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3,375,271

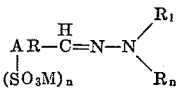
SUN-SCREENING COMPOUNDS

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6 Claims. (Cl. 260—510)

ABSTRACT OF THE DISCLOSURE

Compounds of the formula



wherein AR represents a benzene ring which may be substituted, M is hydrogen, a Group I metal, ammonium or amine, n is an integer from 1 to 3, R_1 and R_2 are independently hydrogen, alkyl, alkenyl, cycloalkyl, or cycloalkenyl, and at least one of R_1 and R_2 is not hydrogen.

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 waterwash. 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.

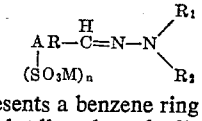
It is still another object of the present invention to provide compositions, and particularly cosmetic compositions, which may be applied to the human skin to protect it against the burning and tanning rays of the sun.

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 objetcs 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 unexpectedly 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 $K=10$ at a given wavelength 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:



(I)

wherein AR represents a benzene ring and R_1 and R_2 may be hydrogen, alkyl, alkenyl, cycloalkyl, cycloalkenyl and substituted derivatives thereof and at least one of R_1 and R_2 is other than hydrogen and n is an integer from 1 to 3, inclusive, and M is hydrogen, a Group I metal, ammonium or amine.

The benzene ring may contain other substituents such as halogen, lower alkyl (C_1 to C_8), substituted lower alkyls, oxy (such as lower alkoxy, lower alkoxy lower alkyl and the like), and carbalkoxy as well as other non-auxochromic groups which do not have a significant bathochromic effect. By significant we mean a shifting of the absorption of more than about 250 A. A group which is specifically to be avoided is nitro as well as more than two oxy substituents. It is also preferred that the compounds do not contain an amino group in the aryl moiety since in general such compounds have inferior light fastness although it is to be understood that the effectiveness thereof over the broad spectrum of the burning and tanning wavelengths is on a par with the other compounds.

Suitable substituents for R_1 and R_2 include all of the well known and the general class of alkyls and various substituted forms thereof such as:

methyl
ethyl
n-propyl
iso-propyl
n-butyl
iso-butyl
tertiary-butyl
secondary-butyl
n-amyl
iso-amyl
tertiary-amyl and the other isomeric amyls
n-hexyl
iso-hexyl and the other isomeric hexyls
n-heptyl
iso-heptyl and the other isomeric heptyls
n-primary nonyl (nonyl-1)
nonyl-(2)
nonyl-(3)
nonyl-(5)
2-methyl-octyl-2
4-ethyl-heptyl-4
2-methyl-4-ethyl-hexyl-4
n-primary octyl
octyl-(2) (capryl)
2-methyl-3-ethyl-pentyl-3
2,2,4-trimethyl-pentyl-4
2-ethyl-hexyl-1
3-ethyl-hexyl-3
2-methyl-heptyl-2
3-methyl-heptyl-3
4-methyl-heptyl-4
n-primary decyl (decyl-1)
decyl-4 (secondary decyl)
2-ethyl-octyl-3 (tertiary decyl)
4-propyl-heptyl-4 (tertiary decyl)
undecyl-1 (n-primary decyl)
undecyl-2 (n-secondary decyl)
dodecyl-1 (n-dodecyl)
tridecyl-1 (n-tridecyl)
tridecyl-7
3-ethyl-undecyl
tetradecyl-1 (n-tetradecyl)
pentadecyl-1 (n-pentadecyl)
pentadecyl-8
hexadecyl (cetyl)
heptadecyl-9
octadecyl-1
2-methyl heptadecyl-2
eicosyl-1
docosyl-1
tricosyl-12
tetracosyl
tricapryl
pentacosyl
hexacosyl
heptacosyl
octacosyl
nonacosyl
myrisyl (30 carbons)
cyanoethyl
cyano-n-propyl
cyano-isopropyl
cyano-n-butyl
cyano-isobutyl
cyano-n-amyl
cyano-isoamyl
cyanohexyl
cyanoheptyl
cyano-n-octyl
cyano-nonyl
cyanodecyl
cyanolauryl
cyanostearyl and the like
carbomethoxyethyl

carbomethoxypropyl
carbomethoxybutyl
carbomethoxyamyl
carbomethoxyhexyl
carbethoxyethyl
carbethoxypropyl
carbethoxybutyl, etc.
carbopropoxyethyl
carbopropoxypropyl
carbopropoxybutyl, etc.
carbobutoxyethyl
carbobutoxybutyl, etc.
chloroethyl
chloropropyl (N-propyl, isopropyl)
chlorobutyl (N-butyl, isobutyl, etc.)
chloroamyl
chlorohexyl
chlorodecyl
chlorolauryl, and the like
bromoethyl
bromopropyl (N-propyl, isopropyl)
bromobutyl (N-butyl, isobutyl, etc.)
bromoamyl
bromohexyl
bromodecyl
bromolauryl, and the like
methoxyethyl
methoxypropyl (N-propyl, isopropyl)
methoxybutyl (N-butyl, isobutyl, etc.)
methoxyamyl
methoxyhexyl
methoxydecyl
methoxylauryl, and the like.
ethoxyethyl
ethoxypropyl (N-propyl, isopropyl)
ethoxybutyl (N-butyl, isobutyl, etc.)
ethoxyamyl
ethoxyhexyl
ethoxydecyl
ethoxylauryl, and the like
allyl
methallyl
crotyl
butenyl-1
pentenyl-1
γ-isopropyl allyl
2-methyl-octenyl-6 and the like
cyclopropyl
cyclobutyl
cyclopentyl
cyclohexyl
cyclopentenyl (-2)
cyclopentenyl (-3)
cyclopentenyl (-4)
cyclohexenyl (-2)
cyclohexenyl (-3)
cyclohexenyl (-4)
cyclohexenyl (-5)
2-methyl cyclohexenyl(-4-)
4-chlorocyclohexyl
4-allyl cyclohexyl
3-bromocyclohexyl
2-isopropyl cyclohexyl
3-n-propyl cyclohexyl
4(2-chloroethyl) cyclohexyl
3-methyl-4-chlorocyclohexyl
3,4-dibromocyclohexyl
2,4-dimethylcyclohexyl

Similar substituents may be present in the benzene ring with the proviso as pointed out above that it is preferred that the carbon chain be no greater than about 8 carbon atoms. Also, as mentioned above, the benzene ring may contain halogen substituents such as chlorine, bromine, iodine and fluorine as well as alkyl sulfonyls such as

methyl sulfonyl, ethyl sulfonyl, carboxamido, N-methylcarboxamide, N-ethylcarboxamide, N,N-dimethylcarboxamide, N,N-diethylcarboxamide, sulfonamide, etc.

The general procedure for preparing the compounds of this invention involves a condensation of the sulfobenzene aldehyde with the N-alkylated hydrazine or N,N-dialkylated hydrazine (or the substituted alkylated forms thereof). 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 (o-formyl benzene sulfonic acid)
4-chloro-2-sulfobenzaldehyde
5-chloro-2-sulfobenzaldehyde
6-chloro-2-sulfobenzaldehyde
3-sulfobenzaldehyde
4-bromo-3-sulfobenzaldehyde
4-chloro-3-sulfobenzaldehyde
4-fluoro-3-sulfobenzaldehyde
4-iodo-3-sulfobenzaldehyde
2,6-dichloro-3-sulfobenzaldehyde
4-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-hexoxy-4-sulfobenzaldehyde
2-ethoxyethyl-4-sulfobenzaldehyde
2-carboethoxyethyl-4-sulfobenzaldehyde
2-cyano-4-sulfobenzaldehyde
2-cyanoethyl-4-sulfobenzaldehyde
3-methoxy-4-sulfobenzaldehyde
3-methyl-2-sulfobenzaldehyde
3-methyl-6-sulfobenzaldehyde
4-chloro-3-methyl-6-sulfobenzaldehyde
4-methoxy-3-sulfobenzaldehyde
4-isopropoxy-3-sulfobenzaldehyde
4-carbethoxy-3-sulfobenzaldehyde
4-bromo-3-ethyl-6-sulfobenzaldehyde
4-ethoxy-3-isobutyl-6-sulfobenzaldehyde
4-cyano-3-methyl-6-sulfobenzaldehyde
2,4-disulfobenzaldehyde
5-chloro-2,4-disulfobenzaldehyde
6-chloro-2,4-disulfobenzaldehyde
6-ethoxy-2,4-disulfobenzaldehyde
5-cyano-2,4-disulfobenzaldehyde
5-chloroethyl-2,4-disulfobenzaldehyde
3-methyl-2,4-disulfobenzaldehyde
2,5-disulfobenzaldehyde
2,6-disulfobenzaldehyde
3,5-disulfobenzaldehyde
2-methoxy3,5-disulfobenzaldehyde
2,4,6-trisulfobenzaldehyde

Examples of specific hydrazines are:

methyl hydrazine
ethyl hydrazine
n-propyl hydrazine
isopropyl hydrazine
n-butyl hydrazine
n-pentyl hydrazine
n-hexyl hydrazine
iso octyl hydrazine
undecyl hydrazine
stearyl hydrazine
sec.-n-octyl hydrazine
dodecyl hydrazine
hydrazine acetic acid
hydrazine acetic acid methyl ester
hydrazine acetic acid ethyl ester
hydrazine acetic acid isobutyl ester
hydrazine acetic acid isooctyl ester
hydrazine acetic acid hexadecyl ester
α-hydrazine propionic acid
α-hydrazine propionic acid methyl ester
α-hydrazine propionic acid ethyl ester
α-hydrazine propionic acid n-propyl ester
α-hydrazine propionic acid isooctyl ester
α-hydrazine hexanoic acid ethyl ester
hydrazine acetic acid, methoxy ethyl ester
hydrazine acetamide
hydrazine N-methyl acetamide
N,N-dimethyl hydrazine
N,N-diethyl hydrazine
N-methyl-N-ethyl hydrazine
N-methyl-N-butyl hydrazine
N-methyl-N-isobutyl hydrazine
N,N-di-n-propyl hydrazine
N,N-dibenzyl hydrazine
N,N-diisobutyl hydrazine
N,N-dipentyl hydrazine
N,N-dicyclohexyl hydrazine
allyl hydrazine
N,N-diallyl hydrazine
cyclopentyl hydrazine
cyclohexyl hydrazine
4-chlorocyclohexyl hydrazine
4-(2-chloroethyl) cyclohexyl hydrazine
pentenyl(-1) hydrazine
crotyl hydrazine
γ-hydrazino propyleneglycol
($CH_2OHCHOHCH_2NHNH_2$)
β-chloroethyl hydrazine
β-cyanoethyl hydrazine
β-methoxyethyl hydrazine
γ-chloropropyl hydrazine
β-chloropropyl hydrazine
carbethoxyethyl ethyl hydrazine

In the following examples which will serve to illustrate the present invention, parts are by weight unless otherwise indicated.

EXAMPLE 1

To 2.4 liters of ethyl alcohol in a 5 liter flask there are added 525 g. (2 moles) of 2-sulfobenzaldehyde and 152 cc. of N,N-dimethylhydrazine (2 moles). The contents are refluxed for 2 hours and thereafter the reaction mixture is cooled. A copious formation of crystals results upon cooling. These are separated from the liquor by filtration. The solids are washed with 800 cc. of ethyl alcohol. The yield is 350 g. which is about 70% of theory. The resulting product has a K_{max} of 49 at 3010 A. and at 3300 A. a K_{max} of 45, demonstrating thereby the broad absorption characteristics of this compound to the burning and tanning rays of solar radiation.

EXAMPLE 2

The compound of Example 1 is made up as a 2% (by weight) solution in water and applied to the skin. A dry film of about 0.5 mil results. After 4 hours' exposure to summer sun, the protected areas of skin show no discernible burning and when compared to completely covered skin there is just a faint discernible difference.

The skin after exposure is rinsed in clear water, dried and exposed again for 4 hours as above. A slight sunburning results. Untreated skin shows a severe reddening. This demonstrates not only the superior protection

afforded by the product of this invention but also its apparent substantivity to skin.

EXAMPLE 3

Example 1 is repeated employing 2 moles of the following sulfo-containing benzaldehydes:

A. 4-chloro-2-sulfobenzaldehyde
C. 4-iodo-3-sulfobenzaldehyde
D. 2,6-dichloro-3-sulfobenzaldehyde
E. 2-methyl-4-sulfobenzaldehyde
F. 2-methylsulfonyl-4-sulfobenzaldehyde
G. 2-ethoxy-4-sulfobenzaldehyde
H. 2-n-hexyloxy-4-sulfobenzaldehyde
J. 2-ethoxyethyl-4-sulfobenzaldehyde
K. 2-carboethoxyethyl-4-sulfobenzaldehyde
L. 2-cyano-4-sulfobenzaldehyde
M. 2-cyanoethyl-4-sulfobenzaldehyde
O. 4-chloro-3-methyl-6-sulfobenzaldehyde
P. 2,4-disulfobenzaldehyde
Q. 3-sulfobenzaldehyde
R. 2,4,6-trisulfobenzaldehyde

EXAMPLE 4

Examples 3A through 3O are each repeated using 2 moles of the following hydrazine compounds:

A. Methyl hydrazine
B. Isooctyl hydrazine
C. Hydrazine acetic acid
D. Hydrazine acetic acid ethyl ester
G. Hydrazine acetamide
H. N-methyl, N-ethyl hydrazine
I. N,N-dibenzyl hydrazine
J. N,N-dipentyl hydrazine
K. N,N-dicyclohexyl hydrazine
L. Cyclopentyl hydrazine
M. Allyl hydrazine
N. Crotyl hydrazine
O. N,N-diallyl hydrazine
P. β-Methoxyethyl hydrazine
Q. 1-cyclopentenyl-1-hydrazine

EXAMPLE 5

Example 2 is repeated employing the compounds prepared in Examples 3 and 4. Excellent results are obtained.

EXAMPLE 6

Examples 2 and 5 are repeated employing the full salts of the sulfonic acids by the treatment of the 1% aqueous solutions with the following base in stoichiometric amounts:

A. Sodium hydroxide
B. Potassium hydroxide
C. Ammonium hydroxide
D. Methyl amine
E. Isopropyl amine
F. Monoethanolamine
G. Triethanolamine
H. Monoisopropanolamine

EXAMPLE 7

Examples 2 and 5 are repeated employing the following concentration (by weight) of absorber:

A. 0.5%
B. 2.0%

EXAMPLE 8

Example 6 is repeated using the following concentrations (by weight) of absorber:

A. 0.5%
B. 3.0%
C. 5.0%

EXAMPLE 9

The compounds of Examples 3P and 3R as well as the compounds formed from the aldehydes of 3P and 3R with the hydrazines of Examples 4C and 4E as the full sodium salts readily form 10% aqueous solutions and even higher concentrations may be obtained.

EXAMPLE 10

Example 2 is repeated except that 2% by weight of polyvinyl pyrrolidone (K=30) is also added to the aqueous solution as a film former.

EXAMPLE 11

Example 10 is repeated employing the following (by weight) as binders in place of the one of Example 10:

A. 2% vinyl pyrrolidone (70%)-vinylacetate (30%) interpolmer, K=45
B. 2% sodium alginate
C. Starch

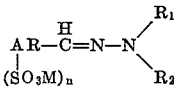
Excellent results are obtained in Examples 10 and 11 after the first 4 hour exposure, but in the second exposure the results are inferior to Example 2 since some of the absorber which remains in the film formers is washed away in the washing prior to the second exposure.

The sun-screen agents of, and used in this invention, are most advantageously applied from aqueous media in view of the ease of application from such a system, as well as the obvious economics thereof. In addition, from such aqueous compositions the sun-screen agents exhibit an outstanding substantivity for the skin which, as pointed out above, makes them particularly outstanding in resisting removal by water, but which does not prevent their ready removability using a slightly alkaline medium such as a soap or the like. It is of course clear that one may use these compounds not only in aqueous media as exemplified above, but they may be used in water-oil systems such as emulsions and the like, including both water-in-oil and oil-in-water emulsions, and they may also be employed in purely or partially organic systems using water-miscible or water-immiscible solvents along with any desired water-soluble, solvent-soluble or water- or solvent-insoluble solid materials such as the usual plasticizers, dyestuffs, pigments, film-formers, fillers and the like. The amount of sun-screen agent in any of such compositions is patently not critical, and any concentration may be used depending upon the desired amount of sun-screen agent to be deposited on the skin. As little as 0.05% in water results in readily discernible and marked protection against the burning rays of the sun. There is obviously no upper limit since it is even possible to apply some of these, or even all of the sun-screen agents described herein in the 100% active form. The preferred range of concentration, however, for most applications, lies between about 0.1% by weight and about 10%, and most preferably from about 0.5% to about 5% by weight based on the weight of the total composition to be applied to the skin. It may also be desirable to employ the sun-screen agents herein disclosed in combination with other sun-screen agents, and it is clear, therefore, that such mixtures as well as mixtures of the compounds described herein are contemplated in the compositions and for the uses towards which the present invention is directed.

Other variations in and modifications of the described processes which will be obvious to those skilled in the art can be made in this invention without departing from the scope or spirit thereof.

We claim:

1. A compound of the formula:



wherein

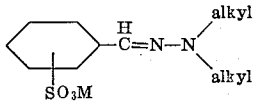
(a) AR represents a benzene ring or a substituted benzene ring containing halogen, lower alkyl, lower alkyl sulfonyl, carboxamido, lower alkoxy, lower alkoxy lower alkyl, carbalkoxy, carbalkoxy lower alkyl, cyano, cyanoalkyl, or halo alkyl,

(b) R_1 and R_2 are independently hydrogen, alkyl, alkenyl, cycloalkyl or cycloalkenyl and at least one of the groups R_1 and R_2 is not hydrogen,

(c) M is hydrogen, a Group I metal, ammonium or amine, and

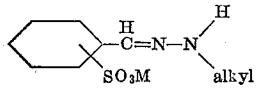
(d) *n* is an integer from 1 to 3, inclusive.

2. A compound of the formula:



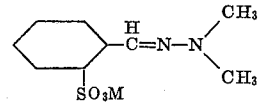
wherein M is selected from the group consisting of hydrogen, Group I metals, ammonium and amine.

3. A compound of the formula:



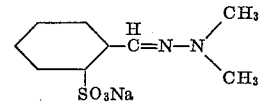
wherein M is selected from the group consisting of hydrogen, Group I metals, ammonium and amine.

4. A compound of the formula:

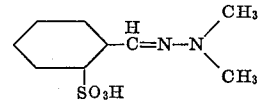


wherein M is selected from the group consisting of hydrogen, Group I metals, ammonium and amine.

5. A compound of the formula:



6. A compound of the formula:



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UNITED STATES PATENT OFFICE

CERTIFICATE OF CORRECTION

Patent No. 3,375,271 March 26, 1968

Sigmund C. Catino et al.

It is certified that error appears in the above identified patent and that said Letters Patent are hereby corrected as shown below:

Column 1, lines 9 to 16, that portion of the formula reading

 should read 

Column 7, line 25, "30" should read -- 3R --.

Signed and sealed this 24th day of March 1970.

(SEAL)
Attest:

Edward M. Fletcher, Jr.
Attesting Officer

WILLIAM E. SCHUYLER, JR.
Commissioner of Patents