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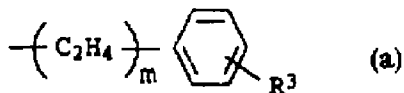
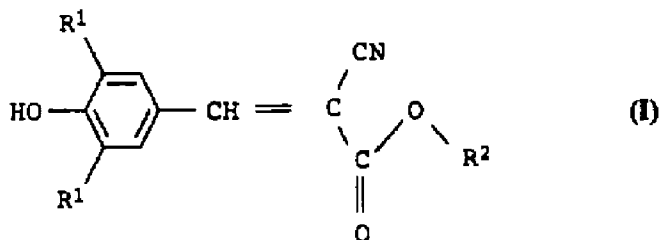
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(51) Int.Cl.<sup>6</sup> C07C 255/41, A61K 7/42

(30) 1995/10/20 (195 39 189.6) DE

(54) **ESTERS BENZYLIDENECYANACETIQUES SUBSTITUES**

(54) **SUBSTITUTED BENZYLIDENECYANOACETIC ESTERS**



(57) Composés de formule (I) dans laquelle R<sup>1</sup> est un i-propyle, un i-butyle ou un t-butyle, R<sup>2</sup> est un alkyle de 6 à 14 atomes de carbone, (a), (b) où R<sup>3</sup> désigne un H ou un alkyle en C<sub>1</sub>-C<sub>4</sub>, et m, n = 0 ou 1.

(57) The invention concerns compounds of the formula (I) in which R<sup>1</sup> = iso-propyl, iso-butyl or t-butyl and R<sup>2</sup> = alkyl with 6-14 C-atoms, (a), (b), R<sup>3</sup> being H or C<sub>1</sub>-C<sub>4</sub> alkyl and m and n being 0 or 1.

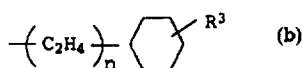
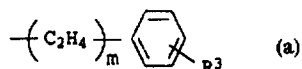
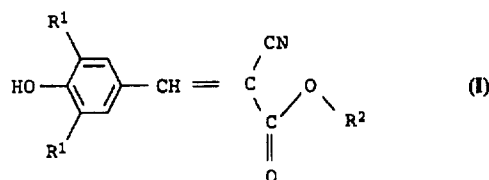


**PCT**  
WELTORGANISATION FÜR GEISTIGES EIGENTUM  
Internationales Büro  
INTERNATIONALE ANMELDUNG VERÖFFENTLICHT NACH DEM VERTRAG ÜBER DIE  
INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES PATENTWESENS (PCT)

|  |           |  |
|--|-----------|--|
| <p>(51) Internationale Patentklassifikation<sup>6</sup> :<br/><b>A61K 7/42, G03C 1/815</b></p>   | <b>A1</b> | <p>(11) Internationale Veröffentlichungsnummer: <b>WO 97/15279</b></p> <p>(43) Internationales Veröffentlichungsdatum: 1. Mai 1997 (01.05.97)</p>  |
| <p>(21) Internationales Aktenzeichen: PCT/EP96/04417</p> <p>(22) Internationales Anmeldedatum: 11. Oktober 1996 (11.10.96)</p> <p>(30) Prioritätsdaten:<br/>195 39 189.6      20. Oktober 1995 (20.10.95)      DE</p> <p>(71) Anmelder (für alle Bestimmungsstaaten ausser US): BASF AKTIENGESELLSCHAFT [DE/DE]; D-67056 Ludwigshafen (DE).</p> <p>(72) Erfinder; und<br/>(75) Erfinder/Anmelder (nur für US): TRENTMANN, Beate [DE/DE]; Kranichweg 5, D-68307 Mannheim (DE).</p> <p>(74) Gemeinsamer Vertreter: BASF AKTIENGESELLSCHAFT; D-67056 Ludwigshafen (DE).</p> |           | <p>(81) Bestimmungsstaaten: AU, CA, CN, JP, US, europäisches Patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).</p> <p><b>Veröffentlicht</b><br/><i>Mit internationalem Recherchenbericht.<br/>Vor Ablauf der für Änderungen der Ansprüche zugelassenen Frist. Veröffentlichung wird wiederholt falls Änderungen eintreffen.</i></p> |

(54) Title: SUBSTITUTED BENZYLIDENECYANOACETIC ACID ESTERS

(54) Bezeichnung: SUBSTITUIERTE BENZYLIDENCYANESSIGESTER



(57) Abstract

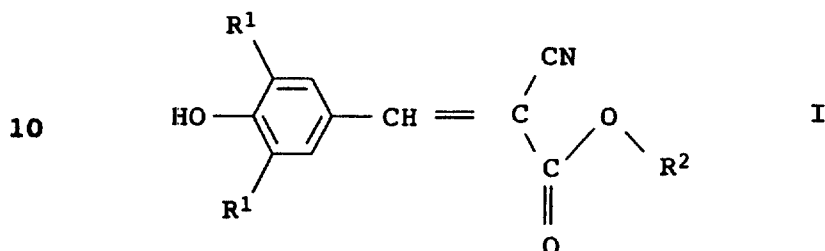
The invention concerns compounds of the formula (I) in which R<sup>1</sup> = iso-propyl, iso-butyl or t-butyl and R<sup>2</sup> = alkyl with 6-14 C-atoms, (a), (b), R<sup>3</sup> being H or C<sub>1</sub>-C<sub>4</sub> alkyl and m and n being 0 or 1.

(57) Zusammenfassung

Verbindung der Formel (I), worin R<sup>1</sup> = i-Propyl, i-Butyl oder t-Butyl, R<sup>2</sup> = Alkyl mit 6-14 C-Atomen, (a), (b), mit R<sup>3</sup> = H oder C<sub>1</sub>-C<sub>4</sub>-Alkyl und m, n = 0 oder 1 bedeuten.

## Substituted benzylidenecyanoacetic esters

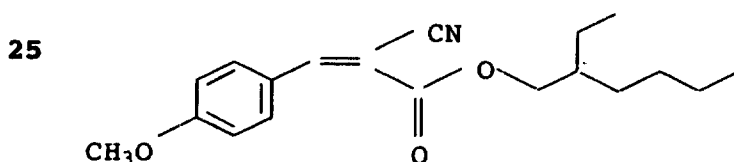
The present invention relates to substituted  
5 benzylidenecyanoacetic esters of the formula I



15 to the use thereof as sunscreen agents, to the use thereof in  
cosmetic products, and to cosmetic compositions comprising these  
compounds.

Sunscreen agents based on substituted benzylidenecyanoacetic  
20 esters are known.

BE 757 036 describes, inter alia, the compound

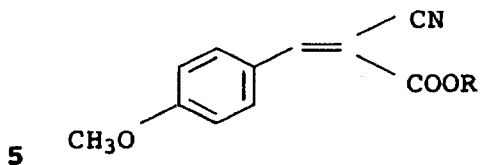


30 as light-sensitive photomaterial.

DE 10 87 902 describes condensates of benzaldehydes with  
compounds containing active methylene groups. Among many other  
compounds, mention is also made of condensates of  
35 4-hydroxy-3,5-di-t-butylbenzaldehyde with diethyl malonate,  
cyanoacetic ester, malononitrile or malonic acid (page 1, second  
column, group VI). These compounds are described as suitable  
light stabilizers for films, sheets, fibers and filaments.

40 DE 28 16 819 describes substituted benzylidenecyanoacetic esters  
of the following structure as UV-A filters:

45



it being found that, with regard to possible substitution on the aromatic ring, para monosubstitution represents the optimum and, in turn, the methoxy radical confers optimal properties here.

10 Concerning the radical R, it is found that compounds with R = n-hexyl, n-octyl, n-decyl, isononyl, and isodecyl are most suitable.

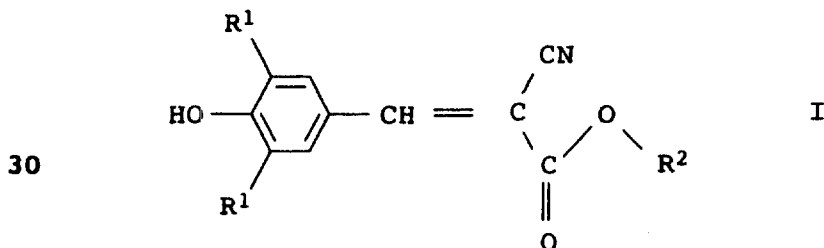
Since cosmetic sunscreen agents must, besides the photoproperties

15 such as suitable absorption maximum, high specific extinction and photostability, have a number of other use properties such as good oil solubility, pH stability, oxidation stability, thermal stability, minimum intrinsic color and no intrinsic odor and, moreover, must also be toxicologically acceptable, it is an

20 object of the present invention to optimize the previously disclosed products in respect of the abovementioned properties.

We have found that this object is achieved in that compounds of the formula I

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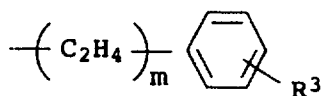
where

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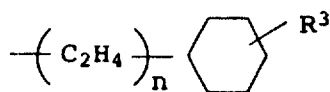
R<sup>1</sup> is i-propyl, i-butyl or t-butyl,

R<sup>2</sup> is alkyl with 6-14 carbon atoms,

40



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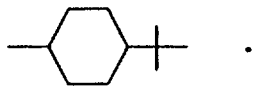
with R<sup>3</sup> = H or C<sub>1</sub>-C<sub>4</sub>-alkyl

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and m, n = 0 or 1,

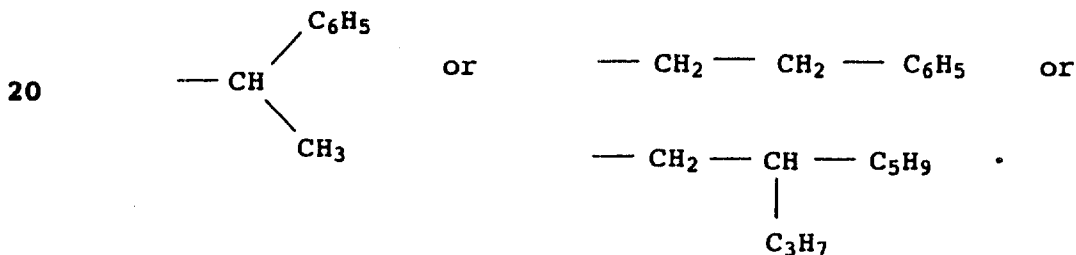
have better properties in respect of many of the abovementioned requirements, especially in respect of the photostability, than  
5 prior art compounds.

Particularly suitable sunscreen agents have been found to be compounds of the formula I where both R<sup>1</sup> radicals are tert-butyl and R<sup>2</sup> is a branched alkyl radical with 8-12 carbon atoms or  
10 -C<sub>2</sub>H<sub>4</sub>-C<sub>6</sub>H<sub>5</sub> or



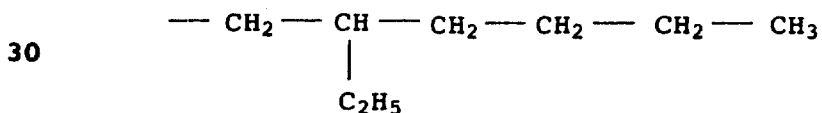
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Moreover R<sup>2</sup> can be, for example, the radical



25

A particularly advantageous compound of the formula I is the one in which both R<sup>1</sup> radicals are tert-butyl and R<sup>2</sup> is



The compounds according to the invention can be prepared in a  
35 conventional way from the corresponding benzaldehydes and cyanoacetic esters in a Knoevenagel condensation (see, for example, Organikum, 1988 edition, page 459). The corresponding cyanoacetic esters were prepared by transesterification of a commercially obtainable cyanoacetic ester with the appropriate  
40 alcohol in a conventional way.

The compounds according to the invention are particularly suitable as light stabilizers for materials which are attacked by UV rays, for example filaments, fibers, sheets, films and other  
45 plastic moldings.

## 4

The compounds according to the invention are particularly suitable for protecting the human skin from UV rays. They can be used in a wide variety of cosmetic and medicinal products such as sun oils, sun creams, sun lotions, sun gels, lipsticks, skin  
5 creams, hair gels and non-greasy gels.

## Examples

## Example 1

10

2-Phenylethyl

3,5-di-tertiary-butyl-4-hydroxybenzylidenecyanoacetate

5.9 g of 3,5 di-tertiary-butyl-4-hydroxybenzaldehyde are [sic]  
15 dissolved in 50 ml of toluene.

4.7 g of 2-phenylethyl cyanoacetate, 0.1 g of piperidine and  
0.25 g of acetic acid were heated to reflux. 0.4 g of H<sub>2</sub>O was  
removed azeotropically in 2 h. The mixture was cooled, washed  
20 with water and with sodium bicarbonate solution, dried and  
concentrated. The crude product was recrystallized.  
Yield: 9.9 g (98%).

## Example 2

25

2-Ethylhexyl 3,5-di-tertiary-butyl-4-hydroxybenzylidene-  
cyanoacetate

28.1 g of 3,5-di-tertiary-butyl-4-hydroxybenzaldehyde were  
30 dissolved in 60 ml of toluene. 21.7 g of 2-ethylhexyl  
cyanoacetate, 0.27 g of piperidine and 0.67 g of acetic acid were  
added. The mixture was heated to reflux, and about 2 g of water  
were removed azeotropically. The clear solution was washed, dried  
and concentrated.  
35 Yield: 46.2 g of pale yellow oil (93%).

## Example 3

4-Tertiary-butylcyclohexyl 3,5-di-tertiary-butyl-4-hydroxy-  
40 benzylidenecyanoacetate

5.4 g of 3,5-di-tertiary-butyl-4-hydroxybenzaldehyde were  
dissolved in 50 ml of toluene. 5.9 g of  
4-tertiary-butylcyclohexyl cyanoacetate, 0.1 g of piperidine and  
45 0.25 g of acetic acid were added. 0.4 g of water was removed  
azeotropically under reflux. The mixture was washed, dried and

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concentrated.

Yield: 10.6 g (96%) of crystals

Properties:

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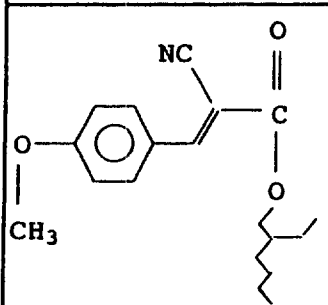
| Example | $\lambda_{\max}$<br>[nm] | $E_1^A$ | Solubility | Photostability |
|---------|--------------------------|---------|------------|----------------|
| 1       | 356                      | 484     | good       | 98%            |
| 2       | 357                      | 638     | very good  | 99%            |
| 3       | 355                      | 623     | good       | 92%            |

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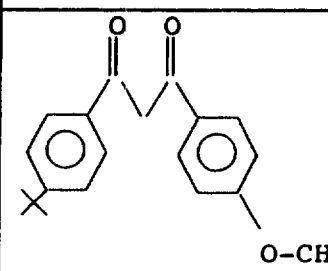
The solubility was determined by dissolving the substances in  $C_{12}$ - $C_{15}$ -alkyl benzoates at room temperature.

15 The photostability was determined by irradiating a solution of the appropriate compound with a Heräus Sun-Test apparatus for 30 min. The amount of the compound still present is indicated as a percentage of the initial amount.

20 Comparative Example 1

|   | $\lambda_{\max}$<br>[nm] | $E_1^A$ | Solubility | Photostability |
|---|--------------------------|---------|------------|----------------|
| 25<br><br>30 | 342                      | 904     | very good  | 79%            |

Comparative Example 2

|  | $\lambda_{\max}$<br>[nm] | $E_1^A$ | Solubility | Photostability |
|--|--------------------------|---------|------------|----------------|
| 35<br><br>40<br>Parsol 1789 | 357                      | 638     | good       | 55%            |

Parsol 1789 is a licenced commercial product (UV-A filter).

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## 6

It is evident that the compounds according to the invention display surprising advantages, especially in the important property of photostability, compared with a known compound of similar structure and compared with a licenced commercial  
5 product.

## Use Examples

- 10 Cosmetic compositions in which the compounds according to the invention can be used with particular advantage are indicated below.

General method for producing emulsions for cosmetic purposes:  
15

All the oil-soluble ingredients are heated to 85°C in a stirred vessel.

- 20 When all the ingredients have melted and are in the form of a liquid phase, the aqueous phase is incorporated with homogenization.

- 25 While stirring, the emulsion is cooled to about 40°C, perfume is added, and the mixture is then homogenized and cooled to 25°C while stirring continuously.

## Composition for the lip salve

- 30  
ad 100 Eucerinum anhydricum  
10.00 Glycerol  
10.00 Titanium dioxide  
0.5-10 Compound from Example 1  
35 8.00 Octyl methoxycinnamate  
5.00 Zinc oxide  
4.00 Castor oil  
4.00 Pentaerythrithyl [sic] stearate/caprate/caprylate  
adipate [sic]  
40 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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## 7

## Composition for sunblocker with micropigments

|    |        |   |
|----|--------|---|
|    | ad 100 | Water   |
|    | 10.00  | Parsol MCX octyl methoxycinnamate [sic]             |
| 5  | 6.00   | PEG-7-hydrogenated castor oil                       |
|    | 6.00   | Titanium dioxide                                    |
|    | 0.5-10 | Compound from Example 1                             |
|    | 5.00   | Mineral oil   |
|    | 5.00   | Isoamyl p-methoxycinnamate                          |
| 10 | 5.00   | Propylene glycol                                    |
|    | 3.00   | Jojoba oil  |
|    | 3.00   | 4-Methylbenzylidene camphor                         |
|    | 2.00   | PEG-45/dodecyl glycol copolymer                     |
|    | 1.00   | Butyl methoxydibenzoylmethane                       |
| 15 | 1.00   | Dimethicone   |
|    | 0.50   | PEG-40-hydrogenated castor oil                      |
|    | 0.50   | Tocopheryl acetate                                  |
|    | 0.50   | Phenoxyethanol                                      |
|    | 0.20   | EDTA  |
| 20 |        | Non-greasy gel                                      |
|    | ad 100 | Water   |
|    | 8.00   | Octyl methoxycinnamate                              |
| 25 | 7.00   | Titanium dioxide                                    |
|    | 0.5-10 | Compound of Example 2                               |
|    | 5.00   | Glycerol  |
|    | 5.00   | PEG-25 PABA   |
|    | 1.00   | 4-Methylbenzylidene camphor                         |
| 30 | 0.40   | Acrylates C10-C30 alkyl acrylate crosspolymer [sic] |
|    | 0.30   | Imidazolidinyl urea                                 |
|    | 0.25   | Hydroxyethyl cellulose                              |
|    | 0.25   | Sodium methylparaben                                |
|    | 0.20   | Disodium EDTA                                       |
| 35 | 0.15   | Fragrance   |
|    | 0.15   | Sodium propylparaben                                |
|    | 0.10   | Sodium hydroxide                                    |

40

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## 8

## Sun cream (SPF 20)

|    |        |                                 |
|----|--------|---------------------------------|
|    | ad 100 | Water                           |
|    | 8.00   | Octyl methoxycinnamate          |
| 5  | 8.00   | Titanium dioxide                |
|    | 6.00   | PEG-7-hydrogenated castor oil   |
|    | 0.5-10 | Compound of Example 2           |
|    | 6.00   | Mineral oil                     |
|    | 5.00   | Zinc oxide                      |
| 10 | 5.00   | Isopropyl palmitate             |
|    | 5.00   | Imidazolidinyl urea             |
|    | 3.00   | Jojoba oil                      |
|    | 2.00   | PEG-45/dodecyl glycol copolymer |
|    | 1.00   | 4-Methylbenzylidene camphor     |
| 15 | 0.60   | Magnesium stearate              |
|    | 0.50   | Tocopheryl acetate              |
|    | 0.25   | Methylparaben                   |
|    | 0.20   | Disodium EDTA                   |
|    | 0.15   | Propylparaben                   |

20

## Sun cream, water-resistant

|    |        |                                 |
|----|--------|---------------------------------|
|    | ad 100 | Water                           |
|    | 8.00   | Octyl methoxycinnamate          |
| 25 | 5.00   | PEG-7-hydrogenated castor oil   |
|    | 5.00   | Propylene glycol                |
|    | 4.00   | Isopropyl palmitate             |
|    | 4.00   | Caprylic/capric triglyceride    |
|    | 0.5-10 | Compound of Example 2           |
| 30 | 4.00   | Glycerol                        |
|    | 3.00   | Jojoba oil                      |
|    | 2.00   | 4-Methylbenzylidene camphor     |
|    | 2.00   | Titanium dioxide                |
|    | 1.50   | PEG-45/dodecyl glycol copolymer |
| 35 | 1.50   | Dimethicone                     |
|    | 0.70   | Magnesium sulfate               |
|    | 0.50   | Magnesium stearate              |
|    | 0.15   | Fragrance                       |

## 40 Sun lotion (SPF 6)

|    |        |                               |
|----|--------|-------------------------------|
|    | ad 100 | Water                         |
|    | 10.00  | Mineral oil                   |
|    | 6.00   | PEG-7-hydrogenated castor oil |
| 45 | 5.00   | Isopropyl palmitate           |
|    | 3.50   | Octyl methoxycinnamate        |
|    | 0.5-10 | Compound of Example 2         |

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|         |                                 |
|---------|---------------------------------|
| 3.00    | Caprylic/capric triglyceride    |
| 3.00    | Jobba oil                       |
| 2.00    | PEG-45/dodecyl glycol copolymer |
| 0.70    | Magnesium sulfate               |
| 5 0.60  | Magnesium stearate              |
| 0.50    | Tocopheryl acetate              |
| 0.30    | Glycerol                        |
| 0.25    | Methylparaben                   |
| 0.15    | Propylparaben                   |
| 10 0.05 | Tocopherol                      |

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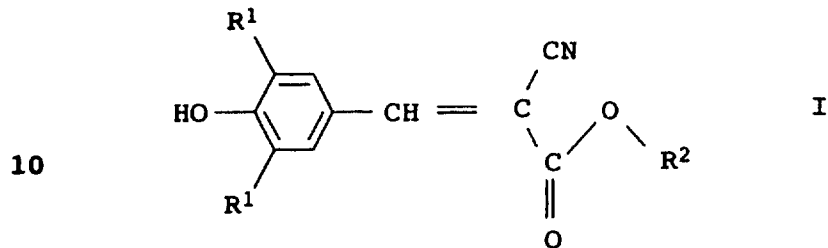
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We claim:

1. A compound of the formula I

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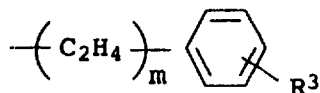
where

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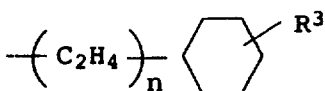
R<sup>1</sup> is i-propyl, i-butyl or t-butyl,

R<sup>2</sup> is alkyl with 6-14 carbon atoms,

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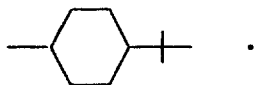
with R<sup>3</sup> = H or C<sub>1</sub>-C<sub>4</sub>-alkyl  
and m, n = 0 or 1.

30 2. A compound of the formula I as claimed in claim 1, where

R<sup>1</sup> is t-butyl and

R<sup>2</sup> is a branched alkyl radical with 8-12 carbon atoms,  
-C<sub>2</sub>H<sub>4</sub>-C<sub>6</sub>H<sub>5</sub> or

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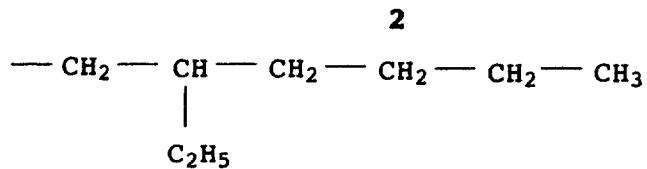


40 3. A compound of the formula I as claimed in claim 1, where

R<sup>1</sup> is t-butyl and

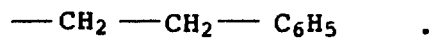
R<sup>2</sup> is

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or



4. The use of a compound as claimed in claim 1 as sunscreen  
10 agent or light stabilizer.
5. The use of a compound as claimed in claim 1 in cosmetic  
products.
- 15 6. A cosmetic composition which comprises as sunscreen agent a  
compound as claimed in claim 1 alone or together with other  
UV-A or UV-B filters.

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