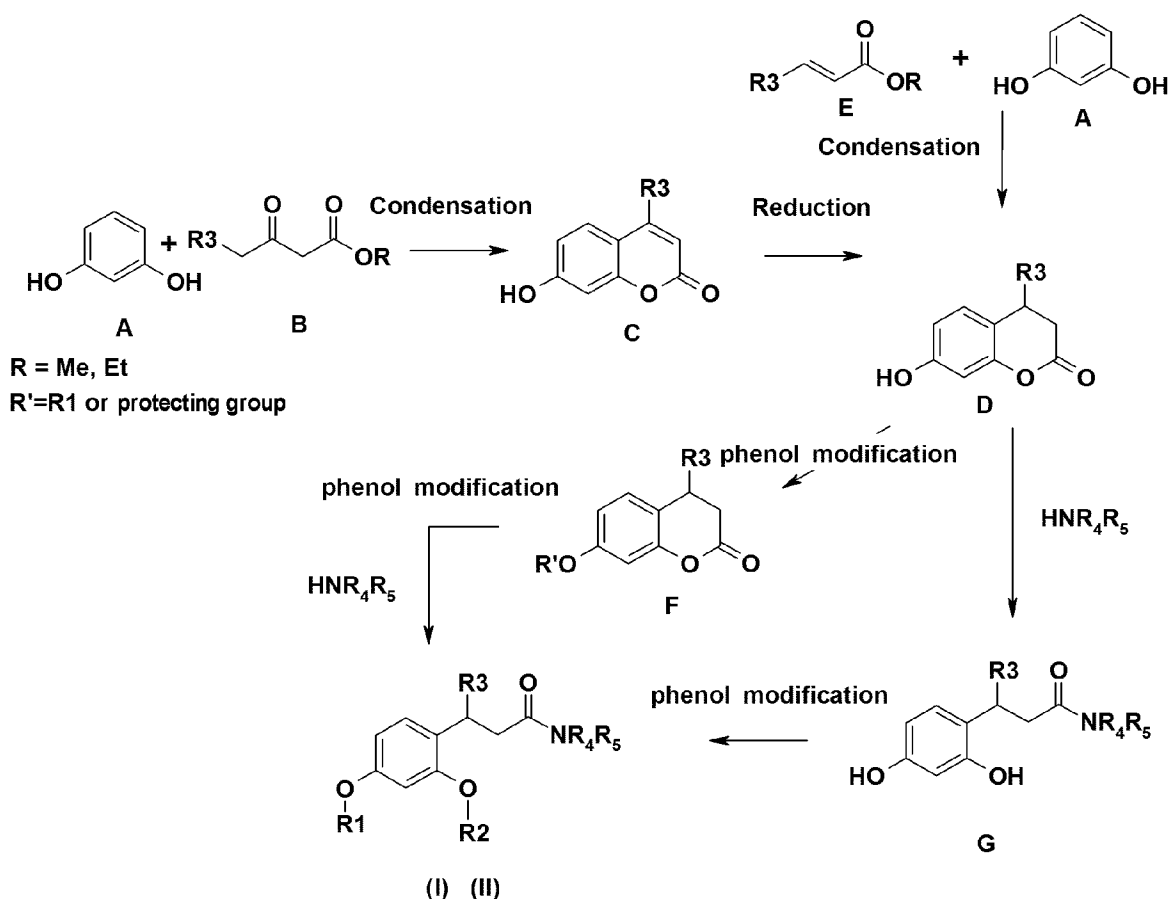
38		2-(3-(2,4-dihydroxyphenyl)-N-methylbutanamido)acetic acid
39		2-(3-(2,4-dihydroxyphenyl)butanamido)propanoic acid
40		2-(3-(2,4-dihydroxyphenyl)butanamido)-3-phenylpropanoic acid
41		3-(2,4-dihydroxyphenyl)butanamide
42		ethyl (S)-2-(3-(2,4-dihydroxyphenyl)butanamido)propanoate
43		ethyl (R)-2-(3-(2,4-dihydroxyphenyl)butanamido)propanoate
44		(S)-2-(3-(2,4-dihydroxyphenyl)butanamido)propanoic acid
45		(R)-2-(3-(2,4-dihydroxyphenyl)butanamido)propanoic acid
46		methyl 2-(3-(2,4-dihydroxyphenyl)butanamido)-4-methylpentanoate

47		(R)-2-(3-(2,4-dihydroxyphenyl)butanamido)-4-methylpentanoic acid
48		ethyl 2-(3-(2,4-dihydroxyphenyl)butanamido)-3-phenylpropanoate
49		3-(2-ethoxy-4-hydroxyphenyl)-N-ethylbutanamide
50		3-(4-ethoxy-2-hydroxyphenyl)-N-ethylbutanamide
51		(R)-2-(3-(2,4-dihydroxyphenyl)butanamido)-3-phenylpropanoic acid
52		3-(2,4-diisopropoxyphenyl)-N-ethylbutanamide
53		3-(2,4-dipropoxyphenyl)-N-ethylbutanamide

54		N-ethyl-3-(4-hydroxy-2-isopropoxyphenyl)butanamide
55		N-ethyl-3-(4-hydroxy-2-propoxyphenyl)butanamide
56		N-ethyl-3-(2-hydroxy-4-isopropoxyphenyl)butanamide
57		N-ethyl-3-(2-hydroxy-4-propoxyphenyl)butanamide
58		3-(2,4-dihydroxyphenyl)-N-ethyl-N-(2-hydroxyethyl)butanamide
59		3-(2,4-dihydroxyphenyl)-1-(morpholin-4-yl)butan-1-one

The compositions of the invention may be prepared according to scheme 1 below.

Scheme 1



According to this scheme 1, the synthesis of compounds (I) and (II) proceeds via the key intermediate of dihydrocoumarin type D, the synthesis of which is described, inter alia, in WO 2005/085 169. A person skilled in the art can adapt the strategy therefrom as a function of the groups R3.

Resorcinol A can react in the presence of a beta-keto ester B to give the coumarin C. This coumarin is reduced by catalytic hydrogenation under the conditions known to those skilled in the art to give D.

D may also be obtained from resorcinol A in the presence of an alpha,beta-unsaturated ester E. The lactone function of D is then opened in the presence of an amine NHR₄R₅ optionally with prior modifications of the phenol functions via strategies known to those skilled in the art in terms of reaction and protection/deprotection (formation of esters, ethers or glycosylations).

Production of the derivatives C and D via reaction between A and B or A and E may be performed especially in the presence of an organic solvent that may be chosen

from toluene, tetrahydrofuran, heptane, isooctane, methyltetrahydrofuran, methyl ethyl ketone, methyl isobutyl ketone, dioxane, ethyl acetate, isopropyl acetate and isododecane, and mixtures thereof, especially at a temperature of between 15 and 200°C, optionally in the presence of a catalyst (acid or basic) as described in the publications: Synthesis of 7-hydroxycoumarins by Pechmann reaction using Nafion resin/silica nanocomposites as catalysts: Laufer MC, Hausmann H, Hölderich WF, *J of Catalysis*, **2003**, 218, 315-320; Synthesis of 7-hydroxycoumarins catalysed by solid acid catalysts Hoefnagel A, Gunnewegh E, Downing R, van Bekkum H, *J Chem Soc Chem Commun*, **1995**, 225-226; in particular in the presence of an acid catalyst such as sulfuric acid, methanesulfonic acid, triflic acid or para-toluenesulfonic acid, sulfonic resins such as Dowex® or Amberlyst® resins (sold by Aldrich).

The compounds of formulae (I) and (II) for which R1 and/or R2 (R'1 and/or R'2) denote a group COR6 (COR'6) may be obtained by acetylation/esterification. The acetylation/esterification reaction may be performed with acetic anhydride (or anhydride R6COOCOR6) or acetyl chloride (or R6COCl), especially in the presence of an aprotic solvent such as toluene, pyridine or tetrahydrofuran. The acetylation reaction may be selective by employing protecting groups on the functions that do not need to be acetylated and by performing a deprotection reaction after acetylation, according to the known techniques of organic synthesis.

The opening reaction of the lactone D with amines NHR4R5 may optionally be performed in the presence of an organic solvent, especially tetrahydrofuran, dioxane, dimethylformamide, dimethyl sulfoxide, 2-methyltetrahydrofuran, dichloromethane; toluene, methanol or ethanol; optionally in the presence of a catalyst chosen from Lewis or Brønsted acid catalysts and basic catalysts, such as potassium carbonate, triethylamine or diisopropylethylamine; optionally by heating to a temperature of between 15°C and 200°C, especially between 20°C and 150°C.

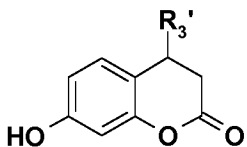
In addition, when the final compounds (I) and (II) bear a free carboxylic acid on radicals R4 and/or R5 (R'4 and/or R'5), the latter may be obtained by saponification using mineral bases, for instance NaOH or LiOH in the presence of protic or aprotic solvents, for instance ethanol or tetrahydrofuran or water at temperatures ranging between

0 and 100°C. The salts obtained are then reacidified in the presence of standard mineral or organic acids, for instance: hydrochloric acid, citric acid.

5 All of these steps may also make use of protection/deprotection strategies usually used in organic chemistry and compiled in the book *Protecting Groups in Organic Synthesis*, Greene, Wuts, Wiley Interscience, depending on the nature of the radicals.

10 Selective glycosylation strategies are known to those skilled in the art and may be found especially in the book *Handbook of Chemical Glycosylation*, A. V. Demchenko, Wiley VCH.

Thus, the present application also relates to a process for preparing a compound of formula (II) as defined previously, which consists in

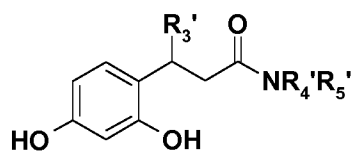
(i) reacting a compound of formula D , in which R3' is as defined above, by hydrogenation for the purpose of ring opening in the presence of a catalyst such as Pd/C, said compound of formula D possibly having been protected beforehand on the hydroxyl group with a protecting group such as the benzyl group, and then

15

(ii) reacting the compound obtained in step (i) with a compound of formula HNR₄R₅, in the presence of an organic solvent, especially tetrahydrofuran, dioxane, dimethylformamide, dimethyl sulfoxide, 2-methyltetrahydrofuran, dichloromethane; toluene, methanol or ethanol; optionally in the presence of a catalyst chosen from Lewis or Brønsted acid catalysts and basic catalysts, such as potassium carbonate, triethylamine or diisopropylethylamine; optionally by heating to a temperature of between 15°C and 200°C, especially between 20°C and 150°C, to give the compound of formula G

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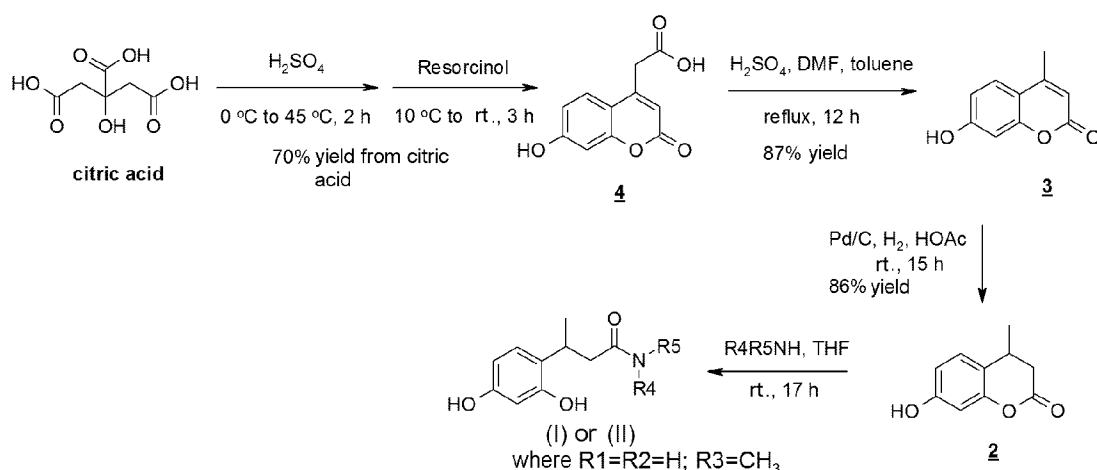
, in which R3', R4' and R5' are as defined above, said compound of formula G being able subsequently to undergo modification of the hydroxyl groups to give said compound of formula (I).

The various schemes below describe the various synthetic routes for obtaining the compounds of formulae (I) and (II).

In these schemes, "rt" means room temperature.

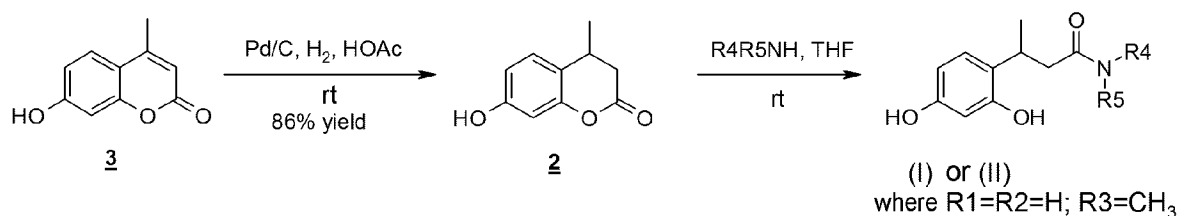
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Scheme 2



According to this scheme 2, the compound of formula (I) or (II) in which $\text{R}_1 = \text{R}_2 = \text{H}$ and $\text{R}_3 = \text{CH}_3$ and R_4 and R_5 have the definitions given above, may be obtained via a succession of five steps in a satisfactory overall yield. With reference to the literature, A. Gharde and B. Ghiya *Journal of the Indian Chemistry Society*, 1992, 69 (7), 397, an adapted procedure was used to access compound **4** with concentrated sulfuric acid and also a solvent and a catalyst. Subsequent decarboxylation at reflux in the presence of H_2SO_4 produces compound **3**. Hydrogenation in HOAc in the presence of the catalyst Pd/C makes it possible to obtain the lactone **2**, which can be readily reacted by nucleophilic substitution with primary or secondary amines to give the compound of formula (I) or (II) in which $\text{R}_1 = \text{R}_2 = \text{H}$ and $\text{R}_3 = \text{CH}_3$ and R_4 and R_5 have the definitions reported above.

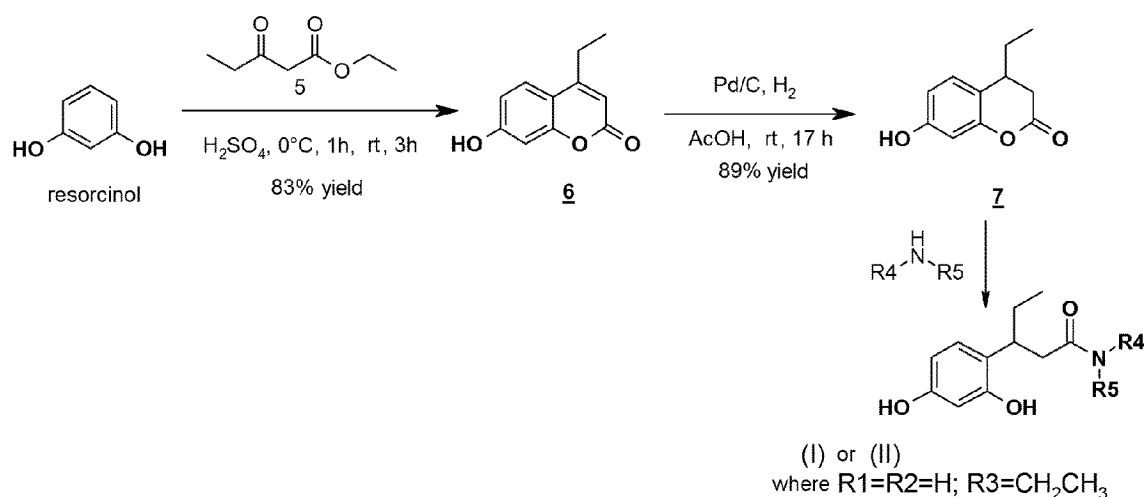
Scheme 3



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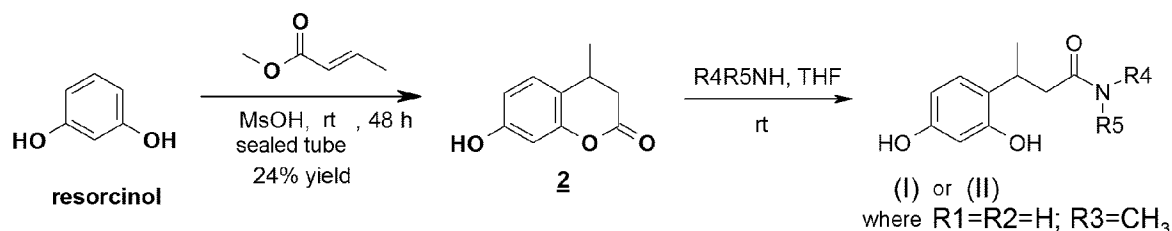
Alternatively, the compound of formula (I) or (II) in which $R_1 = R_2 = H$ and $R_3 = CH_3$ and R_4 and R_5 have the definitions reported above, may also be obtained via an optimized route represented by this scheme 3. Compound **3** is in fact commercially available (7-hydroxy-4-methylcoumarin). Consequently, the same method can then be applied directly starting with this compound in the same manner as has already been described in scheme 2 above to obtain compound **2** and then the compound of formula (I) or (II) in which $R_1 = R_2 = H$ and $R_3 = CH_3$ and R_4 and R_5 have the meanings reported above.

Scheme 4



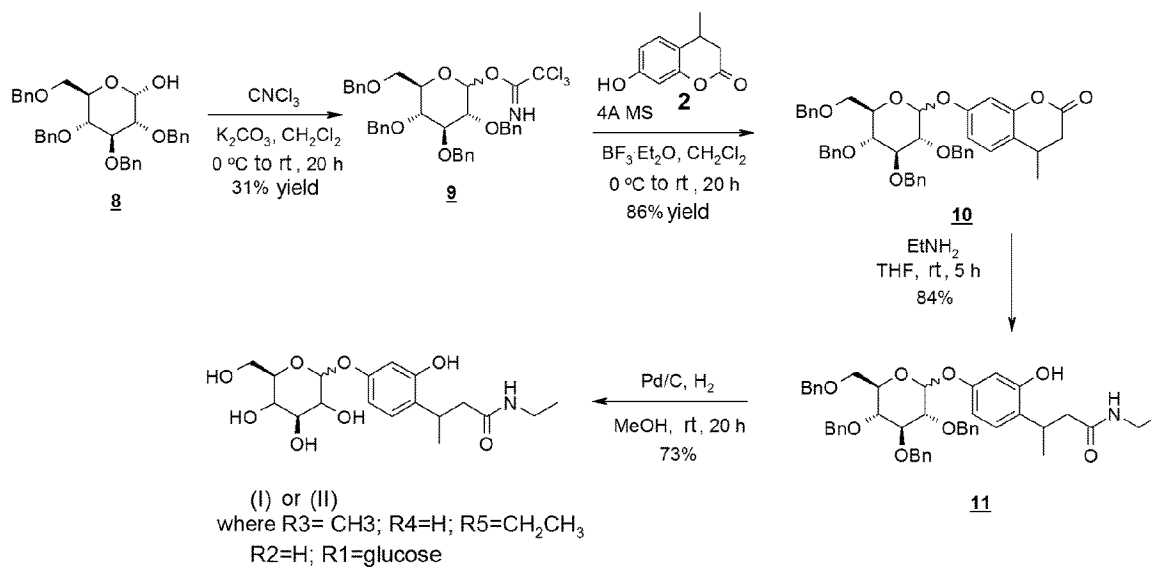
According to scheme 4, the reagents ethyl propionylacetate **5** and resorcinol react in the same manner as in scheme 2 above to give compound **6**, which may be converted into the final product in accordance with the same steps as those mentioned above. A description of this chemistry may be found in the following document: *Asian Journal of Chemistry*, **2010**, 22 (7), 5694-5698.

Scheme 5



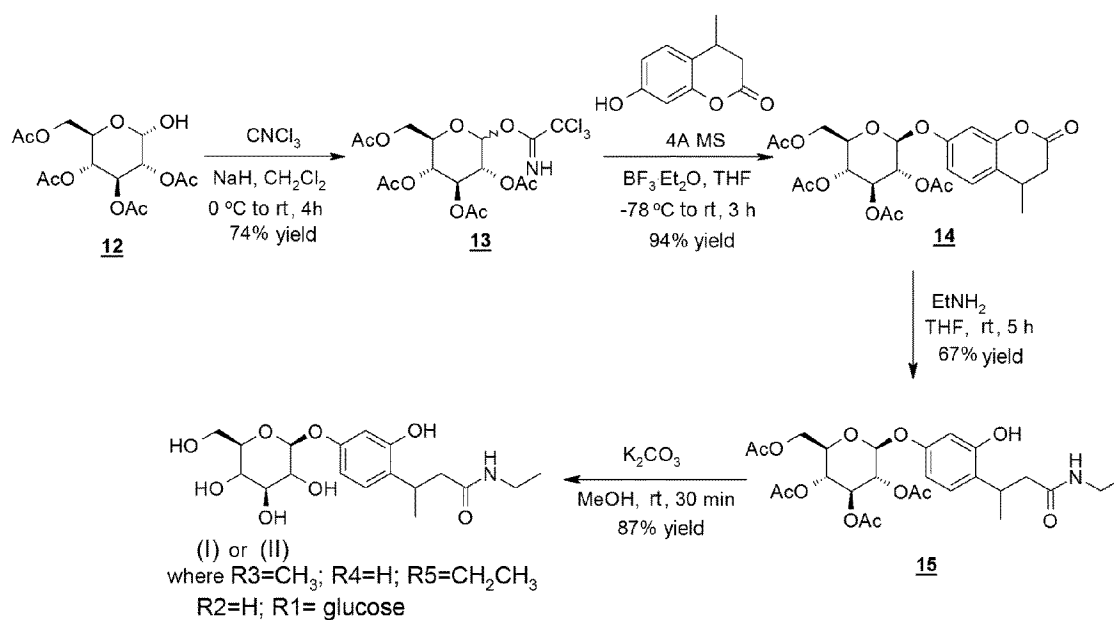
According to scheme 5, resorcinol is reacted with methyl crotonate in the presence of excess MSOH to give 7-hydroxy-4-methyl-3,4-dihydrocoumarin **2**. A yield of 24% may thus be obtained. The final step is identical to that already described above.

5

Scheme 6

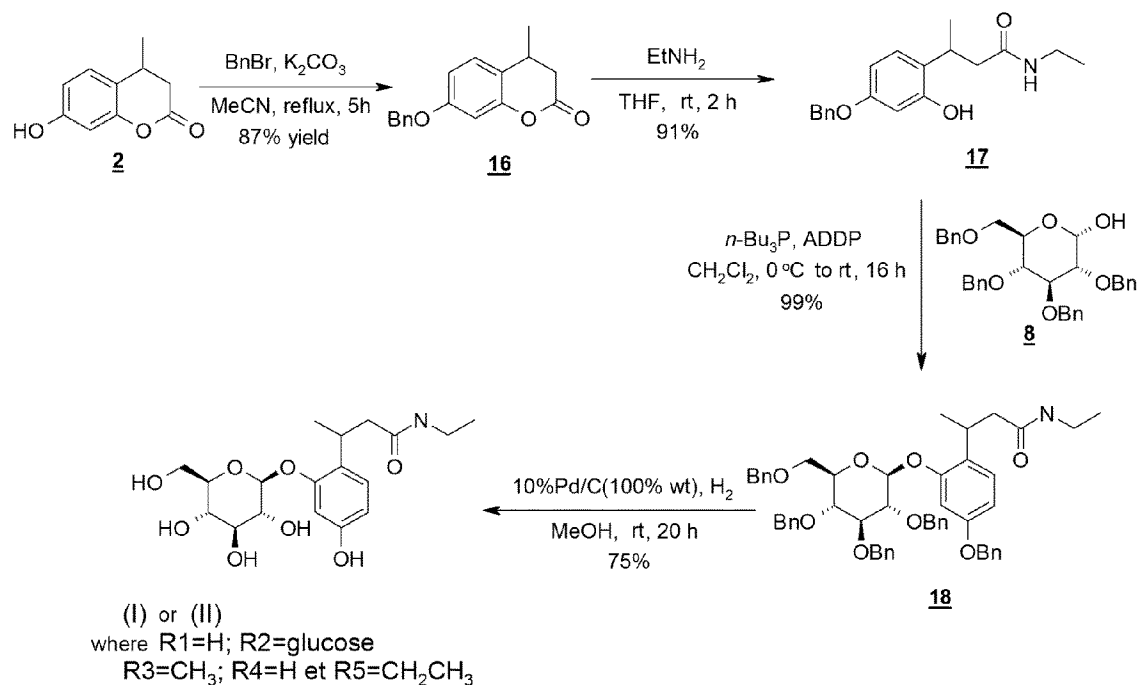
10

According to scheme 6, the glycoside of formula (I) or (II) may be obtained by performing the Schmidt glycosylation reaction in the presence of the trichloroacetimidate glycosyl donor **9**, which is reacted with compound **2** to give the anomer **10** followed by a nucleophilic substitution and then removal of the benzyl groups.

Scheme 7

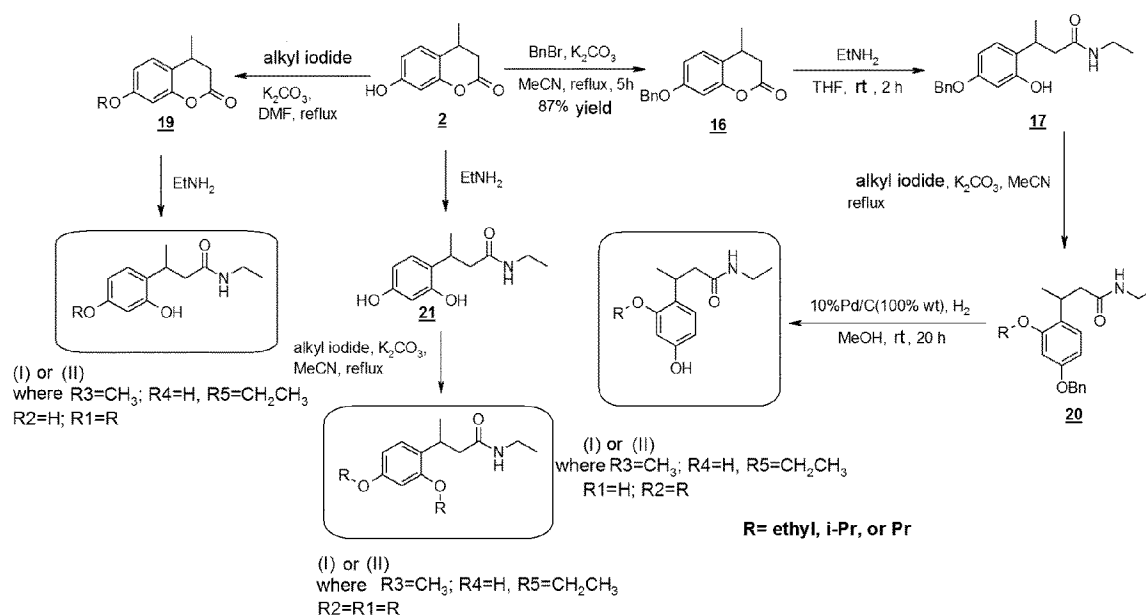
According to scheme 7, the glycoside of formula (I) or (II) may be obtained by performing the Schmidt glycosylation reaction. The beta anomer is obtained. An anomeric effect is observed due to the neighboring position of the acetyl group in compound **13**. The subsequent deprotection is advantageously performed under very mild conditions.

Scheme 8



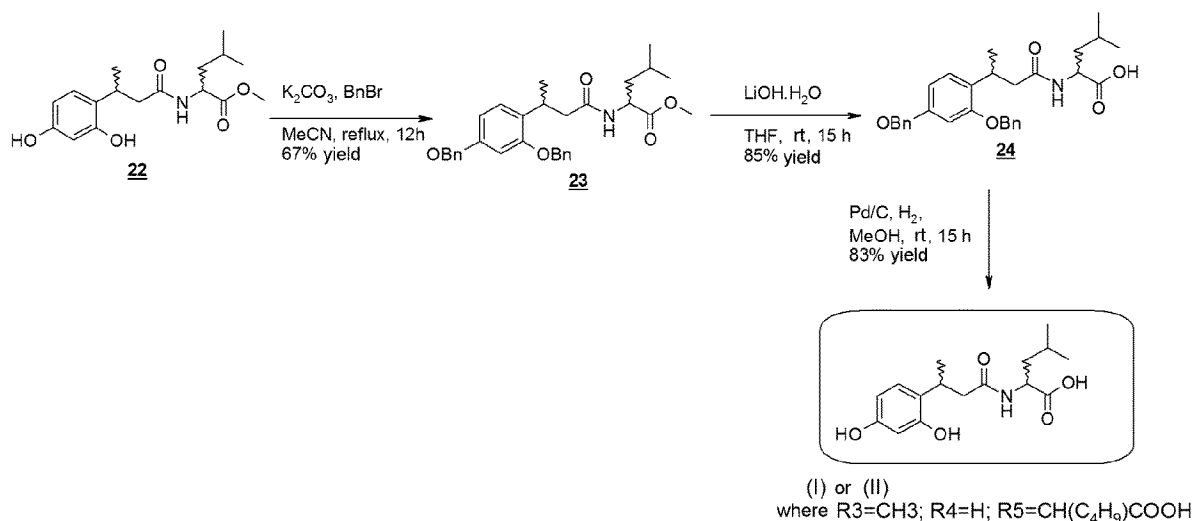
According to scheme 8, the beta anomer of glycoside **18** was synthesized via the Mitsunobu reaction starting with the protected glucopyranose alpha anomer **8** and the mono-benzyl resorcinol compound **17**.

Scheme 9



As illustrated by this scheme 9, the resorcinol derivatives according to the present invention may be obtained according to various processes.

Scheme 10



Scheme 10 illustrates a synthetic route in which the compound in accordance with the invention shows yet another example of meaning for the radical R5.

The compounds of formula (I) or (II) according to the invention find a most particular application in the cosmetic field.

The composition according to the invention comprises, in a physiologically acceptable medium, a compound of formula (I) or (II) as described previously.

The term “physiologically acceptable medium” is intended to mean a medium that is compatible with human keratin materials such as the skin of the body or of the face, the lips, the mucous membranes, the eyelashes, the nails, the scalp and/or the hair.

Compound (I) or (I) may be present in the composition according to the invention in an amount that may be between 0.01% and 10% by weight, preferably between 0.1% and 5% by weight, especially between 0.5% and 3% by weight, relative to the total weight of the composition.

The composition according to the invention is advantageously a cosmetic composition: it may comprise adjuvants usually used in the cosmetic field.

Mention may be made especially of water; organic solvents, especially C2-C6 alcohols; oils, especially hydrocarbon-based oils and silicone oils; waxes, pigments, fillers,

dyes, surfactants, emulsifiers; cosmetic active agents, UV-screening agents, polymers, thickeners, preserving agents, fragrances, bactericides, ceramides, odor absorbers, antioxidants.

These optional cosmetic adjuvants may be present in the composition in a proportion of from 0.001% to 80% by weight and especially from 0.1% to 40% by weight relative to the total weight of the composition. In any case, these adjuvants, and the proportions thereof, will be chosen by those skilled in the art such that the advantageous properties of the compounds according to the invention are not, or are not substantially, adversely affected by the envisaged addition.

As active agents, it will be advantageous to introduce into the composition according to the invention at least one compound chosen from: desquamating agents; calmatives, organic or mineral photoprotective agents, moisturizers; depigmenting agents; anti-glycation agents; NO-synthase inhibitors; agents for stimulating the synthesis of dermal or epidermal macromolecules and/or for preventing their degradation; agents for stimulating fibroblast and/or keratinocyte proliferation or for stimulating keratinocyte differentiation; muscle relaxants and/or dermo-decontracting agents; tensioning agents; anti-pollution agents and/or free-radical scavengers; agents acting on the capillary circulation; agents acting on the energy metabolism of cells; and mixtures thereof.

The composition according to the invention may be in any galenical form normally used in the cosmetic field, and especially in the form of an aqueous or aqueous-alcoholic solution, which is optionally gelled, a dispersion of the lotion type, which is optionally a two-phase lotion, an oil-in-water or water-in-oil or multiple (for example W/O/W or O/W/O) emulsion, an aqueous gel, a dispersion of oil in an aqueous phase by means of spherules, these spherules possibly being polymer nanoparticles such as nanospheres and nanocapsules or, better still, lipid vesicles of the ionic and/or nonionic type; aqueous or oily gels. These compositions are prepared according to the usual methods. A composition in the form of an emulsion, in particular an oil-in-water emulsion, is preferably used according to this invention.

The composition according to the invention may constitute a skincare composition, and especially a cleansing, protecting, treating or care cream for the face, the hands, the feet, the major anatomical folds or the body (for example day creams, night creams, makeup-removing creams, foundation creams or anti-sun creams); a fluid

foundation, a makeup-removing milk, a protective or care body milk or an anti-sun milk; a skincare lotion, gel or mousse, such as a cleansing lotion.

5 The invention is illustrated in greater detail by the following nonlimiting examples.

Example 1: Synthesis of compound 1 / N-butyl-3-(2,4-dihydroxyphenyl)butanamide

10 To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (600 mg, 3.4 mmol) in 10 ml of THF was added n-butylamine (990 mg, 13.5 mmol). The reaction mixture was stirred at room temperature for 15 hours. The mixture was then poured into 200 ml of water and extracted three times with EtOAc. The combined organic layers were washed three times with water, concentrated and dried under vacuum. The crude product is further purified by chromatography on a column of silica gel, eluting with a mixture of petroleum
15 ether/ EtOAc = 3/ 1 to give 960 mg of compound 1 in the form of a white solid in a yield of 97%.

The MS and NMR spectra are in accordance with the desired product.

20 **Example 2: Synthesis of compound 2 / 3-(2,4-dihydroxyphenyl)-N-(3-methoxypropyl)butanamide**

To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (600 mg, 3.4 mmol) in 10 ml of THF was added 3-methoxypropylamine (630 mg, 6.7 mmol). The reaction mixture was stirred at room temperature for 15 hours. The mixture was then poured into 200 ml of water and extracted three times with EtOAc. The combined organic layers were
25 washed three times with water, concentrated and dried under vacuum. The crude product is further purified by chromatography on a column of silica gel, eluting with a mixture of petroleum ether/ EtOAc = 1/ 1 to give 800 mg of compound 2 in the form of a colorless oil in 90% yield.

The MS and NMR spectra are in accordance with the desired product.

Example 3: Synthesis of compound 3 / N-(4-hydroxyphenethyl)-3-(2,4-dihydroxyphenyl)butanamide

To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (600 mg, 3.4 mmol) in 20 ml of THF was added tyramine in 4.0 ml of DMF (1.0 g, 7.3 mmol). The reaction mixture was stirred at room temperature for 15 hours. The mixture was then poured into 200 ml of water and extracted three times with EtOAc. The combined organic layers were washed three times with water, concentrated and dried under vacuum. The crude product is further purified by chromatography on a column of silica gel, eluting with a mixture of petroleum ether/ EtOAc = 3/ 1 to give 1.0 g of compound 3 in the form of a white solid in 94% yield.

The MS and NMR spectra are in accordance with the desired product.

Example 4: Synthesis of compound 4 / 3-(2,4-dihydroxyphenyl)-N-ethylbutanamide

To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (700 mg, 3.9 mmol) in 10 ml of THF was added a 65% aqueous solution of ethylamine (1.0 ml, 14.4 mmol). The reaction mixture was stirred at room temperature for 15 hours. The mixture was then poured into 200 ml of water and extracted three times with EtOAc. The combined organic layers were washed three times with water, concentrated and dried under vacuum. The crude product was further purified by chromatography on a column of silica gel, eluting with a mixture of petroleum ether/ EtOAc = 1/ 1 to give 550 mg of compound 4 in the form of a white solid in a yield of 63%.

Melting point = 130°C

The MS and NMR spectra are in accordance with the desired product.

Example 5: synthesis of compound 9 / N-butyl-3-(2,4-dihydroxyphenyl)-4-methylpentanamide

The synthetic route shown in scheme 4 given in the description was used.

Resorcinol (1.1 g, 10 mmol) was added to a mixture of ethyl isobutyrylacetate (2.37 g, 15 mmol) and concentrated H₂SO₄ (9.8 g, 100 mmol) at 0°C. The mixture was stirred at 0°C for 1 hour and then stirred at room temperature for 3 hours. After this, the mixture was poured into ice-water and extracted three times with ethyl acetate. The organic

layer was concentrated and dried under vacuum. The resulting residue was purified by chromatography on silica gel (eluent: 4/1 petroleum ether/ethyl acetate) to give 1.21 g of 7-hydroxy-4-isopropylcoumarin in the form of a white solid in a yield of 60%.

5 A mixture of 7-hydroxy-4-isopropylcoumarin (1.2 g, 5.9 mol) and 10% Pd/C (180 mg, 15% by weight) in 20 ml of HOAc was stirred under hydrogen at room temperature for 36 hours. The mixture was filtered through a pad of Celite to remove the Pd/C. The filtrate was concentrated and dried under vacuum. The resulting residue was purified by chromatography on silica gel (eluent: 4/1 petroleum ether/ethyl acetate) to give 987 mg of 7-hydroxy-4-isopropyl-3,4-dihydrocoumarin in the form of a white solid in a
10 yield of 82%.

To a solution of 7-hydroxy-4-isopropyl-3,4-dihydrocoumarin (412 mg, 2.0 mmol) in 15 ml of THF was added n-butylamine (165 mg, 2.26 mmol). The reaction mixture was stirred at room temperature for 24 hours. The mixture was then concentrated and dried under vacuum. The resulting residue was purified by chromatography on silica
15 gel (eluent: 2/1 petroleum ether/ethyl acetate) to give 500 mg of N-butyl-3-(2,4-dihydroxyphenyl)-4-methylpentanamide in the form of a pink solid in a yield of 91%.

The MS and NMR spectra are in accordance with the desired product.

Example 6: synthesis of compound 10 / N-butyl-3-(2,4-dihydroxyphenyl)pentanamide
20

The synthetic route shown in scheme 4 given in the description was used.

1,3-Dihydroxybenzene (1.1 g, 10 mmol) was added to a mixture of ethyl propionylacetate (2.16 g, 15 mmol) and concentrated H₂SO₄ (9.8 g, 100 mmol) at 0°C. The mixture was stirred at 0°C for 1 hour and then stirred at room temperature for 3 hours.
25 After this, the mixture was poured into ice water and stirred at 0°C for 30 minutes, resulting in the precipitation of a white solid. The solid was collected by filtration and dried under vacuum. The solid was then washed twice with dichloromethane to give 1.58 g of 7-hydroxy-4-ethylcoumarin in the form of a white solid in a yield of 83%.

A mixture of 7-hydroxy-4-ethylcoumarin (1.5 g, 7.9 mol) and 10% Pd/C (225
30 mg, 15% by weight) in 30 ml of HOAc was stirred under hydrogen at room temperature for 17 hours. The mixture was filtered through a pad of Celite to remove the Pd/C. The filtrate was concentrated and dried under vacuum. The resulting residue was purified by

chromatography on silica gel (eluent: 4/1 petroleum ether/ethyl acetate) to give 1.3 g of 7-hydroxy-4-ethyl-3,4-dihydrocoumarin in the form of a white solid in a yield of 85%.

To a solution of 7-hydroxy-4-ethyl-3,4-dihydrocoumarin (360 mg, 1.88 mmol) in 10 ml of THF was added n-butylamine (165 mg, 2.26 mmol). The reaction mixture was stirred at room temperature for 17 hours. The mixture was then concentrated and dried under vacuum. The resulting residue was purified by chromatography on silica gel (eluent: 2/1 petroleum ether/ethyl acetate) to give 374 mg of N-butyl-3-(2,4-dihydroxyphenyl)pentanamide in the form of a pink solid in a yield of 75%.

The MS and NMR spectra are in accordance with the desired product.

Example 7: synthesis of compound 11 / ethyl 2-(3-(2,4-dihydroxyphenyl)butanamido)-3-phenylpropanoate

A mixture of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (562 mg, 3.16 mmol) and ethyl DL-phenylalaninate (610 mg, 3.16 mmol) was heated at 120°C for 5 hours. The mixture was cooled to room temperature and extracted with EtOAc. The organic layer was concentrated and dried under vacuum. The crude product was further purified by chromatography on a column of silica gel, eluting with CH₂Cl₂/MeOH = 500/ 3 to give 850 mg of compound 11 in the form of a yellow solid in 73% yield.

The MS and NMR spectra are in accordance with the desired product.

Example 8: synthesis of compound 12 / 3-(2,4-dihydroxyphenyl)-N,N-diethylbutanamide

To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (500 mg, 2.8 mmol) in 20 ml of THF were added diethylamine (408 mg, 5.6 mmol) and the catalyst DMAP. The reaction mixture was stirred at room temperature for 15 hours. The mixture was then poured into 100 ml of water and extracted three times with EtOAc. The combined organic layers were washed three times with water, concentrated and dried under vacuum. The crude product is further purified by chromatography on a column of silica gel, eluting with a mixture of petroleum ether/ EtOAc = 3/ 1 to give 360 mg of compound 12 in the form of a white solid in a yield of 51%.

The MS and NMR spectra are in accordance with the desired product.

Example 9: synthesis of compound 13 / N,N-dibutyl-3-(2,4-dihydroxyphenyl)butanamide

To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (500 mg, 2.8 mmol) in 20 ml of THF was added dibutylamine (544 mg, 4.2 mmol). The reaction mixture was refluxed for 15 hours. After cooling to room temperature, the mixture was poured into 100 ml of water and extracted three times with EtOAc. The combined organic layers were washed three times with water, concentrated and dried under vacuum. The crude product is further purified by chromatography on a column of silica gel, eluting with a mixture of petroleum ether/ EtOAc = 3/ 1 to give 730 mg of compound 13 in the form of a pink oil in 84.6% yield.

The MS and NMR spectra are in accordance with the desired product.

Example 10: synthesis of compound 14 / 3-(2,4-dihydroxyphenyl)-N-propylbutanamide

To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (900 mg, 5.0 mmol) in 20 ml of THF was added n-propylamine (590 mg, 10.0 mmol). The reaction mixture was stirred at room temperature for 15 hours. The mixture was then poured into 100 ml of water and extracted three times with EtOAc. The combined organic layers were washed three times with water, concentrated and dried under vacuum. The crude product is further purified by chromatography on a column of silica gel, eluting with a mixture of petroleum ether/ EtOAc = 3/ 1 to give 600 mg of compound 14 in the form of a violet-colored syrup in a yield of 50.6%.

The MS and NMR spectra are in accordance with the desired product.

Example 11: synthesis of compound 15 / 3-(2,4-dihydroxyphenyl)-N-pentylbutanamide

To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (900 mg, 5.0 mmol) in 20 ml of THF was added amylamine (870 mg, 10.0 mmol). The reaction mixture was stirred at room temperature for 15 hours. The mixture was then poured into 100 ml of water and extracted three times with EtOAc. The combined organic layers were washed three times with water, concentrated and dried under vacuum. The crude product is further purified by chromatography on a column of silica gel, eluting with a mixture of

petroleum ether/ EtOAc = 3/ 1 to give 900 mg of compound 15 in the form of a violet-colored syrup in a yield of 68%.

The MS and NMR spectra are in accordance with the desired product.

5 **Example 12: synthesis of compound 16 / 3-(2,4-dihydroxyphenyl)-N-hexylbutanamide**

To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (1.0 g, 5.6 mmol) in THF were added 20 ml of hexylamine (1.13 g, 11.2 mmol). The reaction mixture was stirred at room temperature for 15 hours. The mixture was then poured into 100 ml of water and extracted three times with EtOAc. The combined organic layers were washed three times with water, concentrated and dried under vacuum. The crude product is further purified by chromatography on a column of silica gel, eluting with a mixture of petroleum ether/ EtOAc = 3/ 1 to give 1.2 g of compound 16 in the form of a white solid in a yield of 77%.

15 The MS and NMR spectra are in accordance with the desired product.

Example 13: synthesis of compound 17 / 3-(2,4-dihydroxyphenyl)-N-(3-ethoxypropyl)butanamide

To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (1.0 g, 5.6 mmol) in 20 ml of THF was added 3-ethoxy-1-propylamine (1.15 g, 11.2 mmol). The reaction mixture was stirred at room temperature for 15 hours. The mixture was then poured into 100 ml of water and extracted three times with EtOAc. The combined organic layers were washed three times with water, concentrated and dried under vacuum. The crude product is further purified by chromatography on a column of silica gel, eluting with a mixture of petroleum ether/ EtOAc = 3/ 1 to give 0.95 g of compound 17 in the form of a violet-colored syrup in a yield of 60%.

The MS and NMR spectra are in accordance with the desired product.

30 **Example 14: synthesis of compound 18 / 3-(2,4-dihydroxyphenyl)-N-isopropylbutanamide**

To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (0.8 g, 0.45 mmol) in 3 ml of THF was added isopropylamine (0.47 ml, 0.54 mmol). After stirring at room

temperature for 5 hours, the solvent was removed under vacuum. The residue was purified by chromatography on silica gel (dichloromethane/methanol = 50/ 1) to give 0.85 g of compound 18 in the form of a pink solid in a yield of 80%.

The MS and NMR spectra are in accordance with the desired product.

5

Example 15: synthesis of compound 19 / 3-(2,4-dihydroxyphenyl)-N-isopropylbutanamide

To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (1.0 g, 0.56 mmol) in 3 ml of THF was added isobutylamine (0.62 ml, 0.62 mmol). After stirring at room temperature for 5 hours, the solvent was removed under vacuum. The residue was purified by chromatography on silica gel (dichloromethane/methanol = 50/ 1) to give 1.2 g of compound 19 in the form of a violet-colored solid in a yield of 85%.

The MS and NMR spectra are in accordance with the desired product.

15

Example 16: synthesis of compound 20 / 3-(2,4-dihydroxyphenyl)-N-isopentylbutanamide

To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (1.0 g, 0.56 mmol) in 5 ml of THF was added isoamylamine (0.72 ml, 0.62 mmol). After stirring at room temperature for 5 hours, the solvent was removed under vacuum. The residue was purified by chromatography on silica gel (dichloromethane/methanol = 60/ 1) to give 1.29 g of compound 20 in the form of a violet-colored solid in a yield of 81%.

The MS and NMR spectra are in accordance with the desired product.

Example 17: synthesis of compound 21 / 3-(2,4-dihydroxyphenyl)-N-(4-methylpentyl)butanamide

To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (1.0 g, 0.56 mmol) in 10 ml of THF were added 4-methylpentylamine (0.85 g, 0.62 mmol) and DIPEA (1.08 ml, 0.62 mmol). After stirring at room temperature for 20 hours, the solvent was removed under vacuum. The residue was purified by chromatography on silica gel (petroleum ether /ethyl acetate = 2/ 1) to give 0.7 g of compound 21 in the form of a pink solid in a yield of 45%.

30

The MS and NMR spectra are in accordance with the desired product.

Example 18: synthesis of compound 22 / N-cyclohexyl-3-(2,4-dihydroxyphenyl)butanamide

To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (356 mg, 2.0 mmol) in 10 ml of THF was added cyclohexylamine (238 mg, 2.4 mmol). The mixture was stirred at room temperature for 16 hours. The mixture was concentrated under reduced pressure. The resulting residue was purified by chromatography on silica gel (eluent: 50/1 dichloromethane/methanol) to give 430 mg of compound 22 in the form of a pink solid in a yield of 87

The MS and NMR spectra are in accordance with the desired product.

Example 19: synthesis of compound 23 / N-(cyclohexylmethyl)-3-(2,4-dihydroxyphenyl)butanamide

To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (356 mg, 2.0 mmol) in 10 ml of THF was added cyclohexanemethylamine (271 mg, 2.4 mmol). The mixture was stirred at room temperature for 16 hours. The mixture was concentrated under reduced pressure. The resulting residue was purified by chromatography on silica gel (eluent: 50/1 dichloromethane/methanol) to give 560 mg of compound 23 in the form of a pink solid in a yield of 96%.

The MS and NMR spectra are in accordance with the desired product.

Example 20: synthesis of compound 24 / N-(4-hydroxy-3-methoxyphenethyl)-3-(2,4-dihydroxyphenyl)butanamide

To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (900 mg, 5.0 mmol) in 20 ml of THF and 20 ml of DMF were added 4-hydroxy-3-methoxyphenethylamine hydrochloride (1.1 g, 5.4 mmol) and DMAP (660 mg, 5.4 mmol). The reaction mixture was stirred at room temperature for 15 hours. 200 ml of water were then poured into the mixture, which was extracted three times with EtOAc. The combined organic layers were washed three times with water, concentrated and dried under vacuum. The crude product is further purified by chromatography on a column of silica gel, eluting with a mixture of petroleum ether/ EtOAc = 1/ 1 to give 1.1 g of compound 24 in the form of a purple solid in a yield of 63%.

The MS and NMR spectra are in accordance with the desired product.

Example 21: synthesis of compound 25 / ethyl 2-(3-(2,4-dihydroxyphenyl)butanamido)propanoate

5 To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (356 mg, 2.0 mmol) in 15 ml of DMF were added ethyl 2-aminopropanoate hydrochloride (370 mg, 2.4 mmol) and triethylamine (263 mg, 2.6 mmol). The mixture was heated at 120°C and reacted for 5 hours. After cooling the mixture, 30 ml of water were added thereto and the mixture was extracted with ethyl acetate. The organic layers were dried over sodium sulfate and
10 filtered. The filtrate was concentrated under reduced pressure. The resulting residue was purified by chromatography on silica gel (eluent: 50/1 dichloromethane/methanol) to give 324 mg of compound 25 in the form of a pink syrup in a yield of 55%.

The MS and NMR spectra are in accordance with the desired product.

15 **Example 22: synthesis of compound 5 / methyl 2-(3-(2,4-dihydroxyphenyl)butanamido)-4-methylpentanoate**

A mixture of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (1.42 g, 8 mmol) and methyl 2-amino-4-methylpentanoate (1.39 g, 9.6 mmol) was heated at 120°C for 4 hours. After cooling to room temperature, the mixture was purified by chromatography on silica
20 gel (dichloromethane/methanol = 40/ 1) to give 2.0 g of compound 5 in the form of a brown syrup in a yield of 77%.

The MS and NMR spectra are in accordance with the desired product.

25 **Example 23: synthesis of compound 26 / 3-(2,4-dihydroxyphenyl)-N,N-bis(2-methoxyethyl)butanamide**

To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (1.42 g, 8 mmol) in 10 ml of THF was added bis(2-methoxyethyl)amine (1.6 g, 12 mmol) at room temperature. The reaction mixture was stirred at room temperature for 16 hours. The solvent was removed under reduced pressure. The resulting residue was purified by chromatography on
30 silica gel (dichloromethane/methanol = 50/ 1) to give 1.9 g of compound 26 in the form of a pink syrup in a yield of 75%.

The MS and NMR spectra are in accordance with the desired product.

Example 24: synthesis of compound 27 / ethyl 2-(3-(2,4-dihydroxyphenyl)-N-methylbutanamido)acetate

To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (890 mg, 5 mmol) and TEA (657 mg, 6.5 mmol) in 10 ml of DMF was added ethyl 2-(methylamino)acetate hydrochloride (924 mg, 6 mmol) at room temperature. The reaction mixture was heated at 120°C for 4 hours. After cooling to room temperature, the mixture was poured into 50 ml of water and extracted with EtOAc. The organic layer was collected and concentrated under reduced pressure. The resulting residue was purified by chromatography on silica gel (dichloromethane/methanol = 30/ 1) to give 964 mg of compound 27 in the form of a violet-colored syrup in 65% yield.

The MS and NMR spectra are in accordance with the desired product.

Example 25: synthesis of compound 28 / 3-(2,4-dihydroxyphenyl)-N-(3-heptanyl)butanamide

To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (534 mg, 3.0 mmol) in 25 ml of THF were added 3-heptanamine hydrochloride (547 mg, 3.6 mmol) and triethylamine (394 mg, 1.3 mmol). The mixture was stirred at room temperature for 17 hours. The mixture was filtered and washed three times with ethyl acetate. The filtrate was concentrated under reduced pressure. The resulting residue was purified by chromatography on silica gel (eluent: 50/1 dichloromethane/methanol) to give 550 mg of compound 28 in the form of a pink syrup in a yield of 65%.

The MS and NMR spectra are in accordance with the desired product.

Example 26: synthesis of compound 30 / 3-(2,4-dihydroxyphenyl)-N-(2-hydroxyethyl)butanamide

To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (1.0 g, 5.6 mmol) in 30 ml of THF was added 2-aminoethanol (410 mg, 6.7 mmol). The reaction mixture was stirred at room temperature for 15 hours. The mixture was then poured into 200 ml of water and extracted three times with EtOAc. The combined organic layers were washed three times with water, concentrated and dried under vacuum. The crude product is further purified by chromatography on a column of silica gel, eluting with a mixture of petroleum

ether/ EtOAc = 2/ 1 to give 400 mg of compound 30 in the form of a white solid in a yield of 40%.

The MS and NMR spectra are in accordance with the desired product.

5 **Example 27: synthesis of compound 31 / ethyl 2-(3-(2,4-dihydroxyphenyl)butanamido)acetate**

To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (810 mg, 4.5 mmol) in 15 ml of DMF were added glycine ethyl ester hydrochloride (945 mg, 6.8 mmol) and DMAP (830 mg, 6.8 mmol). The reaction mixture was heated at 120°C for 4 hours. The mixture was then cooled to room temperature and 100 ml of 1N HCl was poured into EtOAc and extracted three times. The combined organic layers were washed three times with water, concentrated and dried under vacuum. The crude product is further purified by chromatography on a column of silica gel, eluting with a mixture of petroleum ether/ EtOAc = 3/ 1 to give 800 mg of compound 31 in the form of a white solid in a yield of 63%.

The MS and NMR spectra are in accordance with the desired product.

20 **Example 28: synthesis of compound 32 / 2-(3-(2,4-dihydroxyphenyl)butanamido)acetic acid**

To a solution of compound 24 (735 mg, 2.6 mmol) in 10 ml of THF was added LiOH (129 mg, 3.1 mmol) in 1.2 ml of water. The reaction mixture was stirred at room temperature for 15 hours. The mixture was then acidified with concentrated HCl. The mixture was concentrated and dried under vacuum, and the resulting residue was purified by chromatography on a column of silica gel, eluting with a mixture of CH₂Cl₂/ MeOH = 30/ 1 to give 275 mg of compound 32 in the form of a white solid in a yield of 42%.

The MS and NMR spectra are in accordance with the desired product.

30 **Example 29: synthesis of compound 29 / N-ethyl-3-(2-hydroxy-4-((2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yloxy)phenyl)butanamide**

The synthetic route shown in scheme 7 given in the description was used.

To a solution of 2,3,4,6-tetra-O-acetyl- α -D-glucopyranose compound **12** (according to scheme 7) (1 g, 2.87 mmol) in 15 ml of dry CH_2Cl_2 were added 60% NaH (57 mg, 1.44 mmol, 0.5 eq.) and trichloroacetonitrile (1.44 ml, 14.4 mmol) under nitrogen at 0°C. After stirring at room temperature for 4 hours, the solvent was removed under vacuum. The residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 15/ 1 to 6/ 1) to give 1.05 g of compound **13** (according to scheme 7) in the form of a colorless oil in a yield of 74%.

To a solution of compound **13** (according to scheme 7) (1.02 g, 2.1 mmol) and 4Å molecular sieves in 10 ml of THF was added 7-hydroxy-4-methyl-3,4-dihydrocoumarin (0.37 g, 2.1 mmol) under nitrogen. After cooling to -78°C, 1 M boron trifluoride etherate in THF was added dropwise to the mixture. The mixture was then stirred at this temperature for 3 hours and then poured into water and extracted twice with dichloromethane. The combined extracts were washed once with saturated aqueous sodium bicarbonate solution, once with water and once with brine, in this order, dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel (dichloromethane/petroleum ether = 1/ 1 to 1/ 4) to give 1 g of compound **14** (according to scheme 7) in the form of a white solid in a yield of 94%.

To a solution of compound **14** (according to scheme 7) (0.98 g, 1.9 mmol) in 8 ml of THF was added aqueous 65% ethylamine solution (0.2 g, 2.9 mmol). After stirring at room temperature for 5 hours, the solvent was removed under vacuum. The residue was purified by chromatography on silica gel (dichloromethane/methanol = 300/ 1) to give 0.7 g of compound **15** (according to scheme 7) in the form of a white solid in a yield of 67%.

To a solution of compound **15** (according to scheme 7) (0.64 g, 1.16 mmol) in 15 ml of methanol was added potassium carbonate (0.32 g, 2.3 mmol). After stirring at room temperature for 30 minutes, the mixture was filtered and the filtrate was evaporated. The residue was purified by chromatography on silica gel (dichloromethane/methanol = 6/ 1 to 2/ 1) to give 0.39 g of compound 29 in the form of a white solid in a yield of 87%.

The MS and NMR spectra are in accordance with the desired product.

Example 30: synthesis of compound 33 / N-ethyl-3-(4-hydroxy-2-((2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yloxy)phenyl)butanamide

The synthetic route shown in scheme 8 given in the description was used.

To a solution of compound **2** (according to scheme 8) (2.0 g, 11.2 mmol) in 20 ml of MeCN were added K₂CO₃ (2.0 g, 14.6 mmol) and BnBr (1.5 ml, 12.4 mmol). After stirring at reflux for 5 hours, the mixture was filtered. The filtrate was evaporated under vacuum. The residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate 15/ 1) to give 2.6 g of compound **16** (according to scheme 7) in the form of a white solid in a yield of 87%.

To a solution of compound **16** (according to scheme 8) (2.6 g, 9.7 mmol) in 15 ml of THF was added aqueous 65% ethylamine solution (0.87 g, 12.6 mmol). After stirring at room temperature for 2 hours, the solvent was removed under vacuum. The residue was washed with ether to give 2.76 g of compound **17** (according to scheme 8) in the form of a white solid in a yield of 91%.

To a solution of compound **17** (according to scheme 8) (0.54 g, 1.0 mmol) and 2,3,4,6-tetra-O-benzyl- α -D-glucopyranose (0.31 g, 1.0 mmol) in 15 ml of CH₂Cl₂ were added tributylphosphate (0.37 ml, 1.5 mmol) and ADDP (1,1'-(azobiscarbonyl)dipiperidine) (0.38 g, 1.5 mmol) at 0°C under a nitrogen atmosphere. After stirring at room temperature for 16 hours, the mixture was filtered. The filtrate was concentrated under vacuum. The residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 3/ 1) to give 0.45 g of compound **18** (according to scheme 8) in the form of a white oil in a yield of 99%.

To a solution of compound **18** (according to scheme 8) (0.78 g, 0.93 mmol) in 20 ml of methanol was added 0.78 g of Pd/C. After stirring at room temperature under hydrogen for 20 hours, the mixture was filtered. The filtrate was evaporated under vacuum. The residue was purified by chromatography on silica gel (dichloromethane/methanol = 10/1 to 6/ 1) to give 0.27 g of compound 33 in the form of a white solid in a yield of 75%.

The MS and NMR spectra are in accordance with the desired product.

Example 31: synthesis of compound 34 / N-ethyl-3-(2-hydroxy-4-((3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yloxy)phenyl)butanamide

The synthetic route shown in scheme 6 given in the description was used.

To a solution of 2,3,4,6-tetra-O-benzyl- α -D-glucopyranose compound **8** (according to scheme 6) (2 g, 3.7 mmol) in 40 ml of dry CH_2Cl_2 were added K_2CO_3 (0.66 g, 4.8 mmol, 1.3 eq.) and trichloroacetonitrile (1.48 ml, 14.8 mmol) under nitrogen at 0°C . After stirring at room temperature for 20 hours, the mixture was filtered. The solvent was removed under vacuum. The residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate 10/ 1) to give 0.77 g of compound **9** in the form of a colorless oil in a yield of 31%.

To a solution of compound **9** (according to scheme 6) (0.77 g, 1.1 mmol) and 4Å molecular sieves in 10 ml of CH_2Cl_2 was added 7-hydroxy-4-methyl-3,4-dihydrocoumarin (0.2 g, 1.1 mmol) under nitrogen. After cooling to 0°C , 1 M boron trifluoride etherate (0.18 ml, 1.5 mmol) in THF was added dropwise to the mixture. The mixture was then stirred at room temperature for 20 hours and poured into water and extracted twice with dichloromethane. The combined extracts were washed once with saturated aqueous sodium bicarbonate solution, once with water and once with brine, in this order, dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel (dichloromethane/petroleum ether = 1/ 1 to 3/ 1) to give 0.66 g of compound **10** (according to scheme 6) in the form of a yellow oil in a yield of 86%.

To a solution of compound **10** (according to scheme 6) (0.66 g, 0.94 mmol) in 10 ml of THF was added aqueous 65% ethylamine solution (0.13 g, 1.88 mmol). After stirring at room temperature for 2 hours, the solvent was removed under vacuum. The residue was washed with ether to give 0.59 g of compound **11** (according to scheme 6) in the form of a colorless oil in a yield of 84%.

To a solution of compound **11** (according to scheme 6) (0.58 g, 0.78 mmol) in 15 ml of methanol was added 0.58 g of 10% Pd/C. After stirring at room temperature under nitrogen for 20 hours, the mixture was filtered. The filtrate was evaporated under vacuum. The residue was purified by chromatography on silica gel (dichloromethane/methanol = 5/ 1) to give 0.22 g of compound **34** in the form of a white solid in a yield of 73%.

The MS and NMR spectra are in accordance with the desired product.

Example 32: synthesis of compound 35 / 4-(4-(ethylamino)-4-oxobutan-2-yl)-1,3-phenylene diacetate

The synthetic route shown in scheme 9 given in the description was used.

To a solution of 3-(2,4-dihydroxyphenyl)-N-butanamide (1.338 g, 6.0 mmol) in 40 ml of THF was added TEA (1.8 g, 18 mmol), followed by slow addition of acetyl chloride (1.4 g, 18 mmol) to the mixture at 0°C in an ice bath. The mixture was stirred at room temperature for 18 hours. The mixture was concentrated under reduced pressure. The resulting residue was purified by chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/ 1) to give 1.62 g of compound 35 in the form of a white powder in a yield of 88%.

Melting point: 83°C

The MS and NMR spectra are in accordance with the desired product.

Example 33: synthesis of compound 36 / 4-(4-(ethylamino)-4-oxobutan-2-yl)-1,3-phenylene diheptanoate

The synthetic route shown in scheme 9 given in the description was used.

To a solution of 3-(2,4-dihydroxyphenyl)-N-butanamide (1.115 g, 5.0 mmol) in 30 ml of THF was added TEA (1.515 g, 15 mmol), followed by slow dropwise addition of heptanoyl chloride (2.235 g, 15 mmol) to the mixture at 0°C in an ice bath. The mixture was stirred at room temperature for 18 hours. The mixture was concentrated under reduced pressure. The resulting residue was purified by chromatography on silica gel (eluent: petroleum ether/ EtOAc = 2/ 1) to give 1.2 g of compound 36 in the form of a white powder in a yield of 54%.

Melting point: 51°C

The MS and NMR spectra are in accordance with the desired product.

Example 34: synthesis of compound 37 / 2-(3-(2,4-dihydroxyphenyl)butanamido)-4-methylpentanoic acid

The synthetic route shown in scheme 10 given in the description was used.

To a solution of methyl 2-(3-(2,4-dihydroxyphenyl)butanamido)-4-methylpentanoate (2.57 g, 8.0 mmol) in 60 ml of MeCN were added K₂CO₃ (3.3 g, 23.9 mmol) and BnBr (4.1 g, 24.0 mmol). The reaction mixture was refluxed for 12 hours. After cooling to room temperature, the mixture was filtered and the filtrate was concentrated and dried. The resulting residue was purified by chromatography on a column of silica gel,

using dichloromethane, to obtain 2.7 g of methyl 2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)-4-methylpentanoate in the form of a white powder in a yield of 67%.

To a solution of methyl 2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)-4-methylpentanoate (2.66 g, 5.3 mmol) in 25 ml of THF was added LiOH (290 mg, 6.9 mmol) in 6.0 ml of water. The reaction mixture was stirred for 15 hours. 100 ml of water were added and the mixture was acidified with 6 N HCl to pH = 2 and extracted twice with EtOAc. The combined organic layers were washed three times with water and concentrated and dried. The resulting residue was purified by chromatography on silica gel (dichloromethane/methanol = 500/ 2) to give 2.2 g of 2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)-4-methylpentanoic acid in the form of a white powder in a yield of 85%.

A mixture of compound **24** (according to scheme 10) (2.2 g, 4.5 mmol) and 200 mg of 10% Pd/C in 50 ml of MeOH was stirred under a hydrogen atmosphere at room temperature for 15 hours. The reaction mixture was filtered and the filtrate was concentrated and dried. The resulting residue was purified by chromatography on silica gel (dichloromethane/methanol = 500/ 20) to give 1.15 g of 2-(3-(2,4-dihydroxyphenyl)butanamido)-4-methylpentanoic acid in the form of a white powder in a yield of 83%.

Melting point: 115.6°C

The MS and NMR spectra are in accordance with the desired product.

Example 35: synthesis of compound 38 / 2-(3-(2,4-dihydroxyphenyl)-N-methylbutanamido)acetic acid

The synthetic route shown in scheme 10 given in the description was used.

To a solution of ethyl 2-(3-(2,4-dihydroxyphenyl)-N-methylbutanamido)acetate (2.7 g, 9.15 mmol) in 60 ml of MeCN were added K₂CO₃ (3.3 g, 23.9 mmol) and BnBr (3.9 g, 22.8 mmol). The reaction mixture was refluxed for 12 hours. After cooling to room temperature, the mixture was filtered and the filtrate was concentrated and dried. The resulting residue was purified by chromatography on a silica gel column, using dichloromethane, to give 4.3 g of ethyl 2-(3-(2,4-bis(benzyloxy)phenyl)-N-methylbutanamido)acetate in the form of a white powder in a yield of 99%.

To a solution of ethyl 2-(3-(2,4-bis(benzyloxy)phenyl)-N-methylbutanamido)acetate (4.3 g, 9.1 mmol) in 50 ml of THF was added LiOH (465 mg, 11.1 mmol) in 8.0 ml of water. The reaction mixture was stirred for 15 hours. 200 ml of water were added and the mixture was acidified with 6 N HCl to pH = 2 and then extracted
5 twice with EtOAc. The combined organic layers were washed three times with water and concentrated and dried. The resulting residue was purified by chromatography on silica gel (dichloromethane/methanol = 500/ 2) to give 3.5 g of 2-(3-(2,4-bis(benzyloxy)phenyl)-N-methylbutanamido)acetic acid in the form of a white powder in a yield of 85%.

A mixture of 2-(3-(2,4-bis(benzyloxy)phenyl)-N-methylbutanamido)acetic acid
10 (3.5 g, 7.8 mmol) and 400 mg of 10% Pd/C in 80 ml of MeOH was stirred under hydrogen at room temperature for 15 hours. The reaction mixture was filtered and the filtrate was concentrated and dried. The resulting residue was purified by chromatography on silica gel (dichloromethane/methanol = 500/ 20) to give 1.5 g of 2-(3-(2,4-dihydroxyphenyl)-N-methylbutanamido)acetic acid in the form of a white powder in a yield of 72%.

15 Melting point: 143.7°C

The MS and NMR spectra are in accordance with the desired product.

Example 36: synthesis of compound 39 / 2-(3-(2,4-dihydroxyphenyl)butanamido)propanoic acid

20 The synthetic route shown in scheme 10 given in the description was used.

To a solution of 7-hydroxy-4-methylchroman-2-one (1 g, 5.6 mmol) in 20 ml of DMF were added ethyl 2-aminopropanoate hydrochloride (1.0 g, 6.7 mmol) and triethylamine (0.97 ml, 6.7 mmol). After stirring at 80°C for 20 hours, the mixture was filtered. The filtrate was poured into water and extracted twice with ethyl acetate. The
25 combined extracts were washed with water and brine, dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel (dichloromethane/methanol = 50/ 1) to give 1.1 g of ethyl 2-(3-(2,4-dihydroxyphenyl)butanamido)propanoate in the form of a yellow syrup in a yield of 67%.

Synthesis of ethyl 2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)propanoate: To a
30 solution of methyl 2-(3-(2,4-dihydroxyphenyl)butanamido)propanoate (1.0 g, 3.4 mmol) in acetonitrile were added K₂CO₃ (1.17 g, 8.5 mmol) and benzyl bromide (0.89 ml, 7.5 mmol). After stirring at 80°C for 20 hours, the mixture was filtered and evaporated under vacuum.

The residue was purified by chromatography on silica gel (dichloromethane petroleum ether = 1/ 2) to give 0.94 g of ethyl 2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)propanoate in the form of a white solid in a yield of 58%.

To a solution of methyl 2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)propanoate
5 (0.85 g, 1.8 mmol) in 10 ml of methanol was added a solution of LiOH (98 mg, 2.3 mmol) in 2 ml of water at 0°C. The mixture was stirred at room temperature for 20 hours. The solvent was then concentrated under vacuum. The residue was purified by chromatography on silica gel (dichloromethane/methanol = 30/ 1 to 10/ 1) to give 0.77 g of 2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)propanoic acid in the form of a white solid in a yield of
10 96%.

To a solution of 2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)propanoic acid (0.77 g, 1.72 mmol) in 20 ml of methanol was added Pd/C. The mixture was stirred at room temperature under hydrogen for 20 hours. The mixture was filtered through Celite® 545 (Sigma). The filtrate was concentrated under vacuum. The residue was purified by
15 chromatography on silica gel (dichloromethane/methanol = 8/ 1) to give 0.25 g of 2-(3-(2,4-dihydroxyphenyl)butanamido)propanoic acid in the form of a white solid in a yield of 54%.

Melting point: 55°C

The MS and NMR spectra are in accordance with the desired product.

20

Example 37: synthesis of compound 40 / 2-(3-(2,4-dihydroxyphenyl)butanamido)-3-phenylpropanoic acid

The synthetic route shown in scheme 10 given in the description was used.

To a solution of 7-hydroxy-4-methylchroman-2-one (0.94 g, 5.3 mmol) in 25
25 ml of DMF were added ethyl L-phenylalaninate hydrochloride (1.45 g, 6.3 mmol) and triethylamine (0.91 ml, 6.3 mmol). After stirring at 80°C for 20 hours, the mixture was filtered. The filtrate was poured into water and extracted twice with ethyl acetate. The combined extracts were washed with water and brine, dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel
30 (dichloromethane/methanol = 50/ 1) to give 1 g of ethyl 2-(3-(2,4-dihydroxyphenyl)butanamido)-3-phenylpropanoate in the form of a yellow syrup in a yield of 51%.

To a solution of ethyl 2-(3-(2,4-dihydroxyphenyl)butanamido)-3-phenylpropanoate (1.0 g, 2.7 mmol) in 25 ml of acetonitrile were added K_2CO_3 (0.93 g, 6.7 mmol) and benzyl bromide (0.71 ml, 5.9 mmol). After stirring at 80°C for 20 hours, the mixture was filtered and evaporated under vacuum. The residue was purified by chromatography on silica gel (dichloromethane ether/petroleum ether = 4/ 1) to give 0.82 g of ethyl 2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)-3-phenylpropanoate in the form of a white solid in a yield of 55%.

To a solution of ethyl 2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)-3-phenylpropanoate (0.81 g, 1.5 mmol) in 8 ml of methanol was added a solution of LiOH (80 mg, 1.9 mmol) in 1.9 ml of water at 0°C. The mixture was stirred at room temperature for 20 hours. The solvent was then concentrated under vacuum. The residue was purified by chromatography on silica gel (dichloromethane/methanol = 25/ 1 to 8/ 1) to give 0.76 g of 2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)-3-phenylpropanoic acid in the form of a white solid in a yield of 99%.

To a solution of 2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)-3-phenylpropanoic acid (0.76 g, 1.45 mmol) in 20 ml of methanol was added Pd/C. The mixture was stirred at room temperature under hydrogen for 20 hours. The mixture was filtered through Celite® 545 (Sigma). The filtrate was concentrated under vacuum. The residue was purified by chromatography on silica gel (dichloromethane/methanol = 10/ 1) to give 0.26 g of 2-(3-(2,4-dihydroxyphenyl)butanamido)-3-phenylpropanoic acid in the form of a white solid in a yield of 52%.

Melting point: 95.4°C

The MS and NMR spectra are in accordance with the desired product.

Example 38: synthesis of compound 41 / 3-(2,4-dihydroxyphenyl)butanamide

To a solution of 7-hydroxy-4-methylchroman-2-one (1.2 g, 6.7 mmol) in 50 ml of THF was added ammonia (5 ml). After stirring at room temperature for 2 hours, the solvent was removed under vacuum. The residue was purified by chromatography on silica gel (EtOAc/petroleum ether = 1/ 1) to give 1.04 g of compound 41 in the form of a pink solid in a yield of 79%.

Melting point: 144-145°C

The MS and NMR spectra are in accordance with the desired product.

Example 39: synthesis of compound 42 / ethyl (S)-2-(3-(2,4-dihydroxyphenyl)butanamido)propanoate

To a solution of 7-hydroxy-4-methylchroman-2-one (3.56 mg, 20 mmol) in 80 ml of DMF were added L-alanine ethyl ester hydrochloride (CAS: 1115-59-9) (3.7 g, 24 mmol) and triethylamine (3.5 ml, 24 mmol). The mixture was heated at 80°C and reacted for 15 hours. After cooling the mixture, 150 ml of water were added and the mixture was extracted three times with ethyl acetate. The organic layers were dried over sodium sulfate and filtered. The filtrate was concentrated under reduced pressure. The resulting residue was purified by chromatography on silica gel (eluent: 50/1 dichloromethane/methanol) to give 2.9 g of compound 42 in the form of a white powder in a yield of 49%.

Melting point: 68-69°C

The MS and NMR spectra are in accordance with the desired product.

Example 40: synthesis of compound 43 / ethyl (R)-2-(3-(2,4-dihydroxyphenyl)butanamido)propanoate

To a solution of 7-hydroxy-4-methylchroman-2-one (2.85 g, 16.0 mmol) in 40 ml of DMF were added D-ethyl 2-aminopropanoate hydrochloride (2.95 g, 19.2 mmol) and triethylamine (2.77 ml, 19.2 mmol). After stirring at 80°C for 20 hours, the mixture was filtered. The filtrate was poured into water and extracted twice with ethyl acetate. The combined extracts were washed with water and brine, dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel (dichloromethane/methanol = 50/ 1) to give 2.2 g of ethyl (R)-2-(3-(2,4-dihydroxyphenyl)butanamido)propanoate in the form of a white solid in a yield of 47%.

Melting point: 55°C

The MS and NMR spectra are in accordance with the desired product.

Example 41: synthesis of compound 44 / (S)-2-(3-(2,4-dihydroxyphenyl)butanamido)propanoic acid

The synthetic route shown in scheme 10 given in the description was used.

To a solution of ethyl (S)-2-(3-(2,4-dihydroxyphenyl)butanamido)propanoate (2.95 g, 10.0 mmol) in 50 ml of acetonitrile were added K_2CO_3 (2.76 g, 20.0 mmol) and benzyl bromide (2.4 ml, 20.0 mmol). After stirring at 80°C for 20 hours, the mixture was filtered and evaporated under vacuum. The residue was purified by chromatography on silica gel (dichloromethane ether/petroleum ether = 1/ 2) to give 3.36 g of ethyl (S)-2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)propanoate in the form of a white solid in a yield of 70%.

To a solution of ethyl (S)-2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)propanoate (3.33 g, 7.0 mmol) in 35 ml of methanol was added a solution of LiOH (385 mg, 9.1 mmol) in 7 ml of water. The mixture was stirred at room temperature for 20 hours. The solvent was then concentrated under reduced pressure. The residue was purified by chromatography on silica gel (dichloromethane/methanol = 30/ 1 to 10/ 1) to give 0.87 g of (S)-2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)propanoic acid in the form of a white solid in a yield of 28%.

To a solution of (S)-2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)propanoic acid (0.87 g, 1.95 mmol) in 20 ml of methanol was added 10% Pd/C (87 mg). The mixture was stirred at room temperature under hydrogen for 20 hours. The mixture was filtered. The filtrate was concentrated under vacuum to give 495 mg of compound 44 in the form of a white solid in a yield of 95%.

Melting point: 87-88°C

The MS and NMR spectra are in accordance with the desired product.

Example 42: synthesis of compound 45 / (R)-2-(3-(2,4-dihydroxyphenyl)butanamido)propanoic acid

The synthetic route shown in scheme 10 given in the description was used.

To a solution of 7-hydroxy-4-methylchroman-2-one (2.85 g, 16.0 mmol) in 40 ml of DMF were added D-ethyl 2-aminopropanoate hydrochloride (2.95 g, 19.2 mmol) and triethylamine (2.77 ml, 19.2 mmol). After stirring at 80°C for 20 hours, the mixture was filtered. The filtrate was poured into water and extracted twice with ethyl acetate. The combined extracts were washed with water and brine, dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel

(dichloromethane/methanol = 50/ 1) to give 2.2 g of ethyl (R)-2-(3-(2,4-dihydroxyphenyl)butanamido)propanoate in the form of a white solid in a yield of 47%.

To a solution of ethyl (R)-2-(3-(2,4-dihydroxyphenyl)butanamido)propanoate (1.66 g, 5.6 mmol) in 30 ml of acetonitrile were added K₂CO₃ (1.94 g, 14 mmol) and
5 benzyl bromide (1.48 ml, 12.4 mmol). After stirring at 80°C for 20 hours, the mixture was filtered and evaporated under vacuum. The residue was purified by chromatography on silica gel (dichloromethane/methanol = 500/ 1) to give 2.42 g of ethyl (R)-2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)propanoate in the form of a white solid in a yield of 91%.

10 To a solution of ethyl (R)-2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)propanoate (2.42 g, 5.1 mmol) in 45 ml of methanol was added a solution of LiOH (0.28 mg, 6.6 mmol) in 6 ml of water at 0°C. The mixture was stirred at room temperature for 20 hours. The solvent was then concentrated under vacuum. The residue was purified by chromatography on silica gel
15 (dichloromethane/methanol = 50/ 1) to give 2.1 g of (R)-2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)propanoic acid in the form of a white solid in a yield of 92%.

To a solution of (R)-2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)propanoic acid (2 g, 4.5 mmol) in 10 ml of methanol and 10 ml of THF was added Pd/C. The mixture
20 was stirred at room temperature under hydrogen for 20 hours. The mixture was filtered through Celite® 545 (Sigma). The filtrate was concentrated under vacuum. The residue was purified by chromatography on silica gel (dichloromethane/methanol = 15/ 1 to give 0.95 g of compound 45 in the form of a white solid in a yield of 79%.

Melting point: 130.5°C

25 The MS and NMR spectra are in accordance with the desired product.

Example 43: synthesis of compound 46 / methyl 2-(3-(2,4-dihydroxyphenyl)butanamido)-4-methylpentanoate

A mixture of 7-hydroxy-4-methyl-chroman-2-one (1.78 g, 10.0 mmol) and D-leucine methyl ester hydrochloride (5845-53-4) (1.82 g, 10.0 mmol) and TEA (1.1 g, 10.9
30 mmol) in 40 ml of DMF was heated at 120°C for 4 hours. After cooling to room temperature, 100 ml of water were poured into EtOAc and extracted twice. The combined

organic layers were washed three times with water and then concentrated and dried. The resulting residue was purified by chromatography on silica gel (dichloromethane/methanol = 40/ 1) to give 1.3 g of compound 46 in the form of a pink powder in a yield of 40%.

Melting point: 55-58°C

5 The MS and NMR spectra are in accordance with the desired product.

Example 44: synthesis of compound 47 / (R)-2-(3-(2,4-dihydroxyphenyl)butanamido)-4-methylpentanoic acid

The synthetic route shown in scheme 10 given in the description was used.

10 To a solution of methyl (R)-2-(3-(2,4-dihydroxyphenyl)butanamido)-4-methylpentanoate (2.5 g, 7.7 mmol) in 60 ml of MeCN were added K₂CO₃ (3.0 g, 21.7 mmol) and BnBr (3.42 g, 20.0 mmol). The reaction mixture was refluxed for 12 hours. After cooling to room temperature, the mixture was filtered and the filtrate was concentrated to dryness. The resulting residue was purified by chromatography on a
15 column of silica gel, using dichloromethane, to give 3.48 g of methyl (R)-2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)-4-methylpentanoate in the form of a white powder in a yield of 89%.

To a solution of methyl (R)-2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)-4-methylpentanoate (3.48 g, 6.9 mmol) in 60 ml of THF was added LiOH (580 mg, 13.8
20 mmol) in 10.0 ml of water. The reaction mixture was stirred for 15 hours. 100 ml of water were added and the mixture was acidified with 6 N HCl to pH = 2 and then extracted twice with EtOAc. The combined organic layers were washed three times with water and concentrated and dried. The resulting residue was purified by chromatography on silica gel (dichloromethane/methanol = 500/ 2) to give 3.0 g of (R)-2-(3-(2,4-
25 bis(benzyloxy)phenyl)butanamido)-4-methylpentanoic acid in the form of a white powder in a yield of 91%.

A mixture of (R)-2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)-4-methylpentanoic acid (2.9 g, 6.1 mmol) and 300 mg of 10% Pd/C in 80 ml of MeOH was stirred under hydrogen at room temperature for 15 hours. The reaction mixture was filtered
30 and the filtrate was concentrated and dried. The resulting residue was purified by chromatography on silica gel (dichloromethane/methanol = 500/ 20) to give 1.15 g of (R)-

2-(3-(2,4-dihydroxyphenyl)butanamido)-4-methylpentanoic acid in the form of a white powder in a yield of 89%.

Melting point: 78-82°C

The MS and NMR spectra are in accordance with the desired product.

5

Example 45: synthesis of compound 48 / ethyl (R)-2-(3-(2,4-dihydroxyphenyl)butanamido)-3-phenylpropanoate

To a solution of 7-hydroxy-4-methylchroman-2-one (1.3 g, 7.3 mmol) in 30 ml of DMF were added ethyl D-phenylalaninate hydrochloride (2 g, 8.7 mmol) and triethylamine (1.26 ml, 8.7 mmol). After stirring at 80°C for 20 hours, the mixture was filtered. The filtrate was poured into water and extracted twice with ethyl acetate. The combined extracts were washed with water and brine, dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 3/ 1 to 1/ 1) to give 1 g of compound 48 in the form of a yellow syrup in a yield of 44%.

Melting point: 100°C

The MS and NMR spectra are in accordance with the desired product.

Example 46: synthesis of compound 6 / 3-(2,4-dihydroxyphenyl)-N-ethylbutanamide

The synthetic route shown in scheme 9 given in the description was used.

To a solution of 3-(2,4-dihydroxyphenyl)-N-butanamide (0.447 g, 2.0 mmol) in iodoethane were added 40 ml of MeCN (0.686 g, 4.4 mmol) and K₂CO₃ (0.608 g, 4.4 mmol). The mixture was refluxed for 18 hours. The mixture was concentrated under reduced pressure. The resulting residue was purified by chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 1/ 1) to give 0.30 g of compound 6 in the form of a white powder in a yield of 54%.

Melting point: 100°C

The MS and NMR spectra are in accordance with the desired product.

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Example 47: synthesis of compound 49 / 3-(2-ethoxy-4-hydroxyphenyl)-N-ethylbutanamide

The synthetic route shown in scheme 9 given in the description was used.

To a solution of 7-hydroxy-4-methylchroman-2-one (5 g, 28.1 mmol) in 100 ml of acetonitrile were added potassium carbonate (4.65 g, 33.7 mmol) and bromomethylbenzene (5.76 g, 33.7 mmol) at room temperature. The mixture was refluxed for 6 hours. After cooling to room temperature, the mixture was filtered. The filtrate was concentrated under reduced pressure. The residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10/ 1) to give 6.87g of 7-(benzyloxy)-4-methylchroman-2-one in the form of a colorless oil in a yield of 91%.

To a solution of 7-(benzyloxy)-4-methylchroman-2-one (2.68 g, 10 mmol) in 20 ml of THF were added dropwise 5 ml of 65% ethylamine solution. After stirring at room temperature for 2 hours, the solvent was removed under vacuum. The residue was purified by chromatography on silica gel (petroleum ether acetate/ethyl acetate = 1/ 1 to give 3 g of 3-(4-(benzyloxy)-2-hydroxyphenyl)-N-butanamide in the form of a white solid in a yield of 96%.

To a solution of 3-(4-(benzyloxy)-2-hydroxyphenyl)-N-butanamide (1 g, 3.2 mmol) iodomethane was added in 50 ml of THF (0.593 g, 3.8 mmol) and potassium carbonate (0.525 g, 3.8 mmol). The mixture was refluxed for 4 hours. After cooling to room temperature, the mixture was filtered and washed with THF. The filtrate was evaporated under vacuum. The resulting residue was purified by chromatography on silica gel (petroleum ether acetate/ethyl acetate = 10/ 1) to give 0.966 g of 3-(4-(benzyloxy)-2-ethoxyphenyl)-N-butanamide in the form of a white solid in a yield of 88%.

To a solution of 3-(4-(benzyloxy)-2-ethoxyphenyl)-N-butanamide (600 mg, 1.76mmol) in 30 ml of acetic acid were added 100 mg of Pd/C. The mixture was stirred under hydrogen and heated at 100°C for 6 hours. After cooling to room temperature, the mixture was filtered. The filtrate was concentrated under reduced pressure. The resulting residue was purified by chromatography on silica gel (dichloromethane/methanol = 80/ 1 to 60/ 1) to give 0.67 mg of compound 49 in the form of a white solid in a yield of 78%.

The MS and NMR spectra are in accordance with the desired product.

Example 48: synthesis of compound 50 / 3-(4-ethoxy-2-hydroxyphenyl)-N-ethylbutanamide

The synthetic route shown in scheme 9 given in the description was used.

To a solution of 7-hydroxy-4-methylchroman-2-one (0.784 g, 4.4 mmol) in 15 ml of acetone were added iodomethane (0.967 g, 6.2 mmol) and potassium carbonate (1.546 g, 11.2 mmol), in that order. The mixture was refluxed for 20 hours. After cooling to room temperature, the mixture was filtered and washed with acetone. The filtrate was evaporated under vacuum. The resulting residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10/ 1) to give 0.65 g of 7-ethoxy-4-methylchroman-2-one in the form of a colorless oil in a yield of 72%.

To a solution of 7-ethoxy-4-methylchroman-2-one (0.61 g, 2.96 mmol) in 15 ml of THF were added dropwise 65% ethylamine solution (0.41 g, 5.92 mmol). After stirring at room temperature for 20 hours, the solvent was removed under vacuum. The residue was purified by chromatography on silica gel (dichloromethane/methanol = 80/ 1 to 60/ 1) to give 0.67 g of compound 50 in the form of a white solid in a yield of 90%.

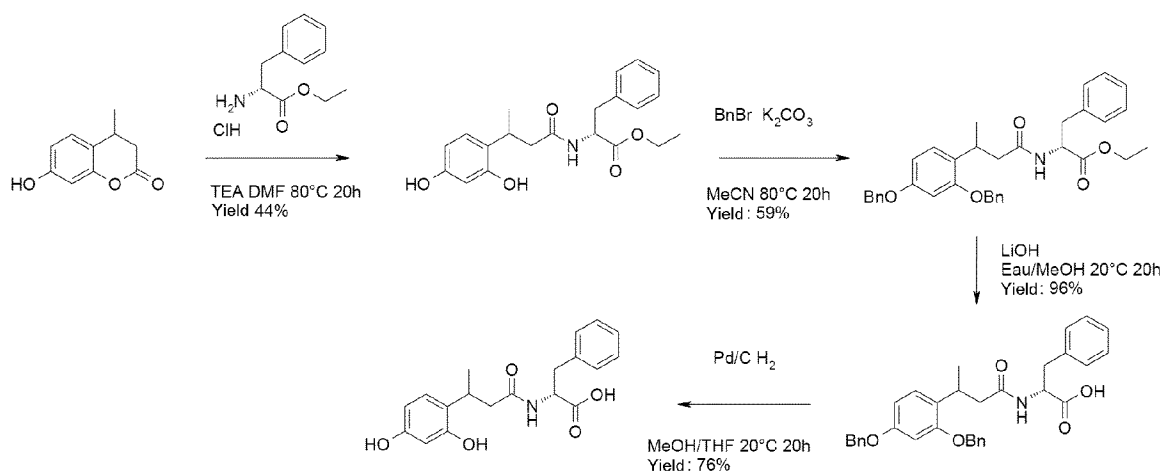
Melting point: 150°C

The MS and NMR spectra are in accordance with the desired product.

Example 49: synthesis of compound 51 / (R)-2-(3-(2,4-dihydroxyphenyl)butanamido)-3-phenylpropanoic acid

The synthetic route shown in scheme 11 below was used.

Scheme 11



To a solution of 7-hydroxy-4-methylchroman-2-one (1.3 g, 7.3 mmol) in 30 ml of DMF were added ethyl D-phenylalaninate hydrochloride (2 g, 8.7 mmol) and triethylamine (1.26 ml, 8.7 mmol). After stirring at 80°C for 20 hours, the mixture was filtered. The filtrate was poured into water and extracted twice with ethyl acetate. The

combined extracts were washed with water and brine, dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 3/ 1 to 1/ 1) to give 1 g of ethyl (R)-2-(3-(2,4-dihydroxyphenyl)butanamido)-3-phenylpropanoate in the form of a yellow syrup in a yield of 44%.

To a solution of ethyl (R)-2-(3-(2,4-dihydroxyphenyl)butanamido)-3-phenylpropanoate (1.21 g, 3.26 mmol) in 30 ml of acetonitrile were added K₂CO₃ (1.13 g, 8.15 mmol) and benzyl bromide (0.86 ml, 7.18 mmol). After stirring at 80°C for 20 hours, the mixture was filtered and evaporated under vacuum. The residue was purified by chromatography on silica gel (dichloromethane ether/petroleum ether = 4/ 1) to give 1.05 g of ethyl (R)-2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)-3-phenylpropanoate in the form of a white solid in a yield of 59%.

To a solution of ethyl (R)-2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)-3-phenylpropanoate (1.05 g, 1.9 mmol) in 15 ml of methanol was added a solution of LiOH (104 mg, 2.4 mmol) in 2.4 ml of water at 0°C. The mixture was stirred at room temperature for 20 hours. The solvent was then concentrated under vacuum. The residue was purified by chromatography on silica gel (dichloromethane/methanol = 25/ 1 to 8/ 1) to give 0.95 g of (R)-2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)-3-phenylpropanoic acid in the form of a white solid in a yield of 96%.

To a solution of (R)-2-(3-(2,4-bis(benzyloxy)phenyl)butanamido)-3-phenylpropanoic acid (1.4 g, 2.7 mmol) in 10 ml of methanol and 15 ml of THF was added Pd/C. The mixture was stirred at room temperature under hydrogen for 20 hours. The mixture was filtered through Celite® 545 (Sigma). The filtrate was concentrated under vacuum. The residue was purified by chromatography on silica gel (dichloromethane/methanol = 10/ 1) to give 0.7 mg of compound 51 in the form of a white solid in a yield of 76%.

Melting point: 114.2°C

The MS and NMR spectra are in accordance with the desired product.

Example 50: synthesis of compound 52 / 3-(2,4-diisopropoxyphenyl)-N-ethylbutanamide

The synthetic route shown in scheme 9 given in the description was used.

To a solution of 3-(2,4-dihydroxyphenyl)-N-butanamide (0.893 g, 4.0 mmol) in 60 ml of MeCN were added 2-iodopropane (3.4 g, 20.0 mmol) and K₂CO₃ (2.76 g, 20.0 mmol). The mixture was refluxed for 18 hours. After cooling, the mixture was filtered. The filtrate was concentrated under reduced pressure. The resulting residue was purified by chromatography on silica gel (eluent: petroleum ether/ EtOAc = 2/ 1) to give 0.928 g of 3-(2,4-diisopropoxyphenyl)-N-butanamide in the form of a white powder in a yield of 75%.

Melting point: 111°C

The MS and NMR spectra are in accordance with the desired product.

Example 51: synthesis of compound 53 / 3-(2,4-dipropoxyphenyl)-N-ethylbutanamide

To a solution of 3-(2,4-dihydroxyphenyl)-N-butanamide (0.447 g, 2.0 mmol) in 30 ml of MeCN were added 1-iodopropane (1.36 g, 8.0 mmol) and K₂CO₃ (1.104 g, 8.0 mmol). The mixture was refluxed for 18 hours. After cooling, the mixture was filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by chromatography on silica gel (eluent: petroleum ether/ EtOAc = 2/ 1) to give 0.4 g of compound 53 in the form of a white powder in a yield of 65%.

Melting point: 82°C

The MS and NMR spectra are in accordance with the desired product.

Example 52: synthesis of compound 54 / N-ethyl-3-(4-hydroxy-2-isopropoxyphenyl)butanamide

The synthetic route shown in scheme 9 given in the description was used.

To a solution of 3-(4-(benzyloxy)-2-isopropoxyphenyl)-N-butanamide (940 mg, 2.64 mmol) in 30 ml of acetic acid were added 100 mg of Pd/C. The mixture was stirred under hydrogen and heated at 100°C for 6 hours. After cooling to room temperature, the mixture was filtered. The filtrate was concentrated under reduced pressure. The resulting residue was purified by chromatography on silica gel (dichloromethane/methanol = 80/ 1 to 60/ 1) to give 458 mg of compound 54 in the form of a white solid in a yield of 65%.

The MS and NMR spectra are in accordance with the desired product.

Example 53: synthesis of compound 55 / N-ethyl-3-(4-hydroxy-2-propoxyphenyl)butanamide

The synthetic route shown in scheme 9 given in the description was used.

To a solution of 3-(4-(benzyloxy)-2-propoxyphenyl)-N-butanamide (1.12 g, 3.16 mmol) in 30 ml of acetic acid were added 200 mg of Pd/C. The mixture was stirred under hydrogen and heated at 100°C for 6 hours. After cooling to room temperature, the mixture was filtered. The filtrate was concentrated under reduced pressure. The resulting residue was purified by chromatography on silica gel (dichloromethane/methanol = 80/ 1 to 60/ 1) to give 689 mg of compound 55 in the form of a white solid in a yield of 82%.

The MS and NMR spectra are in accordance with the desired product.

Example 54: synthesis of compound 56 / N-ethyl-3-(2-hydroxy-4-isopropoxyphenyl)butanamide

To a solution of N-ethyl-3-(2-(benzyloxy)-4-isopropoxyphenyl)butanamide (0.41 g, 1.86 mmol) in 10 ml of THF was added dropwise 65% ethylamine solution (0.17 g, 3.72 mmol). Once the reaction was complete, 10 ml of petroleum ether were added to the mixture. The mixture was stirred at room temperature for 30 minutes. The precipitate was then filtered off and washed with petroleum ether. The residue was dried under vacuum to give 0.41 g of compound 56 in the form of a white solid in a yield of 83%.

Melting point: 221.6°C

The MS and NMR spectra are in accordance with the desired product.

Example 55: synthesis of compound 57 / N-ethyl-3-(2-hydroxy-4-propoxyphenyl)butanamide

To a solution of N-ethyl-3-(2-(benzyloxy)-4-propoxyphenyl)butanamide (0.3 g, 1.36 mmol) in 10 ml of THF was added dropwise 65% ethylamine solution (0.19 g, 2.72 mmol). Once the reaction was complete, 10 ml of petroleum ether were added to the mixture. The mixture was stirred at room temperature for 30 minutes. The precipitate was then filtered off and washed with petroleum ether. The residue was dried under vacuum to give 0.23 g of compound 57 in the form of a white solid in a yield of 68%.

Melting point: 238.3°C

The MS and NMR spectra are in accordance with the desired product.

Example 56: synthesis of compound 58 / 3-(2,4-dihydroxyphenyl)-N-ethyl-N-(2-hydroxyethyl)butanamide

To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (1 g, 5.6 mmol) in 10 ml of THF was added 2-(ethylamino)ethanol (0.75 g, 11.2 mmol) at room temperature. The reaction mixture was stirred at room temperature for 24 hours. The solvent was removed under reduced pressure. The resulting residue was purified by chromatography on silica gel (dichloromethane/methanol = 9/ 1) to give 1.2 g of compound 58 in the form of a gum in a yield of 79%.

The MS and NMR spectra are in accordance with the desired product.

Example 57: synthesis of compound 59 / 3-(2,4-dihydroxyphenyl)-1-(morpholin-4-yl)butan-1-one

To a solution of 7-hydroxy-4-methyl-3,4-dihydrocoumarin (1 g, 5.6 mmol) in 10 ml of THF was added 2-(ethylamino)ethanol (0.73 g, 11.2 mmol) at room temperature. The reaction mixture was stirred at room temperature for 16 hours. The solvent was removed under reduced pressure. The resulting residue was purified by chromatography on silica gel (dichloromethane/methanol = 9/ 1) to give 1.2 g of compound 58 in the form of an off-white solid in a yield of 80%.

The MS and NMR spectra are in accordance with the desired product.

Example 58: Demonstration of the depigmenting activity

The efficacy was demonstrated on the basis of the following test:

For the evaluations of the effect of prevention or of decrease of pigmentation of the skin and/or of lightening of this skin, the examples are carried out in the following way.

The measurement of the depigmenting activity (reduction of melanin production) of compounds of formula (I) was performed by assaying normal human melanocytes *in vitro* as follows.

First of all, normal human melanocytes are cultured and dispensed into 384 wells. After 24 hours, the culture medium was replaced with a medium containing compounds of formula (I) to be evaluated. The cells were incubated for 72 hours before

measurement of the final optical density, which measures the amount of melanin produced by the melanocytes. A dose effect is performed using a wide concentration range of the compounds evaluated. Thus, by making the concentrations and the melanin measurements correspond, it is possible to determine an IC₅₀ in μM : concentration at which 50% decrease in melanin synthesis is achieved.

The compounds of formulae (I) and/or (II) showed a strong depigmenting effect.

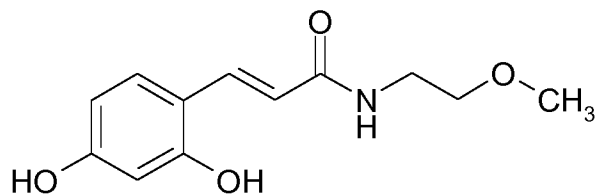
Various test campaigns were conducted and collated in Tables 2, 3, 4 and 5 below.

Table 2

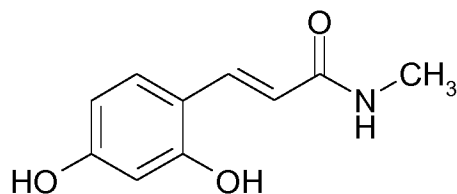
Compound No.	IC ₅₀ (μM)	Maximum concentration tested (μM)
25	0.00586	3
5	0.00586	3
23	0.00825	3
3	0.0158	3
1	0.0235	3
4	0.0303	3
15	0.0315	3
16	0.0325	3
20	0.0338	3
18	0.037	3
22	0.0425	3
14	0.0462	3
21	0.0783	3
2	0.125	3
24	0.137	3

These results were compared with compounds described in the prior art, and more particularly

- in patent application WO 2004/017 936:

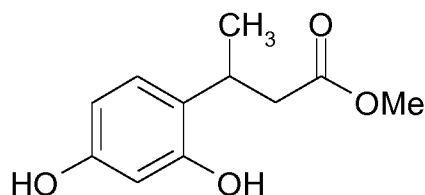


(A). For this compound (A), the IC₅₀ value is 0.241 μ M.



(B). For this compound (B), the IC₅₀ value is 0.26 μ M, and

5 - in patent application WO 2005/085 169:



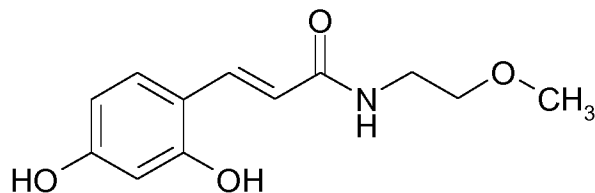
(C). For this compound (C), the IC₅₀ value is 3 μ M.

Table 3

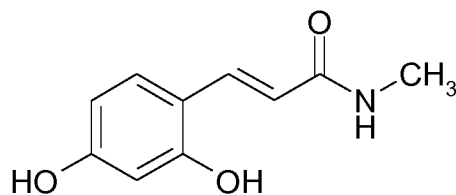
Compound No.	IC ₅₀ (μ M)	Maximum concentration tested (μ M)
1	0.391	200
3	0.391	200
4	0.391	200
20	0.391	200
23	0.391	200
5	0.391	200
2	0.649	200
30	0.852	200
31	1.7	200
27	1.81	200
34	2.7	200

10 These results were compared with compounds described in the prior art, and more particularly

- in patent application WO 2004/017 936:

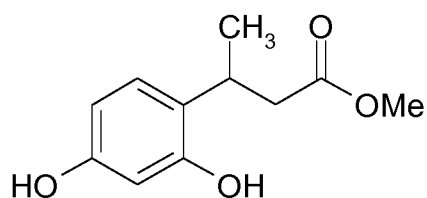


(A). For this compound (A), the IC₅₀ value is 19.1 μ M.



(B). For this compound (B), the IC₅₀ value is 24 μ M, and

- in patent application WO 2005/085 169:



(C). For this compound (C), the IC₅₀ value is 108 μ M.

10

Table 4

Compound No.	IC ₅₀ (μ M)	Maximum concentration tested (μ M)
1	0.391	200
2	0.391	200
3	0.391	200
4	0.391	200
6	29.2	200
12	1.08	200
14	0.391	200
17	0.539	200
19	0.581	200
24	0.391	200
26	3.37	200

27	0.391	200
28	0.874	200
9	97.2	200
10	20.8	200
35	0.391	200
36	4.26	200
38	72.7	200
39	13.5	200
40	42.1	200
41	2.87	200
43	1.23	200
44	48.3	200
45	111	200
46	2.15	200
58	22.2	200
59	28	200

Table 5

Compound No.	IC50 (μ M)	Maximum concentration tested (μ M)
4	1.38	200
26	11	200
58	22.2	200
59	28	200

5

Example 59: Cosmetic composition

A skin depigmenting composition is prepared, comprising (in grams):

Compound 25	2 g
PEG 400	68 g
Ethanol	30 g

10

The composition applied to the skin makes it possible to attenuate brown spots.

Example 60: gel

A skin depigmenting gel is prepared, comprising (% by weight):

Compound 4 0.25%

5 Carbomer (Carbopol 981 from Lubrizol) 1%

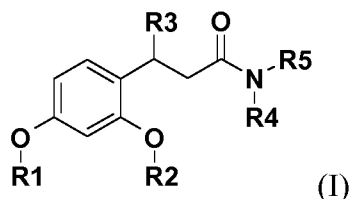
Preserving agent qs

Water qs 100%

The composition applied to the skin makes it possible to attenuate brown spots.

CLAIMS

1. Compound of formula (I) for its use for depigmenting, lightening and/or bleaching the skin



in which

R1 and **R2** independently denote:

- a) H;
- b) a saturated C_1 - C_{20} or unsaturated C_2 - C_{20} , linear or branched C_3 - C_{20} , or cyclic C_3 - C_8 alkyl radical,
- c) a radical S^* denoting a monosaccharide sugar radical or a polysaccharide sugar radical comprising from 2 to 5 saccharide units, preferably from 2 to 3 saccharide units, preferentially a sugar radical comprising 1 or 2 saccharide units (monosaccharide or disaccharide), said monosaccharide or polysaccharide radical S^* being connected to the rest of the molecule via a bond between the carbon atom C1 of one of the sugars of said monosaccharide or polysaccharide radical, this bond possibly being α or β anomeric,

d) a radical COR6 in which

R6 denotes a saturated linear C_1 - C_{20} alkyl radical, an unsaturated linear C_2 - C_{20} alkyl radical, a branched saturated or unsaturated C_3 - C_{20} radical or a C_3 - C_8 cycloalkyl radical,

R3 denotes a saturated C_1 - C_{20} or unsaturated C_2 - C_{20} , linear or branched C_3 - C_{20} , or cyclic C_3 - C_8 alkyl radical,

R4 and **R5** independently denote

- a) H;
- b) a saturated C_1 - C_{20} or unsaturated C_2 - C_{20} or branched C_3 - C_{20} , or cyclic C_3 - C_8 alkyl radical, optionally interrupted with one or more non-adjacent heteroatoms or groups, especially one to three, chosen from N, O, -CO- and combinations thereof such

as -NHCO-, -NHCONH-, and/or optionally substituted with one or more identical or different groups, especially one to three, chosen from:

i) -OR₇

ii) -SR₇

5 iii) -NR₇R₈

iv) -CONHR₇

v) -CONR₇R₈

vi) -COOR₇

vii) -NHCONHR₇

10 viii) -C(O)(C₁-C₄)alkyl

ix) a saturated or unsaturated non-aromatic (hetero)cyclic group, said (hetero)cyclic group being optionally substituted with one or more hydroxyls, especially one to three, and/or with one or more C₁-C₈ alkoxy and/or C₁-C₈ alkyl radicals, especially one to three; one of the chain members of the (hetero)cyclic group possibly being a carbonyl group

15

x) a C₅-C₁₂ (hetero)aryl group optionally substituted with one or more hydroxyl radicals, especially one to three, and/or with one or more C₁-C₈ alkoxy and/or C₁-C₈ alkyl radicals, especially one to three

xi) -NH-C=NH(NH₂) (guanidine group)

20 **R₇** and **R₈**, which may be identical or different, being chosen from H, a saturated linear C₁-C₁₀ alkyl group, an unsaturated linear C₂-C₁₀ alkyl group, a saturated or unsaturated branched C₃-C₁₀ alkyl group, and a C₃-C₈ cycloalkyl group; a (C₁-C₄)alkyl(C₆)(hetero)aryl group optionally containing a nitrogen atom, especially a benzyl group; an acetyl radical;

25 **R₇** and **R₈** possibly forming with the nitrogen that bears them a 5- to 8-membered heterocycle, which may contain one or more heteroatoms or groups chosen from N, O, -CO-, especially one to three, and/or optionally substituted with a C₁-C₁₀ hydrocarbon-based chain;

c) NR₉R₁₀

30 with **R₉** and **R₁₀** denoting a radical chosen from

i) -H

ii) a saturated linear C₁-C₁₀ or unsaturated C₂-C₁₀ or branched C₃-C₁₀ or cyclic C₃-C₈ alkyl group, optionally interrupted with one or more heteroatoms or groups chosen from N, O, -CO and combinations thereof such as -NHCO-, -NHCONH-, and/or optionally substituted with one or more identical or different C₁-C₈ alkyl groups, especially one to three

iii) a C₅-C₁₂ (hetero)aryl group, optionally containing one or more heteroatoms chosen from O, N and S, especially one to three, optionally substituted with one or more hydroxyls and/or with one or more C₁-C₈ alkoxy radicals, especially one to three; R₉ and R₁₀ possibly forming with the nitrogen that bears them a 5- to 8-membered heterocycle, which may contain one or more heteroatoms or groups chosen from N, O and -CO-, especially one to three, and/or optionally substituted with a C₁-C₁₀ hydrocarbon-based chain optionally containing one or more radicals chosen from hydroxyl and C₁-C₄ alkoxy, especially one to three;

d) OR₁₁

with **R₁₁** denoting a radical chosen from:

i) -H

ii) a saturated linear C₁-C₁₀ or branched C₃-C₁₀ or cyclic C₃-C₈ alkyl group,

R₄ and **R₅** possibly forming with the nitrogen that bears them a 5- to 8-membered heterocycle, which may contain one or more heteroatoms or groups chosen from N, O, -CO-, especially one to three, and/or optionally substituted with a C₁-C₁₀ hydrocarbon-based chain;

and also the salts thereof, the solvates thereof and the optical and/or geometrical isomers thereof, including enantiomers and diastereoisomers, and the racemic mixtures thereof, alone or as a mixture.

2. Compound of formula (I) for its use for depigmenting, lightening and/or bleaching the skin according to Claim 1, characterized in that

R₁ and **R₂** independently denote

a) H;

b) a saturated C₁-C₁₀ or unsaturated C₂-C₁₀, linear or branched C₃-C₁₀, or cyclic C₃-C₆ alkyl radical

c) a radical S* as defined previously and in particular a glucosyl, xylosyl, mannosyl, fucosyl or maltosyl radical

d) a radical COR6 in which

R6 denotes a saturated linear C₁-C₁₅ alkyl radical, an unsaturated linear C₂-C₁₅ alkyl radical or a branched saturated or unsaturated C₃-C₁₅ alkyl radical,

R3 denotes a saturated linear C₁-C₁₀ alkyl radical, an unsaturated linear C₂-C₁₀ alkyl radical, a branched saturated or unsaturated C₃-C₁₀ alkyl radical or a C₃-C₆ cycloalkyl radical,

R4 and R5 independently denote

a) -H;

b) a saturated linear C₁-C₁₅ alkyl radical, an unsaturated linear C₂-C₁₅ alkyl radical, a saturated or unsaturated branched C₃-C₁₅ alkyl radical or a C₃-C₈ cycloalkyl radical, optionally interrupted with one or more non-adjacent heteroatoms or groups chosen from N, O and -CO- and combinations thereof such as -NHCO-, -NHCONH-, especially one to three, and/or optionally substituted with one or more identical or different groups, especially one or two, chosen from:

i) -OR7 -OR7 such as a methyl or ethyl or isopropyl radical

ii) -SR7

iii) -NR7R8

iv) -CONHR7

v) -CONR7R8

vi) -COOR7

vii) -NHCONHR7

viii) -C(O)(C₁-C₄)alkyl

ix) a saturated or unsaturated non-aromatic (hetero)cyclic group, said (hetero)cyclic group being optionally substituted with one or more hydroxyls and/or with one or more C₁-C₈ alkoxy and/or C₁-C₈ alkyl radicals, especially one to three;

x) a C₅-C₁₂ (hetero)aryl group optionally substituted with one or more hydroxyl radicals, especially one to three, and/or with one or more C₁-C₈ alkoxy and/or C₁-C₈ alkyl radicals, especially one to three

xi) -NH-C=NH(NH₂) (guanidine group)

R7 and **R8**, which may be identical or different, being chosen from H, a saturated linear C₁-C₁₀ alkyl group, an unsaturated linear C₂-C₁₀ alkyl group, a saturated or unsaturated branched C₃-C₁₀ alkyl group, and a C₃-C₈ cycloalkyl group; a (C₁-C₄)alkyl(C₆)(hetero)aryl group optionally containing a nitrogen atom, especially a benzyl group; an acetyl radical;

R7 and **R8** possibly forming with the nitrogen that bears them a 5- to 8-membered heterocycle, which may contain one or more heteroatoms or groups chosen from N, O, -CO-, and/or optionally substituted with a C₁-C₁₀ hydrocarbon-based chain, especially one to three;

R4 and **R5** possibly forming with the nitrogen that bears them a 5- to 8-membered heterocycle, which may contain one or more heteroatoms or groups chosen from N, O, -CO-, and/or optionally substituted with a C₁-C₁₀ hydrocarbon-based chain such as pyrrolidine, piperidine, morpholine or piperazine;

and also the salts thereof, the solvates thereof and the optical and/or geometrical isomers thereof, including enantiomers and diastereoisomers, and the racemic mixtures thereof, alone or as a mixture.

3. Compound of formula (I) for its use for depigmenting, lightening and/or bleaching the skin according to Claim 1 or 2, characterized in that

R1 and **R2** independently denote

a) H;

b) a saturated linear C₁-C₆ alkyl radical, an unsaturated linear C₂-C₆ alkyl radical or a branched saturated or unsaturated C₃-C₆ alkyl radical, such as ethyl, isopropyl and n-propyl radicals

c) a radical S* denoting a monosaccharide sugar radical or a polysaccharide sugar radical comprising from 2 to 5 saccharide units, preferably from 2 to 3 saccharide units, preferentially a sugar radical comprising 1 or 2 saccharide units (monosaccharide or disaccharide), said monosaccharide or polysaccharide radical S* being connected to the rest of the molecule via a bond between the carbon atom C₁ of one of the sugars of said monosaccharide or polysaccharide radical, this bond possibly being α or β anomeric, S* in particular denoting a glucose radical

d) a radical COR6 in which

R6 denotes a saturated linear C₁-C₁₅ alkyl radical, such as a methyl or hexyl radical

R3 denotes a saturated linear C₁-C₆ alkyl radical, a saturated or unsaturated
5 branched C₃-C₆ alkyl radical or a C₃-C₆ cycloalkyl radical, such as a methyl, ethyl or isopropyl radical

R4 and **R5** independently denote

a) -H;

b) a linear C₁-C₁₅ alkyl group, a branched saturated or unsaturated C₃-C₁₅ alkyl
10 group or a C₃-C₈ cycloalkyl group, optionally interrupted with one or more non-adjacent heteroatoms or groups chosen from N, O and -CO- and combinations thereof such as -NHCO-, -NHCONH-, especially one to three, and/or optionally substituted with one or more identical or different groups, especially one to three, chosen from:

i) -OR7 such as a methyl or ethyl or isopropyl radical

15 ii) -SR7 such as SH or SMe

iii) -NR7R8 such as NH₂

iv) -CONHR7 such as CONH₂

v) -COOR7 such as CO₂Me, CO₂Et and CO₂iPr

vi) a saturated or unsaturated non-aromatic (hetero)cyclic group such as
20 cyclohexyl, optionally substituted with one or more hydroxyl radicals, especially one to three, and/or with one or more C₁-C₄ alkoxy or C₁-C₄ alkyl radicals, especially one to three; one of the chain members possibly being a carbonyl group

vii) a C₅-C₁₂ (hetero)aryl group such as a phenyl, imidazolyl or indolyl radical, optionally substituted with one or more hydroxyl radicals, especially one to three, and/or
25 with one or more C₁-C₈ alkoxy and/or C₁-C₈ alkyl radicals, especially one to three

R7 and **R8**, which may be identical or different, being chosen from H, a saturated linear C₁-C₆ alkyl group, a branched saturated or unsaturated C₃-C₆ alkyl group and a (C₁-C₄)alkyl(C₆)(hetero)aryl group optionally containing a nitrogen atom, especially a benzyl group; an acetyl radical;

30 **R7** and **R8** possibly forming with the nitrogen that bears them a 5- to 8-membered heterocycle, which may contain one or more heteroatoms or groups chosen

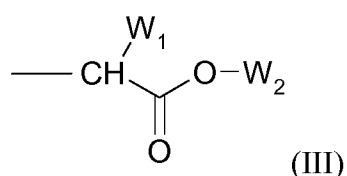
from N, O, -CO-, especially one to three, and/or optionally substituted with a C₁-C₁₀ hydrocarbon-based chain;

R4 and **R5** possibly forming with the nitrogen that bears them a heterocycle chosen from pyrrolidine, piperidine, morpholine and piperazine;

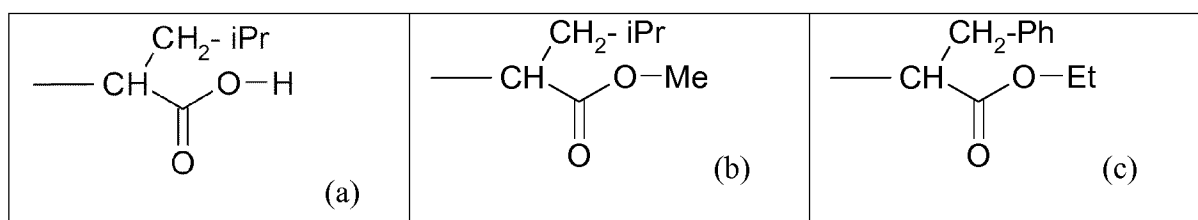
5 and also the salts thereof, the solvates thereof and the optical and/or geometrical isomers thereof, including enantiomers and diastereoisomers, and the racemic mixtures thereof, alone or as a mixture.

4. Compound of formula (I) for its use for depigmenting, lightening and/or
10 bleaching the skin according to the preceding claim, characterized in that the radical R4 is chosen from H, methyl, ethyl, n-butyl and -(CH₂)_xOMe radicals with x denoting an integer ranging from 1 to 4, limits inclusive, in particular -(CH₂)₂OMe.

5. Compound of formula (I) for its use for depigmenting, lightening and/or
15 bleaching the skin according to either of Claims 3 and 4, characterized in that the radical R5 is chosen from a hydrogen atom, the radicals: n-butyl; -(CH₂)_xOT with x denoting an integer ranging from 1 to 4, limits inclusive, and T denoting a methyl or ethyl radical, in particular -(CH₂)₃OMe, -(CH₂)₃OEt, -(CH₂)₂OMe, -(CH₂)₂OEt; ethyl; n-propyl; n-pentyl; n-hexyl; isopropyl; isobutyl; -(CH₂)_x-iPr, with x denoting an integer ranging from 1 to 4,
20 limits inclusive, in particular -(CH₂)₂OMe; cyclohexyl; -CH₂-cyclohexyl; a radical of formula (III)

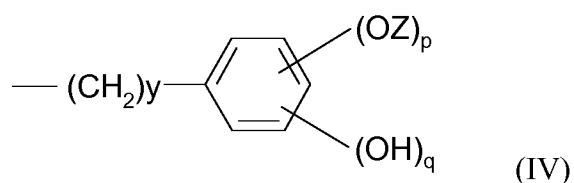


in which W1 denotes a saturated linear or branched C₁-C₆ alkyl radical optionally substituted with a phenyl radical and W2 denotes H or a saturated linear or
25 branched C₁-C₄ alkyl radical, such as the radicals of formulae (a) to (i) below:



$\begin{array}{c} \text{CH}_2\text{-Ph} \\ \\ \text{---CH} \text{---} \text{C(=O)O-H} \\ \\ \text{O} \end{array}$ (d)	$\begin{array}{c} \text{CH}_3 \\ \\ \text{---CH} \text{---} \text{C(=O)O-H} \\ \\ \text{O} \end{array}$ (e)	$\begin{array}{c} \text{CH}_3 \\ \\ \text{---CH} \text{---} \text{C(=O)O-Et} \\ \\ \text{O} \end{array}$ (f)
$\begin{array}{c} \text{H} \\ \\ \text{---CH} \text{---} \text{C(=O)O-Et} \\ \\ \text{O} \end{array}$ (g)	$\begin{array}{c} \text{H} \\ \\ \text{---CH} \text{---} \text{C(=O)O-H} \\ \\ \text{O} \end{array}$ (h)	$\begin{array}{c} \text{H} \\ \\ \text{---CH} \text{---} \text{C(=O)O-} \text{---} \text{C(CH}_3)_2 \\ \\ \text{O} \end{array}$ (i)

or alternatively a radical of formula (IV)



with y denoting an integer between 1 and 4, limits inclusive,

p being equal to 0, 1, 2 or 3,

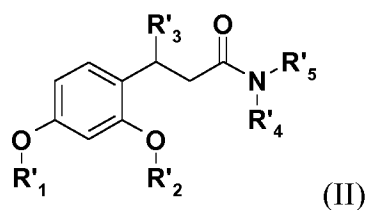
q being equal to 0, 1, 2 or 3, and $p+q < 6$

Z denoting a saturated linear $\text{C}_1\text{--C}_4$ alkyl radical such as methyl,

such as the radicals (j) and (k) below:

$\text{---}(\text{CH}_2)_2\text{---} \text{C}_6\text{H}_4\text{---OH} \quad (\text{j})$	$\text{---}(\text{CH}_2)_2\text{---} \text{C}_6\text{H}_3(\text{OMe})(\text{OH}) \quad (\text{k})$
---	--

6. Compounds of formula (II) below:



in which:

R'1 and **R'2** independently denote

a) H;

b) a saturated $\text{C}_1\text{--C}_{20}$ or unsaturated linear or branched $\text{C}_3\text{--C}_{20}$, or cyclic $\text{C}_3\text{--C}_8$ alkyl radical,

c) a radical S* denoting a monosaccharide sugar radical or a polysaccharide sugar radical comprising from 2 to 5 saccharide units, preferably from 2 to 3 saccharide units, preferentially a sugar radical comprising 1 or 2 saccharide units (monosaccharide or disaccharide), said monosaccharide or polysaccharide radical S* being connected to the rest of the molecule via a bond between the carbon atom C1 of one of the sugars of said monosaccharide or polysaccharide radical, this bond possibly being α or β anomeric,

d) a radical COR'6

in which R'6 denotes a saturated linear C₁-C₂₀ alkyl radical, an unsaturated linear C₂-C₂₀ alkyl radical, a branched saturated or unsaturated C₃-C₂₀ radical or a C₃-C₈ cycloalkyl radical,

it being understood that R'1 and R'2 cannot simultaneously denote a methyl radical,

R'3 denotes a saturated C₁-C₂₀ or unsaturated C₂-C₂₀, linear or branched C₃-C₂₀, or cyclic C₃-C₈ alkyl radical,

R'4 and **R'5** independently denote

a) -H;

b) a saturated C₁-C₂₀ or unsaturated C₂-C₂₀ or branched C₃-C₂₀, or cyclic C₃-C₈ alkyl radical, optionally interrupted with one or more non-adjacent heteroatoms or groups, chosen from N, O, -CO- and combinations thereof such as -NHCO-, -NHCONH-, especially one to three, and/or optionally substituted with one or more identical or different groups, especially one to three, chosen from:

i) -OR'7

ii) -SR'7

iii) -NR'7R'8

iv) -CONHR'7

v) -CONR'7R'8

vi) -COOR'7

vii) -NHCONHR'7

viii) -C(O)(C₁-C₄)alkyl

ix) a saturated or unsaturated non-aromatic (hetero)cyclic group, said (hetero)cyclic group being optionally substituted with one or more hydroxyls, especially one to three, and/or with one or more C₁-C₈ alkoxy or C₁-C₈ alkyl radicals, especially one to three; one of the chain members possibly being a carbonyl group;

5 x) a C₅-C₁₂ (hetero)aryl group optionally substituted with one or more hydroxyl radicals, especially one to three, and/or with one or more C₁-C₈ alkoxy and/or C₁-C₈ alkyl radicals, especially one to three

xi) -NH-C=NH(NH₂) (guanidine group)

R'7 and **R'8**, which may be identical or different, being chosen from H, a
10 saturated linear C₁-C₁₀ alkyl group, an unsaturated linear or branched C₂-C₁₀ alkyl group, a saturated or unsaturated branched C₃-C₁₀ alkyl group, and a C₃-C₈ cycloalkyl group; a (C₁-C₄)alkyl(C₆)(hetero)aryl group optionally containing a nitrogen atom, especially a benzyl group; an acetyl radical;

R'7 and R'8 possibly forming with the nitrogen that bears them a 5- to 8-
15 membered heterocycle, which may contain one or more heteroatoms or groups chosen from N, O, -CO-, especially one to three, and/or optionally substituted with a C₁-C₁₀ hydrocarbon-based chain;

c) NR'9R'10

R'9 and **R'10** denoting a radical chosen from

20 i) -H

ii) a saturated linear C₁-C₁₀ or unsaturated C₂-C₁₀ or branched C₃-C₁₀ or cyclic C₃-C₈ alkyl group, optionally interrupted with one or more non-adjacent heteroatoms or groups chosen from N, O, -CO and combinations thereof such as -NHCO-, -NHCONH-, especially one to three, and/or optionally substituted with one or more identical or different
25 C₁-C₈ alkyl groups, especially one to three;

iii) a C₅-C₁₂ (hetero)aryl group, optionally containing one or more non-adjacent heteroatoms chosen from O, N and S, especially one to three, optionally substituted with one or more hydroxyls and/or with one or more C₁-C₈ alkoxy radicals, especially one to three; R9 and R10 possibly forming with the nitrogen that bears them a 5- to 8-membered
30 heterocycle, which may contain one or more heteroatoms or groups chosen from N, O and -CO-, especially one to three, and/or optionally substituted with a C₁-C₁₀ hydrocarbon-

based chain optionally containing one or more radicals chosen from hydroxyl and C₁-C₄ alkoxy, especially one to three;

d) OR'11

with R'11 denoting a radical chosen from:

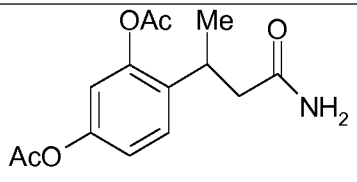
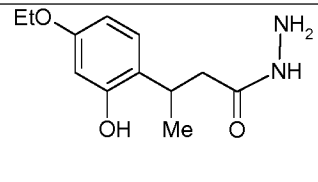
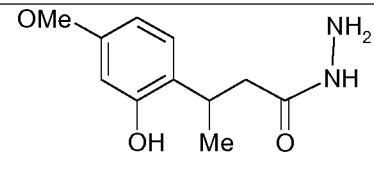
i) -H

ii) a saturated linear C₁-C₁₀ or branched C₃-C₁₀ or cyclic C₃-C₈ alkyl group,

R'4 and R'5 possibly forming with the nitrogen that bears them a 5- to 8-membered heterocycle, which may contain one or more heteroatoms or groups chosen from N, O, -CO-, especially one to three, and/or optionally substituted with a C₁-C₁₀ hydrocarbon-based chain,

and also the salts thereof, the solvates thereof and the optical and/or geometrical isomers thereof, including enantiomers and diastereoisomers, and the racemic mixtures thereof,

with the exception of the following 3 compounds:

		
CAS 200056-48-0	CAS = 24535-08-8	CAS = 1020241-68-2

7. Compound of formula (II) according to the preceding claim, characterized in that

R'1 and **R'2** independently denote

a) H;

b) a saturated linear C₁-C₁₀ alkyl radical, an unsaturated linear or branched C₂-C₁₀ alkyl radical, a branched saturated or unsaturated C₃-C₁₀ alkyl group or a C₃-C₆ cycloalkyl group,

c) a radical S* denoting a monosaccharide sugar radical or a polysaccharide sugar radical comprising from 2 to 5 saccharide units, preferably from 2 to 3 saccharide units, preferentially a sugar radical comprising 1 or 2 saccharide units (monosaccharide or disaccharide), said monosaccharide or polysaccharide radical S* being connected to the rest of the molecule via a bond between the carbon atom C1 of one of the sugars of said

monosaccharide or polysaccharide radical, this bond possibly being α or β anomeric; and in particular a glucosyl, xylosyl, mannosyl, fucosyl or maltosyl radical

d) a group COR'6 in which

5 R'6 denotes a saturated linear C₁-C₁₅ alkyl group or an unsaturated linear C₂-C₁₅ alkyl group

it being understood that R'1 and R'2 cannot simultaneously denote a methyl radical

10 **R'3** denotes a saturated linear C₁-C₁₀ alkyl radical, an unsaturated linear C₂-C₁₀ alkyl radical, a branched saturated or unsaturated C₃-C₁₀ alkyl radical or a C₃-C₆ cycloalkyl radical,

R'4 and **R'5** independently denote

a) -H;

15 b) a linear C₁-C₁₅ alkyl radical, an unsaturated linear C₂-C₁₅ alkyl radical, a saturated or unsaturated branched C₃-C₁₅ radical or a C₃-C₈ cycloalkyl radical, optionally interrupted with one or more heteroatoms or groups chosen from N, O and -CO- and a combination thereof such as -NHCO-, -NHCONH-, especially one to three, and/or optionally substituted with one or more identical or different groups, especially one to three, chosen from:

20 i) -OR'7 such as a methyl or ethyl or isopropyl radical

ii) -SR'7

iii) -NR'7R'8

iv) -CONHR'7

v) -CONR'7R'8

25 vi) -COOR'7

vii) -NHCONHR'7

viii) -C(O)(C₁-C₄)alkyl

ix) a saturated or unsaturated non-aromatic heterocyclic group, said (hetero)cyclic group being optionally substituted with one or more hydroxyl radicals, 30 especially one to three, and/or with one or more C₁-C₈ alkoxy or C₁-C₈ alkyl radicals, especially one to three; one of the chain members possibly being a carbonyl group;

x) a C₅-C₁₂ (hetero)aryl group optionally substituted with one or more hydroxyl radicals, especially one to three, and/or with one or more C₁-C₈ alkoxy and/or C₁-C₈ alkyl radicals, especially one to three

xi) -NH-C=NH(NH₂) (guanidine group)

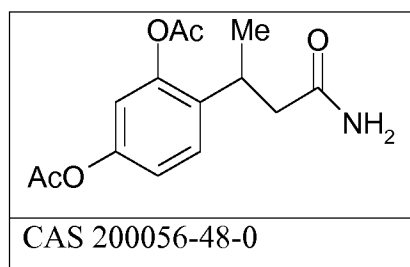
5 **R'7** and **R'8**, which may be identical or different, being chosen from H, a saturated linear C₁-C₁₀ alkyl group, an unsaturated linear C₂-C₁₀ alkyl radical, a saturated or unsaturated branched C₃-C₁₀ alkyl radical, and a C₃-C₈ cycloalkyl radical; a (C₁-C₄)alkyl(C₆)(hetero)aryl group optionally containing a nitrogen atom, especially a benzyl group; an acetyl radical;

10 **R'7** and **R'8** possibly forming with the nitrogen that bears them a 5- to 8-membered heterocycle, which may contain one or more heteroatoms or groups chosen from N, O, -CO-, especially one to three, and/or optionally substituted with a C₁-C₁₀ hydrocarbon-based chain;

15 **R'4** and **R'5** possibly forming with the nitrogen that bears them a 5- to 8-membered heterocycle, which may contain one or more heteroatoms or groups chosen from N, O and -CO-, especially one or two, and/or optionally substituted with a C₁-C₁₀ hydrocarbon-based chain such as pyrrolidine, piperidine, morpholine or piperazine;

20 and also the salts thereof, the solvates thereof and the optical and/or geometrical isomers thereof, including enantiomers and diastereoisomers, and the racemic mixtures thereof,

and with the exception of the following compound:



8. Compound of formula (II) according to either of Claims 6 and 7, characterized in that

25 **R'1** and **R'2** independently denote

a) H;

b) a saturated linear C₁-C₆ alkyl group or an saturated or unsaturated branched C₃-C₆ alkyl group such as ethyl, isopropyl and n-propyl radicals

c) a radical S^* denoting a monosaccharide sugar radical or a polysaccharide sugar radical comprising from 2 to 5 saccharide units, preferably from 2 to 3 saccharide units, preferentially a sugar radical comprising 1 or 2 saccharide units (monosaccharide or disaccharide), said monosaccharide or polysaccharide radical S^* being connected to the rest of the molecule via a bond between the carbon atom C1 of one of the sugars of said monosaccharide or polysaccharide radical, this bond possibly being α or β anomeric, S^* in particular denoting a glucose radical

d) a group $COR'6$

with $R'6$ denoting a saturated linear C_1 - C_{15} alkyl radical or an unsaturated linear C_2 - C_{15} group, preferably a saturated linear C_1 - C_{15} alkyl radical, such as a methyl or hexyl radical

it being understood that $R'1$ and $R'2$ cannot simultaneously denote a methyl radical

$R'3$ denotes a saturated linear C_1 - C_6 alkyl radical, an unsaturated linear C_2 - C_{10} alkyl radical, a saturated or unsaturated branched C_3 - C_6 alkyl radical or a C_3 - C_6 cycloalkyl radical, such as a methyl, ethyl or isopropyl radical

$R'4$ and $R'5$ independently denote

a) $-H$;

b) a saturated linear C_1 - C_{15} alkyl radical, an unsaturated linear C_2 - C_{15} alkyl radical, a saturated or unsaturated branched C_3 - C_{15} radical or a C_3 - C_8 cycloalkyl radical, optionally interrupted with one or more non-adjacent heteroatoms or groups chosen from N, O and $-CO-$ and combinations thereof such as $-NHCO-$, $-NHCONH-$, especially one to three, and/or optionally substituted with one or more identical or different groups, especially one to three, chosen from:

i) $-OR7$ such as a methyl or ethyl or isopropyl radical

ii) $-SR7$ such as SH or SMe

iii) $-NR7R8$ such as NH_2

iv) $-CONHR7$ such as $CONH_2$

v) $-COOR7$ such as CO_2Me , CO_2Et and CO_2iPr

vi) a saturated or unsaturated non-aromatic (hetero)cyclic group such as cyclohexyl, optionally substituted with one or more hydroxyl radicals, especially one to

three, and/or with one or more C₁-C₄ alkoxy or C₁-C₄ alkyl radicals, especially one to three;

vii) a C₅-C₁₂ (hetero)aryl group such as a phenyl, imidazolyl or indolyl radical, optionally substituted with one or more hydroxyl radicals, especially one to three, and/or
5 with one or more C₁-C₈ alkoxy and/or C₁-C₈ alkyl radicals, especially one to three

viii) -NH-C=NH(NH₂) (guanidine group)

R'7 and **R'8**, which may be identical or different, being chosen from H, a saturated linear C₁-C₁₀ alkyl group, an unsaturated linear C₂-C₁₀ alkyl group, a saturated or unsaturated branched C₃-C₁₀ alkyl group, and a C₃-C₈ cycloalkyl group; a (C₁-
10 C₄)alkyl(C₆)(hetero)aryl group optionally containing a nitrogen atom, especially a benzyl group; an acetyl radical;

R'7 and **R'8** possibly forming with the nitrogen that bears them a 5- to 8-membered heterocycle, which may contain one or more heteroatoms or groups especially one or two, chosen from N, O, -CO-, and/or optionally substituted with a C₁-C₁₀
15 hydrocarbon-based chain;

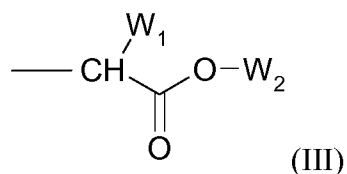
R'4 and R'5 possibly forming with the nitrogen that bears them a heterocycle chosen from pyrrolidine, piperidine, morpholine and piperazine,

and also the salts thereof, the solvates thereof and the optical and/or geometrical isomers thereof, including enantiomers and diastereoisomers, and the racemic
20 mixtures thereof.

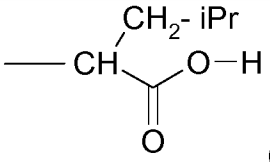
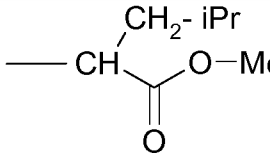
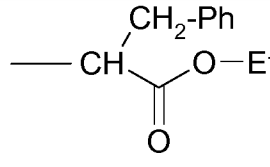
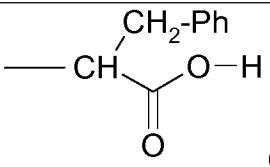
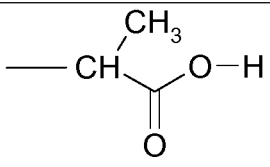
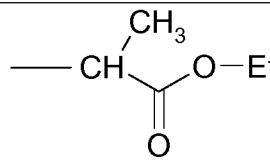
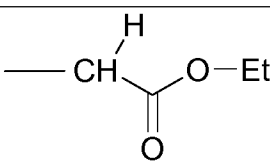
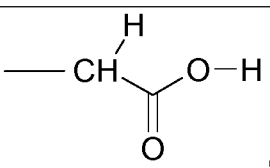
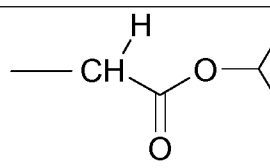
9. Compound of formula (II) according to the preceding claim, characterized in that R'4 is chosen from H, methyl, ethyl, n-butyl and -(CH₂)_xOMe radicals with x denoting an integer ranging from 1 to 4, limits inclusive, in particular -(CH₂)₂OMe.

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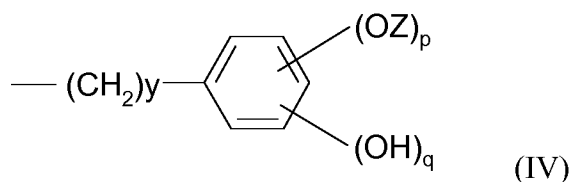
10. Compound of formula (II) according to either of Claims 8 and 9, characterized in that R'5 is chosen from the radicals: n-butyl; -(CH₂)_xOT with x denoting an integer ranging from 1 to 4, limits inclusive, and T denoting a methyl or ethyl radical, in particular -(CH₂)₃OMe, -(CH₂)₃OEt, -(CH₂)₂OMe, ethyl; n-propyl; n-pentyl; n-hexyl;
30 isopropyl; isobutyl; -(CH₂)_x-iPr, x denoting an integer ranging from 1 to 4, limits inclusive, in particular -(CH₂)₂OMe; cyclohexyl; -CH₂-cyclohexyl; a radical of formula (III)



in which W1 denotes a saturated linear or branched C₁-C₆ alkyl radical optionally substituted with a phenyl radical and W2 denotes H or a saturated linear or branched C₁-C₄ alkyl radical, such as the radicals of formulae (a) to (i) below:

5 or alternatively a radical of formula (IV)

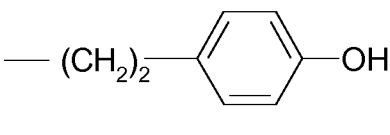
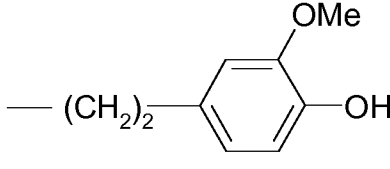


with y denoting an integer between 1 and 4, limits inclusive,

p being equal to 0, 1, 2 or 3,

q being equal to 0, 1, 2 or 3, and p+q < 6

10 Z denoting a saturated linear C₁-C₄ alkyl radical such as methyl, such as the radicals (j) and (k) below:

	
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11. Compound of formula (II) chosen from the following compounds

- N-butyl-3-(2,4-dihydroxyphenyl)butanamide
- 3-(2,4-dihydroxyphenyl)-N-(3-methoxypropyl)butanamide
- N-(4-hydroxyphenethyl)-3-(2,4-dihydroxyphenyl)butanamide
- 3-(2,4-dihydroxyphenyl)-N-ethylbutanamide
- methyl 2-(3-(2,4-dihydroxyphenyl)butanamido)-4-methylpentanoate
- 3-(2,4-diethoxyphenyl)-N-ethylbutanamide
- N-butyl-3-(2,4-dihydroxyphenyl)-4-methylpentanamide
- N-butyl-3-(2,4-dihydroxyphenyl)pentanamide
- ethyl 2-(3-(2,4-dihydroxyphenyl)butanamido)-3-phenylpropanoate
- 3-(2,4-dihydroxyphenyl)-N,N-diethylbutanamide
- N,N-dibutyl-3-(2,4-dihydroxyphenyl)butanamide
- 3-(2,4-dihydroxyphenyl)-N-propylbutanamide
- 3-(2,4-dihydroxyphenyl)-N-pentylbutanamide
- 3-(2,4-dihydroxyphenyl)-N-hexylbutanamide
- 3-(2,4-dihydroxyphenyl)-N-(3-ethoxypropyl)butanamide
- 3-(2,4-dihydroxyphenyl)-N-isopropylbutanamide
- 3-(2,4-dihydroxyphenyl)-N-isobutylbutanamide
- 3-(2,4-dihydroxyphenyl)-N-isopentylbutanamide
- 3-(2,4-dihydroxyphenyl)-N-(4-methylpentyl)butanamide
- N-cyclohexyl-3-(2,4-dihydroxyphenyl)butanamide
- N-(cyclohexylmethyl)-3-(2,4-dihydroxyphenyl)butanamide
- N-(4-hydroxy-3-methoxyphenethyl)-3-(2,4-dihydroxyphenyl)butanamide
- ethyl 2-(3-(2,4-dihydroxyphenyl)butanamido)propanoate
- 3-(2,4-dihydroxyphenyl)-N,N-bis(2-methoxyethyl)butanamide
- ethyl 2-(3-(2,4-dihydroxyphenyl)-N-methylbutanamido)acetate
- 3-(2,4-dihydroxyphenyl)-N-(heptan-3-yl)butanamide
- N-ethyl-3-(2-hydroxy-4-((2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)-tetrahydro-2H-pyran-2-yloxy)phenyl)butanamide
- 3-(2,4-dihydroxyphenyl)-N-(2-hydroxyethyl)butanamide
- ethyl 2-(3-(2,4-dihydroxyphenyl)butanamido)acetate
- 2-(3-(2,4-dihydroxyphenyl)butanamido)acetic acid
- N-ethyl-3-(4-hydroxy-2-((2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)-

tetrahydro-2H-pyran-2-yloxy)phenyl)butanamide

- N-ethyl-3-(2-hydroxy-4-((3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)-tetrahydro-2H-pyran-2-yloxy)phenyl)butanamide
- 4-(4-(ethylamino)-4-oxobutan-2-yl)-1,3-phenylene diacetate
- 4-(4-(ethylamino)-4-oxobutan-2-yl)-1,3-phenylene diheptanoate
- 2-(3-(2,4-dihydroxyphenyl)butanamido)-4-methylpentanoic acid
- 2-(3-(2,4-dihydroxyphenyl)-N-methylbutanamido)acetic acid
- 2-(3-(2,4-dihydroxyphenyl)butanamido)propanoic acid
- 2-(3-(2,4-dihydroxyphenyl)butanamido)-3-phenylpropanoic acid
- 3-(2,4-dihydroxyphenyl)butanamide
- ethyl (S)-2-(3-(2,4-dihydroxyphenyl)butanamido)propanoate
- ethyl (R)-2-(3-(2,4-dihydroxyphenyl)butanamido)propanoate
- (S)-2-(3-(2,4-dihydroxyphenyl)butanamido)propanoic acid
- (R)-2-(3-(2,4-dihydroxyphenyl)butanamido)propanoic acid
- methyl 2-(3-(2,4-dihydroxyphenyl)butanamido)-4-methylpentanoate
- (R)-2-(3-(2,4-dihydroxyphenyl)butanamido)-4-methylpentanoic acid
- ethyl 2-(3-(2,4-dihydroxyphenyl)butanamido)-3-phenylpropanoate
- 3-(2-ethoxy-4-hydroxyphenyl)-N-ethylbutanamide
- 3-(4-ethoxy-2-hydroxyphenyl)-N-ethylbutanamide
- (R)-2-(3-(2,4-dihydroxyphenyl)butanamido)-3-phenylpropanoic acid
- 3-(2,4-diisopropoxyphenyl)-N-ethylbutanamide
- 3-(2,4-dipropoxyphenyl)-N-ethylbutanamide
- N-ethyl-3-(4-hydroxy-2-isopropoxyphenyl)butanamide
- N-ethyl-3-(4-hydroxy-2-propoxyphenyl)butanamide
- N-ethyl-3-(2-hydroxy-4-isopropoxyphenyl)butanamide
- N-ethyl-3-(2-hydroxy-4-propoxyphenyl)butanamide
- 3-(2,4-dihydroxyphenyl)-N-ethyl-N-(2-hydroxyethyl)butanamide
- 3-(2,4-dihydroxyphenyl)-1-(morpholin-4-yl)butan-1-one

and also the salts thereof, the solvates thereof and the optical and/or geometrical isomers thereof, including enantiomers and diastereoisomers, and the racemic mixtures thereof, and is in particular ethyl 2-(3-(2,4-

dihydroxyphenyl)butanamido)propanoate or one of its salts, solvates or optical and/or geometrical isomers thereof.

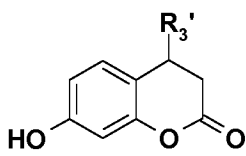
12. Composition comprising, in a physiologically acceptable medium, at least one compound of formula (II) according to any one of Claims 6 to 11.

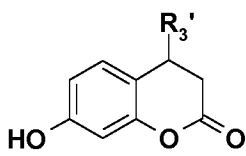
13. Composition according to the preceding claim, characterized in that said compound of formula (II) is present in an amount of between 0.01% and 10% by weight, preferably between 0.1% and 5% by weight and in particular between 0.5% and 3% by weight, relative to the total weight of the composition.

14. Non-therapeutic cosmetic process for depigmenting, lightening and/or bleaching keratin materials, especially the skin, comprising the application of the composition according to Claim 12 or 13 or of a composition comprising a compound of formula (I) according to any one of Claims 1 to 5.

15. Non-therapeutic cosmetic use of at least one compound of formula (I) or (II) according to any one of Claims 1 to 11, as an agent for bleaching, lightening and/or depigmenting keratin materials, especially the skin.

16. Process for preparing a compound of formula (II) as defined in Claim 6, which consists in

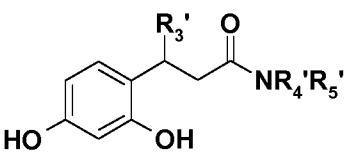


(i) reacting a compound of formula D , in which R₃' is as defined in Claim 6, by hydrogenation for the purpose of ring opening in the presence of a catalyst such as Pd/C, said compound of formula D having possibly been protected beforehand on the hydroxyl group with a protecting group such as the benzyl group, and then

(ii) reacting the compound obtained in step (i) with a compound of formula HNR₄R₅, in the presence of an organic solvent, especially tetrahydrofuran, dioxane, dimethylformamide, dimethyl sulfoxide, 2-methyltetrahydrofuran,

dichloromethane; toluene, methanol or ethanol; optionally in the presence of a catalyst chosen from Lewis or Brønsted acid catalysts and basic catalysts, such as potassium carbonate, triethylamine or diisopropylethylamine; optionally by heating to a temperature of between 15°C and 200°C, especially between 20°C

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and 150°C, to give the compound of formula G , in which R3', R4' and R5' are as defined in Claim 6, said compound of formula G being able subsequently to undergo modification of the hydroxyl groups to give said compound of formula (II).

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2016/080911

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07C235/34 C07C235/36 C07D295/185 C07C231/02 A61K8/42
A61K8/49 A61K8/60 A61Q19/02

ADD.

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07C A61K A61Q C07D

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2004/017936 A1 (UNILEVER PLC [GB]; UNILEVER NV [NL]; LEVER HINDUSTAN LTD [IN]) 4 March 2004 (2004-03-04) cited in the application claims; examples	1-16
A	WO 2005/085169 A1 (UNILEVER PLC [GB]; UNILEVER NV [NL]; LEVER HINDUSTAN LTD [IN]; HARICHI) 15 September 2005 (2005-09-15) cited in the application claims; examples	1-16
A	FR 2 991 985 A1 (OREAL [FR]) 20 December 2013 (2013-12-20) claims; examples	1-16
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Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

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

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

"&" document member of the same patent family

Date of the actual completion of the international search

27 February 2017

Date of mailing of the international search report

06/03/2017

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Ginoux, Claude

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2016/080911

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
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X	----- JIAN SHANG ET AL: "Highly enantioselective asymmetric hydrogenation of (E)-[beta],[beta]-disubstituted [alpha],[beta]-unsaturated Weinreb amides catalyzed by Ir(i) complexes of SpinPhox ligands", CHEMICAL COMMUNICATIONS - CHEMCOM., vol. 48, no. 42, 1 January 2012 (2012-01-01), page 5172, XP055294937, ISSN: 1359-7345, DOI: 10.1039/c2cc30812f compound 2d -----	1-4

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2016/080911

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