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(54) Title: SILYLATED COMPOUNDS AS PRECURSORS FOR SELF-TANNING COMPOSITIONS

(57) Abstract: The use of silylated compounds as precursors of skin self-tanning substances in self-tanning compositions is described.
Silylated compounds as precursors for self-tanning compositions

The present invention relates to the use of silylated compounds as precursors for self-tanning compositions, to novel silylated compounds, to processes for their preparation, and to cosmetic formulations comprising these silylated compounds.

Skin self-tanning substances are substances which produce brown dyes upon contact with the skin as a result of a chemical reaction with the keratin in the skin without the action of natural or artificial light (J. Eichler, Kontakte (Merck, Darmstadt), 1981, 3, 24). Typically, these compounds contain aldol, ketol or dicarbonyl groups in the molecule, dihydroxyacetone (DHA) being the best known representative.

The following compounds are also of importance:
glyceraldehyde, 6-aldo-D-fructose, hydroxymethylglyoxal, muconaldehyde, malealdehyde, substituted succinaldehydes, erythrulose, dihydroxyacetone (as monomer or dimer), methylglyoxal (pyruvaldehyde), substituted 4,4'-dihydroxyrazolin-5-ones, as described in EP-A-0903342.

These compounds react with free amino groups in the skin in a Maillard reaction to give brown-coloured substances in the stratum corneum. This reaction is complete after 4 to 12 hours. The tan achieved cannot be washed off and is removed only with normal skin desquamation, i.e. it takes approximately 5 to 15 days until the skin is completely decoloured.

However, the practical use of self-tanning active ingredients, for example DHA, in self-tanning compositions has disadvantages, such as inadequate stability and high reactivity with other formulation components (discoloration, formation of unpleasant odours), poor solubility in nonpolar organic solvents (virtually insoluble) and difficult formulatability.

Surprisingly, it has been found that by silylating the skin self-tanning substances listed above, it is possible to prepare precursors of these substances which no longer have these disadvantages. Following hydrolysis or enzymatic cleavage of these active ingredient precursors on the skin, the self-tanning substances are again released.
The present invention thus provides for the use of silylated derivatives as precursors of skin self-tanning substances in self-tanning compositions.

In particular, the partially or completely silylated derivatives of the following skin self-tanning substances are of importance:
glyceraldehyde, 6-aldo-D-fructose, hydroxymethylglyoxal, muconialdehyde, malealdehyde, substituted succinodialdehydes, erythrulose, dihydroxyacetone (as monomer or dimer), methylglyoxal (pyruvaldehyde), substituted 4,4'-dihydroxypyrazolin-5-ones, as described in EP-A-0903342.

Preference is given according to the invention to using compounds of the formulae

\[ \text{(1a) } \quad \text{(1b) } \quad \text{(1c) } \quad \text{(1d) } \quad \text{(1e) or (1f) } \]

in which

\( R_1, R_2, R_3 \text{ and } R_4 \) independently of one another are hydrogen or a radical of the formula

\[ \text{(1g) } \quad \text{is } C_1-C_5 \text{alkyl; ary1; } C_6-C_{10} \text{ary1; and } C_1-C_{18} \text{alkyl;} \]

where in the formulae (1a) to (1f) at least one of the radicals \( R_1, R_2, R_3 \) and \( R_4 \) is a radical of the formula (1g).

\( C_1-C_5 \text{alkyl and } C_1-C_{18} \text{alkyl are straight-chain or branched alkyl radicals, for example methyl, ethyl, } n\text{-propyl, isopropyl, } n\text{-butyl, sec-butyl, tert-butyl, amy1, isoamy1 or tert-amy1, heptyl, octyl, isooctyl, nonyl, decyl, undecyl, dodecyl, tetradecyl, pentadecyl or hexadecyl.} \)

\( C_6-C_{10} \text{Ary1 is naphthyl and preferably phenyl.} \)
Particular preference is given according to the invention to using compounds of the formulae

(2a)  
(2b)  
(2c)  

(2d)  
(2e)  
(2f)  

(3a)  
(3b)  
(3c)  

(4a)  
(4b)  

(4c)  

(5a)  
(5b)  
(5c)  

(6a)  
(6b)  
(6c)  

in which, in the formulae given above,
A is a radical of the formula (1g).
Particular preference is given to using compounds in which, in formula (1g),
\[ R_5 \] is methyl or ethyl.

Very particular preference is given according to the invention to using the compounds of the formulae

\[
(7) \quad H_2 C-\overset{\text{CH}_3}{\text{Si}}-O-\overset{\text{CH}_2}{\text{O}}-\overset{\text{CH}_2}{\text{O}}-\overset{\text{Si}}{\text{CH}_3} \quad \text{and} \quad (8) \quad (\text{CH}_3)\text{Si}-O-\overset{\text{O}}{\overset{\text{O}}{\overset{\text{O}}{\overset{\text{O}}{\text{Si}}} \text{Si}}} (\text{CH}_3)\text{Si}.
\]

The soluble precursors of skin self-tanning substances used according to the invention are prepared in a manner known per se. The process comprises silylating the skin self-tanning substances glyceraldehyde, 6-aldo-D-fructose, hydroxymethylglyoxal, muconialdehyde, malealdehyde, substituted succindialdehydes, erythulose, dihydroxyacetone, methylglyoxal (pyruvaldehyde), substituted 4,4'-dihydroxypyrrolin-5-ones with a suitable silylating agent.

The process for the preparation of the compounds of the formulae (1a) to (1f) comprises reacting dihydroxyacetone in monomeric or dimeric form with a suitable silylating reagent.

Some of the compounds of the formulae (1) to (8) are known compounds and some are novel compounds.

The novel compounds are those of the formulae

\[
(1a) \quad R_1 O-\overset{\text{O}}{\overset{\text{O}}{\overset{\text{O}}{\overset{\text{O}}{\text{R}_2}}; \quad (1b) \quad \text{or} \quad (1c) \quad \text{or} \quad (1d) \quad \text{or} \quad (1e) \quad \text{or} \quad (1f) \quad \text{or} \quad (1g).
\]

\[ R_1, R_2, R_3 \text{ and } R_4 \text{ independently of one another are hydrogen or a radical of the formula} \]
where in the formulae (1a) to (1f) at least one of the radicals R₁, R₂, R₃ and R₄ is a radical of the formula (1g), and the following compounds are not included:

- compounds of the formula (1a), in which A and R₁ are at the same time a radical of the formula

\[
\begin{align*}
(1a') & \quad \text{CH}_3 \\
& \quad \text{Si} \quad \text{t-butyl or (1a'')} \\
& \quad \text{CH}_3 \\
& \quad \text{Si} \quad \text{t-butyl} \\
& \quad \text{CH}_3 \\
& \quad \text{Si} \quad \text{t-butyl} \\
\end{align*}
\]

- compounds of the formula (1a) in which A is a radical of the formulae (1a') or (1a'') and R₁ is hydrogen;
- compounds of the formula (1c) in which R₁ and R₂ are a radical of the formula (1a');
- compounds of the formula (1d) in which R₁, R₂, R₃ and R₄ are a radical of the formula

\[
(1a'') \quad \text{CH}_3 \\
& \quad \text{Si} \quad \text{CH}_3 \\
\]

The novel compounds are prepared by reacting dihydroxyacetone, which is in crystalline form as a dimer of the formula

\[
\begin{align*}
(10) & \quad \text{H} \quad \text{O} \\
& \quad \text{O} \quad \text{H} \\
& \quad \text{O} \quad \text{H} \\
& \quad \text{O} \quad \text{H} \\
& \quad \text{O} \quad \text{H} \\
\end{align*}
\]
with a silylating reagent of the formula \( X^{\text{RSi}} \), in which

\[
X = \text{halogen, -CN, -NHSi(R_5)_2R_6, -OSi(R_5)_2R_6, -N(CH_2CH_3)_2, -N(CH_3)_2, -NH(CO)NHSi(R_5)_2R_6}
\]

and

\( R_5 \) and \( R_6 \) are as defined above.

Through suitable choice of the reaction conditions during the silylation reaction it is possible to obtain the compounds of the formulae (1a) to (1f).

The reaction temperature is between -40 and 150°C, preferably 0 and 100°C.

Suitable solvents are halogenated aliphatic and aromatic hydrocarbons, for example chlorobenzene, dichlorobenzene, dichloromethane, trichloromethane or tetrachloromethane, dipolar aprotic solvents, for example dimethylformamide, sulfolane or acetonitrile, ethers, for example tetrahydrofuran, diethyl ether, tert-butyl methyl ether or dioxane, aromatic hydrocarbons, for example toluene, xylene or benzene, or aliphatic hydrocarbons, for example petroleum ether or hexane.

The reactions can also be carried out without solvents by using an excess of the silylating reagent.

Auxiliary bases used are inorganic and/or organic bases, for example triethylamine, trimethylamine, ethyldiisopropylamine, pyridine or imidazole.

Silylating reagents \( X^{\text{RSi}} \) and methods are generally known and described in

The invention further provides a cosmetic formulation comprising
2 to 15% by weight, preferably 5 to 10% by weight, of a precursor or of two or more
precursors of the formula (1), and customary cosmetic carriers or auxiliaries.

Because of its physicochemical properties, the precursor is sensitive to hydrolysis and
cannot therefore be used in the customarily used cosmetic W/O or O/W formulations or in
other customary cosmetic formulations in which the water phase comes into direct contact
with the phase which contains the precursor.

Of particular suitability, therefore, for incorporating the precursor are water-free formulations
or systems in which the water-containing phase and the active ingredient phase are not in
direct contact with one another and are only mixed together upon application (2-chamber or
multichamber systems).

Water-free systems which can be used are, for example, oils based on triglycerides or
mineral oils, and also silicone oils in the form of sprays or as liquid. Silicone oils may also be
used in semisolid form, in the form of "silicone gels". A further variant is oleogels which
contain thickened triglycerides. Likewise suitable are water-free powders and aerosols.

The customary cosmetic carriers or auxiliaries which are present in the cosmetic composition
according to the invention include various oil components, such as fats, oils, silicone oil etc.,
further substances such as allantoin, thickeners, water-free preservatives, perfume oils,
antioxidants, for example vitamin E, carotinoids or HALS compounds.

Moreover, the composition according to the invention can also comprise further UV
protection substances from the following classes of substance:
1. p-aminobenzoic acid derivatives, for example 2-ethylhexyl 4-dimethylaminobenzoate;
2. salicylic acid derivatives, for example 2-ethylhexyl salicylate;
3. benzophenone derivatives, for example 2-hydroxy-4-methoxybenzophenone and its 5-
sulfonic acid derivative;
4. dibenzoylmethane derivatives, for example 1-(4-tert-butylphenyl)-3-(4-
methoxyphenyl)propane-1,3-dione;
5. diphenyl acrylates, for example 2-ethylhexyl 2-cyano-3,3-diphenyl acrylate and 3-
benzofuranyl 2-cyanoacrylate;
6. 3-imidazol-4-ylacrylic acid and esters;
8. polymeric UV absorbers, for example the benzylidene malonate derivatives described in EP-A-709,080;
9. cinnamic acid derivatives, for example the 2-ethylhexyl 4-methoxycinnamate or isoamyl 4-methoxycinnamate disclosed in US-A-5,601,811 and WO 97/00851;
10. camphor derivatives, for example 3-(4′-methyl)benzylidenebornan-2-one, 3-benzylidenebornan-2-one, N-[2(and 4)-2-oxoborn-3-ylidenemethyl]benzyl]acrylamide polymer, 3-(4′-trimethylammonium)benzylidenebornan-2-one methylsulfate, 3,3′-(1,4-phenylenedimethine)bis(7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-methanesulfonic acid) and salts, 3-(4′-sulfo)benzylidenebornan-2-one and salts;
12. 2-hydroxyphenylbenzotriazole derivatives;
13. hydroxyphenyl-s-triazine compounds, for example the compounds described in US-A-5,955,060;
14. 2-phenylbenzimidazole-5-sulfonic acid and salts thereof;
15. menthyl o-aminobenzoate;
16. TiO₂ (with various coatings), ZnO and mica.

The UV absorbers described in “Sunscreens”, Eds. N.J. Lowe, N.A. Shaath, Marcel Dekker, Inc., New York and Basle or in Cosmetics & Toiletries (107), 50 ff (1992) can also be used as additional UV protection substances in the cosmetic composition according to the invention.

To improve the shade of brown, the substances/formulations according to the invention can also be used together with amino acids (e.g. tryptophan, cysteine, histidine, arginine, lysine, tyrosine, aspartic acid, methionine, proline, phenylalanine, hydroxyproline, leucine, glycine, isoleucine, threonine, serine, valine, alanine, cystine).

The examples below illustrate the invention.
General procedure

1 equivalent of the skin self-tanning compound is suspended in dichloromethane. 1.1 equivalents of triethylamine are added per hydroxyl group, and 1.1 equivalents of trimethylchlorosilane per hydroxyl group are added dropwise at room temperature. The mixture is then stirred for 16h at RT, treated with some kieselguhr and filtered. The filtrate is evaporated under reduced pressure at 30°C. The residue is treated with hexane and thoroughly stirred for 30 min under a protective gas. Insoluble constituents are filtered off and the filtrate is evaporated at 30°C under reduced pressure. This gives solids, oils or liquids which release the skin self-tanning active ingredients after contact with water.

Example 1: Preparation of dihydroxyacetone derivatives

Dihydroxyacetone (45.1 g, 0.5 mol) in the form of the dimer and triethylamine (106.3 g, 1.05 mol) are suspended in dichloromethane (400 ml) and, at about 5°C, a solution of trimethylchlorosilane (108.6 g, 1.0 mol) in 100 ml of dichloromethane is slowly added dropwise. The mixture is then stirred for 16 h at room temperature, treated with some kieselguhr and filtered. The filtrate is concentrated by evaporation under reduced pressure at 30°C. The residue is treated with 200 ml of hexane and thoroughly stirred for 30 min under a protective gas. Insoluble constituents are filtered off and the filtrate is concentrated by evaporation at 30°C at reduced pressure.

The colourless liquid which remains (mixture of various silylation products of dihydroxyacetone) releases skin self-tanning active ingredients after contact with water.

Bulb-tube distillation in a high vacuum or fractional distillation in a high vacuum are used to isolate individual compounds.

Furthermore, separation into the individual components can be carried out by preparative column chromatography.

1,3-bis(Trimethylsiloxy)-2-propanone is isolated as colourless liquid.

Yield: 38%

b.p. (0.46-0.27 mbar): 44-51°C

$^1$H-NMR (360 MHz, CDCl$_3$): $\delta=0.01$ (s, 18H, CH$_3$), 4.24 (s, 4H, CH$_2$)

$^{13}$C-NMR (90 MHz, CDCl$_3$): $\delta=0.16$ (CH$_3$), 67.43 (CH$_2$), 209 (C=O).
Example 2: Demonstration of the action

0.02 mol/l of lysine are dissolved in a phosphate buffer system in accordance with DIN 19268 (pH 7). 10 ml of this solution are treated with 0.002 mol of 1,3-bis(trimethylsiloxy)-2-propanone and the mixture is stirred at 32-35°C for 72 h.

As comparison, 10 ml of the lysine solution are treated with 0.002 mol of dihydroxyacetone and stirred at 32 - 35°C for 72 h.

In both cases a comparable brown coloration is obtained after 72 h. In the case of the use of 1,3-bis(trimethylsiloxy)-2-propanone, the brown coloration develops more slowly.

Comparable brown colorations are also obtained if, instead of 1,3-bis(trimethylsiloxy)-2-propanone, the crude product from the reaction between dihydroxyacetone and trimethylchlorosilane liquid (mixture of various silylation products of dihydroxyacetone) is used.
Example 3: Water-free formulations
Instead of 1,3-bis(trimethylsiloxy)-2-propanone it is also possible to use the crude product from the reaction between dihydroxyacetone and trimethylchlorosilane (mixture of different silylation products of dihydroxyacetone).

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<td>Vaseline</td>
<td>Petrolatum</td>
<td>50-80</td>
</tr>
<tr>
<td>Lanolin</td>
<td>Lanolin</td>
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</tr>
<tr>
<td>Mineral oil</td>
<td>Paraffinum Liquidum</td>
<td>10-30</td>
</tr>
<tr>
<td>1,3-bis(Trimethylsiloxy)-2-propane</td>
<td></td>
<td>5-10</td>
</tr>
<tr>
<td>Tocopherol</td>
<td>Tocopherol</td>
<td>0.1-1.0</td>
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<td>Corn germ oil</td>
<td>Zea Mays</td>
<td>1-5</td>
</tr>
<tr>
<td>Castor oil</td>
<td>Castor Oil</td>
<td>1-5</td>
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<table>
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<td>Isododecane</td>
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<td>1,3-bis(Trimethylsiloxy)-2-propanone</td>
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<tr>
<td>Permethyl 106A/Highpoint Chem. USA</td>
<td>Polysobutene</td>
<td>2</td>
</tr>
<tr>
<td>Gel Base/Brooks</td>
<td>Isododecane&amp;Mixed Ethylene Copolymer</td>
<td>ad 100</td>
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### C.

<table>
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<tr>
<td>Calendula oil</td>
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<td>Mineral oil</td>
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<td>5.0</td>
</tr>
<tr>
<td>Paprika extract, oil-soluble</td>
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<tr>
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### D.

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<th>%</th>
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<tbody>
<tr>
<td>Soya oil</td>
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<td>Myritol 318</td>
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<td>Corn germ oil</td>
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### E.

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<td>IPP</td>
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<td>Cetiol HE</td>
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<td>3.00</td>
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### G.

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<tbody>
<tr>
<td>DC 345</td>
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<td>80-90</td>
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<td>Dimethicone/Vinyl Dimethicone Crosspolymer</td>
<td>10-20</td>
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<tr>
<td>1,3-bis(Trimethylsiloxy)-2-propanone</td>
<td></td>
<td>2-15</td>
</tr>
<tr>
<td>Perfume</td>
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### H.

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<td>Magnesium carbonate</td>
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<td>1,3-bis(Trimethylsiloxy)-2-propanone</td>
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WHAT IS CLAIMED IS:

1. The use of silylated derivatives of glyceraldehyde, 6-aldo-D-fructose, hydroxymethylglyoxal, muconialdehyde, malealdehyde, substituted succindialdehydes, erythrulose, dihydroxyacetone, methylglyoxal (pyruvaldehyde) and substituted 4,4'-
dihydroxypyrazolin-5-ones as precursors of skin self-tanning substances in self-tanning compositions.

2. The use according to claim 1, which relates to compounds of the formulae

\[
(1a) \quad \begin{array}{c}
\text{O} \\
R_1 \\
\text{O} \\
R_2 \\
\text{H} \\
R_3 \\
\text{O} \\
R_4 \\
\end{array}
\quad ; \quad
(1b) \quad \begin{array}{c}
\text{O} \\
R_1 \\
\text{O} \\
R_2 \\
\text{H} \\
R_3 \\
\text{O} \\
R_4 \\
\end{array}
\quad ; \quad
(1c) \quad \begin{array}{c}
\text{H} \\
R_1 \\
\text{O} \\
R_2 \\
\text{O} \\
R_3 \\
\text{O} \\
R_4 \\
\end{array}
\quad ; \quad
(1d) \quad \begin{array}{c}
\text{O} \\
R_1 \\
\text{O} \\
R_2 \\
\text{O} \\
R_3 \\
\text{O} \\
R_4 \\
\end{array}
\quad ;
\]

\[
(1e) \quad \begin{array}{c}
\text{O} \\
R_1 \\
\text{O} \\
R_2 \\
\text{O} \\
R_3 \\
\text{O} \\
R_4 \\
\end{array}
\quad \text{or} \quad
(1f) \quad \begin{array}{c}
\text{O} \\
R_1 \\
\text{O} \\
R_2 \\
\text{O} \\
R_3 \\
\text{O} \\
R_4 \\
\end{array}
\]

in which

\[
R_1, R_2, R_3 \text{ and } R_4 \text{ independently of one another are hydrogen or a radical of the formula}
\]

\[
(1g) \quad \begin{array}{c}
\text{Si} \\
R_5 \\
\text{O} \\
R_6 \\
\text{O} \\
R_7 \\
\text{O} \\
R_8 \\
\end{array}
\quad ;
\]

\[
R_5 \quad \text{is } C_1-C_5 \text{alkyl; aryl; } C_1-C_9 \text{aryl; and}
\]

\[
R_6 \quad C_1-C_{16} \text{alkyl;}
\]

where

in the formulae (1a) to (1f) at least one of the radicals \( R_1, R_2, R_3 \) and \( R_4 \) is a radical of the formula (1g).

3. The use according to claim 2, which relates to compounds of the formulae

\[
(2a) \quad \begin{array}{c}
\text{O} \\
A \\
\text{O} \\
A \\
\text{O} \\
A \\
\text{O} \\
A \\
\end{array}
\quad ; \quad
(2b) \quad \begin{array}{c}
\text{O} \\
A \\
\text{O} \\
A \\
\text{H} \\
A \\
\text{O} \\
A \\
\end{array}
\quad ; \quad
(2c) \quad \begin{array}{c}
\text{O} \\
A \\
\text{O} \\
A \\
\text{H} \\
A \\
\text{O} \\
A \\
\end{array}
\quad ;
\]
in which
A is a radical of the formula (1g).

4. The use according to claim 2, which relates to compounds of the formulae

(3a) \( \text{HOC}_\text{A} \); (3b) \( \text{HOC}_\text{A} \); or (3c) \( \text{HOC}_\text{A} \);

in which
A is a radical of the formula (1g).

5. The use according to claim 2, which relates to compounds of the formulae

(4a) \( \text{AOC}_\text{A} \); (4b) \( \text{HOC}_\text{A} \); or

(4c) \( \text{AOC}_\text{A} \)

in which
A is a radical of the formula (1g).

6. The use according to claim 2, which relates to compounds of the formulae

(5a) \( \text{AOC}_\text{A} \); (5b) \( \text{HOC}_\text{A} \); or (5c) \( \text{HOC}_\text{A} \)

in which
A is a radical of the formula (1g).

7. The use according to claim 2, which relates to compounds of the formulae

(6a) \[ \text{O} \quad \text{O} \quad \text{O} \quad \text{A} \quad \text{O} \quad \text{A} \]
(6b) \[ \text{O} \quad \text{O} \quad \text{OH} \quad \text{A} \]
(6c) \[ \text{O} \quad \text{O} \quad \text{H} \quad \text{O} \quad \text{A} \]

in which
A is a radical of the formula (1g).

8. The use according to any one of claims 2 to 7, wherein, in formula (1g),
\( R_5 \) is methyl or ethyl.

9. The use according to claim 1 or 2, which relates to the compound of the formula

(7) \[ \text{CH}_3 \quad \text{Si} \quad \text{O} \quad \text{CH}_2 \quad \text{O} \quad \text{Si} \quad \text{CH}_3 \]

10. The use according to claim 1 or 2, which relates to the compound of the formula

(8) \[ \text{(CH}_3\text{)}_3\text{Si} \quad \text{O} \quad \text{O} \quad \text{Si(CH}_3\text{)}_3 \]

11. A process for the preparation of soluble precursors of skin self-tanning substances, which comprises silylating the skin self-tanning substances glyceraldehyde, 6-aldo-D-fructose, hydroxymethylglyoxal, mucodialdehyde, malealdehyde, substituted succindialdehydes, erythrulose, dihydroxyacetone, methylglyoxal (pyruvaldehyde), substituted 4,4'-dihydroxypyrizolin-5-ones with a suitable silylating agent.

12. A process for the preparation of the compounds of the formulae (1a) to (1f) according to claim 1, which comprises reacting dihydroxyacetone in monomeric or dimereric form with a suitable silylating reagent.
13. A cosmetic formulation comprising
2 to 15% by weight of a precursor or two or more precursors of the formula (1), and
customary cosmetic carriers or auxiliaries.

14. A cosmetic formulation according to claim 13, which is free from water.

15. A cosmetic formulation according to claim 13 or 14, which additionally comprises a UV
filter.

16. A compound of the formula

\[
\begin{align*}
(1a) & \quad \text{O} \quad \text{O} \\
(1b) & \quad \text{O} \quad \text{O} \\
(1c) & \quad \text{O} \quad \text{O} \\
(1d) & \quad \text{O} \quad \text{O} \\
(1e) & \quad \text{O} \quad \text{O} \\
(1f) & \quad \text{O} \quad \text{O}
\end{align*}
\]

in which
\[R_1, R_2, R_3 \text{ and } R_4 \text{ independently of one another are hydrogen or a radical of the formula}
\]

\[
\begin{align*}
(1g) & \quad \text{O} \quad \text{O} \\
\end{align*}
\]

\[R_5 \quad \text{is } C_1-C_8 \text{alkyl; ary1; } C_1-C_8 \text{aryl; and}
\]

\[R_6 \quad C_1-C_{18} \text{alkyl;
}\]

where
in the formulae (1a) to (1f) at least one of the radicals \(R_1, R_2, R_3 \text{ and } R_4\) is a radical of the
formula (1g), and the following compounds are not included:
- compounds of the formula (1a), in which A and R1 are at the same time a radical of the
formula
- compounds of the formula (1a) in which A is a radical of the formulae (1a') or (1a'') and R₁ is hydrogen;
- compounds of the formula (1c) in which R₁ and R₂ are a radical of the formula (1a');
- compounds of the formula (1d) in which R₁, R₂, R₃ and R₄ are a radical of the formula (1a'').
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K7/42 A61K7/48 C07F7/18

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)

IPC 7 A61K C07F

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

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

EPO-Internal, WPI Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<td>A</td>
<td>WO 97 33560 A (SCHERING PLOUGH HEALTHCARE)</td>
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<td>18 September 1997 (1997-09-18)</td>
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<td>A</td>
<td>US 4 956 174 A (JUNINO ALEX ET AL)</td>
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<td>JEONG, L. S. ET AL.: NUCLEOSIDES &amp; NUCLEOTIDES,</td>
<td>12</td>
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<tr>
<td></td>
<td>vol. 17, no. 8, 1998, pages 1473-1487, X000952971</td>
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<td>page 1478, last paragraph</td>
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Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* "A" document defining the general state of the art which is not considered to be of particular relevance
* "E" earlier document but published on or after the international filing date
* "L" document which may throw doubts on priority claims or which is cited to establish the publication date of another citation or other special reason (as specified)
* "O" document referring to an oral disclosure, use, exhibition or other means
* "P" document published prior to the international filing date but later than the priority date claimed

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

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

"Y" document of particular relevance; the claimed invention cannot be considered novel or 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

"Z" document member of the same patent family

Date of the actual completion of the international search: 2 August 2001

Date of mailing of the international search report: 10/08/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epp nl,
Fax (+31-70) 340-3010

Authorized officer

Beyss, E.
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<td>ARREGUIN LOZANO, B. ET AL.: &quot;Gas chromatography of trimethylsilyl sugars at various temperatures&quot; JOURNAL OF CHROMATOGRAPHIC SCIENCE, 8 April 1970 (1970-04-08), XP000926035 page 187 -page 191</td>
<td>16</td>
</tr>
<tr>
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<td>Publication date</td>
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<tr>
<td>WO 9733560 A</td>
<td>18-09-1997</td>
<td>AU 723825 B</td>
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