HYDRAZONE SUN-SCREENING COMPOUNDS

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15 Claims

ABSTRACT OF THE DISCLOSURE

An essentially colorless compound useful as a sun-screening agent, such compound having the formula:

\[
R \overset{\text{H}}{\underset{\text{V}}{\overset{\text{Ar}}{\text{C}=\text{N}\text{N}}}} \overset{\text{H}}{\underset{\text{Y}}{\overset{\text{Ar}}{\text{C}}}}
\]

wherein in the free acid form (Ar₁) and (Ar₂) represent benzene rings; Y and Z are salt-forming groups selected from —SO₂H and —COOH; R is an aliphatic radical, e.g., alkyl, hydroxyalkyl, cyclohexyl; and n and m are integers from 1 to 3. Such compounds have absorption maxima within the range 2900 A. to about 3500 A.

This invention relates to new and useful sun-screen compounds, to compositions containing such compounds, and to methods for protecting the human skin against the burning, tanning and degradation effects of sunlight, and in particular to cosmetic compositions incorporating the novel compounds of this invention which are outstandingly useful for protecting the skin against sunlight.

Sun-screening compounds in general have been developed which afford quite satisfactory protection against the burning rays of the sun but which would permit the tanning rays to be transmitted. In the approximate range of from about 2900 to 3100 A. we find the most detrimental burning wavelengths in the sun’s rays. The effect of these wavelengths on the human skin is to produce a severe burning, reddening, blistering and edema which is characteristic of many burns. Obviously, this is not only not desirable from an esthetic point of view, but is a severe detriment to human health. In order, therefore, to overcome this effect of the burning rays of the sun, quite satisfactory compounds have been heretofore employed to screen out these burning rays. On the assumption and general acceptance by the public that tanning is a desirable phenomenon and is somewhat related to “good health,” the public has been educated to accept the numerous products currently available to screen out the burning rays of the sun but to permit tanning to occur. Within recent years it has become generally accepted that while tanning may have some beneficial effects especially in that it protects the skin from further burning where there is continued exposure to the sun, nevertheless tanning in and of itself is associated with a general deterioration of the skin due to the effect of the actinic radiation thereon. While the great majority of people are not severely affected by tanning, there are a great number who are so sensitive to even the tanning rays of the sun that exposure to these wavelengths creates serious health hazards. Others have not quite accepted the notion that tanning is beautifying and would prefer to remain untanned. Consequently, for those who must have protection against both burning and tanning rays of the sun, and for those who do not desire to be tanned, there has been a need for a broad spectrum sun-screening composition, which would give adequate protection to the skin, which would be sufficiently stable under conditions of use to remain effective for several hours, which could be readily applied to the skin, and which would not be readily removable such as by simple water-wash. The need for the latter characteristic is evident since it would leave one with a false sense of security if the material were so readily removable as, for example, in bathing.

In order, therefore, to achieve the ends of the present invention it is necessary to provide a composition which has an outstanding filtering action on those rays of the sun from about 2900 A. to about 3500 A.; the range of from about 3200 A. to 3500 A. encompassing the tanning wavelengths present in sunlight.

One of the objects, therefore, of the present invention is to provide outstanding and useful compounds which have excellent filtering action on the ultraviolet rays of solar light and particularly those wavelengths of from about 2900 A. to about 3500 A.

It is still another object of the present invention to provide compositions, and particularly cosmetic compositions, which may be applied to the human skin to protect it against the burning and tanning rays of the sun.

It is a still further object of the present invention to provide processes for preparing the compounds with which the present invention is concerned and further, to provide processes for protecting the human skin against the burning and tanning rays of the sun.

Other objects will appear hereinafter as the description proceeds.

In accordance with the objects of the present invention, it has now been discovered that a class of compounds hereinafter to be described has outstanding screening characteristics for the burning and tanning rays of the sun, and particularly those wavelengths in the ultraviolet region of from about 2900 A. to about 3500 A., and that such compounds have outstanding K values as well as unexpected superior light fastness and stability upon exposure to ultraviolet radiation. The K value is a measure of the efficiency of the compound to filter out specified wavelengths of light. A compound with a K value of 1 is one which, at a concentration of 0.1% in a thickness of 1 cm. reduces the light transmitted to 10% of the incident radiation. Thus, a compound with a K = 10 has a given wave-length in a concentration of 0.1% will reduce the transmitted radiation to 10% of the incident radiation with a thickness of only 1 mm.

The compounds of the present invention and those which are employed in the compositions and processes of this invention have the following general formula:

\[
\overset{\text{H}}{\underset{\text{V}}{\overset{\text{Ar}}{\text{C}=\text{N}\text{N}}}} \overset{\text{H}}{\underset{\text{Y}}{\overset{\text{Ar}}{\text{C}}}}
\]

wherein \((\text{Ar}_1)\) and \((\text{Ar}_2)\) represent benzene rings; Y and Z are salt or salt-forming groups, particularly sulfonic or carboxylic; \(n=1\) to 3; \(m=1\) to 3; and R is an aliphatic radical and preferably lower alkyl of 1 to 6 carbon atoms.

The preferred compounds of this invention have the following general formula:

\[
\overset{\text{H}}{\underset{\text{V}}{\overset{\text{Ar}}{\text{C}=\text{N}\text{N}}}} \overset{\text{H}}{\underset{\text{Y}}{\overset{\text{Ar}}{\text{C}}}}
\]

wherein \((\text{Ar}_1)\) and \((\text{Ar}_2)\) are benzene rings; Z is —SO₂H or —COOH; \(n\) and \(m\) have values from 1 to 3; R is lower alkyl of from 1 to 6 carbon atoms; and M is hydrogen or a salt-forming cation which preferably...
is an alkali metal anion, e.g., sodium, potassium, lithium, etc., or ammonium or amine.

Suitable R groups and as representative of aliphatic groupings there are:

alkyl of 1 to 50 carbon atoms
alkenyl of 3 to 50 carbon atoms
cycloalkyl of 3 to 50 carbon atoms
cycloalkenyl of 5 to 30 carbon atoms
haloalkyl of 1 to 50 carbon atoms (e.g., chloroethyl, bromopropyl, fluoramyl, iodopentyl, etc.)
haloalkenyl of 3 to 50 carbon atoms
cyanoalkyl of 1 to 50 carbon atoms
hydroxyalkyl of 1 to 50 carbon atoms
carbalkoxyalkyl of 3 to 50 carbon atoms
alkoxyalkyl of 2 to 50 carbon atoms
hydroxycarboxyalkyl of 2 to 50 carbon atoms

as well as the cyan-, hydroxy-, alkoxy-, carboxy-, hydroxy-alkoxy-derivatives of alkynes.

The benzene nuclei may contain, in addition to the sodium-derivatives, other substituents which are non-chromophoric (i.e., avoid chromophores such as nitro,azo, azopy and the like). Such groups as the following are suitable:

hydroxy
halogen
alkyl (as R above)
substituted alkyl (as R above)
alkenyl (as R above)
substituted alkenyl (as R above)
cyano
alkylsulfonyl (e.g., $-SO_2\text{CH}_3$)
carboxamido
sulfonyamido, etc.

Since an oxy group (i.e., hydroxy, alkoxy or alkenoxy) is an auxochrome and is band chromic in its effect, no more than one of such groups should be present since the absorption maxima of compounds with two or more oxy groups would in most instances be too close, if not in a visible region of the spectrum, tending thereby to lessen the effectiveness of these compounds for the use as sunscreen agents as herein contemplated. It is also preferred that the compounds of, and used in, this invention do not contain amine groups, particularly bonded directly to the benzene nuclei since such compounds, in general, have inferior light fastness albeit they may have satisfactory absorption characteristics for the purposes of the present invention.

The general procedure for preparing the compounds of this invention involves a condensation of a sulfone- or carboxybenzene aldehyde with a sulfone- or carboxyphenyl (R-substituted) hydrazine. The condensation may be carried out in an aqueous medium especially since the reactants are, in general, soluble in water or in any selected solvent medium and isolated in the usual way by distillation, extraction, crystallization or precipitation. Usually, refluxing of the reactants with the aldehyde in the form of the sodium salt results in high yields after about 1 to 2 hours of refluxing. Among suitable aldehydes which may be employed as reactants in preparing the compounds of this invention are:

2-sulfobenzaldehyde
2-chloro-4-sulfobenzaldehyde
2-methyl-4-sulfobenzaldehyde
2-ethyl-4-sulfobenzaldehyde
2-n-butyl-4-sulfobenzaldehyde
2-methylsulfonyl-4-sulfobenzaldehyde
2-carboxamido-4-sulfobenzaldehyde
2-methoxy-4-sulfobenzaldehyde
2-ethoxy-4-sulfobenzaldehyde
2-n-hexyloxy-4-sulfobenzaldehyde
2-hydroxyethyl-4-sulfobenzaldehyde
2-hydroxy-4-sulfobenzaldehyde
2-ethoxyethyl-4-sulfobenzaldehyde
2-carboxethoxyethyl-4-sulfobenzaldehyde
2-cyano-4-sulfobenzaldehyde
2-cyanomethyl-4-sulfobenzaldehyde
3-hydroxy-4-sulfobenzaldehyde
3-methoxy-4-sulfobenzaldehyde
3-hydroxy-6-sulfobenzaldehyde
3-methoxy-6-sulfobenzaldehyde
3-methyl-2-sulfobenzaldehyde
3-methyl-6-sulfobenzaldehyde
4-chloro-3-methyl-6-sulfobenzaldehyde
4-methoxy-3-sulfobenzaldehyde
4-isoproxy-3-sulfobenzaldehyde
4-carbethoxy-3-sulfobenzaldehyde
4-bromo-3-ethyl-6-sulfobenzaldehyde
4-ethoxy-3-isobutyl-6-sulfobenzaldehyde
4-cyano-3-methyl-6-sulfobenzaldehyde
4,2,4-disulfobenzaldehyde
5-chloro-2,4-disulfobenzaldehyde
6-chloro-2,4-disulfobenzaldehyde
6-ethoxy-2,4-disulfobenzaldehyde
5-cyano-2,4-disulfobenzaldehyde
5-chloroethyloxy-2,4-disulfobenzaldehyde
3-methyl-2,4-disulfobenzaldehyde
2,5-disulfobenzaldehyde
2,6-disulfobenzaldehyde
6-hydroxy-3-methyl-5-sulfobenzaldehyde
3,5-disulfobenzaldehyde
2-hydroxy-3,5-disulfobenzaldehyde
2-methoxy-3,5-disulfobenzaldehyde
2,3,5-trisulfobenzaldehyde
2-formyl benzoic acid
3-formyl benzoic acid
4-formyl benzoic acid
2-chloro-3-formyl benzoic acid
2,6-dichloro-3-formyl benzoic acid
2,4,6-trichloro-3-formyl benzoic acid
2-chloro-4-formyl benzoic acid
2,5-dichloro-4-formyl benzoic acid
2,3,6-trichloro-4-formyl benzoic acid
4-formyl-o-toluic acid
4-isoproxy-3-formyl benzoic acid
4-cyano-3-formyl benzo acid
4-chloro-3-formyl benzoic acid
4-carbethoxy-3-formyl benzoic acid
4-fluoro-3-formyl benzoic acid
4-propenyl-3-formyl benzoic acid
4-methylsulfonfyl-3-formyl benzoic acid

Examples of suitable phenyl hydrazines are as follows:

1-methyl-1-(p-sulfophenyl) hydrazine
1-ethyl-1-(p-sulfophenyl) hydrazine
1-isopropanol-1-(p-sulfophenyl) hydrazine
1-n-hexyl-1-(p-sulfophenyl) hydrazine
1-methyl-1-(3-sulfo-4-methyl phenyl) hydrazine
1-ethyl-1-(3-sulfo-4-methyl phenyl) hydrazine
1-methyl-1-(2-methyl-3-sulfo phenyl) hydrazine
1-ethyl-1-(2-methyl-3-sulfo phenyl) hydrazine
1-methyl-1-(2-methyl-5-sulfo phenyl) hydrazine
1-n-propyl-1-(2-methyl-5-sulfo phenyl) hydrazine
1-ethyl-1-(3-sulfo-4-ethyl phenyl) hydrazine
1-methyl-1-(2-sulfo-4-chlorophenyl) hydrazine
1-methyl-1-(2-sulfo-4-methylphenyl) hydrazine
1-n-propyl-1-(2-sulfo-4-methylphenyl) hydrazine
Among the general methods for preparing the hydrazine compounds used in the present invention, mention might be made of nitrosating the N-alkyl aniline, reducing to the hydrazine with zinc in acetic acid and sulfonating with oleum. Alternatively, the N-alkyl anilines may be sulfonated first and then nitrosated and reduced. When the N-alkyl aniline contains a para substituent such as alkyl, halogen, cyano, sulfonyl, carbalkoxy and the like, the sulfonation will take place in the ortho position. Where these substituents are ortho or meta, sulfonation will be para. The general reaction and specific compounds and conditions can be found in Helv. Chim. Acta 29, 1965–66 (1942).

The carboxy phenyl hydrazines can be prepared in a similar manner by nitrosating and reducing the corresponding carboxy anilines.

In the following examples which will serve only to illustrate the present invention and are not to be deemed limiting thereof, parts by weight unless otherwise indicated.

Example 1

Into a 3-liter flask equipped with a stirrer, thermometer, reflex condenser and heating mantle, there are charged the following ingredients:

24.3 g. of 1-methyl-1-(p-sulphonyl) hydrazine (molecular weight 188; \( K_{\text{max}} = 69.2 \text{ at } 253 \text{ nm} \))
52.5 g. sodium salt of 2-sulphobenzaldehyde (88.2% pure; molecular weight 186)
120 ml. of ethanol and 30.6 g. of sodium acetate crystals

The mixture is stirred for 2½ hours at reflux and there-after it is cooled to 10° C. in an ice bath. The resultant crystals are filtered and the filter cake washed with 240 ml. of cold ethanol. The press-cake is then slurried in 750 ml. of water and to the slurry there is added a teaspooon of decolorizing carbon, after which the mass is filtered. To the filtrate there is added slurry at room temperature, isopropanol until the formation of crystals is noted. The entire mass is then cooled to 10° C. and then filtered and dried at 40° C. in a vacuum oven. There is obtained a yield of 77 g. product which has a \( K_{\text{max}} \) equal to 70 at 360 nm and which is identified as 1-methyl-1-(p-sulphonyl)-2-sulphophenyl hydrazono sodium salt.

Example 2

Example 1 is repeated employing in place of the sodium salt of 2-sulphobenzaldehyde, the same weight of 2-sulphobenzaldehyde (i.e., 46.3 g. on a 100% basis). The product is 1-methyl-1-(p-sulphonyl)-2-sulphophenyl hydrazono sodium salt.

Example 3

Example 1 is once again repeated using an equivalent weight on a 100% basis of 2.4-disulpho benzaldehyde. The product obtained is 1-methyl-1-(2,4-disulphophenyl)-2-sulphophenyl hydrazono sodium salt.

Example 4

Example 2 is repeated except that in place of the p-sulphonated hydrazine used in that example, there is used an equal weight of the o-sulphonated product. The product obtained is 1-methyl-1-(o-sulphonyl)-2-sulphophenyl hydrazono sodium salt.

Example 5

Example 4 is repeated except that in place of the o-sulphonated hydrazine, there is used an equivalent weight of the o-carboxylated hydrazine. The product obtained is 1-methyl-1-(o-carboxyphenyl)-2-sulphophenyl hydrazono sodium salt.

Example A

The product of Example 1 is incorporated into a neutral detergent composition in the form of a bar, and which
contains as the main detergents ingredient a cocanut oil acid ester of sodium isethionate. The amount of the product of Example 1 which is used is 0.2% by weight based on the total weight of the detergent bar. The bar is then used separately by five individuals in a bathing procedure, and thereafter the five persons are exposed to the afternoon's summer sun for two hours. A similar group of five persons uses a similar detergent bar but devoid of the product of Example 1, and these individuals are similarly exposed as the first group. Each of the persons in the second group, after exposure, shows considerable reddening of the skin whereas none of the persons in the first group has any visible evidence of sunburn. This performance demonstrates not only the excellent sunscreen characteristics of the compound of Example 1, but also its outstanding substantivity for human skin from the detergent bar which is used for bathing.

Example B

The procedure of Example A is repeated except that in place of a detergent bar, there is used a conventional bar of soap (pH about 10) containing 0.3% of the product of Example 1. Comparable results are obtained as in Example A.

Example C

The product of Example 1 is prepared as a 10% by weight solution in water, and to this solution there is immersing a sample of cellulose textile material which has been previously dyed with a dark red cotton dye. After removal and drying of the sample, it is placed in a vadeometer along with a similarly dyed sample which has not been treated with the product of Example 1. After four hours exposure, the untreated sample shows severe fading whereas the treated goods shows no fading of the dyeing.

Examples 6–25

In the following examples, Example 1 is repeated except that in place of 2-sulfobenzaldehyde, there are used the following benzaldehydes in equivalent amounts:

<table>
<thead>
<tr>
<th>Example</th>
<th>Compound</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>4-chloro-2-sulfobenzaldehyde</td>
</tr>
<tr>
<td>7</td>
<td>4-hydroxy-2-sulfobenzaldehyde</td>
</tr>
<tr>
<td>8</td>
<td>4-bromo-3-sulfobenzaldehyde</td>
</tr>
<tr>
<td>9</td>
<td>2,6-dichloro-3-sulfobenzaldehyde</td>
</tr>
<tr>
<td>10</td>
<td>2-methyl-4-sulfobenzaldehyde</td>
</tr>
<tr>
<td>11</td>
<td>2-methyloxononyl-4-sulfobenzaldehyde</td>
</tr>
<tr>
<td>12</td>
<td>2-carboxamido-4-sulfobenzaldehyde</td>
</tr>
<tr>
<td>13</td>
<td>2-ethoxy-4-sulfobenzaldehyde</td>
</tr>
<tr>
<td>14</td>
<td>2-cyano-4-sulfobenzaldehyde</td>
</tr>
<tr>
<td>15</td>
<td>2-cyanoehtyl-4-sulfobenzaldehyde</td>
</tr>
<tr>
<td>16</td>
<td>3-hydroxy-4-sulfobenzaldehyde</td>
</tr>
<tr>
<td>17</td>
<td>3-methyl-4-sulfobenzaldehyde</td>
</tr>
<tr>
<td>18</td>
<td>5-chloro-2,4-desulfobenzaldehyde</td>
</tr>
<tr>
<td>19</td>
<td>3-chloro-2,5-desulfobenzaldehyde</td>
</tr>
<tr>
<td>20</td>
<td>2-chloro-3-formylbenzoic acid</td>
</tr>
<tr>
<td>21</td>
<td>4-formyl-3-toluid acid</td>
</tr>
<tr>
<td>22</td>
<td>4-carboxyethoxy-3-formyl benzoic acid</td>
</tr>
<tr>
<td>23</td>
<td>4-propenyl-3-formyl benzoic acid</td>
</tr>
<tr>
<td>24</td>
<td>4-methylsulfonyl-3-formyl benzoic acid</td>
</tr>
<tr>
<td>25</td>
<td>3-formyl benzoic acid</td>
</tr>
</tbody>
</table>

In the following examples, Example 1 is repeated replacing the sulphonylhydrazine used therein by the following hydrazines in equivalent amounts:

<table>
<thead>
<tr>
<th>Example</th>
<th>Compound</th>
</tr>
</thead>
<tbody>
<tr>
<td>26</td>
<td>1-ethyl-1-(p-sulfophenyl) hydrazine</td>
</tr>
<tr>
<td>27</td>
<td>1-n-hexyl-1-(p-sulfophenyl) hydrazine</td>
</tr>
<tr>
<td>28</td>
<td>1-methyl-1-(3-sulfo-4-methyl phenyl) hydrazine</td>
</tr>
<tr>
<td>29</td>
<td>1-n-propyl-1-(2-sulfo-5-methylphenyl) hydrazine</td>
</tr>
<tr>
<td>30</td>
<td>1-methyl-1-(2,6-diulso-4-methyl phenyl) hydrazine</td>
</tr>
<tr>
<td>31</td>
<td>1-hydroxycarbonyl-1-(4-sulfo-phenyl) hydrazine</td>
</tr>
<tr>
<td>32</td>
<td>1-cyclohexyl-1-(2-chloro-4-sulfo-phenyl) hydrazine</td>
</tr>
<tr>
<td>33</td>
<td>1-methyl-1-(4-carboxyphenyl) hydrazine</td>
</tr>
<tr>
<td>34</td>
<td>1-ethyl-1-(3-carboxyphenyl) hydrazine</td>
</tr>
<tr>
<td>35</td>
<td>1-methyl-1-(5-chloro-6-carboxyphenyl) hydrazine</td>
</tr>
</tbody>
</table>

We claim:
1. An essentially colorless compound of the formula:

   \[
   R \begin{array}{c}
   \text{N} \\
   \text{X} \\
   \text{Y} \\
   \text{Z}
   \end{array}
   \]

   wherein in the free acid form
   (1) \((Ar)_1\) and \((Ar)_2\) represent benzene rings;
   (2) \(Y\) and \(Z\) are salt-forming groups selected from sulfinic acid and carboxyl;
   (3) \(R\) is a radical selected from alkyl, hydroxalkyl, and cyclohexyl; and
   (4) \(n\) and \(m\) are integers from 1 to 3;

   the compound having an absorption maxima within the range of 2900 A. to about 3500 A.
2. A compound as defined in claim 1 wherein
   (1) \(Y\) and \(Z\) are sulfinic acid; and
   (2) \(R\) is alkyl.
3. A compound as defined in claim 2 wherein
   (1) \(n\) and \(m\) are 1.
4. A compound as defined in claim 2 wherein \(n\) is 2 and \(m\) is 1.
5. A compound as defined in claim 3 wherein \(R\) is alkyl of 1 to 6 carbon atoms.
6. A compound as defined in claim 5 wherein \(Y\) is in the 2-position and \(Z\) is in the 4-position.
7. A compound as defined in claim 6 wherein \(R\) is methyl.
8. A compound as defined in claim 6 wherein \(Y\) and \(Z\) are carboxyl.
9. A compound as defined in claim 6 wherein \(Y\) is sulfinic acid and \(Z\) is carboxyl.
10. A compound as defined in claim 8 wherein \(R\) is alkyl of 1 to 6 carbon atoms and \(n\) and \(m\) are 1.
11. A compound as defined in claim 9 wherein \(R\) is alkyl of 1 to 6 carbon atoms and \(n\) and \(m\) are 1.
12. A water-soluble salt of a compound as defined in claim 1.
13. A water-soluble salt of a compound as defined in claim 3 wherein the cation is selected from the class consisting of alkali metal, ammonium, and amine cations.

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