

**BICYCLIC AROMATIC COMPOUNDS AND THEIR USE IN HUMAN
OR VETERINARY MEDICINE, AS WELL AS IN COSMETOLOGY**

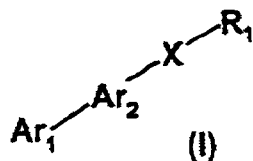
The invention relates, as novel and useful industrial products, to biaromatic compounds. It also
5 relates to the use of these novel compounds in pharmaceutical compositions intended for a use in human or veterinary medicine, or alternatively in cosmetic compositions.

The compounds according to the invention have
10 pronounced activity in the fields of cell differentiation and proliferation, and find applications more particularly in the topical and systemic treatment of dermatological complaints associated with a keratinization disorder,
15 dermatological (or other) complaints with an inflammatory and/or immunoallergic component, and dermal or epidermal proliferations, whether they are benign or malignant. These compounds can also be used in the treatment of degenerative diseases of connective
20 tissue, to combat ageing of the skin, whether this is light-induced or chronological ageing, and to treat cicatrization disorders. They moreover find an application in the ophthalmological field, in particular in the treatment of corneopathies.

25 The compounds according to the invention can also be used in cosmetic compositions for body and hair hygiene.

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The present invention relates to compounds which can be represented by the general formula (I) below:

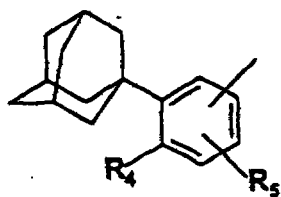


in which:

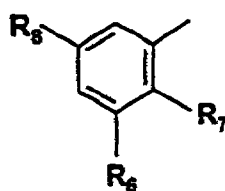
- 5 - R₁ represents (i) the radical -CH₃
 (ii) the radical -CH₂OR₂
 (iii) the radical -CO-R₃

R_2 and R_3 having the meaning given below,

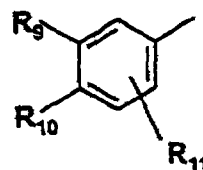
10 of formulae (a)-(c) below:



(a)



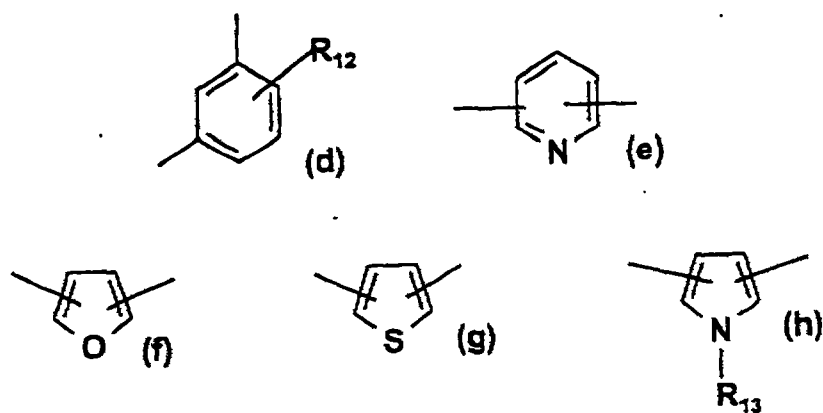
(b)



(C)

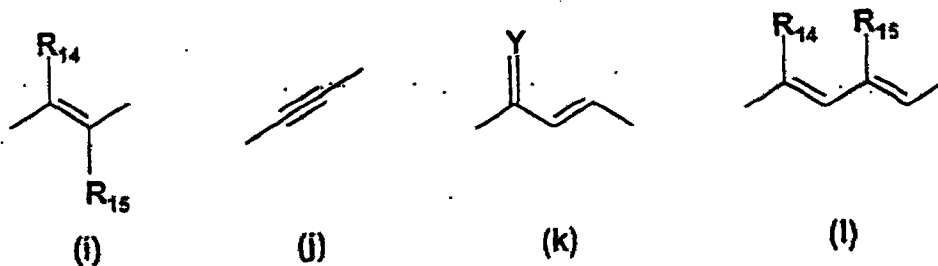
$R_4, R_5, R_6, R_7, R_8, R_9, R_{10}$ and R_{11} having the meanings given below,

- Ar₂ represents a radical chosen from the radicals of formulae (d)-(h) below:



R_{12} and R_{13} having the meaning given below,

- X represents a radical chosen from the radicals of formulae (i)-(l),



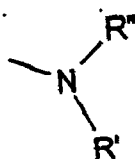
R_{14} , R_{15} and Y having the meanings given below,

5 - R_2 represents a hydrogen atom, a lower alkyl radical or a radical CO- R_{16}

R_{16} having the meaning given below,

- R_3 represents:

- (a) a hydrogen atom,
 (b) a lower alkyl radical,
 (c) a radical of formula:



- R' and R" having the meaning given below,

(d) a radical $-OR_{17}$

R_{17} having the meaning given below,

- R_4 represents a hydrogen atom, a polyether
5 radical, a lower alkyl radical or a radical OR_{18}

R_{18} having the meanings below,

- R_5 represents a hydrogen atom, a lower alkyl
radical, a polyether radical or a radical OR_{19}

R_{19} having the meanings below,

10 - R_6 represents a tert-butyl radical,

- R_7 represents a lower alkyl radical, a polyether
radical or a radical OR_{20}

R_{20} having the meanings below,

- R_6 and R_7 taken together can form, with the
15 adjacent aromatic ring, a 6-membered ring optionally
substituted with methyl groups and/or optionally
interrupted by an oxygen or sulphur atom,

- R_8 represents a tert-butyl, adamantyl, aryl or
aralkyl radical,

20 - R_9 and R_{10} taken together form, with the adjacent
aromatic ring, a 5- or 6-membered ring optionally
substituted with methyl groups and/or optionally
interrupted by an oxygen or sulphur atom,

- R_{11} represents a hydrogen atom, a lower alkyl
25 radical containing from 1 to 9 carbon atoms, a hydroxyl
radical, an alkoxy radical, a polyether radical or a
radical $-OR_{21}$

R_{21} having the meaning given below,

- R_{12} represents a hydrogen atom, a hydroxyl radical, an alkoxy radical, a polyether radical or a radical $-OR_{22}$

R_{22} having the meaning given below,

5 - R_{13} represents a hydrogen atom, a lower alkyl radical or a radical $-COR_{23}$

R_{23} having the meaning given below,

- R_{14} and R_{15} , which may be identical or different, represent a hydrogen atom or a lower alkyl radical,

10 - Y represents an oxygen atom or a CH_2 radical,

- R_{16} represents a lower alkyl radical,

- R_{17} represents a hydrogen atom, a linear or branched alkyl radical containing from 1 to 20 carbon atoms, an alkenyl radical, a mono- or polyhydroxyalkyl radical, an optionally substituted aryl or aralkyl radical or a sugar residue,

15 - R' and R'' , which may be identical or different, represent a hydrogen atom, a lower alkyl radical, a mono- or polyhydroxyalkyl radical, an optionally substituted aryl radical or an amino acid residue, or alternatively, taken together, form a heterocycle,

20 - R_{18} , R_{19} and R_{20} , which may be identical or different, represent a hydrogen atom, a lower alkyl radical, an alkenyl radical, a mono- or

25 polyhydroxyalkyl radical, an aryl radical, an optionally substituted aralkyl radical or a radical

$-(CH_2)_n-R_{24}$,

n and R_{24} having the meanings below,

- R_{21} and R_{22} , which may be identical or different, represent an alkenyl radical, a mono- or polyhydroxyalkyl radical, an aryl radical, an optionally substituted aralkyl radical or a radical

5 - $(CH_2)_n-R_{24}$,

n and R_{24} having the meanings below,

- R_{23} represents a lower alkyl radical,

- R_{24} represents a heterocycle, a monohydroxyalkyl radical, a thiol radical optionally substituted with a
10 lower alkyl, an amino radical optionally substituted with at least one lower alkyl, a radical $-COOR_{25}$, or a radical $-CON(R_{26})R_{27}$,

R_{25} , R_{26} and R_{27} having the meanings below,

- R_{25} represents a hydrogen atom or a lower alkyl
15 radical,

- R_{26} and R_{27} are identical or different and represent a hydrogen atom, a lower alkyl radical, or an optionally substituted aryl radical, or else taken together form a heterocycle,

20 - n is an integer such that $2 \leq n \leq 9$,

with the conditions that:

- when Ar_1 represents the radical of formula (c) and X represents the radicals of formula (i) or (j), then

• R_{11} represents the radical $-OR_{21}$ or a polyether

25 radical, or

• Ar_2 represents the radical of formula (d) where R_{12}

represents the radical $-OR_{22}$ or a polyether radical,

- the compounds of formula (I) are different from:

R_{11} represents a methoxymethoxy radical in an ortho position relative to the substituent Ar_2 when Ar_1 represents the radical of formula (c), X represents the radical of formula (i), R_{12} represents hydrogen and R_1 represents the radical COR_3 where R_3 represents the radical $-OR_{17}$ and R_{17} represents hydrogen,

R_{12} represents a methoxymethoxy radical in an ortho or para position relative to the substituent Ar_1 when Ar_1 represents the radical of formula (c), X represents the radical of formula (i), R_{11} represents a methyl radical in an ortho position relative to Ar_2 , R_1 represents the radical COR_3 where R_3 represents the radical $-OR_{17}$ and R_{17} represents hydrogen.

The invention is also directed towards the salts of the compounds of formula (I) when R_1 represents a carboxylic acid function, and the geometrical and optical isomers of the said compounds of formula (I).

When the compounds according to the invention are in the form of salts, they are preferably salts of an alkali metal or alkaline-earth metal, or alternatively of zinc or of an organic amine.

According to the present invention, the term "lower alkyl radical" means a radical containing from 1 to 12, preferably from 1 to 9, carbon atoms, advantageously the methyl, ethyl, propyl, isopropyl, butyl, tert-butyl, pentyl, hexyl, heptyl, nonyl, decyl and dodecyl radicals.

The expression "linear or branched alkyl

radical containing from 1 to 20 carbon atoms" means in particular the methyl, ethyl, propyl, isopropyl, tert-butyl, octyl and 2-ethylhexyl radicals.

The term "alkoxy radical" means a radical
 5 preferably containing 1 to 9 carbon atoms, in particular the methoxy, propyloxy, pentyloxy and heptyloxy radicals.

The term "monohydroxyalkyl" or
 "polyhydroxyalkyl" radical should be understood as a
 10 radical containing from 1 to 6 carbon atoms and from 1 to 5 hydroxyl groups.

Among the monohydroxyalkyl radicals, the preferred radical is one containing 2 or 3 carbon atoms, in particular a 2-hydroxyethyl, 2-hydroxypropyl
 15 or 3-hydroxypropyl radical.

Among the polyhydroxyalkyl radicals, the preferred radical is one containing from 3 to 6 carbon atoms and from 2 to 5 hydroxyl groups, such as the 2,3-dihydroxypropyl, 2,3,4-trihydroxybutyl and 2,3,4,5-
 20 tetrahydroxypentyl radicals or the pentaerythritol residue.

The term "aryl radical" preferably means a phenyl radical optionally substituted with at least one halogen, a lower alkyl, a hydroxyl, an alkoxy, a nitro
 25 function, a polyether radical or an amino function optionally protected with an acetyl group or optionally substituted with at least one lower alkyl.

The term "aralkyl radical" preferably means a

benzyl or phenethyl radical optionally substituted with at least one halogen, a lower alkyl, a hydroxyl, an alkoxy, a nitro function, a polyether radical or an amino function optionally protected with an acetyl group or optionally substituted with at least one lower alkyl.

Among the alkenyl radicals, the preferred radical is one containing from 2 to 5 carbon atoms and containing one or more ethylenic unsaturations, such as, more particularly, the allyl radical.

The term "polyether radical" means a radical containing from 1 to 6 carbon atoms and from 1 to 3 oxygen or sulphur atoms, such as the methoxymethyl ether, methoxyethoxymethyl ether or methylthiomethyl ether radicals.

Among the sugar residues, the preferred residue is one derived, for example, from glucose, galactose, mannose or glucuronic acid.

Among the amino acid residues, the preferred residue is one derived, for example, from at least one of the 20 amino acids of L or D configuration constituting mammalian proteins. They are chosen more particularly from the residues derived from lysine, glycine or aspartic acid.

Among the heterocycles, the preferred radical is a piperidino, morpholino, pyrrolidino or piperazino radical, optionally substituted in position 4 with a C_1 - C_6 alkyl radical or with a mono- or polyhydroxyalkyl

radical as defined above.

Among the compounds of formula (I) above falling within the context of the present invention, mention may be made of the following:

- 5 - 3-(3',5'-di-tert-butyl-2'-methoxy-3-biphenyl)-
acrylic acid,
- 3-(2'-benzyloxy-3',5'-di-tert-butyl-6-hydroxy-3-
biphenyl)acrylic acid,
- 3-(3',5'-di-tert-butyl-6-hydroxy-2'-pentyloxy-3-
10 biphenyl)acrylic acid,
- 3-(3',5'-di-tert-butyl-6-hydroxy-2'-methoxy-3-
biphenyl)acrylic acid,
- 3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-
tetrahydro-2-naphthyl)-4-methoxymethoxyphenyl]acrylic
15 acid,
- 3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-
tetrahydro-2-naphthyl)-4-hydroxyphenyl]acrylic acid,
- [4-methoxymethoxy-3-(3,5,5,8,8-pentamethyl-5,6,7,8-
tetrahydro-2-naphthyl)phenyl]propynoic acid,
- 20 - 3-[3-(3-propyloxy-5,5,8,8-tetramethyl-5,6,7,8-
tetrahydro-2-naphthyl)-4-methoxymethoxyphenyl]acrylic
acid,
- 3-[3-(3-pentyloxy-5,5,8,8-tetramethyl-5,6,7,8-
tetrahydro-2-naphthyl)-4-methoxymethoxyphenyl]acrylic
25 acid,
- 3-(5'-adamantan-1-yl-4'-methoxy-2'-methyl-3-
biphenyl)acrylic acid,
- 3-(5'-adamantan-1-yl-6'-hydroxy-4'-methoxy-2'-methyl-

- 3-biphenyl)acrylic acid,
- 3-(5'-adamantan-1-yl-4'-methoxy-6-methoxymethoxy-2'-methyl-3-biphenyl)acrylic acid,
- 3-{4-methoxy-3-[3-(3-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-acrylic acid,
- 5 - 3-{4-methoxy-3-[3-(4-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-acrylic acid,
- 10 3-{3-[3-(6-hydroxyhexyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid,
- 3-{3-[3-(7-hydroxyheptyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid,
- 15 - 3-{3-[3-(5-hydroxypentyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid,
- 3-{3-[3-(3-hydroxypropyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid,
- 20 - 3-[3-(1-methoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylic acid,
- 3-[3-(1-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylic acid,
- 25 - 3-(3'-adamantan-1-yl-4'-hydroxy-3-biphenyl)acrylic acid,
- 5-[4-methoxy-3-(5,5,8,8-tetramethyl-5,6,7,8-



- tetrahydro-2-naphthyl)phenyl]-3-methylpenta-2,4-dienoic acid,
- 5-[4-methoxymethoxy-3-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]-3-methylpenta-2,4-dienoic acid,
- 5 - 5-[4-hydroxy-3-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]-3-methylpenta-2,4-dienoic acid,
- 3-{3-[3-(5-tert-butoxycarbonylpentyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid,
- 10 - 3-{3-[3-(7-tert-butoxycarbonylheptyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid,
- 15 - 3-{3-[3-(7-carboxyheptyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid,
- 3-{3-[3-(5-carboxypentyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid,
- 20 - 3-{3-[3-(5-carbamoylpentyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid,
- 3-{3-[3-(7-carbamoylheptyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid,
- 25 - 3-{4-methoxy-3-[5,5,8,8-tetramethyl-3-(2-morpholin-4-ylethoxy)-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylic acid,

acid,

- 3-{4-methoxy-3-[5,5,8,8-tetramethyl-3-(2-piperidin-1-ylethoxy)-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylic acid,

5 - 3-{4-methoxy-3-[3-(2-methoxymethoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylic acid,

- 3-{4-methoxy-3-[3-(3-methoxymethoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylic acid,

10 - 3-{4-methoxy-3-[3-(4-methoxymethoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylic acid,

- 3-{4-methoxy-3-[3-(3-hydroxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-acrylic acid,

15 - 3-[4-fluoro-3-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylic acid,

- 3-{4-hydroxy-3-[3-(3-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-acrylic acid,

20 - 3-{4-hydroxy-3-[3-(4-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-acrylic acid,

25 - 3-{4-hydroxy-3-[3-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-acrylic acid,

- 3-{4-hydroxy-3-[3-(4-chlorobenzyloxy)-5,5,8,8-

- tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl)-
acrylic acid,
- 3-[4-hydroxy-3-(3-methoxymethoxy-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylic acid,
- 5 - 3-(3',5'-di-tert-butyl-6-hydroxy-2'-propyloxy-3-
biphenylyl)acrylic acid,
- 3-(3',5'-di-tert-butyl-6-hydroxy-2'-butyloxy-3-
biphenylyl)acrylic acid,
- 3-(2'-butoxy-3',5'-di-tert-butyl-6-methoxy-3-
10 biphenylyl)acrylic acid,
- 3-(3',5'-di-tert-butyl-6-methoxy-2'-propoxy-3-
biphenylyl)acrylic acid,
- 3-[4-hydroxy-3-(5,5,8,8-tetramethyl-4-propoxy-
5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylic acid,
- 15 - 3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-
tetrahydro-2-naphthyl)-4-methoxyphenyl]acrylic acid,
- ethyl 3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-
tetrahydro-2-naphthyl)-4-methoxyphenyl]acrylate,
- 3-methyl-5-[3-(3,5,5,8,8-pentamethyl-5,6,7,8-
20 tetrahydro-2-naphthyl)phenyl]penta-2,4-dienoic acid,
- 3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-
tetrahydro-2-naphthyl)-4-methoxyphenyl]prop-2-en-1-ol;
- 3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-
tetrahydro-2-naphthyl)-4-methoxyphenyl]propenal,
- 25 - N-ethyl 3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl)-4-methoxyphenyl]-
acrylamide,
- 3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-

- tetrahydro-2-naphthyl)-4-methoxyphenyl]-1-morpholin-4-yl-propenone,
- N-(4-hydroxyphenyl)-3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxyphenyl]acrylamide,
 - 5 - 5-(5'-adamantan-1-yl-4'-methoxy-2'-methyl-3-biphenyl)-3-methylpenta-2,4-dienoic acid,
 - 5-[4-methoxymethoxy-3-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]-3-methylpenta-2,4-dienoic
 - 10 acid,
 - 5-[4-hydroxy-3-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]-3-methylpenta-2,4-dienoic acid,
 - 4-[3-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]penta-2,4-dienoic acid,
 - 15 - 5-(3',5'-di-tert-butyl-2'-methoxy-3-biphenyl)-3-methylpenta-2,4-dienoic acid,
 - 5-(3',5'-di-tert-butyl-2'-propoxy-3-biphenyl)-3-methylpenta-2,4-dienoic acid,
 - 20 - 5-(2'-butoxy-3',5'-di-tert-butyl-3-biphenyl)-3-methylpenta-2,4-dienoic acid,
 - 5-(2'-butoxy-3',5'-di-tert-butyl-6-hydroxy-3-biphenyl)-3-methylpenta-2,4-dienoic acid,
 - 5-(3',5'-di-tert-butyl-6-hydroxy-2'-propoxy-3-biphenyl)-3-methylpenta-2,4-dienoic acid,
 - 25 - 5-(3',5'-di-tert-butyl-6-hydroxy-2'-methoxy-3-biphenyl)-3-methylpenta-2,4-dienoic acid.

According to the present invention, the

compounds of formula (I) which are more particularly preferred are those for which at least one, and preferably all, of the following conditions are satisfied:

- 5 - R_1 represents the radical $-CO-R_3$
 - Ar_2 represents the radicals of formula (d)
 or (e)
 - R_{11} represents the radical $-O-R_{21}$,
 - R_7 represents the radical $-O-R_{20}$.

10 A subject of the present invention is also the processes for preparing the compounds of formula (I), in particular according to the reaction scheme given in Figure 1.

 The derivatives of formula (Ia) can be
 15 obtained (Fig. 1) from aldehyde or ketone derivatives (5), according to a Horner-type reaction with a lithium or sodium derivative of a phosphonate (7), it being possible for the carbonyl compounds (5) to be obtained:

 - either by a coupling reaction between a
 20 boronic acid (3) and a halo derivative (4). This reaction is carried out in the presence of a palladium catalyst, for example tetrakis(triphenylphosphine)-palladium according to the conditions described by N. Miyaura et al. Synthetic Communications (1981)

25 11(7), 513-519.

 The boronic acid derivative (3) can be obtained, for example, from the halo derivative (1) by conversion into the lithium derivative (2) and then reaction with

trimethyl borate and hydrolysis.

- or by a coupling reaction between a zinc derivative (8) and a halo ester derivative (9) in the presence of a catalyst, for example a palladium or
5 nickel derivative (NiCl_2dppe), followed by conversion of the ester function (10) into an alcohol (11) and oxidation into an aldehyde (5).

The compounds of formula (Ib) can be obtained (Fig. 1) from the acetylenic derivative (6) by reaction
10 with n-butyllithium and then carboxylation in the presence of CO_2 .

The acetylenic compounds (6) can be obtained either:

- from the aldehyde derivatives (5) (when R_3 is a hydrogen atom), by reaction with carbon
15 tetrabromide and triphenylphosphine to give a 2'2'-dibromostyrene derivative which is converted into an acetylenic derivative by a non-nucleophilic base such as n-butyllithium in an aprotic solvent such as
20 tetrahydrofuran,

- from the ketone derivatives (5) (when R_3 is a lower alkyl) by a sequence of reactions comprising treatment with a base such as lithium diisopropylamide, then with a dialkyl phosphate chloride and again with
25 lithium diisopropylamide.

When R_1 represents a $-\text{COOH}$ radical, the compounds are prepared:

- either by protecting R_1 with a protecting

group of alkyl, allylic or tert-butyl type.

Conversion to the free form can be carried out:

- in the case of an alkyl protecting group,
5 using sodium hydroxide or lithium hydroxide in an alcoholic solvent such as methanol or in THF.

- in the case of an allylic protecting group,
using a catalyst such as certain transition metal complexes in the presence of a secondary amine such as
10 morpholine.

- in the case of a protecting group of tert-butyl type, using trimethylsilane iodide.

When R_1 represents an alcohol function, the compounds can be obtained:

15 - from the corresponding aldehyde derivatives by the action of an alkyl metal hydride, such as sodium borohydride, in an alcoholic solvent (for example methanol),

.. - from the acid derivatives by reduction with
20 lithium aluminium hydride.

When R_1 represents an aldehyde function, the compounds can be obtained from the alcohol derivatives by oxidation in the presence of manganese oxide, pyridinium dichromate or Swern's reagent.

25 When R_1 represents an amide function, the compounds can be obtained from the corresponding carboxylic derivatives by reaction with aliphatic, aromatic or heterocyclic amines either via an acid

chloride or in the presence of dicyclohexylcarbodiimide or carbonyldiimidazole.

Some of these compounds bind to the RXR receptors, some having agonist activity, others having
5 antagonist activity. The preferred compounds have antagonist activity.

The binding and transactivation properties as RXR-receptor agonists can be determined by methods known in the art, such as, for example: Levin et al.,
10 Nature 1992, **355**, 359-61; Allenby et al., Proc. Natl. Acad. Sci., 1993, **90**, 30-4.

The RXR-agonist activity can also be determined by the test described in French patent application No. 95/07301 filed on 19 June 1995 by the
15 Applicant. This test comprises the following steps: (i) a sufficient amount of a compound which is an active ligand for at least one receptor of the superfamily of steroidal/thyroid nuclear receptors other than a ligand specific for the RXR receptors and which can
20 heterodimerize with the RXRs, such as an RAR-agonist molecule, is applied topically to a part of the skin of a mammal; (ii) a molecule capable of having RXR-agonist activity is administered systemically or topically to this same part of the skin of the mammal before, during
25 or after step (i), and (iii) the response on the part of the mammal's skin thus treated is evaluated. Thus, the response to a topical application to a mammal's ear of an RAR-agonist molecule which corresponds to an

increase in the thickness of this ear can be increased by the systemic or topical administration of an RXR-receptor agonist molecule.

The RXR α -antagonist activity can be evaluated in the transactivation test by determination of the dose (IC₅₀) which gives 50% inhibition of the transactivating activity of an RXR α -selective agonist: 6-[1-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)cyclopropyl]nicotinic acid (CD 3127) according to the following procedure:

HeLa cells are co-transfected with an expression vector coding for RXR α (p565-RXR α) and a reporter plasmid containing the response element 1/2 CRBP II cloned upstream of the thymidine kinase heterologous promoter and of the chloramphenicol-acetyl-transferase (CAT) reporter gene. Eighteen hours after co-transfection, the cells are treated with a fixed concentration of CD 3127 and increasing concentrations of the molecule to be evaluated. After treatment for twenty-four hours, the CAT activity is assayed by ELISA. The fixed concentration of CD3127 used is 10⁻⁸M and corresponds to its EC₅₀.

A subject of the present invention is thus, as a medicinal product, the compounds of formula (I) as defined above.

The compounds according to the invention are particularly suitable in the following fields of treatment:

- 1) for treating dermatological complaints associated with a keratinization disorder which has a bearing on differentiation and on proliferation, in particular for treating common acne, comedones, polymorphonuclear leukocytes, rosacea, nodulocystic acne, acne conglobata, senile acne and secondary acnes such as solar, medication-related or occupational acne,
- 2) for treating other types of keratinization disorder, in particular ichthyosis, ichthyosiform states, Darier's disease, palmoplantar keratoderma, leucoplasias and leucoplasiform states, and cutaneous or mucous (buccal) lichen,
- 3) for treating other dermatological complaints associated with a keratinization disorder with an inflammatory and/or immunoallergic component and, in particular, all forms of psoriasis, whether it is cutaneous, mucous or ungual psoriasis and even psoriatic rheumatism, or alternatively cutaneous atopy, such as eczema or respiratory atopy or alternatively gingival hypertrophy; the compounds can also be used in certain inflammatory complaints which have no keratinization disorder,
- 4) for treating all dermal or epidermal proliferations, whether benign or malignant and whether they are of viral origin or otherwise, such as common warts, flat warts and verruciform epidermodysplasia, it being also possible for the oral or florid papillomatoses and the proliferations to be induced by

ultraviolet radiation, in particular in the case of basocellular and spinocellular epithelioma,

5) for treating other dermatological disorders such as bullosis and collagen diseases,

5 6) for treating certain ophthalmological disorders, in particular corneopathies,

7) for repairing or combating ageing of the skin, whether this is light-induced or chronological ageing, or for reducing actinic keratoses and pigmentations, or

10 any pathologies associated with chronological or actinic ageing,

8) for preventing or curing the stigmata of epidermal and/or dermal atrophy induced by local or systemic corticosteroids, or any other form of cutaneous

15 atrophy,

9) for preventing or treating cicatrization disorders or for preventing or repairing stretch marks, or alternatively for promoting cicatrization,

10) for combating disorders of sebaceous functioning
20 such as the hyperseborrhoea of acne or simple seborrhoea,

11) in the treatment or prevention of cancerous or precancerous states,

12) in the treatment of inflammatory complaints such

25 as arthritis,

13) in the treatment of any general or skin complaint of viral origin,

14) in the prevention or treatment of alopecia,

- 15) in the treatment of dermatological or general complaints having an immunological component,
- 16) in the treatment of complaints of the cardiovascular system such as arteriosclerosis,
- 5 hypertension, non-insulin-dependent diabetes and obesity,
- 17) in the treatment of skin disorders due to an exposure to U.V. radiation.

In the therapeutic fields mentioned above,

10 the compounds according to the invention may be employed advantageously in combination with other compounds of retinoid-type activity, with D vitamins or derivatives thereof, with corticosteroids, with anti-free-radical agents, α -hydroxy or α -keto acids or

15 derivatives thereof, or alternatively ion-channel blockers. The expression "D vitamins or derivatives thereof" means, for example, vitamin D₂ or D₃ derivatives and in particular 1,25-dihydroxyvitamin D₃.

The expression "anti-free-radical agents" means, for

20 example, α -tocopherol, superoxide dismutase, ubiquinol or certain metal-chelating agents. The expression " α -hydroxy or α -keto acids or derivatives thereof" means, for example, lactic, malic, citric, glycolic, mandelic, tartaric, glyceric or ascorbic acid or the salts,

25 amides or esters thereof. Lastly, the term "ion-channel blockers" means, for example, Minoxidil (2,4-diamino-6-piperidinopyrimidine 3-oxide) and derivatives thereof.

A subject of the present invention is also

medicinal compositions containing at least one compound of formula (I) as defined above, one of the optical or geometrical isomers thereof or one of the salts thereof.

5 A subject of the present invention is thus a novel medicinal composition intended in particular for treating the abovementioned complaints, and which is characterized in that it comprises, in a pharmaceutically acceptable support which is compatible
10 with the mode of administration selected for this composition, at least one compound of formula (I), one of the optical or geometrical isomers thereof or one of the salts thereof.

 The compounds according to the invention may
15 be administered enterally, parenterally, topically or ocularly.

 Via the enteral route, the medicinal products may be in the form of tablets, gelatin capsules, sugar-coated tablets, syrups, suspensions, solutions,
20 powders, granules, emulsions, microspheres or nanospheres or polymeric or lipid vesicles which enable controlled release. Via the parenteral route, the compositions may be in the form of solutions or suspensions for infusion or for injection.

25 The compounds according to the invention are generally administered at a daily dose of about 0.01 mg/kg to 100 mg/kg of body weight taken in 1 to 3 doses.

Via the topical route, the pharmaceutical compositions based on compounds according to the invention are more particularly intended for the treatment of the skin and the mucosae and may be in the form of ointments, creams, milks, salves, powders, impregnated pads, solutions, gels, sprays, lotions or suspensions. They may also be in the form of microspheres or nanospheres or polymeric or lipid vesicles or polymeric patches and hydrogels which enable controlled release. These topical-route compositions may either be in anhydrous form or in aqueous form, depending on the clinical indication.

Via the ocular route, they are mainly eyedrops.

These compositions for topical or ocular use contain at least one compound of formula (I) as defined above, or one of the optical or geometrical isomers thereof or alternatively one of the salts thereof, at a concentration preferably of between 0.001% and 5% by weight relative to the total weight of the composition.

The compounds of formula (I) according to the invention also find an application in the cosmetic field, in particular in body and hair hygiene and especially for treating skin types with a tendency towards acne, for promoting the regrowth of the hair, for combating hair loss, for combating the greasy appearance of the skin or the hair in protection against the harmful effects of the sun or in the

treatment of physiologically dry skin types, and for preventing and/or combating light-induced or chronological ageing.

In the cosmetic field, the compounds
5 according to the invention can moreover be employed advantageously in combination with other compounds of retinoid-type activity, with D vitamins or derivatives thereof, with corticosteroids, with anti-free-radical agents, α -hydroxy or α -keto acids or derivatives
10 thereof, or alternatively with ion-channel blockers, all of these various products being as defined above.

The present invention is thus also directed towards a cosmetic composition which is characterized in that it comprises, in a cosmetically acceptable
15 support which is suitable for topical application, at least one compound of formula (I) as defined above or one of the optical or geometrical isomers thereof or one of the salts thereof, it being possible for this cosmetic composition to be, in particular, in the form
20 of a cream, a milk, a lotion, a gel, microspheres or nanospheres or polymeric or lipid vesicles, a soap or a shampoo.

The concentration of compound of formula (I) in the cosmetic compositions according to the invention
25 is advantageously between 0.001% and 3% by weight relative to the entire composition.

The medicinal and cosmetic compositions according to the invention can also contain inert

additives or even pharmacodynamically or cosmetically active additives or combinations of these additives and, in particular: wetting agents; depigmenting agents such as hydroquinone, azelaic acid, caffeic acid or
 5 kojic acid; emollients; moisturizing agents such as glycerol, PEG 400, thiamorpholinone and derivatives thereof, or urea; anti-seborrhoea or anti-acne agents such as S-carboxymethylcysteine, S-benzylcysteamine, the salts and the derivatives thereof, or benzoyl
 10 peroxide; antibiotics such as erythromycin and esters thereof, neomycin, clindamycin and esters thereof, and tetracyclines; antifungal agents such as ketoconazole or 4,5-polymethylene-3-isothiazolinones; agents for promoting the regrowth of the hair, such as Minoxidil
 15 (2,4-diamino-6-piperidinopyrimidine 3-oxide) and derivatives thereof, Diazoxide (7-chloro-3-methyl-1,2,4-benzothiadiazine 1,1-dioxide) and Phenytoin (5,5-diphenylimidazolidine-2,4-dione); non-steroidal anti-inflammatory agents; carotenoids and, in
 20 particular, β -carotene; anti-psoriatic agents such as anthraline and derivatives thereof and, lastly, eicosa-5,8,11,14-tetraynoic acid and eicosa-5,8,11-triynoic
 acid, the esters and the amides thereof.

The compositions according to the invention
 25 may also contain flavour-enhancing agents, preserving agents such as para-hydroxybenzoic acid esters, stabilizing agents, moisture regulators, pH regulators, osmotic pressure modifiers, emulsifying agents, UV-A

and UV-B screening agents, and antioxidants such as α -tocopherol, butylhydroxyanisole or butylhydroxytoluene.

Several examples for obtaining active compounds of formula (I) according to the invention, as well as various concrete formulations based on such compounds, will now be given for illustrative purposes and with no limiting nature.

A. EXAMPLES OF COMPOUNDS

EXAMPLE 1

3-(3',5'-Di-tert-butyl-2'-methoxy-3-biphenyl)acrylic acid

(a) 2-Bromo-4,6-di-tert-butylanisole

6 g (21 mmol) of 2-bromo-4,6-di-tert-butylphenol and 60 ml of DMF are introduced into a round-bottomed flask under a stream of nitrogen. 694 mg (29 mmol) of sodium hydride (80% in oil) are added portionwise and the mixture is stirred until the evolution of gas has ceased. 1.45 ml (23.2 mmol) of iodomethane are then added and the mixture is stirred at room temperature for three hours. The reaction medium is poured into ice-cold water and extracted with ethyl acetate, and the organic phase is separated out after settling has taken place, dried over magnesium sulphate and evaporated. The residue obtained is purified by chromatography from a column of silica eluted with heptane. After evaporation of the solvents, 6.1 g (98%) of the expected product are collected in

the form of a colourless oil.

^1H NMR (d, CDCl_3): 1.3 (s, 9H); 1.4 (s, 9H); 3.9 (s, 3H); 7.3 (d, $J = 2.3$ Hz, 1H); 7.4 (d, $J = 2.3$ Hz, 1H).

(b) 2-Methoxy-3,5-di-tert-butylphenylboronic acid.

5 6 g (20.1 mmol) of 2-bromo-4,6-di-tert-butylanisole and 50 ml of THF are introduced into a three-necked flask under a stream of nitrogen. 9.7 ml (24.1 mmol) of n-butyllithium (2.5M in hexane) are added dropwise, at -78°C , and the mixture is stirred
10 for 15 minutes. At this same temperature, 7 ml (30.1 mmol) of triisopropyl borate are added with stirring for 2 hours. 20 ml of hydrochloric acid (1N) are added at -50°C and the mixture is allowed to warm to room temperature. The reaction medium is extracted
15 with ethyl ether and the organic phase is separated out after settling has taken place, dried over magnesium sulphate and evaporated. The solid obtained is triturated from heptane, filtered off and dried. 4 g (75%) of the expected boronic acid are collected, which
20 product is used without further purification for the rest of the synthesis.

^1H NMR (d, CDCl_3): 1.3 (s, 9H); 1.4 (s, 9H); 3.8 (s, 3H); 6.0 (s, 2H); 7.5 (d, $J = 2.5$ Hz, 1H); 7.7 (d, $J = 2.5$ Hz, 1H).

25 (c) 3-(3',5'-Di-tert-butyl-2'-methoxy-3-biphenyl)acrylic acid

2.2 g (8.3 mmol) of 2-methoxy-3,5-di-tert-butylphenylboronic acid, 942 mg (4.15 mmol) of 3-bromocinnamic acid and 70 ml of DME are introduced into a three-necked flask under a stream of nitrogen.

5 11.4 ml of aqueous potassium carbonate solution (2M) are added dropwise and the reaction medium is degassed.

144 mg (0.12 mmol) of

tetrakis(triphenylphosphine)palladium(0) are then added and the mixture is refluxed for 20 hours. Water and

10 ethyl acetate are added to the reaction medium and this mixture is acidified to pH 1 with hydrochloric acid.

The organic phase is separated out after settling has taken place, washed with water, dried over magnesium sulphate and evaporated. The residue obtained is

15 purified by chromatography on a column of silica eluted with a mixture of heptane and ethyl acetate (75/25).

After evaporation of the solvents, 990 mg (66%) of 3-(3',5'-di-tert-butyl-2'-methoxy-3-biphenyl)acrylic acid with a melting point of 182-3°C are collected.

20 ¹H NMR (d, DMSO): 1.1 (s, 9H); 1.2 (s, 9H); 3.0 (s, 3H);

6.4 (d, J = 16 Hz, 1H); 7.0 (d, J = 2.3 Hz, 1H); 7.1

(d, J = 2.3 Hz, 1H); 7.3-7.6 (m, 5H).

EXAMPLE 23-(2'-Benzyloxy-di-tert-butyl-6-hydroxy-3-biphenyl)acrylic acid

(a) 3-Bromo-4-hydroxybenzaldehyde

5 15 g (123 mmol) of 4-hydroxybenzaldehyde,
687 mg (12.3 mmol) of iron powder, 200 ml of
dichloromethane and 10 ml of THF are introduced into a
500 ml three-necked flask under nitrogen atmosphere.
The mixture is cooled to 0°C, 19.60 g (123 mmol) of
10 bromine are added dropwise and this mixture is stirred
at room temperature for one hour. Saturated sodium
thiosulphate solution is added, the dichloromethane is
evaporated off, the residue is extracted with ethyl
acetate, the organic phase is separated out after
15 settling has taken place, washed with water to neutral
pH and dried over magnesium sulphate, and the solvents
are evaporated off. The residue obtained is purified by
chromatography on a column of silica eluted with an
eluting system composed of 80% heptane and 20%
20 dichloromethane. After evaporation of the solvents,
9.7 g (39%) of a white cottony powder with a melting
point of 121-124°C are collected.

(b) 3-Bromo-4-methoxymethoxybenzaldehyde

9 g (44.7 mmol) of 3-bromo-4-hydroxy-
25 benzaldehyde, 30 ml of THF and 30 ml of DMF are
introduced into a 250 ml round-bottomed flask under a
nitrogen atmosphere. 1.48 g (49.2 mmol) of 80% sodium

hydride are added portionwise, the mixture is stirred for thirty minutes at room temperature and 4.32 g (52.7 mmol) of methoxymethyl chloride are added dropwise. The reaction medium is stirred for one hour at room temperature, acidified with 1N hydrochloric acid and extracted with ethyl acetate. The organic phase is separated out after settling has taken place, washed with water to neutral pH and dried over magnesium sulphate, and the solvents are evaporated off. 11.5 g (100%) of an orange-coloured oil are collected.

(c) Ethyl 3-(3-bromo-4-methoxymethoxyphenyl)acrylate.

12 g (53 mmol) of triethyl phosphonoacetate and 50 ml of THF are introduced into a three-necked flask under a stream of nitrogen. 2.45 g (81.6 mmol) of sodium hydride (80% in oil) are added portionwise and the mixture is stirred until the evolution of gas has ceased. A solution of 10 g (40.8 mmol) of 3-bromo-4-methoxymethoxybenzaldehyde in 50 ml of THF is then added and this mixture is stirred at room temperature for one hour. The reaction medium is poured into water, acidified with hydrochloric acid and extracted with ethyl acetate, and the organic phase is separated out after settling has taken place, dried over magnesium sulphate and evaporated. The residue obtained is purified by chromatography on a column of silica eluted with a mixture of heptane and ethyl acetate (90-10).

After evaporation of the solvents, 9.6 g (74%) of ethyl 3-(3-bromo-4-methoxymethoxyphenyl)acrylate with a melting point of 63-65°C are collected.

(d) 2-Benzyloxy-3,5-di-tert-butylbromobenzene

5 In a similar manner to that of Example 1(a), by reaction of 6 g (21 mmol) of 2-bromo-4,6-di-tert-butylphenol with 2.8 ml (23.2 mmol) of benzyl bromide, 7.4 g (94%) of the expected product are obtained in the form of a colourless oil.

10 ¹H NMR (d, CDCl₃): 1.3 (s, 9H); 1.4 (s, 9H); 5.1 (s, 2H); 7.25-7.45 (m, 5H); 7.55-7.6 (m, 2H).

(e) 2-Benzyloxy-3,5-di-tert-butylphenylboronic acid

In a similar manner to that of Example 1(b), by reaction of 7.2 g (19.3 mmol) of 2-benzyloxy-3,5-di-tert-butylbromobenzene with 6.7 ml (29 mmol) of triisopropyl borate, 4.29 g (65%) of the expected boronic acid are obtained.

15 ¹H NMR (d, CDCl₃): 1.35 (s, 9H); 1.45 (s, 9H); 5.1 (s, 2H); 5.9 (s, 2H); 7.3-7.55 (m, 6H); 7.7 (d, J = 2.5 Hz, 1H);

(f) Ethyl 3-(2'-benzyloxy-3',5'-di-tert-butyl-6'-methoxymethoxy-3-biphenyl)acrylate

In a similar manner to that of Example 1(c), by reaction of 3.24 g (9.53 mmol) of 2-benzyloxy-3,5-di-tert-butylphenylboronic acid with 2 g (6.35 mmol) of

25

ethyl 3-(3-bromo-4-methoxymethoxyphenyl)acrylate, 2.4 g (71%) of the expected ethyl ester are obtained.

¹H NMR (d, CDCl₃): 1.1 (t, J = 7 Hz, 3H); 1.35 (s, 9H); 1.45 (s, 9H); 3.5 (s, 3H); 4.25 (q, J = 7 Hz, 2H); 4.5 (s, 2H); 5.1 (s, 2H); 6.3 (d, J = 16 Hz, 1H); 6.9-7.0 (m, 2H); 7.15-7.25 (m, 5H); 7.4-7.5 (m, 2H); 7.6-7.7 (m, 2H).

(g) Ethyl 3-(2'-benzyloxy-3',5'-di-tert-butyl-6-hydroxy-3-biphenyl)acrylate

2.14 g (4 mmol) of the above ethyl ester, 10 ml of THF and 10 ml of ethanol are introduced into a round-bottomed flask. 1 ml of concentrated sulphuric acid is added and the mixture is stirred at room temperature for 24 hours. The reaction medium is poured into water and extracted with ethyl acetate, and the organic phase is separated out after settling has taken place, washed with water, dried over magnesium sulphate and evaporated. The residue obtained is triturated from heptane, filtered and dried. 1.93 g (100%) of the expected product are collected.

¹H NMR (d, CDCl₃): 1.3 (t, J = 7 Hz, 3H); 1.35 (s, 9H); 1.45 (s, 9H); 4.25 (q, J = 7 Hz, 2H); 4.5-4.7 (m, 2H); 6.4 (d, J = 16 Hz, 1H); 7.0 (d, J = 8 Hz, 1H); 7.0-7.1 (m, 2H); 7.25 (s, 1H); 7.3-7.4 (m, 3H); 7.45-7.50 (m, 2H); 7.6 (s, 1H); 7.7 (d, J = 6 Hz, 1H).

(h) 3-(2'-benzyloxy-3',5'-di-tert-butyl-6-hydroxy-3-

biphenyl)acrylic acid

1.93 g (4 mmol) of ethyl 3-(2'-benzyloxy-3',5'-di-tert-butyl-6-hydroxy-3-biphenyl)acrylate, 20 ml of THF, 2 ml of methanol and 4 ml of sodium hydroxide solution (10N) are introduced into a round-bottomed flask. The reaction medium is refluxed for 12 hours, poured into water, acidified to pH 1 with hydrochloric acid and extracted with ethyl acetate, and the organic phase is separated out after settling has taken place, dried over magnesium sulphate and evaporated. The residue obtained is triturated from heptane, filtered and dried. 1.6 g (87%) of 3-(2'-benzyloxy-3',5'-di-tert-butyl-6-hydroxy-3-biphenyl)acrylic acid with a melting point of 230-1°C are collected.

¹H NMR (d, CDCl₃): 1.3 (s, 9H); 1.5 (s, 9H); 4.6 (s, 2H); 6.3 (d, J = 16 Hz, 1H); 7.0-7.1 (m, 3H); 7.2-7.3 (m, 4H); 7.4-7.5 (m, 2H); 7.6 (s, 1H); 7.7 (d, J = 16 Hz, 1H); 8.1 (m, 1H).

20 EXAMPLE 3

3-(3',5'-Di-tert-butyl-6-hydroxy-2'-pentyloxy-3-biphenyl)acrylic acid

(a) 3,5-Di-tert-butyl-2-pentyloxybromobenzene

In a similar manner to that of Example 1(a), by reaction of 6 g (21 mmol) of 2-bromo-4,6-di-tert-butylphenol with 3 ml (23.2 mmol) of iodopentane, 7.3 g (98%) of the expected product are obtained in the form

of a colourless oil.

¹H NMR (d, CDCl₃): 0.9 (t, J = 7 Hz, 3H); 1.35 (s, 9H);
1.45 (s, 9H); 1.3-1.5 (m, 4H); 1.8-2.0 (m, 2H); 4.0 (q,
J = 7 Hz, 2H); 7.3 (d, J = 2.5 Hz, 1H); 7.4 (d, J = 2.5
5 Hz, 1H).

(b) 3,5-Di-tert-butyl-2-pentyloxyphenylboronic acid

In a similar manner to that of Example 1(b),
by reaction of 7.26 g (20.5 mmol) of 3,5-di-tert-butyl-
2-pentyloxybromobenzene with 7.1 ml (30.75 mmol) of
10 triisopropyl borate, 6.4 g (98%) of the expected
boronic acid are obtained.

¹H NMR (d, CDCl₃): 0.9 (t, J = 7 Hz, 3H); 1.2-1.5 (m,
4H); 1.35 (s, 9H); 1.45 (s, 9H); 1.85-1.95 (m, 2H);
3.8-4.0 (m, 2H); 6.1 (s, 1H); 6.8-7.6 (m, 3H).

15 (c) Ethyl 3-(3',5'-di-tert-butyl-6-methoxymethoxy-2'-
pentyloxy-3-biphenyl)acrylate

In a similar manner to that of Example 1(c),
by reaction of 3 g (9.5 mmol) of 3,5-di-tert-butyl-2-
pentyloxyphenylboronic acid with 2 g (6.35 mmol) of
20 ethyl 3-(3-bromo-4-methoxymethoxyphenyl)acrylate, 2.1 g
(65%) of the expected ethyl ester are obtained.

¹H NMR (d, CDCl₃): 0.7 (t, J = 7 Hz, 3H); 1.0 (m, 4H);
1.2 (m, 5H); 1.25 (s, 9H); 1.35 (s, 9H); 3.2-3.3 (m,
2H); 3.35 (s, 3H); 4.2 (q, J = 7 Hz, 2H); 5.1 (s, 2H);
25 6.25 (d, J = 16 Hz, 1H); 7.05 (d, J = 2.5 Hz, 1H); 7.15
(d, J = 8.5 Hz, 1H); 7.3 (d, J = 2.5 Hz, 1H); 7.4 (dd,

$J = 8.5$ Hz and 2.5 Hz, $1H$); 7.5 (d, $J = 2.5$ Hz, $1H$);
 7.6 (d, $J = 16$ Hz, $1H$).

(d) Ethyl 3-(3',5'-di-tert-butyl-6-hydroxy-2'-
 pentyloxy-3-biphenyl)acrylate

5 In a similar manner to that of Example 2(g),
 starting with 1.84 g (3.6 mmol) of the above ethyl
 ester, 1.6 g (88%) of the expected product are
 obtained.

1H NMR (d, $CDCl_3$): 0.85 (t, $J = 7$ Hz, $3H$); $0.9-1.3$ (m,
 10 $7H$); 1.35 (s, $9H$); 1.45 (s, $9H$); $1.45-1.6$ (m, $2H$); $3.5-$
 3.65 (m, $2H$); 4.3 (q, $J = 7$ Hz, $2H$); 6.35 (d, $J = 16$
 Hz, $1H$); 7.05 (d, $J = 8$ Hz, $1H$); 7.15 (d, $J = 2.4$ Hz,
 $1H$); 7.4 (d, $J = 2.4$ Hz, $1H$); $7.5-7.6$ (m, $2H$); 7.7 (d,
 $J = 16$ Hz, $1H$).

15 (e) 3-(3',5'-Di-tert-butyl-6-hydroxy-2'-pentyloxy-3-
 biphenyl)acrylic acid

In a similar manner to that of Example 2(h),
 starting with 1.62 g (3.2 mmol) of ethyl 3-(3',5'-di-
 tert-butyl-6-hydroxy-2'-pentyloxy-3-

20 biphenyl)acrylate, 1.2 g (86%) of 3-(3',5'-di-tert-
 butyl-6-hydroxy-2'-pentyloxy-3-biphenyl)acrylic acid
 with a melting point of $166-7^\circ C$ are obtained.

1H NMR (d, $CDCl_3$): 0.8 (t, $J = 7$ Hz, $3H$); $1.1-1.25$ (m,
 $4H$); 1.35 (s, $9H$); 1.45 (s, $9H$); 1.6 (t, $J = 7$ Hz, $2H$);
 25 $3.5-3.6$ (m, $2H$); 6.4 (d, $J = 16$ Hz, $1H$); 7.1 (d, $J = 8$
 Hz, $1H$); 7.2 (s, $1H$); 7.4 (m, $2H$); $7.5-7.6$ (m, $2H$); 7.8

(d, $J = 16$ Hz, 1H).

EXAMPLE 4

3-(3',5'-Di-tert-butyl-6-hydroxy-2'-methoxy-3-biphenyl)acrylic acid

- 5 (a) Ethyl 3-(3',5'-di-tert-butyl-2'-methoxy-6-methoxymethoxy-3-biphenyl)acrylate

In a similar manner to that of Example 1(c), by reaction of 2.18 g (8.26 mmol) of 3,5-di-tert-butyl-2-pentyloxyphenylboronic acid with 2 g (6.35 mmol) of
10 ethyl 3-(3-bromo-4-methoxymethoxyphenyl)acrylate, 2 g (70%) of the expected ethyl ester are obtained.

^1H NMR (d, CDCl_3): 1.2-1.3 (m, 3H); 1.35 (s, 9H); 1.45 (s, 9H); 3.3 (s, 3H); 3.4 (s, 3H); 3.8 (q, $J = 7$ Hz, 2H); 5.15 (s, 2H); 6.35 (d, $J = 16$ Hz, 1H); 7.1 (d, $J =$
15 2 Hz, 1H); 7.2 (d, $J = 8$ Hz, 1H); 7.35 (d, $J = 2$ Hz, 1H); 7.5 (dd, $J = 8$ Hz and $J = 2$ Hz, 1H); 7.6 (d, $J = 2$ Hz, 1H); 7.7 (d, $J = 16$ Hz, 1H).

- (b) Ethyl 3-(3',5'-di-tert-butyl-6-hydroxy-2'-methoxy-3-biphenyl)acrylate

20 In a similar manner to that of Example 2(g), starting with 1.45 g (3.17 mmol) of the above ethyl ester, 1.25 g (96%) of the expected product are

obtained:

^1H NMR (d, CDCl_3): 1.1-1.2 (m, 4H); 1.35 (s, 9H); 1.45 (s, 9H); 3.5 (s, 3H); 4.25 (q, $J = 7$ Hz, 2H); 6.35 (d,
25 $J = 16$ Hz, 1H); 7.05 (d, $J = 8$ Hz, 1H); 7.15 (d, $J =$

2.3 Hz, 1H); 7.4 (d, $J = 2.3$ Hz, 1H); 7.5-7.6 (m, 2H);
7.7 (d, $J = 16$ Hz, 1H).

(c) 3-(3',5'-Di-tert-butyl-6-hydroxy-2'-methoxy-3-biphenyl)acrylic acid

5 In a similar manner to that of Example 2(h), starting with 1.23 g (3 mmol) of ethyl 3-(3',5'-di-tert-butyl-6-hydroxy-2'-methoxy-3-biphenyl)acrylate, 800 mg (69%) of 3-(3',5'-di-tert-butyl-6-hydroxy-2'-methoxy-3-biphenyl)acrylic acid with a melting point
10 of 166-7°C are obtained.

^1H NMR (d, CDCl_3): 1.35 (s, 9H); 1.45 (s, 9H); 3.5 (s, 3H); 6.4 (d, $J = 16$ Hz, 1H); 7.1 (d, $J = 8$ Hz, 1H); 7.2 (d, $J = 2.5$ Hz, 1H); 7.45 (d, $J = 2.5$ Hz, 1H); 7.5-7.6 (m, 2H); 7.8 (d, $J = 16$ Hz, 1H).

15 EXAMPLE 5

3-(3-(3-Benzoyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxymethoxyphenyl)acrylic acid

(a) 3-Benzoyloxy-2-bromo-5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalene
20 tetrahydronaphthalene

In a similar manner to that of Example 1(a), by reaction of 5 g (25 mmol) of 3-hydroxy-2-bromo-5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalene with 3.5 ml (29.5 mmol) of benzyl bromide, 6.15 g (66%) of
25 the expected product are obtained.

^1H NMR (CDCl_3): 1.20 (s, 6H); 1.24 (s, 6H); 1.64 (s,

4H); 5.12 (s, 2H); 6.82 (s, 1H Ar); 7.21 to 7.50 (m, 6H Ar).

(b) 3-Benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylboronic acid

5 In a similar manner to that of Example 1(b), by reaction of 6.15 g (16.5 mmol) of 3-benzyloxy-2-bromo-5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalene with 5.7 ml (24.7 mmol) of triisopropyl borate, 3.5 g (62%) of the expected boronic acid with a melting point
10 of 125-6°C are obtained.

¹H NMR (CDCl₃): 1.26 (s, 6H); 1.29 (s, 6H); 1.68 (s, 4H); 5.12 (s, 2H); 5.83 (s, 2H); 6.88 (s, 1H Ar); 7.35 to 7.43 (m, 5H Ar); 7.80 (s, 1H Ar).

(c) Ethyl 3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxymethoxy-phenyl]acrylate
15

In a similar manner to that of Example 1(c), by reaction of 3.4 g (10 mmol) of 3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylboronic acid
20 with 3.17 g (10 mmol) of ethyl 3-(3-bromo-4-methoxymethoxy-phenyl)acrylate, 3 g (56%) of the expected ethyl ester are obtained.

¹H NMR (CDCl₃): 1.27 (s, 12H); 1.33 (t, J = 7.1 Hz, 3H); 1.69 (s, 4H); 3.31 (s, 3H); 4.25 (q, J = 7.1 Hz, 2H);
25 5.01 (s, 2H); 5.06 (s, 2H); 6.32 (d, J = 15.9 Hz, 1H); 6.89 (s, 1H Ar); 7.19 (s, 1H Ar); 7.21 to 7.31 (m, 6H

Ar), 7.46 (dd, $J = 8.6$ Hz, $J = 2.3$ Hz, 1H Ar); 7.52 (d, $J = 2.3$ Hz, 1H Ar); 7.567 (d, $J = 15.9$ Hz, 1H).

(d) 3-[3-(3-Benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxymethoxy-phenyl]acrylic
5 acid

In a similar manner to that of Example 2(h), starting with 1.3 g (2.46 mmol) of the above ethyl ester, 1 g (90%) of 3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxymethoxyphenyl]acrylic acid with a melting point
10 of 161-3°C are obtained.

^1H NMR (CDCl_3): 1.27 to 1.28 (m, 12H); 1.69 (s, 4H); 3.32 (s, 3H); 5.01 (s, 2H); 5.07 (s, 2H); 6.33 (d, $J = 16$ Hz, 1H); 6.70 (s, 1H Ar); 7.20 (s, 1H Ar); 7.21 to
15 7.31 (m, 6H Ar); 7.48 (dd, $J = 8.6$ Hz, $J = 2.1$ Hz, 1H Ar); 7.55 (d, $J = 2$ Hz, 1H Ar); 7.55 (d, $J = 2$ Hz, 1H).

^{13}C NMR (CDCl_3): 1099, 32.11, 33.91, 34.69, 35.33, 56.20, 70.76, 95.02, 111.13, 115.23, 115.36, 125.11, 125.76, 127.08, 127.61, 127.68, 128.49, 129.25, 129.76,
20 129.83, 132.29, 137.37, 137.72, 145.74, 147.05, 153.85, 157.49; 172.54.

EXAMPLE 6

3-[3-(3-Benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-hydroxyphenyl]acrylic acid
25 (a) Ethyl 3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-hydroxyphenyl]acrylate

In a similar manner to that of Example 2(g), starting with 1.8 g (3.4 mmol) of ethyl 3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxymethoxyphenyl]acrylate, 1.2 g (72%) of ethyl 3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-hydroxyphenyl]acrylate are obtained.

¹H NMR (CDCl₃): 1.25 to 1.29 (m, 12H); 1.31 (t, J = 7.1 Hz, 3H); 1.70 (s, 4H); 4.26 (q, J = 7.1 Hz, 2H); 5.07 (s, 2H); 6.33 (d, J = 16 Hz, 1H); 6.81 (s, 1H OH); 6.99 (s, 1H Ar); 7.01 (d, J = 9.8 Hz, 1H Ar); 7.23 (s, 1H Ar); 7.26 to 7.32 (m, 5H Ar); 7.42 (d, J = 2.1 Hz, 1H Ar); 7.49 (dd, J = 8.3 Hz, J = 2.1 Hz, 1H Ar); 7.69 (d, J = 16 Hz, 1H).

(b) 3-[3-(3-Benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-hydroxyphenyl]acrylic acid

In a similar manner to that of Example 2(h), starting with 1.2 g (2.47 mmol) of the above ethyl ester, 980 mg (98%) of 3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-hydroxyphenyl]acrylic acid with a melting point of 123-4°C are obtained.

¹H NMR (CDCl₃): 1.28 to 1.30 (m, 12H); 1.70 (s, 4H); 5.08 (s, 2H); 6.35 (d, J = 15.7 Hz, 1H); 6.38 (s, 1H); 7.00 (s, 1H Ar); 7.04 (d, J = 7.5 Hz, 1H Ar); 7.24 (s, 1H Ar); 7.25 to 7.37 (m, 5H Ar); 7.45 (d, J = 2 Hz, 1H Ar); 7.52 (dd, J = 8.4 Hz, J = 2 Hz, 1H Ar); 7.80 (d, J

= 15.9 Hz, 1H).

¹³C NMR (CDCl₃): 31.88, 32.02, 34.00, 34.65, 34.99,
35.08, 72.30, 112.66, 114.70, 118.16, 124.49, 127.07,
127.23, 127.64, 128.30, 128.68, 129.22, 130.55, 132.19,
5 136.06, 139.95, 147.01, 147.08, 152.48, 156.45, 172.75.

EXAMPLE 7

[4-Methoxymethoxy-3-(3,5,5,8,8-pentamethyl-5,6,7,8-
tetrahydro-2-naphthyl)phenyl]propynoic acid

(a) 2',2'-Dibromo-4-methoxymethoxy-3-(3,5,5,8,8-
10 pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]-
ethylene

4.95 g (14.71 mmol) of 4-methoxymethoxy-3-
(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)-
phenyl]carboxaldehyde and 50 ml of dichloromethane are
15 introduced into a round-bottomed flask. 9.75 g
(29.4 mmol) of carbon tetrabromide and 15.45 g
(58.84 mmol) of triphenylphosphine are added in
succession and the mixture is stirred at room
temperature for two hours. The reaction medium is
20 evaporated and the residue obtained is purified by
chromatography on a silica column eluted with
dichloromethane. 6.75 g (88%) of the expected product
are collected.

(b) [4-Methoxymethoxy-3-(3,5,5,8,8-pentamethyl-5,6,7,8-
25 tetrahydro-2-naphthyl)phenyl]acetylene

7.6 g (12.9 mmol) of 2',2'-dibromo-4-

- methoxymethoxy-3-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]ethylene and 50 ml of THF are introduced under a stream of nitrogen into a three-necked flask. 11 ml (27.1 mmol) of a solution of
- 5 n-butyllithium (2.5M in hexane) are added dropwise at -78°C and the mixture is allowed to return to room temperature. The reaction medium is poured into water and extracted with ethyl ether and the organic phase is decanted, dried over magnesium sulphate and evaporated.
- 10 The residue obtained is purified by chromatography on a silica column eluted with a mixture of heptane and ethyl acetate (98:2). After evaporation of the solvents, 3.68 g (79%) of the expected acetylenic derivative are collected in the form of a yellow oil.
- 15 (c) Ethyl [4-methoxymethoxy-3-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]propynoate
- 3.65 g (10.1 mmol) of the above acetylenic derivative and 60 ml of THF are introduced under a stream of nitrogen into a three-necked flask. 4.45 ml
- 20 (11.1 mmol) of n-butyllithium (2.5M in hexane) are added dropwise at -78°C and the mixture is stirred for thirty minutes. 1.15 ml (12.1 mmol) of ethyl chloroformate are added at -78°C and the mixture is allowed to return to room temperature. The reaction
- 25 medium is poured into an aqueous ammonium chloride solution and extracted with ethyl ether and the organic phase is decanted, dried over magnesium sulphate and

evaporated. The residue obtained is purified by chromatography on a silica column eluted with a mixture of heptane and ethyl acetate (98:2). After evaporation of the solvents, 4.14 g (95%) of ethyl [4-methoxy-methoxy-3-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]propynoate are collected in the form of a yellow oil.

(d) [4-Methoxymethoxy-3-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]propynoic acid

In a similar manner to that of Example 2(h), starting from 439 mg (1 mmol) of ethyl [4-methoxymethoxy-3-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]propynoate, 375 mg (91%) of [4-methoxymethoxy-3-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]propynoic acid with a melting point of 168-170°C are obtained.

EXAMPLE 8.

3-[3-(3-Propyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxymethoxyphenyl]acrylic acid

(a) Ethyl 3-[3-(3-propyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxymethoxyphenyl]-acrylate

In a similar manner to that of Example 1(c), by reaction of 3 g (10.4 mmol) of (3-propyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)boronic acid

(preparation described in WO 97/33881) with 3.2 g (10.1 mmol) of ethyl 3-(3-bromo-4-methoxymethoxyphenyl)acrylate (prepared in Example 2(c)), after chromatography on a silica column and elution with a mixture of heptane and ethyl acetate (98:2), 2.1 g (43%) of the expected ethyl ester are obtained.

(b) 3-[3-(3-Propyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxymethoxyphenyl]acrylic acid

In a similar manner to that of Example 2(h), starting from 724 mg (1.5 mmol) of ethyl 3-[3-(3-propyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxymethoxyphenyl]acrylate, 620 mg (91%) of 3-[3-(3-propyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxymethoxyphenyl]acrylic acid with a melting point of 170-1°C are obtained.

EXAMPLE 9

3-[3-(3-Pentyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxymethoxyphenyl]acrylic acid

(a) 2-Bromo-3-pentyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalene

In a similar manner to that of Example 1(a), by reaction of 5 g (25 mmol) of 3-bromo-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthol with 3.9 ml (29.5 mmol) of 5-iodopentane, 7 g (79%) of the expected

product are obtained in the form of a colourless oil.

(b) (3-Pentyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)boronic acid

In a similar manner to that of Example 1(b),
 5 starting from 6.9 g (19.5 mmol) of 2-bromo-3-pentyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalene, 4.68 g (75%) of the expected boronic derivative are obtained.

(c) Ethyl 3-[3-(3-pentyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxymethoxyphenyl]-acrylate

In a similar manner to that of Example 1(c),
 by reaction of 4 g (12.6 mmol) of (3-pentyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)boronic acid
 15 with 2.64 g (8.4 mmol) of ethyl 3-[3-(3-bromo-4-methoxymethoxyphenyl)acrylate (prepared in Example 2(c)), after chromatography on a silica column eluted with a mixture of heptane and ethyl acetate (98:2), 3.2 g (75%) of the expected ethyl ester are
 20 obtained.

(d) 3-[3-(3-Pentyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxymethoxyphenyl]acrylic acid

In a similar manner to that of Example 2(h),
 25 starting from 1.7 g (3.26 mmol) of ethyl 3-[3-(3-

pentyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxymethoxyphenyl]acrylate, 1.35 g (86%) of 3-[3-(3-pentyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxymethoxyphenyl]acrylic acid with a melting point of 178-80°C are obtained.

EXAMPLE 10

3-(5'-Adamantan-1-yl-4'-methoxy-2'-methyl-3-biphenyl)acrylic acid

(a) 4-Bromo-3-methylphenol

80.0 g (740 mmol) of 3-methylphenol and 400 ml of glacial acetic acid are introduced under a nitrogen atmosphere into a 2 litre three-necked flask. The mixture is cooled to 15°C, 38 ml (742 mmol) of bromine are added dropwise, and the mixture is stirred at 15°C for three hours. The reaction medium is poured into 1 litre of water and extracted with ethyl ether, the organic phase is decanted, washed with water to neutral pH and dried over magnesium sulphate, and the solvents are evaporated. The residue obtained is triturated in heptane, filtered and dried. 70 g (50%) of a white powder with a melting point of 55-56°C are collected.

(b) 2-(1-Adamantyl)-4-bromo-3-methylphenol

70.0 g (376 mmol) of 4-bromo-3-methylphenol, 63 g (414 mmol) of 1-adamantanol, 500 ml of heptane and 50 ml of dichloromethane are introduced under a

nitrogen atmosphere into a 2000 ml round-bottomed flask. 20 ml (376 mmol) of 98% sulphuric acid are added dropwise and the mixture is stirred at room temperature for 3 hours. The reaction medium is poured into water, neutralized to a pH of 8-9 with sodium bicarbonate solution, and extracted with ethyl acetate, the organic phase is decanted, washed with water to neutral pH and dried over magnesium sulphate, and the solvents are evaporated. The residue obtained is triturated in heptane, filtered and dried. 59 g (49%) of a pinky white powder with a melting point of 139-141°C are collected.

(c) 2-(1-Adamantyl)-4-bromo-5-methylanisole

8 g (24.9 mmol) of 2-(1-adamantyl)-4-bromo-3-methylphenol, 75 ml of DMF and 25 ml of THF are introduced under a stream of nitrogen into a 250 ml three-necked flask. 880 mg (27.4 mmol) of sodium hydride (75% in oil) are added in small portions and the mixture is stirred until the evolution of gas is at an end. Then 1.9 ml (30 mmol) of iodomethane are added and the mixture is stirred at room temperature for two hours. The reaction medium is poured into ice-water and extracted with ethyl ether and the organic phase is decanted, dried over magnesium sulphate and evaporated. The residue obtained is triturated in heptane, filtered and dried. 6.44 g (77%) of pale-beige powder with a melting point of 129-131°C are collected.

(d) 5-(1-Adamantyl)-4-methoxy-2-methylphenylboronic acid

6 g (17.9 mmol) of 2-(1-adamantyl)-4-bromo-5-methylanisole and 40 ml of THF are introduced under a stream of nitrogen into a 250 ml three-necked flask. 7.9 ml (19.7 mmol) of n-butyllithium (2.5M in hexane) are added dropwise at -78°C and the mixture is stirred for 15 minutes; at this same temperature, 5 ml (21.5 mmol) of triisopropyl borate are added and the mixture is stirred for 30 minutes. 20 ml of hydrochloric acid (1N) are added at -50°C and the mixture is allowed to return to room temperature. The reaction medium is extracted with ethyl ether and the organic phase is decanted, dried over magnesium sulphate and evaporated. The solid obtained is triturated in heptane, filtered and dried. 4.75 g (88%) of the expected boronic acid with a melting point of $276-278^{\circ}\text{C}$ are collected, which will be used as it is for the remainder of the synthesis.

(e) 3-(5'-Adamantan-1-yl-4'-methoxy-2'-methyl-3-biphenyl)acrylic acid

1.0 g (3.33 mmol) of 5-(1-adamantyl)-4-methoxy-2-methylphenylboronic acid obtained above, 580 mg (2.56 mmol) of 3-bromocinnamic acid and 30 ml of DME are introduced under a stream of nitrogen into a 100 ml three-necked flask. 4.5 ml of an aqueous potassium carbonate solution (2M) are added dropwise

and the reaction medium is degassed. Then 150 mg (0.13 mmol) of tetrakis(triphenylphosphine)palladium(0) are added and the mixture is heated at reflux for 2 hours. Water and ethyl acetate are added to the reaction medium, which is acidified to a pH of 1 with hydrochloric acid (1N). The organic phase is decanted, washed with water, dried over magnesium sulphate and evaporated. The residue obtained is purified by chromatography on a silica column eluted with a mixture of heptane and ethyl acetate (85:15). After evaporation of the solvents, 750 mg of a thick gel are collected, which is left to crystallize under a stream of nitrogen. The yellow crystals thus obtained are recrystallized from ethanol, filtered and dried to give 452 mg (44%) of 3-(5'-adamantan-1-yl-4'-methoxy-2'-methyl-3-biphenyl)acrylic acid with a melting point of 194-6°C.

¹H NMR (CDCl₃): 1.76 (br, 6H), 2.05 (br, 3H), 2.10 (br, 6H), 2.26 (s, 3H), 3.88 (s, 3H), 6.48 (d, J = 15.8 Hz, 1H), 6.78 (s, 1H Ar), 7.07 (s, 1H Ar), 7.35 to 7.51 (m, 4H Ar), 7.84 (d, J = 15.8 Hz, 1H Ar).

EXAMPLE 11

3-(5'-Adamantan-1-yl-6-hydroxy-4'-methoxy-2'-methyl-3-biphenyl)acrylic acid

(a) Ethyl 3-(3-bromo-4-hydroxyphenyl)acrylate

In a similar manner to that of Example 2(g), by reaction of 10.1 g (20.3 mmol) of ethyl 3-(3-bromo-

4-methoxymethoxyphenyl)acrylate obtained in
 Example 2(c) with 5.4 ml (102 mmol) of 98% sulphuric
 acid, 3.9 g of ethyl 3-(3-bromo-4-hydroxyphenyl)-
 acrylate (49%) are obtained in the form of a white
 5 powder with a melting point of 112-3°C.

(b) Ethyl 3-(5'-adamantan-1-yl-6-hydroxy-4'-methoxy-2'-
 methyl-3-biphenyl)acrylate

In a similar manner to that of Example 1(c),
 by reaction of 3.0 g (10 mmol) of 5-(1-adamantyl)-4-
 10 methoxy-2-methylphenylboronic acid obtained in
 Example 10(d) with 2.25 g (8.33 mmol) of
 ethyl 3-(3-bromo-4-hydroxyphenyl)acrylate obtained
 above, 570 mg (15%) of a white powder with a melting
 point of 164-6°C are obtained.

15 (c) 3-(5'-Adamantan-1-yl-6-hydroxy-4'-methoxy-2'-
 methyl-3-biphenyl)acrylic acid

In a similar manner to that of Example 2(h),
 starting from 270 mg (0.6 mmol) of ethyl 3-(5'-
 adamantan-1-yl-6-hydroxy-4'-methoxy-2'-methyl-3-
 20 biphenyl)acrylate obtained above, 190 mg (76%) of a
 white powder which undergoes decomposition commencing
 at 120°C are obtained.

¹H-NMR. (CDCl₃): 1.76 (br, 6H), 2.07 (br, 9H), 2.13 (s, 3H),
 3.89 (s, 3H), 5.20 (br, 1H), 6.31 (d,
 25 J = 15.75 Hz, 1H), 6.83 (s, 1H), 7.00 (d, J = 9.25 Hz,
 1H), 7.48 (dd, J₁ = 9.25 Hz, J₂ = 2.0 Hz, 1H), 7.74 (d,

$J = 15.75 \text{ Hz, 1H}$).

EXAMPLE 12

3-(5'-Adamantan-1-yl-4'-methoxy-6-methoxymethoxy-2'-methyl-3-biphenyl)acrylic acid

- 5 (a) Ethyl 3-(5'-adamantan-1-yl-4'-methoxy-6-methoxymethoxy-2'-methyl-3-biphenyl)acrylate

In a similar manner to that of Example 2(b), by reaction of 300 mg (0.67 mmol) of ethyl 3-(5'-adamantan-1-yl-6-hydroxy-4'-methoxy-2'-methyl-3-biphenyl)acrylate obtained in Example 11(b) with
10 64 mg (0.8 mmol) of methoxymethyl chloride, 320 mg (97%) of a white gel are obtained.

$^1\text{H NMR}$ (CDCl_3): 1.32 (t, $J = 7.00 \text{ Hz}$, 3H), 1.75 (br, 6H), 2.04+2.09 (br+br, 6H+3H), 2.14 (s, 3H), 3.37 (s, 3H), 3.87 (s, 3H), 4.25 (q, $J = 7.0 \text{ Hz}$, 2H), 5.11 (s, 2H), 6.33 (d, $J = 15.8 \text{ Hz}$, 1H), 6.76 (s, 1H), 7.00 (s, 1H), 7.20 (d, $J = 8.5 \text{ Hz}$, 1H), 7.36 (d, $J = 2.25 \text{ Hz}$, 1H), 7.46 (dd, $J_1 = 8.5 \text{ Hz}$, $J_2 = 2.25 \text{ Hz}$, 1H), 7.66 (d, $J = 15.8 \text{ Hz}$, 1H).

- 20 (b) 3-(5'-Adamantan-1-yl-4'-methoxy-6-methoxymethoxy-2'-methyl-3-biphenyl)acrylic acid

In a similar manner to that of Example 2(h), starting from 300 mg (0.61 mmol) of ethyl 3-(5'-adamantan-1-yl-4'-methoxy-6-methoxymethoxy-2'-methyl-3-biphenyl)acrylate obtained above, 200 mg (71%) of a
25 white powder which undergoes decomposition commencing

at 113°C are obtained.

¹H NMR (CDCl₃): 1.76 (br, 6H), 2.04 (br, 3H), 2.09 (br, 6H), 2.14 (s, 3H), 3.38 (s, 3H), 3.87 (s, 3H), 5.13 (s, 2H), 6.34 (d, J = 15.75 Hz, 1H), 6.76 (s, 1H), 7.00 (s, 1H), 7.22 (d, J = 8.5 Hz, 1H), 7.39 (d, J = 2.25 Hz, 1H), 7.49 (dd, J₁ = 8.5 Hz, J₂ = 2.25 Hz, 1H), 7.76 (d, J = 15.75 Hz, 1H).

EXAMPLE 13

3-(4-Methoxy-3-[3-(3-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl]-acrylic acid

(a) 2-Bromo-3-methoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalene

In a similar manner to that of Example 1(a), by reaction of 100 g (353 mmol) of 3-bromo-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthol with 32 ml (406 mmol) of methoxymethyl chloride, 100 g (86%) of the expected product are obtained in the form of a beige powder with a melting point of 69-71°C.

(b) 3-Methoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylboronic acid

In a similar manner to that of Example 1(b), by reaction of 90 g (275 mmol) of 2-bromo-3-methoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalene obtained above, 70 g (87%) of the expected product are obtained in the form of a white powder with

a melting point of 130-132°C.

(c) 3-Bromo-4-methoxybenzaldehyde

In a similar manner to that of Example 1(a),
by reaction of 50 g (270 mmol) of 3-bromo-4-
5 hydroxybenzaldehyde (obtained in accordance with
Example 2(a)) and 20.2 ml (338 mmol) of iodomethane,
48 g (83%) of the expected product are obtained in the
form of a white powder with a melting point of 48-50°C.

(d) Ethyl 3-(3-bromo-4-methoxyphenyl)acrylate

10 In a similar manner to that of Example 2(c),
by reaction of 46 g (214 mmol) of 3-bromo-4-
methoxybenzaldehyde obtained above and 55.2 ml
(278 mmol) of triethyl phosphonoacetate, 47 g (77%) of
the expected product are obtained in the form of white
15 flakes with a melting point of 76-78°C.

(e) Ethyl 3-[4-methoxy-3-(3-methoxymethoxy-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]-
acrylate

In a similar manner to that of Example 1(c),
20 by reaction of 53.3 g (182 mmol) of 3-methoxymethoxy-
5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl-
boronic acid obtained in Example 13(b) and 40 g
(140 mmol) of ethyl 3-(3-bromo-4-methoxyphenyl)acrylate
obtained above, 63 g (99%) of the expected product are
25 obtained in the form of a thick yellow oil.

¹H NMR (CDCl₃): 1.23 to 1.35 (m, 15H), 1.70 (s, 4H),
 3.34 (s, 3H), 3.81 (s, 3H), 4.25 (q, J = 7.25 Hz, 2H),
 5.03 (s, 2H), 6.32 (d, J = 15.75 Hz, 1H), 9.95 (d,
 J = 9.0 Hz, 1H), 7.13 (s, 1H), 7.42 to 7.66 (m, 2H),
 5 7.67 (d, J = 15.75 Hz, 1H).

(f) Ethyl 3-[3-(3-hydroxy-5,5,8,8-tetramethyl, 5,6,7,8-tetrahydro-2-naphthyl)-4-methoxyphenyl]acrylate

In a similar manner to that of Example 2(g),
 by reaction of 63 g (140 mmol) of ethyl 3-[4-methoxy-3-
 10 (3-methoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylate obtained above
 and 22 ml (420 mmol) of sulphuric acid, 42.5 g (75%) of
 the expected product are obtained in the form of a
 pale-yellow powder with a melting point of 147-149°C.

15 (g) Ethyl 3-{4-methoxy-3-[3-(3-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-phenyl}acrylate.

In a similar manner to that of Example 1(a),
 by reaction of 1 g (2.45 mmol) of ethyl 3-[3-(3-
 20 hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxyphenyl]acrylate obtained above with
 4 ml (3 mmol) of 3-methoxybenzyl chloride, 1.30 g
 (100%) of the expected product are obtained in the form
 of a yellow oil.

25 ¹H NMR (CDCl₃): 1.24 to 1.35 (m, 15H), 1.69 (s, 4H),
 3.69 (s, 3H), 3.76 (s, 3H), 4.25 (q, J = 7.0 Hz, 2H),

5.0 (s, 2H), 6.30 (d, J = 16.0 Hz, 1H), 6.75 to 6.96 (m, 5H), 7.16 to 7.22 (m, 2H), 7.45 to 7.51 (m, 2H), 7.67 (d, J = 16.0 Hz, 1H).

(h) 3-{4-Methoxy-3-[3-(3-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-acrylic acid

In a similar manner to that of Example 2(h), starting from 1.3 g (2.45 mmol) of ethyl 3-{4-methoxy-3-[3-(3-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylate obtained above, 830 mg (67%) of the expected product are obtained in the form of a white powder with a melting point of 168-170°C.

EXAMPLE 14

15 3-{4-Methoxy-3-[3-(4-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-acrylic acid

(a) Ethyl 3-{4-methoxy-3-[3-(4-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylate

In a similar manner to that of Example 1(a), by reaction of 1.23 g (3 mmol) of ethyl 3-[3-(3-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxyphenyl]acrylate obtained in Example 13(f) with 490 µl (3.6 mmol) of 4-methoxybenzyl chloride, 1.58 g (100%) of the expected product are

obtained in the form of a yellow oil.

¹H NMR (CDCl₃): 1.21 to 1.35 (m, 15H), 1.69 (s, 4H),
 3.75 (s, 3H), 3.77 (s, 3H), 4.25 (q, J = 7.0 Hz, 2H),
 4.93 (s, 2H), 6.29 (d, J = 16.0 Hz, 1H), 6.80 to 6.94
 5 (m, 4H), 7.15 to 7.18 (m, 2H), 7.31 (d, J = 8.5 Hz,
 1H), 7.44 to 7.50 (m, 2H), 7.66 (d, J = 16.25 Hz, 1H).

(b) 3-{4-Methoxy-3-[3-(4-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-acrylic acid

10 In a similar manner to that of Example 2(h),
 starting from 1.58 g (3 mmol) of ethyl 3-{4-methoxy-3-[3-(4-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylate obtained above,
 1.1 g (71%) of the expected product are obtained in the
 15 form of a white powder with a melting point of 201-203°C.

EXAMPLE 15

3-{3-[3-(6-Hydroxyhexyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic
 20 acid

(a) Ethyl 3-{3-[3-(6-hydroxyhexyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylate.

In a similar manner to that of Example 1(a),
 25 by reaction of 1.4 g (3.4 mmol) of ethyl 3-[3-(3-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-

naphthyl)-4-methoxyphenyl]acrylate obtained in Example 13(f) with 540 μ l (4.1 mmol) of 1-bromohexanol, 850 mg (50%) of the expected product are obtained in the form of a yellow oil.

5 ^1H NMR (CDCl_3): 1.23 to 1.35 (m, 19H), 1.43 to 1.70 (m, 8H), 3.56 (q, $J = 5.5$ Hz, 2H), 3.81 (s, 3H), 3.90 (t, $J = 5.0$ Hz, 2H), 4.25 (q, $J = 7.25$ Hz, 2H), 6.31 (d, $J = 16.0$ Hz, 1H), 6.85 (s, 1H), 6.96 (d, $J = 8.5$ Hz, 1H), 7.20 (s, 1H), 7.47 (dd, $J_1 = 8.25$ Hz, $J_2 =$
10 2.25 Hz, 1H), 7.52 (d, $J = 2.25$ Hz, 1H), 7.67 (d, $J = 16.0$ Hz, 1H).

(b) 3-{3-[3-(6-Hydroxyhexyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid

15 In a similar manner to that of Example 2(h), starting from 850 mg (1.67 mmol) of ethyl 3-{3-[3-(6-hydroxyhexyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylate
obtained above, 510 mg (63%) of the expected product
20 are obtained in the form of a white powder with a melting point of 118-120°C.

EXAMPLE 16

3-{3-[3-(7-Hydroxyheptyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic
25 acid.

(a) Ethyl 3-{3-[3-(7-hydroxyheptyloxy)-5,5,8,8-

tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylate

1.23 g (3 mmol) of ethyl 3-[3-(3-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl]acrylate obtained in Example 13(f), 440 mg (3.2 mmol) of potassium carbonate, 540 μ l (3.5 mmol) of 1-bromoheptanol and 30 ml of butanone are introduced into a round-bottomed flask. The mixture is heated at reflux for 8 hours, the reaction medium is poured into water, acidified to a pH of 1 with hydrochloric acid and extracted with ethyl ether, and the organic phase is decanted, dried over magnesium sulphate and evaporated. 1.57 g (100%) of the expected product in the form of a yellow oil are collected.

¹H NMR (CDCl₃): 1.26 (s, 6H), 1.32 (s, 6H), 1.08 to 1.7 (m, 17H), 3.5 to 3.7 (m, 2H), 3.81 (s, 3H), 3.89 (t, J = 6.25 Hz, 2H), 4.24 (q, J = 7.0 Hz, 2H), 6.3 (d, J = 16.0 Hz, 1H), 6.84 (s, 1H), 6.95 (d, J = 8.25 Hz, 1H), 7.19 (s, 1H), 7.47 (dd, J₁ = 8.25 Hz, J₂ = 2.25 Hz, 1H), 7.50 (d, J = 2.25 Hz, 1H), 7.67 (d, J = 16.0 Hz, 1H).

(b) 3-{3-[3-(7-Hydroxyheptyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid

In a similar manner to that of Example 2(h), starting from 1.57 g (3 mmol) of ethyl 3-{3-[3-(7-hydroxyheptyloxy)-5,5,8,8-tetramethyl-5,6,7,8-

tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylate
 obtained above, 700 mg (47%) of the expected product
 are obtained in the form of a white powder with a
 melting point of 105-107°C.

5 **EXAMPLE 17**

3-{3-[3-(5-Hydroxypentyloxy)-5,5,8,8-tetramethyl-
 5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic
 acid

(a) Ethyl 3-{3-[3-(5-acetoxypentyloxy)-5,5,8,8-
 10 tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-
 methoxyphenyl}acrylate

In a similar manner to that of Example 1(a),
 by reaction of 1.20 g (2.90 mmol) of ethyl 3-[3-(3-
 hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-
 15 naphthyl)-4-methoxyphenyl]acrylate obtained in
 Example 13(f) with 727 mg (3.48 mmol) of 5-bromopentyl
 acetate, 1.42 g (92%) of the expected product are
 obtained in the form of a yellow oil.

¹H NMR (CDCl₃): 1.26 to 1.37 (m, 17H), 1.50 to 1.67 (m,
 20 4H), 1.70 (s, 4H), 2.01 (s, 3H), 3.80 (s, 3H), 3.80 to
 4.00 (m, 4H), 4.25 (q, J = 7.25 Hz, 2H), 6.30 (d, J =
 J = 15.75 Hz, 1H), 6.84 (s, 1H), 6.94 (d, J = 8.25 Hz,
 1H), 7.17 (s, 1H), 7.44 to 7.48 (m, 2H), 7.66 (d,
 J = 16.0 Hz, 1H).

25 (b) 3-{3-[3-(5-Hydroxypentyloxy)-5,5,8,8-tetramethyl-
 5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic

acid

In a similar manner to that of Example 2(h), starting from 1.42 g (2.65 mmol) of ethyl 3-{3-[3-(5-acetoxypentyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylate
 5 obtained above, 730 mg (60%) of the expected product are obtained in the form of a white powder with a melting point of 115-117°C.

EXAMPLE 18

10 3-{3-[3-(3-Hydroxypropyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid

(a) Ethyl 3-{3-[3-(3-Hydroxypropyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylate
 15 methoxyphenyl}acrylate

In a similar manner to that of Example 16(a), by reaction of 1.2 g (2.9 mmol) of ethyl 3-[3-(3-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylate obtained in
 20 Example 13(f) with 490 mg (3.5 mmol) of 1-bromopropanol; 632 mg (47%) of the expected product are obtained in the form of a yellow oil.

¹H NMR (CDCl₃): 1.27 to 1.35 (m, 9H), 1.70 (s, 4H), 1.85 to 1.92 (m, 2H), 1.96 (br, 1H), 3.64 (m, 2H), 3.82 (s, 3H), 4.09 (t, J = 5.5 Hz, 2H), 4.25 (q, J = 7.25 Hz, 2H), 6.31 (d, J = 16.0 Hz, 1H), 6.87 (s, 1H), 6.96 (d, J = 8.5 Hz, 1H), 7.15 (s, 1H), 7.44 (d, J = 2.25 Hz,

25

1H), 7.49 (dd, $J_1 = 8.5$ Hz, $J_2 = 2.25$ Hz, 1H), 7.66 (d, $J = 16.0$ Hz, 1H).

(b) 3-{3-[3-(3-Hydroxypropyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic
5 acid

In a similar manner to that of Example 2(h), starting from 632 mg (1.35 mmol) of ethyl 3-{3-[3-(3-hydroxypropyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylate
10 obtained above, 449 mg (75%) of the expected product are obtained in the form of a white powder with a melting point of 198-200°C.

EXAMPLE 19

3-[3-(1-Methoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylic acid
15

(a) 1-Methoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalene

In a similar manner to that of Example 1(a), by reaction of 8.65 g (42.4 mmol) of 5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthol with 3.55 ml.
20 (46.6 mmol) of methoxymethyl chloride, 10.5 g (100%) of the expected product are obtained.

(b) 1-Methoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthaleneboronic acid

25 1 g (4 mmol) of 1-methoxymethoxy-5,5,8,8-



tetramethyl-5,6,7,8-tetrahydronaphthalene and 12 ml of THF are introduced into a round-bottomed flask. The mixture is cooled to -78°C and 630 μl (4.2 mmol) of TMEDA and then 3.4 ml (4.4 mmol) of sec-BuLi (1.3M) are added dropwise. The mixture is stirred at -78°C for 1 hour and then 1.4 ml (6 mmol) of triisopropyl borate are added and the mixture is allowed to return to room temperature. 3 ml of hydrochloric acid (5%) are added at -40°C and the mixture is stirred at room temperature for 1 hour. The reaction medium is poured into water and extracted with ethyl acetate and the organic phase is decanted, dried over magnesium sulphate and evaporated. The residue obtained is purified by chromatography on a silica column eluted with a mixture of dichloromethane and methanol (98:2). 900 mg (77%) of the expected boronic derivative in the form of a pale-yellow oil are collected.

(c) 3-[3-(1-Methoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylic acid

In a similar manner to that of Example 1(c), by reaction of 3.4 g (11.6 mmol) of 1-methoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthalene-boronic acid with 1.32 g (5.8 mmol) of 3-bromocinnamic acid, trituration in heptane gives 1.4 g (62%) of 3-[3-(1-methoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylic acid in the form of a white powder with a melting point of $188-9^{\circ}\text{C}$.



EXAMPLE 203-[3-(1-Benzoyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylic acid

(a) Methyl 3-[3-(1-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylate

1.24 g (3.15 mmol) of 3-[3-(1-methoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylic acid obtained in Example 19(c), 15 ml of methanol and 15 ml of THF are introduced into a round-bottomed flask. 620 μ l of concentrated sulphuric acid are added and the mixture is stirred at room temperature for eight hours and heated at reflux for two hours. The reaction medium is poured into water and extracted with ethyl ether and the organic phase is decanted, dried over magnesium sulphate and evaporated. 1.1 g (100%) of methyl 3-[3-(1-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylate with a melting point of 197-8°C are collected.

(b) Methyl 3-[3-(1-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylate

In a similar manner to that of Example 1(a), by reaction of 500 mg (1.37 mmol) of methyl 3-[3-(1-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylate with 180 μ l (1.5 mmol) of benzyl bromide, 550 mg (88%) of the expected product are obtained in the form of a yellow oil.



(c) 3-[3-(1-Benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylic acid

In a similar manner to that of Example 2(h), starting from 498 mg (1.01 mmol) of ethyl 3-[3-(1-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylate, 360 mg (82%) of 3-[3-(1-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylic acid with a melting point of 153-4°C are obtained.

10 EXAMPLE 21

3-{3-[3-(5-tert-Butoxycarbonylpentyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid

(a) tert-Butyl 6-bromohexanoate

15 1.95 g (10 mmol) of 6-bromohexanoic acid dissolved in 10 ml of dichloromethane are introduced under a stream of nitrogen into a round-bottomed flask. A solution of 4.37 g (20 mmol) of tert-butyl 2,2,2-trichloroacetimidate in 20 ml of cyclohexane is added
20 dropwise, followed immediately by 200 µl of trifluoroborane etherate. The mixture is stirred at room temperature for 5 minutes, 5 g of sodium bicarbonate are added, and the mixture is stirred for 1 minute. The suspension obtained is placed on a silica
25 column which has been wetted beforehand with cyclohexane and the latter is eluted with a 8:2 cyclohexane/ethyl acetate mixture. After evaporation of



the solvents, 1.63 g (65%) of a colourless oil are obtained.

¹H NMR (CDCl₃): 1.45 (s, 9H), 1.44 to 1.70 (m, 4H), 1.87 (m, 2H), 2.23 (t, J = 7.5 Hz, 2H), 3.41 (t, J =
5 6.75 Hz, 2H).

(b) Ethyl 3-{3-[3-(5-tert-Butoxycarbonylpentyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylate

In a similar manner to that of Example 1(a),
10 by reaction of 2.36 g (5.8 mmol) of ethyl 3-[3-(3-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxyphenyl]acrylate obtained in
Example 13(f) with 1.6 g (6.3 mmol) of tert-butyl
6-bromohexanoate obtained above, 3.3 g (100%) of the
15 expected product are obtained in the form of a yellow oil.

¹H NMR (CDCl₃): 1.21 to 1.75 (m, 32H), 2.13 (t, J =
7.25 Hz, 2H), 3.80 (s, 3H), 3.88 (t, J = 6.25 Hz, 2H),
4.25 (q, J = 7.0 Hz, 2H), 6.30 (d, J = 16.0 Hz, 1H),
20 6.83 (s, 1H), 6.94 (d, J = 8.75 Hz, 1H), 7.16 (s, 1H),
7.44 to 7.48 (m, 2H), 7.66 (d, J = 16.0 Hz, 1H).

(c) 3-{3-[3-(5-tert-Butoxycarbonylpentyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid

25 A solution of 1.0 g (1.7 mmol) of ethyl
3-{3-[3-(5-tert-butoxycarbonylpentyloxy)-5,5,8,8-



tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylate obtained above dissolved in 25 ml of THF is placed in a round-bottomed flask and 730 mg (17 mmol) of lithium hydroxide and 2 ml of water are added. The mixture is heated at the reflux of the THF for 8 hours and stirred at room temperature for 48 hours, the reaction medium is poured into water, acidified to a pH of 1 with hydrochloric acid and extracted with ethyl ether, and the organic phase is decanted, dried over magnesium sulphate, filtered and evaporated. The residue obtained is chromatographed on a silica column eluted with a 8:2 heptane/ethyl acetate mixture. After evaporation of the solvents, 126 mg (14%) of a white powder with a melting point of 130-132°C are collected.

EXAMPLE 22

3-{3-[3-(7-tert-Butoxycarbonylheptyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid

(a) tert-Butyl 8-Bromooctanoate

In a similar manner to that of Example 21(a), starting from 3 g (13.4 mmol) of 8-bromooctanoic acid, 3 g (80%) of a pale-yellow oil are obtained.

¹H NMR (CDCl₃): 1.29 to 1.37 (m, 6H), 1.44 (s, 9H), 1.50 to 1.75 (m, 2H), 1.75 to 1.95 (m, 2H), 2.20 (t, J = 7.5 Hz, 2H), 3.40 (t, J = 6.75 Hz, 2H).



(b) Ethyl 3-{3-[3-(7-tert-butoxycarbonylheptyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylate

In a similar manner to that of Example 1(a),
 5 by reaction of 3.82 g (9.34 mmol) of ethyl 3-[3-(3-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxyphenyl]acrylate obtained in
 Example 13(f) with 3 g (10.7 mmol) of tert-butyl
 8-bromooctanoate obtained above, 4.36 g (77%) of the
 10 expected product are obtained in the form of a yellow
 oil.

^1H NMR (CDCl_3): 1.26 to 1.13 (m, 21H), 1.44 (s, 9H),
 1.43 to 1.65 (m, 4H), 1.70 (s, 4H), 2.16 (t, J =
 7.25 Hz, 2H), 3.80 (s, 3H), 3.88 (t, J = 6.5 Hz, 2H),
 15 4.24 (q, J = 7.0 Hz, 2H), 6.30 (d, J = 15.75 Hz, 1H),
 6.84 (s, 1H), 6.93 (d, J = 8.25 Hz, 1H), 7.17 (s, 1H),
 7.43 to 7.49 (m, 2H), 7.66 (d, J = 15.75 Hz, 1H).

(c) 3-{3-[3-(7-tert-butoxycarbonylheptyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxy-
 20 phenyl}acrylic acid

In a similar manner to that of Example 21(c),
 starting from 1.15 g (1.9 mmol) of ethyl 3-{3-[3-(7-tert-butoxycarbonylheptyloxy)-5,5,8,8-tetramethyl-
 5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylate
 25 obtained above, 363 mg (33%) of the expected product
 are obtained in the form of a white powder with a
 melting point of 126-128°C.

This Sheet Has Been Replaced



EXAMPLE 23

3-{3-[3-(7-Carboxyheptyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid

- 5 (a) Ethyl 3-{3-[3-(7-carboxyheptyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylate

A solution of 3.75 g (6.18 mmol) of ethyl 3-{3-[3-(7-tert-butoxycarbonylheptyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylate obtained in Example 22(b) dissolved in 60 ml of dichloromethane is placed in a round-bottomed flask, 4.76 ml (61.8 mmol) of trifluoroacetic acid are added, and the mixture is stirred at room temperature for 4 hours. The reaction medium is poured into water and extracted with ethyl ether, and the organic phase is decanted, dried over magnesium sulphate, filtered and evaporated.

15 3.4 g (100%) of the expected product are obtained in the form of a white foam.

¹H NMR (CDCl₃): 1.26 to 1.35 (m, 21H), 1.50 to 1.67 (m, 4H), 1.70 (s, 4H), 2.30 (t, J = 7.5 Hz, 2H), 3.80 (s, 3H), 3.88 (t, J = 6.25 Hz, 2H), 4.25 (q, J = 7.25 Hz, 2H), 6.31 (d, J = 15.75 Hz, 1H), 6.84 (s, 1H), 6.94 (d, J = 8.25 Hz, 1H), 7.17 (s, 1H), 7.44 to 7.49 (m, 2H), 7.67 (d, J = 16.0 Hz, 1H).



(b) 3-{3-[3-(7-Carboxyheptyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid

In a similar manner to that of Example 2(h), starting from 1 g (1.8 mmol) of ethyl 3-{3-[3-(7-carboxyheptyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylate obtained above, 830 mg (88%) of the expected product are obtained in the form of a white powder with a melting point of 212-214°C.

EXAMPLE 24

3-{3-[3-(5-Carboxypentyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid

(a) Ethyl 3-{3-[3-(5-carboxypentyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylate

In a similar manner to that of Example 23(a), starting from 2.3 g (3.97 mmol) of ethyl 3-{3-[3-(5-tert-butoxycarbonylpentyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylate obtained in Example 21(b), 2.1 g (100%) of the expected product are obtained in the form of a white foam.

¹H NMR (CDCl₃): 1.24 to 1.42 (m, 17H), 1.55 to 1.70 (m, 8H), 2.28 (t, J = 7.0 Hz, 2H), 3.80 (s, 3H), 3.91 (t, J = 5.75 Hz, 2H), 4.25 (q, J = 7.25 Hz, 2H), 6.32 (d, J = 15.75 Hz, 1H), 6.84 (s, 1H), 6.95 (d, J = 9.0 Hz,



1H), 7.19 (s, 1H), 7.46 to 7.50 (m, 2H), 7.69 (d, J = 16.0 Hz, 1H).

(b) 3-{3-[3-(5-carboxypentyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic
5 acid

In a similar manner to that of Example 2(h), starting from 900 mg (1.72 mmol) of ethyl 3-{3-[3-(5-carboxypentyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylate
10 obtained above, 647 mg (76%) of the expected product are obtained in the form of a white powder with a melting point of 166-168°C.

EXAMPLE 25

3-{3-[3-(5-Carbamoylpentyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic
15 acid

(a) Ethyl 3-{3-[3-(5-Carbamoylpentyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylate

20 A solution of 1.27 g (2.43 mmol) of ethyl 3-{3-[3-(5-carboxypentyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylate obtained in Example 24(a) dissolved in 35 ml of dichloromethane is introduced into a round-bottomed
25 flask, 505 µl (2.55 mmol) of dicyclohexylamine are added, and the mixture is stirred for 10 minutes. Then



186 μ l (2.55 mmol) of thionyl chloride are added dropwise and the mixture is stirred at room temperature for 10 minutes. The reaction medium is evaporated to dryness, the residue obtained is taken up in ethyl ether, the suspension is filtered and the filtrate is evaporated. The residue obtained is dissolved in 15 ml of THF and the solution is introduced dropwise under nitrogen into a three-necked flask containing 20 ml of THF, 405 μ l (2.92 mmol) of triethylamine and 160 μ l of a 34% aqueous ammonia solution (2.67 mmol). The mixture is stirred at room temperature for 30 minutes, the reaction medium is poured into water, acidified to a pH of 1 with 1N hydrochloric acid and extracted with ethyl ether, and the organic phase is decanted, dried over magnesium sulphate, filtered and evaporated. The residue obtained is purified by chromatography on a silica column eluted with a mixture of heptane and ethyl acetate (80:20). After evaporation of the solvents, 750 mg (60%) of the expected product are obtained in the form of a white powder with a melting point of 133-135°C.

(b) 3-{3-[3-(5-Carbamoylpentyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid

25 In a similar manner to that of Example 2(h), starting from 900 mg (1.4 mmol) of ethyl 3-{3-[3-(5-carbamoylpentyloxy)-5,5,8,8-tetramethyl-5,6,7,8-



tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylate
 obtained above, 190 mg (27%) of the expected product
 are obtained in the form of a white powder with a
 melting point of 179-181°C.

5 **EXAMPLE 26**

3-{3-[3-(7-Carbamoylheptyloxy)-5,5,8,8-tetramethyl-
 5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic
 acid

(a) Ethyl 3-{3-[3-(7-carbamoylpentyloxy)-5,5,8,8-
 10 tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-
 methoxyphenyl}acrylate

In a similar manner to that of Example 25(a),
 starting from 1.5 g (2.70 mmol) of ethyl 3-{3-[3-(7-
 carboxyheptyloxy)-5,5,8,8-tetramethyl-5,6,7,8-
 15 tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylate
 obtained in Example 23(a), 1 g (68%) of the expected
 product is obtained in the form of a beige powder with
 a melting point of 132-134°C.

(b) 3-{3-[3-(7-Carbamoylheptyloxy)-5,5,8,8-tetramethyl-
 20 5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic
 acid

In a similar manner to that of Example 2(h),
 starting from 1 g (1.8 mmol) of ethyl 3-{3-[3-(7-
 carbamoylheptyloxy)-5,5,8,8-tetramethyl-5,6,7,8-
 25 tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylate
 obtained above, 700 mg (74%) of the expected product



are obtained in the form of a white powder with a melting point of 199-201°C.

EXAMPLE 27

3-{4-Methoxy-3-[5,5,8,8-tetramethyl-3-(2-morpholin-4-yl-ethoxy)-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylic acid

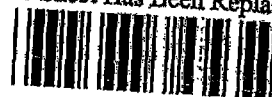
(a) Ethyl 3-{4-methoxy-3-[5,5,8,8-tetramethyl-3-(2-morpholin-4-yl-ethoxy)-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylate

In a similar manner to that of Example 16(a), by reaction of 1.4 g (3.4 mmol) of ethyl 3-[3-(3-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxyphenyl]acrylate obtained in Example 13(f) with 760 mg (4.08 mmol) of 4-(2-chloroethyl)-morpholine hydrochloride, 1.5 g (85%) of the expected product are obtained in the form of a yellow oil.

¹H NMR (CDCl₃): 1.27 (s, 6H), 1.29 to 1.35 (m, 9H), 1.70 (s, 4H), 2.37 (m, 4H), 2.60 (t, J = 5.75 Hz, 2H), 3.59 (m, 4H), 3.81 (s, 3H), 4.05 (t, J = 5.50 Hz, 2H), 4.25 (q, J = 7.0 Hz, 2H), 6.30 (d, J = 15.75 Hz, 1H), 6.85 (s, 1H), 6.91 to 6.95 (m, 1H), 7.16 (s, 1H), 7.44 to 7.49 (m, 2H), 7.65 (d, J = 16.0 Hz, 1H).

(b) 3-{4-Methoxy-3-[5,5,8,8-tetramethyl-3-(2-morpholin-4-yl-ethoxy)-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-acrylic acid

In a similar manner to that of Example 2(h),



starting from 1.5 g (2.9 mmol) of ethyl 3-{4-methoxy-3-[5,5,8,8-tetramethyl-3-(2-morpholin-4-yl-ethoxy)-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylate obtained above, 1.17 g (83%) of the expected product are
 5 obtained in the form of a white powder which undergoes decomposition commencing at 140°C.

¹H NMR (CD₃OD (Ref.: α at δ = 2.85 ppm)): 0.79 (s, 6H), 0.87 (s, 6H), 1.26 (s, 4H), 1.90 (m, 4H), 2.18 (t, J = 5.0 Hz, 2H), 3.07 (m, 4H), 3.31 (s, 3H), 3.61 (t, J =
 10 5.0 Hz, 2H), 5.91 (d, J = 15.75 Hz, 1H), 6.45 (s, 1H), 6.56 (d, J = 8.5 Hz, 1H), 6.62 (s, 1H), 6.87 (d, J = 1.75 Hz, 1H), 7.01 to 7.09 (m, 2H).

EXAMPLE 28

3-{4-Methoxy-3-[5,5,8,8-tetramethyl-3-(2-piperidin-1-yl-ethoxy)-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylic acid
 15

(a) Ethyl 3-{4-methoxy-3-[5,5,8,8-tetramethyl-3-(2-piperidin-1-yl-ethoxy)-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylate

20 In a similar manner to that of Example 16(a), by reaction of 1.4 g (3.4 mmol) of ethyl 3-[3-(3-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxyphenyl]acrylate obtained in Example
 13(f) and 760 mg (4.08 mmol) of 1-(2-chloroethyl)-piperidine hydrochloride, 1.57 g (89%) of the expected
 25 product are obtained in the form of a colourless oil.

¹H NMR (CDCl₃): 1.22 to 1.38 (m, 16H), 1.46 to 1.55 (m,



4H), 1.69 (m, 5H), 2.36 (m, 4H), 2.60 (t, $J = 6.25$ Hz, 2H), 3.81 (s, 3H), 4.05 (t, $J = 6.0$ Hz, 2H), 4.24 (q, $J = 7.25$ Hz, 2H), 6.30 (d, $J = 16.0$ Hz, 1H), 6.85 (s, 1H), 6.93 (d, $J = 9.25$ Hz, 1H), 7.16 (s, 1H), 7.44 to 5 7.48 (m, 2H), 7.66 (d, $J = 16.0$ Hz, 1H).

(b) 3-{4-Methoxy-3-[5,5,8,8-tetramethyl-3-(2-piperidin-1-yl-ethoxy)-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-acrylic acid

In a similar manner to that of Example 2(h), starting from 1.57 g (3 mmol) of ethyl 3-{4-methoxy-3-[5,5,8,8-tetramethyl-3-(2-piperidin-1-yl-ethoxy)-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylate obtained above, 900 mg (61%) of the expected product are obtained in the form of a white powder with a melting 15 point of 251-253°C.

EXAMPLE 29

3-{4-Methoxy-3-[3-(2-methoxymethoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-acrylic acid

20 (a) 2-Methoxymethoxybenzaldehyde

In a similar manner to that of Example 1(a), by reaction of 30 g (245 mmol) of 2-hydroxybenzaldehyde with 21 ml (270 mmol) of methoxymethyl chloride, 40.7 g (100%) of the expected product are obtained in the form 25 of an off-white oil.

^1H NMR (CDCl_3): 3.53 (s, 3H), 5.31 (s, 2H), 7.09 (t, $J =$



7.5 Hz, 1H), 7.22 (d, $J = 8.25$ Hz, 1H), 7.50 to 7.57 (m, 1H), 7.85 (dd, $J_1 = 7.75$ Hz, $J_2 = 1.75$ Hz, 1H), 10.51 (s, 1H).

(b) (2-Methoxymethoxyphenyl)methanol

5 A solution of 40 g (241 mmol) of 2-methoxymethoxybenzaldehyde dissolved in 250 ml of THF is introduced under a stream of nitrogen into a 2-litre round-bottom flask, and 3.65 g (96 mmol) of lithium aluminium hydride are added in small portions. The
10 reaction medium is stirred at room temperature for 15 minutes, before being hydrolysed slowly with a saturated ammonium chloride solution and is then acidified to a pH of 1 with a 1N hydrochloric acid solution. The reaction medium is extracted with ethyl
15 acetate, the organic phase is decanted, dried over magnesium sulphate and filtered, and the filtrate is evaporated. 39.2 g (96%) of a colourless oil are collected.

^1H NMR (CDCl_3): 2.29 (m, 1H), 3.49 (s, 3H), 4.80 (d, $J =$
20 6.0 Hz, 2H), 5.25 (s, 2H), 6.98 to 7.12 (m, 2H), 7.23 to 7.34 (m, 2H).

(c) 2-Methoxymethoxybenzyl chloride

5.0 g (29.7 mmol) of (2-methoxymethoxy-phenyl)methanol obtained above, 90 ml of
25 dichloromethane and 8.27 ml (59.5 mmol) of triethylamine are introduced in succession under a



stream of nitrogen into a 250 ml three-necked flask. Then 2.76 g (35.7 mmol) of methanesulphonyl chloride are added dropwise and the mixture is stirred at room temperature for 1 hour. The reaction medium is

5 hydrolysed with hydrochloric acid and extracted with dichloromethane, the organic phase is dried over magnesium sulphate and filtered, and the filtrate is evaporated. The orange oil obtained is purified by chromatography on a silica column eluted with a mixture

10 of ethyl acetate and heptane (1:9). After evaporation of the solvents, 3.0 g (55%) of the expected product in the form of a yellow oil are collected.

^1H NMR (CDCl_3): 3.50 (s, 3H), 4.67 (s, 2H), 3.25 (s, 2H), 6.99 (td, $J_1 = 7.5$ Hz, $J_2 = 1.0$ Hz, 1H), 7.11 (d, $J = 7.75$ Hz, 1H), 7.24 to 7.38 (m, 2H).

15

(d) Ethyl 3-{4-methoxy-3-[3-(2-methoxymethoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylate

In a similar manner to that of Example 1(a),

20 by reaction of 2.5 g (6.12 mmol) of ethyl 3-[3-(3-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxyphenyl]acrylate obtained in Example 13(f) with 1.26 g (6.73 mmol) of 2-methoxymethoxybenzyl chloride obtained above, 3.2 g (94%) of the expected

25 product are obtained in the form of a yellow oil.

^1H NMR (CDCl_3): 1.27 to 1.35 (m, 15H), 1.69 (s, 4H), 3.43 (s, 3H), 3.74 (s, 3H), 4.25 (q, $J = 7.0$ Hz, 2H),



5.07 (s, 2H), 5.18 (s, 2H), 6.29 (d, J = 16.0 Hz, 1H),
 6.90 to 6.95 (m, 3H), 7.06 (d, J = 7.5 Hz, 1H), 7.15 to
 7.21 (m, 3H), 7.47 (dd, J₁ = 8.5 Hz, J₂ = 2.25 Hz, 1H),
 7.52 (d, J = 2.25 Hz, 1H), 7.66 (d, J = 16.0 Hz, 1H).

5 (e) 3-{4-Methoxy-3-[3-(2-methoxymethoxybenzyloxy)-
 5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-
 naphthyl]phenyl}acrylic acid

In a similar manner to that of Example 2(h),
 starting from 1.0 g (1.8 mmol) of ethyl 3-{4-methoxy-3-
 10 [3-(2-methoxymethoxybenzyloxy)-5,5,8,8-tetramethyl-
 5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylate obtained
 above, 760 mg (80%) of the expected product are
 obtained in the form of a white powder with a melting
 point of 159-161°C.

15 **EXAMPLE 30**

3-{4-Methoxy-3-[3-(3-methoxymethoxybenzyloxy)-5,5,8,8-
 tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-
 acrylic acid

(a) 3-Methoxymethoxybenzaldehyde

20 In a similar manner to that of Example 1(a),
 by reaction of 30 g (245 mmol) of 3-hydroxybenzaldehyde
 with 21 ml (270 mmol) of methoxymethyl chloride, 40.7 g
 (100%) of the expected product are obtained in the form
 of a chestnut-brown oil.

25 ¹H NMR (CDCl₃): 3.49 (s, 3H), 5.23 (s, 2H), 7.27 to 7.32
 (m, 1H), 7.42 to 7.55 (m, 3H), 9.97 (s, 1H).



(b) (3-Methoxymethoxyphenyl)methanol

In a similar manner to that of Example 29(b), by reaction of 40 g (240 mmol) of 3-methoxymethoxybenzaldehyde with 3.65 g (96 mmol) of lithium aluminium hydride, 40.7 g (100%) of the expected product are
 5 obtained in the form of a colourless oil.

^1H NMR (CDCl_3): 1.83 (br, 1H), 3.48 (s, 3H), 4.67 (s, 2H), 5.18 (s, 2H), 6.94 to 7.06 (m, 3H), 7.24 to 7.31 (m, 1H).

10 (c) 3-Methoxymethoxybenzyl chloride

In a similar manner to that of Example 29(c), by reaction of 5.0 g (29.7 mmol) of (3-methoxymethoxyphenyl)methanol with 8.27 ml (59.5 mmol) of triethylamine and 2.76 ml (35.7 mmol) of
 15 methanesulphonyl chloride, 2.66 g (48%) of the expected product are obtained in the form of a yellow oil.

^1H NMR (CDCl_3): 3.48 (s, 3H), 4.55 (s, 2H), 5.22 (s, 2H), 6.97 to 7.07 (m, 3H), 7.24 to 7.30 (m, 1H).

(d) Ethyl 3-{4-methoxy-3-[3-(3-methoxymethoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylate
 20

In a similar manner to that of Example 1(a), by reaction of 2.5 g (6.12 mmol) of ethyl 3-[3-(3-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxyphenyl]acrylate obtained in Example
 25 13(f) with 1.26 g (6.73 mmol) of 3-methoxymethoxybenzyl



chloride obtained above, 2.90 g (85%) of the expected product are obtained in the form of a yellow oil.

¹H NMR (CDCl₃): 1.27 to 1.35 (m, 15H), 1.69 (s, 4H),
3.43 (s, 3H), 3.77 (s, 3H), 4.24 (q, J = 7.25 Hz, 2H),
5 4.99 (s, 2H), 5.09 (s, 2H), 6.31 (d, J = 15.75 Hz, 1H),
6.88 to 6.96 (m, 5H), 7.16 to 7.23 (m, 2H), 7.45 to
7.51 (m, 2H), 7.67 (d, J = 15.75 Hz, 1H).

(e) 3-{4-Methoxy-3-[3-(3-methoxymethoxybenzyloxy)-
5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-
10 naphthyl]phenyl}acrylic acid

In a similar manner to that of Example 2(h),
starting from 1.0 g (1.79 mmol) of ethyl 3-{4-methoxy-
3-[3-(3-methoxymethoxybenzyloxy)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylate obtained
15 above, 813 mg (85%) of the expected product are
obtained in the form of a white powder with a melting
point of 144-146°C.

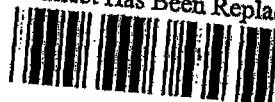
EXAMPLE 31

3-{4-Methoxy-3-[3-(4-methoxymethoxybenzyloxy)-5,5,8,8-
20 tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-
acrylic acid

(a) 4-Methoxymethoxybenzaldehyde

In a similar manner to that of Example 1(a),
by reaction of 30. g (245 mmol) of 4-hydroxybenzaldehyde.
25 with 21 ml (270 mmol) of methoxymethyl chloride, 40.7 g
(100%) of the expected product are obtained in the form

This Sheet Has Been Replaced



of an orange oil.

^1H NMR (CDCl_3): 3.49 (s, 3H), 5.28 (s, 2H), 7.15 (d, $J = 8.75$ Hz, 2H), 7.84 (d, $J = 8.75$ Hz, 2H), 9.9 (s, 1H)

5 (b) (4-Methoxymethoxyphenyl)methanol

In a similar manner to that of Example 29(b), by reaction of 40 g (240 mmol) of 4-methoxymethoxybenzaldehyde with 3.65 g (96 mmol) of lithium aluminium hydride, 15 g (37%) of the expected product are

10 obtained in the form of a colourless oil.

^1H NMR (CDCl_3): 1.71 (t, $J = 5.75$ Hz, 1H), 3.47 (s, 3H), 4.61 (d, $J = 5.75$ Hz, 2H), 5.17 (s, 2H), 7.02 (d, $J = 8.5$ Hz, 2H), 7.29 (d, $J = 8.5$ Hz, 2H).

(c) 4-Methoxymethoxybenzyl chloride

15 In a similar manner to that of Example 29(c),

by reaction of 5.0 g (29.7 mmol) of (4-methoxymethoxyphenyl)methanol with 8.27 ml (59.5 mmol) of triethylamine and 2.76 ml (35.7 mmol) of methanesulphonyl chloride, 2.66 g (48%) of the expected

20 product are obtained in the form of a yellow oil.

^1H NMR (CDCl_3): 3.47 (s, 3H), 4.56 (s, 2H), 5.17 (s, 2H), 7.02 (d, $J = 8.75$ Hz, 2H), 7.31 (d, $J = 8.75$ Hz, 2H).

(d) Ethyl 3-{4-methoxy-3-[3-(4-methoxymethoxy-

25 benzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-



naphthyl]phenyl}acrylate

In a similar manner to that of Example 1(a),
by reaction of 2.5 g (6.12 mmol) of ethyl 3-[3-(3-
hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-
5 naphthyl)-4-methoxyphenyl]acrylate obtained in Example
13(f) with 1.26 g (6.73 mmol) of 4-methoxymethoxybenzyl
chloride obtained above, 3.0 g (87%) of the expected
product are obtained in the form of a white powder with
a melting point of 106-108°C.

10 (e) 3-{4-Methoxy-3-[3-(4-methoxymethoxybenzyloxy)-
5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-
naphthyl]phenyl}acrylic acid

In a similar manner to that of Example 2(h),
starting from 1.0 g (1.79 mmol) of ethyl 3-{4-methoxy-
15 3-[3-(4-methoxymethoxybenzyloxy)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylate obtained
above, 877 mg (91%) of the expected product are
obtained in the form of a white powder with a melting
point of 184-186°C.

20 **EXAMPLE 32**

3-{4-Methoxy-3-[3-(3-hydroxybenzyloxy)-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-
acrylic acid.

(a). Ethyl 3-{4-methoxy-3-[3-(3-hydroxybenzyloxy)-
25 5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-
naphthyl]phenyl}acrylate

This Sheet Has Been Replaced



In a similar manner to that of Example 2(g) but in ethanol as solvent, starting from 1.9 g

(3.4 mmol) of ethyl 3-{4-methoxy-3-[3-(3-methoxy-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-

5 tetrahydro-2-naphthyl]phenyl}acrylate obtained in Example 30(d), 1.38 g (79%) of the expected product are obtained in the form of a white powder with a melting point of 131-133°C.

(b) 3-{4-methoxy-3-[3-(3-hydroxybenzyloxy)-5,5,8,8-

10 tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-acrylic acid

In a similar manner to that of Example 2(h), starting from 1.11 g (2.16 mmol) of ethyl 3-{4-methoxy-

3-[3-(3-hydroxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-

15 tetrahydro-2-naphthyl]phenyl}acrylate obtained above, 1.0 g (95%) of the expected product are obtained in the form of a white powder with a melting point of 229-231°C.

EXAMPLE 33

20 3-[4-Fluoro-3-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylic acid

In a similar manner to that of Example 1(c), by reaction of 2.0 g (8.12 mmol) of 3,5,5,8,8-

pentamethyl-5,6,7,8-tetrahydro-2-naphthylboronic acid,

25 (prepared in Example 5(a) of the patent WO 97/33881) and 1.54 g (6.25 mmol) of 3-(3-bromo-4-fluorophenyl)-



acrylic acid, 1.45 g (63%) of the expected product are obtained in the form of a beige powder with a melting point of 181-183°C.

EXAMPLE 34

5 3-{4-Hydroxy-3-[3-(3-methoxybenzyloxy)-5,5,8,8-
 tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-
 acrylic acid

(a) 2-Bromo-3-(3-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalene

10 In a similar manner to that of Example 1(a), by reaction of 5.0 g (17.7 mmol) of 2-bromo-3-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalene with 3.0 g (19.4 mmol) of 3-methoxybenzyl chloride, 7.14 g (100%) of the expected product are obtained in the form
 15 of a chestnut-brown oil.

¹H NMR (CDCl₃): 1.21 (s, 6H), 1.24 (s, 6H), 1.64 (s, 4H), 3.82 (s, 3H), 5.09 (s, 2H), 6.83 to 6.87 (m, 2H), 7.03 to 7.08 (m, 2H), 7.29 (m, 1H), 7.43 (s, 1H).

(b) 3-(3-Methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylboronic acid

20 In a similar manner to that of Example 1(b), starting from 7.10 g (17.6 mmol) of 2-bromo-3-(3-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalene obtained above, 4.85 g (74%) of
 25 the expected product are obtained in the form of a slightly tacky beige powder.



¹H NMR (CDCl₃): 1.26 (s, 6H), 1.29 (s, 6H), 1.67 (s, 4H), 3.81 (s, 3H), 5.06 (s, 2H), 6.85 to 7.0 (m, 3H), 7.31 (t, J = 7.75 Hz, 1H), 7.78 (s, 1H).

(c) Ethyl 3-(3-bromo-4-methoxymethoxyphenyl)acrylate

5 In a similar manner to that of Example 2(c), by reaction of 30 g (122 mmol) of ethyl 3-(3-bromo-4-methoxymethoxyphenyl)acrylate obtained above with 30.27 g (135 mmol) of triethyl phosphonoacetate, 34.6 g (90%) of the expected product are obtained in the form
10 of white crystals with a melting point of 64-66°C.

(d) Ethyl 3-(3-bromo-4-hydroxyphenyl)acrylate

In a similar manner to that of Example 2(g), starting from 30 g (95 mmol) of ethyl 3-(3-bromo-4-methoxymethoxyphenyl)acrylate obtained above, 25.8 g
15 (100%) of the expected product are obtained in the form of a white powder with a melting point of 113-115°C.

(e) Ethyl 3-{4-hydroxy-3-[3-(3-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylate.

20 In a similar manner to that of Example 1(c), by reaction of 1.0 g (3.7 mmol) of ethyl 3-(3-bromo-4-hydroxyphenyl)acrylate obtained above with 1.77 g (4.8 mmol) of 3-(3-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylboronic acid
25 obtained in Example 34(c), 630 mg (33%) of the expected



product are obtained in the form of a colourless oil.

¹H NMR (CDCl₃): 1.25 to 1.36 (m, 15H), 1.70 (s, 4H),
 3.78 (s, 3H), 4.26 (q, J = 7.25 Hz, 2H), 4.99 (s, 2H),
 6.32 (d, J = 15.75 Hz, 1H), 6.84 (d, J = 8.5 Hz, 2H),
 5 6.93 (s, 1H), 6.98 to 7.02 (m, 2H), 7.19 (d, J =
 8.5 Hz, 1H), 7.25 (s, 1H), 7.40 (d, J = 2.25 Hz, 1H),
 7.69 (d, J = 15.75 Hz, 1H).

(f) 3-{4-Hydroxy-3-[3-(3-methoxybenzyloxy)-5,5,8,8-
 tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-
 10 acrylic acid

In a similar manner to that of Example 2(h),
 starting from 600 mg (1.16 mmol) of ethyl 3-{4-hydroxy-
 3-[3-(3-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-
 tetrahydro-2-naphthyl]phenyl}acrylate obtained above,
 15 539 mg (95%) of the expected product are obtained in
 the form of a white powder with a melting point of
 197-199°C.

EXAMPLE 35

3-{4-Hydroxy-3-[3-(4-methoxybenzyloxy)-5,5,8,8-
 20 tetramethyl-5,6,7,8-tetrahydro-2-
 naphthyl]phenyl}acrylic acid

(a) 2-Bromo-3-(4-methoxybenzyloxy)-5,5,8,8-
 tetramethyl-5,6,7,8-tetrahydronaphthalene.

In a similar manner to that of Example 1(a),
 25 by reaction of 5.0 g (17.7 mmol) of 3-hydroxy-2-bromo-
 5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalene with



3.0 g (19.4 mmol) of 4-methoxybenzyl chloride, 7.14 g (100%) of the expected product are obtained in the form of a chestnut-brown oil.

¹H NMR (CDCl₃): 1.21 (s, 6H), 1.24 (s, 6H), 1.64 (s, 4H), 3.81 (s, 3H), 5.04 (s, 2H), 6.83 (s, 1H), 6.92 (d, J = 7.5 Hz, 2H), 7.39 (d, J = 7.5 Hz, 2H), 7.43 (s, 1H).

(b) 3-(4-Methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylboronic acid.

10 In a similar manner to that of Example 1(b), starting from 7.14 g (17.7 mmol) of 2-bromo-3-(4-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalene obtained above, 3.55 g (54%) of the expected product are obtained in the form of an orange oil.

¹H (CDCl₃): 1.28 (s, 12H), 1.57 (s, 4H), 3.82 (s, 3H), 5.03 (s, 2H), 5.78 (s, 2H), 6.89 (s, 1H), 6.93 (d, J = 8.75 Hz, 1H), 7.35 (d, J = 8.5 Hz, 1H), 7.78 (s, 1H).

20 (c) Ethyl 3-(4-hydroxy-3-[3-(4-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylate.

In a similar manner to that of Example 1(c), by reaction of 1.0 g (3.7 mmol) of ethyl 3-(3-bromo-4-hydroxyphenyl)acrylate obtained in Example 34(d) with 2.0 g (5.5 mmol) of 3-(4-methoxybenzyloxy)-5,5,8,8-



tetramethyl-5,6,7,8-tetrahydro-2-naphthylboronic acid obtained above, 930 mg (49%) of the expected product are obtained in the form of a colourless oil.

¹H NMR (CDCl₃): 1.29 (s, 12H), 1.34 (t, J = 7.0 Hz, 3H),
 5 1.70 (s, 4H), 3.72 (s, 3H), 4.26 (q, J = 7.25 Hz, 2H),
 5.02 (s, 2H), 6.33 (d, J = 15.75 Hz, 1H), 6.70 (s, 1H),
 6.80 to 6.87 (m, 3H), 7.02 (d, J = 7.25 Hz, 2H), 7.18
 to 7.25 (m, 2H), 7.42 (d, J = 2.25 Hz, 1H), 7.48 (d,
 J = 8.5 Hz, 1H), 7.69 (d, J = 16.0 Hz, 1H).

10 (d) 3-{4-Hydroxy-3-[3-(3-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylic acid.

In a similar manner to that of Example 2(h), starting from 930 mg (1.8 mmol) of ethyl 3-{4-hydroxy-
 15 3-[3-(4-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylate obtained above, 800 mg (91%) of the expected product are obtained in the form of a white powder with a melting point of 170-172°C.

20 **EXAMPLE 36**

3-{4-Hydroxy-3-[3-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylic acid.

(a) 2-Bromo-3-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-
 25 5,6,7,8-tetrahydronaphthalene.

In a similar manner to that of Example 1(a),



by reaction of 5.0 g (17.7 mmol) of 3-hydroxy-2-bromo-5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalene with 3.67 g (19.4 mmol) of 4-fluorobenzyl bromide, 4.3 g (62%) of the expected product are obtained in the form of light chestnut-brown crystals with a melting point of 74-76°C.

(b) 3-(4-Fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylboronic acid.

In a similar manner to that of Example 1(b), starting from 4.3 g (11.0 mmol) of 2-bromo-3-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalene obtained above, 3.24 g (83%) of the expected product are obtained in the form of an orange oil.

¹H NMR (CDCl₃): 1.27 (s, 6H), 1.29 (s, 6H), 1.67 (s, 4H), 5.08 (s, 2H), 5.81 (s, 2H), 7.06 to 7.13 (m, 2H), 7.38 to 7.43 (m, 2H), 7.80 (s, 1H).

(c) Ethyl 3-{4-hydroxy-3-[3-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylate.

In a similar manner of Example 1(c), by reaction of 1.0 g (3.7 mmol) of ethyl 3-(3-bromo-4-hydroxyphenyl)acrylate obtained in Example 34(d) with 1.97 g (5.5 mmol) of 3-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylboronic acid obtained above, 825 mg (44%) of the expected product



are obtained in the form of a white solid with a melting point of 123-125°C.

- (d) 3-{4-Hydroxy-3-[3-(3-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylic acid.

In a similar manner to that of Example 2(h), starting from 800 mg (1.6 mmol) of ethyl 3-{4-hydroxy-3-[3-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylate obtained above, 425 mg (56%) of the expected product are obtained in the form of a white powder with a melting point of 157-159°C.

EXAMPLE 37

- 3-{4-Hydroxy-3-[3-(4-chlorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylic acid.

(a) 2-Bromo-3-(4-chlorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalene.

In a similar manner to that of Example 1(a), by reaction of 5.0 g (17.7 mmol) of 3-hydroxy-2-bromo-5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalene with 3.12 g (19.4 mmol) of 4-chlorobenzyl chloride, 7.22 g (100%) of the expected product are obtained in the form of pale chestnut-brown crystals with a melting point of 108-110°C.

This Sheet Has Been Replaced



(b) 3-(4-Chlorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylboronic acid.

In a similar manner to that of Example 1(b), starting from 7.14 g (17.5 mmol) of 2-bromo-3-(4-chlorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalene obtained above, 3.50 g (54%) of the expected product are obtained in the form of an orange oil.

¹H NMR (CDCl₃): 1.26 (s, 6H), 1.29 (s, 6H), 1.67 (s, 4H), 5.09 (s, 2H), 5.72 (s, 2H), 6.84 (s, 1H), 7.37 (m, 4H), 7.80 (s, 1H).

(c) Ethyl 3-{4-hydroxy-3-[3-(4-chlorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylate.

In a similar manner to that of Example 1(c), by reaction of 1.0 g (3.7 mmol) of ethyl 3-(3-bromo-4-hydroxyphenyl)acrylate obtained in Example 34(d) with 2.05 g (5.5 mmol) of 3-(4-chlorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylboronic acid obtained above, 590 mg (30%) of the expected product are obtained in the form of a white solid with a melting point of 152-154°C.

(d) 3-{4-Hydroxy-3-[3-(4-chlorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylic acid.

In a similar manner to that of Example 2(h),



starting from 580 mg (1.12 mmol) of ethyl 3-{4-hydroxy-3-[3-(4-chlorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylate obtained above, 382 mg (70%) of the expected product are obtained in the form of a white powder with a melting point of 147-149°C.

EXAMPLE 38

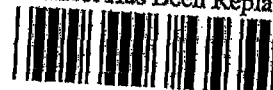
3-[4-Hydroxy-3-(3-methoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylic acid.

- 10 (a) Ethyl 3-(4-hydroxy-3-[3-methoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl)acrylate.

In a similar manner to that of Example 1(c), by reaction of 1.0 g (3.7 mmol) of ethyl 3-(3-bromo-4-hydroxyphenyl)acrylate obtained in Example 34(d) with 1.6 g (5.5 mmol) of 3-methoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylboronic acid obtained in Example 13(b), 150 mg (9%) of the expected product are obtained in the form of a white solid with a melting point of 101-103°C.

- (d) 3-{4-Hydroxy-3-[3-methoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylic acid.

In a similar manner to that of Example 2(h), starting from 150 mg (0.34 mmol) of ethyl 3-{4-hydroxy-3-[3-methoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-



tetrahydro-2-naphthyl]phenyl}acrylate obtained above, 100 mg (72%) of the expected product are obtained in the form of a white powder with a melting point of 191-193°C.

5 **EXAMPLE 39**

3-(3',5'-Di-tert-butyl-6-hydroxy-2'-propyloxy-3-biphenyl)acrylic acid.

(a) 1-Bromo-3,5-di-tert-butyl-2-propyloxybenzene.

In a similar manner to that of Example 1(a),
10 by reaction of 15 g (52.6 mmol) of 6-bromo-2,4-di-tert-butylphenol with 7.4 g (57.9 mmol) of 1-bromopropane, 17.2 g (100%) of the expected product are obtained in the form of orange crystals with a melting point of 41-43°C.

15 (b) 2-Propyloxy-3,5-di-tert-butylphenylboronic acid.

In a similar manner to that of Example 1(b), starting from 16.0 g (48.9 mmol) of 1-bromo-3,5-di-tert-butyl-2-propyloxybenzene obtained above, 9.1 g (63%) of the expected product are obtained in the form
20 of a white powder with a melting point of 104-106°C.

(c) Ethyl 3-(3',5'-di-tert-butyl-6-hydroxy-2'-propyloxy-3-biphenyl)acrylate.

In a similar manner to that of Example 1(c),
by reaction of 1.0 g (3.7 mmol) of ethyl 3-(3-bromo-4-hydroxyphenyl)acrylate obtained in Example 34(d) with
25



2.14 g (7.33 mmol) of 2-propyloxy-3,5-di-tert-butylphenylboronic acid obtained above, 70 mg (4%) of the expected product are obtained in the form of a colourless oil.

5 ^1H NMR (CDCl_3): 0.85 (t, $J = 7.5$ Hz, 3H), 1.34 (s, 9H), 1.40 (t, $J = 7.75$ Hz, 3H), 1.45 (s, 9H), 1.55 to 1.59 (m, 2H), 3.43 to 3.65 (m, 2H), 4.27 (q, $J = 8.25$ Hz, 2H), 6.37 (d, $J = 15.75$ Hz, 1H), 7.05 (d, $J = 8.25$ Hz, 1H), 7.16 (d, $J = 2.5$ Hz, 1H), 7.30 (s, 1H), 7.43 (d, 10 $J = 2.5$ Hz, 1H), 7.50 to 7.55 (m, 2H), 7.72 (d, $J = 16.0$ Hz, 1H).

(d) 3-(3',5'-Di-tert-butyl-6-hydroxy-2'-propyloxy-3-biphenyl)acrylic acid:

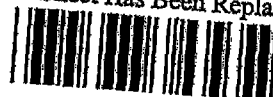
In a similar manner to that of Example 2(h),
15 starting from 70 mg (0.16 mmol) of ethyl 3-(3',5'-di-tert-butyl-6-hydroxy-2'-propyloxy-3-biphenyl)acrylate obtained above, 50 mg (75%) of the expected product are obtained in the form of a white powder with a melting point of 187-189°C.

20 **EXAMPLE 40**

3-(3',5'-Di-tert-butyl-6-hydroxy-2'-butyloxy-3-biphenyl)acrylic acid.

(a) 1-Bromo-3,5-di-tert-butyl-2-butyloxybenzene.

In a similar manner to that of Example 1(a),
25 by reaction of 15 g (52.6 mmol) of 2-bromo-4,6-di-tert-butylphenol with 7.93 g (57.9 mmol) of 1-bromobutane,



17.7 g (100%) of the expected product are obtained in the form of an orange oil.

^1H NMR (CDCl_3): 0.99 (t, $J = 7.5$ Hz, 3H), 1.28 (s, 9H), 1.39 (s, 9H), 1.45 to 1.60 (m, 2H), 1.80 to 1.92 (m, 2H), 4.03 (t, $J = 7.0$ Hz, 2H), 7.27 (d, $J = 2.5$ Hz, 1H), 7.39 (d, $J = 2.5$ Hz, 1H).

(b) 2-Butyloxy-3,5-di-tert-butylphenylboronic acid.

In a similar manner to that of Example 1(b), starting from 16.0 g (46.8 mmol) of 1-bromo-3,5-di-tert-butyl-2-butyloxybenzene obtained above, 14 g (97%) of the expected product are obtained in the form of a white powder with a melting point of 92-94°C.

(c) Ethyl 3-(3',5'-di-tert-butyl-6-hydroxy-2'-butyloxy-3-biphenyl)acrylate.

In a similar manner to that of Example 1(c), by reaction of 6.2 g (22.8 mmol) of ethyl 3-(3-bromo-4-hydroxyphenyl)acrylate obtained in Example 34(d) with 14 g (45.7 mmol) of 2-butyloxy-3,5-di-tert-butylphenylboronic acid obtained above, 700 mg (7%) of the expected product are obtained in the form of a yellow oil.

^1H NMR (CDCl_3): 0.78 (t, $J = 7.5$ Hz, 3H), 1.31 to 1.56 (m, 25H), 3.20 to 3.66 (m, 2H), 4.27 (q, $J = 7.25$ Hz, 2H), 6.37 (d, $J = 16.0$ Hz, 1H), 7.06 (d, $J = 8.25$ Hz, 1H), 7.16 (d, $J = 2.5$ Hz, 1H), 7.30 (s, 1H), 7.43 (d, $J = 2.25$ Hz, 1H), 7.49 to 7.55 (m, 2H), 7.72 (d,



$J = 16.0 \text{ Hz, 1H}$).

(d) 3-(3',5'-Di-tert-butyl-6-hydroxy-2'-butoxy-3-biphenyl)acrylic acid.

In a similar manner to that of Example 2(h),
 5 starting from 430 mg (0.95 mmol) of ethyl 3-(3',5'-di-tert-butyl-6-hydroxy-2'-butoxy-3-biphenyl)acrylate obtained above, 300 mg (74%) of the expected product are obtained in the form of a white powder with a melting point of 194-196°C.

10 EXAMPLE 41

3-(2'-Butoxy-3',5'-di-tert-butyl-6-methoxy-3-biphenyl)acrylic acid.

(a) Ethyl 3-(2'-butoxy-3',5'-di-tert-butyl-6-methoxy-3-biphenyl)acrylate.

15 In a similar manner to that of Example 1(a), by reaction of 230 mg (0.5 mmol) of ethyl 3-(3',5'-di-tert-butyl-6-hydroxy-2'-butoxy-3-biphenyl)acrylate obtained in Example 40(c) with 82 mg (0.58 mmol) of iodomethane, 230 mg (100%) of the expected product are
 20 obtained in the form of a yellow oil.

$^1\text{H NMR}$ (CDCl_3): 0.67 (t, $J = 7.25 \text{ Hz}$, 3H), 1.07 (m, 2H), 1.25 to 1.36 (m, 14H), 1.43 (s, 9H), 3.40 (br, 2H), 3.84 (s, 3H), 4.25 (q, $J = 7.0 \text{ Hz}$, 2H), 6.33 (d, $J = 15.5 \text{ Hz}$, 1H), 6.98 (d, $J = 8.5 \text{ Hz}$, 1H), 7.11 (d, $J = 2.25 \text{ Hz}$, 1H), 7.35 (d, $J = 2.5 \text{ Hz}$, 1H), 7.48 (dd, $J_1 = 8.5 \text{ Hz}$, $J_2 = 2.25 \text{ Hz}$, 1H), 7.56 (d, $J = 2.25 \text{ Hz}$,



1H), 7.68 (d, J = 15.75 Hz, 1H).

(b) 3-(2'-Butoxy-3',5'-di-tert-butyl-6-methoxy-3-biphenyl)acrylic acid.

In a similar manner to that of Example 2(h),
5 starting from 230 mg (0.51 mmol) of ethyl 3-(2'-butoxy-3',5'-di-tert-butyl-6-methoxy-3-biphenyl)acrylate obtained above, 120 mg (55%) of the expected product are obtained in the form of a white powder with a melting point of 204-206°C.

10 **EXAMPLE 42**

3-(3',5'-Di-tert-butyl-6-methoxy-2'-propoxy-3-biphenyl)acrylic acid.

(a) Ethyl 3-(3',5'-di-tert-butyl-6-methoxy-2'-propoxy-3-biphenyl)acrylate.

15 In a similar manner to that of Example 1(c), by reaction of 1.0 g (3.5 mmol) of ethyl 3-(3-bromo-4-methoxyphenyl)acrylate obtained in Example 13(d) with 1.54 g (5.26 mmol) of 2-propyloxy-3,5-di-tert-butylphenylboronic acid obtained in Example 39(b),
20 1.20 g (76%) of the expected product are obtained in the form of a white powder with a melting point of 107-109°C.

(b) 3-(3',5'-Di-tert-butyl-6-methoxy-2'-propoxy-3-biphenyl)acrylic acid.

25 In a similar manner to that of Example 2(h),



starting from 1.0 g (2.2 mmol) of ethyl 3-(3',5'-di-
tert-butyl-6-methoxy-2'-propoxy-3-biphenyl)acrylate
obtained above, 800 mg (85%) of the expected product
are obtained in the form of a white powder with a
5 melting point of 207-209°C.

EXAMPLE 43

3-[4-Hydroxy-3-(5,5,8,8-tetramethyl-4-propoxy-5,6,7,8-
tetrahydro-2-naphthyl)phenyl]acrylic acid

(a) 3-Bromo-5,5,8,8-tetramethyl-5,6,7,8-
10 tetrahydronaphth-1-ol

9.73 g (73 mmol) of aluminium chloride are
introduced together with 80 ml of dichloromethane under
a stream of nitrogen into a 2 litre three-necked flask;
and a solution of 25 g (145 mmol) of 3-bromophenol in
15 100 ml of dichloromethane is added dropwise, and the
mixture is stirred at room temperature for 15 minutes.
Then a solution of 26.2 g (143 mmol) of 2,5-dichloro-
2,5-dimethylhexane in 100 ml of dichloromethane is run
in and the mixture is stirred at room temperature for 1
20 hour. Then a solution of 40 g (218 mmol) of 2,5-
dichloro-2,5-dimethylhexane in 200 ml of
dichloromethane is added in four portions with one hour
of stirring between each addition and the mixture is
stirred for 15 hours. The dichloromethane is evaporated
25 from the reaction medium, the residue is taken up in
ethyl acetate and water, and the organic phase is
decanted, dried over magnesium sulphate, filtered and



evaporated. The residue obtained is purified by chromatography on silica, eluting first with heptane and then with a 95:5 heptane/ethyl acetate mixture. After evaporation of the solvents, 30 g (73%) of the expected product are obtained in the form of oily black crystals.

^1H NMR (CDCl_3): 1.25 (s, 6H), 1.38 (s, 6H), 1.58 to 1.67 (m, 4H), 4.99 (s, 1H), 6.25 (d, $J = 2.0$ Hz, 1H), 7.04 (d, $J = 2.0$ Hz, 1H).

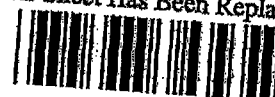
10 (b) 2-Bromo-4-propyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalene.

In a similar manner to that of Example 1(a), by reaction of 18 g (63.6 mmol) of 3-bromo-5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphth-1-ol obtained in the preceding example with 8.61 g (70 mmol) of 1-bromopropane, 16.2 g (78%) of the expected product are obtained in the form of yellow crystals with a melting point of 86-88°C.

(c) 4-Propyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylboronic acid.

In a similar manner to that of Example 1(b), starting from 16.0 g (49.2 mmol) of 2-bromo-4-propyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalene obtained above, 6.2 g (46%) of the expected product are obtained in the form of a white powder with a melting point of 230-232°C.

This Sheet Has Been Replaced



(d) Ethyl 3-[4-hydroxy-3-(5,5,8,8-tetramethyl-4-propoxy-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylate.

In a similar manner to that of Example 1(c), by reaction of 1.0 g (3.7 mmol) of ethyl 3-(3-bromo-4-hydroxyphenyl)acrylate obtained in Example 34(d) with 1.61 g (5.5 mmol) of 4-propyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylboronic acid obtained in Example 43(c), 640 mg (40%) of the expected product are obtained in the form of a white powder with a melting point of 114-116°C.

(e) 3-[4-Hydroxy-3-(5,5,8,8-tetramethyl-4-propoxy-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylic acid.

In a similar manner to that of Example 2(h), starting from 640 mg (1.47 mmol) of ethyl 3-[4-hydroxy-3-(5,5,8,8-tetramethyl-4-propoxy-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylate obtained above, 270 mg (45%) of the expected product are obtained in the form of a white powder with a melting point of 209-211°C.

EXAMPLE 44

20 3-[4-Methoxy-3-[3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl]acrylic acid.

(a) Ethyl 3-[4-methoxy-3-[3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl]acrylate.

25 In a similar manner to that of Example 1(a), by reaction of 1.40 g (3.4 mmol) of ethyl 3-[3-(3-



hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxyphenyl]acrylate obtained in Example 13(f) with 450 μ l (3.77 mmol) of benzyl bromide, 1.64 g (97%) of the expected product are obtained in the form of a yellow oil.

^1H NMR (CDCl_3): 1.28 to 1.35 (m, 15H), 1.69 (s, 4H), 3.76 (s, 3H), 4.25 (q, $J = 7.0$ Hz, 2H), 5.02 (s, 2H), 6.30 (d, $J = 15.75$ Hz, 1H), 6.89 (s, 1H), 6.93 (d, $J = 8.25$ Hz, 1H), 7.19 (s, 1H), 7.20 to 7.35 (m, 5H), 7.43 to 7.52 (m, 2H), 7.67 (d, $J = 16.0$ Hz, 1H).

(b) 3-{4-Methoxy-3-[3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylic acid.

In a similar manner to that of Example 2(h), starting from 1.64 g (3.3 mmol) of ethyl 3-{4-methoxy-3-[3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylate obtained above, 1.27 g (82%) of the expected product are obtained in the form of a white powder with a melting point of 200-202°C.

EXAMPLE 45

20 3-Methyl-5-[3-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]penta-2,4-dienoic acid.

(a) 3-(3,5,5,8,8-Pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)benzaldehyde.

In a similar manner to that of Example 1(c), by reaction of 2.0 g (8.12 mmol) of 3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthylboronic acid



(prepared in Example 5(a) of the patent WO 97/33881) and 1.89 g (10.15 mmol) of 3-bromobenzaldehyde, 3.10 g (100%) of the expected product are obtained in the form of a white powder with a melting point of 99-101°C.

- 5 (b) Ethyl 3-methyl-5-[3-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]penta-2,4-dienoate.

In a similar manner to that of Example 2(c), by reaction of 2.0 g (6.53 mmol) of 3-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)benzaldehyde
10 obtained in the preceding example and 1.90 g (7.20 mmol) of triethyl 3-methyl-4-phosphonocrotonate, 1.80 g (66%) of the expected product are obtained in the form of a white powder with a melting point of
15 83-85°C.

- (c) 3-Methyl-5-[3-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]penta-2,4-dienoic acid.

In a similar manner to that of Example 2(h), starting from 1.00 g (2.4 mmol) of ethyl 3-methyl-5-[3-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]penta-2,4-dienoate obtained above and
20 after separation of the isomers on a fine silica column (7-35 µm) eluted with a 95:5 heptane/ethyl acetate mixture, 420 mg (45%) of the expected product are
25 obtained in the form of a white powder with a melting point of 218-220°C.



B. EXAMPLES OF TESTS

The biological tests carried out correspond to those described in the present application. The results obtained are collated in the following table:

Compound No.	RXR binding	RXR α transactivation	
	K _o (nM)	Agonist AC ₅₀ (nM)	Antagonist IC ₅₀ (nM)
1	394	384	-----
2	23	inactive	920
3	10	inactive	729
4	17	165	-----
5	76	inactive	4000
6	14	inactive	505
7	153	32	-----
8	235	inactive	1100
9	231	inactive	631

C. FORMULATION EXAMPLES**1) ORAL ROUTE**

(a) The following composition is prepared in the form of a 0.8 g tablet

Compound of Example 3	0.005 g
Pregelatinized starch	0.265 g
Microcrystalline cellulose	0.300 g

This Sheet Has Been Replaced



Lactose 0.200 g

Magnesium stearate 0.030 g

For the treatment of acne, 1 to 3 tablets
will be administered to an adult individual per day for
5 3 to 6 months, depending on the severity of the case
treated.

(b) A drinkable suspension for packaging in 5 ml vials
is prepared:

	Compound of Example 2	0.050 g
10	Glycerol	0.500 g
	70% sorbitol	0.500 g
	Sodium saccharinate	0.010 g
	Methyl parahydroxybenzoate	0.040 g
	Flavouring	qs
15	Purified water	qs 5 ml

For the treatment of acne, 1 vial will be
administered to an adult individual per day for
3 months, depending on the severity of the case
treated.

20 (c) The following formulation for packaging in gelatin
capsules is prepared:

	Compound of Example 5	0.025 g
	Corn starch	0.060 g
	Lactose qs	0.300 g

25 The gelatin capsules used consist of gelatin,
titanium oxide and a preserving agent.



In the treatment of psoriasis, 1 gelatin capsule will be administered to an adult individual per day for 30 days.

2) TOPICAL ROUTE

- 5 (a) The following nonionic water-in-oil cream is prepared:

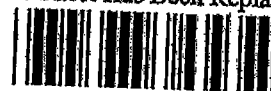
	Compound of Example 6	0.100 g
	Mixture of emulsifying lanolin	
	alcohols, waxes and refined oils,	
10	sold by the company BDF under the	
	name "anhydrous Eucerin"	39.900 g
	Methyl para-hydroxybenzoate	0.075 g
	Propyl para-hydroxybenzoate	0.075 g
	Sterile demineralized water qs . . .	100.000 g

- 15 This cream will be applied to psoriatic skin once or twice a day for 30 days.

- (b) A gel is prepared by making the following formulation:

	Compound of Example 18	0.050 g
20	Base erythromycin	4.000 g
	Butylhydroxytoluene	0.050 g
	Hydroxypropylcellulose sold by	
	the company Hercules under the	
	name "Klucel HF"	2.000 g
25	Ethanol (at 95°) qs	100.000 g

This gel will be applied to skin affected



with dermatitis or acneic skin 1 to 3 times a day for 6 to 12 weeks, depending on the severity of the case treated.

(c) An anti-seborrhoeic lotion is prepared by mixing
5 together the following ingredients:

Compound of Example 4	0.030 g
Propylene glycol	5.000 g
Butylhydroxytoluene	0.100 g
Ethanol (at 95°) qs	100.000 g

10 This lotion will be applied twice a day to a seborrhoeic scalp, and a significant improvement is observed within a period of between 2 and 6 weeks.

(d) A cosmetic composition to combat the harmful
effects of the sun is prepared by mixing together the
15 following ingredients:

Compound of Example 25	1.000 g
Benzylidenecamphor	4.000 g
Fatty acid triglycerides	31.000 g
Glyceryl monostearate	6.000 g
20 Stearic acid	2.000 g
Cetyl alcohol	1.200 g
Lanolin	4.000 g
Preserving agents	0.300 g
Propylene glycol	2.000 g
25 Triethanolamine	0.500 g
Fragrance	0.400 g



Demineralized water qs 100.000 g

This composition will be applied daily and makes it possible to combat light-induced ageing.

(e) The following nonionic oil-in-water cream is

5 prepared:

	Compound of Example 38	0.500 g
	Vitamin D3	0.020 g
	Cetyl alcohol	4.000 g
	Glyceryl monostearate	2.500 g
10	PEG-50 stearate	2.500 g
	Karite butter	9.200 g
	Propylene glycol	2.000 g
	Methyl para-hydroxybenzoate	0.075 g
	Propyl para-hydroxybenzoate	0.075 g
15	Sterile demineralized water qs	100.000 g

This cream will be applied to psoriatic skin once or twice a day for 30 days.

(f) A topical gel is prepared by mixing together the following ingredients:

20	Compound of Example 19	0.050 g
	Ethanol	43.000 g
	α -tocopherol	0.050 g
	Carboxyvinyl polymer sold under	
	the name "Carbopol 941" by the	
25	company "Goodrich"	0.500 g
	Triethanolamine as an aqueous	



solution at 20% by weight 3.800 g
 Water 9.300 g
 Propylene glycol qs 100.000 g

This gel will be applied in the treatment of
 5 acne 1 to 3 times a day for 6 to 12 weeks, depending on
 the severity of the case treated.

(g) A hair lotion to combat hair loss and to promote
 regrowth of the hair is prepared by mixing together the
 following ingredients:

10 Compound of Example 41 0.05 g
 Compound sold under the name
 "Minoxidil" 1.00 g
 Propylene glycol 20.00 g
 Ethanol 34.92 g
 15 Polyethylene glycol (molecular
 mass = 400) 40.00 g
 Butylhydroxyanisole 0.01 g
 Butylhydroxytoluene 0.02 g
 Water qs 100.00 g

20 This lotion will be applied twice a day for
 3 months to a scalp which has suffered considerable
 hair loss.

(h) An anti-acne cream is prepared by mixing together
 the following ingredients:

25 Compound of Example 13 0.050 g
 Retinoic acid 0.010 g



Mixture of glycerol stearate and
polyethylene glycol stearate (75 mol),
sold under the name "Gelot 64" by
the company "Gattefosse" 15.000 g

5 Kernel oil polyoxyethylenated with
6 mol of ethylene oxide, sold
under the name "Labrafil M2130 CS"
by the company "Gattefosse" 8.000 g

Perhydrosqualene 10.000 g

10 Preserving agents qs

Polyethylene glycol (molecular
mass = 400) 8.000 g

Disodium salt of ethylenediamine-
tetraacetic acid 0.050 g

15 Purified water qs 100.000 g

This cream will be applied to skin affected
with dermatitis or to acneic skin 1 to 3 times a day
for 6 to 12 weeks.

(i) An oil-in-water cream is prepared by making the
20 following formulation:

Compound of Example 29 0.020 g

Betamethasone 17-valerate 0.050 g

S-Carboxymethylcysteine 3.000 g

Polyoxyethylene stearate (40 mol of
25 ethylene oxide) sold under the name
"Myrj 52" by the company "Atlas" . . . 4.000 g

Sorbitan monolaurate, polyoxyethylene



with 20 mol of ethylene oxide, sold
under the name "Tween 20" by the
company "Atlas" 1.800 g
Mixture of glyceryl mono- and
5 distearate sold under the name
"Geleol" by the company "Gattefosse". 4.200 g
Propylene glycol 10.000 g
Butylhydroxyanisole 0.010 g
Butylhydroxytoluene 0.020 g
10 Cetostearyl alcohol 6.200 g
Preserving agents qs
Perhydrosqualene 18.000 g
Mixture of caprylic/capric
triglycerides sold under the name
15 "Miglyol 812" by the company "Dynamit
Nobel" 4.000 g
Triethanolamine (99% by weight) . . 2.500 g
Water qs 100.000 g
This cream will be applied twice a day to
20 skin affected with dermatitis, for 30 days.

(j) The following oil-in-water cream is prepared:

Lactic acid 5.000 g
Compound of Example 33 0.020 g
Polyoxyethylene stearate (40 mol of
25 ethylene oxide) sold under the name
"Myrj 52" by the company "Atlas" . . 4.000 g
Sorbitan monolaurate, polyoxyethylene

with 20 mol of ethylene oxide, sold

under the name "Tween 20" by the

company "Atlas" 1.800 g

Mixture of glyceryl mono- and

5 distearate sold under the name

"Geleol" by the company "Gattefosse". 4.200 g

Propylene glycol 10.000 g

Butylhydroxyanisole 0.010 g

Butylhydroxytoluene 0.020 g

10 Cetostearyl alcohol 6.200 g

Preserving agents qs

Perhydrosqualene 18.000 g

Mixture of caprylic/capric

triglycerides sold under the name

15 "Miglyol 812" by the company "Dynamit

Nobel" 4.000 g

Water qs 100.000 g

This cream will be applied once a day and

helps to combat ageing, whether this is light-induced

20 or chronological ageing.

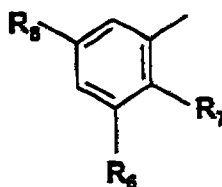
CLAIMS

$$\text{Ar}_1-\text{Ar}_2-\text{X}-\text{R}_1 \quad (\text{I})$$

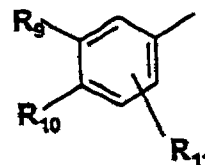
5 - R₁ represents (i) the radical -CH₃
 (ii) the radical -CH₂OR₂
 (iii) the radical -CO-R₃

- Ar_1 represents a radical chosen from the radicals

(a)



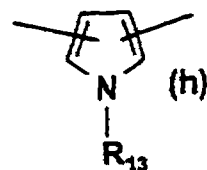
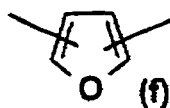
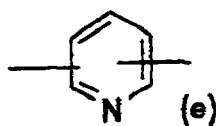
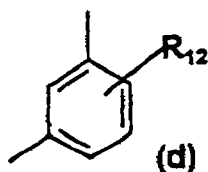
(b)



(c)

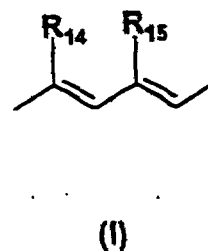
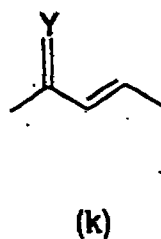
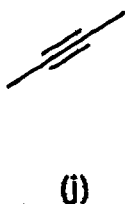
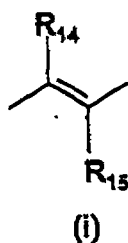
- Ar₂ represents a radical chosen from the radicals of formulae (d)-(h) below:





R_{12} and R_{13} having the meaning given below,

- X represents a radical chosen from the radicals of formulae (i)-(l),



R_{14} , R_{15} and Y having the meanings given below,

5 - R_2 represents a hydrogen atom, a lower alkyl radical or a radical $\text{CO}-R_{16}$

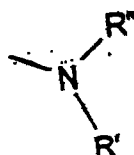
R_{16} having the meaning given below,

- R_3 represents:

(a) a hydrogen atom,

(b) a lower alkyl radical,

(c) a radical of formula:



- R' and R" having the meaning given below,

(d) a radical $-OR_{17}$

R_{17} having the meaning given below,

- R_4 represents a hydrogen atom, a polyether
5 radical, a lower alkyl radical or a radical OR_{18}

R_{18} having the meanings below,

- R_5 represents a hydrogen atom, a lower alkyl
radical, a polyether radical or a radical OR_{19}

R_{19} having the meanings below,

10 - R_6 represents a tert-butyl radical,

- R_7 represents a lower alkyl radical, a polyether
radical or a radical OR_{20}

R_{20} having the meanings below,

- R_6 and R_7 taken together can form, with the
15 adjacent aromatic ring, a 6-membered ring optionally
substituted with methyl groups and/or optionally
interrupted by an oxygen or sulphur atom,

- R_8 represents a tert-butyl, adamantyl, aryl or
aralkyl radical,

20 - R_9 and R_{10} taken together form, with the adjacent
aromatic ring, a 5- or 6-membered ring optionally
substituted with methyl groups and/or optionally
interrupted by an oxygen or sulphur atom,

- R_{11} represents a hydrogen atom, a lower alkyl
25 radical containing from 1 to 9 carbon atoms, a hydroxyl
radical, an alkoxy radical, a polyether radical or a
radical $-OR_{21}$

R_{21} having the meaning given below,



- R_{12} represents a hydrogen atom, a hydroxyl radical, an alkoxy radical, a polyether radical or a radical $-OR_{22}$

R_{22} having the meaning given below,

5 - R_{13} represents a hydrogen atom, a lower alkyl radical or a radical $-COR_{23}$

R_{23} having the meaning given below,

- R_{14} and R_{15} , which may be identical or different, represent a hydrogen atom or a lower alkyl radical,

10 - Y represents an oxygen atom or a CH_2 radical,

- R_{16} represents a lower alkyl radical,

- R_{17} represents a hydrogen atom, a linear or branched alkyl radical containing from 1 to 20 carbon atoms, an alkenyl radical, a mono- or polyhydroxyalkyl radical, an optionally substituted aryl or aralkyl radical or a sugar residue,

15

- R' and R'' , which may be identical or different, represent a hydrogen atom, a lower alkyl radical, a mono- or polyhydroxyalkyl radical, an optionally substituted aryl radical or an amino acid residue, or alternatively, taken together, form a heterocycle,

20

- R_{18} , R_{19} and R_{20} , which may be identical or different, represent a hydrogen atom, a lower alkyl radical, an alkenyl radical, a mono- or polyhydroxyalkyl radical, an aryl radical, an optionally substituted aralkyl radical or a radical

25

$-(CH_2)_n-R_{24}$,

n and R_{24} having the meanings below,



- R_{21} and R_{22} , which may be identical or different, represent an alkenyl radical, a mono- or polyhydroxyalkyl radical, an aryl radical, an optionally substituted aralkyl radical or a radical

5 - $(CH_2)_n-R_{24}$,

n and R_{24} having the meanings below,

- R_{23} represents a lower alkyl radical,

- R_{24} represents a heterocycle, a monohydroxyalkyl radical, a thiol radical optionally substituted with a lower alkyl, an amino radical optionally substituted with at least one lower alkyl, a radical $-COOR_{25}$, or a radical $-CON(R_{26})R_{27}$,

R_{25} , R_{26} and R_{27} having the meanings below,

- R_{25} represents a hydrogen atom or a lower alkyl radical,

- R_{26} and R_{27} are identical or different and represent a hydrogen atom, a lower alkyl radical, or an optionally substituted aryl radical, or else taken together form a heterocycle,

20 - n is an integer such that $2 \leq n \leq 9$,

with the conditions that:

- when Ar_1 represents the radical of formula (c) and X represents the radicals of formula (i) or (j); then

• R_{11} represents the radical $-OR_{21}$ or a polyether radical, or

• Ar_2 represents the radical of formula (d) where R_{12} represents the radical $-OR_{22}$ or a polyether radical,

- the compounds of formula (I) are different from:



R_{11} represents a methoxymethoxy radical in an ortho position relative to the substituent Ar_2 when Ar_1 represents the radical of formula (c), X represents the radical of formula (i), R_{12} represents hydrogen and R_1 represents the radical COR_3 where R_3 represents the radical $-OR_{17}$ and R_{17} represents hydrogen,

R_{12} represents a methoxymethoxy radical in an ortho or para position relative to the substituent Ar_1 when Ar_1 represents the radical of formula (c), X represents the radical of formula (i), R_{11} represents a methyl radical in an ortho position relative to Ar_2 , R_1 represents the radical COR_3 where R_3 represents the radical $-OR_{17}$ and R_{17} represents hydrogen, and the optical and geometrical isomers of the said compounds of formula (I), as well as the salts thereof.

2. Compounds according to Claim 1, characterized in that they are in the form of salts of an alkali metal or alkaline-earth metal, of zinc, of an organic amine or of an inorganic or organic acid.

3. Compounds according to either of Claims 1 and 2, characterized in that the lower alkyl radicals are chosen from the methyl, ethyl, isopropyl, butyl, tert-butyl and hexyl radicals.

4. Compounds according to one of the preceding claims, characterized in that the linear or branched alkyl radicals containing from 1 to 20 carbon atoms are chosen from the methyl, ethyl, tert-butyl, propyl, octyl and 2-ethylhexyl radicals.



5. Compounds according to one of the preceding claims, characterized in that the alkoxy radicals are chosen from the methoxy, propyloxy, pentyloxy and heptyloxy radicals.

5 6. Compounds according to one of the preceding claims, characterized in that the monohydroxyalkyl radicals correspond to radicals containing 2 or 3 carbon atoms, in particular a 2-hydroxyethyl, 2-hydroxypropyl or 3-hydroxypropyl
10 radical.

7. Compounds according to one of the preceding claims, characterized in that the polyhydroxyalkyl radicals are chosen from the 2,3-dihydroxypropyl, 2,3,4-trihydroxybutyl and
15 2,3,4,5-tetrahydroxypentyl radicals and the pentaerythritol residue.

8. Compounds according to one of the preceding claims, characterized in that the aryl radicals correspond to a phenyl radical, optionally
20 substituted with at least one halogen, a lower alkyl, a hydroxyl, an alkoxy, a nitro function, a polyether radical or an amino function optionally protected with an acetyl group or optionally substituted with at least one lower alkyl.

25 9. Compounds according to one of the preceding claims, characterized in that the aralkyl radicals are chosen from a benzyl or phenethyl radical optionally substituted with at least one halogen, a



lower alkyl, a hydroxyl, an alkoxy, a nitro function, a polyether radical or an amino function optionally protected with an acetyl group or optionally substituted with at least one lower alkyl.

5 10. Compounds according to one of the preceding claims, characterized in that the alkenyl radicals correspond to radicals containing from 2 to 5 carbon atoms and containing one or more ethylenic unsaturations.

10 11. Compounds according to any one of the preceding claims, characterized in that the polyether radicals are chosen from the methoxymethyl ether, methoxyethoxymethyl ether and methylthiomethyl ether radicals.

15 12. Compounds according to one of the preceding claims, characterized in that the sugar residues are chosen from the group consisting of glucose, galactose, mannose and glucuronic acid residues.

20 13. Compounds according to any one of the preceding claims, characterized in that the amino acid residues are chosen from the group consisting of residues derived from lysine, glycine or aspartic acid.

25 14. Compounds according to any one of the preceding claims, characterized in that the heterocyclic radicals are chosen from the group consisting of piperidino, morpholino, pyrrolidino or piperazino radicals, optionally substituted in position



4 with a C_1 - C_6 alkyl radical or with a mono- or polyhydroxyalkyl radical.

15. Compounds according to Claim 1, characterized in that they are taken, alone or as
- 5 mixtures, from the group consisting of:
- 3-(3',5'-di-tert-butyl-2'-methoxy-3-biphenyl)-acrylic acid,
 - 3-(2'-benzyloxy-3',5'-di-tert-butyl-6-hydroxy-3-biphenyl)acrylic acid,
 - 10 - 3-(3',5'-di-tert-butyl-6-hydroxy-2'-pentyloxy-3-biphenyl)acrylic acid,
 - 3-(3',5'-di-tert-butyl-6-hydroxy-2'-methoxy-3-biphenyl)acrylic acid,
 - 3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxymethoxyphenyl]acrylic
 - 15 acid,
 - 3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-hydroxyphenyl]acrylic acid,
 - [4-methoxymethoxy-3-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]propynoic acid,
 - 20 - 3-[3-(3-propyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxymethoxyphenyl]acrylic acid,
 - 3-[3-(3-pentyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxymethoxyphenyl]acrylic
 - 25 acid,
 - 3-(5'-adamantan-1-yl-4'-methoxy-2'-methyl-3-biphenyl)acrylic acid,



- 3-(5'-adamantan-1-yl-6-hydroxy-4'-methoxy-2'-methyl-3-biphenyl)acrylic acid,
- 3-(5'-adamantan-1-yl-4'-methoxy-6-methoxymethoxy-2'-methyl-3-biphenyl)acrylic acid,
- 5 - 3-{4-methoxy-3-[3-(3-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-acrylic acid,
- 3-{4-methoxy-3-[3-(4-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-
- 10 acrylic acid,
- 3-{3-[3-(6-hydroxyhexyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid,
- 3-{3-[3-(7-hydroxyheptyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic
- 15 acid,
- 3-{3-[3-(5-hydroxypentyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid,
- 20 - 3-{3-[3-(3-hydroxypropyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid,
- 3-[3-(1-methoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylic acid,
- 25 - 3-[3-(1-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylic acid,
- 3-(3'-adamantan-1-yl-4'-hydroxy-3-biphenyl)acrylic acid,



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- 5-[4-methoxy-3-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]-3-methylpenta-2,4-dienoic acid,
- 5-[4-methoxymethoxy-3-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]-3-methylpenta-2,4-dienoic acid,
- 5 - 5-[4-hydroxy-3-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]-3-methylpenta-2,4-dienoic acid,
- 5-[4-hydroxy-3-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]-3-methylpenta-2,4-dienoic acid,
- 10 - 3-{3-[3-(5-tert-butoxycarbonylpentyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid,
- 3-{3-[3-(7-tert-butoxycarbonylheptyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid,
- 15 - 3-{3-[3-(7-carboxyheptyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid,
- 3-{3-[3-(5-carboxypentyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid,
- 20 - 3-{3-[3-(5-carbamoylpentyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid,
- 3-{3-[3-(5-carbamoylpentyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid,
- 25 - 3-{3-[3-(7-carbamoylheptyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-4-methoxyphenyl}acrylic acid,
- 3-{4-methoxy-3-[5,5,8,8-tetramethyl-3-(2-morpholin-4-

- ylethoxy)-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylic acid,
- 3-{4-methoxy-3-[5,5,8,8-tetramethyl-3-(2-piperidin-1-ylethoxy)-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylic acid,
- 5 - 3-{4-methoxy-3-[3-(2-methoxymethoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylic acid,
- 3-{4-methoxy-3-[3-(3-methoxymethoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylic acid,
- 10 - 3-{4-methoxy-3-[3-(4-methoxymethoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}acrylic acid,
- 3-{4-methoxy-3-[3-(3-hydroxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-acrylic acid,
- 15 - 3-[4-fluoro-3-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylic acid,
- 20 - 3-{4-hydroxy-3-[3-(3-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-acrylic acid,
- 3-{4-hydroxy-3-[3-(4-methoxybenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-acrylic acid,
- 25 - 3-{4-hydroxy-3-[3-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-acrylic acid,

- 3-{4-hydroxy-3-[3-(4-chlorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]phenyl}-acrylic acid,
- 3-[4-hydroxy-3-(3-methoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylic acid,
- 5 - 3-(3',5'-di-tert-butyl-6-hydroxy-2'-propyloxy-3-biphenyl)acrylic acid,
- 3-(3',5'-di-tert-butyl-6-hydroxy-2'-butyloxy-3-biphenyl)acrylic acid,
- 10 - 3-(2'-butoxy-3',5'-di-tert-butyl-6-methoxy-3-biphenyl)acrylic acid,
- 3-(3'5'-di-tert-butyl-6-methoxy-2'-propoxy-3-biphenyl)acrylic acid,
- 3-[4-hydroxy-3-(5,5,8,8-tetramethyl-4-propoxy-5,6,7,8-tetrahydro-2-naphthyl)phenyl]acrylic acid,
- 15 - 3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxyphenyl]acrylic acid,
- ethyl 3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxyphenyl]acrylate,
- 20 - 3-methyl-5-[3-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]penta-2,4-dienoic acid,
- 3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxyphenyl]prop-2-en-1-ol,
- 3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxyphenyl]propenal,
- 25 - N-ethyl 3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxyphenyl]-acrylamide,

- 3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxyphenyl]-1-morpholin-4-yl-propenone,
- N-(4-hydroxyphenyl)-3-[3-(3-benzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-4-methoxyphenyl]acrylamide,
- 5 - 5-(5'-adamantan-1-yl-4'-methoxy-2'methyl-3-biphenyl)-3-methylpenta-2,4-dienoic acid,
- 5-[4-methoxymethoxy-3-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]-3-methylpenta-2,4-dienoic acid,
- 10 - 5-[4-hydroxy-3-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]-3-methylpenta-2,4-dienoic acid,
- 15 - 4-[3-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)phenyl]penta-2,4-dienoic acid,
- 5-(3',5'-di-tert-butyl-2'-methoxy-3-biphenyl)-3-methylpenta-2,4-dienoic acid,
- 5-(3',5'-di-tert-butyl-2'-propoxy-3-biphenyl)-3-methylpenta-2,4-dienoic acid;
- 20 - 5-(2'-butoxy-3',5'-di-tert-butyl-3-biphenyl)-3-methylpenta-2,4-dienoic acid,
- 5-(2'-butoxy-3',5'-di-tert-butyl-6-hydroxy-3-biphenyl)-3-methylpenta-2,4-dienoic acid,
- 25 - 5-(3',5'-di-tert-butyl-6-hydroxy-2'-propoxy-3-biphenyl)-3-methylpenta-2,4-dienoic acid,
- 5-(3',5'-di-tert-butyl-6-hydroxy-2'-methoxy-3-biphenyl)-3-methylpenta-2,4-dienoic acid.

16. Compounds according to Claim 1, characterized in that they have at least one, and preferably all, of the following characteristics:

- R_1 represents the radical $-CO-R_3$
- 5 - Ar_2 represents the radicals of formula (d) or (e),

- R_{11} represents the radical $-O-R_{21}$,
- R_7 represents the radical $-O-R_{20}$.

17. Compounds according to any one of the preceding claims, for use as medicinal products.

18. Compounds according to Claim 17, for use as a medicinal product intended for treating dermatological complaints associated with a keratinization disorder which has a bearing on differentiation and on proliferation, in particular for treating common acne, comedones, polymorphonuclear leukocytes, rosacea, nodulocystic acne, acne conglobata, senile acne and secondary acnes such as solar, medication-related or occupational acne; for treating other types of keratinization disorder, in particular ichthyosis, ichthyosiform states, Darier's disease, palmoplantar keratoderma, leucoplasias and leucoplasiform states, and cutaneous or mucous (buccal) lichen; for treating other dermatological complaints associated with a keratinization disorder with an inflammatory and/or immunoallergic component and, in particular, all forms of psoriasis, whether it is cutaneous, mucous or unguinal psoriasis and even

psoriatic rheumatism, or alternatively cutaneous atopy, such as eczema or respiratory atopy or alternatively gingival hypertrophy; the compounds can also be used in certain inflammatory complaints which have no

5 keratinization disorder; for treating all dermal or epidermal proliferations, whether benign or malignant and whether they are of viral origin or otherwise, such as common warts, flat warts and verruciform epidermodysplasia, it being also possible for the oral

10 or florid papillomatoses and the proliferations to be induced by ultraviolet radiation, in particular in the case of basocellular and spinocellular epithelioma; for treating other dermatological disorders such as bullosis and collagen diseases; for treating certain

15 ophthalmological disorders, in particular corneopathies; for repairing or combating ageing of the skin, whether this is light-induced or chronological ageing, or for reducing actinic keratoses and pigmentations, or any pathologies associated with

20 chronological or actinic ageing; for preventing or curing the stigmata of epidermal and/or dermal atrophy induced by local or systemic corticosteroids, or any other form of cutaneous atrophy; for preventing or treating cicatrization disorders or for preventing or

25 repairing stretch marks, or alternatively for promoting cicatrization, for combating disorders of sebaceous functioning such as the hyperseborrhoea of acne or simple seborrhoea; in the treatment or prevention of

cancerous or precancerous states, more particularly
promyelocytic leukaemia; in the treatment of
inflammatory complaints such as arthritis; in the
treatment of any general or skin complaint of viral
5 origin; in the prevention or treatment of alopecia; in
the treatment of dermatological complaints having an
immunological component; in the treatment of complaints
of the cardiovascular system such as arteriosclerosis,
hypertension, non-insulin-dependent diabetes and
10 obesity; in the treatment of skin disorders due to an
exposure to U.V. radiation.

19. Pharmaceutical composition,
characterized in that it comprises, in a
pharmaceutically acceptable support, at least one of
15 the compounds as defined in any one of Claims 1 to 16.

20. Composition according to Claim 19,
characterized in that the concentration of compound(s)
according to one of Claims 1 to 16 is between 0.001%
and 5% by weight relative to the entire composition.

20 21. Cosmetic composition, characterized in
that it comprises, in a cosmetically acceptable
support, at least one of the compounds as defined in
any one of Claims 1 to 16.

22. Composition according to Claim 21,
25 characterized in that the concentration of compound(s)
according to one of Claims 1 to 16 is between 0.001%
and 3% by weight relative to the entire composition.

23. Use of a cosmetic composition as defined

in either of Claims 21 and 22, for body or hair
hygiene.