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Shelston IP, Level 21 60 Margaret Street, Sydney, NSW, 2000
- (56) Related Art
RUPPIN C. ET AL: "Synthesis of Enol Esters from Terminal Alkynes Catalyzed By Ruthenium Complexes"
YANAGISAWA M. ET AL: "Aldol Reaction of Enol Esters Catalyzed by Cationic Species Paired with Tetrakis(pentafluorophenyl)borate"
JP 61-293952
HUH, TAE-SONG ET AL: "Kinetics and mechanism of the hydrolysis of enol ester in strong acid solution"

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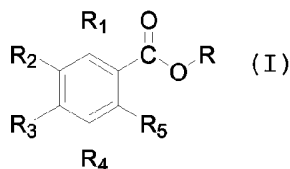
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(54) Title: BENZOIC ACID ESTER COMPOUNDS, COMPOSITIONS, USES AND METHODS RELATED THERETO



(57) Abstract: Benzoic acid ester compounds of formula (I) wherein R and R₁-R₅ have the meanings explained in the description, methods for producing them and use thereof in cosmetic, pharmaceutical, personal care and industrial preparations as sunscreens based on photochemical precursor properties of ultraviolet absorbers.

WO 2006/100225 A3

**BENZOIC ACID ESTER COMPOUNDS, COMPOSITIONS, USES AND
METHODS RELATED THERETO**

Technical field

5 This invention is directed to photochemical precursors of ultraviolet absorbers, especially to benzoic acid ester compounds.

Background of the invention

10 Overexposure to the sun's invisible rays, ultraviolet A (UVA, 320-400 nm) and ultraviolet B (UVB, 290-320 nm) can cause skin damage. The damage can be immediate and long-term, with effects ranging from sunburn, rashes, and cell and tissue damage to premature wrinkling and skin cancer.

15 One particularly deadly form of skin cancer, malignant melanoma, has been on the rise in recent decades, as tanning has become more popular. Over the same period, scientists have warned that the thin layer of ozone that protects life on Earth from the sun's ultraviolet (UV)

20 radiation is being depleted. This allows more UV radiation to get through, adding to the risk of overexposure. Indeed, many skin changes that often are identified with aging actually result from damage by too much sun.

25 Sunscreen is any substance or material that protects the skin from UV radiation. Sunscreens are available in the forms of topical lotion, cream, ointment, gel, or spray that can be applied to the skin; a salve or stick that can be applied to the lips, nose, and eyelids; a

30 moistener in towelettes that can be rubbed against the skin; sunglasses that protect the eyes; and film screen

that can be affixed to the windows of a car, room, or office.

Sunscreens help to prevent sunburn and reduce the harmful effects of the sun such as premature skin aging and skin cancer. But just how much protection they provide is a matter of debate. For many years, experts thought that only UVB was harmful. However, recent research suggests that UVA may be just as dangerous as UVB, although its effects may take longer to show up. In particular, UVA may play a role in causing melanoma. Most sunscreen products contain ingredients that provide adequate protection only against UVB rays. Even those labeled as "broad spectrum" sunscreens may offer only partial protection against UVA radiation. Those containing the ingredient avobenzone (4-*tert*-butyl-4'-methoxydibenzoylmethane) give the most protection against UVA rays.

Sunscreens should be applied between 30 minutes and 2 hours before sun exposure. In general, they should be reapplied after every 80 minutes spent in the water or when perspiring heavily or every 2 hours spent out of the water.

UVB (290-320 nm) is the most erythemogenic solar radiation reaching the surface of the earth. It is also a potent skin carcinogen in animal studies. Sun Protection Factor (SPF) indicates the degree of protection against UVB induced erythema. The US Food and Drug Administration (FDA) regulates sunscreen products as over-the-counter drugs. The Final Over-the-Counter Drug Products Monograph on Sunscreens (Federal Register 1999: 64: 27666-27963) established the conditions for safety, efficacy, and labeling of these products. The SPF is defined as the dose of ultraviolet radiation (UVR) required to produce 1

minimal erythema dose (MED) on protected skin after the application of 2 mg/cm² of product divided by the UVR required to produce 1 MED on unprotected skin.

All sunscreens have a SPF on their labels. The SPF represents the length of time that sunscreen-protected skin can be exposed to UV rays before a minimal redness (erythema) appears, compared to the length of time it takes on unprotected skin. In other words, it indicates how much longer the skin can be exposed to the sun before getting a sunburn. For example, without a sunscreen, an individual might get a sunburn after 20 minutes or less in the sun. By applying a sunscreen of SPF 15, the individual might spend up to 300 minutes under the sun before sunburning, that is 15 times longer than if no protection is used.

Sunscreens with SPF numbers higher than 15 may work better for people who are fair-skinned, live at high altitudes, work or play outdoors much of the day, or perspire heavily. Swimming and perspiration reduce the actual SPF value of many sunscreens, even those that are water-resistant, so it is convenient to reapply the product often.

Table 1 shows some relevant broadly used sunscreen compounds.

Table 1

Drug Name	Concentration %	Absorbance	Protection nm
Avobenzene	2-3	UVA I ¹	320-400
Dioxybenzone	Up to 3	UVB, UVA II ²	250-390
Oxybenzone	Up to 6	UVB, UVA II ²	270-350
Sulisobenzene	Up to 10	UVB, UVA II ²	260-375

¹ 340-400nm; ² 320-340nm

Avobenzone (4-*tert*-butyl-4'-methoxydibenzoylmethane, Parsol 1789, US4387089) provides superior protection through a large portion of the UVA range, including UVA I. Potentially a significant addition to sunscreen products for true broad-spectrum UV protection, concerns have been raised regarding its photostability and its potential to degrade other sunscreen ingredients in products in which it is used.

10 Dioxybenzone (2,2'-dihydroxy-4-methoxybenzophenone, US2853521) is mainly used as an UV-absorber for polymers and coatings. It is used as a stabilizer for polyester film. It is effective against UVB and some UVA light.

15 Oxybenzone (2-hydroxy-4-methoxybenzophenone, US2773903, US2861104, US2861105 and US3073866) absorbs well through UVA II and can be considered a broad-spectrum absorber. It significantly enhances UVB protection when used in a given formula.

20 Sulisobenzene (5-benzoyl-4-hydroxy-2-methoxy-benzenesulfonic acid, GB1136525) extends the coverage beyond the UVB range and into the UVA range, helping to obtain broad-spectrum sunscreen preparations.

25 Amino-substituted hydroxybenzophenones have been disclosed as photostable UV filters to be used in cosmetic and dermatological compositions (US6409995).

30 Chemical sunscreens "block" the penetration of UV radiation through the epidermis by acting as filters and absorbing and reflecting high energy UV. The sunscreen molecules absorb the high energy UV photons causing the electronic structure to move to a higher energy state.
35 This electronic energy is dissipated by conversion to

vibrational and rotational energy within the molecule, ultimately being transferred to the molecule's environment as heat.

The FDA has taken a position against the continued
5 labeling of high SPF formulations, and has stated that the maximum SPF should not exceed 30 due to the additional costs and risks from increased concentrations of active ingredients. This is in spite of the fact that other than the expected occurrence of occasional
10 allergic, phototoxic, and photoallergic cutaneous reactions, there is virtually no published evidence of harm from using high SPF sunscreen formulations.

There are, in fact, a number of reasons why high SPF formulations (> 30 SPF) may be the best choice for high
15 risk individuals, especially when sun exposure is expected to be extensive. Rubbing, sweating, and water immersion diminish the effectiveness of all sunscreens, requiring frequent re-application of the product even with supposedly waterproof or sweat proof formulations.
20 Another factor that enhances the damaging effects of lengthy exposures is a time-dependent diminution of SPF effect not related to removal of the product from rubbing or washing. Experiments in the hairless mouse model found a significant decrease in measured SPF occurring within
25 the first few hours following sunscreen application. Studies in humans confirm that single applications of an SPF 25 sunscreen are frequently inadequate to prevent erythema, and that multiple applications are required to completely suppress erythema, even from a single day's
30 sun exposure.

A final factor that may not be fully compensated for, even with repeated application, is the effect of multi-day UV exposures. A significant multi-day exposure to

sunlight (e.g., all day Saturday and Sunday) increases the sensitivity of the skin to UV damage on the second day of exposure. This means that even if the sunscreen functions as predicted by the rated SPF to prevent erythema on the first day of exposure, the heightened sensitivity on the second and subsequent days of exposure may lead to erythema development which would not have been predicted based solely on extrapolations of the SPF. In such instances, a sunscreen with an SPF > 30 may provide significantly better protection from UV damage, particularly in susceptible individuals.

Higher SPF sunscreen products have led to the use of multiple individual sunscreen agents used in combinations at maximum concentrations that may interact.

The current focus on erythema as the standard against which sunscreen potency is measured may have led to the assumption that erythema prevention is also the only important goal of sun protection, and ultimately to the FDA's position against sunscreens more potent than 30 SPF. This assumption ignores experimental evidence that significant UV-induced damage occurs prior to the development of perceptible UV-induced redness. Human research using sunburn cells as the measure of UV damage supports the existence of significant sub-erythematous DNA damage in the skin, and the value of high SPF sunscreens in preventing it.

SPF testing is designed to evaluate protection against erythema produced by natural sunlight and, therefore, denotes principally the degree of protection against UVB, since the amount of UVA received from sunlight does not produce significant erythema. The only ingredient approved by the FDA for protection against UVA radiation is avobenzene. However, if a product contains ingredients

that absorb UV between 290-320 nm it can be labeled as a broad-spectrum sunscreen, meaning it will provide protection against both UVB and short wave UVA radiation.

5 Adverse reactions to sunscreen comprise cutaneous problems, such as allergic contact reactions, photocontact reactions, and drying or tightening of the skin. Other side effects are rare, but possible, namely acne, burning, itching, or stinging of the skin, redness or swelling of the skin, rash, with or without blisters
10 that ooze and become crusted, pain in hairy parts of body and pus in hair follicles.

Photostability refers to the ability of a molecule to remain intact with irradiation. Poor photostability is potentially a problem with all UV filters because they
15 are deliberately selected as UVR-absorbing molecules. This issue has been raised specifically with avobenzene, with photolysis demonstrated, especially *in vitro* systems, that simultaneously irradiate and measure transmittance *in situ*. The photostability of the
20 molecules also depends on the solvent or the vehicle used.

Subjective irritation associated with burning or stinging without objective erythema is the most common sensitivity complaint from sunscreens. This irritation is most
25 frequently observed in the eye area. However, persistent objective irritant contact dermatitis is a more common side effect. Virtually all sunscreen ingredients reported to cause contact allergy might be photoallergens. Sunscreen actives seem to have become the leading cause
30 of photocontact allergic reactions. Individuals with preexisting eczematous conditions have a significant predisposition to sensitization associated with their impaired cutaneous barrier. In addition, certain

antibiotics, birth control pills, diuretics, antihistamines, and antidepressants are among the commonly used drugs that can increase sensitivity to the sun's rays.

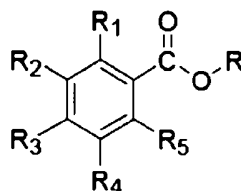
A water resistance claim of two hours means the sunscreen should retain its full SPF protection even after two hours in the water. Even water resistant, sunscreen should be
5 reapplied after any water sports.

It is therefore desirable to discover new sunscreen compounds with a lower risk of side effects, increased photostability, and increased persistence on the skin.

Any discussion of the prior art throughout the specification should in no way be considered as an admission that such prior art is widely known or forms part of common
10 general knowledge in the field.

It is an object of the present invention to overcome or ameliorate at least one of the disadvantages of the prior art, or to provide a useful alternative.

According to a first aspect, the invention provides use of benzoic acid ester compounds of formula (I):



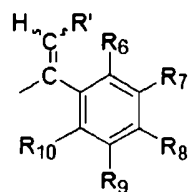
(I)

15

wherein R₁-R₅ are selected independently from hydrogen, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₃-C₆-cycloalkoxy, hydroxy, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, wherein said two alkyl portions of said dialkylamino can form, together with the nitrogen atom to which they are attached, a heterocycle selected from
20 pyrrolidine, piperidine, morpholine and piperazine optionally N-substituted by C₁-C₆-alkyl or C₃-C₆-cycloalkyl, C₃-C₆-cycloalkylamino, C₁-C₆-alkyl-C₃-C₆-cycloalkylamino and C₃-C₆-dicycloalkylamino, or two groups on adjacent ring carbons form a fused O-(CH₂)_m-O group wherein m is 1 or 2, or two groups on adjacent ring carbons form a fused CH=CH-CH=CH group;

25 R is a group selected from (i), (ii), or (iii):

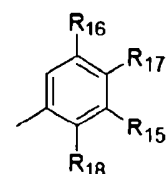
- 8a -



(i)



(ii)



(iii)

wherein R' is selected from hydrogen, C₁-C₆-alkyl or C₃-C₆-cycloalkyl;

R₆-R₁₀ are selected independently from hydrogen, C₁-C₆-alkyl or C₃-C₆-cycloalkyl, C₁-C₆-alkoxy or C₃-C₆-cycloalkoxy, hydroxy, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, wherein said two alkyl portions of said dialkylamino can form, together with the nitrogen atom to which they are attached, a heterocycle selected from pyrrolidine, piperidine, morpholine and piperazine optionally N-substituted by C₁-C₆-alkyl or C₃-C₆-cycloalkyl, C₃-C₆-cycloalkylamino, C₁-C₆-alkyl-C₃-C₆-cycloalkylamino and C₃-C₆-dicycloalkylamino, or two groups on adjacent ring carbons form a fused O-(CH₂)_n-O group wherein n is 1 or 2, or two groups on adjacent ring carbons form a fused CH=CH-CH=CH group;

R₁₁ is selected from hydrogen, C₁-C₆-alkyl and C₃-C₆-cycloalkyl;

R₁₂ is selected from hydrogen, C₁-C₆-alkyl and C₃-C₆-cycloalkyl;

R₁₃ and R₁₄ are selected independently from hydrogen, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₃-C₆-cycloalkoxy, hydroxy, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, wherein said two alkyl portions of said dialkylamino can form, together with the nitrogen atom to which they are attached, a heterocycle selected from pyrrolidine, piperidine, morpholine and piperazine optionally N-substituted by C₁-C₆-alkyl or C₃-C₆-cycloalkyl, C₃-C₆-cycloalkylamino, C₁-C₆-alkyl-C₃-C₆-cycloalkylamino and C₃-C₆-dicycloalkylamino;

or the group OR₁₂ and R₁₄ form a fused O-(CH₂)_p-O group wherein p is 1 or 2; and

R₁₅-R₁₈ are selected independently from hydrogen, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₃-C₆-cycloalkoxy, hydroxy, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, wherein said two alkyl portions of said dialkylamino can form, together with the nitrogen atom to which they are attached, a heterocycle selected from pyrrolidine, piperidine, morpholine and piperazine optionally N-substituted by C₁-C₆-alkyl or C₃-C₆-

cycloalkyl, C₃-C₆-cycloalkylamino, C₁-C₆-alkyl-C₃-C₆-cycloalkylamino and C₃-C₆-dicycloalkylamino, or two groups on adjacent ring carbons from a fused O-(CH₂)_q-O group wherein q is 1 or 2, or two groups on adjacent ring carbons form a fused CH=CH-CH=CH group;

5 or a pharmaceutically acceptable salt thereof,

to prepare a cosmetic or pharmaceutical composition, a personal care composition or an industrial composition comprising an effective amount of at least one of said compounds for protecting a human or animal living body or a material from ultraviolet radiation.

According to a second aspect, the invention provides a cosmetic or pharmaceutical
10 composition, a personal care composition or an industrial composition containing at least a benzoic acid ester compound as defined in the first aspect for protecting a human or animal living body or a material from ultraviolet radiation.

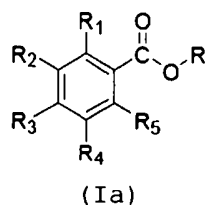
According to a third aspect, the invention provides use of benzoic acid ester compounds according to the first aspect to prepare a cosmetic or pharmaceutical composition
15 characterised by a progressive UV protection depending on the time to sun exposition and the degree of sun radiation.

According to a fourth aspect, the invention provides the use of benzoic acid ester compounds according to the first aspect to prepare a personal care composition characterised by a progressive UV protection depending on the time to sun exposition
20 and the degree of sun radiation.

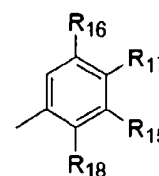
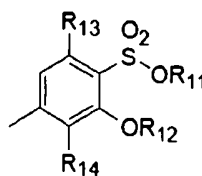
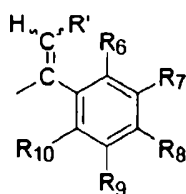
According to a fifth aspect, the invention provides the use of benzoic acid ester compounds according to the first aspect to prepare an industrial composition characterized by a progressive UV protection depending on the time to sun exposition and the degree of sun radiation.

25 According to a sixth aspect, the invention provides the use of benzoic acid ester compounds according to the first aspect to prepare a cosmetic or pharmaceutical composition, a personal care composition or an industrial composition that, upon phototransposition, indicates the amount of UVB radiation received.

According to a seventh aspect, the invention provides a benzoic acid ester compound of formula (Ia):



wherein R is a group selected from (i), (ii) and (iii):



5

wherein R₁-R₅ are selected independently from hydrogen, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₃-C₆-cycloalkoxy, hydroxy, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, wherein said two alkyl portions of said dialkylamino can form, together with the nitrogen atom to which they are attached, a heterocycle selected from pyrrolidine, piperidine, morpholine and piperazine optionally N-substituted by C₁-C₆-alkyl or C₃-C₆-cycloalkyl, C₃-C₆-cycloalkylamino, C₁-C₆-alkyl-C₃-C₆-cycloalkylamino and C₃-C₆-dicycloalkylamino, or two groups on adjacent ring carbons form a fused O-(CH₂)_m-O group wherein m is 1 or 2, or two groups on adjacent ring carbons form a fused CH=CH-CH=CH group;

15 R' is hydrogen;

R₆-R₁₀ are selected independently from hydrogen, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₃-C₆-cycloalkoxy, hydroxy, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, wherein said two alkyl portions of said dialkylamino can form, together with the nitrogen atom to which they are attached, a heterocycle selected from pyrrolidine, piperidine, morpholine and piperazine optionally N-substituted by C₁-C₆-alkyl or C₃-C₆-cycloalkyl, C₃-C₆-cycloalkylamino, C₁-C₆-alkyl-C₃-C₆-cycloalkylamino and C₃-C₆-dicycloalkylamino, or two groups on adjacent ring carbons form a fused O-(CH₂)_n-O

20

group wherein n is 1 or 2, or two groups on adjacent ring carbons form a fused CH=CH-CH=CH group;

R₁₁ is selected from hydrogen, C₁-C₆-alkyl and C₃-C₆-cycloalkyl;

R₁₂ is selected from hydrogen, C₁-C₆-alkyl and C₃-C₆-cycloalkyl;

5 R₁₃ and R₁₄ are selected independently from hydrogen, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₃-C₆-cycloalkoxy, hydroxy, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, wherein said two alkyl portions of said dialkylamino can form, together with the nitrogen atom to which they are attached, a heterocycle selected from pyrrolidine, piperidine, morpholine and piperazine optionally N-substituted by C₁-C₆-
10 alkyl or C₃-C₆-cycloalkyl, C₃-C₆-cycloalkylamino, C₁-C₆-alkyl-C₃-C₆-cycloalkylamino and C₃-C₆-dicycloalkylamino;

or the group OR₁₂ and R₁₄ form a fused O-(CH₂)_p-O group wherein p is 1 or 2;

R₁₅ is selected from 1-pyrrolidinyl, 1-piperidinyl, 4-morpholinyl and 1(4)-piperazinyl optionally 4(1)-substituted by C₁-C₆-alkyl or C₃-C₆-cycloalkyl; and

15 R₁₆ and R₁₈ are selected independently from hydrogen, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₃-C₆-cycloalkoxy, hydroxy, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, wherein said two alkyl portions of said dialkylamino can form, together with the nitrogen atom to which they are attached, a heterocycle selected from pyrrolidine, piperidine, morpholine and piperazine optionally N-substituted by C₁-C₆-
20 alkyl or C₃-C₆-cycloalkyl, C₃-C₆-cycloalkylamino, C₁-C₆-alkyl-C₃-C₆-cycloalkylamino and C₃-C₆-dicycloalkylamino, or two groups on adjacent ring carbons form a fused O-(CH₂)_q-O group wherein q is 1 or 2, or two groups on adjacent ring carbons form a fused CH=CH-CH=CH group;

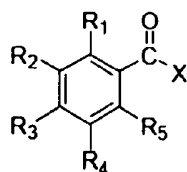
with the proviso that when R₁, R₂, and R₄-R₁₀ are each hydrogen, R₃ cannot be hydrogen
25 or methoxy; and

with the proviso that when R₁-R₇, R₉ and R₁₀ are each hydrogen, R₈ cannot be methyl;

or a pharmaceutically acceptable salt thereof.

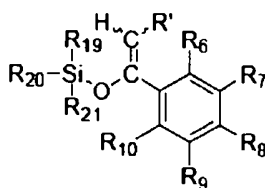
According to an eighth aspect, the invention provides a process to prepare a benzoic acid ester compound as defined in the seventh aspect wherein R is (i), by reacting an acyl
30 halide of formula (II):

- 8e -



(II)

wherein R_1 - R_5 are as defined above, and X is an halogen atom selected from the group consisting of fluorine, chlorine and bromine, with a silylenol of formula (III):



(III)

- 5 wherein R' and R_6 - R_{10} are as defined as above and R_{19} - R_{21} are selected independently from C_1 - C_6 -alkyl, C_3 - C_6 -cycloalkyl and $C_6H_5-(CH_2)_r$, wherein r is 1-4, or two groups can form, together with the silicium atom a ring selected from silolane, sililane and silepane, in the presence of a catalyst selected from the group consisting of mercuric chloride, cuprous chloride and mixtures thereof.
- 10 According to a ninth aspect, the invention provides a benzoic acid compound when prepared by the method according to the eighth aspect.

According to a tenth aspect, the invention provides a method of treating a human or animal body in need of protection from ultraviolet radiation comprising the steps of administering to a subject in need of said treatment a composition comprising an effective amount of a benzoic acid ester compound of formula (I) according to a previous aspect.

15

Unless the context clearly requires otherwise, throughout the description and the claims, the words "comprise", "comprising", and the like are to be construed in an inclusive sense as opposed to an exclusive or exhaustive sense; that is to say, in the sense of

20 "including, but not limited to".

The present invention provides a method for protecting a human or animal living body from ultraviolet radiation comprising treating said human or animal living body with an effective amount of a composition comprising a benzoic acid ester compound with ultraviolet absorbing properties *per se* susceptible to be photochemically converted *in situ* to another sunscreen compound with a higher UV protection. Also the present invention provides a method for protecting a material from ultraviolet radiation comprising treating said material with an effective amount of a composition comprising a benzoic acid ester compound with ultraviolet absorbing properties *in situ* to another sunscreen compound with a higher UV protection.

10 **Brief description of the drawings**

Figure 1 shows the phototransposition kinetics of 1-phenylvinyl 4-methoxybenzoate;

Figure 2 shows the phototransposition kinetics of 1-(4-methoxyphenyl)-vinyl 4-*tert*-butylbenzoate; _____

Figure 3 shows the phototransposition kinetics of 1-(4-*tert*-butylphenyl)-vinyl 4-methoxybenzoate;

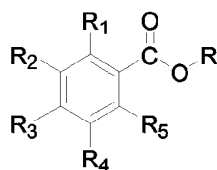
Figure 4 shows the phototransposition kinetics of 4-benzoyloxy-2-methoxybenzenesulfonic acid;

5 Figure 5 shows the phototransposition kinetics of 3-diethylaminophenyl benzoate; and

Figure 6 shows the phototransposition kinetics of 3-methoxyphenyl benzoate.

10 Detailed description of the invention

The present invention relates to a method for protecting a human or animal living body or a material from ultraviolet radiation comprising treating said human or animal living body or material with a composition comprising an effective amount of at least a benzoic acid ester compound of formula (I):



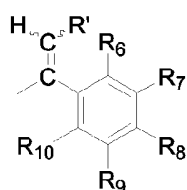
(I)

wherein R₁-R₅ are selected independently from hydrogen, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₃-C₆-cycloalkoxy, hydroxy, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, wherein said two alkyl portions of said dialkylamino can form, together with the nitrogen atom to which they are attached, a heterocycle selected from pyrrolidine, piperidine, morpholine and piperazine optionally N-substituted by C₁-C₆-alkyl or C₃-C₆-cycloalkyl, C₃-C₆-cycloalkylamino, C₁-C₆-alkyl-C₃-C₆-cycloalkylamino and C₃-C₆-dicycloalkylamino, or two groups

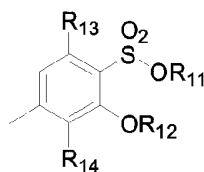
on adjacent ring carbons form a fused O-(CH₂)_m-O group wherein m is 1 or 2, or two groups on adjacent ring carbons form a fused CH=CH-CH=CH group;

R is a group selected from (i), (ii) and (iii):

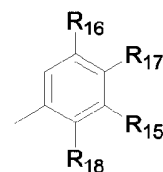
5



(i)



(ii)



(iii)

wherein R' is selected from hydrogen, C₁-C₆-alkyl and C₃-C₆-cycloalkyl;

R₆-R₁₀ are selected independently from hydrogen, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₃-C₆-cycloalkoxy, hydroxy, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, wherein said two alkyl portions of said dialkylamino can form, together with the nitrogen atom to which they are attached, a heterocycle selected from pyrrolidine, piperidine, morpholine and piperazine optionally N-substituted by C₁-C₆-alkyl or C₃-C₆-cycloalkyl, C₃-C₆-cycloalkylamino, C₁-C₆-alkyl-C₃-C₆-cycloalkylamino and C₃-C₆-dicycloalkylamino, or two groups on adjacent ring carbons form a fused O-(CH₂)_n-O group wherein n is 1 or 2, or two groups on adjacent ring carbons form a fused CH=CH-CH=CH group;

R₁₁ is selected from hydrogen, C₁-C₆-alkyl and C₃-C₆-cycloalkyl;

R₁₂ is selected from hydrogen, C₁-C₆-alkyl and C₃-C₆-cycloalkyl;

R₁₃ and R₁₄ are selected independently from hydrogen, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₃-C₆-cycloalkoxy, hydroxy, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, wherein said two alkyl portions of said dialkylamino can form, together with the nitrogen atom to which they are

30

attached, a heterocycle selected from pyrrolidine, piperidine, morpholine and piperazine optionally N-substituted by C₁-C₆-alkyl or C₃-C₆-cycloalkyl, C₃-C₆-cycloalkylamino, C₁-C₆-alkyl-C₃-C₆-cycloalkylamino and C₃-C₆-dicycloalkylamino;

5 or the group OR₁₂ and R₁₄ form a fused O-(CH₂)_p-O group wherein p is 1 or 2; and

R₁₅-R₁₈ are selected independently from hydrogen, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₃-C₆-cycloalkoxy,

10 hydroxy, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, wherein said two alkyl portions of said dialkylamino can form, together with the nitrogen atom to which they are attached, a heterocycle selected from pyrrolidine,

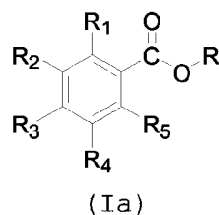
15 piperidine, morpholine and piperazine optionally N-substituted by C₁-C₆-alkyl or C₃-C₆-cycloalkyl, C₃-C₆-cycloalkylamino, C₁-C₆-alkyl-C₃-C₆-cycloalkylamino and C₃-C₆-dicycloalkylamino, or two groups on adjacent ring carbons form a fused O-(CH₂)_q-O group wherein q is 1 or 2,

20 or two groups on adjacent ring carbons form a fused CH=CH-CH=CH group;

or a pharmaceutically acceptable salt thereof.

Some compounds included in formula (I) have not been described previously in the literature. Accordingly, the present invention relates to the new benzoic acid ester compounds of formula (Ia):

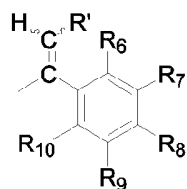
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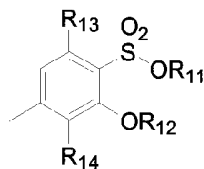
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wherein R is a group selected from (i), (ii) and (iii):

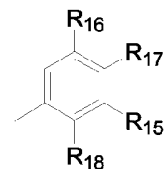
12



(i)



(ii)



(iii)

wherein R_1 - R_5 are selected independently from hydrogen, C_1 - C_6 -alkyl, C_3 - C_6 -cycloalkyl, C_1 - C_6 -alkoxy, C_3 - C_6 -cycloalkoxy, hydroxy, amino, C_1 - C_6 -alkylamino, C_1 - C_6 -dialkylamino, wherein said two alkyl portions of said dialkylamino can form, together with the nitrogen atom to which they are attached, a heterocycle selected from pyrrolidine, piperidine, morpholine and piperazine optionally N-substituted by C_1 - C_6 -alkyl or C_3 - C_6 -cycloalkyl, C_3 - C_6 -cycloalkylamino, C_1 - C_6 -alkyl- C_3 - C_6 -cycloalkylamino and C_3 - C_6 -dicycloalkylamino, or two groups on adjacent ring carbons form a fused $O-(CH_2)_m-O$ group wherein m is 1 or 2, or two groups on adjacent ring carbons form a fused $CH=CH-CH=CH$ group;

R' is hydrogen;

R_6 - R_{10} are selected independently from hydrogen, C_1 - C_6 -alkyl, C_3 - C_6 -cycloalkyl, C_1 - C_6 -alkoxy, C_3 - C_6 -cycloalkoxy, hydroxy, amino, C_1 - C_6 -alkylamino, C_1 - C_6 -dialkylamino, wherein said two alkyl portions of said dialkylamino can form, together with the nitrogen atom to which they are attached, a heterocycle selected from pyrrolidine, piperidine, morpholine and piperazine optionally N-substituted by C_1 - C_6 -alkyl or C_3 - C_6 -cycloalkyl, C_3 - C_6 -cycloalkylamino, C_1 - C_6 -alkyl- C_3 - C_6 -cycloalkylamino and C_3 - C_6 -dicycloalkylamino, or two groups on adjacent ring carbons form a fused $O-(CH_2)_n-O$ group wherein n is 1 or 2, or two groups on adjacent ring carbons form a fused $CH=CH-CH=CH$ group;

R₁₁ is selected from hydrogen, C₁-C₆-alkyl and C₃-C₆-cycloalkyl;

R₁₂ is selected from hydrogen, C₁-C₆-alkyl and C₃-C₆-cycloalkyl;

5 R₁₃ and R₁₄ are selected independently from hydrogen, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₃-C₆-cycloalkoxy, hydroxy, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, wherein said two alkyl portions of said dialkylamino can form, together with the nitrogen atom to which they are
10 attached, a heterocycle selected from pyrrolidine, piperidine, morpholine and piperazine optionally N-substituted by C₁-C₆-alkyl or C₃-C₆-cycloalkyl, C₃-C₆-cycloalkylamino, C₁-C₆-alkyl-C₃-C₆-cycloalkylamino and C₃-C₆-dicycloalkylamino;

15 or the group OR₁₂ and R₁₄ form a fused O-(CH₂)_p-O group wherein p is 1 or 2;

R₁₅ is selected from 1-pyrrolidinyl, 1-piperidinyl, 4-morpholinyl and 1(4)-piperazinyl optionally 4(1)-substituted by C₁-C₆-alkyl or C₃-C₆-cycloalkyl; and

20 R₁₆-R₁₈ are selected independently from hydrogen, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₃-C₆-cycloalkoxy, hydroxy, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, wherein said two alkyl portions of said dialkylamino can form, together with the nitrogen atom to which they are
25 attached, a heterocycle selected from pyrrolidine, piperidine, morpholine and piperazine optionally N-substituted by C₁-C₆-alkyl or C₃-C₆-cycloalkyl, C₃-C₆-cycloalkylamino, C₁-C₆-alkyl-C₃-C₆-cycloalkylamino and C₃-C₆-dicycloalkylamino, or two groups on adjacent ring
30 carbons form a fused O-(CH₂)_q-O group wherein q is 1 or 2, or two groups on adjacent ring carbons form a fused CH=CH-CH=CH group;

with the proviso that when R₁, R₂, and R₄-R₁₀ are each hydrogen, R₃ cannot be hydrogen or methoxy; and

with the proviso that when R_1 - R_7 , R_9 and R_{10} are each hydrogen, R_8 cannot be methyl;
or a pharmaceutically acceptable salt thereof.

5 More preferably the present invention relates to new benzoic acid ester compounds of formula (Ia) wherein in said compounds, when R is (i), R_3 is selected independently from C_1 - C_6 -alkyl, C_3 - C_6 -cycloalkyl, C_1 - C_6 -alkoxy and C_3 - C_6 -cycloalkoxy, R_8 is selected independently
10 from hydrogen, C_1 - C_6 -alkyl, C_3 - C_6 -cycloalkyl, C_1 - C_6 -alkoxy and C_3 - C_6 -cycloalkoxy, and R_1 , R_2 , R_4 - R_7 , R_9 and R_{10} are each hydrogen; when R is (ii), R_1 - R_5 , R_{11} , R_{13} and R_{14} are each hydrogen and R_{12} is C_1 - C_6 -alkyl and C_3 - C_6 -cycloalkyl; and when R is (iii), R_{15} is selected from 1-pyrrolidinyl, 1-
15 piperidinyl, 4-morpholinyl and 1(4)-piperazinyl optionally 4(1)-substituted by C_1 - C_6 -alkyl or C_3 - C_6 -cycloalkyl and R_{16} - R_{18} are each hydrogen;
with the proviso that when R_1 , R_2 , and R_4 - R_{10} are each hydrogen, R_3 cannot be hydrogen or methoxy; and
20 with the proviso that when R_1 - R_7 , R_9 and R_{10} are each hydrogen, R_8 cannot be methyl;
or a pharmaceutically acceptable salt thereof.

The term "pharmaceutically acceptable salt" used herein
25 encompasses any salt formed from organic and inorganic acids, such as hydrobromic, hydrochloric, phosphoric, nitric, sulfuric, acetic, adipic, aspartic, benzenesulfonic, benzoic, citric, ethanesulfonic, formic, fumaric, glutamic, lactic, maleic, malic, malonic, mandelic, methanesulfonic, 1,5-
30 naphthalendisulfonic, oxalic, pivalic, propionic, p-toluenesulfonic, succinic, tartaric acids and the like, or any metal salt wherein the metal is selected from sodium, potassium, lithium, calcium, magnesium, zinc, aluminum and the like, or ammonium salts, or any salt formed from organic
35 bases, such as 2-amino-1-butanol, 2-amino-2-ethyl-1,3-

propanediol, 2-amino-2-methyl-1,3-propanediol,
benzathine, benzyldimethylamine, chlorprocaine, choline,
dibenzylmethylamine, diethanolamine, diisopropanolamine,
ethylenediamine, dimethyl stearamine, meglumine, 2-
5 methyl-2-amino-1-propanol, monoamine glycols,
monoethanolamine, monoisopropanolamine, morpholine, N,N-
dibenzylethylenediamine, N,N-dimethyl-2-amino-2-methyl-1-
propanol, N,N-dimethylaniline, procaine, pyridine,
quinoline, *t*-butyl-dimethylamine, triethanolamine,
10 triethylamine, trihydroxymethylaminomethane,
triisopropanolamine, trimethylamine and the like, and
salts with amino acids such as glycine, lysine, arginine,
taurine, histidine, alanine, valine, cysteine and the
like.

15

The preferred compounds to be used in the methods of the
present invention are shown below:

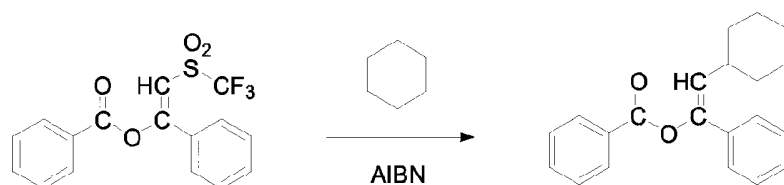
1-phenylvinyl 4-methoxybenzoate;
1-(4-methoxyphenyl)-vinyl 4-*tert*-butylbenzoate;
20 1-(4-*tert*-butylphenyl)-vinyl 4-methoxybenzoate;
1-phenylvinyl 4-*tert*-butylbenzoate;
4-benzoyloxy-2-methoxybenzenesulfonic acid;
3-diethylaminophenyl benzoate;
3-(1-pyrrolidinyl)phenyl benzoate;
25 3-methoxyphenyl benzoate;
phenyl 4-methoxysalicylate; and
3-methoxyphenyl salicylate.

The preferred new compounds of the present invention are
30 shown below:

1-(4-methoxyphenyl)-vinyl 4-*tert*-butylbenzoate;
1-(4-*tert*-butylphenyl)-vinyl 4-methoxybenzoate;
1-phenylvinyl 4-*tert*-butylbenzoate;
4-benzoyloxy-2-methoxybenzenesulfonic acid; and
35 3-(1-pyrrolidinyl)phenyl benzoate.

Compounds of formula (I) when R is (i) can be obtained by a great variety of methods disclosed in the literature. Schemes 1a-1e illustrate some representative synthetic examples thereof.

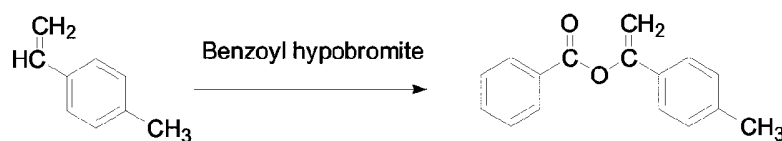
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Xiang, J *et al.*, *J.Amer.Chem.Soc.*, 119(18), <1997>, 4123-4129

Scheme 1a

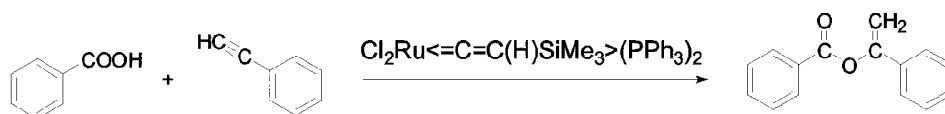
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Edwards; Hodges, *J.Chem.Soc.*, <1954>, 761

Scheme 1b

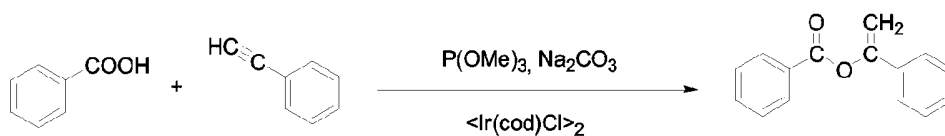
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Opstal, T *et al.*, *Syn.Lett.*, <2003>, 314-320

Scheme 1c

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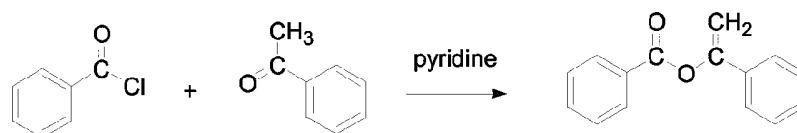


Nakagawa, H *et al.*, *Tetrahedron Lett.*, 44(1), <2003>, 103-106

Scheme 1d

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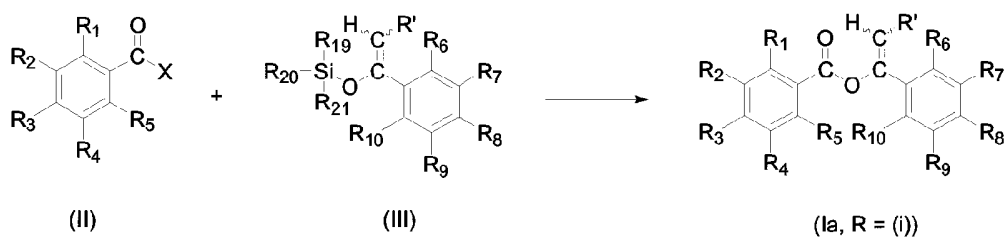


Claisen; Haase, Chem.Ber., 36, <1903>, 3679

Scheme 1e

- 5 Compounds of formula (I) when R is (ii) have not been described yet in the literature, and consequently the present invention relates to said group of compounds *per se*.
- 10 Compounds of formula (I) when R is (iii) are commercially available or can be obtained alternatively by known methods of organic chemistry.

The present invention also relates to a process to
 15 prepare the compounds of formula (Ia). When R is (i), the process comprises reacting an acyl halide of formula (II), wherein R₁-R₅ are as defined above, X is an halogen atom selected from the group consisting of fluorine, chlorine or bromine, preferably chlorine, with a
 20 silylenol of formula (III), wherein R' and R₆-R₁₀ are as defined above and R₁₉-R₂₁ are selected independently from C₁-C₆-alkyl, C₃-C₆-cycloalkyl and C₆H₅-(CH₂)_r-, wherein r is 1-4, or two groups can form, together with the silicium atom a ring selected from silolane, sililane and silepane
 25 (Scheme 2a)



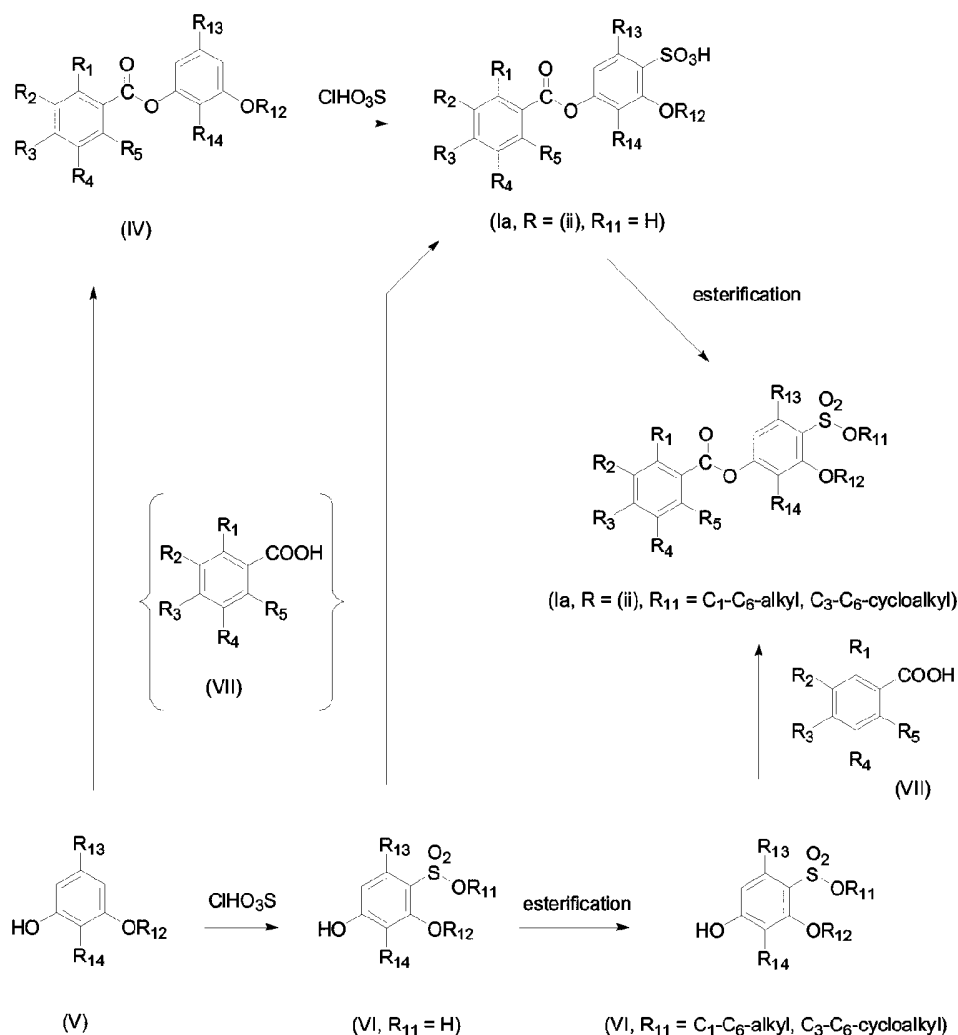
Scheme 2a

Said reaction occurs conveniently in the presence of a catalyst selected from the group consisting of mercuric chloride, cuprous chloride and mixtures thereof. Optional solvents can be selected from N,N-dimethylformamide, N,N-dimethylacetamide, 1-methyl-2-pyrrolidone, 1-methyl-2-piperidone, 1,3-dimethyl-2-imidazolidinone, and the like, and mixtures thereof. Preferably the solvent is 1,3-dimethyl-2-imidazolidinone.

Intermediate silylenols of formula (III) can be prepared by standard chemical methods. However, some intermediate silylenols of formula (III) have not been described previously in the literature and are included in the present invention. A representative of the new intermediate silylenols is 4-*tert*-butylacetophenone trimethylsilylenol.

When R is (ii), the process comprises reacting a benzoic acid ester of formula (IV), wherein R₁-R₅ and R₁₂-R₁₄ are as defined above, with chlorosulfonic acid followed by an optional esterification reaction with C₁-C₆-alkyl-OH or C₃-C₆-cycloalkyl-OH to afford the corresponding C₁-C₆-alkyl or C₃-C₆-cycloalkyl sulfonic ester final compounds. Alternatively the process comprises firstly sulfonating a phenol of formula (V) with chlorosulfonic acid followed by esterification with an acid intermediate (VII) wherein R₁-R₅ are as defined above. Likewise, esterifying the sulfonic acid intermediates (VI) with C₁-C₆-alkyl-OH or C₃-C₆-cycloalkyl-OH provides the corresponding C₁-C₆-alkyl or C₃-C₆-cycloalkyl sulfonic acid esters thereof, which can be esterified with (VII) to afford the corresponding C₁-C₆-alkyl or C₃-C₆-cycloalkyl sulfonic acid ester final compounds (Scheme 2b).

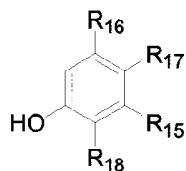
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Scheme 2b

5 When R is (iii), the process comprises reacting an acyl halide of formula (II), wherein R₁-R₅ are as defined above, X is an halogen atom selected from the group consisting of fluorine, chlorine or bromine, preferably chlorine, with a phenol of formula (VIII):

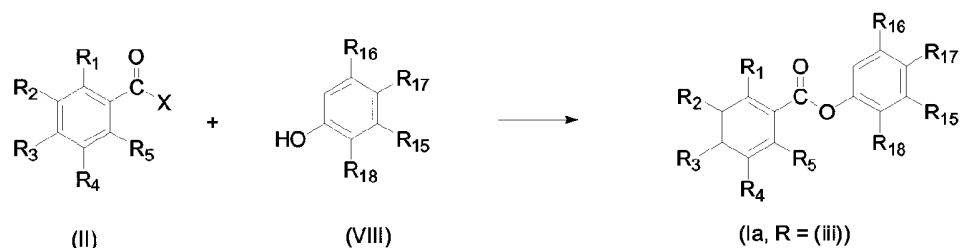
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20

(VIII)

wherein R_{15} - R_{18} are as defined above (Scheme 2c)



5

Scheme 2c

The present invention also relates to the use of benzoic acid ester compounds of formula (I) or salts thereof as photochemical precursors of ultraviolet absorbers.

10

The present invention also relates to compositions containing at least a benzoic acid ester compound of formula (I) or salts thereof.

15

The present invention also relates to cosmetic or pharmaceutical compositions comprising an effective amount of at least a benzoic acid ester compound of formula (I) or an acceptable salt thereof susceptible to be photochemically converted *in situ* to a sunscreen compound with enhanced UV protection ability.

20

The present invention also relates to a method for protecting a human or animal living body from ultraviolet radiation with a cosmetic or pharmaceutical composition comprising an effective amount of at least a benzoic acid ester compound of formula (I) or an acceptable salt thereof susceptible to be photochemically converted *in situ* to a sunscreen compound with enhanced UV protection ability.

25

30

The present invention also relates to a method for protecting a human or animal living body from ultraviolet radiation with a cosmetic or pharmaceutical composition comprising an effective amount of at least a benzoic acid ester compound of formula (I) or an acceptable salt thereof susceptible to be photochemically converted *in situ* to a sunscreen compound with enhanced UV protection ability, wherein the human or animal living body is a human being.

10

Such compositions typically range from 0.01 to 40 wt % based on the total weight of the sunscreen. More typically, the amount falls within the range of 0.05 wt % to 25 wt %. The amount of organic sunscreen compound of formula (I) preferably ranges from about 0.1 wt % to about 15 wt % of the sunscreen formulation.

15

These sunscreen formulations can contain one or more additional organic sunscreen agents for filtering UVB or UVA rays or they may additionally contain one or more metal oxide sunscreen agents such as titanium dioxide or zinc oxide.

20

These sunscreen formulations may additionally contain a carrier and at least one component selected from the group consisting of dispersing agents, preservatives, anti-foams, perfumes, fragrances, oils, waxes, propellants, dyes, pigments, emulsifiers, surfactants, thickeners, humectants, exfoliants and emollients. These sunscreen formulations may be in the form of a cosmetic composition with a cosmetically acceptable carrier and one or more cosmetic adjuvants. The sunscreen formulation can optionally have conventional antioxidants or other stabilizers without UV absorbing characteristics.

25

30

35

Other ingredients referred to above and discussed more particularly below are generally used in an amount from about 0.1 wt % to about 10 wt % of the sunscreen formulation. The balance comprises a cosmetically or pharmaceutically acceptable carrier.

Suitable dispersing agents for the sunscreen formulations include those useful for dispersing organic or inorganic sunscreen agents in either a water phase, oil phase, or part of an emulsion, including, for example, chitosan.

Emulsifiers may be used in the sunscreen formulations to disperse one or more of the compounds of formula (I) or other components of the sunscreen formulation. Suitable emulsifiers include conventional agents such as, for example, glycerol stearate, stearyl alcohol, cetyl alcohol, dimethicone copolyol phosphate, hexadecyl-D-glucoside, octadecyl-D-glucoside, etc.

Thickening agents may be used to increase the viscosity of the sunscreen formulations. Suitable thickening agents include carbomers, acrylate/acrylonitrile copolymers, xanthan gum and combinations of these. The carbomer thickeners include the crosslinked acrylic polymers. The amount of thickener within the sunscreen formulation, on a solids basis without water, may range from about 0.001 to about 5%, preferably from 0.01 to about 1% and optimally from about 0.1 to about 0.5% by weight.

Minor optional adjunct ingredients for the sunscreen formulations to be applied to skin or hair may include preservatives, waterproofing agents, fragrances, anti-foam agents, plant extracts (aloe vera, witch hazel, cucumber, etc) opacifiers, skin conditioning agents and

colorants, each in amounts effective to accomplish their respective functions.

The sunscreen formulations may optionally contain an ingredient which enhances the waterproof properties such as, compounds that form a polymeric film, such as dimethicone copolyol phosphate, diisostearoyl trimethylolpropane siloxysilicate and dilauroyl trimethylolpropane siloxysilicate, chitosan, dimethicone, polyethylene, polyvinylpyrrolidone (PVP), PVP/vinylacetate, PVP/eicosene copolymer, adipic acids/diethylene glycol/glycerine crosspolymer and the like. Waterproofing agents may be present at levels of from about 0.01 to about 10% by weight.

The sunscreen formulations may also optionally contain one or more skin conditioning agents. These include humectants, exfoliants and emollients.

Humectants are polyhydric alcohols intended for moisturizing, reducing scaling and stimulating the removal of built scale from the skin. Typically polyhydric alcohols include polyalkylene glycols and more preferably alkylene polyols and their derivatives. Illustrative are propylene glycol, dipropylene glycol, polypropylene glycol, polyethylene glycol, sorbitol, 2-pyrrolidone-5-carboxylate, hydroxypropyl sorbitol, hexylene glycol, ethoxydiglycol 1,3-butylene glycol, 1,2,6-hexanetriol, glycerin, ethoxylated glycerin, propoxylated glycerin and mixtures thereof. Most preferably the humectant is glycerin. Amounts of humectant can range anywhere from 1 to 30%, preferably from 2 to 20% and optimally from about 5 to 10% by weight of the sunscreen composition.

The exfoliants suitable for use in the present invention may be selected from alpha-hydroxy carboxylic acids, beta hydroxycarboxylic acids and salts of these acids. Most preferred are glycolic, lactic and salicylic acids and
5 their alkali, metal or ammonium salts.

Suitable emollients include those agents known for softening the skin or hair which may be selected from hydrocarbons, fatty acids, fatty alcohols and esters.
10 Petrolatum is a common hydrocarbon type of emollient conditioning agent. Other hydrocarbons that may be employed include alkyl benzoates, mineral oils, polyolefins such as polydecene, and paraffins, such as isohexadecane. Fatty acids and alcohols typically have
15 from about 10 to 30 carbon atoms. Illustrative are myristic, isostearic, hydroxystearic, oleic, linoleic, ricinoleic, behenic and erucic acids and alcohols. Oily ester emollients may be those selected from one or more of the following triglyceride esters, acetoglyceride
20 esters, ethoxylated glycerides, alkyl esters of fatty acids, ether esters, polyhydric alcohol esters and wax esters. Additional emollients or hydrophobic agents include C₁₂ to C₁₅ alkyl benzoates, dioctyladipate, octyl stearate, octyldodecanol, hexyl laurate, octyldodecyl
25 neopentanoate, cyclomethicone, dicapryl ether, dimethicone, phenyl trimethicone, isopropyl myristate, caprylic/capric glycerides, propylene glycol dicaprylate/dicaprate and decyl oleate.

30 The sunscreen formulations may optionally contain one or more inorganic sunscreen agents as discussed above including micro fine surface treated titanium dioxide and micro fine untreated and surface treated zinc oxide. Titanium dioxide in the sunscreen compositions preferably
35 has a mean primary particle size of between 5 and 150 nm

and preferably from 10 to 100 nm. The zinc oxide in the sunscreen compositions preferably has a mean primary particle size of between 5 nm and 150 nm, preferably between 10 nm and 100 nm.

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The sunscreen compositions may also contain one or more additional monomeric organic chromophoric compounds. These can either be UVA, UVB or broad band filters. Examples of suitable UVA sunscreens include benzophenone derivatives, menthyl anthranilate, butyl methoxydibenzoyl methane and benzylidene-dioxoimidazoline derivatives. Examples of suitable UVB sunscreens include cinnamate derivatives, salicylate derivatives, p-aminobenzoic acid derivatives, camphor derivatives, phenylbenzimidazole derivatives and diphenylacrylate derivatives. Examples of suitable broad-band sunscreen include benzotriazole derivatives and triazine derivatives such as anisotriazone. Others include ethylhexyltriazone and diethylhexylbutamidotriazone. Particularly useful organic sunscreen agents that can be introduced are avobenzene, 2-ethylhexyl p-methoxycinnamate, oxybenzone, octyldimethyl p-aminobenzoic acid, dioxybenzone, ethyl-4-[bis(hydroxypropyl)]aminobenzoate, 2-ethylhexyl-2-cyano-3,3-diphenylacrylate, 2-ethylhexylsalicylate, glycerol p-aminobenzoate, 3,3,5-trimethylcyclohexylsalicylate, methylanthranilate, p-dimethylaminobenzoic acid, 2-ethylhexyl p-dimethylaminobenzoate, 2-phenylbenzimidazole-5-sulfonic acid, 2-p-dimethylaminophenyl-5-sulfoniobenzoxazoic acid, sulisobenzene, and mixtures thereof. Examples of useful commercially available organic sunscreen agents that can be introduced include 2-phenylbenzimidazole-5-sulphonic acid, 2-(4-methylbenzylidene)-camphor and 4-isopropylidibenzoylmethane. Although not preferred, the sunscreen formulation may contain an additional

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antioxidant. Examples of suitable antioxidants which provide stability include p-hydroxybenzoic acid and its esters, salicylates, cumarin derivatives, flavones, hydroxy or methoxy substituted benzophenones, uric or
5 tannic acid and its derivatives, hydroquinone, and benzophenones.

In addition to providing sunscreen activity at levels which provide UV absorption, the compounds of formula (I)
10 can be introduced into a skin care formulation, a hair care formulation or other personal care formulations such as cosmetic or pharmaceutical compositions at levels which provide antioxidant activity. These compounds can be used with or without conventional antioxidants in
15 personal care formulations such as hair care, skin care and cosmetic and pharmaceutical compositions.

In the cosmetics field, and in particular for make-up compositions such as foundation compositions, tinted
20 creams, mascaras, blushers and eye shadows, lipsticks and nail varnishes, pigments are being sought which are capable of imparting to these various types of products a varied palette of colorations which are reproducible over time and are insoluble in most of the cosmetic media used
25 such as water and cosmetically acceptable solvents. These pigments should, moreover, be stable at the pHs usually used or encountered in the cosmetics field.

Cosmetic or pharmaceutical products, such as skin
30 lotions, collagen creams, sunscreen, facial make-up, etc., comprise synthetic materials such as antifoams, antioxidants, antiperspirants, colorants, dyes, emollients, emulsifiers, exfoliants, humectants, lipids, moisturizers, perfumes, fragrances, pigments,
35 preservatives, propellants, skin conditioners, solvents,

surfactants, thickeners, water proofing agents, etc.; as well as natural products such as collagen, proteins, mink oil, olive oil, coconut oil, carnauba wax, beeswax, lanolin, cocoa butter, xanthan gum, aloe, etc.

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The present invention also relates to a method to improve the photostability of a sunscreen formulation that comprises adding at least a benzoic acid ester compound of formula (I) or an acceptable salt thereof to said
10 sunscreen composition in an amount sufficient to improve the photostability of said sunscreen agent.

The present invention also relates to a personal care composition which comprises at least a benzoic acid ester
15 compound of formula (I) or an acceptable salt thereof in an amount effective to photostabilize composition ingredients from sun radiation.

The cosmetic, pharmaceutical and personal care
20 compositions can be in the form of creams, ointments, milks, suspensions, powders, oils, lotions, gels, sticks, foams, emulsions, dispersions, sprays and aerosols, and the like. More specific forms include lipsticks, foundations, makeup, loose or press powders, eye blushes,
25 eye shadows, mascaras, nail varnishes, nail lacquers and non permanent dyeing compositions for the hair, and the like.

The present invention also relates to industrial
30 compositions comprising an effective amount of at least a benzoic acid ester compound of formula (I) or an acceptable salt thereof susceptible to be photochemically converted *in situ* to a sunscreen compound with enhanced UV protection ability.

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The present invention also relates to a method for protecting a material from ultraviolet radiation comprising treating said material by an industrial composition comprising an effective amount of at least a
5 benzoic acid ester compound of formula (I) or an acceptable salt thereof susceptible to be photochemically converted *in situ* to a sunscreen compound with enhanced UV protection ability, wherein said material is selected from the group consisting of organic compounds, oils,
10 fats, waxes, gelatins, sunscreens, polymers, such as polyolefins, polyketones, polystyrene, polyvinyl chloride (PVC), polyacrylates, polymethacrylates, polyacrylamides, polyacrylonitriles, polyvinyl alcohol derivatives, polyvinyl acetate derivatives, polyurethanes, polyamides,
15 polyesters, polyureas, polycarbonates, polysiloxanes, polyketimines, radiation curable compositions, resins, such as hydrocarbon resins, phenol/formaldehyde resins, urea/formaldehyde resins, melamine/formaldehyde resins, unsaturated polyester resins, crosslinkable acrylic
20 resins, crosslinked epoxy resins, epoxy/melamine resins, varnishes, cellulose, cellulose-based paper formulations, photographic materials, photographic film paper, metallic products, ceramic products, biocides, natural textile fibers, textile fabrics, dyes, inks, pigments, paints,
25 coatings, adhesives, leathers, woods, rubbers, glasses, lenses, composites, mixtures or blends thereof, and the like.

The compounds of the present invention are particularly
30 useful as ultraviolet light absorber agents for stabilizing a wide variety of materials including, for example, naturally occurring and synthetic organic compounds, oils, fats, waxes, sunscreens, organic dyes and biocides, and particularly various organic artificial
35 polymers used in applications such as photographic

materials, photographic film paper, plastics, artificial textile fibers such as polyamide and polyester, polyurethane, natural textile fibers such as silk, cotton and wool, natural or synthetic rubbers, paints and other coatings, adhesives, resins, natural fibers and laminated UV screening window films, natural polymers such as cellulose and cellulose-base paper formulations, rubber, gelatin and chemically modified homologous derivatives, inks, polysiloxanes, metallic products, wood products, ceramic products, lenses, composites, mixtures or blends thereof, and the like, among others.

Cellulose-based paper formulations uses comprise newsprint, cardboard, posters, packaging, labels, stationery, book and magazine paper, bond typing paper, multi-purpose and office paper, computer paper, xerographic paper, laser and ink-jet printer paper, offset paper, currency paper, and the like.

The compounds of the present invention may also be employed to form light stabilizing compositions. Such light stabilizing compositions may include a variety of other components known in the art including triazines, benzotriazoles, hindered amine light stabilizers, radical scavengers, antioxidants and the like.

The present invention also relates to the use of compounds of formula (I) to prepare cosmetic or pharmaceutical compositions, personal care compositions and industrial compositions that, upon phototransformation, indicate the amount of UVB radiation received.

Polymers which can be stabilized include naturally occurring and synthetic organic materials which may be

mixtures of compounds, including mineral oils, animal and vegetable fats, oils and waxes, or oils, fats or waxes based on synthetic esters (e.g., phthalates, adipates, phosphates or trimellitates) and also mixtures of
5 synthetic esters with mineral oils in any ratio.

The compounds of the present invention are typically employed in amounts from about 0.01 to about 30% by weight, preferably from about 0.05 to about 20% by
10 weight, and most preferably from about 0.1 to about 10% by weight, based on the weight of the material to be stabilized.

The compounds of the present invention can be incorporated into such materials in any one of a variety
15 of conventional procedures, including for example, physical mixing or blending, optionally, with chemical bonding to the material (typically to a polymer), as a component in a light stabilizing or oxidation composition
20 such as a coating or solution, or as a component in a UV screening composition such as a sunscreen composition.

Natural or synthetic rubbers such as natural latex or lattices of carboxylated styrene/butadiene copolymers may
25 be formulated as aqueous emulsions.

Organic dyes encompass azo dyes (diazo, triazo and polyazo), anthraquinones, benzodifuranones, polycyclic aromatic carbonyl dyes, indigoid dyes, polymethines,
30 styryl dyes, di- and triaryl carbonium dyes, phthalocyanines, quinophthalones, sulfur dyes, nitro and nitroso dyes, stilbene dyes, formazan dyes, quinacridones, carbazoles and perylene tetracarboxylic diimides.

When compositions are used in the form of emulsions, they may additionally contain surface-active agents which are well known in the state of the art, such as anionic, nonionic, cationic or amphoteric surface-active agents or mixtures thereof.

These compositions may also contain fatty substances, organic solvents, silicones, thickening agents, softening agents, surfactants, sunscreen agents, anti-free-radical agents, anti-foaming agents, moisturizing agents, fragrances, preserving agents, antioxidants, fillers, sequestering agents, treatment agents such as nonionic, cationic, anionic or amphoteric polymers or mixtures thereof, propellants, and basifying or acidifying agents, or other pigments.

The fatty substances may consist of an oil or a wax or mixtures thereof, fatty acids, fatty alcohols, fatty acid esters, vaseline, paraffin, lanolin, hydrogenated lanolin or acetylated lanolin.

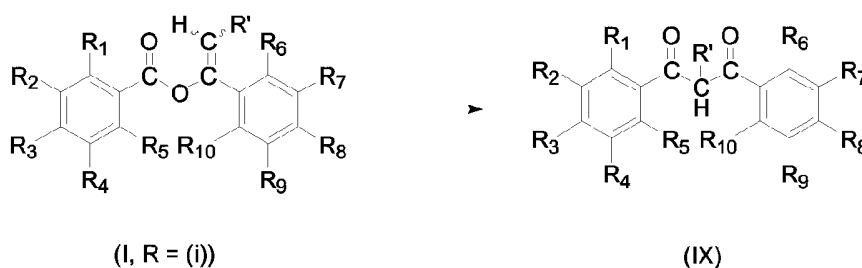
The oils are chosen from animal oils, vegetable oils, mineral oils or synthetic oils and especially hydrogenated palm oil, hydrogenated castor oil, liquid paraffin, paraffin oil, purcellin oil and silicone oils.

The waxes are chosen from animal waxes, fossil waxes, vegetable waxes, mineral waxes or synthetic waxes. Beeswaxes, carnauba wax, candelilla wax, sugar cane wax, Japan wax, ozokerites, montan wax, microcrystalline waxes and paraffin waxes may more particularly be mentioned.

The sunscreen activity of the benzoic acid ester compounds of the present invention is based on efficient

phototransposition reactions showing a high chemical yield.

The phototransposition of compounds of formula (I) when R is (i) provides dibenzoylmethane compounds of formula (IX), according to Scheme 3.



Scheme 3

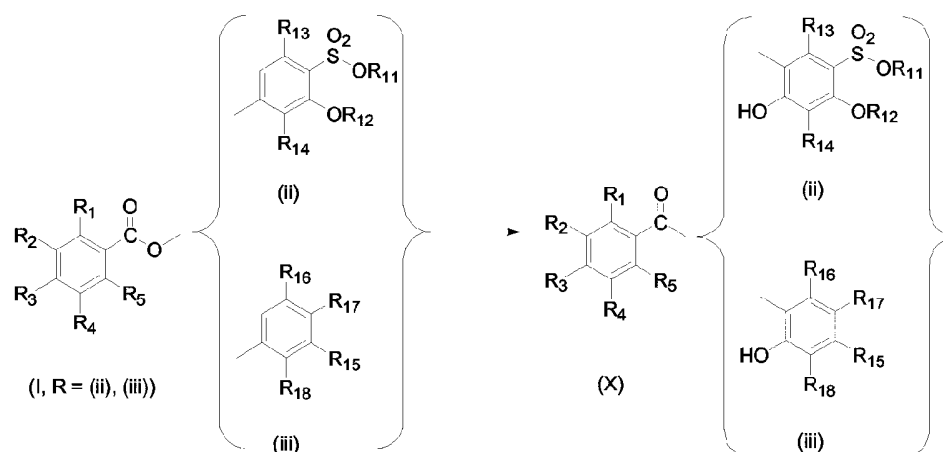
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Such dibenzoylmethane compounds constitute a recognized chemical sunscreen series, being avobenzene the most representative. Thus, phototransposition of both 1-(4-methoxyphenyl)-vinyl 4-*tert*-butylbenzoate and 1-(4-*tert*-butylphenyl)-vinyl 4-methoxybenzoate yields the authorized and widely used avobenzene sunscreen compound.

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The photo-Fries transposition of compounds of formula (I) wherein R is (ii) or (iii) provides benzophenone compounds of formula (X), according to Scheme 4:

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Scheme 4

5 Such benzophenone compounds constitute a recognized and widely used chemical sunscreen series. Dioxybenzone, oxybenzone and sulisobenzene are the most representative compounds in said series. Phototransposition of both 3-methoxyphenylsalicylate and phenyl 4-methoxysalicylate
 10 provides dioxybenzone. Phototransposition of 3-methoxyphenyl benzoate leads to oxybenzone. And phototransposition of 4-benzoyloxy-2-methoxybenzenesulfonic acid leads to sulisobenzene.

15 The photo-Fries transposition of compounds of formula (I) wherein R₁₅ is a dialkylamino group provides a recent sunscreen benzophenone series, being 4-diethylamino-2-hydroxybenzophenone and 2-hydroxy-4-(1-pyrrolidinyl)benzophenone the most representative
 20 compounds in said series. Phototransposition of 3-diethylaminophenyl benzoate and 3-(1-pyrrolidinyl)phenyl benzoate provides 4-diethylamino-2-hydroxybenzophenone and 2-hydroxy-4-(1-pyrrolidinyl)benzophenone respectively.

25

The compounds of formula (I) show a progressive UV protection depending on the time to sun exposition and the degree of sun radiation. This progressive UV protection property is evidenced in their UVB and particularly UVA screening ability. Consequently, the compositions containing compounds of formula (I) constitute a safer method to take sunbaths and produce a more uniform and glamorous tanning than conventional sunscreens. Moreover the compounds resulting from the phototranspositions belong to recognized chemical sunscreen series which ensure the convenience of the method.

Accordingly, the present invention also relates to the use of compounds of formula (I) to prepare cosmetic or pharmaceutical compositions, personal care compositions and industrial compositions characterized by a progressive UV protection depending on the time to sun exposition and the degree of sun radiation.

The following non-limiting examples illustrate the scope of the present invention.

Preparation example 1: 4-Methoxyacetophenone trimethylsilylenol

A solution of 0.82 g (5.5 mmol) of 4-methoxyacetophenone in 3.4 mL of tetrahydrofuran was added to 7 mmol of lithium diisopropylamine (LDA) generated *in situ*. After stirring the solution for 30 minutes, 4.5 mL of trimethylsilyl chloride were added and the mixture was stirred for 17 h at room temperature under nitrogen atmosphere. Then pentane was added, the mixture was filtered to remove the lithium salts and the solvent was evaporated to dryness under reduced pressure. The

obtained crude contained 78% (¹H-NMR) of 4-methoxyacetophenone trimethylsilylenol.

¹H-NMR: 3.78 (s, 3H), 4.32 (d, 1H, J = 2 Hz), 4.79 (d, 1H, J = 2 Hz), 6.85 (d, 2H, J = 9 Hz), 7.52 (d, 2H, J = 9 Hz)

5 Preparation of LDA: Under nitrogen atmosphere, 0.97 mL of distilled diisopropylamine were dissolved in 7 mL of anhydrous tetrahydrofuran at 0°C. Then 4.4 mL of butyl lithium 1.6M in hexane were added and the mixture was stirred for 20 minutes.

10

Preparation example 2: 4-*Tert*-butylacetophenone trimethylsilylenol

15 A solution of 1.25 mL (6.7 mmol) of 4-*tert*-butylacetophenone in 4 mL of tetrahydrofuran was added to LDA (7 mmol) generated *in situ*. After stirring the solution for 30 minutes, 4.5 mL of trimethylsilyl chloride were added and the mixture was stirred for 16 h at room temperature under nitrogen atmosphere. Then

20

pentane was added, the mixture was filtered to remove the lithium salts and the solvent was evaporated to dryness under reduced pressure. The obtained crude contained 100% (¹H-NMR) of 4-*tert*-butylacetophenone trimethylsilylenol.

25 ¹H-NMR: 1.32 (s, 9H), 4.38 (d, 1H, J = 2 Hz), 4.87 (d, 1H, J = 2 Hz), 7.34 (d, 2H, J = 9 Hz), 7.52 (d, 2H, J = 9 Hz)

Preparation example 3: 1-Phenylvinyl 4-*tert*-butylbenzoate

30 A mixture of 4.16 g (21.62 mmol) of acetophenone trimethylsilylenol, 4.33 g (22.01 mmol) of 4-*tert*-butylbenzoyl chloride and 136 mg of mercuric chloride was heated at 100°C for 2 h. The mixture was then left to cool, water was added over the reaction crude and

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extracted with dichloromethane. The organic phase was

dried over magnesium sulfate and the solvent was removed under reduced pressure. A 2.12 g sample was purified by flash chromatography (hexane:dichloromethane 3:1) giving 1.17 g of 1-phenylvinyl 4-*tert*-butylbenzoate. Yield 57%.

5 $^1\text{H-NMR}$: 1.36 (s, 9H), 5.14 (d, 1H, $J = 2$ Hz), 5.58 (d, 1H, $J = 2$ Hz), 7.32 (m, 3H), 7.53 (m, 2H), 8.13 (dt, 2 H, $J = 9$ Hz, 2 Hz).

$^{13}\text{C-NMR}$: 164.63/s -CO-, 157.23/s -C=CH₂, 153.03/s -C-C-(CH₃)₃, 134.28/s -C-C=CH₂, 129.94/d 2 CH aromatic, 128.81/d 1 CH aromatic, 128.41/d 2 CH aromatic, 126.55/s -C-CO-, 125.50/d 2 CH aromatic, 124.81/d 2 CH aromatic, 102.14/t CH₂, 35.26/s -C-(CH₃)₃, 31.18/q 3 CH₃.

IR: 1737, 1642, 1607, 1249 cm⁻¹.

15 **Preparation example 4:** 1-Phenylvinyl 4-methoxybenzoate

A mixture of 2.38 g (12.37 mmol) of acetophenone trimethylsilylenol, 2.15 g (12.60 mmol) of 4-methoxybenzoyl chloride and 93 mg of mercuric chloride was heated at 100°C for 2 h. The mixture was then left to cool to room temperature, and then water was added over the reaction crude, and extracted with dichloromethane. The organic phase was dried over magnesium sulfate and the solvent was removed under reduced pressure. The obtained crude contained 75-85% of 1-phenylvinyl 4-methoxybenzoate as determined by $^1\text{H-NMR}$.

Preparation example 5: 1-(4-Methoxyphenyl)-vinyl 4-*tert*-butylbenzoate

30 4-*tert*-butylbenzoyl chloride (1.78 g, 9 mmol), 0.47 g of cuprous chloride and 4 mL of 1,3-dimethyl-2-imidazolidinone were added to crude 4-methoxyacetophenone trimethylsilylenol (4.3 mmol). After stirring the solution for 21 hours at room temperature, 1 mL of triethylamine and 10 mL of chloroform were added. Then

the solution was chromatographed through flash silica column (hexane/ethyl acetate 10:1). The first collected fraction was purified by flash chromatography (hexane/dichloromethane 3:2) giving 0.34 g of 1-(4-methoxyphenyl)-vinyl 4-*tert*-butylbenzoate. Yield 25%.

¹H-NMR: 1.37 (s, 9H), 3.80 (s, 3H), 5.03 (d, 1H, J = 2 Hz), 5.46 (d, 1H, J = 2 Hz), 6.85 (dt, 2H, J = 2 Hz, 9 Hz), 7.46 (dt, 2H, J = 2 Hz, 9 Hz), 7.52 (dt, 2H, J = 2 Hz, 9 Hz), 8.12 (dt, 2H, J = 2 Hz, 9 Hz).

¹³C-NMR: 164.69/s -CO-, 159.99/s -C-OCH₃, 157.18/s -C=CH₂, 152.83/s -C-C-(CH₃)₃, 129.93/d 2 CH aromatic, 126.94/s 1 CH aromatic, 126.63/s 1 CH aromatic, 126.25/d 2 CH aromatic, 125.50/d 2 CH aromatic, 113.84/d 2 CH aromatic, 100.27/t CH₂, 55.33/q CH₃-O, 35.26/s -C-(CH₃)₃, 31.18/q 3 CH₃.

IR: 1735, 1608, 1512, 1245, 1176, 1095 cm⁻¹.

Mp: 87-89°C

Preparation example 6: 1-(4-*Tert*-butylphenyl)-vinyl 4-methoxybenzoate

4-methoxybenzoyl chloride (2.35 g, 13.8 mmol), 0.65 g of cuprous chloride and 5.6 mL of 1,3-dimethyl-2-imidazolidinone were added to crude 4-*tert*-butylacetophenone trimethylsilylenol (6.7 mmol). After stirring the solution for 20 hours at room temperature, 1.4 mL of triethylamine and 10 mL of chloroform were added. Then the solution was chromatographed through flash silica column (hexane/ethyl acetate 10:1). The first collected fraction was purified twice by flash chromatography (hexane/dichloromethane 3:2 and next, hexane/dichloromethane 4:1) giving 0.14 g of an uncolored oil corresponding to 1-(4-*tert*-butylphenyl)-vinyl 4-methoxybenzoate. Yield 7%.

¹H-NMR: 1.29 (s, 9H), 3.86 (s, 3H), 5.09 (d, 1H, J = 2 Hz), 5.53 (d, 1H, J = 2 Hz), 6.97 (2H), 7.35 (dt, 2 H, J = 2 Hz, 9 Hz), 7.46 (dt, 2H, J = 2 Hz, 9 Hz), 8.15 (dt, 2H, J = 2 Hz, 9 Hz).

5 ¹³C-NMR: 164.37/s -CO-, 163.63/s -C-OCH₃, 153.01/s -C=CH₂, 151.80/s -C-C-(CH₃)₃, 132.06/d 2 CH aromatic, 131.42/s -C-C=CH₂, 125.32/d 2 CH aromatic, 124.48/d 2 CH aromatic, 121.67/s C-CO, 113.72/d 2 CH aromatic, 101.29/t CH₂, 55.44/q CH₃-O, 34.62/s -C-(CH₃)₃, 31.21/q 3 CH₃.

10 IR: 1732, 1606, 1510, 1246, 1167, 1090 cm⁻¹.

Preparation example 7: 4-Benzoyloxy-2-methoxybenzene-sulfonic acid

15 A solution of 0.47 mL (7.01 mmol) of chlorosulfonic acid in 7 mL of dichloromethane was added drop by drop to a solution of 1.6 g (7.01 mmol) of 3-methoxyphenyl benzoate in 12 mL of dichloromethane at 0°C. Once the addition was completed, the mixture was left to react for 18 h at room
20 temperature. The formed precipitate was filtered, giving 300 mg of 4-benzoyloxy-2-methoxybenzenesulfonic acid. Yield 15%.

¹H-NMR: 3.76 (s, 3H), 6.77 (dd, 1H, J = 2 Hz, 8 Hz), 6.94 (d, 1H, J = 2 Hz), 7.62 (m, 2H), 7.76 (m, 2H), 8.15 (m, 25 2H).

¹³C-NMR: 164.23/s CO, 156.84/s C-OCH₃, 151.87/s C-OCOPh, 133.89/d 1 CH aromatic, 133.21/s C-COO, 129.64/d 2 CH aromatic, 128.89/d 1 CH aromatic, 128.81/d 2 CH aromatic, 128.73/s C-SO₃H, 112.03/d 1 CH aromatic, 106.04/d 1 CH
30 aromatic, 55.84/d CH₃.

IR: 3500, 1727, 1264, 1198 cm⁻¹.

Preparation example 8: 3-Diethylaminophenyl benzoate

A mixture of 1.53 g (9.3 mmol) of 3-diethylaminophenol, 1.35 mL (11.8 mmol) of benzoyl chloride and 1 mL of pyridine in 50 mL of toluene was refluxed for 3 hours. The mixture was then left to cool and the solvent was removed by distillation under reduced pressure. The
5 obtained crude was purified by flash chromatography (hexane/ethyl acetate 7:1) providing a red oil fraction (235 mg) containing mainly 3-diethylaminophenyl benzoate.

10 **Preparation example 9:** 3-Methoxyphenyl benzoate

Phosphorus oxychloride (3.16 mL) was added over a mixture of 2.95 g (24.16 mmol) of benzoic acid and 3 g (24.16 mmol) of 3-methoxyphenol, and the resulting mixture was
15 heated at 125°C for 45 minutes under argon atmosphere. The mixture was cooled to room temperature, water was added over the reaction crude and extracted with diethyl ether. The organic phase was dried over magnesium sulfate and the solvent was removed under reduced pressure
20 yielding 5.0 g of a dark red oil. The obtained crude was purified by flash chromatography (hexane/ethyl acetate 10:1) to afford 2.10 g of 3-methoxyphenyl benzoate. Yield 38%.

25 **Preparation example 10:** Phenyl 4-methoxysalicylate

Phosphorus oxychloride (2 mL) was added over a mixture of 2.00 g (11.89 mmol) of 4-methoxysalicylic acid and 2.13 g (22.65 mmol) of phenol, and the resulting mixture was
30 heated at 115°C for 15 minutes under argon atmosphere. The mixture was cooled to room temperature, water was added over the reaction crude and extracted with dichloromethane. The organic phase was dried over magnesium sulfate and the solvent was removed under
35 reduced pressure yielding 4.5 g of a dark red oil. The

obtained crude was purified by flash chromatography (hexane/ethyl acetate 8.5:1) to afford 1.97 g of phenyl 4-methoxysalicylate. Yield 65%.

5 **Preparation example 11: 3-Methoxyphenyl salicylate**

Phosphorus oxychloride (2 mL) was added over a mixture of 2.00 g (14.48 mmol) of salicylic acid and 3.3 mL (28.96 mmol) of 3-methoxyphenol, and the resulting mixture was
10 heated at 115°C for 15 minutes under argon atmosphere. The mixture was cooled to room temperature, water was added over the reaction crude and extracted with dichloromethane. The organic phase was dried over
15 magnesium sulfate and the solvent was removed under reduced pressure yielding 4.0 g of a black oil. The obtained crude was purified by flash chromatography (hexane/ethyl acetate 9:1) to afford 2.36 g of 3-methoxyphenyl salicylate. Yield 85%.

20 **Preparation example 12: 3-(1-pyrrolidinyl)phenyl benzoate**

A mixture of 1.52 g (9.3 mmol) of 3-(1-pyrrolidinyl)phenol, 1.35 mL (11.8 mmol) of benzoyl chloride and 1 mL of pyridine in 50 mL of toluene was
25 refluxed for 3 hours. The mixture was then left to cool and the solvent was removed by distillation under reduced pressure. The obtained crude was purified by flash chromatography (hexane/ethyl acetate 7:1) providing a red oil fraction (233 mg) containing mainly 3-(1-pyrrolidinyl)phenyl benzoate.
30

Phototransposition example 1: Phototransposition of 1-phenylvinyl 4-methoxybenzoate

A solution of 5 mg of 1-phenylvinyl 4-methoxybenzoate in 10 mL of methanol was irradiated with UVB lamps ($60 \text{ W}\cdot\text{m}^{-2}$) for 20 minutes at 35°C . The crude reaction spectrum showed a new absorption band in UVA zone due to
5 dibenzoylmethane fragment. The conversion to benzoyl-4-methoxybenzoyl-methane was observed from the beginning, being the complete conversion in 5 minutes. The phototransposition kinetics is shown in Figure 1.

10 **Phototransposition example 2:** Phototransposition of 1-(4-methoxyphenyl)-vinyl 4-*tert*-butylbenzoate

A sample of 4 mL of a solution containing 0.231 mg of 1-(4-methoxyphenyl)-vinyl 4-*tert*-butylbenzoate in 50 mL of methanol was irradiated with UVB lamps ($60 \text{ W}\cdot\text{m}^{-2}$) for 10
15 minutes at 35°C . The conversion to avobenzene was completed in 5 minutes. The phototransposition kinetics is shown in Figure 2.

20 **Phototransposition example 3:** Phototransposition of 1-(4-*tert*-butylphenyl)-vinyl 4-methoxybenzoate

A sample of 4 mL of a solution containing 0.400 mg of 1-(4-*tert*-butylphenyl)-vinyl 4-methoxybenzoate in 50 mL of methanol was irradiated with UVB lamps ($60 \text{ W}\cdot\text{m}^{-2}$) for 10
25 minutes at 35°C . The conversion to avobenzene was completed in 5 minutes. The phototransposition kinetics is shown in Figure 3.

30 **Phototransposition example 4:** Phototransposition of 4-benzoyloxy-2-methoxybenzenesulfonic acid

A solution containing 5 mg of 4-benzoyloxy-2-methoxybenzenesulfonic acid in 10 mL of methanol was irradiated with UVB lamps ($60 \text{ W}\cdot\text{m}^{-2}$) for 20 minutes at 35°C . The

absorption spectrum was then recorded minute by minute. The conversion to sulisobenzone was complete in 10 minutes. The phototransposition kinetics is shown in Figure 4.

5

Phototransposition example 5: Phototransposition of 3-diethylaminophenyl benzoate

A sample of 4 mL of a solution containing 0.395 mg of 3-diethylaminophenyl benzoate in 50 mL of methanol was irradiated with UVB lamps ($60 \text{ W}\cdot\text{m}^{-2}$) for 20 minutes at 35°C. The phototransformation to 4-diethylamino-2-hydroxybenzophenone was completed in 10 minutes. The phototransposition kinetics is shown in Figure 5.

15 **Phototransposition example 6:** Phototransposition of 3-methoxyphenyl benzoate

A sample of 5 mg of 3-methoxyphenyl benzoate in 10 mL of polydimethylsiloxane (viscosity 10000 cSt) was irradiated with UVB lamps ($60 \text{ W}\cdot\text{m}^{-2}$) for 15 hours and 20 minutes at 35°C. The phototransformation to oxybenzone was completed in 40 minutes. The phototransposition kinetics is shown in Figure 6.

25 **Phototransposition example 7:** Phototransposition of 1-phenylvinyl 4-*tert*-butylbenzoate

A solution of 5 mg of 1-phenylvinyl 4-*tert*-butylbenzoate in 10 mL of *tert*-butanol was irradiated with UVB lamps ($60 \text{ W}\cdot\text{m}^{-2}$) for 5 hours at 35°C. Some different compounds were detected by thin layer chromatography (hexane/ethyl acetate 2:1), one of said compounds being benzoyl-4-*tert*-butylbenzoylmethane, desmethoxyavobenzene, identified by $^1\text{H-NMR}$.

30

Composition example 1: Sunscreen Composition 1

<u>Phase A</u>		<u>Phase B</u>	
Deionized water	60.0 %	Active ingredient	8.75%
Disodium EDTA	0.10 %	Octyl salicylate	5%
Glycerin	1.5%	Aluminum stearate	5%
NaCl	3.0%	Cyclomethicone + Dimethicone	10%
Butylene glycol	2.5%	Cetyl dimethicone	1%
		Cyclomethicone	2%
		ABIC-EM 97	1%
		Fragrance	0.15%
		TOTAL	100.00 %

5

Procedure

Phase B ingredients were combined. The mixture was stirred and heated to 70-75°C. Phase A ingredients were combined. The mixture was heated to 70-75°C while stirring. Phase B was added to phase A while stirring. Preservative was added. The mixture was stirred, allowing to cool to room temperature.

10

Composition example 2: Sunscreen Oil/Water Spray Lotion

	<u>Phase A-1</u>	% w/w
Active ingredient 1		7.50%
Active ingredient 2		2.50%
Dicapryl ether		4.50%
Dimethicone		2.00%
Stearyl alcohol		0.60%
PPG-2 Ceteareth-9 ¹		0.40%
Steareth-10		0.50%
Glyceryl stearate + PEG-100 stearate ²		2.80%
	<u>Phase A-2</u>	
Titanium dioxide + Simethicone + Alumina ³		5.00%
	<u>Phase B-1</u>	
Demineralized water		66.10%
Chitosan + water ⁴		2.00%
Glycerin USP		2.50%
Dimethicone copolyol phosphate		2.50%
	<u>Phase B-2</u>	
Polyquaternium 37 + Mineral oil + PPG-1 trideceth-6 ⁵		0.40%
	<u>Phase C</u>	
Propylene glycol + DMDM Hydantoin + Methylparaben + Propylparaben ⁶		0.70%
	TOTAL	100.00
		%

¹ Eumulgin® L (Henkel)² Ariacel® 165 (ICI)5 ³ Eusolex® T-2000 (Rona)⁴ Hydagen® CMF (Henkel)⁵ Salcare® SC 95 (Ciba)⁶ Paragon® II (McIntyre)10 Procedure

The A-1 ingredients were combined; the mixture was stirred and heated to 60°C until all solids were dissolved. A-2 was dispersed in A-1 with agitation. The

B-1 ingredients were combined; the mixture was stirred and heated to 60°C. B-2 was dispersed in B-1 with agitation. A was added to B while stirring vigorously. The mixture was gently homogenized allowing to cool to
 5 40°C. C was added to A/B; the mixture was gently homogenized until mixture was uniform. The mixture was stirred with another mixer allowing mixture to reach 25°C prior to packaging. Dispensing is made conveniently by a high shear pump spray device.

10

Composition example 3: Sunscreen Cream

<u>Phase A</u>	% w/w
Deionized water	39.73%
Carbomer (2% aq. solution)	15.00%
Propylene glycol	5.00%
Methylparaben	0.20%
Propylparaben	0.10%
Triethanolamine (99%)	0.45%
Tetrasodium EDTA	0.02%
<u>Phase B</u>	
Active ingredient 1	5.00%
Active ingredient 2	3.00%
Active ingredient 3	4.50%
Glyceryl stearate + PEG-100 stearate ¹	1.00%
Cyclomethicone	5.00%
Glyceryl stearate	4.00%
Stearic acid	2.50%
Isostearyl isostearate	10.00%
Hydrogenated castor oil	2.00%
C ₁₂₋₁₅ alcohol benzoates ²	2.50%
TOTAL	100.00%

¹ Ariacel® 165 (ICI)² Finsolv® TN (Finetex)

15

Procedure

Phase A ingredients were added to a main vessel under impeller agitation. The mixture was heated to 75-80°C. Phase B ingredients were combined; the suspension was heated and mixed to 85°C. Phase B was added slowly to batch and mixed for 15 minutes at 85°C. After removing the mixture from heat, it was switched to paddle mixing and cooled to room temperature.

10 **Composition example 4:** Water/Oil Broad Spectrum Sunscreen Lotion

	% w/w
Active ingredient 1	7.50%
Active ingredient 2	5.00%
Octyl stearate	2.00%
Dicapryl ether	3.00%
Cyclomethicone	4.00%
Dimethicone	2.00%
PEG-30 Dipolyhydroxystearate ¹	1.30%
Laurylmethicone copolyol	2.30%
Behanemidopropyl dimethylamine behenate	0.50%
Titanium dioxide + Alumina + Simethicone ²	8.00%
Deionized water qs	61.00%
Propylene glycol	2.00%
NaCl	0.80%
Propylene glycol + DMDM Hydantoin + Methylparaben + Propylparaben ³	0.60%
TOTAL	100.00%

¹ Ariacel® P135 (ICI)

² Eusolex® T-2000 (Rona)

15 ³ Paragon® II (McIntyre)

Composition example 5: UVA/UVB Sun Protection Cream with Avobenzone

	<u>Phase A-1</u>	% w/w
Water (demineralized)		67.80%
Disodium EDTA		0.05%
Propylene glycol		3.00%
Methylparaben		0.15%
	<u>Phase A-2</u>	
Carbomer		0.20%
	<u>Phase B</u>	
Isopropyl myristate		2.00%
Cetyl alcohol + Glyceryl stearate + PEG-75 Stearate + Cetetch 20 + Steareth 20 ¹		4.00%
Active ingredient		3.50%
Homomethyl salicylate		7.00%
Octyl salicylate		7.00%
Avobenzone		3.00%
Dimethicone		1.00%
C30-38 Olefin + Isopropyl maleate + MA copolymer		1.00%
	<u>Phase C</u>	
Triethanolamine (99%)		0.30%
	<u>Phase D</u>	
Preservatives		qs
	TOTAL	100.00
		%

¹ Emulium Delta® (Gattefosse)

5 ² Performa® V 1608 (New Phase Technologies)

Procedure

Phase A-1 ingredients were combined; the mixture was
 10 heated to 50°C while stirring until methylparaben was
 dissolved. A-2 was dispensed in A-1 with a sifter. The
 resulting mixture A was heated to 65°C. Phase B
 ingredients were combined; the mixture was heated to 65-
 70°C while stirring until solids were dissolved. B was

added to A. The mixture was homogenized and C was added at 55-60°C. Homogenizing was continued allowing mixture to cool to 40-45°C. Phase D was added; the mixture was stirred with propeller mixer until uniform. pH was adjusted to 6.5-7.0 with triethanolamine.

Composition example 6: Oil/water Sunscreen Lotion

	<u>Phase A</u>	% w/w
Active ingredient		3.00%
Isopropyl myristate		4.00%
C ₁₂₋₁₅ Alkyl benzoate ¹		4.00%
Cetyl alcohol		1.50%
Steareth-2		2.00%
Steareth-21		2.50%
Dimethicone		0.50%
	<u>Phase B</u>	
Deionized water		81.07%
Acrylates / C ₁₀₋₃₀ Alkyl Acrylates crosspolymer ²		0.20%
	<u>Phase C</u>	
Triethanolamine (99%)		0.23%
	<u>Phase D</u>	
Phenoxyethanol + Isopropylparaben + Isobutylparaben + Butylparaben ³		1.00%
	TOTAL	100.00%

¹ Finsolv® TN (Finetex)

10 ² Carbopol® ETD 2020 (B F Goodrich)

³ Liquapar® PR (Sutton)

Procedure

15 Phase B was prepared by dispersing Carbopol in water. The dispersion was heated to 70-75°C. Phase A ingredients were combined. The mixture was stirred and heated to 70-75°C. Phase B was added to phase A while stirring. Phase C was added. The mixture was homogenized until it cooled

to 45-40°C. Phase D was added. The mixture was stirred allowing to cool to room temperature.

Composition example 7: Oil/water Sunscreen Lotion with Avobenzone

5

	<u>Phase A</u>	% w/w
Active ingredient		3.00%
Avobenzone		3.00%
Isopropyl myristate		4.00%
C ₁₂₋₁₅ Alkyl benzoate ¹		4.00%
Cetyl alcohol		1.50%
Steareth-2		2.00%
Steareth-21		2.50%
Dimethicone		0.50%
	<u>Phase B</u>	
Deionized water		78.07%
Acrylates / C ₁₀₋₃₀ Alkyl Acrylates crosspolymer ²		0.20%
	<u>Phase C</u>	
Triethanolamine (99%)		0.23%
	<u>Phase D</u>	
Phenoxyethanol + Isopropylparaben + Isobutylparaben + Butylparaben ³		1.00%
	TOTAL	100.00%

¹ Finsolv® TN (Finetex)

² Carbopol® ETD 2020 (B F Goodrich)

³ Liquapar® PR (Sutton)

10 Procedure

Phase B was prepared by dispersing Carbopol in water. The dispersion was heated to 70-75°C. Phase A ingredients were combined. The mixture was stirred and heated to 70-75°C. Phase B was added to phase A while stirring. Phase C was added. The mixture was homogenized until it cooled to 45-40°C. Phase D was added. The mixture was stirred allowing to cool to room temperature.

15

Composition example 8: Sun Care Lipstick

	% w/w
Active ingredient	7.00%
Microcrystalline wax	5.00%
Glyceryl trihydroxystearate	5.00%
Ozokerite	3.40%
Polyglycerolated beeswax	2.10%
Acetylated lanolin	19.45%
Lanolin oil	19.10%
Avocado oil	18.99%
Butene/isobutene copolymer	14.34%
Castor oil	4.81%
Ascorbyl palmitate	0.50%
Mixture of tocopherols in soybean oil (50/50)	0.31%
TOTAL	100.00%

Composition example 9: Sunscreen Gel

	% w/w
Active ingredient 1	8.00%
Active ingredient 2	6.00%
TiO ₂	7.00%
Glycerol	5.00%
PEG-25 <i>p</i> -aminobenzoic acid	5.00%
Acrylates / C ₁₀₋₃₀ Alkyl Acrylates crosspolymer ¹	0.40%
Imidazolidinylurea	0.30%
Hydroxyethylcellulose	0.25%
Sodium methylparaben	0.25%
Disodium EDTA	0.20%
Fragrance	0.15%
Sodium propylparaben	0.15%
Sodium hydroxide	0.10%
Water	qs
TOTAL	100.00%

¹ Carbopol® ETD 2020 (B F Goodrich)

Composition example 10: Sunscreen Cream

	% w/w
Active ingredient 1	7.00%
Active ingredient 2	7.00%
TiO ₂	8.00%
ZnO ₂	5.00%
PEG-7 hydrogenated castor oil	6.00%
Mineral oil	6.00%
Isopropyl palmitate	5.00%
Imidazolidinylurea	0.30%
Jojoba oil	3.00%
PEG-45 dodecyl glycol copolymer	2.00%
Magnesium stearate	0.60%
Tocopheryl acetate	0.50%
Methylparaben	0.25%
Disodium EDTA	0.20%
Propylparaben	0.15%
Water	qs
TOTAL	100.00%

Composition example 11: Water-resistant Sunscreen Cream

	% w/w
Active ingredient 1	8.00%
Active ingredient 2	7.00%
TiO ₂	3.00%
PEG-7 hydrogenated castor oil	5.00%
Propylene glycol	5.00%
Isopropyl palmitate	4.00%
Caprylic / Capric triglyceride	4.00%
Glycerol	4.00%
Jojoba oil	3.00%
PEG-45 dodecyl glycol copolymer	1.50%
Dimethicone	1.50%
Magnesium sulfate	0.70%
Magnesium stearate	0.50%
Fragrance	0.15%
Water	qs
TOTAL	100.00%

Composition example 12: Sunscreen Milk

	% w/w
Active ingredient 1	4.50%
Active ingredient 2	4.00%
Mineral oil	10.00%
PEG-7 hydrogenated castor oil	6.00%
Isopropyl palmitate	5.00%
Caprylic / Capric triglyceride	3.00%
Jojoba oil	3.00%
PEG-45 dodecyl glycol copolymer	2.00%
Magnesium sulfate	0.70%
Magnesium stearate	0.60%
Tocopheryl acetate	0.50%
Glycerol	3.00%
Methylparaben	0.25%
Propylparaben	0.15%
Tocopherol	0.05%
Water	qs
TOTAL	100.00%

Composition example 13: Sunscreen Makeup Powder

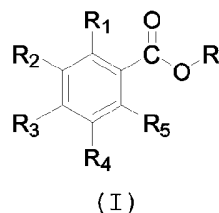
	% w/w
Active ingredient 1	0.12%
Active ingredient 2	0.08%
Talc	76.00%
Polyethylene powder	4.00%
Magnesium carbonate	8.76%
Isopropyl myristate	1.20%
Liquid petrolatum	1.20%
Sorbitol	4.00%
Bordeaux 5B pigment	0.52%
Victoria Blue Lake pigment	0.12%
Titanium mica	4.00%
TOTAL	100.00%

Composition example 14: Sunscreen Nail Varnish

	% w/w
Active ingredient	0.30%
Nitrocellulose	6.43%
Toluensulfonamide formaldehyde resin	5.81%
Acetyltributyl citrate	3.83%
Butyl acetate	12.85%
Ethyl acetate	5.54%
Stearalkonium hectorite	0.80%
Citric acid	0.04%
Victoria Blue Lake pigment	0.01%
TiO ₂	0.45%
Bordeaux 5B pigment	0.04%
Titanium mica	0.35%
Isopropyl alcohol	4.60%
Toluene	qs
TOTAL	100.00%

CLAIMS

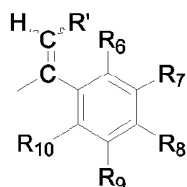
1. Use of benzoic acid ester compounds of formula (I):



5

wherein R_1 - R_5 are selected independently from hydrogen, C_1 - C_6 -alkyl, C_3 - C_6 -cycloalkyl, C_1 - C_6 -alkoxy, C_3 - C_6 -cycloalkoxy, hydroxy, amino, C_1 - C_6 -alkylamino, C_1 - C_6 -dialkylamino, wherein said two alkyl portions of said dialkylamino can form, together with the nitrogen atom to which they are attached, a heterocycle selected from pyrrolidine, piperidine, morpholine and piperazine optionally N-substituted by C_1 - C_6 -alkyl or C_3 - C_6 -cycloalkyl, C_3 - C_6 -cycloalkylamino, C_1 - C_6 -alkyl- C_3 - C_6 -cycloalkylamino and C_3 - C_6 -dicycloalkylamino, or two groups on adjacent ring carbons form a fused $O-(CH_2)_m-O$ group wherein m is 1 or 2, or two groups on adjacent ring carbons form a fused $CH=CH-CH=CH$ group;

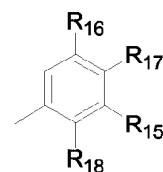
20 R is a group selected from (i), (ii) and (iii):



(i)



(ii)



(iii)

wherein R' is selected from hydrogen, C_1 - C_6 -alkyl and C_3 - C_6 -cycloalkyl;

25 R_6 - R_{10} are selected independently from hydrogen, C_1 - C_6 -alkyl, C_3 - C_6 -cycloalkyl, C_1 - C_6 -alkoxy, C_3 - C_6 -cycloalkoxy, hydroxy, amino, C_1 - C_6 -alkylamino, C_1 - C_6 -dialkylamino,

wherein said two alkyl portions of said dialkylamino can form, together with the nitrogen atom to which they are attached, a heterocycle selected from pyrrolidine, piperidine, morpholine and piperazine optionally N-

5 substituted by C₁-C₆-alkyl or C₃-C₆-cycloalkyl, C₃-C₆-cycloalkylamino, C₁-C₆-alkyl-C₃-C₆-cycloalkylamino and C₃-C₆-dicycloalkylamino, or two groups on adjacent ring carbons form a fused O-(CH₂)_n-O group wherein n is 1 or 2, or two groups on adjacent ring carbons form a fused

10 CH=CH-CH=CH group;

R₁₁ is selected from hydrogen, C₁-C₆-alkyl and C₃-C₆-cycloalkyl;

R₁₂ is selected from hydrogen, C₁-C₆-alkyl and C₃-C₆-cycloalkyl;

15 R₁₃ and R₁₄ are selected independently from hydrogen, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₃-C₆-cycloalkoxy, hydroxy, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, wherein said two alkyl portions of said dialkylamino can form, together with the nitrogen atom to which they are

20 attached, a heterocycle selected from pyrrolidine, piperidine, morpholine and piperazine optionally N-substituted by C₁-C₆-alkyl or C₃-C₆-cycloalkyl, C₃-C₆-cycloalkylamino, C₁-C₆-alkyl-C₃-C₆-cycloalkylamino and C₃-C₆-dicycloalkylamino;

25 or the group OR₁₂ and R₁₄ form a fused O-(CH₂)_p-O group wherein p is 1 or 2; and

R₁₅-R₁₈ are selected independently from hydrogen, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₃-C₆-cycloalkoxy, hydroxy, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino,

30 wherein said two alkyl portions of said dialkylamino can form, together with the nitrogen atom to which they are attached, a heterocycle selected from pyrrolidine, piperidine, morpholine and piperazine optionally N-substituted by C₁-C₆-alkyl or C₃-C₆-cycloalkyl, C₃-C₆-cycloalkylamino, C₁-C₆-alkyl-C₃-C₆-cycloalkylamino and C₃-

35

C₆-dicycloalkylamino, or two groups on adjacent ring carbons form a fused O-(CH₂)_q-O group wherein q is 1 or 2, or two groups on adjacent ring carbons form a fused CH=CH-CH=CH group;

5 or a pharmaceutically acceptable salt thereof,
to prepare a cosmetic or pharmaceutical composition, a personal care composition or an industrial composition comprising an effective amount of at least one of said compounds for protecting a human or animal living body or
10 a material from ultraviolet radiation.

2. Use of claim 1 wherein, in the benzoic acid ester compound, when R is (i), R₃ is selected independently from methoxy and *tert*-butyl, R₈ is selected independently from
15 hydrogen, methoxy and *tert*-butyl, and R', R₁, R₂, R₄, R₅, R₆, R₇, R₉ and R₁₀ are each hydrogen; when R is (ii), R₁, R₂, R₃, R₄, R₅, R₁₁, R₁₃ and R₁₄ are each hydrogen and R₁₂ is methyl; and when R is (iii), R₁ is selected independently from hydrogen and hydroxy, R₃ is selected independently
20 from hydrogen and methoxy, R₁₅ is selected independently from hydrogen, diethylamino, 1-pyrrolidinyl and methoxy, and R₂, R₄, R₅, R₁₆, R₁₇ and R₁₈ are each hydrogen.

3. Use of claim 2, wherein the benzoic acid ester
25 compound is selected from the group consisting of:

1-phenylvinyl 4-methoxybenzoate;
1-(4-methoxyphenyl)-vinyl 4-*tert*-butylbenzoate;
1-(4-*tert*-butylphenyl)-vinyl 4-methoxybenzoate;
1-phenylvinyl 4-*tert*-butylbenzoate;
30 4-benzoyloxy-2-methoxybenzenesulfonic acid;
3-diethylaminophenyl benzoate;
3-(1-pyrrolidinyl)phenyl benzoate;
3-methoxyphenyl benzoate;
phenyl 4-methoxysalicylate; and
35 3-methoxyphenyl salicylate.

4. Use of benzoic acid ester compounds as defined in any one of claims 1 to 3 as photochemical precursors of ultraviolet absorbers.
5. Use according to any one of claims 1 to 4, wherein the human or animal living body is a human being.
- 5 6. A cosmetic or pharmaceutical composition, a personal care composition or an industrial composition containing at least a benzoic acid ester compound as defined in any one of claims 1 to 5 for protecting a human or animal living body or a material form ultraviolet radiation.
7. The cosmetic or pharmaceutical composition according to claim 6 comprising an
10 effective amount of at least a benzoic acid ester compound susceptible to be photochemically converted *in situ* to a sunscreen compound with enhanced UV protection ability.
8. The cosmetic or pharmaceutical composition according to claim 7, wherein said composition is selected from creams, ointments, milks, suspensions, powders, oils,
15 lotions, gels, sticks, foams, emulsions, dispersions, sprays, aerosols, lipsticks, foundations, makeup, loose or press powders, eye blushes, eye shadows, mascaras, nail varnishes, nail lacquers, and non permanent dyeing compositions for the hair.
9. The cosmetic or pharmaceutical composition according to any one of claims 6 to 8, wherein the effective amount of the benzoic acid ester compound ranges from 0.01 to
20 40 wt % based on the total weight of the sunscreen.
10. The cosmetic or pharmaceutical composition according to claim 9, wherein the effective amount of the benzoic acid ester compound ranges from 0.05 to 25 wt % based on the total weight of the sunscreen.
11. The cosmetic or pharmaceutical composition according to claim 10, wherein the
25 effective amount of the benzoic acid ester compound ranges from 0.1 to 15 wt % of the sunscreen formulation.

12. Use of benzoic acid ester compounds according to any one of claims 1 to 5 to prepare a cosmetic or pharmaceutical composition characterised by a progressive UV protection depending on the time to sun exposition and the degree of sun radiation.
13. A cosmetic or pharmaceutical composition as defined in claim 12, wherein said
5 composition is selected from creams, ointments, milks, suspensions, powders, oils, lotions, gels, sticks, foams, emulsions, dispersions, sprays, aerosols, lipsticks, foundations, makeup, loose or press powders, eye blushes, eye shadows, mascaras, nail varnishes, nail lacquers and non permanent dyeing compositions for the hair.
14. The cosmetic or pharmaceutical composition according to claim 13, wherein the
10 effective amount of the benzoic acid ester compound ranges from 0.01 to 40 wt % based on the total weight of the sunscreen.
15. The cosmetic or pharmaceutical composition according to claim 14, wherein the effective amount of the benzoic acid ester compound ranges from 0.05 to 25 wt % based on the total weight of the sunscreen.
16. The cosmetic or pharmaceutical composition according to claim 15, wherein the
15 effective amount of the benzoic acid ester compound ranges from 0.1 to about 15 wt % of the sunscreen formulation.
17. The personal care composition according to claim 6 wherein the benzoic acid ester compound photostabilizes composition ingredients from sun radiation.
18. The personal care composition according to claim 17, wherein said composition is
20 selected from creams, ointments, milks, suspensions, powders, oils, lotions, gels, sticks, foams, emulsions, dispersions, sprays, aerosols, lipsticks, foundations, makeup, loose or press powders, eye blushes, eye shadows, mascaras, nail varnishes, nail lacquers and non permanent dyeing compositions for the hair.
19. The use of benzoic acid ester compounds according to any one of claims 1 to 5 to
25 prepare a personal care composition characterised by a progressive UV protection depending on the time to sun exposition and the degree of sun radiation.

20. A personal care composition as defined in claim 19, wherein said composition is selected from creams, ointments, milks, suspensions, powders, oils, lotions, gels, sticks, foams, emulsions, dispersions, sprays, aerosols, lipsticks, foundations, makeup, loose or press powders, eye blushes, eye shadows, mascaras, nail varnishes, nail lacquers and non
5 permanent dyeing compositions for the hair.
21. The use of an industrial composition as defined in any one of claims 1 to 5, wherein said material is selected from the group consisting of organic compounds, oils, fats, waxes, gelatins, sunscreens, polymers, radiation curable compositions, resins, varnishes, cellulose, cellulose-based paper formulations, photographic materials,
10 photographic film paper, metallic products, ceramic products, biocides, natural textile fibers, textile fabrics, dyes, inks, pigments, paints, coatings, adhesives, leathers, woods, rubbers, glasses, lenses, composites, mixtures or blends thereof.
22. An industrial composition as defined in claim 21 comprising an effective amount of at least a benzoic acid ester compound susceptible to be photochemically converted *in*
15 *situ* to a sunscreen compound with enhanced UV protection ability.
23. The industrial composition according to claim 21 or claim 22 wherein the effective amount of the benzoic acid ester compound ranges from 0.01 to 30% by weight, based on the weight of the material to be stabilized.
24. The industrial composition according to claim 23 wherein the effective amount of
20 the benzoic acid ester compound ranges from 0.05 to 20% by weight, based on the weight of the material to be stabilized.
25. The industrial composition according to claim 24 wherein the effective amount of the benzoic acid ester compound ranges from 0.1 to 10% by weight, based on the weight of the material to be stabilized.
- 25 26. The industrial composition according to any one of claims 21 to 25, wherein said polymers are selected from polyolefins, polyketones, polystyrene, polyvinyl chloride (PVC), polyacrylates, polymethacrylates, polyacrylamides, polyacrylonitriles, polyvinyl alcohol derivatives, polyvinyl acetate derivatives, polyurethanes, polyamides, polyesters, polyureas, polycarbonates, polysiloxanes, polyketimines, composites, mixtures or blends
30 thereof.

27. The industrial composition according to any one claims 21 to 25, wherein said resins are selected from hydrocarbon resins, phenol/formaldehyde resins, urea/formaldehyde resins, melamine/formaldehyde resins, unsaturated polyester resins, crosslinkable acrylic resins, crosslinked epoxy resins, epoxy/melamine resins, composites, mixtures or blends thereof.

28. The industrial composition as defined in claim 21 or according to claim 24 or claim 25, wherein said natural textile fibers are selected from silk, cotton and wool, composites, mixtures or blends thereof.

29. The use of benzoic acid ester compounds according to any one of claims 1 to 5 to prepare an industrial composition characterized by a progressive UV protection depending on the time to sun exposition and the degree of sun radiation.

30. An industrial composition as defined in claim 29 comprising a material selected from the group consisting of organic compounds, oils, fats, waxes, gelatins, sunscreens, polymers, radiation curable compositions, resins, varnishes, cellulose, cellulose-based paper formulations, photographic materials, photographic film paper, metallic products, ceramic products, biocides, natural textile fibers, textile fabrics, dyes, inks, pigments, paints, coatings, adhesives, leathers, woods, rubbers, glasses, lenses, composites, mixtures or blends thereof.

31. The industrial composition according to claim 29 or claim 30, wherein the effective amount of the benzoic acid ester compound ranges from 0.01 to 30% by weight, based on the weight of the material to be stabilized.

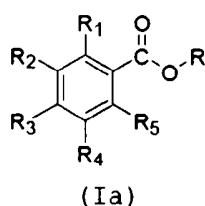
32. The industrial composition according to claim 31, wherein the effective amount of the benzoic acid ester compound ranges from 0.05 to 20% by weight, based on the weight of the material to be stabilized.

33. The industrial composition according to claim 29 or claim 30, wherein the effective amount of the benzoic acid ester compound ranges from 0.1 to 10% by weight, based on the weight of the material to be stabilized.

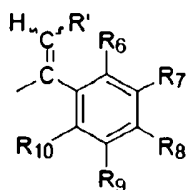
34. The industrial composition according to any one of claims 30 to 33, wherein said polymers are selected from polyolefins, polyketones, polystyrene, polyvinyl chloride

(PVC), polyacrylates, polymethacrylates, polyacrylamides, polyacrylonitriles, polyvinyl alcohol derivatives, polyvinyl acetate derivatives, polyurethanes, polyamides, polyesters, polyureas, polycarbonates, polysiloxanes, polyketimines, composites, mixtures or blends thereof.

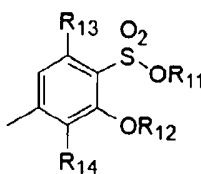
- 5 35. The industrial composition according to any one of claims 30 to 33, wherein said resins are selected from hydrocarbon resins, phenol/formaldehyde resins, urea/formaldehyde resins, melamine/formaldehyde resins, unsaturated polyester resins, crosslinkable acrylic resins, crosslinked epoxy resins, epoxy/melamine resins, composites, mixtures or blends thereof.
- 10 36. The industrial composition according to any one of claims 30 to 33, wherein said natural textile fibers are selected from silk, cotton and wool, composites, mixtures or blends thereof, and the like.
37. The use of benzoic acid ester compounds according to any one of claims 1 to 5 to prepare a cosmetic or pharmaceutical composition, a personal care composition or an industrial composition that, upon phototransposition, indicates the amount of UVB radiation received.
- 15 38. A benzoic acid ester compound of formula (Ia):



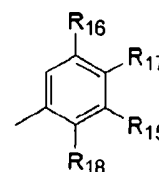
wherein R is a group selected from (i), (ii) and (iii):



(i)



(ii)



(iii)

- wherein R₁-R₅ are selected independently from hydrogen, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₃-C₆-cycloalkoxy, hydroxy, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, wherein said two alkyl portions of said dialkylamino can form, together with the nitrogen atom to which they are attached, a heterocycle selected from
- 5 pyrrolidine, piperidine, morpholine and piperazine optionally N-substituted by C₁-C₆-alkyl or C₃-C₆-cycloalkyl, C₃-C₆-cycloalkylamino, C₁-C₆-alkyl-C₃-C₆-cycloalkylamino and C₃-C₆-dicycloalkylamino, or two groups on adjacent ring carbons form a fused O-(CH₂)_m-O group wherein m is 1 or 2, or two groups on adjacent ring carbons form a fused CH=CH-CH=CH group;
- 10 R' is hydrogen;
- R₆-R₁₀ are selected independently from hydrogen, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₃-C₆-cycloalkoxy, hydroxy, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, wherein said two alkyl portions of said dialkylamino can form, together with the nitrogen atom to which they are attached, a heterocycle selected from pyrrolidine,
- 15 piperidine, morpholine and piperazine optionally N-substituted by C₁-C₆-alkyl or C₃-C₆-cycloalkyl, C₃-C₆-cycloalkylamino, C₁-C₆-alkyl-C₃-C₆-cycloalkylamino and C₃-C₆-dicycloalkylamino, or two groups on adjacent ring carbons form a fused O-(CH₂)_n-O group wherein n is 1 or 2, or two groups on adjacent ring carbons form a fused CH=CH-CH=CH group;
- 20 R₁₁ is selected from hydrogen, C₁-C₆-alkyl and C₃-C₆-cycloalkyl;
- R₁₂ is selected from hydrogen, C₁-C₆-alkyl and C₃-C₆-cycloalkyl;
- R₁₃ and R₁₄ are selected independently from hydrogen, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₃-C₆-cycloalkoxy, hydroxy, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, wherein said two alkyl portions of said dialkylamino can form, together
- 25 with the nitrogen atom to which they are attached, a heterocycle selected from pyrrolidine, piperidine, morpholine and piperazine optionally N-substituted by C₁-C₆-alkyl or C₃-C₆-cycloalkyl, C₃-C₆-cycloalkylamino, C₁-C₆-alkyl-C₃-C₆-cycloalkylamino and C₃-C₆-dicycloalkylamino;
- or the group OR₁₂ and R₁₄ form a fused O-(CH₂)_p-O group wherein p is 1 or 2;
- 30 R₁₅ is selected from 1-pyrrolidinyl, 1-piperidinyl, 4-morpholinyl and 1(4)-piperazinyl optionally 4(1)-substituted by C₁-C₆-alkyl or C₃-C₆-cycloalkyl; and

R₁₆-R₁₈ are selected independently from hydrogen, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₃-C₆-cycloalkoxy, hydroxy, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, wherein said two alkyl portions of said dialkylamino can form, together with the nitrogen atom to which they are attached, a heterocycle selected from pyrrolidine, piperidine, morpholine and piperazine optionally N-substituted by C₁-C₆-alkyl or C₃-C₆-cycloalkyl, C₃-C₆-cycloalkylamino, C₁-C₆-alkyl-C₃-C₆-cycloalkylamino and C₃-C₆-dicycloalkylamino, or two groups on adjacent ring carbons form a fused O-(CH₂)_q-O group wherein q is 1 or 2, or two groups on adjacent ring carbons form a fused CH=CH-CH=CH group;

with the proviso that when R₁, R₂, and R₄-R₁₀ are each hydrogen, R₃ cannot be hydrogen or methoxy; and

with the proviso that when R₁-R₇, R₉ and R₁₀ are each hydrogen, R₈ cannot be methyl; or a pharmaceutically acceptable salt thereof.

39. The benzoic acid ester compound according to claim 38, wherein in said compound, when R is (i), R₃ is selected independently from C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₃-C₆-cycloalkoxy, R₈ is selected independently from hydrogen, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy and C₃-C₆-cycloalkoxy, and R₁, R₂, R₄-R₇, R₉ and R₁₀ are each hydrogen; when R is (ii), R₁-R₅, R₁₁, R₁₃ and R₁₄ are each hydrogen and R₁₂ is C₁-C₆-alkyl and C₃-C₆-cycloalkyl; and when R is (iii), R₁₅ is selected from 1-pyrrolidinyl, 1-piperidinyl, 4-morpholinyl and 1(4)-piperazinyl optionally 4(1)-substituted by C₁-C₆-alkyl or C₃-C₆-cycloalkyl and R₁₆-R₁₈ are each hydrogen;

with the proviso that when R₁, R₂, and R₄-R₁₀ are each hydrogen, R₃ cannot be hydrogen or methoxy; and

with the proviso that when R₁-R₇, R₉ and R₁₀ are each hydrogen, R₈ cannot be methyl; or a pharmaceutically acceptable salt thereof.

40. The benzoic acid ester compound according to claim 39, wherein said compound is selected from the group consisting of:

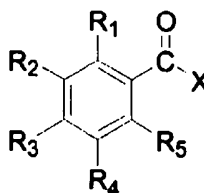
1-(4-methoxyphenyl)-vinyl 4-*tert*-butylbenzoate;

1-(4-*tert*-butylphenyl)-vinyl 4-methoxybenzoate;

1-phenylvinyl 4-*tert*-butylbenzoate;

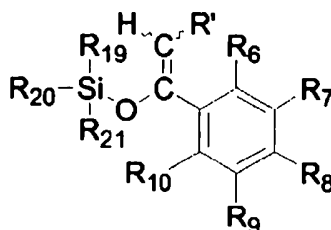
4-benzoyloxy-2-methoxybenzenesulfonic acid; and
3-(1-pyrrolidinyl)phenyl benzoate.

41. A process to prepare a benzoic acid ester compound as defined in claim 38
5 wherein R is (i), by reacting an acyl halide of formula (II):



(II)

wherein R₁-R₅ are as defined above, and X is an halogen atom selected from the group consisting of fluorine, chlorine and bromine, with a silylenol of formula (III):



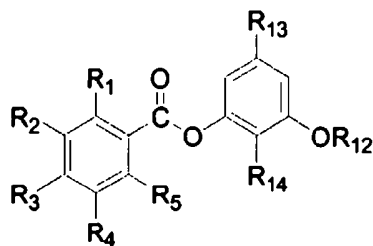
(III)

- 10 wherein R' and R₆-R₁₀ are as defined above and R₁₉-R₂₁ are selected independently from C₁-C₆-alkyl, C₃-C₆-cycloalkyl and C₆H₅-(CH₂)_r, wherein r is 1-4, or two groups can form, together with the silicium atom a ring selected from silolane, sililane and silepane, in the presence of a catalyst selected from the group consisting of mercuric chloride, cuprous chloride and mixtures thereof.

15

42. The process according to claim 41, wherein X is chlorine and R₁₉-R₂₁ are each methyl.

43. A process to prepare a benzoic acid ester compound as defined in claim 38,
20 wherein R is (ii), by reacting a benzoic acid ester of formula (IV):

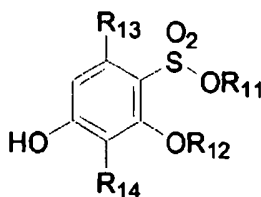


(IV)

wherein R₁-R₅ and R₁₂-R₁₄ are as defined above, with chlorosulfonic acid followed by an optional esterification reaction with C₁-C₆-alkyl-OH or C₃-C₆-cycloalkyl-OH.

5

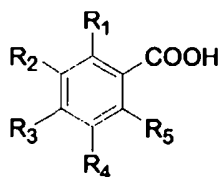
44. A process to prepare a benzoic acid ester compound as defined in claim 38 wherein R is (ii) and R₁₁ is hydrogen, by esterifying an intermediate (VI):



(VI)

wherein R₁₁ is hydrogen and R₁₂-R₁₄ are as defined above, with an acid intermediate

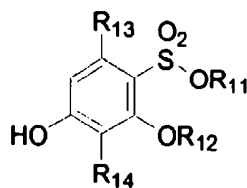
10 (VII):



(VII)

wherein R₁-R₅ are as defined above.

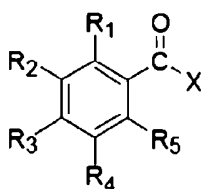
45. A process to prepare a benzoic acid ester compound as defined in claims 38 and 15 44 wherein R is (ii), by esterifying the intermediate (VI):



(VI)

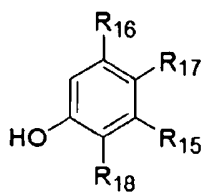
wherein R_{11} is C_1 - C_6 -alkyl or C_3 - C_6 -cycloalkyl and R_{12} - R_{14} are as defined above, with (VII).

- 5 46. A process to prepare a benzoic acid ester compound as defined in claim 38 wherein R is (iii), by reacting an acyl halide of formula (II):



(II)

wherein R_1 - R_5 are as defined above, and X is an halogen atom selected from the group consisting of fluorine, chlorine and bromine, with a phenol of formula (VIII):



(VIII)

10

wherein R_{15} - R_{18} are as defined above.

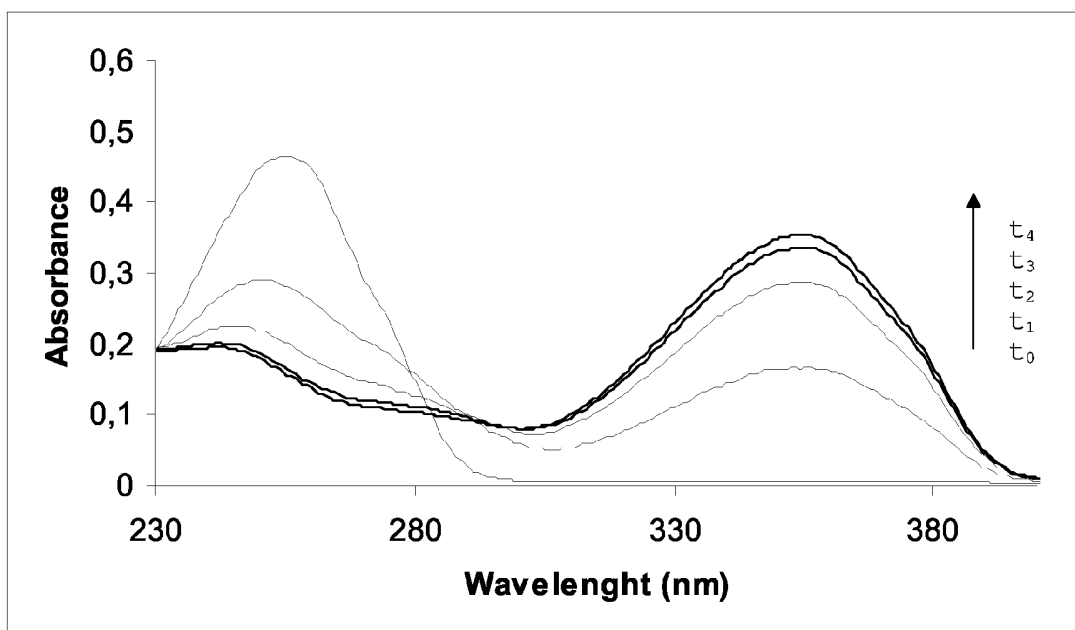
47. The process according to claim 46, wherein X is chlorine.

48. The silylenol of formula (III) as defined in claim 41 which is 4-*tert*-butylacetophenone trimethylsilylenol.

- 15 49. A benzoic acid compound when prepared by the method according to any one of claims 41 to 47.

50. A method of treating a human or animal body in need of protection from ultraviolet radiation comprising the steps of administering to a subject in need of said treatment a composition comprising an effective amount of a benzoic acid ester compound of formula (I) according to any one of claims 1 to 5.

- 5 51. Use of benzoic acid ester compounds of formula (I); a cosmetic or pharmaceutical composition, a personal care composition or an industrial composition containing at least a benzoic acid ester compound; a benzoic acid ester compound of formula (Ia); a process to prepare a benzoic acid ester compound; a benzoic acid ester compound when prepared by the method; a method of treating a human or animal body in need of protection from
- 10 ultraviolet radiation substantially as herein described with reference to any one of the embodiments of the invention illustrated in the accompanying drawings and/or examples.



Wavelength (nm)

t_0	0
t_1	30 s
t_2	1 min
t_3	2 min
t_4	3 min

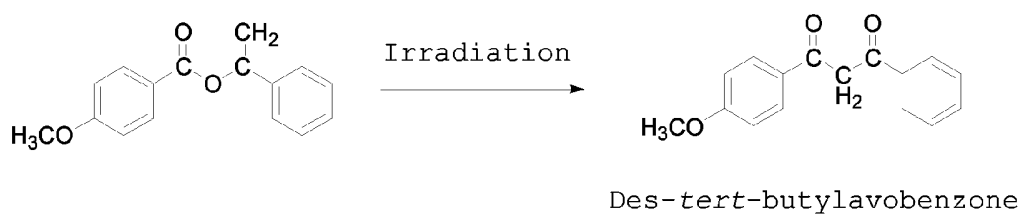
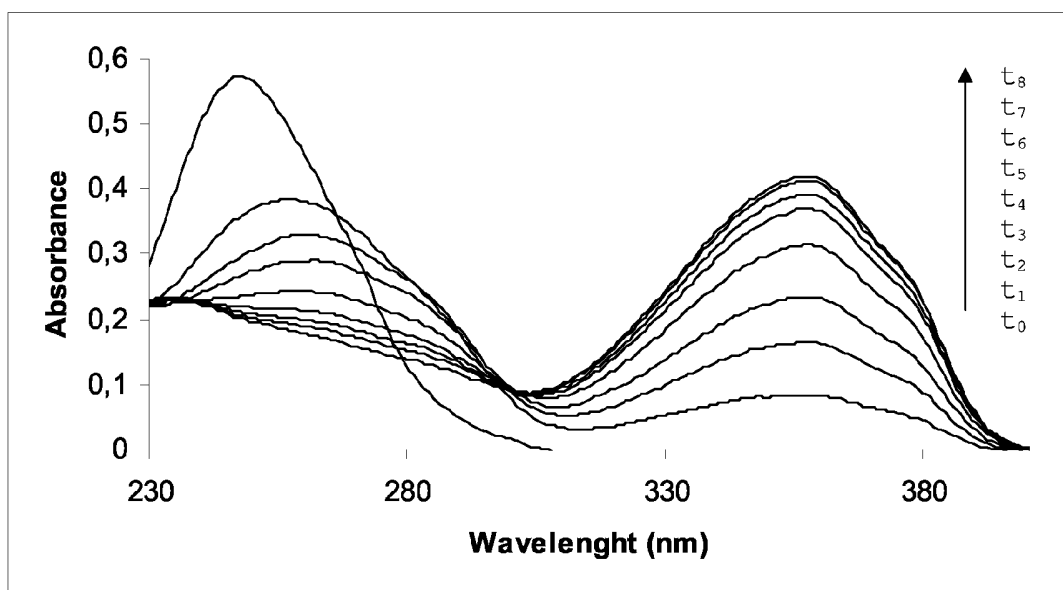


FIG. 1



Wavelength (nm)

t_0	0
t_1	20 s
t_2	40 s
t_3	1 min
t_4	2 min
t_5	3 min
t_6	4 min
t_7	5 min
t_8	10 min

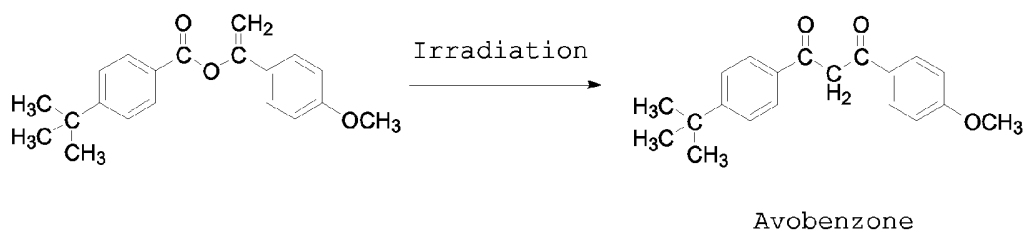
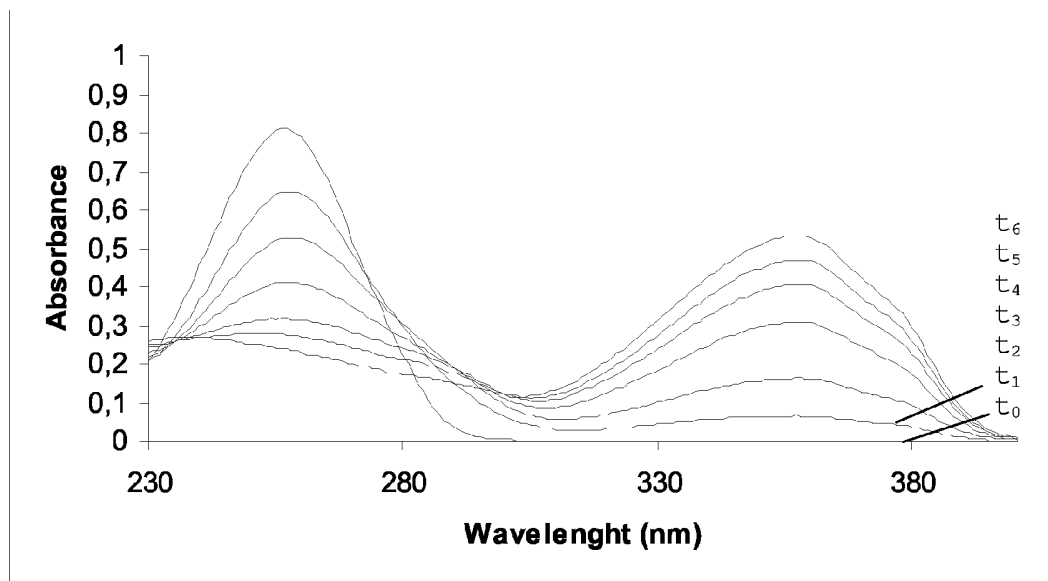


FIG. 2



Wavelength (nm)

t_0	0
t_1	20 s
t_2	40 s
t_3	1 min
t_4	2 min
t_5	3 min
t_6	10 min

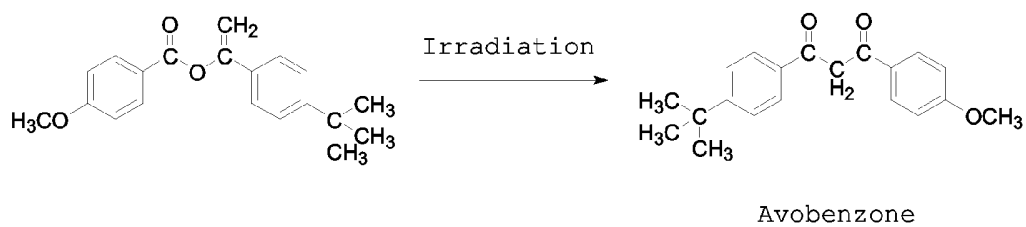
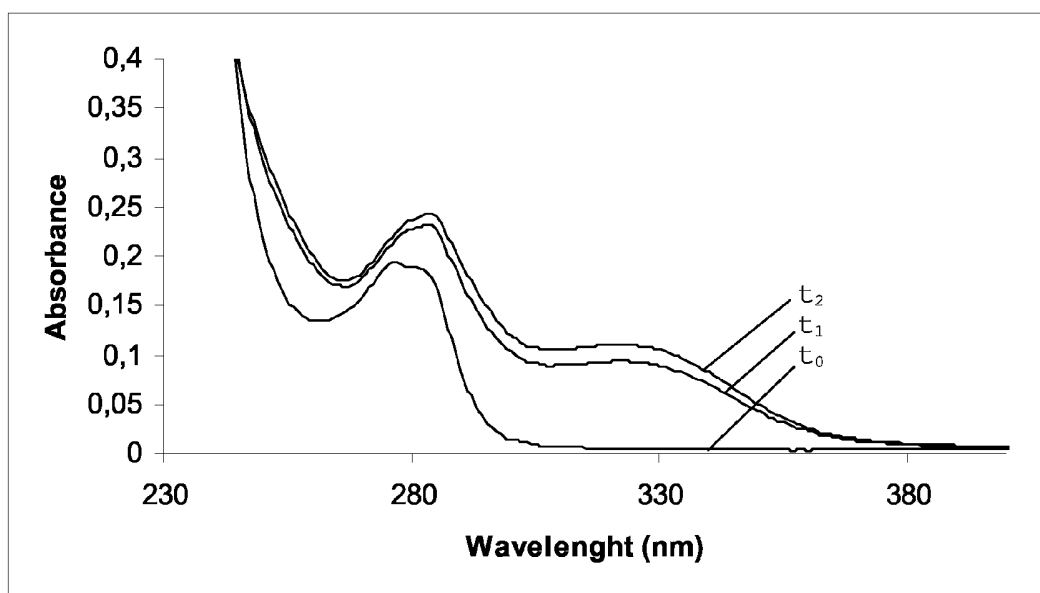


FIG. 3



Wavelength (nm)

t_0	0
t_1	1 min
t_2	2 min

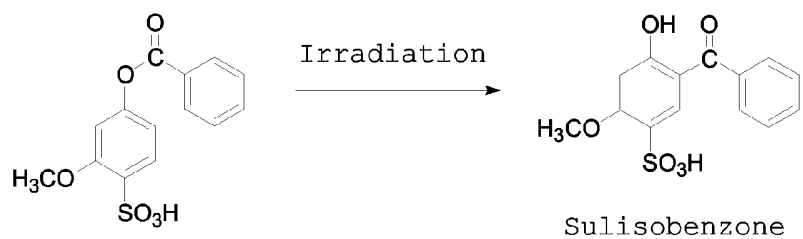
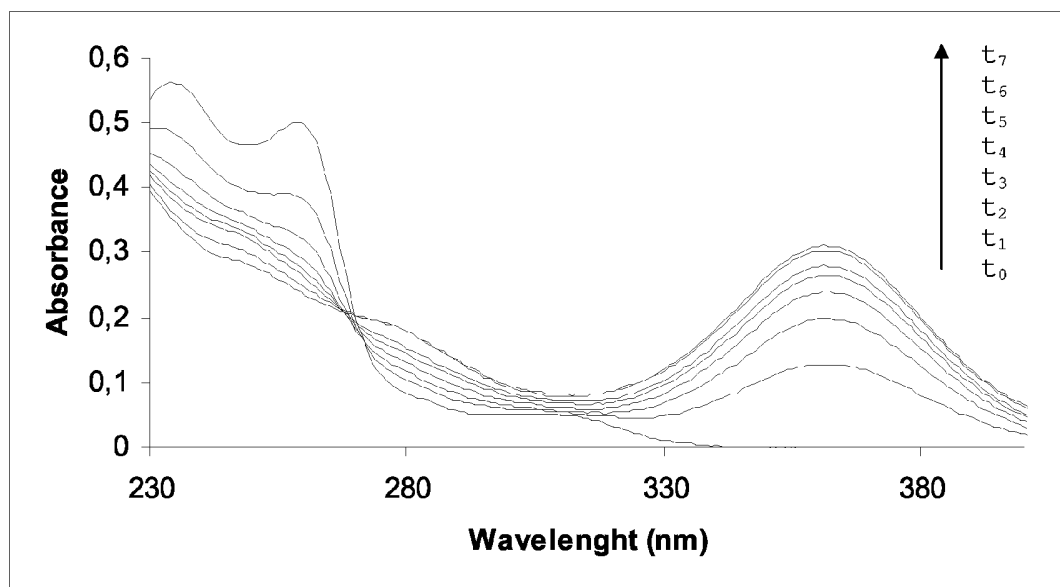


FIG. 4



Wavelength (nm)

t_0	0
t_1	1 min
t_2	2 min
t_3	3 min
t_4	4 min
t_5	5 min
t_6	10 min
t_7	20 min

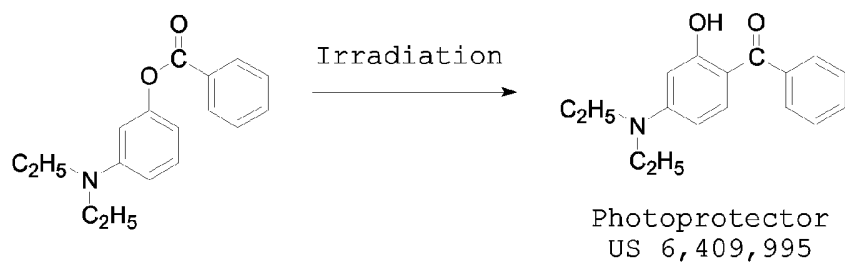
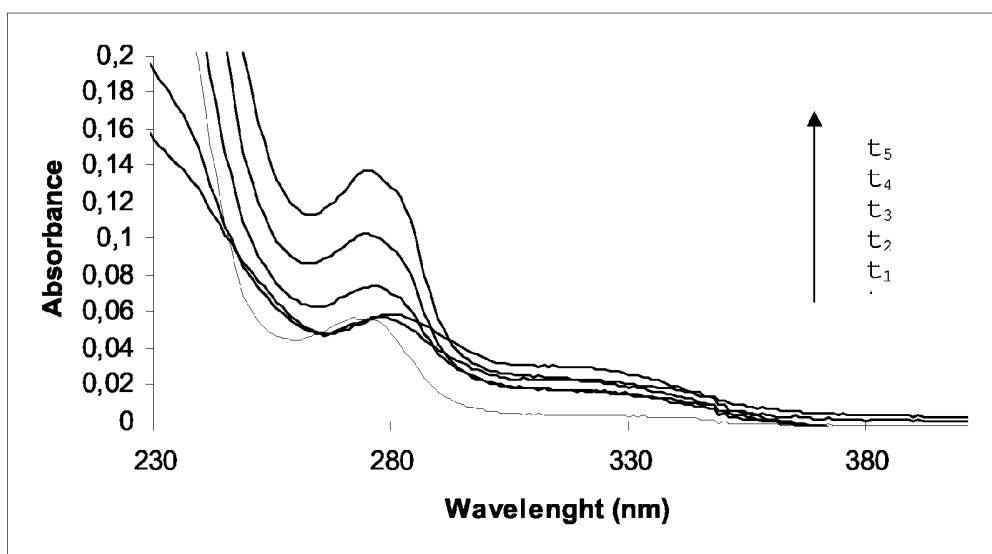


FIG. 5



Wavelength (nm)

t ₀	0
t ₁	2 min
t ₂	4 min
t ₃	6 min
t ₄	9 min
t ₅	20 min

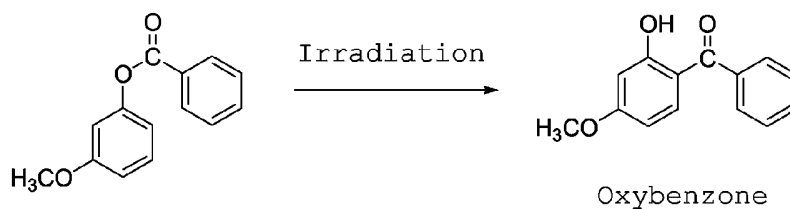


FIG. 6