

**Title:** POLYMERIC ULTRAVIOLET LIGHT ABSORBERS

![Chemical Structure](image)

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The present invention relates to polymeric ultraviolet light-absorbing compounds and processes for their production and relates particularly but not exclusively to polymeric ultraviolet light-absorbing compounds being copolymers of acrylic acid with the ultraviolet light-absorbing monomers of the invention and with other ultraviolet light-absorbing compounds. The ultraviolet light-absorbing compounds are of general formula (I), in which: R represents -(alk)\_n-O- or -(CH\_2-CH\_2O)\_n in which alk is a divalent straight or branched alkyl, aryl or alkaryl radical having 1 to 20 carbon atoms and n is from 1 to 1000, R' represents -OH, NH\_2, -NHR'\_2 or -NR'\_2 in which R' represents a straight or branched alkyl, aryl or alkaryl radical having from 1 to 20 carbon atoms. The polymers have a spreadability and lubricity which is conductive to their rubbing into the skin either alone or when formulated in sunscreen lotions, creams or suspensions.
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POLYMERIC ULTRAVIOLET LIGHT ABSORBERS

TECHNICAL FIELD

The present invention relates to polymeric ultraviolet light-absorbing compounds and processes for their production and relates particularly but not exclusively to polymeric ultraviolet light-absorbing compounds being copolymers of acrylic acid with the ultraviolet light-absorbing monomers of the invention and with other ultraviolet light-absorbing compounds. It is desirable that such compounds have a spreadability and lubricity which is conducive to their rubbing into the skin either alone or when formulated in sunscreen lotions, creams or suspensions; as well these compounds should desirably have relatively low skin permeability and relatively low water solubility; all these properties make these polymeric compounds suitable as sunscreen agents either alone or when formulated in sunscreen lotions, creams or suspensions.

BACKGROUND ART

As is well-known a sunscreen agent should have the property of absorbing ultraviolet light and, especially, in the region 300-310nm since this is a particularly damaging radiation to the human skin. In recent decades many publications and patents (for reviews see Bailey and Vogl, J Macromol. Sci. – Rev. 1976, C14(2), 257-93 and Tirrell, Polymer News, 1981, 7, 104-110) relate to such ultraviolet light-absorbing agents which are polymeric in order to achieve lower water solubility (which reduces losses of the agents after application and then, swimming) and/or skin permeability (which reduces the possibility of dermal toxicity or allergy). However, although there have been very many syntheses in the various research laboratories, to our knowledge there has been no commercialisation in spite of the great advantages claimed for these polymeric compounds. In our view which is drawn from our experimentation and reading in this field, this results from the very difficult compromise in that whenever practical levels of the ultraviolet light-absorbing components are included in the polymer, hydrophobic and intractable properties result and which prohibit formulation in creams, lotions or suspensions. We have found these difficulties invariably result, either when the ultraviolet absorbing component is conjugated to polymer or included as comonomer (see the earlier references for a description of these methods).

We have discovered that copolymers of acrylic acid with ultraviolet light-absorbing monomers do not have these intractable properties and
particularly, have a spreadability and lubricity which favours their formulation in creams, lotions or suspensions and even, may be rubbed into the skin alone to form efficacious, sun-protecting barriers. Especially, although it does not restrict the scope of this invention, it has been discovered that acrylic acid may be copolymerised with new, ultraviolet light-absorbing comonomers.

**DISCLOSURE OF THE INVENTION**

Thus, the present invention therefore provides ultraviolet light-absorbing compounds, of general formula (I):

\[
\text{C-O-R-C-CH=CH}_2
\]

(\text{I})

in which:

- \(R\) represents \(-(\text{alk})_n\)- or \(-(\text{CH}_2\text{CH}_2\text{O})_n\)- in which alk is a divalent straight or branched alkyl, aryl or alkaryl radical having 1 to 20 carbon atoms and \(n\) is from 1 to 1000.

- \(R'\) represents \(-\text{OH}, \text{NH}_2\), \(-\text{NR}^n_2\) or \(-\text{NR}^n_2\) in which \(R''\) represents a straight or branched alkyl, aryl or alkylaryl radical having from 1 to 20 carbon atoms.

The invention also provides a process for the manufacture of compounds of formula (I) as hereinbefore defined which comprises reacting a compound of formula (II):

\[
\text{C-OH}
\]

(\text{II})
in which R' is as hereinbefore defined, or an ester or acyl halide derivative thereof with a diol of formula (III)

\[ \text{HO-R-H} \] (III)

in which R is hereinbefore defined and then reacting the intermediate product so formed with acrylic acid or an acyl halide derivative thereof.

Preferably n is from 1 to 10 and particularly preferred compounds of formula (I) are those in which

- R is \(-\text{CH}_2\text{CH}_2\text{O}^-\) and R' is 2-OH or
- R is \(-\text{CH}_2\text{CH}_2\text{O}^-\) and R' is 4-N(CH_3)_2.

Among the various analogues of general formula (I) which are available from this invention, we prefer to use the comonomer 2-acryloxyethyl salicylate since it allows good lubricity and spreadability, together with the retention of maximum ultraviolet absorption.

Other preferred compounds of formula (I) include

2-acryloxy(polyoxyethylene) salicylate, 2-acryloxyethyl-4-N,N'-dimethylaminobenzoate, 4-acryloxy-2-hydroxybenzophenone.

The invention also provides polymeric compounds, being copolymers of acrylic acid and/or methacrylic acid with compounds of general formula (I) and/or with any other one or a number of ultraviolet light-absorbing monomers.

Such other ultraviolet light-absorbing monomers include vinyl or acrylate derivatives of 2-acryloxydibenzoylmethane, 2-hydroxy-4'-vinyl-dibenzoylmethane, oxalanilides, hydroxy benzoyl benzoic acids, 6-aza-1,2-dihydro-3H-1,4-benzodiazepine, 5-styrylpyrazoles, 7-azobenzimidazoles, benzal-3-alkyl-2H-benzothiazoloazines, p- or m- hydroxycinnamic acids, hydroxyphenylcarbamates, 4-methyl-N-(2-hydroxybenzylidene)aniline, 4-hydroxy-N-(2-hydroxybenzylidene)aniline, N-(3-hydroxybenzylidene)aniline, (4-hydroxybenzaldehyde) phenylhydrazine, benzaldehyde-4-hydroxyphenylhydrazone, N-(4-hydroxybenzylidene)benzylamine, 4,5-dihydro-5-oxo-1-phenyl-4-(phenylazo)-1H-pyrazole-3-carboxylic acid sodium salt, 4,5-dihydro-5-oxo-1-(4-sulfophenyl)-4-[(4-sulfophenyl)azo]-1H-pyrazole-3-carboxylic acid, 4,5-dihydro-5-oxo-1-(4-sulfophenyl)-4-[(4-sulfophenyl)azo]-1H-pyrazole-3-carboxylic acid trisodium salt, 1-[(4-sulfophenyl)azo]-2-naphthol-6-sulfonic acid, 1-[(4-sulfophenyl)azo]-2-naphthol-6-sulfonic acid disodium salt, 8-hydroxy-5,7-dinitro-2- naphthalenesulfonic acid, 8-hydroxy-5,7-dinitro-2-naphthalenesulfonic acid disodium salt, 1-hydroxy-2,4-dinitronaphthalene, 1-hydroxy-2,4- dinitronaphthalene sodium salt.
2-(1,3-dioxy-2-indanyl)quinoline, 2-(5-sulfo-1,3-dioxy-2-indanyl)-7-quinolinesulfonic acid, 2-(5-sulfo-1,3-dioxy-2-indanyl)-7-quinoline-sulfonic acid disodium salt; of monoarylidenecyclopentanones, diarylidene-cyclopentanones, monoarylidenecyclohexanones, diarylidene cyclohexanones, aryldeneacryloic acid esters, beta-acylidenevaleric acid esters, 3-cinnamoyl-4-hydroxy-6-methyl-2-pyrones; 2-(g-dimethylamino- benzylidene)cyclopentanones, B-aminoalkylidenecyclohexanones, B-amino- alkylidenecyclopentanones, 2-acetyl-5-phenyl-2,4-pentadienoic acid esters, chalcones, dibenzoylmethanes, 2-hydroxybenzophenones, 2-hydroxy-phenyl- benzotriazoles, 2,2'-diphenyldisulfonates, alpha-methylcinnamyl-malonates, urocanic acid esters, 6,7-dialkyl-2-phenylindoles, indomethacins, alpha-10-dimethylphenothiazine-2-acetic acids, kojic acids, tropolones, cinnamaldehydes, ethoxylated diphenylamines, ethoxylated- alpha-naphthols, camphors, pyridine maleates, benzaldehydrolides, bis(aminobenzoate)esters and cinnamic acid sulfophenylamides. (When the plural case is used, known analogues of the parent ultraviolet light absorbing monomers are meant to be included). One or more of these monomers can be copolymerised with acrylic acid and/or methacrylic acid.

Further, this application is not limited to copolymerisation of the abovementioned monomers with acrylic acid and/or methacrylic acid and includes the covalent bonding to those monomers of one or more known ultraviolet chromophores which have been suitably functionalised to enable bonding. It will be apparent to those skilled in the art, the variety of functional groups that can be used to attach the ultraviolet chromophores to acrylic acid and/or methacrylic acid: this may best be achieved for example, between a compound containing one or more active hydrogen atoms connected to oxygen, nitrogen, sulphur, phosphorous and in some cases, one or more acidic hydrogens attached to carbon; thus according to known art, a linkage may be made through this active hydrogen by way of bonds such as acetal, ketal, carbonyl, alkenyl, alkyl, alkylnyl, amide, amidine, amine, aminoether, arene, carbamate, ester, diazo, disulphide, ester, epoxide, peroxide, imide, imine, isothiocyanate, lactone, peptide, selenide, sulhide, sulphinic ester, sulphonamide, sulphone, sulphonic ester, sulphoxide, thioacetal, thioamide, thiocarbamate, thiocyanate, thiol ester, urea, thiourea, urethane and xanthate.

Usually, other (non-ultraviolet light-absorbing) monomers are not needed or used in these polymeric compounds, but they may be included so long as they do not unduly detract from the desired properties. Because
the various polymeric compounds which are provided by this invention are often similar in structure, conveniently, they may be often blended without undue incompatibilities in creams, lotions or suspensions to resultant, wide and/or uniform ultraviolet light-absorption across the spectrum.

The polymeric compounds of the invention are ultraviolet light-absorbing, have attractive spreadability and lubricity on the skin and usually, relatively low skin permeability or/and relatively low water solubility which are desirable when used alone, or as an ingredient for a sunscreen preparation.

The invention is not limited by the choice of copolymerising monomer, but when compounds of formula I in which R' is -2-OH are used, we have discovered that the invention additionally provides a polymeric compound which has been observed to often reduce any dermal irritation/inflammation attributable to any other ingredients of a base-cream or lotion or suspension for example, in which it may be formulated.

In a further aspect the invention provides a process for producing ultraviolet absorbing polymers by copolymerising at least one ultraviolet absorbing monomer, including compounds of formula I, with acrylic acid and/or methacrylic acid.

The special properties of the copolymers of the invention allow spreadability and lubricity even at high content (up to about 90% molar) of the ultraviolet light-absorbing monomers. This high content is very desirable as it maximises absorption and thus minimises the amount of ultraviolet light-absorber needed in a formulation or polymer blend to achieve the desired level of ultraviolet light-absorption.

The invention also provides ultraviolet light-absorbing formulations which include, in addition to the usual carriers and excipients known for such formulations, compounds of formula I or one or more of the ultraviolet light-absorbing copolymers of the invention. Such formulations find use in protecting surfaces (including skin) from the effects of ultraviolet light.

The copolymers of the invention may also be formulated into polymer blends with other non ultraviolet light-absorbing polymers.

BEST MODES OF CARRYING OUT THE INVENTION

The invention will now be illustrated by following non-limitative examples:
Example 1

(a) 2-acryloxyethyl salicylate and (b) analogue: 2-acryloxy(polyoxyethylene) salicylate

(a) Sulphuric acid (120ml, 2.16mol) was added to a mixture of salicylic acid (300.0g, 2.16mol) and ethylene glycol (600ml, 10.8mol). The resulting mixture was heated with occasional swirling on a steam bath for 2 hours. The cooled solution was poured into water (3.0l) and the product extracted into ether (3 x 600ml). The combined extracts were washed with saturated sodium hydrogen carbonate solution (600ml) then dried and concentrated. The ester was distilled under reduced pressure (ca. 280g, 70%).

Acryl chloride (112ml, 1.38mol) in dichloromethane (112ml) was added dropwise to a stirred cooled solution of the salicylate (250g, 1.37mol) and triethylamine (190ml, 1.37mol) in dichloromethane (1.25l). The mixture was allowed to come to room temperature over 20 hours. The mixture was poured into water (300ml) and the organics washed with dilute hydrochloric acid, water and saturated sodium hydrogen carbonate solution (all 300ml). The dried solution was concentrated to give the acrylate as an oil (290g, 90%). bp 260°/250 Pa. Found C, 60.8; H, 5.2%; C_{12}H_{12}O_{5} requires C, 61.0; H, 5.1%. 'H n.m.r. (CDCl₃): 84.1 - 4.6 (4H, m, -OCH₂CH₂-O-); 5.5-8.0 (7H, m, ArH and vinyl H); 10.4 (1H, s, -OH). U.V.: λ max (logε): 307 (3.46), 236 (3.94), 212nm (4.05).

Close examination of the N.M.R. spectrum and the gas chromatogram shows the presence also, of 2-hydroxyethyl-2-acryloxybenzoate.

(b) A mixture of salicylic acid (16.8g), PEG 200 (110ml) and sulphuric acid (7ml) was heated at 90-100° for 15 hours. After cooling the mixture was poured into water and extracted with dichloromethane. The extracts were washed with water, saturated sodium hydrogen carbonate solution and brine. Removal of solvent gave an oil (29.1g, 74%).

'H n.m.r. (CDCl₃): 82.9 (1H, s, -CH₂OH); 3.3-4.0 (13H, m, -OCH₂CH₂-O-); 4.3-4.6 (2H, m, -CH₂Q); 6.5-7.9 (4H, m, ArH); 10.6 (1H, s, ArOH).

Acryl chloride (3ml) in dichloromethane (5ml) was added dropwise to the salicylate (10g) and triethylamine (5ml) in dichloromethane (40ml) with stirring and cooling with ice salt. After 19 hours poured into water and the organics separated. The aqueous was extracted with dichloromethane then the combined organics were washed with dilute hydrochloric acid, water, saturated sodium hydrogen carbonate solution and brine. Removal of
solvent from the dried solution gave an oil (11.36g, 86%). 'H n.m.r. 
(CDC13): 63.1-3.9 (10H, m, -OCH2CH2O-); 4.1-4.5 (4H, m, 
-OCH2CH2O-); 5.5-6.5 (3H, m, vinyl H); 6.6-7.9 (4H, m, ArH); 10.6 (1H, 
s, -ArOH).

Example 2

2-acryloxyethyl 4,N,N'dimethylaminobenzoate

A solution of the acid (17.54g) in dmf (80ml) was added dropwise to a 
stirred suspension of sodium hydride (3.2g, 80%) in dmf (50ml). The 
mixture was then stirred overnight. 2-Chloroethanol (7.2ml) was added 
dropwise to the stirred solution. At the completion of the addition the 
mixture was stirred at room temperature for 2 hours then heated overnight. 
The solid gradually dissolved and left a further 24 hours then poured into 
water. The product was extracted into ethyl acetate. The extracts were 
filtered from a little insoluble material which was washed with ethyl 
acetate. The filtrate was dried over MgSO4 then concentrated to a light 
tan solid (ca. 19g) which was recrystallised from petrol/chloroform mp 
94-96°. First recrystallisation (8.95g); second recrystallisation (2.45g) 
mp 99-101° with prior softening. Total (11.4g, 51%). 'H n.m.r. (CDCl3): 
5.2.9 (7H, s, -NMe2 and -OH), 3.7-4.4 (4H, AA'BB'm, -OCH2CH2O-): 
5.3-7.9 (4H, AA'BB'm, ArH).

A solution of acryl chloride (5ml) in dichloromethane (10ml) was 
added dropwise to a stirred, cooled solution of the benzoate (8.95g) in 
triethylamine (7ml) in CH2Cl2 (60ml). The mixture was allowed to come 
to room temperature overnight then poured into water and the product 
extracted into dichloromethane. The extracts were washed with dilute 
hydrochloric acid and water, dried over MgSO4 and then concentrated to an 
oil which solidified on cooling (7g, 62%). 'H n.m.r. (CDCl3): 82.9 
(6H, s, -NMe2); 4.4 (4H, s, -OCH2CH2O-); 5.5-7.9 (7H, m, ArH and 
viny1 H).

Example 3

4-acryloxy-2-hydroxybenzophenone

According to CIBA Limited British Patent 898 065:

2,4-dihydroxybenzophenone (120.0g, 0.560mol) was dissolved in a solution of 
sodium hydroxide (22.6g, 0.565mol) in methanol (480ml) and the solvent 
evaporated. To the residual solid was added toluene (1.2l). Acryl chloride (46.6ml, 0.573mol) was added dropwise to the cooled stirred 
mixture. The mixture was allowed to come to room temperature and was then 
heated to just below reflux. The salt was filtered and washed with a
little toluene (ca. 150ml). The filtrate was concentrated to give the acrylate as a yellow oil (158.20g, crude) which was precipitated in ethanol (500ml) to give a yellowish solid mp79-80° (71.65g, 48%). The mother liquor was further concentrated to yield yellow crystals (10.67g, 7%). A third crop was obtained by recrystallisation from ethanol to yield yellow crystals (16.35g, 11% mp80°. Total: 98.67g, 66%. 'H n.m.r. (CDCl₃): 65.8-7.9 (11H, m, ArH and vinyl H); 12.3 (1H, s, –OH). U.V.: λMeOH max (logε): 325 (4.06), 265 (4.29), 210nm (4.41).

**Example 4**

(a) and (b) Copolymers of acrylic acid and 2-acryloxyethyl salicylate; (c) acrylic acid and 2-acryloxyvinylpolyoxyethylene salicylate; (d) and (e) Copolymers of Methacrylic acid/acrylic acid and 2-acryloxyethyl salicylate

(a) A solution of the acrylate (26.2g, 0.111mol), acrylic acid 7.5ml, 0.109mol) and benzoyl peroxide (0.8g) in toluene (100ml) was added dropwise to toluene (480ml) at 100° with stirring. At the completion of the addition the mixture was stirred at 100° for 90 minutes then allowed to cool. The 25% salicylate copolymer is a white granular, easily ground solid; soluble in dmf, dmso, dilute base (NaOH); slightly soluble in acetone, methanol, chloroform; insoluble in water, sea water, petrol. The product was collected and air dried on filter paper overnight (16.8g). 'H n.m.r. (d₆-dmso): 80.6-3.9 (hump, –CH₂CH₂–); 4.3 (bs, –OCH₂CH₂O–); 5.5-8.0 (m, ArH); 10.3 (bs, ArOH); 12.0 (hump, –CO₂H).

(b) A solution of the acrylate (290g, 1.23mol), acrylic acid (9.4ml, 0.137mol) and benzoyl peroxide (4.7g) in ethyl acetate (290ml) was added dropwise to ethyl acetate (1.45l) at reflux with stirring. At the completion of the addition, the mixture was stirred at reflux for 2 hours, then allowed to cool. The resulting solution was diluted with ethyl acetate (1.16l). The product was isolated by spray precipitation into light petroleum (30l) to yield a fine white powder that was air dried on filter paper overnight (200g, 66%).

The 80% salicylate copolymer is a white powdery solid; soluble in chloroform, toluene, ethyl acetate, 2-butane, acetone; insoluble in petrol, water, sea water, ethanol. 'H n.m.r. (CDCl₃): 80.6-3.3 (hump, –CH₂CH₂–); 3.6-5.5 (bs, –OCH₂CH₂O–); 6.5-8.0 (m, ArH); 10.5 (bs, –OH). U.V.: (39.6mg⁻¹l⁻²) λCHCl₃ max (Aₘ₉₅): 309 (0.433), 242nm (0.924).

(c) A solution of benzoyl peroxide (120mg) in toluene (10ml) and a solution of acrylic acid (1.2ml) and the acrylate (7.36g) in toluene (10ml)
were added simultaneously (separately) to toluene (70ml) with mechanical stirring between 120° and 140°. At the completion of the addition, the mixture was stirred at 120°-140° for 2 hours, then allowed to cool. The precipitate was collected and washed with toluene (1.7g). Soluble in dms, dmf, dilute sodium hydroxide solution; insoluble in water, sea water, toluene, chloroform, petrol and methanol. *H n.m.r. (d_6-dms): 81.0-2.8 (hump, \(-\text{CH}_2\text{-CH}-, \text{CO}_2\text{H}\)); 2.8-4.7 (m, \(-\text{OCH}_2\text{-CH}_2\text{O}\\cdot\text{-})\); 6.7-8.0 (m, ArH); 10.3 (hump, ArOH).

(d) A solution of the acrylate (30g, 0.127mol), methacrylic acid (1.2ml, 0.014mol) and benzoyl peroxide (0.48g) in ethyl acetate (30ml) was added dropwise to ethyl acetate (150ml) at reflux with stirring. At the completion of the addition, the mixture was stirred at reflux for 2 hours, then allowed to cool. The resulting solution was diluted with ethyl acetate (120ml). The product was isolated by spray precipitation into light petroleum (3l) to yield a fine white powder that was air dried on filter paper overnight (21g), 66%).

(e) Prepared for example 4(d) above substituting for methacrylic acid, a mixture of acrylic acid (0.72ml, 0.011mol) and methacrylic acid (0.30ml, 3.5mmol).

**Example 5**

(a) Copolymer of acrylic acid and 2-acryloyloxyethyl-4-N,N'-dimethylaminobenzoate (b) copolymer of methacrylic acid and 2-acryloyloxyethyl-4-N,N'-dimethylaminobenzoate

(a) Nitrogen was bubbled through a solution of the acrylate (7g) in toluene (130ml) for 30 minutes. Then acrylic acid (1.8ml) and AIBN (0.11g) were added. The mixture was heated at 110-120° for 2 hours. A solid formed which coagulated. The mixture was allowed to cool and the solid collected. Washed with toluene, dried at the pump then on filter papers overnight. The granular material (4g) was ground up and dried under vacuum. *H n.m.r. (CDCl_3, d_6-dms): 50.8-2.7 (hump, \(-\text{CH}_2\text{-CH}-\)); 2.9 (bs, \(-\text{NMe}_2\): 4.3 (bs, \(-\text{OCH}_2\text{-CH}_2\text{O}\\cdot\text{-})\); 6.3-8.5 (m, ArH and \(-\text{CO}_2\text{H}\)).

U.V.: \(\lambda\text{MeOH max. (loge): 310 (4.38); 229nm (3.78). Soluble in dms, dmf; insoluble in other organics, water and sea water.}

(b) Nitrogen was bubbled through a solution of the acrylate (7g) in toluene (130ml) for 30 minutes. Then methacrylic acid (2.2ml) and AIBN (0.11g) were added. The mixture was heated at 110-120° for 2 hours. A solid formed which coagulated. The mixture was allowed to cool and the solid collected. Washed with toluene, dried at the pump then on filter papers overnight. The
granular material (4g) was ground up and dried under vacuum.

**Example 6**

**Copolymer of acrylic acid, 2-acryloxyethyl salicylate and 4-acryloxy-2-hydroxybenzophenone**

A solution of the benzophenone monomer (2.66g, 9.9mmol), salicylate monomer (2.34g, 9.9mmol), acrylic acid (0.075ml, 1.09mmol) and benzoyl peroxide (70mg) in a 50% mixture of ethyl acetate and toluene (15ml) was added dropwise to a 50% solution of ethyl acetate and toluene (35ml) at 100-110°C with stirring. At the completion of the addition, the mixture was stirred at 100-110°C for four hours. The product was isolated by spray precipitation from light petroleum (ca. 500ml) to yield an off-white powder (3.42g, 68%). The salicylate benzophenone terpolymer is a cream to pale yellow powder; soluble in ethyl acetate, acetone; slightly soluble in toluene; insoluble in water, sea water, petrol and methanol. 'H n.m.r. (CDCl₃): 81.0-3.3 (hump, -CH₂CH₂-); 4.4 (bs, -OCH₂CH₂O-); 6.3-8.0 (m, ArH); 10.4 (bs, -OH); 12.2 (bs, -OH). U.V.: (43.2mgl⁻¹)

λ-CHCl₃, max. (Aₘₓ): 320 (0.540); 268 (1.186); 244nm (1.061).

**Example 7**

(a) and (b) Copolymers of acrylic acid and 4-acryloxy-2-hydroxybenzophenone; (c) Copolymer of methacrylic acid and 4-acryloxy-2-hydroxybenzophenone

(a) A solution of the acrylate (26.0g, 96.9mmol), acrylic acid (6.5ml, 94.8mmol) and benzoyl peroxide (1g) in toluene (90ml) was added dropwise with stirring to toluene (430ml) at 100°C. Two additions of benzoyl peroxide (1g) in toluene (5ml) were made at 2 hourly intervals. Thirty minutes after a precipitate formed the mixture was allowed to cool. The solid was collected and air dried (20.0g). 33% benzophenone copolymer (cream to pale yellow granular solid) soluble in dmf, dmso, dilute sodium hydroxide solution; insoluble in water. The 80% benzophenone copolymer is a cream to pale yellow powder soluble in chloroform, ethyl acetate, acetone; slightly soluble in toluene; insoluble in water, sea water, petrol and ethanol. 'H n.m.r. (CDCl₃, d₆-dmso): 80.9-3.3 (hump, -CH₂CH₂-, -CO₂H); 6.1-8.0 (m, ArH); 11.8 (bs, ArOH).

(b) A solution of the benzophenone acrylate (40.0g, 0.149mol), acrylic acid (1.14ml, 16.6mmol) and benzoyl peroxide (550mg) in a 50% mixture of ethyl acetate and toluene (200ml) was added dropwise to a 50% solution of ethyl acetate and toluene (280ml) at reflux with stirring. At the completion of the addition, the mixture was stirred at reflux for 4
hours. The product was isolated by precipitation into petroleum (ca. 4.01) to yield an off-white powder (35.21g, 85%). 'H n.m.r. (CDCl₃): 6.1.5-3.8 (hump, -CH₂CH-); 6.3-8.0 (m, ArH); 12.1 (bs, ArOH). U.V. (40.4mg l⁻¹) λCHCl₃ max. (A_max): 333 (0.783), 268nm (1.993).

(c) A solution of the benzophenone acrylate (40.0g, 0.149mol), methacrylic acid (11.41ml), 16.6mol) and benzoyl peroxide (550mg) in a 50% mixture of ethyl acetate and toluene (200ml) was added dropwise to a 50% solution of ethyl acetate and toluene (280ml) at reflux with stirring. At the completion of the addition, the mixture was stirred at reflux for 4 hours. The product was isolated by precipitation into petroleum (ca. 4.01) to yield an off-white powder (35.21g, 85%).

Example 8

Formulations: Spreadability and Lubricity on Skin

(a) Base formulation:

PART A: Crodamol PC (20g; a propylene glycol fatty acid ester), crodamol CAP (20g; mixed fatty acid esters), crillet 3 (2g; sorbitan monostearate), cetyl alcohol (2g), stearic acid (6g) and super hartolan (2g; lanolin alcohols) were heated until the mixture was homogeneous then allowed to cool.

PART B: Triethanolamine (3g) and glycerol (6g) were dissolved in water (110ml).

PART C: Dowicil 200 (20mg; preservative) was dissolved in water (20ml) and to this was added collasol (6g; collagen). Part A (11g) and Part B (25ml) were heated to 60° then B added to A and then allowed to cool with constant stirring. Then, Part C (5ml) was added with stirring.

(b) The salicylate copolymer (8g; example 4(a)) was suspended in Part A (22ml) at 60°. Part B (8ml) at 60° was added with stirring, cooled with stirring, then Part C (10ml) was added.

The resulting sunscreen lotion was tested for its sunscreen factor according to Australian Standard 2604 "Sunscreen Products - Evaluation and Classification" of 1986, and gave a sunscreen protecting factor score on average of 9. Similar results were recorded when the copolymer within the formulation (example 8(b)) was rubbed into the skin - neat and dry, without being dispersed into the base formulation.

(c) The polymer (370g; 4(b)) was dry ground for several hours then water (2.59l), glycerol (111g) and triethanolamine (96.2g) were added. Grinding continued for about 7 hours. The mill was emptied (ca. 90% recovery) and the slurry heated with stirring to 60°. Crodamol CAP (370g),
crodamol PC (370g), polysorbate 60 (74g), cetyl alcohol (37g), pristerene (stearic acid) (185g) and super hartolain (55.5g) were heated to 60°. 992g of this was added to the aqueous with stirring (ca. 400rpm) and left to cool overnight with stirring. 440g of a mixture of collasol (111g), Dowicil 200 (7.4g) and water (370ml) was then added. Perfume (13.3g) was then added.

An evaluation of the sunscreen protecting factor according to Australian Standard gave scores of 10-15+. The same formulation was appraised equally with a leading commercial brand during a panel test among 13 subjects during a weekend's swimming and bathing; during this period the water insolubility of the screening film was noted and was consistent with all laboratory results.

(d) The polymer (10g; example 4(b)) was dry ground for 15 minutes then with a solution of triethanolamine (2.6g), glycerol (3g) in water (70ml). The pot was decanted to give 81g. 28g of Part A was then added at 60°. It was cooled with stirring and then Part C (12.3ml) was added.

(e) Triethanolamine (0.39g) and glycerol (0.45g) were dissolved in water (10.5ml); terpolymer (1.5g; example 6) was dry ground then ground further with the above solution. Part A (3.31g) and the above (9.61g) were heated to 60-70°; Part A was then added to Part B with stirring. The resulting mixture was allowed to cool with stirring (temp. below 30°). Part C (1.48g) was then added with stirring.

(f) Copolymer (4.4g; example 7(a)) was suspended in Part A (11g) at 60°; then Part B (25ml) was added with stirring at 60° and the resulting mixture was allowed to cool to 30° with stirring Part C (5.5g) was then added with stirring.

(g) The salicylate copolymer (5g, example 4(b)) and the benzophenone copolymer (5g, example 7(b)) were ground in a ball mill for several hours. A solution of glycerol (3g) and triethanolamine (2.6g) in water (70ml) was added and grinding continued. The suspension was decanted then heated with stirring to 60°. Part A (28.9g) at 60° was added with stirring and the mixture allowed to cool to 30°. Then Part C (13ml) was added with stirring.

(h) The copolymers of Examples 4–7 inclusive, as well as the formulations of this Example were subjectively tested in a panel of 13 of mixed sexes and ages, for spreadability and lubricity and compared favourably with several commercial sunscreen preparations.
Example 9

Irritations

Percutaneous Absorption and Primary Dermal

(a) Studies were carried out in modified Franz diffusion cells (see Chien "Transdermal Controlled Systemic Medications", Dekker, 1987) of approximately 10ml volume at 37°C. Freshly excised hairless mice skin (ca. 2cm²) was used as the membrane. These were left overnight in contact with the cell solution before applying the material to be studied. Samples were taken at intervals after application, the cell being topped up with fresh solution, and the samples analysed by hplc (Bondapak column).

<table>
<thead>
<tr>
<th>SAMPLE</th>
<th>APPLIED DOSE (mg)</th>
<th>MAX DETECTION mg l⁻¹</th>
<th>PENETRATION: % OF APPLIED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methyl salicylate</td>
<td>2 *</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>15 *</td>
<td>17.3</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>200 *</td>
<td>439</td>
<td>2.2</td>
</tr>
<tr>
<td>Homomenthyl salicylate</td>
<td>15.3 **</td>
<td>27.7</td>
<td>1.8</td>
</tr>
</tbody>
</table>

Polymer: Ex. 4(b) 16.7 ** <1 <0.06%
* Cell solution was 20% polyethylene glycol 400 in 0.9% saline.
** Cell solution was 90% thf in water.

(b) Percutaneous Absorption (Radio-Active)

Synthesis of labelled materials commenced from [carboxyl-¹⁴C] salicylic acid (55 mCi mmol⁻¹). (Amersham Australia Pty Ltd)

[Carboxyl-¹⁴C] methyl salicylate:

Salicylic acid (16.4mg) was combined with labelled acid (2.5mg). The methyl ester was prepared according to the method of "Vogel's Textbook of Practical Organic Chemistry", Longmans, 4th ed. in 30% yield after preparative thin layer chromatography (p.t.l.c.).

Salicylic acid (65.4mg) was combined with labelled acid (22.8mg). The polymer was prepared essentially as described in examples 1(a) and 4(b) above and purified by spray precipitation. The intermediate esters were purified by the p.t.l.c. and obtained in 67% and 37% yield respectively. The polymer was isolated in 16% yield.
5% formulations were prepared of the above materials in the base described above.

The so-formed formulations of methyl ester and polymer were each, respectively, diluted with 4 parts of the formulations of the non-labelled methyl ester and polymer. Samples (ca. 100mg) of each of these blends were then applied to the shaved, dorsal skins of each of 6 albino rabbits. Sacrifice of the animals and examination of their faeces and urine demonstrated that over a period of 24 hours on the skin, an average of 0.8% of the label from the polymer penetrated the skin; 4.3% from the monomer (during this time it was also observed that considerable amounts of the monomer evaporated and were presumably, unavailable for skin-penetration).

(c) Primary Dermal Irritation (Draize)

Draize tests of acute dermal irritation/corrosion were performed on 6 albino rabbits according to the OECD Guidelines for Testing of Chemicals, Section 4 (Health Effects), updated 24.2.87:

<table>
<thead>
<tr>
<th>SAMPLE</th>
<th>SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blank formulation: Example 8(a)</td>
<td>3.2</td>
</tr>
<tr>
<td>Formulation: Example 8(b), Polymer 4(a)</td>
<td>1.7</td>
</tr>
<tr>
<td>Formulation: Polymer 7(a)</td>
<td>1.1</td>
</tr>
<tr>
<td>Formulation: Polymer 4(b)</td>
<td>2.3</td>
</tr>
</tbody>
</table>

* Prepared similarly to example 8(b).

Thus, all formulations give lower scores than their base formulation.
CLAIMS

POLYMERIC ULTRAVIOLET LIGHT-ABSORBERS

1. Ultraviolet light-absorbing compounds, of general formula (I):

in which:

- \( R \) represents \(-(\text{alk})_n\text{O}\) or \( -(\text{CH}_2\text{CH}_2\text{O})_n\) in which \( \text{alk} \) is a
divalent straight or branched alkyl, aryl or alkaryl radical having 1
to 20 carbon atoms and \( n \) is from 1 to 1000

- \( R' \) represents \( \text{OH}, \text{NH}_2, \text{NHR}^{\text{n}} \) or \( \text{-NR}_2^{\text{n}} \) in which \( R' \) represents a
straight or branched alkyl, aryl or alkylaryl radical having from 1
to 20 carbon atoms.

2. Compounds as defined in claim 1, wherein \( n \) is 1 to 10.

3. Compounds as defined in claim 1 or claim 2, wherein \( R \) is
\(-\text{CH}_2\text{CH}_2\text{O}-\).

4. Compounds as defined in any one of claims 1 to 3, wherein \( R' \) is
\( 2\text{-OH} \) or \( 4\text{-N(CH}_3)_2 \).

5. A compound selected from 2-acryloxyethyl salicylate,
2-acryloxypolyoxyethylene salicylate, 2-acryloxyethyl-4-N,N'-dimethylamino-
benzoate, 4-acryloxy-2-hydroxybenzophenone.

6. A process for the manufacture of compounds of formula (I) as
defined in claim 1, which comprises reacting a compound of formula (II)

in which \( R' \) is as defined in claim 1, or an ester or acyl halide
derivative thereof with a diol of formula (III)

in which \( R \) is as defined in claim 1, and then reacting the intermediate
product so formed with acrylic acid and/or methacrylic acid or acyl halide
derivatives thereof.

7. A process as defined in claim 6, which comprises reacting
salicylic acid with ethylene glycol, and then reacting the intermediate product so formed with acryloyl chloride.

8. Copolymers of acrylic acid and/or methacrylic acid with compounds as defined in any one of claims 1 to 5 or with other compounds capable of absorbing ultraviolet light and capable of being polymerised with acrylic acid and/or methacrylic acid.

9. Copolymers as defined in claim 8, wherein the other compounds are vinyl or acrylate derivatives of 2-acryloyldibenzoylmethane, 2-hydroxy-4′-vinylidibenzoylmethane, oxalanilides, hydroxy benzoyl benzoic acids, 6-aza-1,2-dihydro-3H-1,4-benzodiazepine, 5-styrylpyrazoles, 7-azo-benzimidazoles, benzal-3-alkyl-2H-benzothiazoloazines, p- or m- hydroxycinnamic acids, hydroxyphenylcarbamates, 4-methyl-N-(2-hydroxybenzylidene)-aniline, 4-hydroxy-N-(2-hydroxybenzylidene)aniline, N-(3-hydroxybenzylidene)aniline, (4-hydroxybenzaldehyde) phenylhydrazone, benzaldehyde-4-hydroxyphenylhydrazone, N-(4-hydroxybenzylidene)benzylamine, 4,5-dihydro-5-oxo-1-phenyl-4-(phenylazo)-1H-pyrazole-3-carboxylic acid sodium salt, 4,5-dihydro-5-oxo-1-[(4-sulfophenyl)-4-[(4-sulfophenyl)azo]-1H-pyrazole-3-carboxylic acid, 4,5-dihydro-5-oxo-1-[(4-sulfophenyl)azo]-1H-pyrazole-3-carboxylic acid trisodium salt, 1-[(4-sulfophenyl)azo]-2-naphthol-6-sulfonic acid, 1-[(4-sulfophenyl)azo]-2-naphthol-6-sulfonic acid disodium salt, 8-hydroxy-5,7-dinitro-2-naphthalenesulfonic acid, 8-hydroxy-5,7-dinitro-2-naphthalenesulfonic acid disodium salt, 1-hydroxy-2,4-dinitronaphthalene, 1-hydroxy-2,4-dinitronaphthalene sodium salt, 2-((1,3-dioxo-2-indanyl)quinoline, 2-((5-sulfo-1,3-dioxo-2-indanyl)-7-quinolinesulfonic acid, 2-((5-sulfo-1,3-dioxo-2-indanyl)-7-quinolinesulfonic acid disodium salt; of monoarylidenecyclopentanones, diarylidenecyclopentanones, monoarylidenecyclohexanones, diarylidenecyclohexanones, aryldenedepyruvic acid esters, delta-acrylidenevulinc acid esters, 3-cinnamoyl-4-hydroxy-6-methyl-2-pyrones, 2-(g-dimethylaminobenzylidene)cyclopentanones, 6-aminoalkylidenecyclohexanones, 6-aminoalkylidenecyclopentanones, 2-acetyl-5-phenyl-2,4-pentadienoic acid esters, chalcones, dibenzoylmethanes, 2-hydroxybenzophenones, 2-hydroxyphenylbenzotriazoles, 2,2′-diphenyldisulfonates, alpha-methylcinnamalmalonates, urocanic acid esters, 6,7-dialkyl-2-phenylindoles, indomethacines, alpha-10-dimethylphenothiazine-2-acetic acids, kofic acids, tropolones, cinnamaldehydes, ethoxylated diphenylamines, ethoxylated-alpha-napththoic, camphors, pyridine maleates, benzalpthalides, bis(amino-benzoate)esters and cinnamic acid sulfophenylamides.
10. Copolymers as defined in claim 8, wherein the other compounds are known ultraviolet chromophores which have been functionalized to enable bonding to acrylic acid or methacrylic acid.

11. Copolymers as defined in any one of claims 8 to 10, further comprising other monomers polymerisable with acrylic acid and/or methacrylic acid.

12. A copolymer of acrylic acid and 2-acryloxyethyl salicylate.

13. A copolymer of acrylic acid and 2-acryloxypolyoxyethylene salicylate.

14. A copolymer of acrylic acid and 2-acryloxyethyl-4-N,N'-dimethylaminobenzoate.

15. A copolymer of acrylic acid, 2-acryloxyethyl salicylate and 4-acyrloxy-2-hydroxybenzophenone.

16. A copolymer of acrylic acid and 4-acyrloxy-2-hydroxybenzophenone.

17. A copolymer of methacrylic acid and 2-acryloxyethyl salicylate.

18. A copolymer of methacrylic acid and 2-acryloxyethyl 4-N,N'-dimethylaminobenzoate.

19. A copolymer of methacrylic acid and 4-acyrloxy-2-hydroxybenzophenone.

20. A copolymer as defined in any one of claims 8 to 19 containing up to about 90 molar % of ultraviolet light-absorbing monomers.

21. A process for producing copolymers of acrylic acid and/or methacrylic acid with compounds as defined in any one of claims 1 to 5 or with compounds capable of absorbing ultraviolet light and capable of being polymerised with acrylic acid and/or methacrylic acid, which process comprises polymerising acrylic acid and/or methacrylic acid with compounds as defined in any one of claims 1 to 5 or with compounds capable of absorbing ultraviolet light and capable of being polymerised with acrylic acid and/or methacrylic acid.

22. A process as defined in claim 21, carried out in the presence of a polymerisation inducing agent.

23. A process as defined in claim 22, wherein the polymerisation inducing agent is an anionic catalyst, gamma radiation, a free radical catalyst, ultraviolet radiation, electron beam radiation or a combination of two or more thereof.

24. The product of the process of any one of claims 21 to 23.

25. An ultraviolet light absorbing formulation comprising a copolymer as defined in any one of claims 8 to 20 or 24 or a compound as
defined in any one of claims 1 to 5, together with the usual carriers and excipients known for ultraviolet light absorbing formulations.

26. An ultraviolet light stable polymer blend which includes a copolymer as defined in any one of claims 8 to 20 or 24.

27. A substrate coated with a copolymer as defined in any one of claims 8 to 20 or 24.

28. A method for protecting a surface from the effects of ultraviolet light which method comprises applying to said surface an effective amount of a copolymer as defined in any one of claims 8 to 20 or 24 or of a formulation as defined in claim 25.
# INTERNATIONAL SEARCH REPORT

## I. CLASSIFICATION OF SUBJECT MATTER

According to International Patent Classification (IPC) or to both National Classification and IPC

Int. Cl. A 4 C07C 69/84, 101/62, 101/54, 69/54, A61K 7/42, 7/44  
C08L 33/02, 33/14, 51/08, C08G 65/32, C08F 220/30, 220/23, 283/06

## II. FIELDS SEARCHED

<table>
<thead>
<tr>
<th>Classification System</th>
<th>Minimum Documentation Searched</th>
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<tr>
<td>IPC</td>
<td>C07C 69/84, 101/62, 101/54</td>
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</table>

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched

AU : IPC as above

## III. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of Document</th>
<th>Relevant to Claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>DE, A, 2116973 (BAYER AG) 14 December 1972 (14.12.72)</td>
<td>(1-28)</td>
</tr>
</tbody>
</table>
W.P. Ewald et al, "Photopolymerizable Compounds featuring novel co-initiators" pp 560-5. See  
Example 10, Table II | (1-28) |
| X        | Chemdex 3 Database, RN 100012-67-7  
Benzoic acid, 2 hydroxy, 2-[1-oxo-2-propenyl] oxy] ethyl ester | (1-28) |

* Special categories of cited documents:  
"A" document defining the general state of the art which is not considered to be of particular relevance  
"E" earlier document but published on or after the international filing date  
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another document or other special reason (as specified)  
"O" document referred to in the oral proceedings, use, exhibition or other means  
\*m" document published prior to the international filing date or later than the priority date claimed

*E* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  
*X* document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step  
*Y* document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art  
*Z* document member of the same patent family

## IV. CERTIFICATION

Date of the actual completion of the international search  
21 September 1988 (21.09.88)

Date of mailing of the international search report  
29 September 1988 (29.09.88)

International Searching Authority  
Australian Patent Office

Signature of Authorized Officer  
D.E. GLANVILLE
V. OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE

This international search report has not been established in respect of certain claims under Article 17(2) (a) for the following reasons:

1. Claim numbers because they relate to subject matter not required to be searched by this Authority, namely:

2. Claim numbers because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. Claim numbers because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

VI. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This International Searching Authority found multiple inventions in this international application as follows:

4-acryloxy-2-hydroxybenzophenone claimed in claim 5 does not fall within the scope of the invention defined by claim 1.

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the international application.

2. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:

3. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim numbers:

   1-4,6-14,17,18,20-28

4. As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

Remainder on Protest

The additional search fees were accompanied by applicant’s protest.

No protest accompanied the payment of additional search fees.
ANNEX TO THE INTERNATIONAL SEARCH REPORT ON
INTERNATIONAL APPLICATION NO. PCT/AU 88/00180

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

<table>
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<tr>
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<tbody>
<tr>
<td>DE 2116973</td>
<td>BE 781733 FR 2136251 GB 1387908</td>
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<td>US 3821282</td>
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