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Cosmetic preparations containing photostable UV-A filters

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(54) Title: COSMETIC PREPARATIONS CONTAINING PHOTOSTABLE UV-A FILTERS			
(54) Bezeichnung: PHOTOSTABILE UV-A-FILTER ENTHALTENDE KOSMETISCHE ZUBEREITUNGEN			
(57) Abstract Described are cosmetic preparations containing light-screening agents designed to protect the human epidermis against UV light in the region from 280 to 400 nm. The light-screening agents are contained in a carrier compound suitable for cosmetic purposes together with compounds of the formula (I), as given in claim 1, in which R ¹ , R ² and n are as defined in clause 1, which absorb in the UV-B region and are <i>per se</i> prior art for cosmetic preparations, in amounts which are active as photostable UV-A filters.			
(57) Zusammenfassung Lichtschutzmittel enthaltende kosmetische Zubereitungen zum Schutz der menschlichen Epidermis gegen UV-Licht im Bereich von 280 bis 400 nm, in einem kosmetisch geeigneten Träger zusammen mit an sich für kosmetische Zubereitungen bekannten im UV-B-Bereich absorbierenden Verbindungen als photostabile UV-A-Filter wirksame Mengen von Verbindungen der Formel (I) gemäß Anspruch 1 enthalten, in der R ¹ und R ² und n die in Anspruch 1 angegebenen Bedeutungen haben.			

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Cosmetic formulations containing photostable UV-A filters

Abstract

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A sunscreen-containing cosmetic formulation to protect the human epidermis from UV light in the range from 280 to 400 nm, [lacuna] comprises in a cosmetically suitable carrier, together with compounds which absorb in the UV-B region and are known per se
10 for cosmetic formulations, as photostable UV-A filters effective amounts of compounds of the formula I as claimed in claim 1, where R¹ and R² and n have the meanings stated in claim 1.

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Cosmetic formulations containing photostable UV-A filters

Description

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The invention relates to the use of substituted diphenylmalononitriles as photostable UV-A filters in cosmetic formulations to protect the human epidermis from UV radiation, specifically in the range from 320 to 400 nm.

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The sunscreen agents employed in cosmetic formulations have the task of preventing harmful effects of sunlight on the human skin or at least reducing their consequences. In addition, however, these sunscreen agents also serve to protect other ingredients
15 from decomposition or degradation by UV radiation.

The sunlight reaching the surface of the earth contains UV-B (280 to 320 nm) and UV-A (> 320 nm), radiation which is immediately adjacent to the visible light region. The effect on the human
20 skin, especially of UV-B radiation, is manifested by sunburn. Accordingly the industry supplies quite a large number of substances which absorb UV-B radiation and thus prevent sunburn.

Dermatological investigations have now shown that UV-A radiation
25 is also perfectly able to cause skin damage by, for example, damaging the keratin or elastin. This results in a reduction in the elasticity and water-storage capacity of the skin, ie. the skin becomes less supple and is prone to wrinkles. The noticeably high incidence of skin cancer in regions exposed to strong
30 sunlight shows that evidently damage to the genetic information in the cells is also caused by sunlight, specifically by UV-A radiation. All these findings therefore make it appear necessary to develop efficient filter substances for the UV-A region.

35 There is a growing need for sunscreen agents for cosmetic formulations which can be used in particular as UV-A filters and whose absorption maxima should therefore be in the region from about 320 to 380 nm. In order to achieve the desired effect with use of the minimum amount, sunscreen agents of this type should
40 additionally have a highly [sic] specific extinction. In addition, sunscreen agents for cosmetic products must also meet a large number of other requirements, for example good solubility in cosmetic oils, high stability of the emulsions produced with them, toxicological acceptability and little intrinsic odor and
45 color.



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Another requirement which must be met by sunscreen agents is adequate photostability. However, this is only inadequately ensured, if at all, with UV-A absorbing sunscreen agents available to date.

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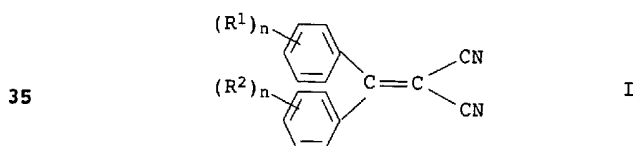
French patent No. 2 440 933 describes 4-(1,1-dimethylethyl)-4'-methoxydibenzoylmethane as UV-A filter. The proposal is to combine this specific UV-A filter, which is sold by GIVAUDAN under the name "PARASOL 1789", with various UV-B
10 filters in order to absorb all UV rays with a wavelength from 280 to 380 nm.

However, this UV-A filter has insufficient photochemical stability, when used alone or in combination with UV-B filters,
15 to ensure permanent protection of the skin during lengthy exposure to the sun, which makes repeated applications at regular and short intervals necessary if effective protection of the skin from all the UV rays is desired.

20 This is why, according to EP 0514491, the UV-A filters with inadequate photostability are to be stabilized by adding 2-cyano-3,3-diphenylacrylic esters which themselves act as filters in the UV-B region.

25 It is an object of the present invention to propose sunscreen agents for cosmetic purposes which absorb in the UV-A region and are photostable.

We have found that this object is achieved by adding compounds of
30 the formula I



where R¹ and R² are identical or different straight-chain or
40 branched aliphatic or cycloaliphatic radicals which are in the para and/or ortho position and have 1 to 18 carbon atoms, and where R¹ can additionally be a hydrogen atom, and where furthermore n is 1 or 2, when these compounds have their
essential absorption in the range from 320 to 380 nm, as UV-A
45 filters in cosmetic formulations to protect the human skin from



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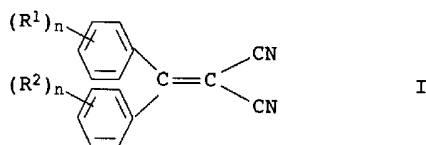
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the sun's rays, together with compounds which absorb in the UV-B region and are known per se for cosmetic formulations.

Aliphatic and cycloaliphatic radicals mean in particular hydrocarbon radicals which may be interrupted by oxygen atoms.

It is preferred in this connection to use compounds of the formula I

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where R^1 and R^2 are identical or different and are straight-chain or branched alkyl radicals having 1 to 18 carbon atoms, in which the alkyl chain can be interrupted by oxygen atoms, and where R^1 can also be hydrogen, and n is 1 and 2.

Particularly suitable compounds of the formula I are those where R^1 and R^2 is [sic] identical or different branched alkoxy radicals which are in the para position and have 3 to 12 carbon atoms, and n is in each case 1, and R^1 can also be hydrogen.

Particularly preferred individual compounds are the following, where R^1 and/or R^2 are in the para position and are

30 n-propoxy	isopropoxy
n-butoxy	1-methylpropoxy
2-methylpropoxy	n-pentoxy
1,1-dimethylpropoxy	3-methylbutoxy
hexoxy	2,2-dimethylpropoxy
35 heptoxy	1-methyl-1-ethylpropoxy
2-ethylhexoxy	and/or octoxy,

and where R^1 can also be hydrogen.

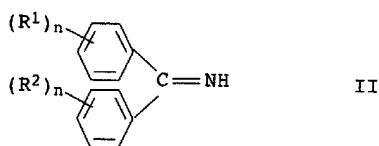
40 The compounds which can be used according to the invention are expediently prepared in a manner known per se by a process disclosed by Georges Charles, Bull.Soc.Chim. 1962, 1559, in which benzophenone is replaced as starting compounds by the corresponding imines of the formula II

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where R^1 and R^2 and n have the meanings indicated above, with malononitrile in polar organic solvents with exclusion of water.

10 This process has several advantages: no catalyst is required; the yields are better and the reaction takes place at lower temperatures. The starting compounds of the formula II can be obtained, for example, by the process of DE-A 4442138.

15 Sunscreen-containing cosmetic formulations are, as a rule, based on a carrier which contains at least one oil phase. However, formulations only with an aqueous (gel) base are also possible. Accordingly, oils, oil-in-water and water-in-oil emulsions, 20 creams and pastes, protective lipstick bases or gels are suitable.

Sunscreen products of these types can accordingly be in liquid, pasty or solid form, for example as water-in-oil creams, 25 oil-in-water creams and lotions, aerosol foam creams, gels, oils, grease pencils, dusting powders, sprays or alcoholic/aqueous solutions.

Examples of conventional oil components in cosmetics are liquid 30 paraffin, glyceryl stearate, isopropyl myristate, diisopropyl adipate, acetylstearyl 2-ethylhexanoate, hydrogenated polyisobutene, petrolatum, caprylic acid/capric acid triglycerides, microcrystalline wax, lanolin and stearic acid.

35 Examples of conventional cosmetic auxiliaries which may be suitable as additives are emulsifiers such as fatty alcohol ethoxylates, sorbitan fatty acid esters or lanolin derivatives, thickeners such as carboxymethylcellulose or crosslinked polyacrylic acid, preservatives and perfumes. Finally, other 40 substances which absorb in the UV-A region and are known per se can also be used if they are stable in the complete system of the combination of UV-B and UV-A filters to be used according to the invention.

45 The present invention furthermore relates to cosmetic formulations which comprise 0.1 to 10% by weight, preferably 1 to 7% by weight, based on the total amount of the cosmetic



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formulation, of one or more of the compounds of the formula I together with compounds which absorb in the UV-B region and are known per se for cosmetic formulations as sunscreen agents, with the compounds of the formula I usually being employed in a smaller amount than the UV-B-absorbing compounds.

Most of the sunscreen agents in the cosmetic formulations used to protect the human epidermis comprise compounds which absorb UV light in the UV-B region, ie. in the range from 280 to 320 nm. Examples of contents of the UV-A absorbers to be used according to the invention are from 10 to 90% by weight, preferably 20 to 50% by weight, based on the total amount of UV-B- and UV-A-absorbing substances.

Any UV-B filter substances are suitable as UV-B filter substances used in combination with the compounds of the formula I to be used according to the invention. Examples which may be mentioned are:

No.	Substance	CAS No. (=acid)
1	4-Aminobenzoic acid	150-13-0
2	3-(4'-Trimethylammonium)benzylidenebornan-2-one [sic] methyl sulfate	52793-97-2
3	3,3,5-Trimethylcyclohexyl salicylate (Homosalatum)	118-56-9
4	2-Hydroxy-4-methoxybenzophenone (Oxybenzonum)	131-57-7
5	2-Phenylbenzimidazole-5-sulfonic acid and its potassium, sodium and triethanolamine salts	27503-81-7
6	3,3'-(1,4-Phenylenedimethine)-bis(7,7-dimethyl-2-oxobicyclo[2.2.1]heptane-1-methanesulfonic acid) and its salts	90457-82-2
7	Polyethoxyethyl 4-bis(polyethoxy)aminobenzoate	113010-52-9
8	2-Ethylhexyl 4-dimethylaminobenzoate	21245-02-3
9	2-Ethylhexyl salicylate	118-60-5
10	2-Isoamyl [sic] 4-methoxycinnamate	7/6/7-10-2
11	2-Ethylhexyl 4-methoxycinnamate	5466-77-3
12	2-Hydroxy-4-methoxybenzophenone-5-sulfone [sic] (Sulisobenzonum) and the sodium salt	4065-45-6
13	3-(4'-Sulfo)benzylidenebornan-2-one [sic] and salts	58030-58-6
14	3-(4'-Methyl)benzylidenebornan-2-one [sic]	36861-47-9
15	3-Benzylidenebornan-2-one	16087-24-8
16	1-(4'-Isopropylphenyl)-3-phenylpropane-1,3-dione	63260-25-9



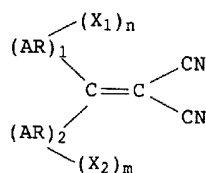
No.	Substance	CAS No. (=acid)
17	4-Isopropylbenzyl salicylate	94134-93-7
5 18	2,4,6-Triamline (o-carbo-2'-ethylhexyl-1'-oxy)-1,3,5-triazine [sic]	88122-99-0
19	3-4-Imidazolylacrylic [sic] acid and its ethyl ester	104-98-3*
20	Ethyl 2-cyano-3,3-diphenylacrylate	5232-99-5
10 21	2'-Ethylhexyl 2-cyano-3,3-diphenylacrylate	6197-30-4
22	Menthyl o-aminobenzoate or: 5-methyl-2-(1-methylethyl) [sic] 2-aminobenzoate	134-09-8
23	Glyceryl p-aminobenzoate or: 1-glyceryl 4-aminobenzoate	136-44-7
15 24	2,2'-Dihydroxy-4-methoxybenzophenone (dioxybenzone)	131-53-3
25	2-Hydroxy-4-methoxy-4-methylbenzophenone (mexonone)	1641-17-4
26	Triethanolamine salicylate	2174-16-5
20 27	Dimethoxyphenylglyoxalic [sic] acid or: Sodium 3,4-dimethoxyphenylglyoxalate [sic]	
28	3-(4'Sulfo)benzylidenebornan-2-one [sic] and its salts	56039-58-8

25 Mention should also finally be made of micronized pigments such as titanium dioxide and zinc oxide.

30 The compounds to be used according to the invention are, as a rule, distinguished by a particularly high absorbance in the UV-A radiation region. They are also readily soluble in cosmetic oils and can easily be incorporated into cosmetic formulations. The emulsions prepared with the compounds I are particularly distinguished by their high stability, the compounds I themselves by their high photostability, and the formulations prepared with 35 I by their pleasant sensation on the skin.

US 3,270,045 (1966) discloses the use of compounds of the formula

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where AR is an aromatic radical and X₁ is also an alkoxy radical, as light stabilizers for organic materials which are altered by UV radiation, especially plastics. Among the large number of substances to be stabilized against UV radiation, such as plastic materials, sheets, foamed materials, whose surface is to be protected, also mentioned are "polishes, creams, lotions and the like". However, the skilled worker is unable to derive the teaching of the present invention from the complete context of this patent, ie. (a) to use these compounds as sunscreen agents for the human skin, (b) to make a selection in respect of UV-A absorbers and (c) to use these in combination with compounds which absorb in the UV-B region and are known per se for cosmetic formulations.

15 This is all the more true since this reference is from 1966 and, as explained at the outset, to date no stable UV-A absorbers have been available for cosmetic application; on the contrary, the development has been in the direction of external stabilization of UV-A absorbers which are unstable on their own.

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Preparation

Example 1

25 General method:

0.2 mol of alkylated benzophenone in 200 ml of heptane is mixed with an equimolar amount of malonitrile [sic] and 20 ml of a catalyst mixture consisting of ammonium [sic] acetate/glacial acetic acid (molar ratio 1:4) and refluxed with a water trap for 20 h. Each hour during the reaction, a further 3 ml of the catalyst mixture are added. Subsequently the remaining catalyst is removed at about 50°C and cooled to room temperature. The products precipitate. This is followed by filtration with suction and crystallization several times from ethyl acetate. Products which result as an oil are purified on a silica gel column with

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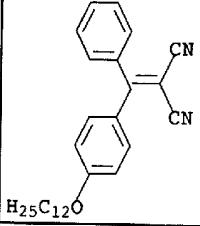
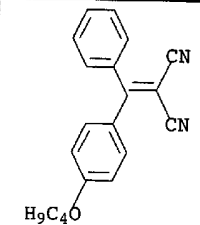
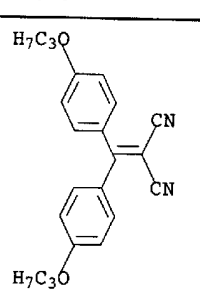
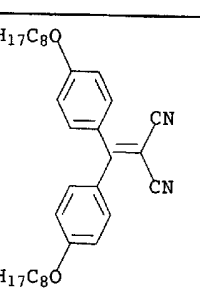
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methylene chloride as eluent (yield: 35 %). Table 1 shows the individual substances prepared.

Table 1

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Compound No.	Structure	λ max. [nm] (CH ₂ CL ₂ [sic])	E ₁ ¹	m.p. [°C]
10 15 1		360	470	64-66
20 25 2		360	630	80-82
30 35 3		344	730	90-94
40 45 4		346	460	oil



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General method for producing emulsions for cosmetic purposes

All the oil-soluble ingredients are heated to 85°C in a stirred vessel. When all the ingredients have melted and are present in the liquid phase, the aqueous phase is incorporated with homogenization. The emulsion is cooled to about 40°C with stirring, is perfumed, homogenized and then cooled to 25°C with continuous stirring.

10 Formulations

Example 2

Composition for lip protection

15	ad 100	Eucerinum anhydricum
	10.00	Glycerol
	10.00	Titanium dioxide
	0.5-10	Compound of Table 1, No. 2
20	8.00	Octyl methoxycinnamate
	5.00	Zinc oxide
	4.00	Castor oil
	4.00	Pentaerythrithil [sic] stearate/caprata/caprylate adipate [sic]
25	3.00	Glyceryl stearate SE
	2.00	Beeswax
	2.00	Microcrystalline wax
	2.00	Quaternium-18 bentonite
	1.50	PEG-45/dodecyl glycol copolymer

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Example 3

Composition for sunblocker with micropigments

35	ad 100	Water
	10.00	Octyl methoxycinnamate [sic]
	6.00	PEG-7-hydrogenated castor oil
	6.00	Titanium dioxide
	0.5-10	Compound of Table 1, No. 4
40	5.00	Mineral oil
	5.00	Isoamyl p-methoxycinnamate
	5.00	Propylene glycol
	3.00	Jojoba oil
	3.00	4-Methylbenzylidene camphor
45	2.00	PEG-45/dodecyl glycol copolymer
	1.00	Butyl methoxydibenzoylmethane
	1.00	Dimethicone



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0.50 PEG-40-hydrogenated castor oil
0.50 Tocopheryl acetate
0.50 Phenoxyethanol
0.20 EDTA

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Example 4

Fat-free gel

10 ad 100 Water
8.00 Octyl methoxycinnamate
7.00 Titanium dioxide
0.5-10 Compound of Table 1, No. 2
5.00 Glycerol
15 5.00 PEG-25 PABA
1.00 4-Methylbenzylidene camphor
0.40 Acrylate C10-C30 alkyl acrylate crosspolymer
0.30 Imidazolidinyl urea
0.25 Hydroxyethyl cellulose
20 0.25 Sodium methylparaben
0.20 Disodium EDTA
0.15 Fragrance
0.15 Sodium propylparaben
0.10 Sodium hydroxide

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Example 5

Sun cream (SPF 20)

30 ad 100 Water
8.00 Octyl methoxycinnamate
8.00 Titanium dioxide
6.00 PEG-7-hydrogenated castor oil
0.5-10 Compound of Table 1, No. 2.
35 6.00 Mineral oil
5.00 Zinc oxide
5.00 Isopropyl palmitate
5.00 Imidazolidinyl urea
3.00 Jojoba oil
40 2.00 PEG-45/dodecyl glycol copolymer
1.00 4-Methylbenzylidene camphor
0.60 Magnesium stearate
0.50 Tocopheryl acetate
0.25 Methylparaben
45 0.20 Disodium EDTA
0.15 Propylparaben



Example 6

Sun cream water-resistant

5	ad 100	Water
	8.00	Octyl methoxycinnamate
	5.00	PEG-7-hydrogenated castor oil
	5.00	Propylene glycol
	4.00	Isopropyl palmitate
10	4.00	Caprylic/capric triglyceride
	0.5-10	Compound in Table 1, No. 3
	4.00	Glycerol
	3.00	Jojoba oil
	2.00	4-Methylbenzylidene camphor
15	2.00	Titanium dioxide
	1.50	PEG-45/dodecyl glycol copolymer
	1.50	Dimethicone
	0.70	Magnesium sulfate
	0.50	Magnesium stearate
20	0.15	Fragrance

Example 7

Sun milk (SPF 6)

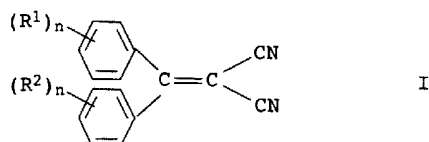
25	ad 100	Water
	10.00	Mineral oil
	6.00	PEG-7-hydrogenated castor oil
	5.00	Isopropyl palmitate
30	3.50	Octyl methoxycinnamate
	0.5-10	Compound in Table 1, No. 2
	3.00	Caprylic/capric triglyceride
	3.00	Jojoba oil
	2.00	PEG-45/dodecyl glycol copolymer
35	0.70	Magnesium sulfate
	0.60	Magnesium stearate
	0.50	Tocopheryl acetate
	0.30	Glycerol
	0.25	Methylparaben
40	0.15	Propylparaben
	0.05	Tocopherol



We claim:

1. The use of compounds of the formula I

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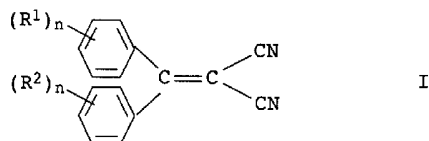


15 where R^1 and R^2 are identical or different straight-chain or branched aliphatic or cycloaliphatic radicals which are in the para and/or ortho position and have 1 to 18 carbon atoms, and where R^1 may additionally be a hydrogen atom, and where

20 furthermore n is 1 or 2, as UV-A filters in cosmetic formulations to protect the human skin from the sun's rays, together with compounds which absorb in the UV-B region and are known per se for cosmetic formulations.

2. The use as claimed in claim 1 of compounds of the formula I

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where R^1 and R^2 are identical or different and are straight-chain or branched alkyl radicals having 1 to 18 carbon atoms, in which the alkyl chain can be interrupted by oxygen atoms, and where R^1 can also be hydrogen, and n is 1 and 2.

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3. The use as claimed in claim 1 of compounds of the formula I, where R^1 and R^2 are identical or different branched alkoxy radicals which are in the para position and have 3 to 12 carbon atoms, and n is in each case 1, and R^1 can additionally be hydrogen.

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4. A sunscreen-containing cosmetic formulation to protect the human epidermis from UV light in the range from 280 to 400 nm, which comprises in a cosmetically suitable carrier, together with compounds which absorb in the UV-B region and are known per se for cosmetic formulations, as photostable

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UV-A filters effective amounts of compounds of the formula I as claimed in claim 1, where R¹ and R² and n have the meanings stated in claim 1.

- 5 5. A sunscreen-containing cosmetic formulation as claimed in claim 4, comprising as UV-A filters compounds of the formula I as claimed in claim 1, where R¹ and R² are identical or different alkoxy radicals having 1 to 18 carbon atoms, and n is 1 or 2, and R¹ can also be a hydrogen atom.
- 10 6. A sunscreen-containing cosmetic formulation as claimed in claim 4, wherein the cosmetically suitable carrier comprises at least one oil phase.

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