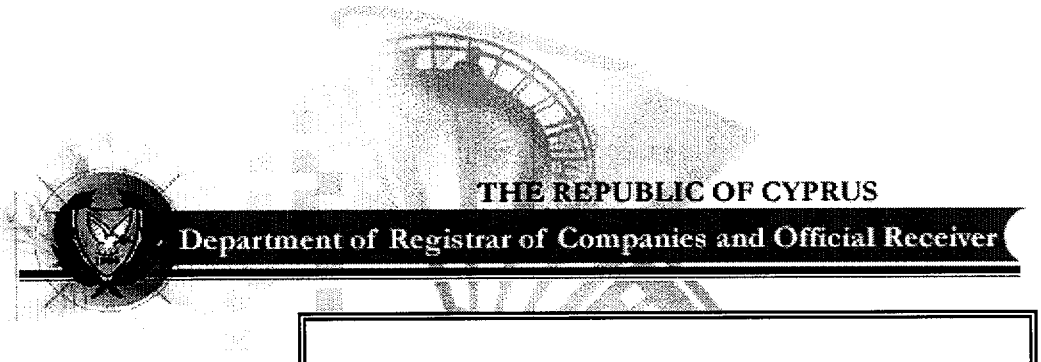

ΚΥΠΡΙΑΚΟ ΓΡΑΦΕΙΟ ΔΙΠΛΩΜΑΤΩΝ ΕΥΡΕΣΙΤΕΧΝΙΑΣ

THE PATENT OFFICE OF CYPRUS

ΑΡΙΘΜΟΣ ΔΗΜΟΣΙΕΥΣΗΣ **CY1726**
PUBLICATION NUMBER

ΑΡΙΘΜΟΣ ΔΗΜΟΣΙΕΥΣΗΣ
ΓΡΑΦΕΙΟΥ ΔΙΠΛΩΜΑΤΩΝ ΕΥΡΕΣΙΤΕΧΝΙΑΣ
ΗΝΩΜΕΝΟΥ ΒΑΣΙΛΕΙΟΥ
UK PATENT OFFICE
PUBLICATION NUMBER GB2185980

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3617637	26 May 1986	

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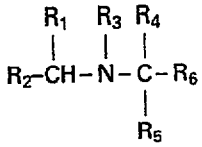
(72) & (74) continued overleaf

(56) Documents cited
Chemical Abstracts Vol 104(9) no 68547e
Chemical Abstracts Vol 98(7) no 53251n
Chemical Abstracts Vol 80(19) no 108368s

(58) continued overleaf

(54) Amine derivatives, processes for their production and their use

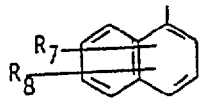
(57) Compounds of formula I



I

wherein

R_1 represents a group of formula



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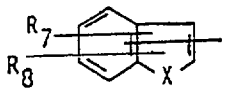

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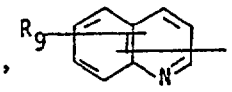
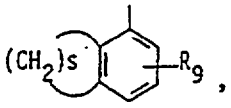


IIc ,



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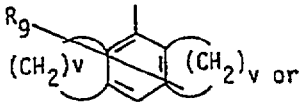
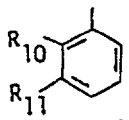


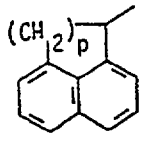
IIe or



IIf

and R_2 represents hydrogen or lower alkyl, or

R_1 and R_2 together with the carbon atom to which they are attached represent a group of formula IIg

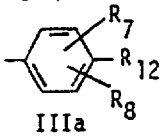


IIg ,

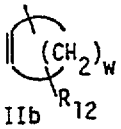
R_4 and R_5 represent independently hydrogen or lower alkyl,

R_3 represents hydrogen, alkyl, cycloalkyl or halogenalkyl and

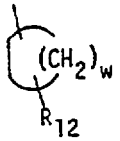
R_6 represents a group of formula



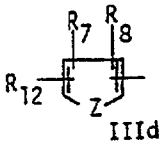
IIIa ,



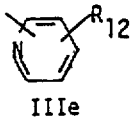
IIIb ,



IIIc



IIId ,



IIIe

or R_2 and R_3 together form a $-(CH_2)_u-$ group wherein u stands for a whole number from 1 to 8 and R_4, R_5 and R_6 have the meanings given above, which compounds are indicated for use as pharmaceuticals and agrochemicals.

GB 2 185 980 A

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Peter Nussbaumer

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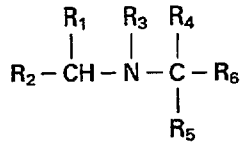
(58) Field of search
No search performed

SPECIFICATION

Amine derivatives, processes for their production and their use

The present invention concerns the use of amine derivatives as antimycotics and agro fungicides as well as certain amine derivatives as such, pharmaceutical and agrochemical compositions containing them and processes for their production.

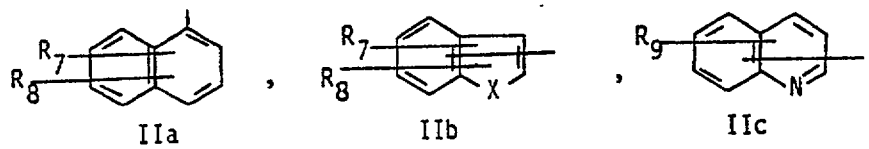
In particular the invention concerns the use of compounds of formula I as antimycotics and agro fungicides



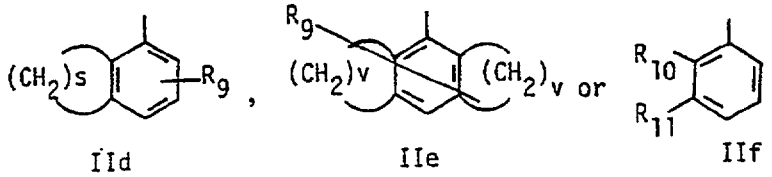
I

wherein

R_1 represents a group of formula



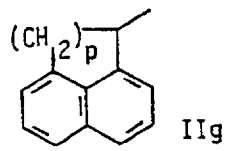
IIa , IIb , IIc



IId , IIe or IIf

and R_2 represents hydrogen or lower alkyl, or

R_1 and R_2 together with the carbon atom to which they are attached represent a group of formula IIg



IIg

whereby in formulae IIa to IIg

R_7 and R_8 represent independently hydrogen, halogen, trifluoromethyl, lower alkyl or lower alkoxy,

R_9 represents hydrogen, halogen, lower alkyl or lower alkoxy,

R_{10} and R_{11} represent independently hydrogen, halogen, trifluoromethyl, lower alkyl, lower alkoxy or lower alkylthio, whereby when one of the R_{10} and R_{11} represents hydrogen, halogen or lower alkoxy the other is other than hydrogen,

X represents oxygen, sulphur, imino, lower alkylimino, $-O-CH_2-$ or $-CH_2-$,

p stands for 1, 2 or 3,

s stands for 3, 4 or 5,

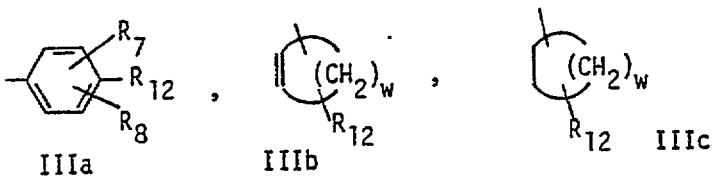
v stands for 3, 4, 5 or 6

whereby one or two of the $-CH_2-$ groups in formula IId may be replaced by oxygen or sulphur,

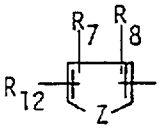
R_4 and R_5 represent independently hydrogen or lower alkyl,

R_3 represents hydrogen, alkyl, cycloalkyl or halogenalkyl and

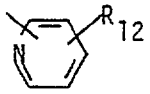
R_6 represents a group of formula



IIIa , IIIb , IIIc



IIId



IIIe

whereby in the formulae IIIa to IIIe

R_7 and R_8 have the meanings given above,

w stands for 2,3,4,5 or 6,

Z represents oxygen, sulphur or NR_3 wherein R_3 has the meaning given above and

R_{12} represents alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, lower alkoxy, lower alkoxycarbonyl, lower alkylthio, phenyl, phenalkyl, trialkylsilyl, dialkylphenylsilyl or halogen, whereby alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, phenyl or phenalkyl may be substituted by phenyl, lower alkoxy, lower alkylthio, phenalkoxy, lower alkoxyphenyl, lower alkylphenyl, halogenphenyl, halogen or an optionally substituted heterocycle; optionally interrupted by carbonyl; or

R_1 represents a group of formula IIa to IIf as defined above,

R_2 and R_3 together form a $-(CH_2)-_u$ group wherein u stands for a whole number from 1 to 8 and R_4, R_5 and R_6 have the meanings given above, in free form or in pharmaceutically acceptable acid addition salt form.

Each lower alkyl moiety preferably contains 1 to 4, especially 2 or 1 carbon atoms. Alkyl moieties contain in particular 1 to 12, especially 2 to 8, more particularly 2 to 6 and preferably 2 to 4 carbon atoms. Each alkenyl or alkynyl contains in particular 3 to 6, especially 3 or 4 carbon atoms e.g. allyl, propenyl or propynyl. Such groups as mentioned above can be straight chained or branched. A preferred cycloalkylidene is cyclohexylidene. Cycloalkyl is to be understood as embracing polycycles such as bornyl or adamantyl but is preferably cyclohexyl, cyclopentyl or cyclopropyl. Conveniently R_7, R_8 and R_9 are independently hydrogen or halogen. X is conveniently sulphur, imino or lower alkylimino.

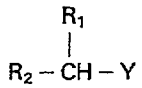
Examples of heterocycles are saturated or unsaturated 5 or 6 membered rings containing one or more heteroatoms selected from nitrogen, oxygen or sulphur-e.g. thiophene. These can contain one or more substituents such as defined for R_7.

R_1 is preferably a group of formula IIc or IId in particular IIa or IIb. R_2 is preferably hydrogen and R_3 conveniently lower alkyl. R_6 is preferably IIIa

Values for p, s, u, v and w are conveniently chosen such that seven- or preferably six- or five-membered rings are formed. Halogen stands for fluorine, chlorine or bromine.

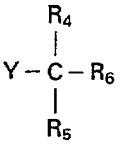
The compounds of the present invention may be prepared by

a) reacting a compound of formula IV



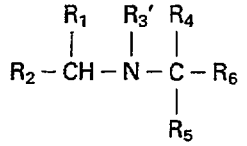
IV

with a compound of formula V



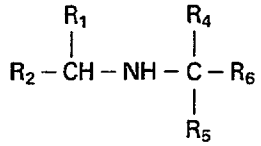
V

b) for preparing a compound of formula Ia



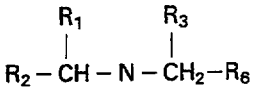
Ia

introducing a R'_3 group into a compound of formula Ib



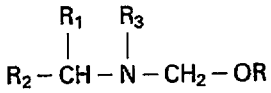
Ib

c)(i) for preparing a compound of formula Ic



Ic

reacting a compound of formula VI



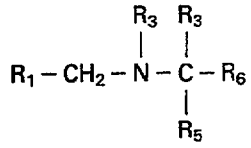
VI

with a compound of formula VII

$R_6 - Me$

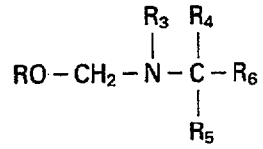
VII or

(ii) for preparing a compound of formula Id



Id

reacting a compound of formula VIa



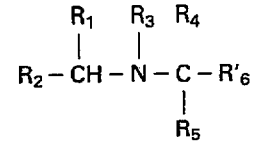
VIa

with a compound of formula VIIa

$R_1 - Me$

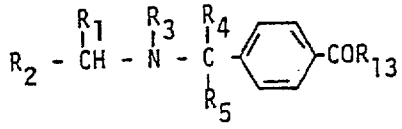
VIIa

d) for preparing a compound of formula Ie



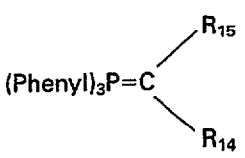
Ie

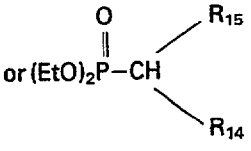
reacting a compound of formula VIb



VIb

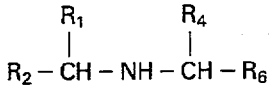
with a Wittig reagent of formula IVb or IVc





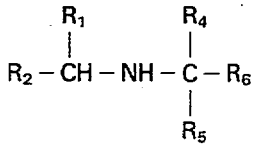
or

e) for preparing a compound of formula If and Ig



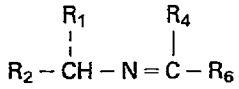
If

and



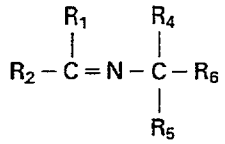
Ig

reducing a Schiff's base of formula Ih, Ii



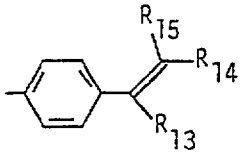
Ih

or



Ii

whereby in the above formulae R, R_2, R_3, R_4, R_5 and R_6 are as defined for formula I, one Y represents a leaving group and the other $-NH-R_3$, R'_3 represents cycloalkyl, halogenalkyl or lower alkyl, R represents lower alkyl, Me represents a metal equivalent, R'_6 represents a group of formula IIIf



IIIf

wherein R_{13}, R_{14} and R_{15} represent independently hydrogen, lower alkyl, lower alkoxy, phenyl, phenalkoxy, lower alkoxyphenyl, lower alkylphenyl, halogenphenyl, halogen or an optionally substituted heterocycle, and recovering the compound obtained in free form or acid addition salt form.

Process a) is carried out in a manner conventional for the preparation of tertiary amines by condensation. The process can be carried out in an inert solvent such as a lower alkanol e.g. ethanol, optionally mixed with water, an aromatic hydrocarbon e.g. benzene or toluene, a cyclic ether e.g. dioxane, or a carboxylic acid dialkylamide e.g. dimethylformamide. The reaction temperature conveniently lies between room temperature and the boiling point of the reaction mixture, preferably room temperature. The process is conveniently carried out in the presence of an acid binding agent e.g. an alkali metal carbonate such as sodium carbonate. The leaving group is conveniently iodine or preferably bromine or chlorine or an organic sulphonyloxy with 1 to 10 carbon atoms e.g. an alkylsulphonyloxy, preferably with 1 to 4 carbom atoms such as mesyloxy or an alkylphenylsulphonyloxy, preferably with 7 to 10 carbon atoms such as tosyloxy.

Process b) is carried out in a manner conventional for the alkylation of secondary amines e.g. by direct alkylation with an alkylating agent e.g. with a halogenide or a sulphate or by reductive alkylation, especially by reaction with a suitable aldehyde and subsequent or simultaneous reduction. Reductive alkylation can conveniently be carried out by reacting a compound of formula Ib in an inert solvent e.g. in a lower alkanol such as methanol, with a corresponding aldehyde. Reduction can be carried out for example with a complex metal hydride such as $NaBH_4$ or $NaCNBH_3$ as reducing agent. It can also be carried out using aqueous NaH_2PO_3-solution (H. Loibner et. al. Tetrahedron Letters *1984*/2535) or formic acid which can serve simultaneously as reducing agent and reaction medium.

Process c) can be carried out in a manner conventional for reactions involving organometal compounds. It is preferably carried out in an inert solvent e.g. in an ether between −20°C and +50°C.

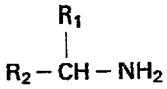
Process d) can be carried out in a manner conventional for Wittig reactions preferably in an aprotic solvent such as a cyclic ether e.g. tetrahydrofuran or an aromatic hydrocarbon e.g. toluene between 20°C and the boiling point of the reaction mixture.

Reduction according to process e) can be carried out for example with a complex hydride such as $NaBH_4$. It is preferably carried out in an inert solvent e.g. in a lower alkanol such as methanol at room temperature.

The final products can be isolated and purified in conventional manner. Free bases of the compounds of formula I can be converted into salt forms and vice versa. Suitable acid addition salts are the hydrochloride, hydrogen fumarate or naphthalin-1,5-disulphonate.

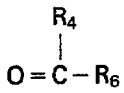
The starting materials of formulae VI and VIa can be prepared by reaction of the corresponding amine of formula IV with formaldehyde and a lower alcohol of formula ROH.

The compounds of formula Ih can be prepared by reaction of a compound of formula IVd



IVd

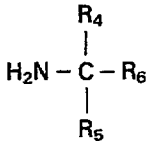
with a compound of formula VIII



VIII

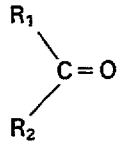
wherein R_1, R_2, R_4 and R_6 are as defined above.

Starting materials of formula Ii can be prepared by reacting a compound of formula IVe



IVe

with a compound of formula IX

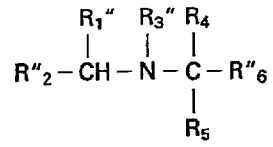


IX

The remaining intermediates are either known or can be prepared analogously to known processes or e.g. as described in the examples.

Some of compounds of formula I are new and also form part of the invention.

These compounds of formula Ij

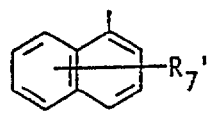


Ij

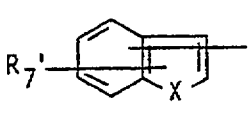
wherein R_4 and R_5 are as defined above and R''_1, R''_2, R''_3, and R''_6 have the same meanings as R_1, R_2, R_3 and R_6 respectively with the proviso that

a) when R''_1 stands for naphthyl, R''_2, R''_3, R_4 and R_5 stand for hydrogen and R''_6 stands for a group IIIa wherein R_8 is hydrogen then R_{12} and R_7 are not both halogen and R_{12} is not halogen or methyl when R_7 is hydrogen.

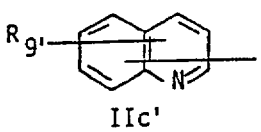
b) when R''_1 stands for a group



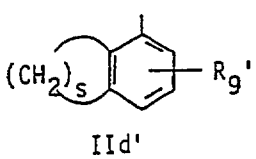
IIa'



IIb'

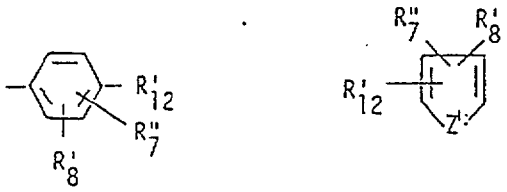


IIc'



IId'

wherein R'_7 and R'_9 represent independently hydrogen, lower alkyl, lower alkoxy or halogen and s stands for 3, 4 or 5, R''_2 represents hydrogen or lower alkyl, X represents oxygen, sulphur or nitrogen and R_4 and R_5 represent hydrogen then R''_6 does not stand for a group



wherein Z' represents oxygen or sulphur, R''_7 represents hydrogen, R'_8 represents hydrogen, halogen or lower alkyl and R'_{12} represents hydrogen, alkyl, cycloalkyl, halogenalkyl or halogen;
in free form or in acid addition salt form.

A preferred group of compounds for use as antimycotics and agro fungicides are those of formula Ij as defined above.

A further preferred group of compounds of formula I are those wherein

a) R_1 represents a group of formula IIa to IIf and R_2 represents hydrogen or lower alkyl or R_1 and R_2 together represent a group of formula IIg whereby in the formulae IIa to IIg R_7 and R_8 represent independently hydrogen, halogen, trifluoromethyl, lower alkyl or lower alkoxy and R_9 represents hydrogen, halogen, lower alkyl or lower alkoxy, R_{10} and R_{11} represent independently hydrogen, lower alkyl, halogen, trifluoromethyl, lower alkoxy or lower alkylthio, whereby when one of R_{10} or R_{11} represents hydrogen, halogen or lower alkoxy the other is not hydrogen, X represents oxygen, sulphur, imino, lower alkylimino or $-CH_2-$, p stands for 1, 2, or 3, u stands for 3, 4 or 5 and v stands for 3, 4, 5 or 6 and in the group of formula IId one or two of the CH_2 groups may be replaced by oxygen or sulphur, R_4 and R_5 represent independently hydrogen or lower alkyl, R_3 represents hydrogen, cycloalkyl, halogenalkyl or alkyl and R_6 represents a group of formula IIIa to IIIe, whereby R_7 and R_8 are as herein-defined, w stands for 2, 3, 4, 5 or 6, Z stands for oxygen, sulphur or $N-R_3$ wherein R_3 is as herein defined and R_{12} represents alkyl, alkenyl, alkynyl, cycloalkylalkyl, lower alkoxy, lower alkylthio, phenyl, phenalkyl, trialkylsilyl, dialkylphenylsilyl or halogen, whereby alkyl, alkenyl, alkynyl, cycloalkylalkyl, phenyl and phenalkyl can be substituted by lower alkoxy; optionally interrupted by carbonyl or

b) R_1 represents a group of formula IIa to IIf as defined under a), R_2 and R_3 represent together $-tCH_2)_u-$ whereby u stands for a whole number from 1 to 8 and R_4, R_5 and R_6 are as herein defined.

A further preferred group of compounds of formula I are those wherein

a) R_1 represents a group of formula IIA or IIb

b) R_2 represents hydrogen or lower alkyl in particular hydrogen,

c) R_3 represents hydrogen or alkyl in particular lower alkyl and

d) R_6 represents a group of formula IIIa

whereby

R_7 and R_8 represent independently, hydrogen, halogen or lower alkoxy in particular hydrogen, X represents $-O-CH_2-$, oxygen or sulphur in particular sulphur, R_4 and R_5 represent independently hydrogen or lower alkyl in particular hydrogen and R_{12} represents alkyl, alkenyl, alkynyl, cycloalkylalkyl, lower alkoxy, lower alkoxycarbonyl, lower alkylthio, phenyl, phenalkyl, trialkylsilyl, dialkylphenylsilyl or halogen whereby alkyl, alkenyl, alkynyl, cycloalkylalkyl, phenyl or phenylalkyl can be substituted by phenyl, lower alkoxy, lower alkylthio, phenalkoxy, lower alkoxyphenyl, lower alkylphenyl, halogenphenyl, halogen or an optionally substituted heterocycle; optionally interrupted by carbonyl.

A further preferred group of compounds of formula I are those wherein R_1 represents a group of formula IIa, IIb, IIc, IId or IIe and R_2 represent hydrogen or lower alkyl or R_1 and R_2 together represent a group of formula IIg whereby R_7 and R_8 represent independently hydrogen, halogen, trifluoromethyl, lower alkyl, lower alkoxy and R_9 represents hydrogen, halogen, lower alkyl or lower alkoxy, R_{10} and R_{11} represent independently hydrogen, lower alkyl, halogen, trifluoromethyl, lower alkoxy or lower alkylthio whereby when one of R_{10} or R_{11} is hydrogen, halogen or lower alkoxy the other is not hydrogen, X represents oxygen, sulphur, imino, lower alkylthio, $-O-CH_2-$ or $-CH_2-$, p stands for 1, 2 or 3, s stands for 3, 4 or 6 and v stands for 3, 4, 5 or 6 and one or two CH_2 groups in formula IId may be replaced by oxygen or sulphur, R_4 and R_5 represent independently hydrogen or lower alkyl, R_3 represents hydrogen, cycloalkyl, halogenalkyl or alkyl and R_6 represents a group of formula IIIa, IIIb, IIIc, IIId or IIIe, whereby R_7 and R_8 are as herein defined, w stands for 2, 3, 4, 5 or 6, Z stands for oxygen, sulphur or N-R_3 wherein R_3 is as defined above and R_{12} is as defined under formula I or R_1 represents a group of formula IIa to IIe, R_2 and R_3 together represent $-(CH_2)_u-$ wherein u is a whole number from 1 to 8 and R_4, R_5 and R_6 are as defined above.

The compounds of formula I possess advantageous chemotherapeutical properties and in particular exhibit on local or oral application an antimycotic activity and are thus indicated for use as pharmaceuticals in particular as antimycotics. This activity can be established on various families and species of mycetes e.g. Trichophyton spp., Aspergillus spp., Microsporum spp., Sporothrix schenckii and Candida spp. both in vitro dilution tests at concentrations of from 0.003 to 50 ug/ml and in vivo in the experimental skin mycosis test on

guinea pigs and in intravaginal-intrauterine or disseminated infections. In the skin mycosis model the test substance is taken up in polyethyleneglycol and rubbed daily for 7 days on the infected skin surface. The antimycotic activity could be observed at concentrations of 0.1 to 2%. The oral activity can be demonstrated in vivo in the guinea pig trichophytosis model in a dosage range of ca. 2 to 70 mg/kg of body weight.

An indicated daily dosage is for example in the range of from 70 to 2000 mg conveniently given in divided doses two to four times daily or in controlled release form; dosage forms suitable for e.g. oral administration comprise from 17.5 to 1000 mg of active ingredient.

The compounds of the invention may be employed in the free base form or in the form of pharmaceutically acceptable acid addition salts. In general these forms exhibit the same order of activity as the free base forms. Examples of such acid addition salts include the hydrochloride, hydrogen fumarate and naphthaline-1,5-disulfonate.

The compounds may be admixed with conventional pharmaceutically acceptable diluents and carriers, and, optionally other excipients and administered orally, topically, i.v. or parenterally in such forms as tablets, capsules, creams, tinctures or injectable preparations.

Such compositions also form part of the invention.

The invention also concerns a method of combatting infections and diseases caused by mycetes comprising administering to a subject in need of such treatment an effective amount of a compound of formula I in free base form or in the form of a pharmaceutically acceptable salt thereof and such compounds for use as pharmaceuticals, in particular as anti-mycotic agents.

The compounds of the invention in free form or in agriculturally acceptable salt or metal complex form are also suitable for combatting phytopathogenic fungi. This fungicidal activity can be demonstrated i.a. in *in vivo* tests against Uromyces appendiculatus (bean rust) on runner beans as well as against other rust fungi (e.g. Hemileia, Puccinia), on coffee, wheat, flax and ornamentals (e.g. pelargonium, snapdragon); and against Erysiphe cichoracearum on cucumber as well as against other powdery mildews (e.g. E. Graminis f. sp. tritici. E. gram. f. sp. hordei, Podosphaera leucotricha, Uncinula recator) on wheat, barley, apple and vines.

The following examples illustrate the invention. All temperatures are given in degrees centigrade.

EXAMPLE 1

N-(5,7-difluoro-1-naphthylmethyl)-N-methyl-4-tert.butylbenzylamine (process a))

To a mixture of 0.3 g of N-methyl-4-tert.butylbenzylamine, 0.25 g of potassium carbonate and 5 ml of abs. dimethylformamide (DMF) are added dropwise 0.4g of 5,7-difluoro-1-bromomethylnaphthalene and the mixture stirred overnight at RT. The solvent is removed under vacuum and the residue partitioned between ether and water. The organic phase is dried and evaporated. The pure product is obtained as an oil following chromatography on silica gel (eluant : hexane/ethylacetate=95/5).

EXAMPLE 2

N-(4-tert.butyl-1-cyclohexenylmethyl)-1-naphthylmethylamine (process e))

2g of 4-tert.Butyl-1-cyclohexenecarbaldehyde, 1.9 g of 1-naphthylmethylamine and 15 ml of toluene are warmed at 70° for 4 hours with a 4 Å molecular sieve. The mixture is filtered, washed through with ether and the filtrate evaporated. The residue is dissolved in 30 ml of absolute methanol and reacted within 1/2 hour with two portions each of 0.5 g of sodium borohydride. The mixture is stirred for 2 hours at room temperature, evaporated and the residue partitioned between water and dichloromethane. The organic phase is dissolved in a little methanol and reacted with an excess of methanolic hydrochloric acid and evaporated to dryness. The residue is recrystallized from isopropanol/ether. By treatment with 1N caustic soda and extraction with ether the title compound is obtained as pure base as an oil, m.p. (hydrochloride): 153-155°.

EXAMPLE 3

N-(4-tert.butyl-1-cyclohexenylmethyl)-N-(1-naphthylmethyl)methylamine (process b))

0.8 g of N-(4-tert.butyl-1-cyclohexenylmethyl)-1-naphthylmethylamine are reacted with 13 ml of 1N NaH_2PO_3-solution and brought into solution by the addition of 15 ml of dioxane. Following addition of 1.1 ml 37% formaline solution the mixture is warmed to 60° for 1/2 hour, made alkaline with caustic soda and extracted with ether. Following drying and evaporation of the organic phase the pure product is obtained as an oil.

EXAMPLE 4

N-Methyl-N-(1-naphthylmethyl)-4-(2-phenyl-2-propyl)benzylamine (process c))

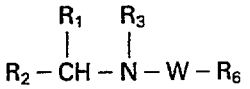
A Grignard reagent is prepared from 3 g of 2-(4-bromophenyl)-2-phenylpropane and 265 mg of magnesium in 25 ml of ether. 2.5 g of N-ethoxymethyl-N-methyl-1-naphthylmethylamine in 5 ml of ether are added dropwise at room temperature with vigorous stirring and the mixture then refluxed for 4 hours. Following addition of sat. aq. ammonium chloride and stirring for 1/2 hour the aqueous phase is extracted with ether. The combined organic phases are dried and the solvent distilled off. By column chromatography on silica gel (eluant: toluene/ethyl acetate=95/5) the pure product is obtained as an oil.

EXAMPLE 5

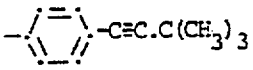
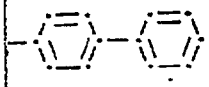
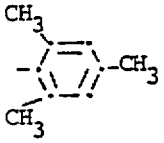
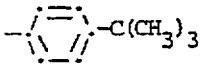
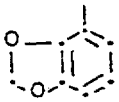
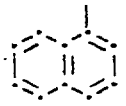
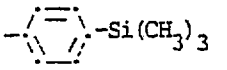
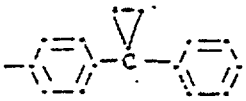
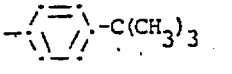
N-Methyl-N-(1-naphthylmethyl)-4-[1-(4-methoxyphenyl)]-ethenyl]benzylamine process d)

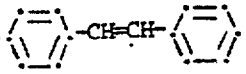
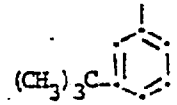
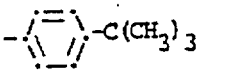
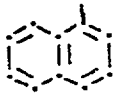
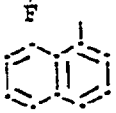
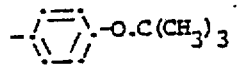
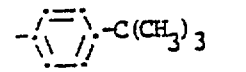
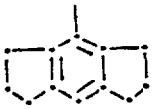
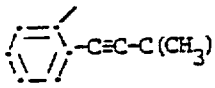
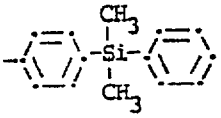
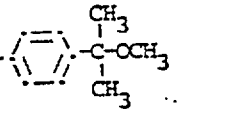
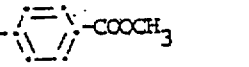
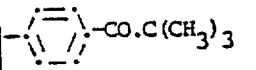
1.37 g of Methyltriphenylphosphonium bromide/sodium amide are stirred for 15 minutes at room temperature in 5 ml of toluene. 1 g of N-methyl-N-(1-naphthylmethyl)-4-(4-methoxybenzoyl)benzylamine are added and the mixture refluxed for 1 1/2 hours. Following concentration the residue is taken up in ether filtered off and the filtrate concentrated and chromatographed over silica gel with toluene. The title compound is obtained as an oil.

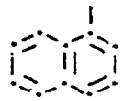
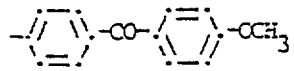
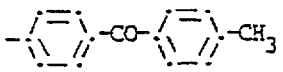
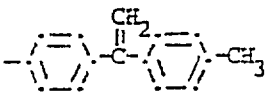
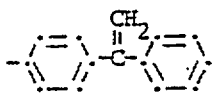
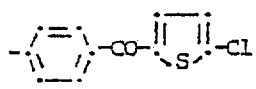
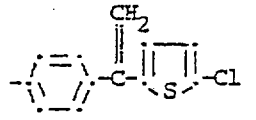
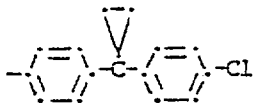
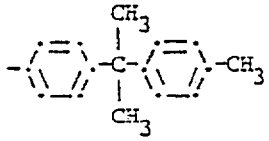
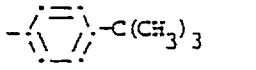
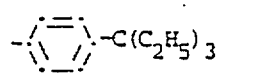
Analogously to Examples 1 to 5 or as otherwise hereinbefore described, the following compounds of formula Ik are obtained

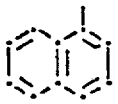
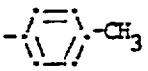
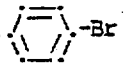
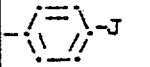
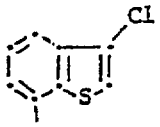
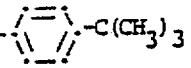
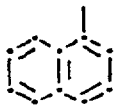
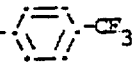
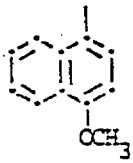
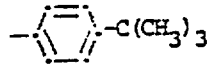
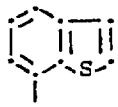
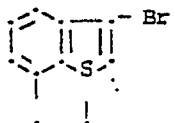
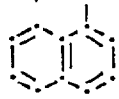
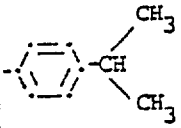


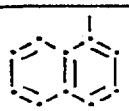
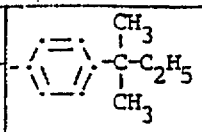
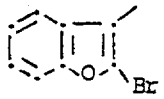
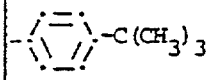
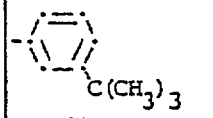
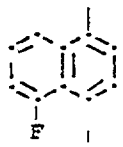
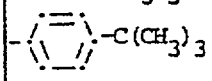
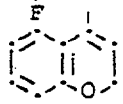
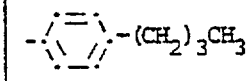
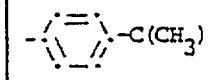
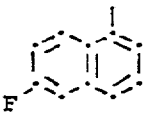
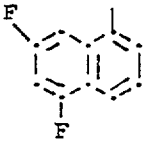
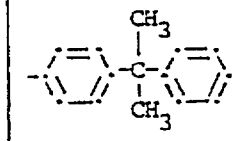
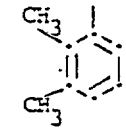
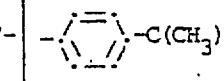
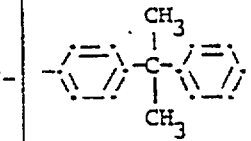
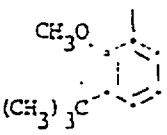
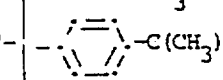
Ik

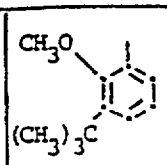
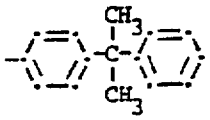
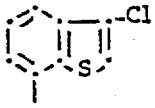
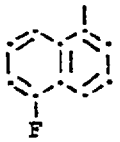
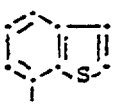
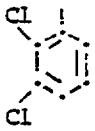
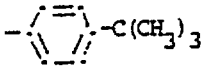
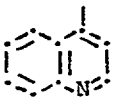
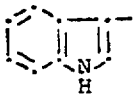
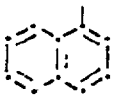
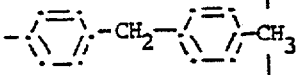
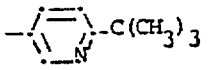
Ex.	R_1	R_2	R_3	W	R_6	
6		H	CH_3	$-CH_2-$		Oil
7	- " -	H	CH_3	-"-		Oil
8	- " -	H	CH_3	-"-		Oil
9	- " -			-"-		Oil
10		H	CH_3	-"-	- " -	Oil
11		H	CH_3	-"-		Oil
12	- " -	H	CH_3	-"-		Oil
13			H	-"-		m.p. 68-72°
14	- " -		CH_3	-"-	- " -	Oil
15		H	CH_3		- " -	Oil

Ex :	R_1	R_2	R_3	W	R_6	
16		H	CH_3	$-CH_2-$		m.p. 90-95°
17		H	CH_3	-"-		Oil
18		H		-"-	- " -	Oil
19		H	CH_3	-"-	- " -	Oil
20		H	CH_3	-"-		m.p. 88.5°
21	- " -	H	$-CH_2CH_2F$	-"-		Oil
22		H	CH_3	-"-	- " -	Oil
23		H	CH_3	-"-		Oil
24	- " -	H	CH_3	-"-		Oil
25	- " -	H	CH_3	-"-		Oil
26	- " -	H	CH_3	-"-		Oil
27	- " -	H	CH_3	-"-		Oil

28		H	CH_3	$-CH_2-$		Oil
29	- " -	H	CH_3	-"-		Oil
30	- " -	H	CH_3	-"-		Oil
31	- " -	H	CH_3	-"-		Oil
32	- " -	H	CH_3	-"-		Oil
33	- " -	H	CH_3	-"-		Oil
34	- " -	H	CH_3	-"-		Oil
35	- " -	H	CH_3	-"-		Oil
36	- " -	H	CH_3	-"-		Oil m.p.(HCl) 205-207°
37	- " -	H	CH_3	-"-		Oil

38		H	CH_3	$-CH_2-$		Oil
39	- " -	H	CH_3	- " -		Oil
40	- " -	H	CH_3	- " -		Oil
41		H	CH_3	- " -		Oil
42		H	C_2H_5	- " -	- " -	Oil m.p.(HCl) 182-184°
43	- " -	H	CH_3	- " -		Oil
44		H	CH_3	- " -		Oil
45		H	CH_3	- " -	- " -	Oil
46		H	CH_3	- " -	- " -	Oil
47		H	CH_3	- " -	- " -	Oil
48		H	H	- " -		Oil
49	- " -	H	CH_3	- " -	- " -	Oil

50		H	CH_3	$-CH_2-$		Oil, m.p.(HCl): 169-171°
51		H	CH_3	-"-		Oil
52		H	CH_3	-"-		Oil
53		H	CH_3	-"-		Oil, m.p.(HCl): 210-214°
54		H	CH_3	- " -	- " -	Oil
55		H	H	-"-		Oil
56	- " -	H	CH_3	-"-	- " -	Oil
57	- " -	H	H	-"-		Oil
58		H	CH_3	-"-	- " -	Oil
59		H	CH_3	-"-		Oil
60		H	CH_3	-"-		Oil
61	- " -	H	CH_3	-"-		Oil
62		H	CH_3	-"-		Oil

63		H	CH_3	$-CH_2-$		Oil
64		H	CH_3	-"-	- " -	Oil
65		H	CH_3	-"-	- " -	Oil, m.p.(HCl): 186-189°
66		H	CH_3	-"-	- " -	Oil
67		H	CH_3	-"-	- " -	Oil
68	- " -	H	CH_3	-"-		Oil
69		H	CH_3	-"-	- " -	Oil
70		H	CH_3	-"-	- " -	Oil
71		H	CH_3	- " -		Oil
72	- " -	H	CH_3	-"-		Oil

The required starting materials can be prepared e.g. as follows:

A) 4-(3,3-Dimethyl-1-butynyl)benzylbromide (for Example 6)

3.35 g of 4-(3,3-Dimethyl-1-butynyl)toluene, 3.47 g of N-bromosuccinimide and 100 mg of dibenzoylperoxide in 50 ml of carbon tetrachloride are refluxed for 8 hours. The mixture is filtered and the solvent removed under vacuum. The pure product is obtained as an oil following chromatography over silica gel using hexane as an eluent.

Analogously to A) the following compounds can be obtained as oils:

B) 4-Bromomethyl-4'-methylbenzophenone (for example 29).

C) 2-(4-Bromomethylphenyl)-2-(4-toluene) propane (for Example 35).

D) 3-tert.Butylbenzylbromide (for Examples 17 and 52).

E) 2-(3,3-dimethyl-1-butynyl)benzylbromide (for Example 23).

F) 4-(2-Methoxy-2-propyl)benzylbromide (for Example 25).

G) 3-(Bromomethyl)-6-tert.butylpyridine (for Example 72).

H) N-Methyl-4-phenylbenzylamine (for Example 7)

10 g of 4-Biphenylcarbaldehyde and 40 ml of 33% ethanolic methylamine are stirred overnight at room temperature with a 4 Å molecular sieve. The mixture is filtered and concentrated under vacuum. The residue is treated in 60 ml of ethanol with 2 g of sodium borohydride and stirred for 3 hours. The solvent is removed under vacuum, the residue partitioned between the ether and water and the organic phase dried and concentrated. The pure base is obtained as an oil following chromatography on silica gel with dichloromethane/ethanol=9/1 as eluant.

Analogously to H) the following compounds can be obtained as oils:

I) N-(2,3-Methylenedioxybenzyl)methylamine (for Example 10).

J) 1-(Naphthylmethyl)cyclopropyl-amine (for Example 18).

K) N-methyl-2,3-dimethylbenzylamine (for Example 60 and 61).

L) N-Ethoxymethyl-N-methyl-1-naphthylmethylamine (for Examples 4, 37, 50 and 71).

21 g of N-methyl-1-naphthylmethylamine and 9 g of abs. ethanol are treated under ice-cooling in portions with 3.6 g of paraformaldehyde and the mixture stirred for 1 hour at room temperature. The reaction mixture is treated with dichloromethane, filtered and concentrated. The pure product is obtained as a pale yellow oil following vacuum distillation (1.3 mbar/135-138°).

M) N-(5,7-Difluoro-1-naphthylmethyl)methylamine (for Examples 1 and 59)

a) *4-(2,4-Difluorophenyl)-4-one-butyric acid*

11.4 g of 1,3-Difluorobenzene and 28 g of aluminiumchloride are taken up in 75 ml of dichloromethane and treated at 38° with 10 g of succinic anhydride in small portions and then refluxed for 6 hours. The mixture is poured onto ice/hydrochloric acid, treated with dichloromethane and stirred for 1/2 hour. The phases are separated, the aqueous phase extracted with dichloromethane and the combined organic phases shaken with dilute caustic soda. The aqueous alkaline solution is washed with ether and made acidic with hydrochloric acid. The precipitate is filtered off under suction, washed with water and dried (m.p. 113-115°).

b) *4-(2,4-Difluorophenyl)butyric acid*

50 g of Zinc, 5 g of mercury (II) chloride, 2.5 ml of conc. hydrochloric acid and 75 ml of water are thoroughly stirred for 10 minutes. The liquid is decanted off and the amalgamated zinc treated with 30ml of water, 75ml of conc. hydrochloric acid, 3 ml of acetic acid and 16 g of 4-(2,4-difluorophenyl)-4-one-butyric acid. The mixture is refluxed for 8 hours whereby 10 ml of conc. hydrochloric acid are added every 2 hours. The organic phase is removed, the solution decanted from the zinc, extracted with toluene and the combined organic phases washed with water, dried and concentrated. The residue is dissolved in excess 1N caustic soda, treated with 200 mg of palladium on active charcoal and hydrogenated for 36 hours at room temperature and normal pressure. The mixture is filtered, made acidic and extracted with ether. The crystalline crude product can be purified by ball-tube distillation at 0.13 mbar/120°, m.p. 45-47°.

c) *5,7-Difluoro-1-tetralone*

120 g of Polyphosphoric acid and 12 g of phosphorous pentoxide are stirred to homogeneity at 60°. 43 g of 4-(2,4-Difluorophenyl)butyric acid are added and the mixture stirred for 11/2 hours at 80°, poured onto ice-water and extracted with ether. The combined organic phases are washed with sodium carbonate solution and sodium chloride solution, dried, stirred with a little active charcoal and evaporated. The crude product can be purified by silica gel chromatography (eluant: hexane/ethylacetate=4/1) or vacuum sublimation at 0.65 mbar/100°, m.p. 89-91°.

d) *5,7-Difluoro-methyl-1-tetralol*

2 g of 5,7-Difluoro-tetralone are dissolved in 20 ml of ether and added to a Grignard reagent prepared from 0.34 g of magnesium and 2 g of methyliodide in ether. After refluxing for 21/2 hours the mixture is poured onto ice/sat. ammonium chloride and stirred 1/2 hour. The aqueous phase is extracted with ether and purified to a colourless oil by column chromatography over silica gel (eluant: toluene/ethylacetate=9/1).

e) *5,7-Difluoro-1-methylnaphthalene*

2.5 g of 5,7-Difluoro-methyl-tetralol, 3.6 g of triphenylmethanol and 2.6 g of trifluoroacetic acid anhydride are refluxed for 5 hours in 16 ml of trifluoroacetic acid. The mixture is poured onto ice-water and extracted with dichloromethane. The organic phase is washed neutral with sodium bicarbonate solution, dried and concentrated. The oily crude product can be purified by chromatography over silica gel (eluant:hexane).

f) *5,7-Difluoro-1-bromomethylnaphthaline*

1.35 g of 5,7-Difluoro-1-methylnaphthaline in 10 ml of carbon tetrachloride are refluxed for 41/2 hours with 1.4 g of N-bromosuccinimide and 50 mg of dibenzoylperoxide. The cooled mixture is fiiltered and the solvent removed under vacuum. The purity of the crystalline crude product is sufficient for further reaction, m.p. 74-76.5°.

g) *N-(5,7-Difluoro-1-naphthylmethyl)methylamine*

2.3 g of 5,7-Difluoro-1-bromomethylnaphthaline are dissolved in 10 ml of ethanol and slowly added dropwise with cooling to 15 ml of a 35% ethanolic methylamino solution. After 1 hour cooling is discontinued and the mixture stirred overnight at room temperature. The solvent is removed under vacuum, the residue taken up in 2N hydrochlorid acid, the aqueous phase washed with ether and made alkaline with solid potassium carbonate. By extraction with ether the title compound is obtained as a colourless oil, m.p. (HCl): 224-228°.

N) 5,8-Difluoro-1-bromomethylnaphthaline (for Example 19)

a) *5,8-Difluoro-4-methyl-1-tetralol*

5 g of 5,8-Difluoro-4-methyl-1-tetralone are dissolved in 75 ml of methanol and treated in small portions with 1 g of sodium borohydride. After 2 hours at room temperature the mixture is concentrated and the residue partitioned between water and ether. The aqueous phase is extracted with ether and the combined organic phases dried and concentrated. Recrystallisation from n-hexane yields the pure product as colourless crystals, m.p. 73-75°.

b) *5,8-Difluoro-1-methylnaphthaline*

3 g of 5,8-Difluoro-4-methyl-1-tetralol are refluxed for 5 hours with 1 g of sulphur. The cold mixture is diluted with ether, filtered and the solvent removed at 0°. The product is purified by column chromatography over silica gel (eluant:hexane).

c) *5,8-Dichloro-1-bromomethylnaphthaline*

Analogous to lf) to obtain the pure compound following chromatography over silica gel (eluant:hexane/ethylacetate=98/2).

O) (5-Fluoro-1-naphthylmethyl)methylamine (for Examples 53 and 65)

a) *5-Fluoro-1-naphthaldehyde*

1.95 g of 5-Fluoro-1-naphthonitrile are dissolved in 40 ml of abs. toluene and cooled to −30°. At this temperature 11 ml of diisobutylaluminiumhydride (20% in toluene) are added dropwise and stirring continued for 2 hours without cooling. The phases are separated, the aqueous solution extracted with toluene and the combined organic phases dried and concentrated. The pure product is obtained as colourless crystals upon recrystallisation from ether/petroleum ether, m.p. 93°.

b) *(5-Fluoro-1-naphthylmethyl)methylamine*

The compound is obtained from 5-fluoro-1-naphthaldehyde and methylamine analogously to Example 2 as a colourless oil.

P) 4-(Dimethylphenylsilyl)benzylbromide (for Example 24)

a) 4-(Dimethylphenylsilyl)toluene

5 g of Bromotoluene are dissolved in 30 ml of tetrahydrofuran and slowly treated at −65° with an equimolar amount of butyllithium in hexane. After 30 minutes at −65° 5 g of dimethylphenylchloridesilane are added dropwise and cooling discontinued. After 2 hours at room temperature the mixture is poured onto ice-water, extracted with dichloromethane and ball-tube distilled (0.13 mbar/95°).

b) *4-(Dimethylphenylsilyl)benzylbromide*

Q) 1-Phenyl-1-(4-bromomethylphenyl)ethylene (for Example 31)

a) *1-Methoxy-1-phenyl-1-tolylethane*

2 g of 1-Phenyl-1-tolylethanol are stirred overnight with 0.56 g of 80% NaH in 50 ml of tetrahydrofuran, 3.7 g of methyliodide added and stirring continued for 6 hours. The mixture is worked up with aq. HCl, extracted with dichloromethane and the oily product purified over a silica gel column with cyclohexane as eluant.

b) *1-Phenyl-1-(4-bromomethylphenyl)ethylene*
Proceeds analogously to A) to obtain, starting from 1-methoxy-1-phenyl-1-tolylethane, the title compound as an oil.

R) 5-Chloro-2-(4-bromomethylbenzoyl)thiophen (for Example 32)
a) *5-Chloro-2-(4-methylbenzoyl)thiophen*
5.17 g of $AlCl_3$ are suspended in 1.2 ml of dichloroethane. 3.84 g of 2-Chlorothiophen and 5 g of p-toluychloride are added dropwise with cooling. Following stirring for 1.5 hours at room temperature the mixture is worked up with aq. HCl, extracted with dichloromethane and the oily product purified on silica gel with toluene as eluant.

b) *5-Chloro-2-(4-bromomethylbenzoyl)thiophen*
Proceeds analogously to A) to obtain, starting from 5-chloro-2-(4-methylbenzoyl)thiophen, the title compound as an oil.

S) 1-(4-Chlorophenyl)-1-(4-aminomethylphenyl)cyclopropane (for Example 34)
a) *1-(4-Chlorophenyl)-1-(4-cyanophenyl)ethylene*
Proceeds analogously to Example 5) starting from 4-chloro-4'-cyanobenzophenone to obtain an oily product which can be directly further reacted.

b) *1-(4-Chlorophenyl)-1-(4-cyanophenyl)cyclopropane*
600 mg of Copper powder are cauterized with 10 mg of iodine in 10 ml of toluene. 1.2 g of Diiodomethane and 500 mg of 1-(4-cyanophenyl)-1-(4-chlorophenyl)-ethylene are added and the mixture refluxed for 140 hours and then filtered and the filtrate concentrated. The oily residue is chromatographed on silica gel with toluene as eluant.

c) *1-(4-Chlorophenyl)-1-(4-aminomethylphenyl)cyclopropane*
230 mg of Lithiumaluminiumhydride are suspended in 10 ml of tetrahydrofuran, 234 mg of 1-(4-chlorophenyl)-1-(4-cyanophenyl)cyclopropane in 5 ml tetrahydrofuran added dropwise and the mixture refluxed for 18 hours. The mixture is then hydrolysed with 1N HCl and extracted with dichloromethane. The oily title compound is directly reacted further.

T) N-Methyl-3-tert.butyl-2-methoxybenzylamine (for Examples 62 and 63)
a) *3-tert.Butyl-2-methoxybenzylbromide*
Proceeds analogously to A) starting from (2-tert.butyl-6-methylphenyl)methylether)as crude product suitable for further reaction.

b) *N-Methyl-3-tert.butyl-2-methoxybenzylamine*
Proceeds analogously to M)g) to obtain a colourless oil.

U) 1-Phenyl-[1-(4-aminomethyl)phenyl]cyclopropane (for Example 12)
Proceeds analogously to S) starting from 1-phenyl-1-(4-cyanophenyl)ethylene to obtain the title compound as an oil.

V) (6-Fluoro-1-naphthylmethyl)methylamine (for Example 58)
Proceeds analogously to O) to obtain the title compound as an oil.

NMR-Spectra

Ex.	Spectra
1	7.9-8.1 (m, 1H); 7.6-7.8 (m,1H); 7.2-7.6 (m, 6H); 6.98 (ddd, J = 10.5 + 8.5 + 2.5Hz, 1H); 3.83 (s, 2H); 3.57 (s, 2H); 2.19 (s, 3H); 1.31 (s, 9H).
2	8.0-8.25 (m, 1H); 7.65-8.0 (m, 2H); 7.30-7.65 (m, 4H); 5.55-5.80 (m, 1H); 4.18 (s, 2H); 3.26 (s, 2H); 1.55-2.30 (m, 5H); 1.50 (s, 1H); 1.0-1.4 (m, 2H); 0.87 (s, 9H).
3	8.2-8.45 (m, 1H); 7.65-7.95 (m, 2H); 7.30-7.65 (m, 4H); 5.55-5.75 (m, 1H); 3.85 (s, 2H); 2.94 (s, 2H); 2.12 (s, 3H); 1.65-2.2 (m, 5H); 1.05-1.50 (m, 2H); 0.86 (s, 9H).
4	8.10-8.34 (m,1H); 7.64-7.95 (m, 2H); 7.03-7.58 (m, 13H); 3.92 (s, 2H); 3.55 (s, 2H); 2.19 (s, 3H); 1.65 (s, 6H).
5	8.20-8.44 (m, 1H); 7.75-7.85 (m, 2H); 7.37-7.58 (m, 4H); 7.23-7.36 (m, 6H); 6.82-6.87 (m, 2H); 5.34-5.38 (m, 2H); 3.95 (s, 2H); 3.81 (s, 3H); 3.60 (s, 2H); 2.21 (s, 3H).

6 8.18-8.36 (m, 1H); 7.65-7.95 (m, 2H); 7.18-7.60 (m, 8H); 3.90 (s, 2H); 3.55 (s, 2H); 2.15 (s, 3H); 1.30 (s, 9H).

7 8.26-8.33 (m, 1H); 7.75-7.88 (m, 2H); 7.28-7.62 (m, 13H); 3.96 (s, 2H); 3.63 (s, 2H); 2.23 (s, 3H).

8 7.64-8.05 (m, 3H); 7.27-7.53 (m, 4H); 6.86 (s, 2H); 3.85 (s, 2H); 3.58 (s, 2H); 2.33 (s, 6H); 2.25 (s, 3H); 2.13 (s, 3H).

9 8.20-9.00 (br, 1H); 7.10-7.95 (m, 10H); 3.75-3.95 (m, 1H); 3.77 (d, 1H, J = 13,5 Hz); 3.00-3.25 (m, 1H); 2.80 (d, 1H, J = 13,5 Hz); 1.45-2.10 (m, 7H); 1.27 (s, 9H).

10 7.32 (s, 4H); 6.70-6.95 (m, 3H); 5.95 (s, 2H); 3.54 (s, 2H); 3.52 (s, 2H); 2.20 (s, 3H); 1.30 (s, 9H).

11 8.15-8.40 (m, 1H); 7.68-7.95 (m, 2H); 7.25-7.65 (m, 8H); 3.94 (s, 2H); 3.60 (s, 2H); 2.20 (s, 3H); 0.24 (s, 9H).

12 8.16-8.27 (m, 1H); 7.70-7.88 (m, 2H); 6.84-7.52 (m, 13H); 3.88 (s, 2H); 3.50 (s, 2H); 2.25 (s, 3H); 1.22-1.28 (m, 4H).

13 7.2-7.85 (m, 10H); 4.9 (dd, J = 7.5 + 4Hz, 1H); 3.95 (s, 2H); 3.74 (dd, J = 18 + 7.5Hz, 1H); 3.25 (dd, J = 18 + 4Hz, 1H); 1.7 (s, 1H); 1.30 (s, 9H).

14 7.2-7.8 (m, 10H); 5.0(dd, J = 7.5 + 4Hz, 1H); 3.25-3.6(m, 4H); 2.19 (s, 3H); 1.30 (s, 9H).

15 8.0-8.25 (m, 1H); 7.7-8.0 (m, 2H); 7.2-7.65 (m, 8H); 3.96 (s, 2H); 3.84 (qua, J = 6.5Hz, 1H); 2.15 (s, 3H); 1.54 (d, J = 6.5Hz, 3H); 1.33 (s, 9H).

16 8.15-8.45 (m, 1H); 7.65-8.0 (m, 2H); 7.15-7.65 (m, 13H); 7.1 (s, 2H); 3.95 (s, 2H); 3.6 (s, 2H); 2.2 (s, 3H).

17 7.15-7.5 (m, 8H); 3.54 (s, 2H); 3.49 (s, 2H); 2.21 (s, 3H); 1.34 (s, 9H); 1.32 (s, 9H).

18 7.95-8.2 (m, 1H); 7.6-7.95 (m, 2H); 7.1-7.6 (m, 8H); 4.1 (s, 2H); 3.73 (s, 2H); 1.7-2.05 (m, 1H); 1.32 (s, 9H); 0.1-0.4 (m, 4H).

19 8.0 (d, J = 8Hz, 1H); 7.76 (d, J = 7Hz, 1H); 7.52 (dd, J = 8 + 7Hz, 1H); 7.25-7.35 (AA'BB'-System, 4H); 7.0-7.13 (m, 2H); 4.11 (d, J = 3Hz, 2H); 3.64 (s, 2H); 2.21 (s, 3H); 1.3 (s, 9H).

20 8.05-8.27 (m, 1H); 6.75-7.90 (m, 10H); 3.90 (s, 2H); 3.53 (s, 2H); 2.18 (s, 3H); 1.30 (s, 9H).

21 8.15-8.40 (m, 1H); 7.65-7.95 (m, 2H); 7.15-7.65 (m, 8H); 4.50 (dt, J = 48 + 5,5Hz, 2H); 4.12 (s, 2H); 3.70 (s, 2H); 2.84 (dt, J = 26 + 5.5Hz, 2H); 1.29 (s, 9H).

22 8.14-8.42 (m, 4H); 7.03 (s, 1H); 3.48 (s, 2H); 3.45 (s, 2H); 2.75-3.05 (m, 8H); 2.08 (s, 3H); 1.85-2.20 (m, 4H); 1.30 (s, 9H).

23 8.16-8.40 (m, 1H); 7.68-7.95 (m, 2H); 7.04-7.64 (m, 7H); 3.99 (s, 2H); 3.81 (s, 2H); 2,22 (s, 3H); 1.36 (s, 9H).

24 8.20-8.42 (m, 1H); 7.70-8.00 (m, 2H); 7.24-7.68 (m, 13H); 4.00 (s, 2H); 3.66 (s, 2H); 2.27 (s, 3H); 0.59 (s, 6H).

25 8.12-8.40 (m, 1H); 7.66-7.95 (m, 2H); 7.20-7.62 (m, 8H); 3.95 (s, 2H); 3.60 (s, 2H); 3.07 (s, 3H); 2.22 (s, 3H); 1.53 (s, 6H).

26 8.20-8.42 (m, 1H); 7.72-8.12 (m, 4H); 7.30-7.68 (m, 6H); 3.95 (s, 2H); 3.90 (s, 3H); 3.62 (s, 2H); 2.20 (s, 3H).

27 8.20-8.42 (m, 1H); 7.26-7.98 (m, 10H); 3.97 (s, 2H); 3.61 (s, 2H); 2.21 (s, 3H); 1.34 (s, 9H).

28 8.20-8.38 (m, 1H); 7.36-7.84 (m, 12H); 6.86-6.98 (m, 2H); 3.98 (s, 2H); 3.86 (s, 3H); 3.64 (s, 2H); 2.21 (s, 3H).

29 8.27-8.39 (m, 1H); 7.24-7.94 (m, 14H); 4.00 (s, 2H); 3.66 (s, 2H); 2.44 (s, 3H); 2.24 (s, 3H).

30 8.24-8.34 (m, 1H); 7.74-7.92 (m, 2H); 7.08-7.60 (m, 12H); 5.40 (s, 2H); 3.95 (s, 2H); 3.60 (s, 2H); 2.34 (s, 3H); 2.20 (s, 3H).

31 8.24-8.35 (m, 1H); 7.74-7.92 (m, 2H); 7.12-7.60 (m, 13H); 5.42-5.47 (m,2H); 3.95 (s, 2H); 3.60 (s, 2H); 2.20 (s, 3H).

32 8.30-8.41 (m, 1H); 7.74-7.96 (m, 4H); 7.36-7.64 (m, 7H); 6.98-7.03 (d, J = 4 Hz, 1H); 4.02 (s, 2H); 3.68 (s, 2H); 2.26 (s, 3H).

33 8.24-8.28 (m, 1H); 7.72-7.85 (m, 3H); 7.34-7.52 (m, 7H); 6.74 (d, J = 4 Hz, 1H); 6.64 (d, J = 4 Hz, 1H); 5.44 (s, 1H); 5.18 (s, 1H); 3.95 (s, 2H); 3.60 (s, 2H); 2.24 (s, 3H).

34 8.18-8.24 (m, 1H); 7.76-7.84 (m, 2H); 7.08-7.48 (m, 12H); 3.92 (s, 2H); 3.54 (s, 2H); 2.17 (s, 3H); 1.20-1.29 (m, 4H).

35 8.16-8.28 (m, 1H); 7.74-7.90 (m, 2H); 7.10-7.57 (m, 12H); 3.96 (s, 2H); 3.60 (s, 2H); 2.25 (s, 3H); 2.21 (s, 3H); 1.64 (s, 6H).

36 8.13-8.35 (m, 1H); 7.64-7.92 (m, 2H); 7.24-7.60 (m, 8H); 3.92 (s, 2H); 3.57 (s, 2H); 2.20 (s, 3H); 1.30 (s, 9H).

37 8.05-8.4 (m, 1H); 7.6-8.0 (m, 2H); 7.1-7.6 (m, 8H); 3.92 (s, 2H); 3.58 (s, 2H); 2.2 (s, 3H); 1.66 (qua, J = 7Hz, 6H); 0.64 (t, J = 7Hz, 9H);

38 8.20-8.35 (m, 1H); 7.70-7.92 (m, 2H); 7.36-7.60 (m, 4H); 7.05-7.35 (m, 4H); 3.90 (s, 2H); 3.56 (s, 2H); 2.32 (s, 3H); 2.18 (s, 3H).

39 8.20-8.36 (m, 1H); 7.70-7.95 (m, 2H); 7.15-7.62 (m, 8H); 3.93 (s, 2H); 3.52 (s, 2H); 2.18 (s, 3H).

40 8.18-8.36 (m, 1H); 7.30-7.96 (m, 8H); 7.00-7.18 (m, 2H); 3.92 (s, 2H); 3.50 (s, 2H); 2.17 (s, 3H).

41 7.70-7.90 (m, 1H); 7.20-7.55 (m, 7H); 3.82 (s, 2H); 3.59 (s, 2H); 2.16 (s, 3H); 1.32 (s, 9H).

42 8.18-8.40 (m, 1H)); 7.16-7.90 (m, 10H); 3.99 (s, 2H); 3.58 (s, 2H); 2.56 (qua, 2H, J = 6,75 Hz); 1.28 (s, 9H); 1.10 (t, 3H, J = 6,75 Hz).

43 8.20-8.42 (m, 1H); 7.30-8.00 (m, 10H); 3.97 (s, 2H); 3.61 (s, 2H); 2.20 (s, 3H).

44 8.10-8.40 (m, 2H); 7.15-7.65 (m, 7H); 6.75 (d, J = 8Hz, 1H); 3.99 (s, 3H); 3.84 (s, 2H); 3.55 (s, 2H); 2.08 (s, 3H); 1.30 (s, 9H).

45 7.75-8.05 (m, 2H); 7.20-7.55 (m, 7H); 3.76 (s, 2H); 3.56 (s, 2H); 2.12 (s, 3H); 1.31 (s, 9H).

46 7.65-7.90 (m, 1H); 7.20-7.55 (m, 8H); 3.82 (s, 2H); 3.60 (s, 2H); 2.18 (s, 3H); 1.31 (s, 9H).

47 7.76 (dd, J = 7 + 3Hz, 1H); 7.2-7.55 (m, 7H); 3.81 (s, 2H); 3.58 (s, 2H); 2.15 (s, 3H); 1.3 (s, 9H).

48 7.95-8.2 (m, 1H); 7.65-7.95 (m, 2H); 7.10-7.6 (m, 8H); 4.23 (s, 2H); 3.88 (s, 2H); 2.9 (sept, J = 7Hz, 1H); 1.73 (s, 1H); 1.23 (d, J = 7Hz, 6H).

49 8.1-8.4 (m, 1H); 7.65-8.0 (m, 2H); 7.10-7.6 (m, 8H); 3.92 (s, 2H); 3.58 (s, 2H); 2.90 (sept, J = 7Hz, 1H); 2.2 (s, 3H); 1.24 (d, J = 7Hz, 6H).

50 8.1-8.35 (m, 1H); 7.7-7.95 (m, 2H); 7.25-7.65 (m, 8H); 3.95 (s, 2H); 3.6 (s, 2H); 2.2 (s, 3H); 1.64 (qua, J = 7.5Hz, 2H); 1.26 (s, 6H); 0.66 (t, J = 7.5Hz, 3H).

51 7.63-7.7 (m, 1H); 7.15-7.45 (m, 7H); 3.59 (s, 2H); 3.55 (s, 2H); 2.22 (s, 3H); 1.32 (s, 9H).

52 8.2-8.45 (m, 1H); 7.65-8.0 (m, 2H); 7.10-7.6 (m, 8H); 3.92 (s, 2H); 3.61 (s, 2H); 2.22 (s, 3H); 1.33 (s, 9H).

53 7.9-8.15 (m, 2H); 7.0-7.6 (m, 8H); 3.9 (s, 2H); 3.56 (s, 2H); 2.19 (s, 3H); 1.3 (s, 9H).

54 6.73-7.48 (m, 8H); 5.75-5.85 (m, 1H); 4.70-4.85 (m, 2H); 3.52 (s, 2H); 3.28 (d, J = 1,5Hz, 2H); 2.20 (s, 3H); 1.31 (s, 9H).

55 7.96-8.18 (m, 1H); 7.62-7.94 (m, 2H); 7.05-7.62 (m, 8H); 4.23 (s, 2H); 3.87 (s, 2H); 2.60 (tr, J = 7,5 Hz, 2H); 2.00 (s, 1H); 1.10-1.80 (m, 4H); 0.91 (tr, J = 7 Hz, 3H).

56 8.15-8.36 (m, 1H); 7.65-7.95 (m, 2H); 7.04-7.62 (m, 8H); 3.92 (s, 2H); 3.58 (s, 2H); 2.60 (tr, J = 7,5 Hz, 2H); 2.20 (s, 3H); 1.10-1.80 (m, 4H); 0.91 (tr, J = 7 Hz, 3H).

57 8.02-8.24 (m,1H); 7.66-8.0 (m, 2H); 7.22-7.64 (m, 8H); 4.26 (s, 2H); 3.90 (s, 2H); 1.69 (s, 1H); 1.33 (s, 9H).

58 8.16-8.40 (m, 1H); 7.60-7.82 (m, 1H); 7.12-7.58 (m, 8H); 3.90 (s, 2H); 3.56 (s, 2H); 2.20 (s, 3H); 1.32 (s, 9H).

59 7.96-8.03 (m, 1H); 7.62-7.70 (m, 1H); 7.48-7.55 (m, 1H); 7.36-7.45 (m, 1H); 7.12-7.32 (m, 9H); 6.97 (ddd, J = 10,5, 8,5 und 2,5 Hz, 1H); 3.82 (s, 2H); 3.54 (s, 2H); 2.19 (s, 3H); 1.67 (s, 6H).

60 7.00-7.45 (m, 7H); 3.52 (s, 2H); 3.50 (s, 2H); 2.27 (s, 6H); 2.13 (s, 3H); 1.31 (s, 9H).

61 7.00-7.45 (m, 12H); 3.52 (s, 2H); 3.50 (s, 2H); 2.30 (s, 3H); 2.27 (s, 3H); 2.15 (s, 3H); 1.70 (s, 6H).

62 6.92-7.60 (m, 7H); 3.78 (s, 3H); 3.61 (s, 2H); 3.52 (s, 2H); 2.19 (s, 3H); 1.40 (s, 9H); 1.31 (s, 9H).

63 6.90-7.60 (m, 12H); 3.78 (s, 3H); 3.61 (s, 2H); 3.51 (s, 2H); 2.19 (s, 3H); 1.68 (s, 6H); 1.40 (s, 9H).

64 7.74-8.02 (m, 1H); 7.12-7.45 (m, 12H); 3.79 (s, 2H); 3.56 (s, 2H); 2.15 (s, 3H); 1.66 (s, 6H).

65 7.90-8.15 (m, 2H); 7.02-7.60 (m, 13H); 3.90 (s, 2H); 3.55 (s, 2H); 2.19 (s, 3H); 1.66 (s, 6H).

66 7.65-7.86 (m, 1H); 7.15-7.55 (m, 13H); 3.82 (s, 2H); 3.59 (s, 2H); 2.18 (s, 3H); 1.68 (s, 6H).

67 7.10-7.60 (m, 12H); 3.67 (s, 2H); 3.58 (s, 2H); 2.22 (s, 3H); 1.68 (s, 6H).

68 7.46-7.56 (m, 1H); 7.25-7.40 (m, 5H); 7.14-7.24 (m, 1H); 3.66 (s, 2H); 3.58 (s, 2H); 2.22 (s, 3H); 1.31 (s, 9H).

69 8.86 (d, J = 5 Hz, 1H); 6.08-6.20 (m, 2H); 7.65-7.73 (m, 1H); 7.46-7.56 (m, 2H); 7.25-7.40 (m, 4H); 3.93 (s, 2H); 3.62 (s, 2H); 2.25 (s, 3H); 1.32 (s, 9H).

70 8.25 (br s, 1H); 7.70-7.77 (m, 1H); 7.05-7.40 (m, 8H); 3.73 (s, 2H); 3.53 (s, 2H); 2.22 (s, 3H); 1.32 (s, 9H).

71 8.20-8.25 (m, 1H); 7.74-7.84 (m, 2H); 7.07-7.47 (m, 12H); 3.93 (s, 2H); 3.92 (s, 2H); 3.55 (s, 2H); 2.29 (s, 3H); 2.18 (s, 3H).

72 8.44-8.60 (m, 1H); 8.16-8.42 (m, 1H); 7.70-7.96 (m, 2H); 7.20-7.68 (m, 6H); 3.98 (s, 2H); 3.56 (s, 2H); 2.22 (s, 3H); 1.35 (s, 9H).

A 7.22-7.48 (m, 4H); 4.46 (s, 2H); 1.30 (s, 9H).

B 7.10-7.80 (m, 8H); 4.48 (s, 2H); 2.26 (s, 3H).

C 7.20 (s, 4H); 7.10 (s, 4H); 4.45 (s, 2H); 2.27 (s, 3H); 1.62 (s, 6H).

D 7.1-7.5 (m, 4H); 4.48 (s, 2H); 1.34 (s, 9H).

E 7.15-7.50 (m, 4H); 4.67 (s, 2H); 1.37 (s, 9H).

F 7.40 (s, 4H); 4.52 (s, 2H); 3.09 (s, 3H); 1.63 (s, 6H).

G 8.50-8.66 (m, 1H); 7.20-7.80 (m, 2H); 4.50 (s, 2H); 1.35 (s, 9H).

H 7.20-7.70 (m, 9H); 3.75 (s, 2H); 2.42 (s, 3H); 1.80 (s, 1H).

I 6.68 (s, 3H); 5.93 (s, 2H); 3.73 (s, 2H); 2.43 (s, 3H); 1.36 (s, 1H).

J 7.85-8.25 (m, 1H); 7.2-7.8 (m, 6H); 4.2 (s, 2H); 2.1 (qui, J = 5Hz, 1H); 1.7 (s, 1H); 0.35 (d, J = 5Hz, 4H).

K 6.95-7.25 (m, 3H); 3.70 (s, 2H); 2.50 (s, 3H); 2.28 (s, 3H); 2.25 (s, 3H); 1.10 (s, 1H).

L 8.05-8.35 (m, 1H); 7.15-8.0 (m, 6H); 4.15 (s, 4H); 3.48 (qua, J = 7 Hz, 2H); 2.45 (s, 3H); 1.2 (t, J = 7 Hz, 3H).

M a) 7.98 (dt, J = 9 + 6,5 Hz, 1H); 6.8-7.1 (m, 2H); 5.8-6.8 (br, 1H); 3.2-3.4 (m, 2H); 2.8 (t, J = 6,5 Hz, 2H).

b) 7.15 (dt, J = 8 + 7 Hz, 1H); 6.7-6.9 (m, 2H); 2.68 (t, J = 7 Hz, 2H); 2.38 (t, J = 7 Hz, 2H); 1.75-2.1 (m, 2H).

c) 7.57 (ddd, J = 9, 2.5 + 1,5 Hz, 1H); 7.02 (ddd, J = 9, 8 + 2,5 Hz, 1H); 2.93 (t, J = 6,5 Hz, 2H); 2.7 (t, J = 6,5 Hz, 2H); 2.0-2.3 (m, 2H).

d) 7.12 (dd, J = 9 + 2,5 Hz, 1H); 6.86 (ddd, J = 9, 8 + 2,5 Hz, 1H); 2.63-2.71 (m, 2H); 1.96 (s, 1H), 1.7-2.0 (m, 4H); 1.51 (s, 3H).

e) 7.8-8.0 (m, 1H); 7.3-7.5 (m, 3H); 6.98 (ddd, J = 10,5, 9 + 2,5 Hz, 1H); 2.6 (s, 3H).

f) 7.85-8.15 (m, 1H); 7.30-7.65 (m, 3H); 6.98 (ddd, J = 10,5, 9 + 2,5 Hz, 1H); 4.80 (s, 2H).

g) 7.80-8.15 (m, 1H); 7.15-7.65 (m, 3H); 6.90 (ddd, J = 10,5, 9 + 2,5 Hz, 1H); 4.02 (s, 2H); 2.48 (s, 3H); 1.38 (s, 1H).

N a) 6.8-6.95 (m, 2H); 5.03-5.1 (m, 1H); 3.09 (sext, J = 7 Hz, 1H); 2.57 (dd, J = 7 + 3 Hz, 1H); 1.7-2.02 (m, 4H); 1.34 (dd, J = 7 + 1,5 Hz, 3H).

b) 7.8-8.1 (m, 1H); 6.8-7.6 (m, 4H); 2.8 (d, J = 7,5 Hz, 3H).

c) 7.8-8.2 (m, 1H); 6.85-7.6 (m, 4H); 5.05 (d, J = 2,5 Hz, 2H).

O a) 10.4 (d, J = 1 Hz, 1H); 9.03 (dt, J = 8.8 + 0.7 Hz, 1H); 8.41 (dqui, J = 7,5 + 0,7 Hz, 1H); 8.05 (dd, J = 7 + 1,3 Hz, 1H); 7.71 (dd, J = 7,5 + 7 Hz, 1H); 7.63 (ddd, J = 8,8, 7,8 + 5,9 Hz, 1H); 7.27 (ddd, J = 10,4, 7,8 + 1,0 Hz, 1H).

b) 8.0-8.16 (m, 1H); 7.85-8.0 (m, 1H); 7.35-7.6 (m, 3H); 7.17 (ddd, J = 10,5, 8 + 1 Hz, 1H); 4.20 (s, 2H); 2.56 (s, 3H); 1.5 (s, 1H).

P a) 7.05-7.60 (m, 9H); 2.35 (s, 3H); 0.52 (s, 6H).

b) 7.10-7.60 (m, 9H); 4.38 (s, 2H); 0.52 (s, 6H).

Q a) 7.10-7.40 (m, 9H); 3.10 (s, 3H); 2.28 (s, 3H); 1.82 (s, 3H).

b) 7.23 (s, 9H); 5.43 (s, 2H); 4.5 (s, 2H).

R a) 7.71 (d, J = 9 Hz, 2H); 7.39 (d, J = 4 Hz, 1H); 7.25 (d, J = 9 Hz, 2H); 6.95 (d, J = 4 Hz, 1H); 2.40 (s, 3H).

b) 7.30-7.90 (m, 5H); 6.97 (d, J = 4 Hz, 1H); 4.50 (s, 2H).

S a) 7.10-7.80 (m, 8H); 5.55 (s, 2H).

b) 7.15-7.70 (m, 8H); 1.30 (s, 4H).

c) 7.15-7.30 (m, 8H); 3.80 (s, 2H); 1.80 (br s, 2H); 1.25 (s, 4H).

T a) 6.90-7.50 (m, 3H); 4.60 (s, 2H); 3.93 (s, 3H); 1.40 (s, 9H).

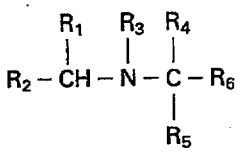
b) 6.85-7.40 (m, 3H); 3.80 (s, 5H); 2.46 (s, 3H); 1.50 (br s, 1H); 1.39 (s, 9H).

U b) 7.00-7.50 (m, 9H); 1.32 (s, 4H).

c) 7.15-7.25 (m, 9H); 3.80 (s, 2H); 1.60 (br s, 2H); 1.25 (s, 4H).

CLAIMS

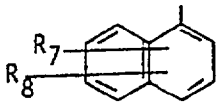
1. Compounds of formula I



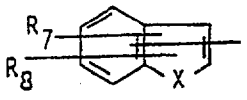
I

wherein

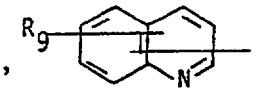
R_1 represents a group of formula



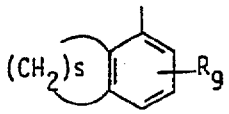
IIa



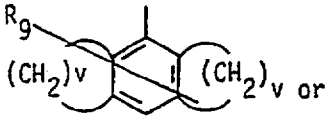
IIb



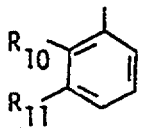
IIc



IId



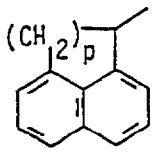
IIe



IIf

and R_2 represents hydrogen or lower alkyl, or

R_1 and R_2 together with the carbon atom to which they are attached represent a group of formula IIg



IIg

whereby in formulae IIa to IIg

R_7 and R_8 represent independently hydrogen, halogen, trifluoromethyl, lower alkyl or lower alkoxy,

R_9 represents hydrogen, halogen, lower alkyl or lower alkoxy,

R_{10} and R_{11} represent independently hydrogen, halogen, trifluoromethyl, lower alkyl, lower alkoxy or lower alkylthio, whereby when one of R_{10} and R_{11} represents hydrogen, halogen or lower alkoxy the other is other than hydrogen,

X represents oxygen, sulphur, imino, lower alkylimino, $-O-CH_2-$ or $-CH_2-$,

p stands for 1, 2 or 3,

s stands for 3, 4 or 5,

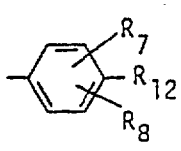
v stands for 3, 4, 5 or 6

whereby one or two of the $-CH_2-$ groups in formula IId may be replaced by oxygen or sulphur,

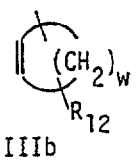
R_4 and R_5 represent independently hydrogen or lower alkyl,

R_3 represents hydrogen, alkyl, cycloalkyl or halogenalkyl and

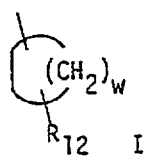
R_6 represents a group of formula



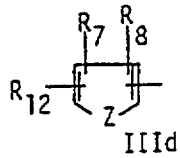
IIIa



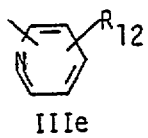
IIIb



IIIc



IIId



IIIe

whereby in the formulae IIIa to IIIe
R_7 and R_8 have the meanings given above,
w stands for 2,3,4,5 or 6,
Z represents oxygen, sulphur or NR_3 wherein R_3 has the meaning given above and
R_{12} represents alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, lower alkoxy, lower alkoxycarbonyl, lower alkylthio, phenyl, phenalkyl, trialkylsilyl, dialkylphenylsilyl or halogen, whereby alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, phenyl or phenalkyl may be substituted by phenyl, lower alkoxy, lower alkylthio, phenalkoxy, lower alkoxyphenyl, lower alkylphenyl, halogenphenyl, halogen or an optionally substituted heterocycle; optionally interrupted by carbonyl; or
R_1 represents a group of formula IIa to IIf as defined above,
R_2 and R_3 together form a $-(CH_2)-_u$ group wherein u stands for a whole number from 1 to 8 and R_4, R_5 and R_6 have the meanings given above, in free form or in pharmaceutically acceptable acid addition salt form for use as systemic pharmaceuticals.

2. Compounds as claimed according to Claim 1 for use as systemic antimycotics.

3. Compounds of formula I as defined in Claim 1 in free form or in agriculturally acceptable salt or metal complex form for use as agrochemicals.

4. Compounds as claimed according to Claim 3 for use in combatting phytophathogenic fungi.

5. A systemic pharmaceutical composition which comprises a compound of formula I in free form or in pharmaceutically acceptable acid addition salt form together with a pharmaceutically acceptable diluent or carrier got up in a form suitable for systemic administration.

6. A composition according to Claim 5 got up in a form suitable for non-topical systemic administration.

7. An agrochemical composition comprising a compound of formula I as defined in Claim 1 in free form or in agriculturally acceptable salt or metal complex form together with an agriculturally acceptable diluent or carrier.

8. A composition according to Claim 5 or 6 or the use according to Claim 1 or 2 wherein in formula I
R_1 represents a group of formula IIa to IIf and R_2 represents hydrogen or lower alkyl or R_1 and R_2 together represent a group of formula IIg whereby in the formulae IIa to IIg R_7 and R_8 represent independently hydrogen, halogen, trifluoromethyl, lower alkyl or lower alkyl and R_9 represents hydrogen, halogen, lower alkyl or lower alkoxy, R_{10} and R_{11} represent independently hydrogen, lower alkyl, halogen, trifluoromethyl, lower alkoxy or lower alkylthio, whereby when one of R_{10} or R_{11} represents hydrogen, halogen or lower alkoxy the other is not hydrogen, X represents oxygen, sulphur, imino, lower alkylamino or $-CH_2-$ p stands for 1, 2 or 3, u stands for 3, 4 or 5 and v stands for 3, 4, 5 or 6 and in the group of formula IId one or two of the CH_2 groups may be replaced by oxygen or sulphur, R_4 and R_5 represent independently hydrogen or lower alkyl, R_3 represents hydrogen, cycloalkyl, halogenalkyl or alkyl and R_6 represents a group of formula IIIa to IIIe, whereby R_7 and R_8 are as herein-defined, w stands for 2, 3, 4, 5 or 6, z stands for oxygen, sulphur or N-R_3 wherein R_3 is as herein defined and R_{12} represents alkyl, alkenyl, alkynyl, cycloalkylalkyl, lower alkoxy, lower alkylthio, phenyl, phenalkyl, trialkylsilyl, dialkylphenylsilyl or halogen, whereby alkyl, alkenyl, alkynyl, cycloalkylalkyl, phenyl and phenalkyl can be substituted by lower alkoxy; optionally interrupted by carbonyl or
b) R_1 represents a group of formula IIa to IIf as defined under a), R_2 and R_3 represent together $-(CH_2)_u-$ whereby u stands for a whole number from 1 to 8 and R_4, R_5 and R_6 are as herein defined.

9. A composition according to Claim 5 or 6 or the use according to Claim 1 or 2 wherein in formula I
(i) a) R_1 represents a group of formula IIa or IIb
b) R_2 represents hydrogen or lower alkyl
c) R_3 represents hydrogen or alkyl
d) R_6 represents a group of formula IIIa
whereby
R_7 and R_8 represent independently, hydrogen, halogen or lower alkoxy, X represents $-O-CH_2-$, oxygen or sulphur
R_4 and R_5 represent independently hydrogen or lower alkyl and R_{12} represents alkyl, alkenyl, alkynyl, cycloalkylalkyl, lower alkoxy, lower alkoxycarbonyl, lower alkylthio, phenyl, phenalkyl, trialkylsilyl, dialkylphenylsilyl or halogen whereby alkyl, alkenyl, alkynyl, cycloalkylalkyl, phenyl or phenylalkyl can be substituted by phenyl, lower alkoxy, lower alkylthio, phenalkoxy, lower alkoxyphenyl, lower alkylphenyl, halogenphenyl, halogen or an optionally substituted heterocycle; optionally interrupted by carbonyl,
(ii) a) R_2 represents hydrogen
b) R_3 represents lower alkyl
c) R_7 and R_8 represent hydrogen
d) X represents sulphur
e) R_4 and R_5 represent hydrogen and the remaining substituents are as defined under (i),
(iii) R_1 represents a group of formula IIa, IIb, IIc, IId or IIe and R_2 represent hydrogen or lower alkyl or R_1 and R_2 together represent a group of formula IIg whereby R_7 and R_8 represent independently hydrogen, halogen, trifluoromethyl, lower alkyl, lower alkoxy and R_9 represents hydrogen, halogen, lower alkyl or lower alkoxy, R_{10} and R_{11} represent independently hydrogen, lower alkyl, halogen, trifluoromethyl, lower alkoxy or lower alkylthio whereby when one of R_{10} or R_{11} is hydrogen, halogen or lower alkoxy the other is not hydrogen, X represents oxygen, sulphur, imino, lower alkylimino, $-O-CH_2-$ or $-CH_2-$, p stands for 1, 2 or 3, s stands for 3, 4

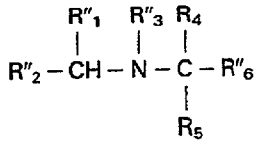
or 6 and v stands for 3, 4, 5 or 6 and one or two CH_2 groups in formula IId may be replaced by oxygen or sulphur, R_4 and R_5 represent independently hydrogen or lower alkyl, R_3 represents hydrogen, cycloalkyl, halogenalkyl or alkyl and R_6 represents a group of formula IIIa, IIIb, IIIc, IIId or IIIe, whereby R_7 and R_8 are as herein defined, w stands for 2, 3, 4, 5 or 6, Z stands for oxygen, sulphur or N-R_3 wherein R_3 is as defined above and R_{12} is as defined under formula I or R_1 represents a group of formula IIa to IIe, R_2 and R_3 together represent $-(CH_2)_u-$ wherein u is a whole number from 1 to 8 and R_4, R_5 and R_6 are as defined above.

10. A composition according to Claim 5 or 6 or the use according to Claim 1 or Claim 2 wherein in formula I

a) R_1 represents naphthyl,
R_2, R_3, R_4 and R_5 represent hydrogen and
R_6 represents a group of formula IIIa,
wherein
R_8 represents hydrogen and
R_7 and R_{12} are as defined in Claim 1 except that they are not both simultaneously halogen and R_{12} is other than halogen or methyl when R_7 is hydrogen or

b) R_1 represents a group of formula IIa, IIb, IIc or IId
wherein
R_8 represents hydrogen,
R_7 and R_9 represent independently hydrogen, lower alkyl, lower alkoxy or halogen,
R_2 represents hydrogen or lower alkyl,
X represents oxygen, sulphur or imino,
R_4 and R_5 represent hydrogen and
R_6 is as defined in Claim 1 except that it does not represent a group of formula IIIa or IIId
wherein
Z represents oxygen or sulphur,
R_7 represents hydrogen
R_8 represents hydrogen, halogen or lower alkyl,
R_{12} represents hydrogen, alkyl, cycloalkyl, halogen alkyl or halogen.

11. A compound of formula Ij

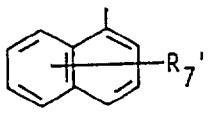


Ij

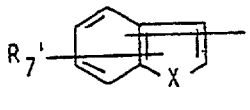
wherein R_4 and R_5 are as defined in Claim 1 and R''_1, R''_2, R''_3 and R''_6 have the same meanings as R_1, R_2, R_3 and R_6 respectively in Claim 1, with the proviso that

a) when R''_1 stands for naphthyl, R''_2, R''_3, R_4 and R_5 stand for hydrogen and R''_6 stands for a group IIIa wherein R_8 is hydrogen then R_{12} and R_7 are not both halogen and R_{12} is not halogen or methyl when R_7 is hydrogen.

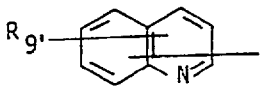
b) when R''_1 stands for a group



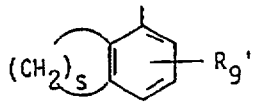
IIa'



IIb'

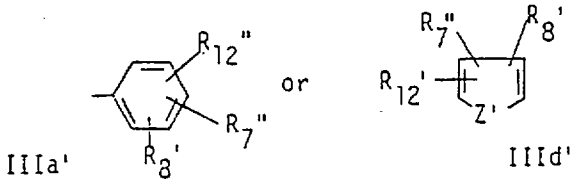


IIc'



IId'

wherein R'_7 and R'_8 represent independently hydrogen, lower alkyl, lower alkoxy or halogen and s stands for 3, 4 or 5, R'_6 represents hydrogen or lower alkyl, X represents oxygen, sulphur or nitrogen and R_4 and R_5 represent hydrogen then R''_6 does not stand for a group



IIIa' IIId'

wherein Z' represents oxygen or sulphur, R''_7 represents hydrogen, R'_8 represents hydrogen, halogen or lower alkyl and R_{12} represents hydrogen, alkyl, cycloalkyl, halogenalkyl or alkyl;
in free form or in acid addition salt form.

12. A compound according to Claim 11 wherein in formula I the substituents are as defined in Claim 8 subject to the provisos given in Claim 11.

13. A compound according to Claim 11 wherein in formula I the substituents are as defined in Claim 9 subject to the provisos given in Claim 11.

14. N-methyl-N-(1-naphthylmethyl)-4-(2-phenyl-2-propyl)benzylamine.

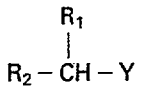
15. The compound according to Claim 14 in acid addition salt form.

16. A pharmaceutical composition comprising a compound of formula I according to any one of Claims 11 to 14 in free form or pharmaceutically acceptable acid addition salt form together with a pharmaceutically acceptable diluent or carrier.

17. A compound of formula I according to any one of Claims 11 to 14 in free form or pharmaceutically acceptable acid addition salt form for use as a pharmaceutical.

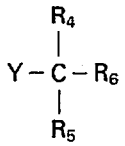
18. A compound of formula I according to any one of Claims 11 to 14 in free form or pharmaceutically acceptable acid addition salt form for use as an antimycotic.

19. A process for preparing a compound of formula Ij according to Claim 11 which comprises
a) reacting a compound of formula IV



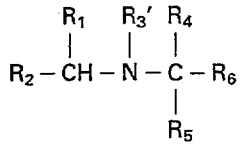
IV

with a compound of formula V



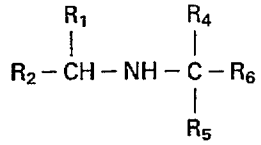
V

b) for preparing a compound of formula Ia



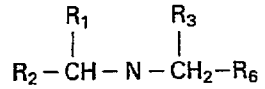
Ia

introducing a $R1_3$ group into a compound of formula Ib



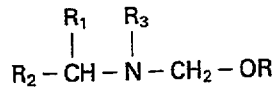
Ib

c)(i) for preparing a compound of formula Ic



Ic

reacting acompound of formula VI



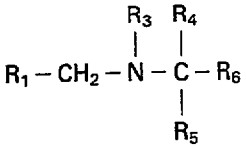
VI

with a compound of formula VII

$R_6 - Me$

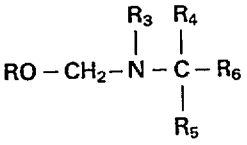
VII or

(ii) for preparing a compound of formula Id



Id

reacting a compound of formula VIa



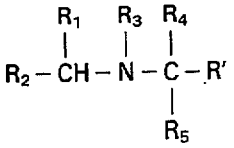
VIa

with a compound of formula VIIa

$R_1 - Me$

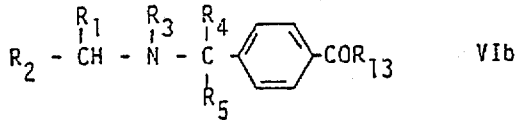
VIIa

d) for preparing a compound of formula Ie



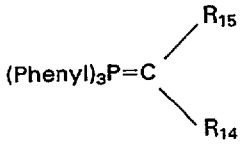
Ie

reacting a compound of formula VIb

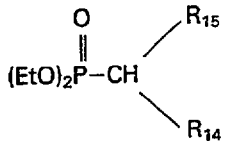


VIb

with a Wittig reagent of formula IVb or IVc

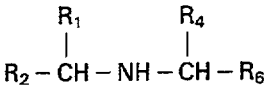


or



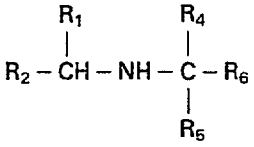
or

e) for preparing a compound of formula If and Ig



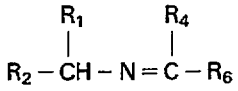
If

and



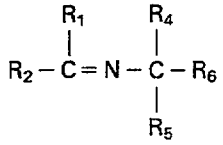
Ig

reducing a Schiff's base of formula Ih, Ii



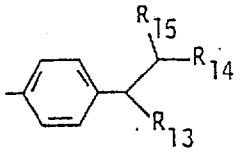
Ih

or



Ii

whereby in the above formulae R, R_2, R_3, R_4, R_5 and R_6 are as defined for formula Ij, one Y represents a leaving group and the other –NH–R_3, R'_3 represents cycloalkyl, halogenalkyl or lower alkyl, R represents lower alkyl, Me represents a metal equivalent, R'_6 represents a group of formula IIIf



IIIf

wherein R_{13}, R_{14} and R_{15} represent independently hydrogen, lower alkyl, lower alkoxy, phenyl, phenalkoxy, lower alkoxyphenyl, lower alkylphenyl, halogenphenyl, halogen or an optionally substituted heterocycle, and recovering the compound obtained in free form or acid addition salt form.

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