



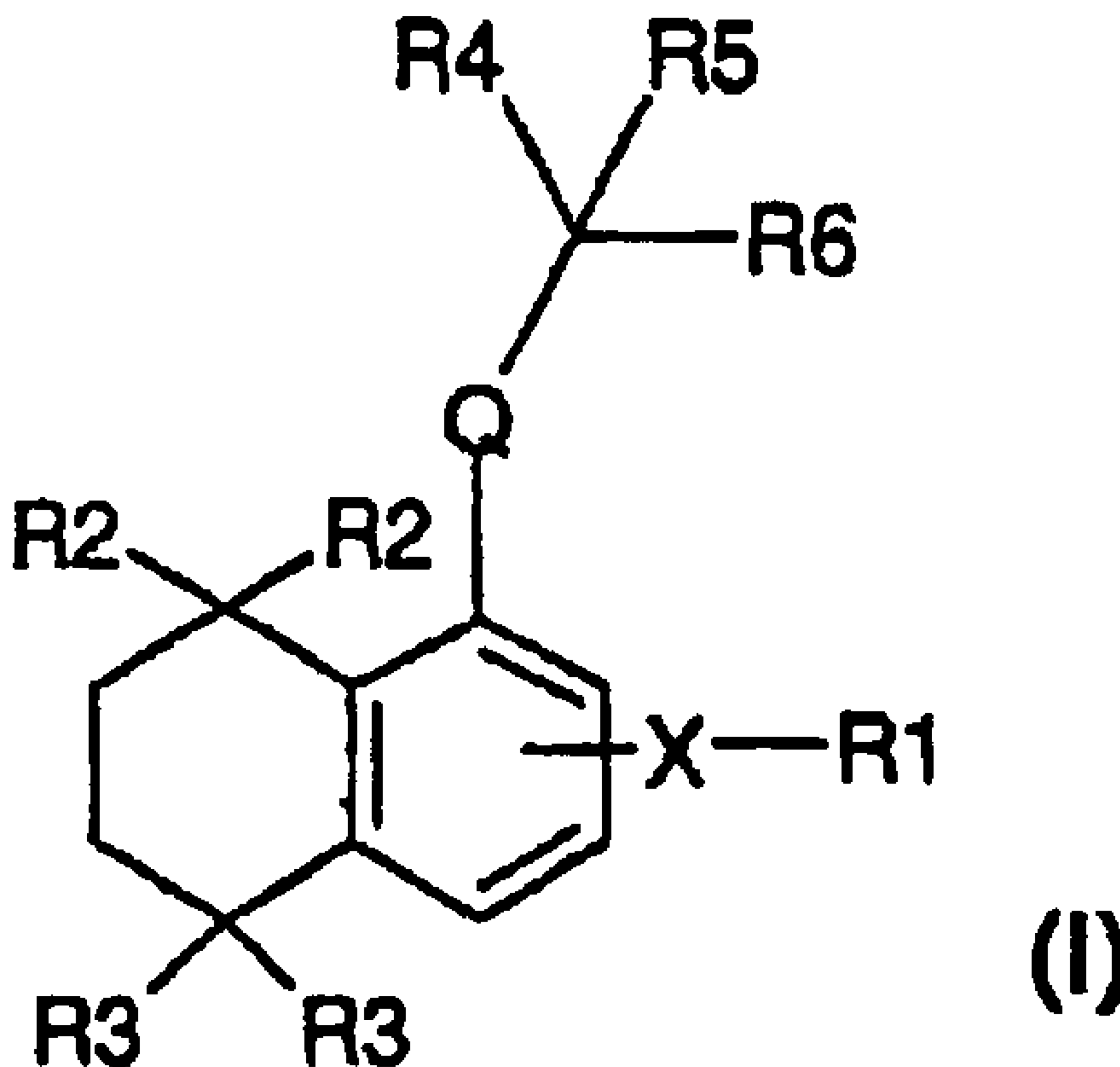
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(54) Titre : LIGANDS INHIBITEURS DES RECEPTEURS RAR
(54) Title: LIGANDS THAT ARE INHIBITORS OF THE RAR RECEPTORS



(57) Abrégé/Abstract:

Novel ligands that are inhibitors of the RAR receptors, process for preparing them and use thereof in human medicine and in cosmetics. The invention relates to novel bicyclic compounds corresponding to the general formula (I) below: R4 R5 X-R6 Q R2

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(74) Agent: ROBIC

(57) Abrégé(suite)/Abstract(continued):

R2 \ X-R1 R3 R3 t~~ and to the method for preparing them, and to their use in pharmaceutical compositions intended for use in human or veterinary medicine, or alternatively in cosmetic compositions.

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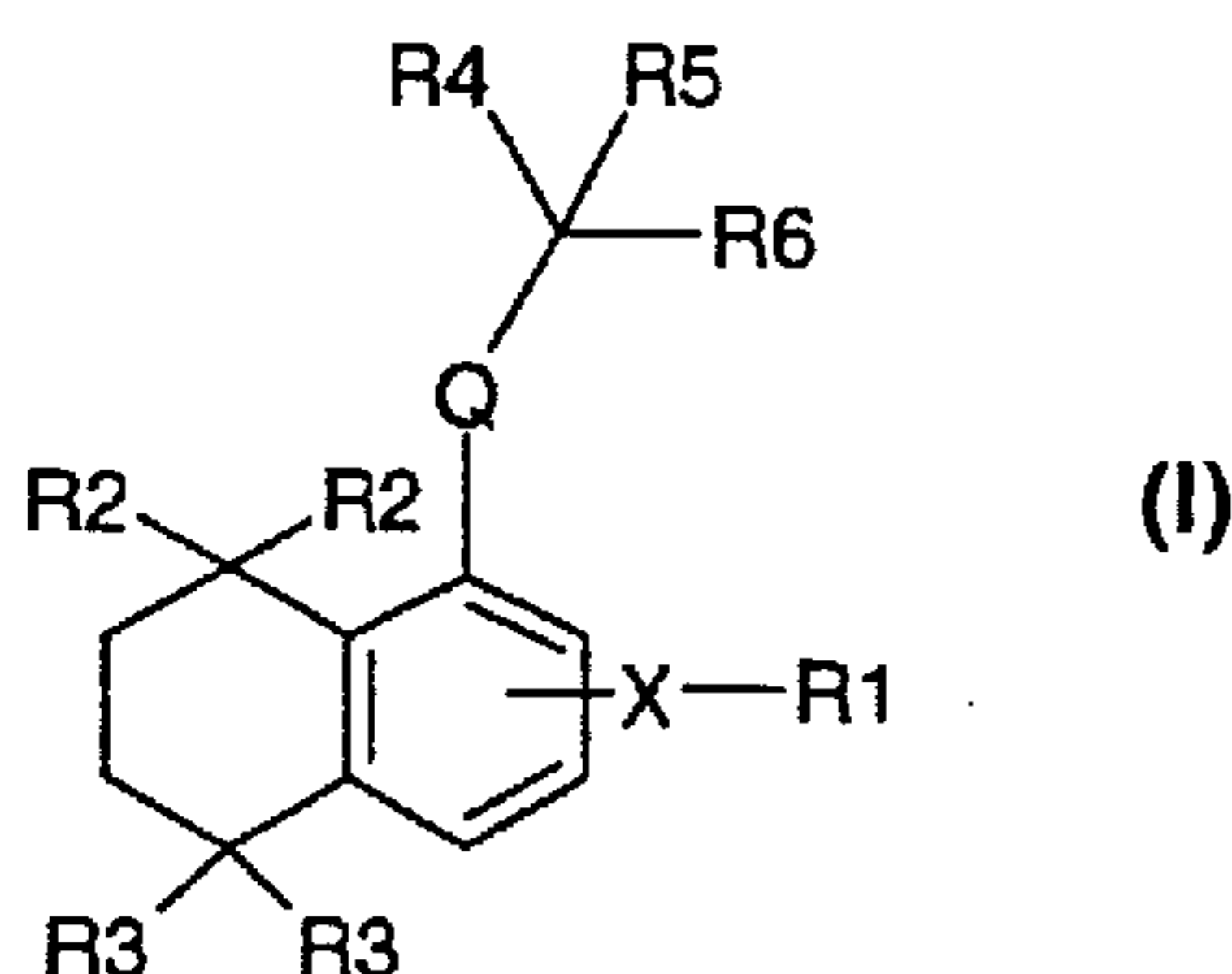
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(54) Title: LIGANDS THAT ARE INHIBITORS OF THE RAR RECEPTORS



(57) Abstract: Novel ligands that are inhibitors of the RAR receptors, process for preparing them and use thereof in human medicine and in cosmetics. The invention relates to novel bicyclic compounds corresponding to the general formula (I) below: R4 R5 X-R6 Q R2 R2 \ X-R1 R3 R3 t~~ and to the method for preparing them, and to their use in pharmaceutical compositions intended for use in human or veterinary medicine, or alternatively in cosmetic compositions.

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LIGANDS THAT ARE INHIBITORS OF THE RAR RECEPTORS

The invention relates to novel bicyclic
5 compounds as novel and useful industrial products. The
invention also relates to the process for preparing
them and to their use in pharmaceutical compositions
for use in human or veterinary medicine, or
alternatively in cosmetic compositions.

10 Compounds with activity of retinoid type
(vitamin A and its derivatives) are widely described in
the literature as having activity in cell proliferation
and differentiation processes. These properties give
this class of compounds high potential in the treatment
15 or prevention of numerous pathologies, and more
particularly in dermatology and cancer. Many biological
effects of retinoids are mediated by modulating the
nuclear retinoic acid receptors (RAR).

The RAR receptors activate transcription by
20 binding to DNA sequence elements, known as RAR response
elements (RARE), in the form of a heterodimer with the
retinoid X receptors (known as RXRs).

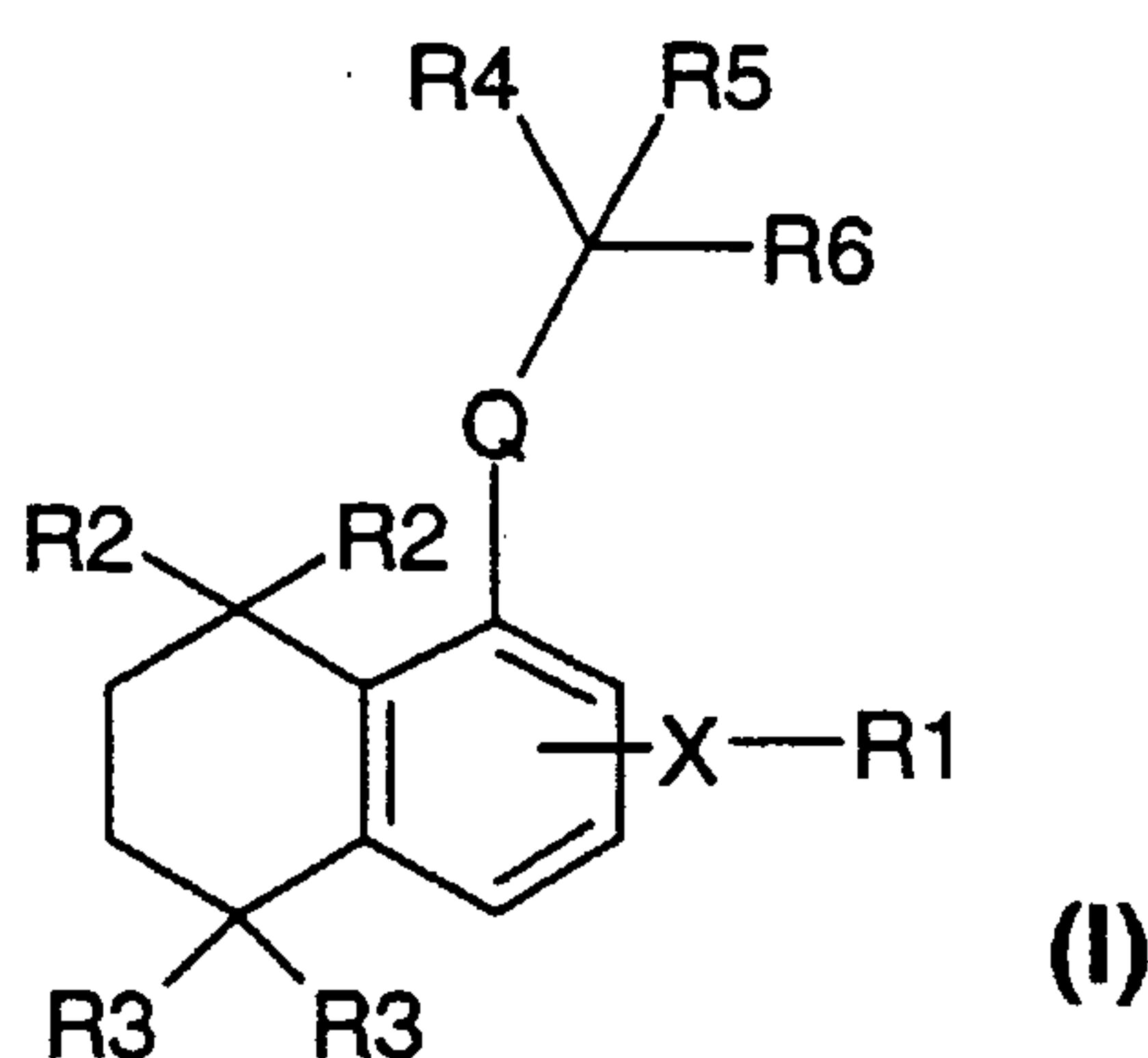
Three subtypes of human RARs have been
identified and described: RAR α , RAR β and RAR γ .

25 The prior art contains a large number of
chemical compounds with inhibitory activity on
receptors of RAR type. Among the prior art documents
that may be mentioned more particularly are patent
EP 0 986 537 which describes heteroethynylated
30 compounds, patent US 6 103 762 which describes

biaromatic compounds whose aromatic nuclei are linked via a divalent propynylene or allenylene radical, patent US 6 150 413 which describes triaromatic compounds, patent US 5 723 499 which describes polycyclic aromatic compounds, and patent US 6 214 878 which describes stilbene compounds. Patent US 6 218 128 describes a family of bicyclic or tricyclic molecules.

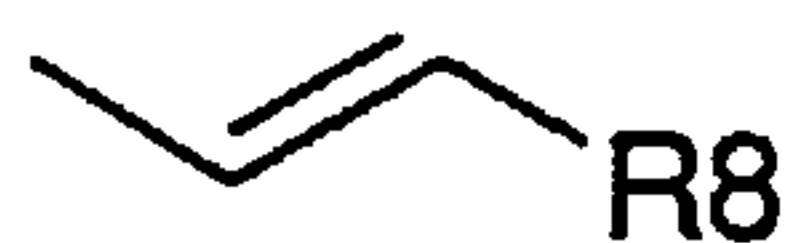
The Applicant has invented novel bicyclic compounds that are inhibitors of the retinoic acid receptors.

Thus, the present invention relates to bicyclic compounds corresponding to the following general formula:



in which:

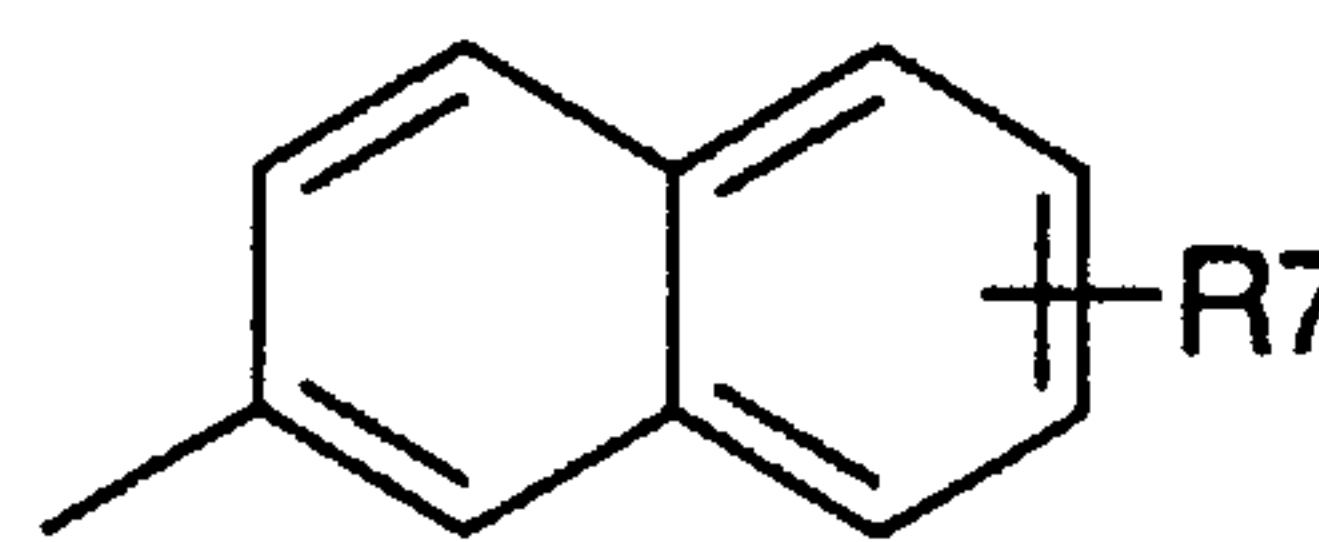
- R_1 represents a radical of formulae (a) to (c) below:



(a)



(b)



(c)

R_7 and R_8 having the meanings given below,

- each of the radicals R_2 and R_3 , which may be identical or different, represent a hydrogen atom or an alkyl radical containing from 1 to 6 carbon atoms,
- 5 - X represents an Se atom, $-CHOH$, $-CH_2$ or $-C=O$,
- Q represents an oxygen atom, a sulphur atom, CH_2 , $-NH$ or $-NR_9$,

R_9 having the meanings given below,

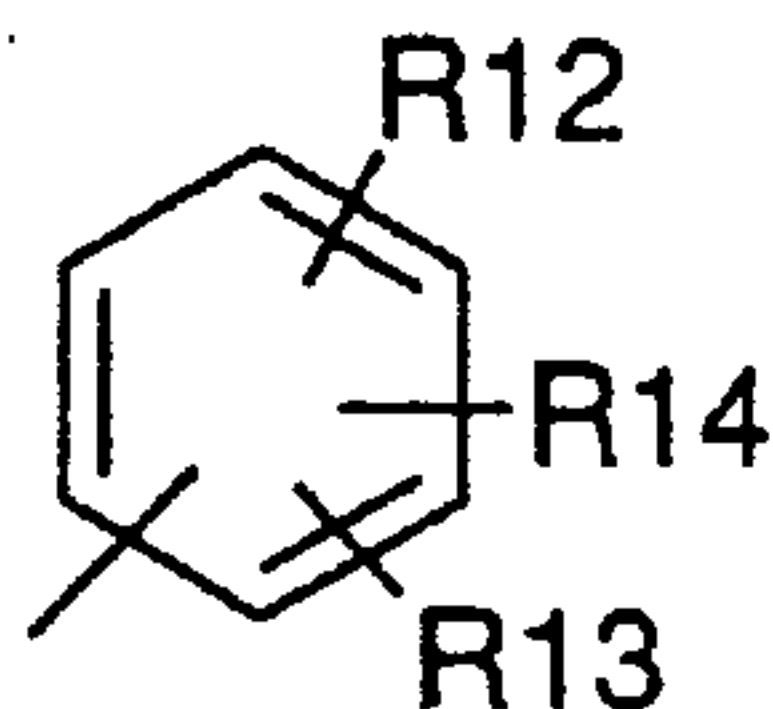
- R_4 and R_5 , which may be identical or different,
- 10 represent a hydrogen atom, an alkyl radical containing from 1 to 6 carbon atoms, or together form an oxo radical,
- R_6 represents a phenyl radical, a naphthyl radical or a heterocyclic radical, R_6 being optionally
- 15 substituted with one or more radicals chosen from an alkyl containing from 1 to 6 carbon atoms, an $-OR_{10}$ radical, a halogen atom, $-CF_3$, $-NH_2$ and a nitrogen atom mono- or disubstituted with an alkyl radical containing from 1 to 6 carbon atoms,

20 R_{10} having the meanings given below,

- R_7 represents a radical $-COR_{11}$,

R_{11} having the meanings given below,

- R_8 represents a radical:



(i)

R_{12} , R_{13} and R_{14} having the meanings given below,

- R_9 represents an alkyl radical containing from 1 to 6 carbon atoms,

5 - R_{10} represents a hydrogen atom or an alkyl radical containing from 1 to 6 carbon atoms,

- R_{11} represents a radical $-OR_{15}$ or a radical $-NR_{15}R_{16}$,

R_{15} and R_{16} having the meanings given below,

- R_{12} and R_{13} , which may be identical or different,
10 represent a hydrogen atom, a halogen atom, an alkyl radical containing from 1 to 6 carbon atoms or a radical $-OR_{17}$,

R_{17} having the meanings given below,

- R_{14} represents a radical $-COR_{18}$,

15 R_{18} having the meanings given below,

- R_{15} , R_{16} and R_{17} , which may be identical or different, represent a hydrogen atom or an alkyl radical containing from 1 to 6 carbon atoms,

- R_{18} represents a radical $-OR_{19}$, or a radical
20 $-NR_{19}R_{20}$,

R_{19} and R_{20} having the meanings given below,

- R_{19} represents a hydrogen atom or an alkyl radical containing from 1 to 6 carbon atoms,

- R_{20} represents a hydrogen atom, an alkyl radical
25 containing from 1 to 6 carbon atoms, or $-OH$,
and the optical isomers, the salts obtained with a pharmaceutically acceptable salt or base, and also the mixtures of the said compounds of formula (I).

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

5 According to the present invention:

The expression "alkyl radical containing from 1 to 6 carbon atoms" preferably means the methyl, ethyl, propyl, isopropyl, butyl, tert-butyl, pentyl, or hexyl radicals.

10 The term "halogen atom" preferably means a fluorine, chlorine, or bromine atom.

The term "heterocycle" means a carbon-based ring of 5 to 8 carbon atoms interrupted with 1 or 2 hetero atoms chosen from sulphur, nitrogen, oxygen and
15 selenium, and preferably a pyridine, pyrimidine or thiophene radical.

Among the compounds corresponding to the general formula (I) above that may be mentioned are the following, alone or as a mixture:

20

4-[4-(3-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

4-[5,5,8,8-tetramethyl-4-(4-methylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

25 4-[4-(4-tert-butylbenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8,-tetrahydro-2-naphthylselanylethynyl]benzoic acid

4-[4-(3,4-difluorobenzyloxy)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic
acid

4-[4-(2,4-difluorobenzyloxy)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic
acid

4-[5,5,8,8-tetramethyl-4-(4-trifluoromethylbenzyloxy)-
5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic
acid

10 4-[5,5,8,8-tetramethyl-4-(2-naphthylmethoxy)-5,6,7,8-
tetrahydro-2-naphthylselanylethynyl]benzoic acid

4-[4-(4-chlorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-
tetrahydro-2-naphthylselanylethynyl]benzoic acid

4-[4-(4-bromobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-
15 tetrahydro-2-naphthylselanylethynyl]benzoic acid

4-[5,5,8,8-tetramethyl-4-(3-methylbenzyloxy)-5,6,7,8-
tetrahydro-2-naphthylselanylethynyl]benzoic acid

4-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-
tetrahydro-2-naphthylselanylethynyl]benzoic acid

20 4-{3-hydroxy-3-[5,5,8,8-tetramethyl-4-(4-
trifluoromethylbenzyloxy)-5,6,7,8-tetrahydro-2-
naphthyl]prop-1-ynyl}benzoic acid

4-{3-hydroxy-3-[5,5,8,8-tetramethyl-4-(4-tert-
butylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthyl]prop-1-
25 ynyl}benzoic acid

4-{3-hydroxy-3-[5,5,8,8-tetramethyl-4-(4-
methylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthyl]prop-1-

ynyl}benzoic acid

4-{3-[4-(4-tert-butylbenzyloxy)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-

ynyl}benzoic acid

5 4-{(E)-3-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}benzoic
acid

6-{1-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]methanoyl}naphthalene-2-
10 carboxylic acid

6-{1-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-1-hydroxymethyl}-
naphthalene-2-carboxylic acid

4-{3-[4-(4-fluorobenzylamino)-5,5,8,8-tetramethyl-
15 5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}-
benzoic acid

4-(3-{4-[(4-fluorobenzyl)methylamino]-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-
oxopropenyl)benzoic acid

20 4-{3-[4-(4-fluorobenzylamino)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-
ynyl}benzoic acid

4-{3-[4-(4-fluorobenzylamino)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}benzoic
25 acid

4-(3-{4-[(4-fluorobenzyl)methylamino]-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

hydroxypropenyl)benzoic acid

4-(3-{4-[(4-fluorobenzyl)methylamino]-5,5,8,8-

tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

hydroxyprop-1-ynyl)benzoic acid

5 4-{3-[4-(4-fluorobenzylsulphanyl)-5,5,8,8-tetramethyl-

5,6,7,8-tetrahydro-2-naphthyl]-3-

hydroxypropenyl}benzoic acid

4-{3-[4-(4-fluorobenzylsulphanyl)-5,5,8,8-tetramethyl-

5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}benzoic

10 acid

4-{3-[4-(4-fluorobenzylsulphanyl)-5,5,8,8-tetramethyl-

5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-

ynyl}benzoic acid

4-{3-[4-(4-fluorobenzylamino)-5,5,8,8-tetramethyl-

15 5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}-2-

hydroxybenzoic acid

4-(3-{4-[(4-fluorobenzyl)methylamino]-tetramethyl-

5,6,7,8-tetrahydro-2-naphthyl}oxopropenyl)-2-

hydroxybenzoic acid

20 4-{3-[4-(4-fluorobenzylamino)-5,5,8,8-tetramethyl-

5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-2-

hydroxybenzoic acid

4-{3-[4-(4-fluorobenzylamino)-5,5,8,8-tetramethyl-

5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}-2-

25 hydroxybenzoic acid

4-(3-{4-[(4-fluorobenzyl)methylamino]-5,5,8,8-

tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

hydroxypropenyl)-2-hydroxybenzoic acid

4-(3-{4-[(4-fluorobenzyl)methylamino]-5,5,8,8-

tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

hydroxyprop-1-ynyl)-2-hydroxybenzoic acid

5 4-{3-[4-(4-fluorobenzylsulphanyl)-5,5,8,8-tetramethyl-

5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}-2-

hydroxybenzoic acid

4-{3-[4-(4-fluorobenzylsulphanyl)-5,5,8,8-tetramethyl-

5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}-2-

10 hydroxybenzoic acid

4-{3-[4-(4-fluorobenzylsulphanyl)-5,5,8,8-tetramethyl-

5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-2-

hydroxybenzoic acid

4-{3-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-

15 5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}-2-

hydroxybenzoic acid

4-{3-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-

5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}-2-

hydroxybenzoic acid

20 4-{3-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-

5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-2-

hydroxybenzoic acid

4-{3-[4-(4-fluorobenzoylamido)-5,5,8,8-tetramethyl-

5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}-

25 benzoic acid

4-(3-{4-[(4-fluoro)methylbenzoylamido]-5,5,8,8-

tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

oxopropenyl)benzoic acid

4-{3-[4-(4-fluorobenzoylamido)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}benzoic acid

5 -(3-{4-[(4-fluoro)methylbenzoylamido]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxypropenyl)benzoic acid

4-{3-[4-(4-fluorobenzoylamido)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}benzoic

10 acid

4-(3-{4-[(4-fluoro)methylbenzoylamido]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}hydroxyprop-1-ynyl)benzoic acid

4-(3-{4-[1-(4-fluorophenyl)-1-methylethoxy]-5,5,8,8-

15 tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxypropenyl)benzoic acid

4-(3-{4-[1-(4-fluorophenyl)-1-methylethoxy]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-oxopropenyl)benzoic acid

20 4-(3-{4-[1-(4-fluorophenyl)-1-methylethoxy]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)benzoic acid

4-{3-[4-(4-methylbenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}-

25 benzoic acid

4-(3-{4-[(4-methylbenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

oxopropenyl)benzoic acid

4-{3-[4-(4-methylbenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}benzoic acid

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4-(3-{4-[(4-methylbenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

10 hydroxypropenyl)benzoic acid

4-(3-{4-[(4-methylbenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)benzoic acid

4-{3-[4-(4-methylbenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}-benzoic acid

15 5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}-benzoic acid

4-{3-[4-(4-methylbenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}benzoic acid

20 4-{3-[4-(4-methylbenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}benzoic acid

4-{3-[4-(4-methylbenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}-2-

25 hydroxybenzoic acid

4-(3-{4-[(4-methylbenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

oxopropenyl)-2-hydroxybenzoic acid

4-{3-[4-(4-methylbenzylamino)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-2-
hydroxybenzoic acid

5 4-{3-[4-(4-methylbenzylamino)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}-2-
hydroxybenzoic acid

4-(3-{4-[(4-methylbenzyl)methylamino]-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

10 hydroxypropenyl)-2-hydroxybenzoic acid

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4-{3-[4-(4-methylbenzylsulphanyl)-5,5,8,8-tetramethyl-

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hydroxybenzoic acid

4-{3-[4-(4-methylbenzylsulphanyl)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}-2-
hydroxybenzoic acid

20 4-{3-[4-(4-methylbenzylsulphanyl)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-2-
hydroxybenzoic acid

4-{3-[4-(4-methylbenzyloxy)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}-2-

25 hydroxybenzoic acid

4-{3-[4-(4-methylbenzyloxy)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}-2-

hydroxybenzoic acid

4-{3-[4-(4-methylbenzyloxy)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-2-
hydroxybenzoic acid

5 4-[3-(4-{[1-(4-methylphenyl)methanoyl]amino}-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-
hydroxypropenyl]benzoic acid

4-[3-(4-{[1-(4-methylphenyl)methanoyl]methylamino}-
5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-
10 oxopropenyl]benzoic acid

4-[3-(4-{[1-(4-methylphenyl)methanoyl]amino}-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-
hydroxyprop-1-ynyl]benzoic acid

4-[3-(4-{[1-(4-methylphenyl)methanoyl]methylamino}-
15 5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-
hydroxypropenyl]benzoic acid

4-[3-(4-{[1-(4-methylphenyl)methanoyl]amino}-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-
oxopropenyl]benzoic acid

20 4-[3-(4-{[1-(4-methylphenyl)methanoyl]methylamino}-
5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-
hydroxyprop-1-ynyl]benzoic acid

4-(3-{4-[1-(4-methylphenyl)-1-methylethoxy]-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

25 hydroxypropenyl)benzoic acid

4-(3-{4-[1-(4-methylphenyl)-1-methylethoxy]-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

oxopropenyl)benzoic acid

4-(3-{4-[1-(4-methylphenyl)-1-methylethoxy]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)benzoic acid

5 4-{3-[4-(4-dimethylaminobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}benzoic acid

4-(3-{4-[(4-dimethylaminobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

10 oxopropenyl)benzoic acid

4-{3-[4-(4-dimethylaminobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}benzoic acid

4-{3-[4-(4-dimethylaminobenzylamino)-5,5,8,8-

15 tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}benzoic acid

4-(3-{4-[(4-dimethylaminobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxypropenyl)benzoic acid

20 4-(3-{4-[(4-dimethylaminobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)benzoic acid

4-{3-[4-(4-dimethylaminobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

25 hydroxypropenyl}benzoic acid

4-{3-[4-(4-dimethylaminobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

oxopropenyl}benzoic acid

4-{3-[4-(4-dimethylaminobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}benzoic acid

5 4-{3-[4-(4-dimethylaminobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}-2-hydroxybenzoic acid

4-(3-{4-[(4-dimethylaminobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

10 oxopropenyl)-2-hydroxybenzoic acid

4-{3-[4-(4-dimethylaminobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-2-hydroxybenzoic acid

4-{3-[4-(4-dimethylaminobenzylamino)-5,5,8,8-

15 tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}-2-hydroxybenzoic acid

4-(3-{4-[(4-dimethylaminobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxypropenyl)-2-hydroxybenzoic acid

20 4-(3-{4-[(4-dimethylaminobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)-2-hydroxybenzoic acid

4-{3-[4-(4-dimethylaminobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

25 hydroxypropenyl}-2-hydroxybenzoic acid

4-{3-[4-(4-dimethylaminobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

oxopropenyl}-2-hydroxybenzoic acid

4-{3-[4-(4-dimethylaminobenzylsulphanyl)-5,5,8,8-

tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

hydroxyprop-1-ynyl}-2-hydroxybenzoic acid

5 4-{3-[4-(4-dimethylaminobenzyloxy)-5,5,8,8-tetramethyl-

5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}-2-

hydroxybenzoic acid

4-{3-[4-(4-dimethylaminobenzyloxy)-5,5,8,8-tetramethyl-

5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}-2-

10 hydroxybenzoic acid

4-{3-[4-(4-dimethylaminobenzyloxy)-5,5,8,8-tetramethyl-

5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-2-

hydroxybenzoic acid

4-[3-(4-{{1-(4-dimethylaminophenyl)methanoyl}amino}-

15 5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-

hydroxypropenyl]benzoic acid

4-[3-(4-{{1-(4-dimethylaminophenyl)methanoyl}-

methylamino}-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-

naphthyl)-3-oxopropenyl]benzoic acid

20 4-[3-(4-{{1-(4-dimethylaminophenyl)methanoyl}amino}-

5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-

hydroxyprop-1-ynyl]benzoic acid

4-[3-(4-{{1-(4-dimethylaminophenyl)methanoyl}methyl-

amino}-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-

25 naphthyl)-3-hydroxypropenyl]benzoic acid

4-[3-(4-{{1-(4-dimethylaminophenyl)methanoyl}amino}-

5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-

oxopropenyl]benzoic acid

4-[3-(4-{[1-(4-dimethylaminophenyl)methanoyl]-
methylamino}-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-
naphthyl)-3-hydroxyprop-1-ynyl]benzoic acid

5 4-(3-{4-[1-(4-dimethylaminophenyl)-1-methylethoxy]-
5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-
hydroxypropenyl)benzoic acid

4-(3-{4-[1-(4-dimethylaminophenyl)-1-methylethoxy]-
5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-
10 oxopropenyl)benzoic acid

4-(3-{4-[1-(4-dimethylaminophenyl)-1-methylethoxy]-
5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-
hydroxyprop-1-ynyl)benzoic acid

4-(3-{4-[2-(4-fluorophenyl)ethyl]-5,5,8,8-tetramethyl-
15 5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxypropenyl)-
benzoic acid

4-(3-{4-[2-(4-fluorophenyl)ethyl]-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl}-3-oxopropenyl)benzoic
acid

20 4-(3-{4-[2-(4-fluorophenyl)ethyl]-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-
ynyl)benzoic acid

4-(3-{4-[2-(4-fluorophenyl)-2-methylpropyl]-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

25 hydroxypropenyl)benzoic acid

4-(3-{4-[2-(4-fluorophenyl)-2-methylpropyl]-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

oxopropenyl)benzoic acid

4-(3-{4-[2-(4-fluorophenyl)-2-methylpropyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)benzoic acid

5 4-(3-{4-[2-(4-methylphenyl)ethyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxypropenyl)-benzoic acid

4-(3-{4-[2-(4-methylphenyl)ethyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-oxopropenyl)benzoic
10 acid

4-(3-{4-[2-(4-methylphenyl)ethyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)benzoic acid

4-(3-{4-[2-(4-methylphenyl)-2-methylpropyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxypropenyl)benzoic acid

15 4-(3-{4-[2-(4-methylphenyl)-2-methylpropyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-oxopropenyl)benzoic acid

20 4-(3-{4-[2-(4-methylphenyl)-2-methylpropyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)benzoic acid

4-(3-{4-[2-(4-dimethylaminophenyl)ethyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

25 hydroxypropenyl)benzoic acid

4-(3-{4-[2-(4-dimethylaminophenyl)ethyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

oxopropenyl)benzoic acid

4-(3-{4-[2-(4-dimethylaminophenyl)ethyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)benzoic acid

5 4-(3-{4-[2-(4-dimethylaminophenyl)-2-methylpropyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxypropenyl)benzoic acid

4-(3-{4-[2-(4-dimethylaminophenyl)-2-methylpropyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

10 oxopropenyl)benzoic acid

4-(3-{4-[2-(4-dimethylaminophenyl)-2-methylpropyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)benzoic acid

4-{3-[4-(4-fluorobenzyloxy)-5,6,7,8-tetrahydro-2-

15 naphthyl]-3-hydroxypropenyl}benzoic acid

4-{3-[4-(4-fluorobenzyloxy)-8,8-dimethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}benzoic acid

4-{3-[4-(4-fluorobenzyloxy)-5,5-dimethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}benzoic acid

20 4-(3-{4-[(4-fluorobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)benzamide

4-(3-{4-[(4-fluorobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

25 hydroxyprop-1-ynyl)-N-hydroxybenzamide

N-ethyl-4-(3-{4-[(4-fluorobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

hydroxyprop-1-ynyl)benzamide

4-{3-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-
ynyl}benzamide

5 4-{3-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-N-
hydroxybenzamide

N-ethyl-4-{3-[4-(4-fluorobenzyloxy)-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

10 hydroxyprop-1-ynyl}benzamide

4-{3-[4-(4-fluorobenzylamino)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-
ynyl}benzamide

4-{3-[4-(4-fluorobenzylamino)-5,5,8,8-tetramethyl-

15 5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-N-
hydroxybenzamide

N-ethyl-4-{3-[4-(4-fluorobenzylamino)-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-
hydroxyprop-1-ynyl}benzamide

20 4-{3-[4-(4-fluorobenzylsulphanyl)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-
ynyl}benzamide

4-{3-(4-(4-fluorobenzylsulphanyl)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-N-

25 hydroxybenzamide

N-ethyl-4-{3-[4-(4-fluorobenzylsulphanyl)-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

hydroxyprop-1-ynyl}benzamide

N-ethyl-4-(3-{4-[(4-fluorobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)-*N*-methylbenzamide

5 *N*-ethyl-4-{3-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-*N*-methylbenzamide

N-ethyl-4-{3-[4-(4-fluorobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

10 hydroxyprop-1-ynyl}-*N*-methylbenzamide

N-ethyl-4-{3-[4-(4-fluorobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-*N*-methylbenzamide

4-(3-{4-[(4-methylbenzyl)methylamino]-5,5,8,8-

15 tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)benzamide

4-(3-{4-[(4-methylbenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)-*N*-hydroxybenzamide

20 *N*-ethyl-4-(3-{4-[(4-methylbenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)benzamide

4-{3-[4-(4-methylbenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-

25 ynyl}benzamide

4-{3-[4-(4-methylbenzyloxy)-5,5,8,8-tetramethyl-

5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-*N*-

hydroxybenzamide

N-ethyl-4-{3-[4-(4-methylbenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}benzamide

5 4-{3-[4-(4-methylbenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}benzamide

4-{3-[4-(4-methylbenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-*N*-

10 hydroxybenzamide

N-ethyl-4-{3-[4-(4-methylbenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}benzamide

4-{3-[4-(4-methylbenzylsulphanyl)-5,5,8,8-tetramethyl-

15 5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}benzamide

4-{3-[4-(4-methylbenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-*N*-hydroxybenzamide

20 *N*-ethyl-4-{3-[4-(4-methylbenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}benzamide

N-ethyl-4-(3-{4-[(4-methylbenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

25 hydroxyprop-1-ynyl)-*N*-methylbenzamide

N-ethyl-4-{3-[4-(4-methylbenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

- hydroxyprop-1-ynyl}-N-methylbenzamide
- N-ethyl-4-{3-[4-(4-methylbenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-N-methylbenzamide
- 5 N-ethyl-4-{3-[4-(4-methylbenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-N-methylbenzamide
- 4-(3-{4-[(4-dimethylaminobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)benzamide
- 10 4-(3-{4-[(4-dimethylaminobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)-N-hydroxybenzamide
- N-ethyl-4-(3-{4-[(4-dimethylaminobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)benzamide
- 15 5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)benzamide
- 4-{3-[4-(4-dimethylaminobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}benzamide
- 20 4-{3-[4-(4-dimethylaminobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-N-hydroxybenzamide
- N-ethyl-4-{3-[4-(4-dimethylaminobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}benzamide
- 25 hydroxyprop-1-ynyl}benzamide
- 4-{3-[4-(4-dimethylaminobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}benzamide

- hydroxyprop-1-ynyl}benzamide
4-{3-[4-(4-dimethylaminobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-N-hydroxybenzamide
- 5 N-ethyl-4-{3-[4-(4-dimethylaminobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}benzamide
4-{3-[4-(4-dimethylaminobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-N-hydroxybenzamide
- 10 hydroxyprop-1-ynyl}benzamide
4-{3-[4-(4-dimethylaminobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-N-hydroxybenzamide
N-ethyl-4-{3-[4-(4-dimethylaminobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}benzamide
- 15 N-ethyl-4-(3-{4-[(4-dimethylaminobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl)-N-methylbenzamide
- 20 N-ethyl-4-{3-[4-(4-dimethylaminobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-N-methylbenzamide
N-ethyl-4-{3-[4-(4-dimethylaminobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-N-methylbenzamide or
- 25 N-ethyl-4-{3-[4-(4-dimethylaminobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-N-methylbenzamide

hydroxyprop-1-ynyl}-N-methylbenzamide.

According to the present invention, the compounds of formula (I) that are more particularly preferred are those for which:

- 5 - R_1 represents (b),
- Q represents an oxygen atom, and
- R_9 represents (i).

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

A general description of the preparation of the compounds of general formulae 6 to 12 is given below.

15 Intermediate 2 may be formed from 3-bromophenol, via a Friedel-Crafts reaction in the presence of aluminium chloride and a corresponding partner, for instance 2,5-dichloro-2,5-dimethylhexane. The compounds of general structure 3 may be obtained by
20 converting the bromide of 2 into an acid or an aldehyde after lithiation with butyllithium, or, in the case where $R = SH$ or SeH , the compounds of general structure 3 may be obtained by lithiation of 3 and attack of the anion formed on the native sulphur or selenium. These
25 compounds may then be converted into the corresponding disulphides or diselenides by spontaneous oxidation in

non-gassed ethanol, after which the compounds 4 may be prepared by forming the sulphide or selenide bromide by the action of bromine on the disulphide or diselenide function, followed by addition of a true alkyne in the presence of copper iodide in dimethylformamide, for example. After O-alkylation of the phenol function of the compounds of structure 4, for example by nucleophilic substitution with a halogenated compound in the presence of sodium hydride, the compounds of structure 6 are obtained after saponification of the ester function, for example by reaction with sodium hydroxide.

In the case where $Q = O$, the compounds 5 may be obtained after O-alkylation of the phenol function of the compounds of structure 3, for example by nucleophilic substitution with a halogenated compound in the presence of sodium hydride. In the case where $Q = S$ or $N-R$, the phenol may first be converted into trifluoromethanesulphonyl by reaction with trifluoromethanesulphonic anhydride, and this intermediate is then coupled with a thiolate or an amine, respectively, in the presence of transition metal complexes, for instance bis-pyridyldichloronickel or dichlorobisphosphinoferrocenylpalladium, respectively. In the case where $Q = CR_{11}R_{12}$ or $C=O$, the compound obtained after reaction of 3 with trifluoromethanesulphonic anhydride may be coupled

according to the Stille procedure with, for example, organotin derivatives, with or without pressure of carbon monoxide, respectively.

The compounds 3 for which $R = COOR'$ may be converted into acids by saponification, and then into methyl ketones by reaction with methyl lithium: the compounds 5 in which $R = COMe$ will thus be obtained.

When the compounds of general structure 5 are obtained, compounds 7 - 12 are obtained in the following manner:

The compounds 7 may be obtained by forming the acids corresponding to the esters 5, followed by conversion of these acids into the acid chlorides thereof, for example by reaction with thionyl chloride. These acid chlorides may then be coupled with organometallic derivatives of naphthylzinc type, or with naphthoic boronic acids, in the presence of catalysts based on transition metals, for example tetrakis(triphenylphosphino)palladium. The precursors of the compounds of general structure 7 are generally obtained in the form of esters: the acids of structure 7 may be obtained by saponification, for example by reaction with sodium hydroxide.

The compounds 8 may be prepared by forming a chalcone bond by reacting the methyl ketone of 5 with a corresponding aromatic aldehyde in the presence of potassium hydroxide.

The compounds of general structure 9 may be prepared from the aldehyde 5 by creating a propargyl alcohol function by addition of a propargyl anion, for example by reaction with ethynyl magnesium bromide, followed by a Sonogashira coupling with an aromatic halide, for instance 4-iodobenzoic acid in the presence of copper salts and a catalyst based on a transition metal complex, for instance tetrakis(triphenylphosphino)palladium.

10 The compounds of general structure 10 may be obtained from the compounds of structure 7, for example after reduction or alkylation of the carbonyl function ($R, R' = OH, H$ or alkyl, respectively), or alternatively by reduction followed by a dehydroxylation ($R, R' =$
15 H, H), or acetalization of the carbonyl function ($R, R' = OR, OR$), or formation of an oxime on the carbonyl function of 7 by reaction with a corresponding hydroxyl or alkoxyamine.

 The compounds of general structure 11 may be
20 obtained from the compounds of structure 8, for example after reduction or alkylation of the carbonyl function ($R, R' = OH, H$ or alkyl, respectively), for example by reaction with sodium borohydride or an alkylmagnesium halide.

25 The compounds of general structure 12 may be prepared from the compounds of structure 9, by oxidation of the benzyl alcohol to a ketone ($R, R' =$

C=O), for example after reaction with manganese oxide, or oxidation followed by the formation of an oxime on the carbonyl function of 9 by reaction with a corresponding hydroxyl or alkoxyamine ($R, R' = C=N-OR$),
5 or dehydroxylation of the benzyl alcohol function ($R, R' = H, H$), for example by reaction with triethylsilane in the presence of boron trifluoride, or by oxidation and formation of an acetal ($R, R' = OR, OR$), or by oxidation and alkylation of the carbonyl
10 function ($R, R' = \text{alkyl}, OH$), for example by addition of an alkylmagnesium halide, or by O-alkylation of the alcohol function of 9 ($R, R' = OR, H$).

The compounds according to the invention have inhibitory properties of RAR-type receptors. This RAR-
15 receptor inhibitory activity is measured in a test of transactivation by means of the dissociation constant K_{dapp} (apparent) and the IC_{50} (concentration that inhibits 50% of the reference agonist activity).

According to the invention, the expression
20 "inhibitor of RAR-type receptors" means any compound which, for at least one of the RAR subtypes, has a dissociation constant K_{dapp} of less than or equal to $1 \mu M$, and an IC_{50} value $\leq 100 \text{ nM}$, in a transactivation test as described in Example 19.

25 The preferred compounds of the present invention have, for at least one of the RAR subtypes, a dissociation constant K_{dapp} of less than or equal to

500 nM and advantageously less than or equal to 100 nM, and an $IC_{50} \leq 25$ nM.

A subject of the present invention is also the compounds of formula (I) as described above, as
5 medicinal products.

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

- 1) for treating dermatological complaints associated
10 with a keratinization disorder relating to cell differentiation and proliferation, especially for treating common acne, comedones, polymorphs, acne rosacea, nodulocystic acne, acne conglobata, senile acne, and secondary acnes such as solar acne,
15 medication-related acne or occupational acne;
- 2) for treating other types of keratinization disorders, especially ichthyosis, ichthyosiform conditions, Darier's disease, palmoplantar keratoderma, leukoplakia and leukoplakiiform conditions, and
20 cutaneous or mucous (buccal) lichen;
- 3) for treating other dermatological complaints with an inflammatory immunoallergic component, with or without cell proliferation disorder, and especially all forms of psoriasis, whether cutaneous, mucous or
25 ungual, and even psoriatic rheumatism, or cutaneous atopy, such as eczema, or respiratory atopy, or alternatively gingival hypertrophy;

- 4) for treating all dermal or epidermal proliferations, whether benign or malignant, and whether of viral origin or otherwise, such as common warts, flat warts and verruciform epidermodysplasia,
5 oral or florid papillomatoses, T lymphoma, and proliferations that may be induced by ultraviolet radiation, especially in the case of basocellular and spinocellular epithelioma, and also any cutaneous precancerous lesion such as keratoacanthomas;
- 10 5) for treating other dermatological disorders such as immune dermatoses, such as lupus erythematosus, immune bullous diseases and collagen diseases, such as scleroderma;
- 6) in the treatment of dermatological or general
15 complaints with an immunological component;
- 7) for treating certain ophthalmological disorders, especially corneopathies,
- 8) for preventing or curing the stigmata of epidermal and/or dermal atrophy induced by local or systemic
20 corticosteroids, or any other form of cutaneous atropy,
- 9) in the treatment of any cutaneous or general complaint of viral origin,
- 10) in the treatment of skin disorders caused by exposure to UV radiation, and also for repairing or
25 combating ageing of the skin, whether photoinduced or chronological ageing, or for reducing pigmentations and actinic keratosis, or any pathology associated with

- chronological or actinic ageing, such as xerosis;
- 11) for combating sebaceous function disorders, such as the hyperseborrhoea of acne or simple seborrhoea;
- 12) for preventing or treating cicatrization disorders, or for preventing or repairing stretch marks, or alternatively for promoting cicatrization;
- 13) in the treatment of pigmentation disorders, such as hyperpigmentation, melasma, hypopigmentation or vitiligo;
- 14) in the treatment of lipid metabolism complaints, such as obesity, hyperlipidaemia, or non-insulin-dependent diabetes;
- 15) in the treatment of inflammatory complaints such as arthritis;
- 16) in the treatment or prevention of cancerous or precancerous conditions;
- 17) in the prevention or treatment of alopecia of various origins, especially alopecia caused by chemotherapy or radiation;
- 18) in the treatment of disorders of the immune system, such as asthma, type I sugar diabetes, multiple sclerosis or other selective dysfunctions of the immune system; and
- 19) in the treatment of complaints of the cardiovascular system, such as arteriosclerosis or hypertension.

A subject of the present invention is also a

pharmaceutical composition comprising, in a physiologically acceptable medium, at least one compound of formula (I) as defined above.

A subject of the present invention is also a novel medicinal composition intended especially for treating the abovementioned complaints, which is characterized in that it comprises, in a pharmaceutically acceptable support that is compatible with the mode of administration selected for this composition, at least one compound of formula (I), an optical isomer thereof or a salt thereof.

The composition according to the invention may be administered enterally, parenterally, topically or ocularly. The pharmaceutical composition is preferably packaged in a form that is suitable for topical application.

Via the enteral route, the composition may be in the form of tablets, gel capsules, dragees, syrups, suspensions, solutions, powders, granules, emulsions, suspensions of microspheres or nanospheres or lipid or polymer vesicles allowing a controlled release. Via the parenteral route, the composition may be in the form of solutions or suspensions for infusion or for injection.

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, in 1 to 3 dosage intakes.

The compounds are used systemically, at a concentration generally of between 0.001% and 10% by weight and preferably between 0.01% and 1% by weight relative to the weight of the composition.

5 Via the topical route, the pharmaceutical composition according to the invention is more particularly intended for treating the skin and mucous membranes and may be in liquid, pasty or solid form, and more particularly in the form of ointments, creams,
10 milks, pomades, powders, impregnated pads, syndets, solutions, gels, sprays, mousses, suspensions, sticks, shampoos or washing bases. It may also be in the form of suspensions of microspheres or nanospheres or of lipid or polymer vesicles or gelled or polymer patches
15 allowing a controlled release.

The compounds are used topically at a concentration generally of between 0.001% and 10% by weight and preferably between 0.01% and 1% by weight, relative to the total weight of the composition.

20 The compounds of formula (I) according to the invention also find an application in cosmetics, in particular in body and hair hygiene and especially for treating acne-prone skin, for promoting regrowth of the hair or for limiting hair loss, for combating the
25 greasy appearance of the skin or the hair, in protection against the harmful aspects of sunlight or in the treatment of physiologically dry skin, and for

preventing and/or combating photoinduced or
chronological ageing.

A subject of the invention is thus also a
composition comprising, in a cosmetically acceptable
5 support, at least one of the compounds of formula (I).

A subject of the invention is also the
cosmetic use of a composition comprising at least one
compound of formula (I) for preventing and/or treating
the signs of ageing and/or dry skin.

10 A subject of the invention is also the
cosmetic use of a composition comprising at least one
compound of formula (I) for body or hair hygiene.

The cosmetic composition according to the
invention containing, in a cosmetically acceptable
15 support, at least one compound of formula (I) or an
optical or geometrical isomer thereof or a salt
thereof, may be especially in the form of a cream, a
milk, a gel, suspensions of microspheres or nanospheres
or lipid or polymer vesicles, impregnated pads,
20 solutions, sprays, mousses, sticks, soaps, shampoos or
washing bases.

The concentration of compound of formula (I)
in the cosmetic composition is preferably between
0.001% and 3% by weight relative to the total weight of
25 the composition.

The pharmaceutical and cosmetic compositions
as described above may also contain inert additives, or

even pharmacodynamically active additives as regards the pharmaceutical compositions, or combinations of these additives, and especially:

- 5 - wetting agents;
- flavour enhancers;
- preserving agents such as para-hydroxybenzoic acid esters;
- stabilizers;
- 10 - moisture regulators;
- pH regulators;
- osmotic pressure modifiers;
- emulsifiers;
- UV-A and UV-B screening agents;
- 15 - antioxidants such as α -tocopherol, butylhydroxyanisole, butylhydroxytoluene, superoxide dismutase, ubiquinol or certain metal-chelating agents;
- depigmenting agents such as hydroquinone, azelaic
- 20 acid, caffeic acid or kojic acid;
- emollients;
- moisturizers, for instance glycerol, PEG 400, thiamorpholinone and its derivatives or urea;
- antiseborrhoeic or antiacne agents, such as
- 25 S-carboxymethylcysteine, S-benzylcysteamine, salts thereof or derivatives thereof, or benzoyl peroxide;
- antibiotics, for instance erythromycin and its

- esters, neomycin, clindamycin and its esters, and tetracyclines;
- antifungal agents such as ketoconazole or poly-4,5-methylene-3-isothiazolidones;
 - 5 - agents for promoting regrowth of the hair, for instance Minoxidil* (2,4-diamino-6-piperidinopyrimidine 3-oxide) and its derivatives, Diazoxide (7-chloro 3-methyl-1,2,4-benzothiadiazine 1,1-dioxide) and Phenytoin*
 - 10 (5,4-diphenylimidazolidine-2,4-dione);
 - non-steroidal anti-inflammatory agents;
 - carotenoids and especially β -carotene;
 - anti-psoriatic agents such as anthralin and its derivatives;
 - 15 - eicosa-5,8,11,14-tetraynoic acid and eicosa-5,8,11-triynoic acid, and esters and amides thereof;
 - retinoids, i.e. natural or synthetic RXR receptor ligands;
 - corticosteroids or oestrogens;
 - 20 - α -hydroxy acids and α -keto acids or derivatives thereof, such as lactic acid, malic acid, citric acid, glycolic acid, mandelic acid, tartaric acid, glyceric acid or ascorbic acid, and also salts, amides or esters thereof, or β -hydroxy acids or
 - 25 derivatives thereof, such as salicylic acid and its salts, amides or esters;
 - ion-channel blockers such as potassium-channel

* Trademarks

blockers;

- or alternatively, more particularly for pharmaceutical compositions, in combination with medicinal products known to interfere with the immune system (for example cyclosporin, FK 506, glucocorticoids, monoclonal antibodies, cytokines or growth factors, etc.).

Needless to say, a person skilled in the art will take care to select the optional compound(s) to be added to these compositions such that the advantageous properties intrinsically attached to the present invention are not, or are not substantially, adversely affected by the envisaged addition.

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

EXAMPLE 1: 4-[4-(3-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

a. 3-Bromo-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-1-naphthyl

60 g (347 mmol) of 3-bromophenol are dissolved in 600 mL of dichloromethane. This solution is added to a solution of 46 g (347 mmol) of aluminium

chloride in 200 mL of dichloromethane. 127 g (694 mmol) of 2,5-dichloro-2,5-dimethylhexane are added in 10 g portions every 40 minutes. The medium is then stirred for 10 hours, after which it is poured onto ice and
5 extracted with dichloromethane. The residue obtained is dissolved in ethyl ether and this organic phase is then washed with 1 N sodium hydroxide solution and then with water. The residue obtained is purified by chromatography (eluent: heptane and then 1/1
10 heptane/dichloromethane). A thick oil is obtained (67 g; yield = 68%).

b. 7-Bromo-5-ethoxymethoxy-1,1,4,4-tetramethyl-1,2,3,4-tetrahydronaphthalene

42 g (148 mmol) of 3-bromo-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-1-naphthyl are dissolved
15 in 400 mL of anhydrous DMF. 7.2 g (178 mmol) of 60% sodium hydride are added portionwise and the reaction medium is stirred for one hour. 16.5 mL (178 mmol) of ethoxymethyl chloride are added dropwise and the medium
20 is stirred at room temperature for 2 hours and then hydrolyzed and extracted with ethyl ether. The organic phase is washed with 1 N sodium hydroxide solution and then three times with water. The residue obtained is purified by chromatography (eluent: heptane). A yellow
25 oil is obtained (m = 45.7 g; yield = 95%).

c. Bis(4-ethoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthalene) diselenide

10 g (30.8 mmol) of 7-bromo-5-ethoxymethoxy-1,1,4,4-tetramethyl-1,2,3,4-tetrahydronaphthalene are dissolved in 200 mL of anhydrous THF. The medium is cooled to -78°C and 20 mL (34 mmol) of 1.7 M tert-butylolithium solution are added dropwise. The medium is stirred for one hour and then added via a cannula to a suspension of 2.68 g (34 mmol) of selenium in 100 mL [lacuna] at -78°C. The reaction medium is warmed to room temperature and then stirred for 2 hours and treated with saturated ammonium chloride solution. The residue obtained after extraction is dissolved in 100 mL of ethanol, and 100 mg of sodium hydroxide are added. The reaction medium is stirred for 12 hours and then concentrated. The desired product is obtained after purification by chromatography (eluent: 95/5 heptane/ethyl acetate) (m = 10 g, yield = 95%).

d. Methyl 4-(4-ethoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylselanylethynyl)benzoate

10 g (14.7 mmol) of bis(4-ethoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthalene) diselenide are dissolved in 200 mL of anhydrous THF and the medium is cooled to -78°C. 13.9 mL (13.9 mmol) of a 1 N solution of bromine in THF are added slowly. The medium is stirred for one hour and 300 mL of DMF are then added, followed by addition of 4.65 g (26.4 mmol) of methyl 4-ethynylbenzoate and 16.8 g of copper iodide. The reaction medium is warmed to room

temperature and stirred for 48 hours, and is then hydrolyzed and extracted with ethyl acetate. A thick oil is obtained after purification by chromatography (eluent: 9/1 heptane/ethyl acetate) (m = 9.8 g; yield = 5 74%).

e. *Methyl 4-(4-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoate*

9 g (18 mmol) of methyl 4-(4-ethoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-
10 naphthylselanylethynyl]benzoate are dissolved in 100 mL of methanol, and 2 mL of sulphuric acid are added. The medium is refluxed for 2 hours and is then hydrolyzed and extracted with dichloromethane. The residue is purified by chromatography (eluent: dichloromethane). A
15 yellow solid is obtained (m = 7.2 g; yield = 90%; m.p. = 139°C).

f. *Methyl 4-[4-(3-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoate*

20 600 mg (1.35 mmol) of methyl 4-(4-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoate are dissolved in 40 mL of 2-butanone. 182 μ l (1.48 mmol) of 3-fluorobenzyl bromide are added, followed by addition of 250 mg (1.8
25 mmol) of potassium carbonate. The reaction medium is refluxed for 10 ten hours and then cooled and filtered. After washing the solid residue obtained with heptane,

a white solid is obtained (m = 683 mg; yield = 92%;
m.p. = 132°C).

g. 4-[4-(3-fluorobenzyloxy)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

5 650 mg (1.2 mmol) of methyl 4-[4-(3-fluorobenzyloxy)-
5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-
naphthylselanylethynyl]benzoate are dissolved in 20 mL
of THF. 10 mL of water are added, followed by addition
of 240 mg (6 mmol) of sodium hydroxide. The medium is
10 stirred for 4 hours at 80°C and then acidified with 1 N
hydrochloric acid and extracted with ethyl acetate. The
residue obtained is purified by chromatography (eluent:
1/1 heptane/ethyl acetate) and then recrystallized in a
heptane/ethyl acetate mixture. A pure yellow
15 crystalline solid is obtained (m = 577 mg; yield = 90%;
m.p. = 206°C).

¹H NMR (DMSO) : 1.31 (s, 6H); 1.40 (s, 6H); 1.63-1.68
(m, 4H); 5.24 (s, 2H); 7.17 (s, 1H); 7.22 (m, 1H);
7.32-7.37 (m, 3H); 7.48 (m, 11H); 7.63 (d, J = 8.2 Hz,
20 2H); 8.01 (d, J = 8.2 Hz, 2H); 13.1 (bs, 1H).

**EXAMPLE 2 - 4-[5,5,8,8-tetramethyl-4-(4-
methylbenzyloxy)-5,6,7,8-tetrahydro-2-
naphthylselanylethynyl]benzoic acid**

a. Methyl 4-[5,5,8,8-tetramethyl-4-(4-
25 methylbenzyloxy)-5,6,7,8-tetrahydro-2-
naphthylselanylethynyl]benzoate

In a manner similar to that of Example 1f, by reacting

600 mg (1.35 mmol) of methyl 4-(4-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylselanylethynyl)benzoate with 250 mg (1.8 mmol) of potassium carbonate and 274 μ L (1.5 mmol) of 4-methylbenzyl bromide. A white solid is obtained (m = 708 mg; yield = 96%; m.p. = 154°C).

b. 4-[5,5,8,8-tetramethyl-4-(4-methylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

10 In a manner similar to Example 1g, by reacting 650 mg (1.2 mmol) of methyl 4-[5,5,8,8-tetramethyl-4-(4-methylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoate with 240 mg of sodium hydroxide. A yellow crystallized solid is obtained (m = 15 580 mg; yield = 91%; m.p. = 254°C).

^1H NMR ($\text{CDCl}_3 + \text{DMSO}$): 1.29 (s, 6H); 1.37 (s, 6H); 1.61-1.64 (m, 4H); 2.40 (s, 3H); 5.04 (s, 2H); 7.0 (s, 1H); 7.16 (m, 3H); 7.17 (m, 2H); 7.45 (d, J = 6.8 Hz, 2H); 8.00 (d, J = 6.8 Hz, 2H)

20 **EXAMPLE 3 - 4-[4-(4-tert-butylbenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid**

a. Methyl 4-[5,5,8,8-tetramethyl-4-(4-tert-butylbenzyloxy)-5,6,7,8-tetrahydro-2-

25 naphthylselanylethynyl]benzoate

In a manner similar to that of Example 1f, by reacting 600 mg (1.38 mmol) of methyl 4-(4-hydroxy-5,5,8,8-

tetramethyl-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoate with 240 mg (1.6 mmol) of potassium carbonate and 300 μ L (1.6 mmol) of 4-tert-butylbenzyl bromide. A white solid is obtained
5 (m = 640 mg; yield = 80%; m.p. = 138°C).

b. 4-[5,5,8,8-tetramethyl-4-(4-tert-butylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

In a manner similar to that of Example 1g, by reacting
10 640 mg (1.2 mmol) of methyl 4-[5,5,8,8-tetramethyl-4-(4-tert-butylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoate with 240 mg of sodium hydroxide. A yellow crystallized solid is obtained (m = 530 mg; yield = 92%; m.p. = 285°C).

15 ^1H NMR (CDCl_3) 1.24 (s, 6H); 1.35 (s, 9H); 1.42 (s, 6H); 1.66 (m, 4H); 5.09 (s, 2H); 7.04 (d, 1H, 1.6Hz); 7.22 (d, 1H, 1.6Hz); 7.40 (dd, 4H, $J_1 = 4\text{Hz}$, $J_2 = 13\text{Hz}$); 7.52 (d, 2H, 8Hz); 8.06 (d, 2H, 8Hz).

EXAMPLE 4 - 4-[4-(3,4-difluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid
20

a. Methyl 4-[5,5,8,8-tetramethyl-4-(3,4-difluorobenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoate

25 In a manner similar to Example 1f, by reacting 600 mg (1.38 mmol) of methyl 4-(4-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoate

with 240 mg (1.6 mmol) of potassium carbonate and 210 μ L (1.6 mmol) of 3,4-difluorobenzyl bromide. A white solid is obtained (m = 680 mg; yield = 86%; m.p. = 118°C).

- 5 b. 4-[5,5,8,8-tetramethyl-4-(3,4-difluorobenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

In a manner similar to that of Example 1g, by reacting 680 mg (1.2 mmol) of methyl 4-[5,5,8,8-tetramethyl-4-(3,4-difluorobenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoate with 240 mg of sodium hydroxide. A yellow crystallized solid is obtained (m = 402 mg; yield = 61%; m.p. = 218°C).

¹H NMR (CDCl₃) 1.32 (s, 6H); 1.39 (s, 6H); 1.66 (m, 4H); 5.06 (s, 2H); 6.94 (d, 1H, 4Hz); 7.14 (m, 2H); 7.23 (m, 1H); 7.28 (d, 1H, 4Hz); 7.51 (d, 2H, 5, 6Hz); 8.07 (d, 2H, 4Hz).

- EXAMPLE 5 - 4-[4-(2,4-difluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid**

a. Methyl 4-(5,5,8,8-tetramethyl-4-(2,4-difluorobenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

In a manner similar to that of Example 1f, by reacting 600 mg (1.38 mmol) of methyl 4-(4-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid with 240 mg

(1.6 mmol) of potassium carbonate and 200 μ L (1.7 mmol) of 2,4-difluorobenzyl bromide. A white solid is obtained (m = 790 mg; yield = 100%; m.p. = 115°C).

b. 4-[5,5,8,8-tetramethyl-4-(2,4-difluorobenzyloxy)-
5 5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

In a manner similar to that of Example 1g, by reacting 790 mg (1.4 mmol) of methyl 4-[5,5,8,8-tetramethyl-4-(2,4-difluorobenzyloxy)-5,6,7,8-tetrahydro-2-
10 naphthylselanylethynyl]benzoate with 240 mg of sodium hydroxide. A yellow crystallized solid is obtained (m = 502 mg; yield = 65%; m.p. = 219°C).

¹H NMR (CDCl₃) 1.31 (s, 6H); 1.37 (s, 6H); 1.65 (m, 4H);
5.12 (s, 2H); 6.90 (m, 2H); 7.03 (d, 1H, 1.6Hz); 7.22
15 (d, 1H, 2Hz); 7.51 (m, 3H); 8.08 (d, 2H, 8Hz).

EXAMPLE 6 - 4-[4-(4-trifluoromethylbenzyloxy)-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

a. Methyl 4-[5,5,8,8-tetramethyl-4-(4-
20 trifluoromethylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoate

In a manner similar to that of Example 1f, by reacting 590 mg (1.3 mmol) of methyl 4-(4-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-
25 naphthylselanylethynyl]benzoate with 240 mg (1.6 mmol) of potassium carbonate and 383 mg (1.6 mmol) of 4-trifluoromethylbenzyl bromide. A white solid is

obtained (m = 840 mg; yield = 100%; m.p. = 156°C).

b. 4-[5,5,8,8-tetramethyl-4-(4-trifluoromethylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

5 In a manner similar to that of Example 1g, by reacting 840 mg (1.4 mmol) of methyl 4-[5,5,8,8-tetramethyl-4-(4-trifluoromethylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoate with 240 mg of sodium hydroxide. A white crystallized solid is obtained (m =
10 614 mg; yield = 72%; m.p. = 253°C).

¹H NMR (DMSO) 1.17 (s, 6H); 1.34 (s, 6H); 1.59 (m, 4H); 5.27 (s, 2H); 7.11 (d, 1H, 4Hz); 7.27 (d, 1H, 4Hz); 7.55 (d, 2H, 8Hz); 7.67 (d, 2H, 8Hz); 7.73 (d, 2H, 8Hz); 7.94 (d, 2H, 8Hz); 13.10 (s, 1H).

15 **EXAMPLE 7 - 4-[5,5,8,8-tetramethyl-4-(naphthylmethoxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid**

a. Methyl 4-[5,5,8,8-tetramethyl-4-(naphthylmethoxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoate

20 In a manner similar to that of Example 1f, by reacting 368 mg (0.8 mmol) of methyl 4-(4-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoate with 140 mg (1 mmol) of potassium carbonate and 221 mg (1 mmol) of
25 2-bromomethylnaphthalene. A white solid is obtained (m = 400 mg; yield = 83%; m.p. = 134°C).

b. 4-[5,5,8,8-tetramethyl-4-(naphthylmethoxy)-

5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

In a manner similar to that of Example 1g, by reacting 400 mg (0.7 mmol) of methyl 4-[5,5,8,8-tetramethyl-4-(naphthylmethoxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoate with 140 mg of sodium hydroxide. A white crystallized solid is obtained (m = 258 mg; yield = 65%; m.p. = 254°C).

¹H NMR (DMSO) 1.25 (s, 6H); 1.35 (s, 6H); 1.58 (m, 4H); 5.31 (s, 2H); 7.19 (d, 1H, 1.6Hz); 7.26 (d, 1H, 1.6Hz); 7.53 (m, 4H); 7.59 (d, 1H, 8Hz); 7.85 (m, 1H); 7.96 (m, 4H); 7.98 (s, 1H).

EXAMPLE 8 - 4-[4-(4-chlorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-

naphthylselanylethynyl]benzoic acid

a. Methyl 4-[5,5,8,8-tetramethyl-4-(4-chlorobenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoate

In a manner similar to that of Example 1f, by reacting 370 mg (0.8 mmol) of methyl 4-(4-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoate with 140 mg (1 mmol) of potassium carbonate and 205 mg (1 mmol) of 4-chlorobenzyl bromide. A white solid is obtained (m = 300 mg; yield = 64%).

b. 4-[5,5,8,8-tetramethyl-4-(4-chlorobenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic

acid

In a manner similar to that of Example 1g, by reacting 300 mg (0.5 mmol) of methyl 4-[5,5,8,8-tetramethyl-4-(4-chlorobenzyloxy)-5,6,7,8-tetrahydro-2-

5 naphthylselanylethynyl]benzoate with 110 mg of sodium hydroxide. A white crystallized solid is obtained (m = 210 mg; yield = 72%, m.p. = 255°C).

¹H NMR (DMSO) 1.24 (s, 6H); 1.32 (s, 6H); 1.59 (m, 4H); 5.15 (s, 2H); 7.10 (s, 1H); 7.26 (s, 1H); 7.43 (d, 2H, 10 8Hz); 7.48 (d, 2H, 8Hz); 7.56 (d, 2H, 8Hz); 7.95 (d, 2H, 8Hz); 13.10 (s, 1H).

EXAMPLE 9 - 4-[4-(4-bromobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8,-tetrahydro-2-naphthylselanylethynyl]benzoic acid

15 a. Methyl 4-[5,5,8,8-tetramethyl-4-(4-bromobenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoate

In a manner similar to that of Example 1f, by reacting 215 mg (0.5 mmol) of methyl 4-(4-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2- 20 naphthylselanylethynyl]benzoate with 80 mg (0.6 mmol) of potassium carbonate and 146 mg (0.6 mmol) of 4-bromobenzyl bromide. A white solid is obtained (m = 320 mg; yield = 100%).

25 b. 4-[5,5,8,8-tetramethyl-4-(4-bromobenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

In a manner similar to that of Example 1g, by reacting 320 mg (0.5 mmol) of methyl 4-[5,5,8,8-tetramethyl-4-(4-bromobenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoate with 110 mg of sodium hydroxide. A white crystallized solid is obtained (m = 240 mg; yield = 66%; m.p. = 265°C).

¹H NMR (DMSO) 1.24 (s, 6H); 1.32 (s, 6H); 1.59 (m, 4H); 5.13 (s, 2H); 7.09 (d, 1H, 1.2Hz); 7.25 (d, 1H, 1.2Hz); 7.41 (d, 2H, 8.4Hz); 7.56 (d, 4H, 7.2Hz); 7.95 (d, 2H, 8Hz); 13.10 (s, 1H).

EXAMPLE 10 - 4-[5,5,8,8-tetramethyl-4-(3-methylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

a. Methyl 4-[5,5,8,8-tetramethyl-4-(3-methylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoate

In a manner similar to that of Example 1f, by reacting 600 mg (1.35 mmol) of methyl 4-(4-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoate with 250 mg (1.8 mmol) of potassium carbonate and 274 µL (1.5 mmol) of 3-methylbenzyl bromide. A white solid is obtained (m = 708 mg; yield 96%; m.p. = 102°C).

b. 4-[5,5,8,8-tetramethyl-4-(3-methylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

In a similar manner to that of Example 1g, by reacting

650 mg (1.2 mmol) of methyl 4-[5,5,8,8-tetramethyl-4-(3-methylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoate with 240 mg of sodium hydroxide. A yellow crystallized solid is obtained

5 (m = 600 mg; yield = 94%; m.p. 225°C).

¹H NMR (DMSO) : 1.29 (s, 6H); 1.38 (s, 6H); 1.62-1.65 (m, 4H); 2.34 (s, 3H); 5.15 (s, 2H); 7.16-7.19 (m, 2H); 7.29-7.31 (m, 4H); 7.63 (d, J = 8.2Hz, 2H); 8.00 (d, J = 8.2Hz, 2H); 13.3 (bs, 1H).

10 **EXAMPLE 11 - 4-[5,5,8,8-tetramethyl-4-(4-methylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid**

a. Methyl 4-[5,5,8,8-tetramethyl-4-(4-fluorobenzyloxy)-5,6,7,8-tetrahydro-2-

15 *naphthylselanylethynyl]benzoate*

In a manner similar to that of Example 1f, by reacting 600 mg (1.35 mmol) of methyl 4-(4-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-

naphthylselanylethynyl]benzoate with 250 mg (1.8 mmol)

20 of potassium carbonate and 185 µL (1.5 mmol) of 4-fluorobenzyl bromide. A white solid is obtained (m = 690 mg; yield = 93%; m.p. = 121°C).

b. 4-[5,5,8,8-tetramethyl-4-(4-fluorobenzyloxy)-5,6,7,8-tetrahydro-2-*naphthylselanylethynyl]benzoic*

25 *acid*

In a manner similar to that of Example 1g, by reacting 650 mg (1.2 mmol) of methyl 4-[5,5,8,8-tetramethyl-4-

(4-fluorobenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoate with 240 mg of sodium hydroxide. A yellow crystallized solid is obtained (m = 619 mg; yield = 98%; m.p. = 228°C).

5 ¹H NMR (DMSO) : 1.14 (s, 6H); 1.21 (s, 6H); 1.45-1.49 (m, 4H); 5.02 (s, 2H); 7.02 (s, 1H); 7.08-7.15 (m, 3H); 7.39-7.42 (m, 2H); 7.47 (d, J = 8.1Hz, 2H); 7.85 (d, J = 8.1Hz, 2H); 12.9 (bs, 1H).

EXAMPLE 12 - 4-{4-hydroxy-3-[5,5,8,8-tetramethyl-4-(4-trifluoromethylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthyl]prop-1-ynyl}benzoic acid

a. 4-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthalenecarbaldehyde

30 g (106 mmol) of 3-bromo-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-1-naphthyl (Example 5a) are dissolved in 500 mL of anhydrous THF. The medium is cooled to -78°C, and 156 mL (265 mmol) of tert-butyllithium are then added dropwise. After 45 minutes at this temperature, 12.3 mL (159 mmol) of dimethylformamide are added. The mixture is warmed to room temperature and then treated with 1 N hydrochloric acid solution and extracted with ethyl acetate. The residue obtained is then purified by chromatography (eluent: 9/1 heptane/ethyl acetate). A white solid is obtained (m = 16.5g; yield = 67%; m.p. = 144°C).

b. 5,5,8,8-tetramethyl-4-(4-trifluoromethylbenzyloxy)-5,6,7,8-tetrahydro-2-

naphthalenecarbaldehyde

In a manner similar to that of Example 1c, by reacting 700 mg (3 mmol) of 4-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthalenecarbaldehyde with 5 160 mg of sodium hydride and 789 mg (3.3 mmol) of 4-trifluoromethylbenzyl bromide. A yellow oil is obtained (m = 1.15 g; yield = 100%).

c. 1-[5,5,8,8-tetramethyl-4-(4-trifluoromethylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthyl]prop-2-yn-1-ol

In a manner similar to that of Example 1f, by reacting 1.15 g (3 mmol) of 5,5,8,8-tetramethyl-4-(4-trifluoromethylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthalenecarbaldehyde with 7.7 mL (7.7 mmol) of 1 N 15 ethynylmagnesium bromide solution. A colourless oil is obtained (m = 1.2 g; yield = 100%).

d. 4-{3-hydroxy-3-[5,5,8,8-tetramethyl-4-(4-trifluoromethylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthyl]prop-1-ynyl}benzoic acid

20 In a manner similar to that of Example 1g, by reacting 1.2 g (2.8 mmol) of 1-[5,5,8,8-tetramethyl-4-(4-trifluoromethylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthyl]prop-2-yn-1-ol with 600 mg (2.4 mmol) of 4-iodobenzoic acid in the presence of 23 mg of copper 25 iodide and 42 mg of bis(triphenylphosphine)dichloropalladium. The desired product is obtained in the form of orange-coloured crystals (m = 930 mg; yield = 72%,

m.p. 222°C).

¹H NMR (DMSO) 1.25 (s, 6H); 1.37 (s, 6H); 1.60 (m, 4H);
5.25 (s, 2H); 5.52 (s, 2H); 6.10 (d, 1H); 6.99 (s, 1H);
7.15 (s, 1H); 7.49 (d, 2H, 8Hz); 7.73 (dd, 4H, 8Hz,
5 12Hz); 7.92 (d, 2H, 8Hz); 13.1 (s, 1H).

EXAMPLE 13 - 4-{3-hydroxy-3-[5,5,8,8-tetramethyl-4-(4-methylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthyl]prop-1-ynyl}benzoic acid

a. 5,5,8,8-tetramethyl-4-(4-methylbenzyloxy)-5,6,7,8-
10 tetrahydro-2-naphthalenecarbaldehyde

In a manner similar to that of Example 1c, by reacting
700 mg (3 mmol) of 4-hydroxy-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthalenecarbaldehyde with
160 mg of sodium hydride and 611 mg (3.3 mmol) of 4-
15 methylbenzyl bromide. A colourless oil is obtained (m =
1.12 g; yield = 100%).

b. 1-[5,5,8,8-tetramethyl-4-(4-methylbenzyloxy)-
5,6,7,8-tetrahydro-2-naphthyl]prop-2-yn-1-ol

In a manner similar to that of Example 1f, by reacting
20 1.12 g (3.3 mmol) of 5,5,8,8-tetramethyl-4-(4-
methylbenzyloxy)-5,6,7,8-tetrahydro-2-
naphthalenecarbaldehyde with 8.7 mL (8.7 mmol) of 1 N
ethynylmagnesium bromide solution. A colourless oil is
obtained (m = 1.22 g; yield = 100%).

25 c. 4-{3-hydroxy-3-[5,5,8,8-tetramethyl-4-(4-
methylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthyl]prop-1-
ynyl}benzoic acid

In a manner similar to that of Example 1g, by reacting 1.22 g (3.3 mmol) of 1-[5,5,8,8-tetramethyl-4-(4-methylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthyl]prop-2-yn-1-ol with 680 mg (2.8 mmol) of 4-iodobenzoic acid in the presence of 27 mg of copper iodide and 49 mg of bis(triphenylphosphine)dichloropalladium. The desired product is obtained in the form of beige-coloured crystals (m = 900 mg; yield = 67%; m.p. = 219°C).

¹H NMR (DMSO) 1.24 (s, 6H); 1.33 (s, 6H); 1.59 (m, 4H); 2.29 (s, 3H); 5.06 (s, 2H); 5.52 (d, 1H, 4.8Hz); 6.10 (d, 1H, 5.6Hz); 7.01 (d, 1H, 1.2Hz); 7.12 (d, 1H, 0.8Hz); 7.18 (d, 2H, 7.6Hz); 7.37 (d, 2H, 8Hz); 7.51 (d, 2H, 8Hz); 7.93 (d, 2H, 8Hz); 13.1 (s, 1H).

EXAMPLE 14 - 4-{3-[4-(4-tert-butylbenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxy-prop-1-ynyl}benzoic acid

a. 4-(4-tert-butylbenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthalenecarbaldehyde

In a manner similar to that of Example 1c, by reacting 700 mg (3 mmol) of 4-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthalenecarbaldehyde with 160 mg of sodium hydride and 600 µL (3.3 mmol) of 4-tert-butylbenzyl bromide. A colourless oil is obtained (m = 1.2 g; yield = 100%).

b. 1-[4-(4-tert-butylbenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]prop-2-yn-1-ol

In a similar manner to that of Example 1f, by reacting

1.2 g (3 mmol) of 4-(4-tert-butylbenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthalenecarbaldehyde with 7.8 mL (7.8 mmol) of 1 N ethynylmagnesium bromide solution. A colourless oil is
5 obtained (m = 760 mg; yield = 63%).

c. 4-{3-[4-(4-tert-butylbenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxy-prop-1-ynyl}benzoic acid

In a manner similar to that of Example 1g, by reacting
10 760 mg (1.9 mmol) of 1-[4-(4-tert-butylbenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]prop-2-yn-1-ol with 390 mg (1.6 mmol) of 4-iodobenzoic acid in the presence of 15 mg of copper iodide and 28 mg of bis(triphenylphosphine)dichloropalladium. The desired
15 product is obtained in the form of white crystals (m = 600 mg; yield = 71%; m.p. = 254°C).

¹H NMR (DMSO) 1.25 (s, 6H); 1.26 (s, 9H); 1.36 (s, 6H); 1.59 (m, 4H); 5.09 (s, 2H); 5.53 (d, 1H, 5.6Hz); 6.10 (d, 1H, 6.4Hz); 7.05 (s, 1H); 7.13 (s, 1H); 7.39 (dd, 20 4H, 8Hz, 16Hz); 7.53 (d, 2H, 8.4Hz); 7.93 (d, 2H, 8.4Hz); 13.10 (s, 1H).

EXAMPLE 15 - 4-{3-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxy-prop-1-ynyl}benzoic acid

25 a. 4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthalenecarbaldehyde

In a manner similar to that of Example 1c, by reacting

700 mg (3 mmol) of 4-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthalenecarbaldehyde with 160 mg of sodium hydride and 410 μ L (3.3 mmol) of 4-fluorobenzyl bromide. A colourless oil is obtained (m = 1.2 g; yield = 100%).

b. 1-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]prop-2-yn-1-ol

In a manner similar to that of Example 1f, by reacting 1.0 g (2.9 mmol) of 4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthalenecarbaldehyde with 4.5 mL (4.5 mmol) of 1 N ethynylmagnesium bromide solution. A colourless oil is obtained (m = 580 mg; yield = 55%).

c. 4-{3-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxy-prop-1-ynyl}benzoic acid

In a manner similar to that of Example 1g, by reacting 580 mg (1.6 mmol) of 1-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]prop-2-yn-1-ol with 330 mg (1.3 mmol) of 4-iodobenzoic acid in the presence of 12 mg of copper iodide and 23 mg of bis(triphenylphosphine)dichloropalladium. The desired product is obtained in the form of beige-coloured crystals (m = 420 mg; yield = 67%; m.p. 188°C).

^1H NMR (DMSO) 1.24 (s, 6H); 1.59 (s, 6H); 5.10 (s, 2H); 5.52 (d, 1H, 4.3Hz); 6.10 (s, 1H); 7.00 (d, 1H, 1.2Hz); 7.13 (d, 1H, 1.2Hz), 7.19 (t, 2H, 8.8Hz); 7.50 (m, 4H);

7.92 (d, 2H, 8.4Hz).

EXAMPLE 16 - 4-{(E)-3-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}benzoic acid

- 5 a. 1-(4-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)ethanone
- 5 g (22 mmol) of 4-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthalenecarbaldehyde (Example 16a) are dissolved in 150 mL of THF. The medium is cooled to 0°C
- 10 and 15 mL (45 mmol) of 3M methylmagnesium bromide solution are then added. After 30 minutes, the medium is treated with saturated ammonium chloride solution and then extracted with ethyl acetate. The residue obtained is dissolved in 40 mL of dichloromethane. A
- 15 solution of 6.5 mL of DMSO (84 mmol) in 50 mL of dichloromethane is then added slowly to a solution, prepared beforehand, of 3.75 mL (43 mmol) of oxalyl chloride in 100 mL of dichloromethane at -78°C. The solution containing the product obtained previously is
- 20 then added to this reaction medium very slowly, followed by addition of 23 mL (165 mmol) of triethylamine. The reaction medium is warmed slowly to room temperature and is then treated with saturated ammonium chloride solution and extracted with
- 25 dichloromethane. The residue is purified by chromatography (eluent: 9/1 heptane/ethyl acetate). A thick yellow oil is obtained (m = 2.6 g; yield = 51%).

b. Methyl 4-[(E)-3-(4-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-oxopropenyl]benzoate
1.4 g (4.9 mmol) of 1-(4-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)ethanone are dissolved in
5 50 mL of methanol. 660 mg (4.4 mmol) of 4-carboxybenzaldehyde and 2.3 mL (20 mmol) of 47% KOH solution are then added. The reaction medium is stirred at 65°C for 48 hours, and then cooled and acidified, and finally extracted with ethyl acetate. The residue
10 obtained is then dissolved in 50 mL of methanol and 1 mL of concentrated sulphuric acid. The reaction medium is stirred at reflux for 12 hours and then cooled, hydrolyzed, and extracted with dichloromethane. The residue obtained is purified by chromatography
15 (eluent: 85/15 heptane/ethyl acetate). A yellow crystallized solid is obtained (m = 390 mg; yield = 20%).

c. Methyl 4-[(E)-3-[4-(4-fluorobenzyloxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)]-3-oxopropenyl]benzoate
20

In a manner similar to Example 1f, by reacting 340 mg (0.85 mmol) of methyl 4-[(E)-3-(4-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-oxopropenyl]benzoate with 140 mg (1 mmol) of potassium
25 carbonate and 120 µL (1 mmol) of 4-fluorobenzyl bromide. The product is obtained in the form of yellow crystals (m = 320 mg; yield = 75%; m.p. = 142°C).

d. 4-((E)-3-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}benzoic acid

In a manner similar to that of Example 1g, by reacting
5 320 mg (0.6 mmol) of methyl 4-((E)-3-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}benzoate with
128 mg (3 mmol) of sodium hydroxide. The desired
product is obtained in the form of a white crystallized
10 solid (m = 170 mg; yield = 55%; m.p. = 241°C).

¹H NMR (DMSO) 1.33 (s, 6H); 1.35 (s, 6H); 1.63 (m, 4H);
5.22 (s, 2H); 7.27 (t, 2H, 8Hz); 7.52 (s, 1H); 7.58
(dd, 2H, 8Hz, 2.4Hz); 7.78 (s, 2H); 8.01 (s, 4H).

EXAMPLE 17 - 6-{1-[4-(4-fluorobenzyloxy)-5,5,8,8-
15 **tetramethyl-5,6,7,8-tetrahydro-2-**
naphthyl]methanoyl}naphthalene-2-carboxylic acid

a. 4-ethoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthalene boronic acid

8.9 g (26 mmol) of 7-bromo-5-ethoxymethoxy-1,1,4,4-tetramethyl-1,2,3,4-tetrahydronaphthalene (Example 5b)
20 are dissolved in 200 mL of anhydrous THF and the
mixture is cooled to -78°C. 12.5 mL (31 mmol) of 2.5M
butyllithium solution are added and the mixture is
stirred for 1 hour. 7.2 mL (31 mmol) of triisopropyl
25 borate are then added and the reaction medium is
stirred at this temperature for 1 hour, then warmed to
room temperature and treated with saturated ammonium

chloride solution. The residue obtained after extraction is washed with heptane. A white powder is obtained (m = 6.8 g; yield = 85%).

b. Methyl 6-[1-(4-ethoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)methanoyl]-2-naphthalenecarboxylate

5 g (16 mmol) of 4-ethoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthalene boronic acid are dissolved in 100 mL of toluene. 26 g (80 mmol) of caesium carbonate are added and the medium is degassed for 15 minutes with a flow of nitrogen. 14 mg (0.8 mmol) of palladium chloride are added, followed by 5.47 g (22 mmol) of methyl 6-chlorocarbonyl-2-naphthalenecarboxylate in 1 g portions. The reaction medium is refluxed for 15 hours and then hydrolysed and extracted with ethyl acetate. The residue obtained is purified by chromatography (eluent: 9/1 heptane/ethyl acetate). The product is then recrystallized from an ethyl acetate/heptane mixture (m = 4.3 g; yield = 59%; m.p. = 96°C).

c. Methyl 6-[1-(4-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)methanoyl]-2-naphthalenecarboxylate

3.5 g (7.6 mmol) of methyl 6-[1-(4-ethoxymethoxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)methanoyl]-2-naphthalenecarboxylate are dissolved in 50 mL of THF and 100 mL of methanol. 1 mL

of concentrated sulphuric acid is added and the reaction medium is heated at 80°C for 2 hours and then cooled and hydrolyzed. A white solid is obtained (m = 2.6 g; yield = 84%; m.p. = 222°C).

- 5 d. Methyl 6-{1-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]methanoyl}-2-naphthalenecarboxylate

In a manner similar to that of Example 1f, by reacting 1.5 g (3.6 mmol) of methyl 6-[1-(4-hydroxy-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)methanoyl]-2-naphthalenecarboxylate with 600 mg (4.5 mmol) of potassium carbonate and 540 µL (4.3 mmol) of 4-fluorobenzyl bromide. The product is obtained in the form of white crystals (m = 320 mg; yield 98%; mp. = 15 179°C).

- e. 6-{1-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]methanoyl}-2-naphthalenecarboxylic acid

In a manner similar to that of Example 1g, by reacting 20 250 mg (0.5 mmol) of methyl 6-{1-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]methanoyl}-2-naphthalenecarboxylate with 40 mg of sodium hydroxide. A white crystallized solid is obtained (m = 235 mg; 25 yield = 66%; m.p. = 277°C).

¹H NMR (DMSO) 1.24 (s, 6H); 1.39 (s, 6H); 1.63-1.66 (m, 4H); 5.15 (s, 2H); 7.20-7.27 (m, 3H); 7.41 (s, 1H):

7.49-7.52 (m, 2H), 7.89 (d, $J = 8.5\text{Hz}$, 1H); 8.06 (d, $J = 8.5\text{Hz}$, 1H); 8.19 (d, $J = 8.7\text{Hz}$, 1H); 8.26 (d, $J = 8.6\text{Hz}$, 1H); 8.37 (s, 1H); 8.70 (s, 1H).

EXAMPLE 18 - 6-{1-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-1-hydroxymethyl}-2-naphthalenecarboxylic acid

245 mg (0.5 mmol) of 6-{1-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]methanoyl}-2-naphthalenecarboxylate are dissolved in 5 mL of THF and 5 mL of methanol, and 28 mg (0.7 mmol) of sodium borohydride are added. The medium is stirred for 1 hour, and then treated with saturated ammonium chloride solution. The residue obtained after extraction is purified by chromatography: a white solid is obtained ($m = 220\text{ mg}$; yield = 89%; m.p. = 212°C).

^1H NMR (DMSO) : 1.20 (s, 6H); 1.27 (s, 6H); 1.53-1.55 (m, 4H); 5.01 (s, 2H); 5.79 (s, 1H); 5.98 (bs, 1H); 6.89 (s, 1H); 7.09-7.17 (m, 3H); 7.44-7.48 (m, 2H); 7.56 (d, $J = 8.6\text{Hz}$, 1H); 7.94-8.02 (m, 4H); 8.53 (s, 1H).

EXAMPLE 19: TRANSACTIVATION TEST

The activation of receptors with an agonist (activator) in HeLa cells leads to the expression of a reporter gene, luciferase, which, in the presence of a substrate, generates light. The activation of the receptors may thus be measured by quantifying the

luminescence produced after incubating the cells in the presence of a reference agonist. The inhibitory products displace the agonist from its site, thus preventing activation of the receptor. The activity is
5 measured by quantifying the reduction in light produced. This measurement makes it possible to determine the inhibitory activity of the compounds according to the invention.

10 Determination of the K_{dapp}:

In this study, a constant is determined which represents the affinity of the molecule for the receptor. Since this value can fluctuate depending on the basal activity and the expression of the receptor,
15 it is referred to as the K_{dapparent} (K_{dApp}).

To determine this constant, "crossed curves" of the test product against a reference agonist, 4-[2-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)propenyl]benzoic acid, are performed in 96-
20 well plates. The test product is used at 10 concentrations and the reference agonist at 7 concentrations. In each well, the cells are in contact with a concentration of the test product and a concentration of the reference agonist, 4-[2-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)propenyl]benzoic acid. Measurements are also
25 taken for the total agonist (4-[2-(5,5,8,8-tetramethyl-

5,6,7,8-tetrahydro-2-naphthyl)propenyl]benzoic acid) and inverse agonist, 4-((E)-3-[4-(4-tert-butylphenyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl]benzoic acid, controls.

5 These crossed curves make it possible to determine the AC₅₀ values (concentration at which 50% activation is observed) for the reference ligand at various concentrations of test product. These AC₅₀ values are used to calculate the Schild regression by
10 plotting a straight line corresponding to the Schild equation ("quantitation in receptor pharmacology" Terry P. Kenakin, *Receptors and Channels*, 2001, 7, 371-385).

 In the case of an antagonist, an IC₅₀ value (concentration that inhibits 50% of the activity) is
15 calculated by plotting the curve of the product at the concentration of the reference ligand that gives 80% activation.

 The HeLa cell lines used are stable transfectants containing the plasmids ERE-βGlob-Luc-SV-
20 Neo (reporter gene) and RAR (α, β, γ) ER-DBD-puro. These cells are inoculated into 96-well plates at a rate of 10 000 cells per well in 100 μl of DMEM medium without phenol red, and supplemented with 10% defatted calf serum. The plates are then incubated at 37°C and 7% CO₂
25 for 4 hours.

 The various dilutions of the test products, of the reference ligand (4-[2-(5,5,8,8-tetramethyl-

5,6,7,8-tetrahydro-2-naphthyl)propenyl]benzoic acid),
 of the 100% control (100 nM 4-[2-(5,5,8,8-tetramethyl-
 5,6,7,8-tetrahydro-2-naphthyl)propenyl]benzoic acid)
 and of the 0% control (500 nM 4-((E)-3-[4-(4-tert-
 5 butylphenyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-
 naphthyl]-3-oxopropenyl}benzoic acid) are added at a
 rate of 5 μ l per well. The plates are then incubated
 for 18 hours at 37°C and 7% CO₂.

The culture medium is removed by turning over
 10 and 100 μ l of a 1:1 PBS/luciferine mixture is added to
 each well. After 5 minutes, the plates are read using
 the luminescence detector.

	RAR alpha		RAR beta		RAR gamma	
	Kdapp (nM)	IC ₅₀ (nM)	Kdapp (nM)	IC ₅₀ (nM)	Kdapp (nM)	IC ₅₀ (nM)
Ex 1	8	14	4	6.5	2	5
Ex 3	15	26.25	30	48	4	10
Ex 4	2	3.5	4	6.4	1	2.5
Ex 5	2	3.5	1	1.6	1	2.5
Ex 10	30	52.5	15	24	4	10
Ex 11	8	14	4	6.4	1	2.5

The results obtained with the compounds
 15 according to the invention clearly show Kdapp values
 $\leq$ 100 nM and an IC₅₀ value $\leq$ 100 nM for at least one of
 the receptor subtypes, this clearly demonstrating a
 reduction in the signal, and in the luminescence in the

presence of the reference agonist. The compounds according to the invention are thus clearly inhibitors of retinoic acid receptors (RAR).

5 EXAMPLE 20: FORMULATION EXAMPLES

This example illustrates various concrete formulations based on the compounds according to the invention.

10 A - ENTERAL ROUTE

(a) 0.2 g tablet

- Compound of Example 16	0.001 g
- Starch	0.114 g
- Dicalcium phosphate	0.020 g
- Silica	0.020 g
- Lactose	0.030 g
- Talc	0.010 g
- Magnesium stearate	0.005 g

(b) Drinkable suspension in 5 ml ampules

- Compound of Example 17	0.001 g
- Glycerol	0.500 g
- 70% sorbitol	0.500 g
- Sodium saccharinate	0.010 g
- Methyl para-hydroxybenzoate	0.040 g
- Flavouring	qs
- Purified water	5 ml

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(c) 0.8 g tablet

- Compound of Example 9	0.500 g
- Pregelatinized starch	0.100 g
- Microcrystalline cellulose	0.115 g
- Lactose	0.075 g
- Magnesium stearate	0.010 g

(d) Drinkable suspension in 10 ml ampules

- Compound of Example 2	0.200 g
- Glycerol	1.000 g
- 70% sorbitol	1.000 g
- Sodium saccharinate	0.010 g
- Methyl para-hydroxybenzoate	0.080 g
- Flavouring	qs
- Purified water qs	10 ml

5 B - PARENTERAL ROUTE

(a) Composition

- Compound of Example 3	0.002 g
- Ethyl oleate	qs 10 g

(b) Composition

- Compound of Example 1	0.05%
- Polyethylene glycol	20%
- 0.9% NaCl solution	qs 100

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(c) Composition

- Compound of Example 3 2.5%
- Polyethylene glycol 400 20%
- 0.9% NaCl solution qs 100

(d) Injectable cyclodextrin composition

- Compound of Example 3 0.1 mg
- β -Cyclodextrin 0.10 g
- Water for injection qs 10.00 g

5 C - TOPICAL ROUTE

(a) Ointment

- Compound of Example 12 0.020 g
- Isopropyl myristate 81.700 g
- Liquid petroleum jelly fluid 9.100 g
- Silica ("Aerosil 200" sold by Degussa) 9.180 g

(b) Ointment

- Compound of Example 15 0.300 g
- White petroleum jelly codex qs 100 g

10

(c) Nonionic water-in-oil cream

- Compound of Example 10 0.100 g
- Mixture of emulsifying lanolin alcohols, waxes and oils ("Anhydrous Eucerin" sold by BDF) 39.900 g

70

- Methyl para-hydroxybenzoate 0.075 g
- Propyl para-hydroxybenzoate 0.075 g
- Sterile demineralized water qs 100 g

(d) Lotion

- Compound of Example 9 0.100 g
- Polyethylene glycol (PEG 400) 69.900 g
- 95% ethanol 30.000 g

(e) Hydrophobic ointment

- Compound of Example 4 0.300 g
- Isopropyl myristate 36.400 g
- Silicone oil ("Rhodorsil 47 V 300"
sold by Rhône-Poulenc) 36.400 g
- Beeswax 13.600 g
- Silicone oil ("Abil 300 000 cst"
sold by Goldschmidt) qs 100 g

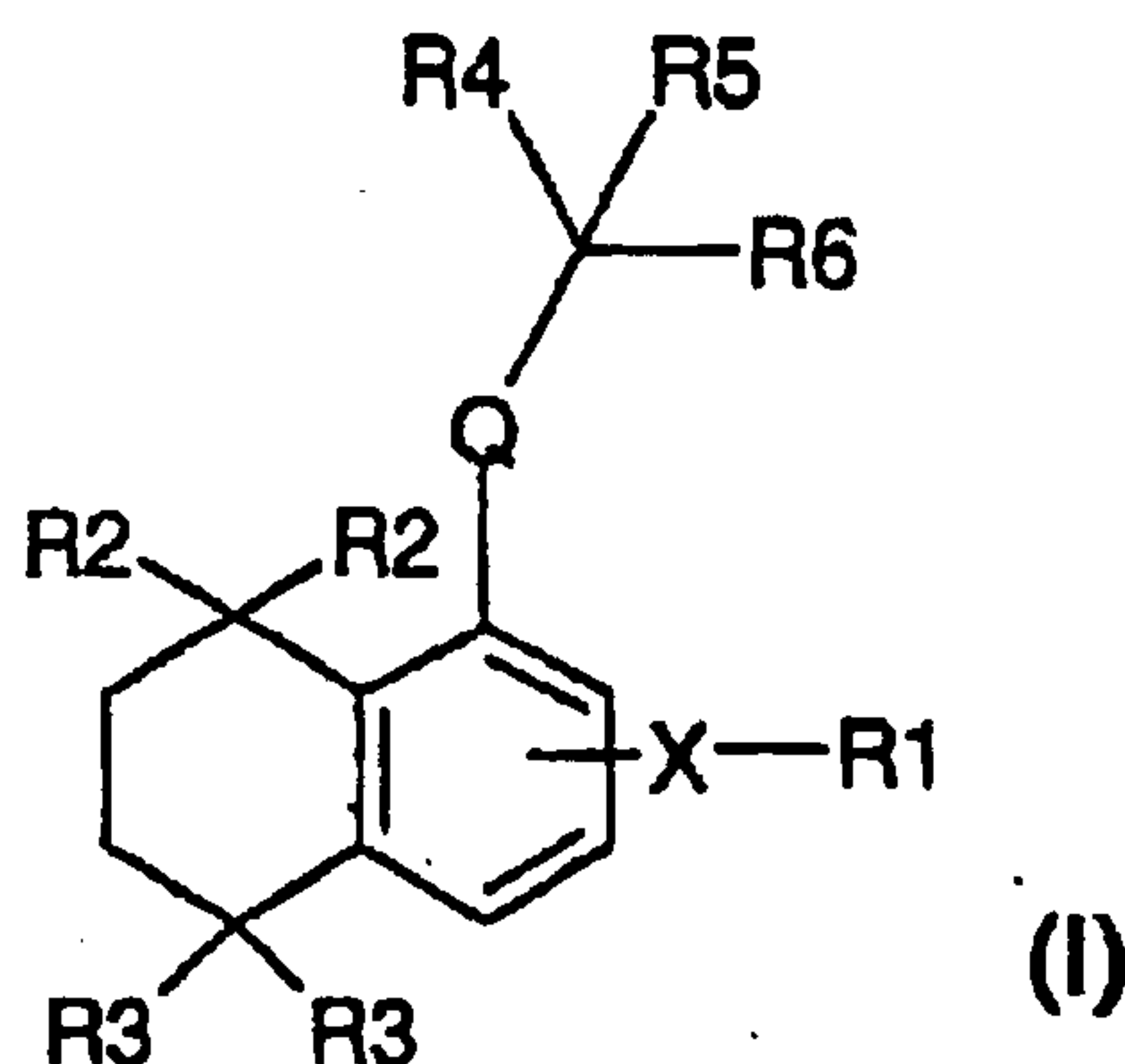
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(f) Nonionic oil-in-water cream

- Compound of Example 6 1.000 g
- Cetyl alcohol 4.000 g
- Glyceryl monostearate 2.500 g
- 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
- Sterile demineralized water qs 100 g

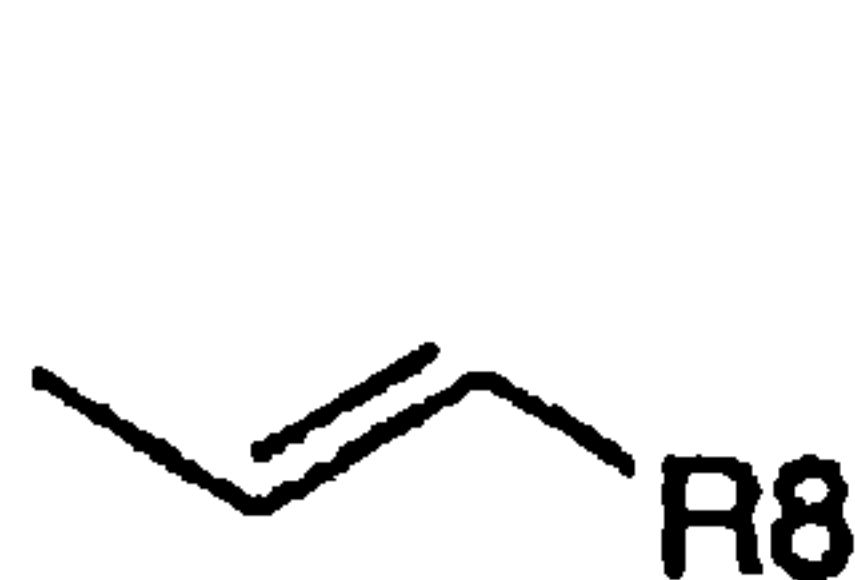
WHAT IS CLAIMED IS:

1. Compounds characterized in that they correspond to formula (I) below:



in which:

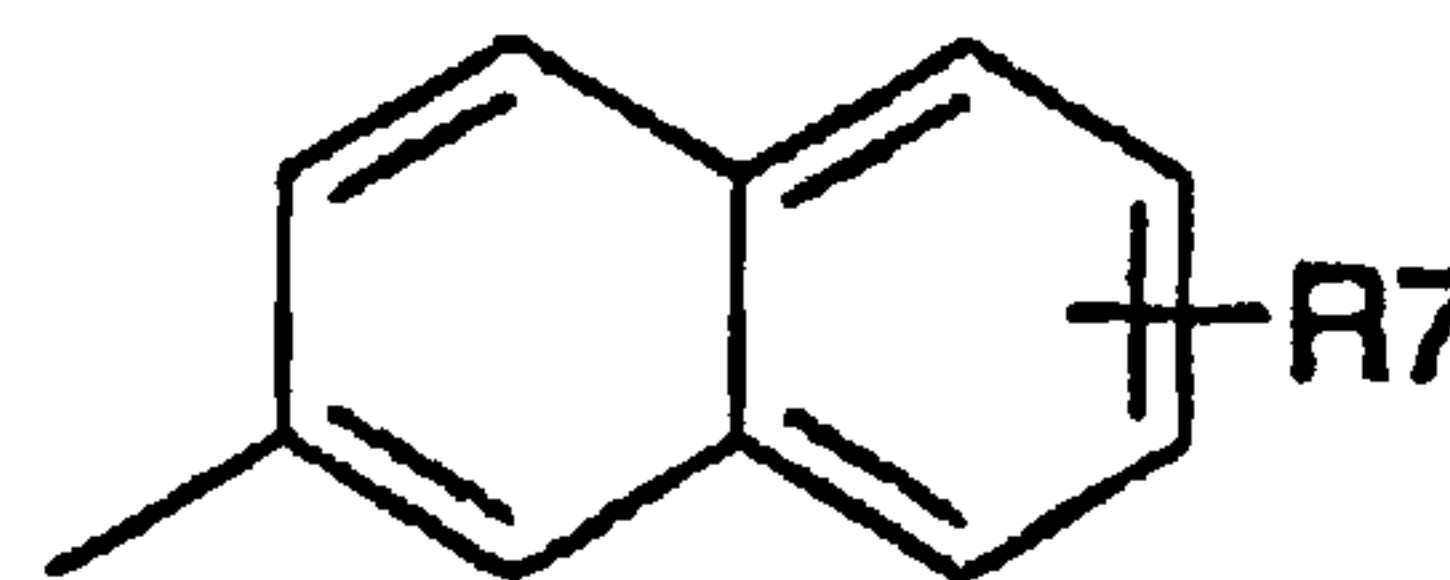
- R₁ represents a radical of formulae (a) to (c) below:



(a)



(b)



(c)

R₇ and R₈ having the meanings given below,

- each of the radicals R₂ and R₃, which is identical or different, represent a hydrogen atom or an alkyl radical containing from 1 to 6 carbon atoms,

- 10 - X represents an Se atom, -CHOH, -CH₂ or C=O,
 - Q represents an oxygen atom, a sulphur atom, CH₂,
 - NH or -NR₉,

R₉ having the meanings given below,

- R₄ and R₅, which is identical or different, represent a hydrogen atom, an alkyl radical containing from 1 to 6 carbon atoms, or together form an oxo radical,
 - R₆ represents a phenyl radical, a naphthyl radical or a heterocyclic radical of the pyridine, pyrimidine or thiophene type, optionally substituted with one or more radicals chosen from an alkyl containing from 1 to 6 carbon atoms, an -OR₁₀

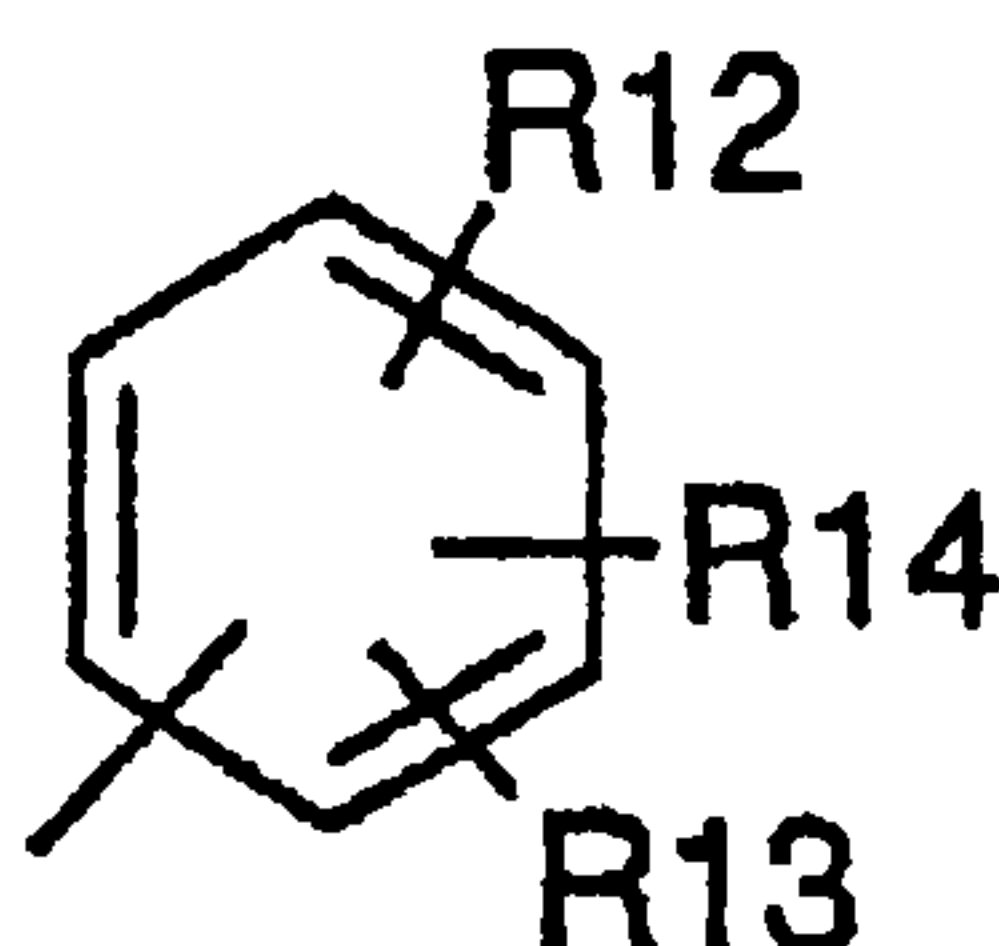
radical, a halogen atom, $-\text{CF}_3$, $-\text{NH}_2$ and a nitrogen atom mono- or disubstituted with an alkyl radical containing from 1 to 6 carbon atoms,

R_{10} having the meanings given below,

- R_7 represents a radical $-\text{COR}_{11}$,

R_{11} having the meanings given below,

- R_8 represents a radical:



(i)

R_{12} , R_{13} and R_{14} having the meanings given below,

- R_9 represents an alkyl radical containing from 1 to 6 carbon atoms,
- 10 - R_{10} represents a hydrogen atom or an alkyl radical containing from 1 to 6 carbon atoms,

- R_{11} represents a radical $-\text{OR}_{15}$ or a radical $-\text{NR}_{15}\text{R}_{16}$

R_{15} and R_{16} having the meanings given below,

- R_{12} and R_{13} , which is identical or different, represent a hydrogen atom, a halogen atom, an alkyl radical containing from 1 to 6 carbon atoms or a radical $-\text{OR}_{17}$,

R_{17} having the meanings given below,

- R_{14} represents a radical $-\text{COR}_{18}$,

R_{18} having the meanings given below,

- 20 - R_{15} , R_{16} and R_{17} , which may be identical or different, represent a hydrogen atom or an alkyl radical containing from 1 to 6 carbon atoms,

- R_{18} represents a radical $-\text{OR}_{19}$ or a radical $-\text{NR}_{19}\text{R}_{20}$,

R_{19} and R_{20} having the meanings given below,

- R₁₉ represents a hydrogen atom or an alkyl radical containing from 1 to 6 carbon atoms,
 - R₂₀ represents a hydrogen atom, an alkyl radical containing from 1 to 6 carbon atoms, or -OH,
- and the optical isomers, the salts obtained with a pharmaceutically acceptable salt or base, of the said compounds of formula (I).

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

10 3. Compounds according to claim 1 or 2, characterized in that the alkyl radicals containing from 1 to 6 carbon atoms are chosen from the methyl, ethyl, propyl, isopropyl, butyl, tert-butyl, pentyl and hexyl radicals.

4. Compounds according to claim 1 or 2, characterized in that the halogen atom is chosen from the group consisting of a fluorine, chlorine or bromine atom.

5. Compounds according to claim 1 or 2, characterized in that the heterocyclic radical is chosen from a pyridine, pyrimidine or thiophene radical optionally substituted with an alkyl radical containing from 1 to 6 carbon atoms.

6. Compounds according to claim 1, characterized in that they are taken, from the group consisting of:

4-[4-(3-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

20 4-[5,5,8,8-tetramethyl-4-(4-methylbenzyloxy)-5,6,7,8-

tetrahydro-2-naphthylselanylethynyl]benzoic acid

4-[4-(4-tert-butylbenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

4-[4-(3,4-difluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

10 4-[4-(2,4-difluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

4-[5,5,8,8-tetramethyl-4-(4-trifluoromethylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

4-[5,5,8,8-tetramethyl-4-(2-naphthylmethoxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

4-[4-(4-chlorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

4-[4-(4-bromobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

20 4-[5,5,8,8-tetramethyl-4-(3-methylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthylselanylethynyl]benzoic acid

4-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-

tetrahydro-2-naphthylselanylethynyl]benzoic acid

4-{3-hydroxy-3-[5,5,8,8-tetramethyl-4-(4-trifluoromethylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthyl]prop-1-ynyl}benzoic acid

4-{3-hydroxy-3-[5,5,8,8-tetramethyl-4-(4-tert-butylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthyl]prop-1-ynyl}benzoic acid

4-{3-hydroxy-3-[5,5,8,8-tetramethyl-4-(4-methylbenzyloxy)-5,6,7,8-tetrahydro-2-naphthyl]prop-1-ynyl}benzoic acid

4-{3-[4-(4-tert-butylbenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}benzoic acid

4-{(E)-3-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}benzoic acid

6-{1-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]methanoyl}naphthalene-2-carboxylic acid

6-{1-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-1-hydroxymethyl}naphthalene-2-carboxylic acid

4-{3-[4-(4-fluorobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}-benzoic acid

4-(3-{4-[(4-fluorobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-oxopropenyl)benzoic acid

4-{3-[4-(4-fluorobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}benzoic acid

10 4-{3-[4-(4-fluorobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}benzoic acid

4-(3-{4-[(4-fluorobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxypropenyl)benzoic acid

4-(3-{4-[(4-fluorobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)benzoic acid

20 4-{3-[4-(4-fluorobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}benzoic acid

4-{3-[4-(4-fluorobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}benzoic acid

4-{3-[4-(4-fluorobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}benzoic acid

4-{3-[4-(4-fluorobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}-2-hydroxybenzoic acid

10 4-(3-{4-[(4-fluorobenzyl)methylamino]tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}oxopropenyl)-2-hydroxybenzoic acid

4-{3-[4-(4-fluorobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-2-hydroxybenzoic acid

4-{3-[4-(4-fluorobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}-2-hydroxybenzoic acid

20 4-(3-{4-[(4-fluorobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxypropenyl)-2-hydroxybenzoic acid

4-(3-{4-[(4-fluorobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

hydroxyprop-1-ynyl)-2-hydroxybenzoic acid

4-{3-[4-(4-fluorobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}-2-hydroxybenzoic acid

4-{3-[4-(4-fluorobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}-2-hydroxybenzoic acid

4-{3-[4-(4-fluorobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-2-

10 hydroxybenzoic acid

4-(3-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl)-2-hydroxybenzoic acid

4-(3-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl)-2-hydroxybenzoic acid

4-(3-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl)-2-hydroxybenzoic acid

20 4-(3-[4-(4-fluorobenzoylamido)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl)benzoic acid

4-(3-{4-[(4-fluoro)methylbenzoylamido]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-oxopropenyl)benzoic acid

4-(3-[4-(4-fluorobenzoylamido)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-

ynyl}benzoic acid

4-(3-{4-[(4-fluoro)methylebenzoylamido]-5,5,8,8-

tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

hydroxypropenyl}benzoic acid

4-{3-[4-(4-fluorobenzoylamido)-5,5,8,8-tetramethyl-

5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}benzoic acid

4-(3-{4-[(4-fluoro)methylbenzoylamido]-5,5,8,8-

tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}hydroxyprop-

10 1-ynyl}benzoic acid

4-(3-{4-[1-(4-fluorophenyl)-1-methylethoxy]-5,5,8,8-

tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

hydroxypropenyl}benzoic acid

4-(3-{4-[1-(4-fluorophenyl)-1-methylethoxy]-5,5,8,8-

tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

oxopropenyl}benzoic acid

4-(3-{4-[1-(4-fluorophenyl)-1-methylethoxy]-5,5,8,8-

tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

hydroxyprop-1-ynyl}benzoic acid

20 4-{3-[4-(4-methylbenzylamino)-5,5,8,8-tetramethyl-

5,6,7,8-tetrahydro-2-naphthyl]-3-

hydroxypropenyl}benzoic acid

4-(3-{4-[(4-methylbenzyl)methylamino]-5,5,8,8-

tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

oxopropenyl)benzoic acid

4-{3-[4-(4-methylbenzylamino)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-
ynyl}benzoic acid

4-{3-[4-(4-methylbenzylamino)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}benzoic
acid

4-(3-{4-[(4-methylbenzyl)methylamino]-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-
10 hydroxypropenyl)benzoic acid

4-(3-{4-[(4-methylbenzyl)methylamino]-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-
hydroxyprop-1-ynyl)benzoic acid

4-{3-[4-(4-methylbenzylsulphanyl)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-
hydroxypropenyl}benzoic acid

4-{3-[4-(4-methylbenzylsulphanyl)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}benzoic
acid

20 4-{3-[4-(4-methylbenzylsulphanyl)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-
ynyl}benzoic acid

4-{3-[4-(4-methylbenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}-2-hydroxybenzoic acid

4-(3-{4-[(4-methylbenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-oxopropenyl)-2-hydroxybenzoic acid

4-{3-[4-(4-methylbenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-2-hydroxybenzoic acid

10 4-{3-[4-(4-methylbenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}-2-hydroxybenzoic acid

4-(3-{4-[(4-methylbenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxypropenyl)-2-hydroxybenzoic acid

4-(3-{4-[(4-methylbenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)-2-hydroxybenzoic acid

20 4-{3-[4-(4-methylbenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}-2-hydroxybenzoic acid

4-{3-[4-(4-methylbenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}-2-hydroxybenzoic acid

4-{3-[4-(4-methylbenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-2-hydroxybenzoic acid

4-{3-[4-(4-methylbenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}-2-hydroxybenzoic acid

10 4-{3-[4-(4-methylbenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}-2-hydroxybenzoic acid

4-{3-[4-(4-methylbenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-2-hydroxybenzoic acid

4-[3-(4-{[1-(4-methylphenyl)methanoyl]amino}-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-hydroxypropenyl]benzoic acid

20 4-[3-(4-{[1-(4-methylphenyl)methanoyl]methylamino}-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-oxopropenyl]benzoic acid

4-[3-(4-{[1-(4-methylphenyl)methanoyl]amino}-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-

hydroxyprop-1-ynyl]benzoic acid

4-[3-(4-([1-(4-methylphenyl)methanoyl]methylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-hydroxypropenyl]benzoic acid

4-[3-(4-([1-(4-methylphenyl)methanoyl]amino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-oxopropenyl]benzoic acid

4-[3-(4-([1-(4-methylphenyl)methanoyl]methylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-

10 hydroxyprop-1-ynyl]benzoic acid

4-(3-(4-[1-(4-methylphenyl)-1-methylethoxy]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-hydroxypropenyl)benzoic acid

4-(3-(4-[1-(4-methylphenyl)-1-methylethoxy]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-oxopropenyl)benzoic acid

4-(3-(4-[1-(4-methylphenyl)-1-methylethoxy]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-

hydroxyprop-1-ynyl)benzoic acid

20 4-{3-[4-(4-dimethylaminobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}benzoic acid

4-(3-{4-[(4-dimethylaminobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-oxopropenyl)benzoic acid

4-{3-[4-(4-dimethylaminobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}benzoic acid

4-{3-[4-(4-dimethylaminobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}benzoic acid

10 4-(3-{4-[(4-dimethylaminobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxypropenyl)benzoic acid

4-(3-{4-[(4-dimethylaminobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)benzoic acid

4-{3-[4-(4-dimethylaminobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}benzoic acid

4-{3-[4-(4-dimethylaminobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}benzoic acid

20 tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}benzoic acid

4-(3-[4-(4-dimethylaminobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

hydroxyprop-1-ynyl}benzoic acid

4-{3-[4-(4-dimethylaminobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}-2-hydroxybenzoic acid

4-(3-{4-[(4-dimethylaminobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-oxopropenyl)-2-hydroxybenzoic acid

4-{3-[4-(4-dimethylaminobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

10 hydroxyprop-1-ynyl}-2-hydroxybenzoic acid

4-{3-[4-(4-dimethylaminobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}-2-hydroxybenzoic acid

4-(3-{4-[(4-dimethylaminobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxypropenyl)-2-hydroxybenzoic acid

4-(3-{4-[(4-dimethylaminobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)-2-hydroxybenzoic acid

20 4-{3-[4-(4-dimethylaminobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}-2-hydroxybenzoic acid

4-{3-[4-(4-dimethylaminobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}-2-hydroxybenzoic acid

4-{3-[4-(4-dimethylaminobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

hydroxyprop-1-ynyl}-2-hydroxybenzoic acid

4-{3-[4-(4-dimethylaminobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}-2-hydroxybenzoic acid

4-{3-[4-(4-dimethylaminobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-oxopropenyl}-2-hydroxybenzoic acid

4-{3-[4-(4-dimethylaminobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-2-

10 hydroxybenzoic acid

4-[3-(4-{[1-(4-dimethylaminophenyl)methanoyl]amino}-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-hydroxypropenyl]benzoic acid

4-[3-(4-{[1-(4-dimethylaminophenyl)methanoyl]-methylamino}-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-oxopropenyl]benzoic acid

4-[3-(4-{[1-(4-dimethylaminophenyl)methanoyl]amino}-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-hydroxyprop-1-ynyl]benzoic acid

20 4-[3-(4-{[1-(4-dimethylaminophenyl)methanoyl]-methylamino}-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-hydroxypropenyl]benzoic acid

4-[3-(4-{[1-(4-dimethylaminophenyl)methanoyl]amino}-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-oxopropenyl]benzoic acid

4-[3-(4-{[1-(4-dimethylaminophenyl)methanoyl]-methylamino}-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-

naphthyl)-3-hydroxyprop-1-ynyl]benzoic acid

4-(3-(4-[1-(4-dimethylaminophenyl)-1-methylethoxy]-
5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-
hydroxypropenyl)benzoic acid

4-(3-(4-[1-(4-dimethylaminophenyl)-1-methylethoxy]-
5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-
oxopropenyl)benzoic acid

4-(3-(4-[1-(4-dimethylaminophenyl)-1-methylethoxy]-
5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-
10 hydroxyprop-1-ynyl)benzoic acid

4-(3-(4-[2-(4-fluorophenyl)ethyl]-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl)-3-
hydroxypropenyl)benzoic acid

4-(3-(4-[2-(4-fluorophenyl)ethyl]-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl)-3-oxopropenyl)benzoic
acid

4-(3-(4-[2-(4-fluorophenyl)ethyl]-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl)-3-hydroxyprop-1-
ynyl)benzoic acid

20 4-(3-(4-[2-(4-fluorophenyl)-2-methylpropyl]-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-
hydroxypropenyl)benzoic acid

4-(3-(4-[2-(4-fluorophenyl)-2-methylpropyl]-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-
oxopropenyl)benzoic acid

4-(3-(4-[2-(4-fluorophenyl)-2-methylpropyl]-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)-3-

hydroxyprop-1-ynyl)benzoic acid

4-(3-{4-[2-(4-methylphenyl)ethyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

hydroxypropenyl)benzoic acid

4-(3-{4-[2-(4-methylphenyl)ethyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-oxopropenyl)benzoic acid

4-(3-{4-[2-(4-methylphenyl)ethyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-

10 ynyl)benzoic acid

4-(3-{4-[2-(4-methylphenyl)-2-methylpropyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

hydroxypropenyl)benzoic acid

4-(3-{4-[2-(4-methylphenyl)-2-methylpropyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

oxopropenyl)benzoic acid

4-(3-{4-[2-(4-methylphenyl)-2-methylpropyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

hydroxyprop-1-ynyl)benzoic acid

20 4-(3-{4-[2-(4-dimethylaminophenyl)ethyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

hydroxypropenyl)benzoic acid

4-(3-{4-[2-(4-dimethylaminophenyl)ethyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

oxopropenyl)benzoic acid

4-(3-{4-[2-(4-dimethylaminophenyl)ethyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

hydroxyprop-1-ynyl)benzoic acid

4-(3-{4-[2-(4-dimethylaminophenyl)-2-methylpropyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxypropenyl)benzoic acid

4-(3-{4-[2-(4-dimethylaminophenyl)-2-methylpropyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-oxopropenyl)benzoic acid

4-(3-{4-[2-(4-dimethylaminophenyl)-2-methylpropyl]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

10 hydroxyprop-1-ynyl)benzoic acid

4-{3-[4-(4-fluorobenzyloxy)-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}benzoic acid

4-{3-[4-(4-fluorobenzyloxy)-8,8-dimethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}benzoic acid

4-{3-[4-(4-fluorobenzyloxy)-5,5-dimethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxypropenyl}benzoic acid

4-(3-{4-[(4-fluorobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)benzamide

20 4-(3-{4-[(4-fluorobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)-N-hydroxybenzamide

N-ethyl-4-(3-{4-[(4-fluorobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)benzamide

4-{3-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-

ynyl)benzamide

4-{3-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-N-
hydroxybenzamide

N-ethyl-4-{3-[4-(4-fluorobenzyloxy)-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-
hydroxyprop-1-ynyl}benzamide

4-{3-[4-(4-fluorobenzylamino)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-

10 ynyl)benzamide

4-{3-[4-(4-fluorobenzylamino)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-N-
hydroxybenzamide

N-ethyl-4-{3-[4-(4-fluorobenzylamino)-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-
hydroxyprop-1-ynyl}benzamide

4-{3-[4-(4-fluorobenzylsulphanyl)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-
ynyl}benzamide

20 4-{3-[4-(4-fluorobenzylsulphanyl)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-N-
hydroxybenzamide

N-ethyl-4-{3-[4-(4-fluorobenzylsulphanyl)-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-
hydroxyprop-1-ynyl}benzamide

N-ethyl-4-{3-[4-[(4-fluorobenzyl)methylamino]-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

hydroxyprop-1-ynyl)-N-methylbenzamide

N-ethyl-4-{3-[4-(4-fluorobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

hydroxyprop-1-ynyl)-N-methylbenzamide

N-ethyl-4-{3-[4-(4-fluorobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

hydroxyprop-1-ynyl)-N-methylbenzamide

N-ethyl-4-{3-[4-(4-fluorobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

10 hydroxyprop-1-ynyl)-N-methylbenzamide

4-(3-{4-[(4-methylbenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

hydroxyprop-1-ynyl)benzamide

4-(3-{4-[(4-methylbenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

hydroxyprop-1-ynyl)-N-hydroxybenzamide

N-ethyl-4-(3-{4-[(4-methylbenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

hydroxyprop-1-ynyl)benzamide

20 4-{3-[4-(4-methylbenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl)benzamide

4-{3-[4-(4-methylbenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl)-N-hydroxybenzamide

N-ethyl-4-{3-[4-(4-methylbenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

hydroxyprop-1-ynyl}benzamide

4-{3-[4-(4-methylbenzylamino)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-
ynyl}benzamide

4-{3-[4-(4-methylbenzylamino)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-N-
hydroxybenzamide

N-ethyl-4-{3-[4-(4-methylbenzylamino)-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

10 hydroxyprop-1-ynyl}benzamide

4-{3-[4-(4-methylbenzylsulphanyl)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-
ynyl}benzamide

4-{3-[4-(4-methylbenzylsulphanyl)-5,5,8,8-tetramethyl-
5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-N-
hydroxybenzamide

N-ethyl-4-{3-[4-(4-methylbenzylsulphanyl)-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-
hydroxyprop-1-ynyl}benzamide

20 N-ethyl-4-{3-[4-[(4-methylbenzyl)methylamino]-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-
hydroxyprop-1-ynyl}-N-methylbenzamide

N-ethyl-4-{3-[4-(4-methylbenzyloxy)-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-
hydroxyprop-1-ynyl}-N-methylbenzamide

N-ethyl-4-{3-[4-(4-methylbenzylamino)-5,5,8,8-
tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

hydroxyprop-1-ynyl)-N-methylbenzamide

N-ethyl-4-(3-[4-(4-methylbenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

hydroxyprop-1-ynyl)-N-methylbenzamide

4-(3-{4-[(4-dimethylaminobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

hydroxyprop-1-ynyl)benzamide

4-(3-{4-[(4-dimethylaminobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

10 hydroxyprop-1-ynyl)-N-hydroxybenzamide

N-ethyl-4-(3-{4-[(4-dimethylaminobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-

hydroxyprop-1-ynyl)benzamide

4-{3-[4-(4-dimethylaminobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-

ynyl)benzamide

4-{3-[4-(4-dimethylaminobenzyloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl)-N-

hydroxybenzamide

20 N-ethyl-4-(3-[4-(4-dimethylaminobenzyloxy)-5,5,8,8-

tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

hydroxyprop-1-ynyl)benzamide

4-{3-[4-(4-dimethylaminobenzylamino)-5,5,8,8-

tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

hydroxyprop-1-ynyl)benzamide

4-{3-[4-(4-dimethylaminobenzylamino)-5,5,8,8-

tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

hydroxyprop-1-ynyl)-N-hydroxybenzamide

N-ethyl-4-{3-[4-(4-dimethylaminobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}benzamide

4-{3-[4-(4-dimethylaminobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}benzamide

4-{3-[4-(4-dimethylaminobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-

10 hydroxyprop-1-ynyl)-N-hydroxybenzamide

N-ethyl-4-{3-[4-(4-dimethylaminobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}benzamide

N-ethyl-4-(3-{4-[(4-dimethylaminobenzyl)methylamino]-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl}-3-hydroxyprop-1-ynyl)-N-methylbenzamide

N-ethyl-4-{3-[4-(4-dimethylaminobenzylloxy)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl}-N-methylbenzamide

20 N-ethyl-4-{3-[4-(4-dimethylaminobenzylamino)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl)-N-methylbenzamide or

N-ethyl-4-{3-[4-(4-dimethylaminobenzylsulphanyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl]-3-hydroxyprop-1-ynyl)-N-methylbenzamide.

7. Compounds according to claim 1 or 2, characterized in that they have the following characteristics:

- R_1 represents (b),
- Q represents an oxygen atom, and
- R_8 represents (i).

8. Compounds according to any one of claims 1 to 7, useful as medicinal products.

9. Use of a compound according to any one of claims 1 to 7 in the manufacture of a composition intended for treating:

- 10 - dermatological complaints associated with a keratinization disorder relating to cell differentiation and proliferation;
- ichthyosis, ichthyosiform conditions, Darier's disease, palmoplantar keratodermas, leukoplakia and leukoplakiform conditions, and cutaneous or mucous (buccal) lichen;
 - dermatological complaints with an inflammatory immunoallergic component, with or without cell proliferation disorder;
 - benign or malignant dermal or epidermal proliferations, of viral or non-viral origin;
 - proliferations which is induced by ultraviolet radiation;
 - precancerous skin lesions;
- 20 - immune dermatoses;
- immune bullous diseases;
 - collagen diseases;
 - dermatological conditions with an immunological component;
 - ophthalmological disorders;
 - stigmata of epidermal and/or dermal atrophy induced by local or systemic corticosteroids, or any other form of cutaneous atrophy;
 - skin complaints of viral origin;

- skin disorders caused by exposure to UV radiation, photoinduced or chronological ageing of the skin, or actinic pigmentations and keratoses;
- pathologies associated with chronological or actinic ageing of the skin;
- disorders of sebaceous function;
- cicatrization disorders or stretch marks; or
- pigmentation disorders.

10. Use according to claim 9, characterized in that the dermatological conditions associated with a keratinization disorder are common acne, comedones, polymorphs, acne rosacea, nodulocystic acne, acne conglobata, senile acne or
10 secondary acnes comprising, medication-related acne or occupational acne.

11. Use according to claim 9, characterized in that the dermatological complaints with an inflammatory immunoallergic component are cutaneous, mucous or ungual psoriasis, psoriatic rheumatism or cutaneous atopy comprising eczema, respiratory atopy or gingival hypertrophy.

12. Use according to claim 9, characterized in that the dermal or epidermal proliferations are common warts, flat warts, verruciform epidermodysplasia, oral or florid papillomatoses, or T lymphoma.

13. Use according to claim 9, characterized in that the proliferations which is induced by ultraviolet radiation are basocellular and spinocellular epithelioma.

20 14. Use according to claim 9, characterized in that the precancerous skin lesions are keratoacanthomas.

15. Use according to claim 9, characterized in that the immune dermatosis is lupus erythematosus.

16. Use according to claim 9, characterized in that the collagen disease is scleroderma.
17. Use according to claim 9, characterized in that the ophthalmological disorders are corneopathies.
18. Use according to claim 9, characterized in that the pathology associated with chronological or actinic ageing is xerosis.
19. Use according to claim 9, characterized in that the disorders of sebaceous function are the hyperseborrhoea of acne or simple seborrhoea.
20. Use according to claim 9, characterized in that the pigmentation disorders are hyperpigmentation, melasma, hypopigmentation and vitiligo.
21. Pharmaceutical composition, characterized in that it comprises, in a physiologically acceptable support, at least one of the compounds as defined in any one of claims 1 to 7.
22. Composition according to claim 21, characterized in that the concentration of compound(s) according to one of claims 1 to 7 is between 0.001% and 10% by weight relative to the total weight of the composition.
23. Composition according to claim 21, characterized in that the concentration of compound(s) according to one of claims 1 to 7 is between 0.01% and 1% by weight relative to the total weight of the composition.
- 20 24. 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 7.

25. Composition according to claim 24, characterized in that the concentration of compound(s) according to one of claims 1 to 7 is between 0.001% and 3% by weight relative to the total weight of the composition.
26. Cosmetic use of a composition as defined in claim 24 or 25, for preventing and/or treating the signs of ageing and/or dry skin.
27. Cosmetic use of a composition as defined in claim 24 or 25, for body or hair hygiene.

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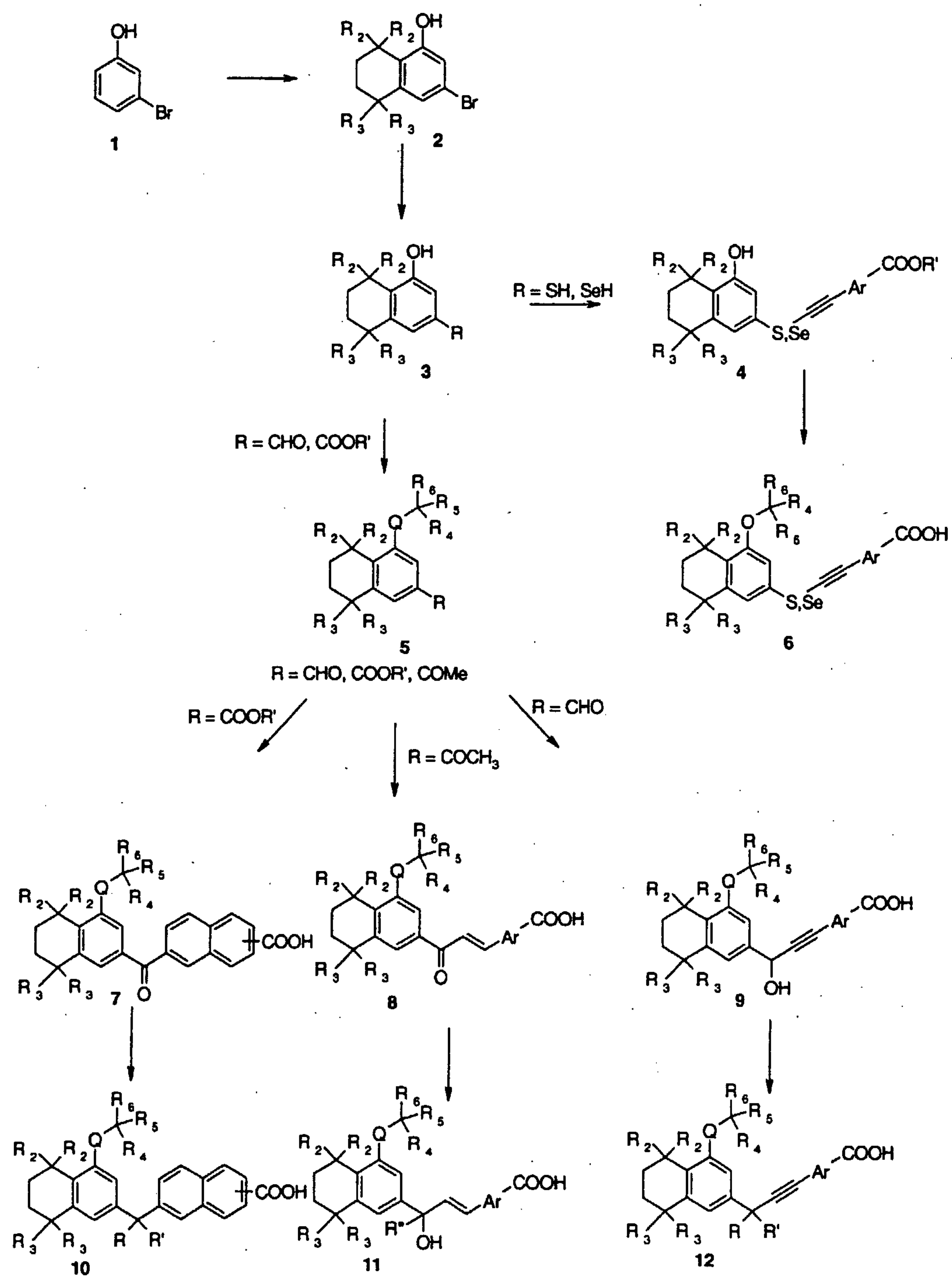
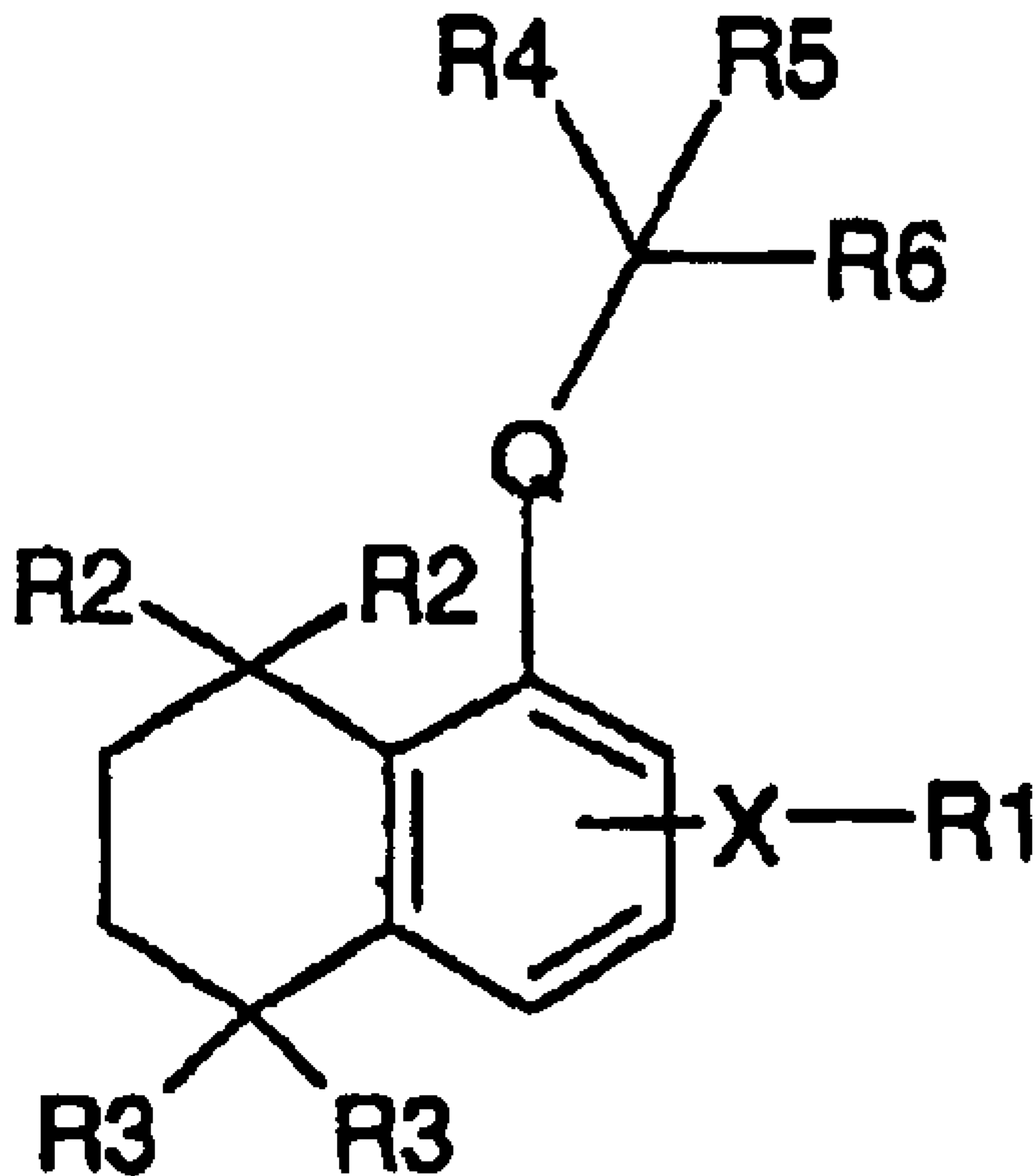


Figure 1



(I)