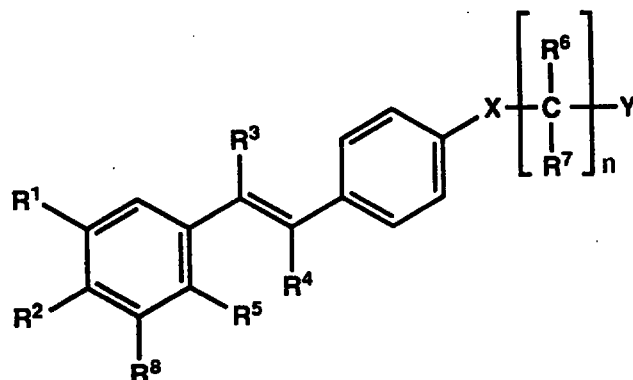


Description

The present invention is concerned with novel stilbene derivatives of the general formula



I

wherein R¹ and R² each independently represent lower-alkyl; or together represent 1,3-propylene, 1,4-butylene and 1,5-pentylene and lower-alkyl-substituted derivatives thereof; one of the residues R³ and R⁴ signifies hydrogen and the other signifies hydrogen or lower-alkyl; R⁶ and R⁷ signify hydrogen or lower-alkyl; R⁵ and R⁸ signify hydrogen, lower-alkyl, lower-alkoxy or halogen; X signifies -O-; Y signifies piperidino, pyrrolidino, morpholino, piperazino, N-methylpiperazino, thiomorpholino, thiomorpholino 4-oxide, thiomorpholino 4,4-dioxide, imidazolino or pyrrolo and n signifies 2, 3 or 4.

Furthermore, the invention is concerned with a process for the manufacture of the compounds of formula I, pharmaceutical preparations based on the compounds of formula I, the compounds of formula I in the treatment and prophylaxis of neoplasms, dermatoses and ageing of the skin as well as the use of the compounds of formula I in the manufacture of pharmaceutical preparations for the treatment and prophylaxis of such disorders.

The term "lower" denotes groups with 1-6 C-atoms. Alkyl and alkoxy groups can be straight-chain or branched, such as methyl, ethyl, propyl, isopropyl, butyl, sec.-butyl or tert.-butyl and methoxy, ethoxy, propoxy, isopropoxy, butoxy, sec.-butoxy and tert.-butoxy, respectively. Halogen embraces fluorine, chlorine, bromine and iodine. An alkyl residue with 3-5 C-atoms in a straight chain, represented by R¹ and R² together, can be branched. Examples of lower-alkyl-substituted derivatives of 1,3-propylene, 1,4-butylene and 1,5-pentylene are the residues

$-\text{C}(\text{CH}_3)_2-\text{CH}_2-\text{C}(\text{CH}_3)_2-$, $-\text{C}(\text{CH}_3)_2-\text{CH}_2\text{CH}_2-\text{C}(\text{CH}_3)_2-$ and $-\text{CH}_2\text{CH}_2-\text{C}(\text{CH}_3)_2-\text{CH}_2\text{CH}_2-$.

The compounds of formula I can be present as trans or cis isomers or cis/trans isomer mixtures. In general, the trans compounds of formula I are preferred.

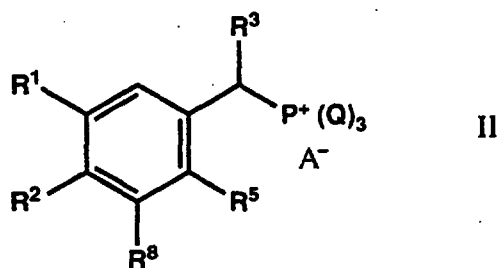
Preferred groups of compounds of formula I are those in which R^1 and R^2 together represent a residue $-\text{C}(\text{CH}_3)_2-\text{CH}_2-\text{C}(\text{CH}_3)_2-$ or $-\text{C}(\text{CH}_3)_2-\text{CH}_2\text{CH}_2-\text{C}(\text{CH}_3)_2-$; R^4 , R^5 and R^8 represent hydrogen; and R^3 represents methyl. Furthermore, the compounds of formula I in which R^1 and R^8 are lower-alkyl, especially tert.-butyl, are of particular interest. Further, 4-[2-[p-[(E)-2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)propenyl]phenoxy]ethyl]morpholine is preferred.

Typical representatives of the compounds in accordance with the invention are the compounds described in the Examples as well as the compounds listed hereinafter:

1-methyl-4-[2-[p-[(E)-2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)propenyl]phenoxy]ethyl]piperazine;
 tetrahydro-4-[2-[p-[(E)-2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)propenyl]phenoxy]ethyl]-2H-1,4-thiazine;
 1-[2-[p-[(E)-2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)propenyl]phenoxy]ethyl]pyrrole;

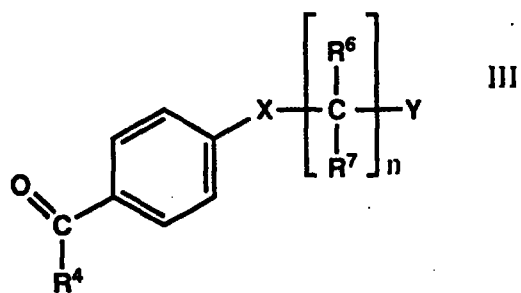
The compounds of formula I can be obtained in accordance with the invention by

a) reacting a compound of the general formula



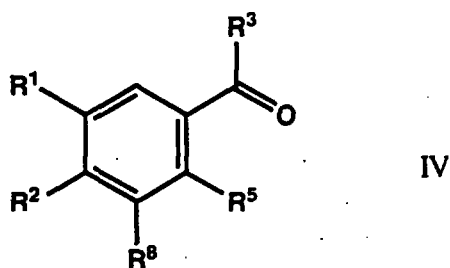
with a compound of the general formula

3

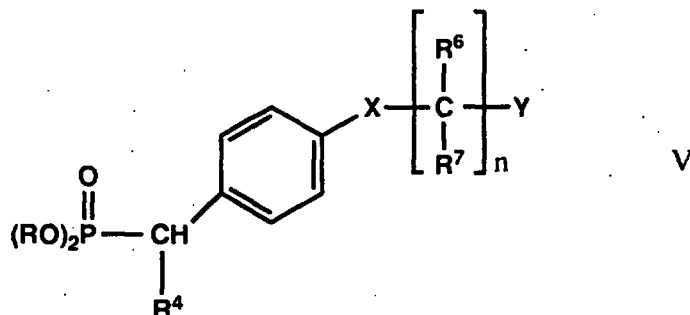


or

b) reacting a compound of the general formula

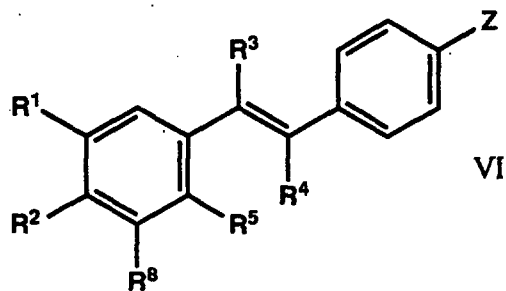


with a compound of the general formula

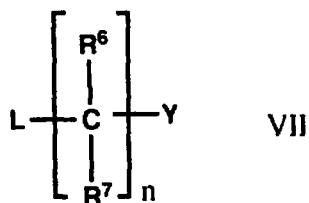


or

c) reacting a compound of the general formula



with a compound of the general formula



wherein in the foregoing formulae II-VII R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , X, Y and n have the significance given above; Q represents aryl; A^- represents an anion of an inorganic or organic acid; R represents a lower alkyl group; Z represents hydroxy, and L represents a leaving group.

The reaction in accordance with process variant a) can be carried out under the usual process conditions of a Wittig reaction. Thereby, the components are reacted with one another in the presence of an acid-binding agent, e.g. in the presence of a strong base such as e.g. butyllithium, sodium hydride, potassium tert.-butylate or the sodium salt of dimethyl sulphoxide, but especially in the presence of an ethylene oxide which is optionally substituted by lower alkyl such as 1,2-butylene oxide, optionally in a solvent, e.g. in an ether such as diethyl ether or tetrahydrofuran or in an aromatic hydrocarbon such as benzene or toluene, in a temperature range lying between room temperature and the boiling point of the reaction mixture.

Of the inorganic acid ions A^- the chloride and bromide ion or the hydrosulphate ion is preferred, of the organic acid ions the tosyloxy ion is preferred. The aryl residue Q is preferably a phenyl residue or a substituted phenyl residue such as p-tolyl.

The reaction according to process variant b) can be carried out under the usual conditions of a Horner reaction. Thereby, the components are condensed with the aid of a base and preferably in the presence of an inert organic solvent, e.g. with the aid of sodium hydride in benzene, toluene, dimethylformamide, DMSO, tetrahydrofuran, dioxan or 1,2-dimethoxyethane, or also with the aid of a sodium alcoholate in an alkanol, e.g. sodium methylate in methanol, in a temperature range lying between 0° and the boiling point of the reaction mixture.

The alkoxy residues RO are preferably lower alkoxy residues with 1-6 carbon atoms such as methoxy or ethoxy.

The reaction according to process variant c) can be carried out in an organic solvent such as dimethylformamide, conven-

iently while heating up to the reflux temperature of the reaction mixture. Examples of leaving groups L are halogen such as chlorine; mesyloxy and tosyloxy.

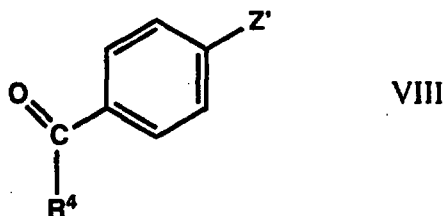
The starting compounds of general formulae II-VII, insofar as they are not known or described herein, can be prepared in analogy to known methods or methods described herein.

Compounds of general formula II and IV and their preparation are described e.g. in German Offenlegungsschriften 2 414 619 and 2 819 213 and European Patent Specification 2 742.

Compounds of general formula III can be prepared starting from p-hydroxy-substituted benzaldehyde or acetophenone, propiophenone or homologues thereof by reaction with a compound of the formula $Y(CR^6, R^7)_nCl$ in the presence of a base such as NaH.

Compounds of general formula V can be prepared starting from p-hydroxy-substituted benzoic acid esters by reaction with a compound of the formula $Y(CR^6, R^7)_nCl$, reduction of the ester group with Dibal or $LiAlH_4$ to the corresponding alcohol, replacement of the hydroxy group by bromine, e.g. by reaction with PBr_3 , and reaction of the bromide with a trialkyl phosphite to give a phosphonate of general formula V.

Compounds of general formula VI in which Z represents hydroxy can be prepared from compounds of general formula II and compounds of the general formula



wherein Z' is a protected hydroxy group, e.g. an acetoxy group,
by a Wittig reaction and subsequent cleavage of the protecting group.

Documents EP-A-58 370 and FR-A-2 599 027 describe arotinoids which have a similar spectrum of activity to the present compounds, but which can contain alkoxy or hydroxy-alkylsulphonyl groups in the terminal phenyl ring. Document EP-

A-51 187 described styryl dyestuffs which contain dimethyl-aminoethylamino groups as substituents on a phenyl ring. Document US-A-3 483 209 describes bis-(phenylalkylamino-alkyl)benzene derivatives which may be substituted by pyrrolidinoethoxy groups in the terminal phenyl rings and which have antibacterial and anti-parasitic activity. Document Chem. Pharm. Bull., 31(6) 2023-2032 (1983) describe spasmolytically-active benzisoxazolyl-phenyl-acrylonitriles which are substituted by morpholino- or piperidino-ethoxy in the phenyl ring.

The biological activity of the compounds in accordance with the invention can be determined e.g. using the test procedures described in German Offenlegungsschrift 3 715 955. In testing the activity against-chemically induced (oral administration of dimethylbenzanthracene) mammary tumours in rats the results compiled hereinafter were obtained with the compound of formula I, 4-[2-[p-[(E)-2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)-propenyl]phenoxy]ethyl]morpholine:

	Dosage [mg/kg/day] p.o.	Rats with tumours [% of controls]	Increase or decrease in the average number of tumours per rat	Increase or decrease in the average tumour volume per rat in mm ³
	50	100	+91	+550
	100	50	-73	- 77
	200	10	-96	- 99
Control group	-	100	+242	+714

The compounds of formula I can be used for the topical and systemic therapy of benign and malignant neoplasms, of pre-malignant lesions as well as, further, for the systemic and topical prophylaxis of the said conditions.

Furthermore, they are suitable for the topical and systemic therapy of acne, psoriasis and other dermatoses which are accompanied by an intensified or pathologically altered cornification, as well as of inflammatory and allergic dermatological conditions. Further, the process products of formula I can also be used for the control of mucous membrane disorders with inflammatory or degenerative or metaplastic changes. Furthermore, the compounds of formula I can be used, preferably in topical preparations, for the treatment and prophylaxis of light-damaged skin (ageing of the skin).

The compositions can be administered enterally, parenterally or topically. For enteral administration there are suitable e.g. compositions in the form of tablets, capsules, dragées, syrups, suspensions, solutions and suppositories. Preparations in the form of infusion or injection solutions are suitable for parenteral administration.

The dosages in which the preparations are administered can vary according to the mode of use and route of use as well as according to the requirements of the patients. In general, daily dosages of about 0.1-100 mg/kg, preferably 1-50 mg/kg, come into consideration for adults.

The preparations can contain inert or pharmacodynamically active additives. Tablets or granulates e.g. can contain a series of binding agents, filler materials, carrier substances or diluents. Liquid preparations can be present, for example, in the form of a sterile solution which is miscible with water. Capsules can contain a filler material or thickening agent in addition to the active substance. Furthermore, there can also be present flavour-improving additives as well as the substances usually used as preserving, stabilizing, moisture-retaining and emulsifying agents, salts for varying the osmotic pressure, buffers and other additives.

The previously mentioned carrier substances and diluents can comprise organic or inorganic substances, e.g. water, gelatine, lactose, starch, magnesium stearate, talc, gum arabic, polyalkylene glycols and the like. It is a prerequisite that all adjuvants used in the manufacture of the preparations are non-toxic.

For topical application the active substances are conveniently used in the form of salves, tinctures, creams, solutions, lotions, sprays, suspensions and the like. Salves and creams as well as solutions are preferred. These preparations intended for topical application can be manufactured by mixing the process products as active ingredients with non-toxic, inert, solid or liquid carriers which are usual in such preparations and which are suitable for topical treatment.

For topical application there are conveniently suitable about 0.1-5%, preferably 0.3-2%, solutions as well as about 0.1-5%, preferably about 0.3-2%, salves or creams.

If desired, an antioxidant e.g. tocopherol, N-methyl- γ -tocopheramine as well as butylated hydroxyanisole or butylated hydroxytoluene, can be admixed with the preparations.

The following Examples illustrate the invention further. The temperatures are given in degrees Celsius.

Example 1

332 g of [1-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)ethyl]triphenylphosphonium bromide are suspended in 1.2 l of tetrahydrofuran. 406 ml of butyllithium (1.6 molar in hexane) are added dropwise thereto at 0°C while stirring. After stirring at 0°C for 1 hour a solution of 120 g of 4-(2-morpholinoethoxy)benzaldehyde in 400 ml of tetrahydrofuran is added dropwise to the dark red solution. After stirring at room temperature for 2 hours the reaction mixture is poured into 3 l of a methanol/water mixture (6:4) and extracted with hexane. The organic phase is washed with water, dried over sodium sulphate and evaporated. The yellowish, crystalline residue is recrystallized from ethyl acetate/hexane and gives 123 g of 4-[2-[p-[(E)-2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)-propenyl]phenoxy]ethyl]morpholine in white crystals, melting point 107-109°C.

The 4-(2-morpholinoethoxy)benzaldehyde used as the starting product can be prepared as follows:

92.8 g of 4-hydroxybenzaldehyde are dissolved in 820 ml of dimethylformamide. After the addition of 228 g of 4-(2-chloroethyl)morpholine and 415 g of finely powdered potassium carbonate the reaction mixture is heated to 100°C overnight under argon and while stirring vigorously. The cooled solution is poured into 3 l of ice-water, extracted with ethyl acetate, washed with water, dried and evaporated. The residual dark oil is distilled in a high vacuum and gives 132 g of 4-(2-morpholinoethoxy)benzaldehyde as a yellowish oil, boiling point 145-150°C/33 Pa.

Example 2

In a manner analogous to Example 1, from 26 g of triphenyl [1-(1,1,3,3-tetramethyl-5-indenyl)ethyl]phosphonium bromide and 10 g of 4-(2-morpholinoethoxy)benzaldehyde there are obtained, after recrystallization from hexane, 13.6 g of 4-[2-[p-[(E)-2-(1,1,3,3-tetramethyl-5-indenyl)propenyl]-

phenoxy]ethyl]morpholine in white crystals, melting point 85-86°C.

Example 3

0.75 g of a 50% suspension of sodium hydride in mineral oil is suspended in 10 ml of dimethylformamide. A solution of 5 g of p-[(E)-2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)-propenyl]phenol in 30 ml of dimethylformamide is added dropwise thereto while stirring at 0°C. After stirring at 0° for 1 hour a solution of 3.6 g of N-(2-chloroethyl)pyrrolidine in 30 ml of dimethylformamide is added dropwise thereto. The reaction mixture is subsequently heated to 70°C for 2 hours, thereafter cooled, poured into ice-water and extracted with ethyl acetate. The organic solution is washed several times with water, dried and evaporated. There is obtained a yellow-brown oil which is purified by filtration over silica gel (eluting agent ethyl acetate + 10% ethanol) and recrystallized from hexane. There are isolated 4.5 g of 1-[2-[p-[(E)-2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)propenyl]phenoxy]ethyl]pyrrolidine in white crystals, melting point 80-82°C.

Example 4

In a manner analogous to Example 3, from 5 g of p-[(E)-2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)propenyl]phenol and 4.7 g of 1-(2-chloroethyl)-piperidine there are obtained 5.2 g of 1-[2-[p-[(E)-2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)-propenyl]phenoxy]ethyl]piperidine in white crystals, melting point 91-93°C.

Example 5

2.1 g of [1-(6,7,8,9-tetrahydro-7,7-dimethyl-5H-benzocyclohepten-2-yl)ethyl]triphenylphosphonium bromide are suspended in 10 ml of toluene and treated at 0°C with 0.5 g of potassium tert-butyrate. After stirring at room temperature for 2 hours a solution of 0.94 g of 4-(2-morpholinoethoxy)-benzaldehyde in 5 ml of toluene is added dropwise thereto and the mixture is stirred at room temperature for 3 hours. After evaporating the majority of the solvent the residue is poured into a mixture of methanol/water (6:4) and extracted several times with hexane. The organic phase is washed with water, dried and evaporated. Recrystallization of the residue from hexane gives 0.4 g of 4-[2-[p-[(E)-2-(6,7,8,9-tetrahydro-7,7-dimethyl-5H-

benzocyclophepten-2-yl)propenyl]phenoxy]ethyl]-morpholine, melting point 78-79°C.

Example 6

Analogously to Example 1, from [1-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)ethyl]triphenylphosphonium bromide and 4-[2-(tetrahydro-4'H-1,4-thiazin-4'-yl)-ethoxy]-benzaldehyde 1',1'-dioxide there is obtained, after stirring at room temperature for 16 hours, working-up, flash chromatography on silica gel with hexane/ethyl acetate (1:2) and crystallization from ethyl acetate/hexane, tetrahydro-4-[2-[p-[(E)-2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)propenyl]-phenoxy]ethyl]-2H-1,4-thiazine 1,1-dioxide of melting point 144-145°C.

The 4-[2-(tetrahydro-4'H-1,4-thiazin-4'-yl)ethoxy]-benzaldehyde 1',1'-dioxide can be prepared as follows:

11.6 g of 4-hydroxybenzaldehyde in 160 ml of dimethylformamide are heated to 100°C under argon for 2 hours with 15.6 g of 4-(2-chloroethyl)-tetrahydro-2H-1,4-thiazine 1,1-dioxide and 21.6 g of powdered potassium carbonate. After cooling the mixture is poured on to 150 g of ice, extracted three times with 300 ml of ethyl acetate and the organic phases are washed twice with 150 ml of water, dried over sodium sulphate and evaporated in a vacuum. The beige, crystalline residue (22.1 g) is used directly for the above Wittig reaction. A sample was chromatographed on silica gel with ethyl acetate/hexane (4:1) and yielded colourless crystals of melting point 101-102°C from ethyl acetate/hexane.

The manufacture of dosage forms containing the compounds of formula I can be effected in the usual manner, e.g. on the basis of the following Examples.

Example A

Hard gelatine capsules can be manufactured as follows:

<u>Ingredients</u>	<u>mg/capsule</u>
1. Spray-dried powder containing 75% of compound I	200
2. Sodium dioctylsulphosuccinate	0.2
3. Sodium carboxymethylcellulose	4.8

4.	Microcrystalline cellulose	86.0
5.	Talc	8.0
6.	Magnesium stearate	<u>1.0</u>
	Total	300

The spray-dried powder, which is based on the active substance, gelatine and microcrystalline cellulose and which has an average particle size of the active substance of $<1 \text{ m}$ (measured by means of autocorrelation spectroscopy), is moistened with an aqueous solution of sodium carboxymethylcellulose and sodium dioctylsulphosuccinate and kneaded. The resulting mass is granulated, dried and sieved, and the granulate obtained is mixed with microcrystalline cellulose, talc and magnesium stearate. The powder is filled into size 0 capsules.

Example B

Tablets can be manufactured as follows:

<u>Ingredients</u>	<u>mg/tablet</u>
1. Compound I as a finely milled powder	500
2. Lactose powd.	100
3. Maize starch white	60
4. Povidone® K30	8
5. Maize starch white	112
6. Talc	16
7. Magnesium stearate	<u>4</u>
Total	800

The finely milled substance is mixed with lactose and a portion of the maize starch. The mixture is moistened with an aqueous solution of Povidone® K30 and kneaded, and the resulting mass is granulated, dried and sieved. The granulate is mixed with the remaining maize starch, talc and magnesium stearate and pressed to tablets of suitable size.

Example C

Soft gelatine capsules can be manufactured as follows:

<u>Ingredients</u>	<u>mg/capsule</u>
1. Compound I	50
2. Triglyceride	<u>450</u>
Total	500

10 g of compound I are dissolved in 90 g of medium-chain triglyceride with stirring, inert gasification and protection from light. This solution is processed as the capsule fill mass to soft gelatine capsules containing 50 mg of active substance.

Example D

A lotion can be manufactured as follows:

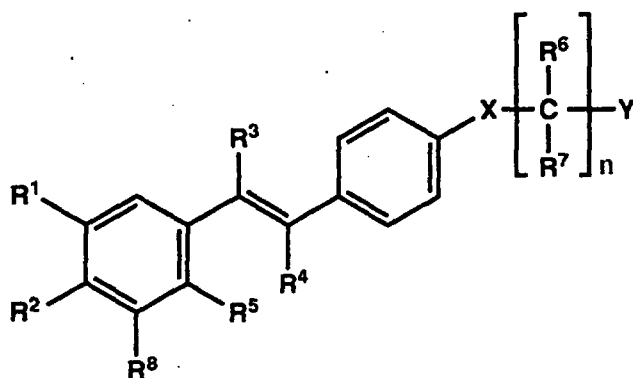
Ingredients

1.	Compound I, finely milled	3.0 g
2.	Carbopol® 934	9.6 g
3.	Sodium hydroxide	q.s. ad pH 6
4.	Ethanol, 94%	50.0 g
5.	Demineralized water	ad 100.0 g

The active substance is incorporated into the ethanol, 94%/water mixture under protection from light. Carbopol® 934 is stirred in until gelling is complete and the pH value is adjusted with sodium hydroxide.

Claims

1. Compounds of the general formula



wherein R¹ and R² each independently represent lower-alkyl; or together represent 1,3-propylene, 1,4-butylene and 1,5-pentylene and lower-alkyl-substituted derivatives thereof; one of the residues R³ and R⁴ signifies hydrogen and the other signifies hydrogen or lower-alkyl; R⁶ and R⁷ signify hydrogen or lower-alkyl; R⁵ and R⁸ signify hydrogen, lower-alkyl, lower-alkoxy or halogen; X signifies -O-; Y signifies piperidino, pyrrolidino, morpholino, piperazino, N-



10 g of compound I are dissolved in 90 g of medium-chain triglyceride with stirring, inert gasification and protection from light. This solution is processed as the capsule fill mass to soft gelatine capsules containing 50 mg of active substance.

Example D

A lotion can be manufactured as follows:

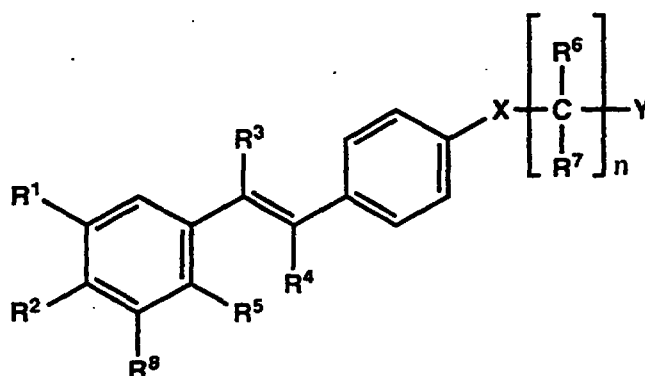
Ingredients

1.	Compound I, finely milled	3.0 g
2.	Carbopol® 934	9.6 g
3.	Sodium hydroxide	q.s. ad pH 6
4.	Ethanol, 94%	50.0 g
5.	Demineralized water	ad 100.0 g

The active substance is incorporated into the ethanol, 94%/water mixture under protection from light. Carbopol® 934 is stirred in until gelling is complete and the pH value is adjusted with sodium hydroxide.

Claims

1. Compounds of the general formula



wherein R¹ and R² each independently represent lower-alkyl; or together represent 1,3-propylene, 1,4-butylene and 1,5-pentylene and lower-alkyl-substituted derivatives thereof; one of the residues R³ and R⁴ signifies hydrogen and the other signifies hydrogen or lower-alkyl; R⁶ and R⁷ signify hydrogen or lower-alkyl; R⁵ and R⁸ signify hydrogen, lower-alkyl, lower-alkoxy or halogen; X signifies -O-; Y signifies piperidino, pyrrolidino, morpholino, piperazino, N-



methylpiperazino, thiomorpholino, thiomorpholino 4-oxide, thiomorpholino 4,4-dioxide, imidazolino or pyrrolo and n signifies 2, 3 or 4 and whereby "lower" denotes groups with 1-6 C atoms.

2. Compounds in accordance with claim 1, in which R^1 and R^2 together represent a residue $-(CH_3)_2C-CH_2CH_2-C(CH_3)_2-$ or $-(CH_3)_2C-CH_2-C(CH_3)_2-$.

3. 4-[2-[p-[(E)-2-(5,6,7,8-Tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)propenyl]phenoxy]ethyl]morpholine as the compound according to claim 1.

4. 4-[2-[p-[(E)-2-(1,1,3,3-Tetramethyl-5-indenyl)-propenyl]phenoxy]ethyl]morpholine,

1-[2-[p-[(E)-2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)propenyl]phenoxy]ethyl]pyrrolidine,

1-[2-[p-[(E)-2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)propenyl]phenoxy]ethyl]piperidine,

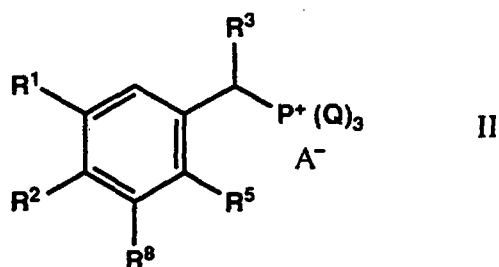
4-[2-[p-[(E)-2-(6,7,8,9-tetrahydro-7,7-dimethyl-5H-benzocyclohepten-2-yl)propenyl]phenoxy]ethyl]morpholine,

tetrahydro-4-[2-[p-[(E)-2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)propenyl]phenoxy]ethyl]-2H-1,4-thiazine 1,1-dioxide as compounds according to claim 1.

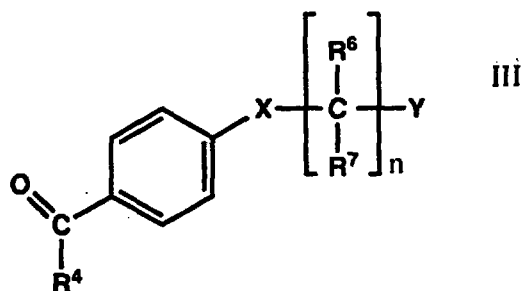
5. The compounds in accordance with claims 1-4 for use as medicaments.

6. A process for the manufacture of the compounds of general formula I of claim 1, characterized by

a) reacting a compound of the general formula

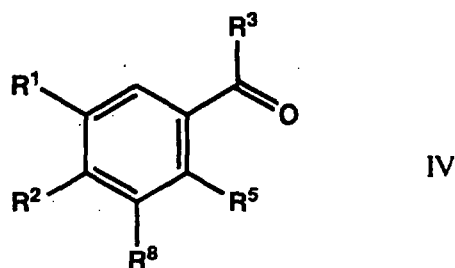


with a compound of the general formula

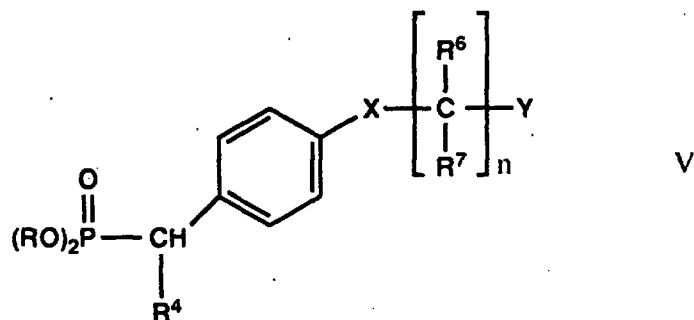


or

b) reacting a compound of the general formula

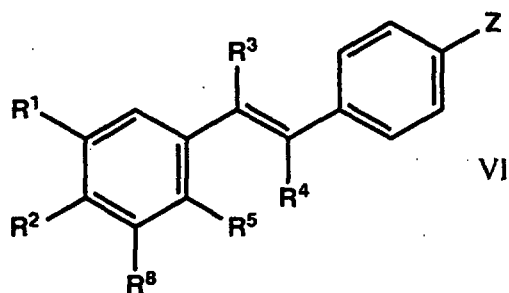


with a compound of the general formula

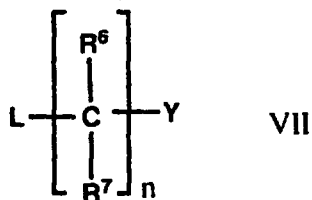


or

c) reacting a compound of the general formula



with a compound of the general formula



wherein in the foregoing formulae II-VII R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, X, Y and n have the significance given above; Q represents aryl; A⁻ represents an anion of an inorganic or organic acid; R represents a lower alkyl group; Z represents hydroxy; and L represents a leaving group.

7. Pharmaceutical preparations containing a compound in accordance with claims 1-4 and usual pharmaceutical adjuvants and carrier materials.

8. The use of the compounds in accordance with claims 1-4 as active substances in the manufacture of pharmaceutical preparations, especially for the treatment of neoplasms, dermatoses and ageing of the skin.