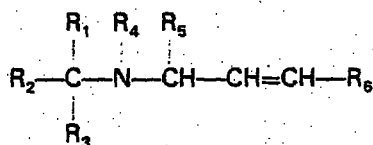


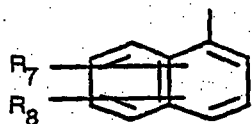
Description

This invention relates to propenylamines, processes for their production, pharmaceutical compositions containing them and their use as pharmaceuticals.

The invention provides compounds of formula I,



wherein a) R_1 represents a group of formula



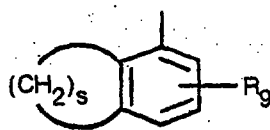
IIa



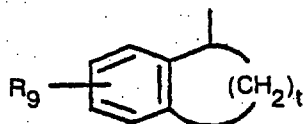
IIb



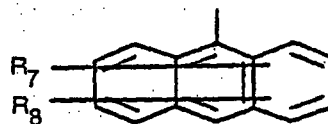
IIc



IIId

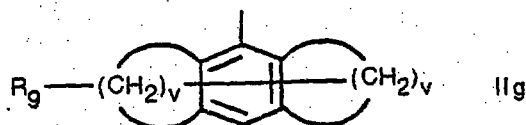


IIe



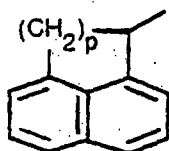
IIIf

or

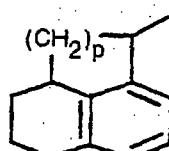


IIg

and R_2 represents hydrogen or lower alkyl, or R_1 and R_2 together represent a group of formula



IIh



IIi

whereby in the formulae IIa to IIi,

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

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

X represents oxygen, sulphur, imino, lower alkyl imino or a radical of formula $-(CH_2)_r-$,

p is 1, 2 or 3,

r is 1, 2 or 3,

s is 3, 4 or 5,

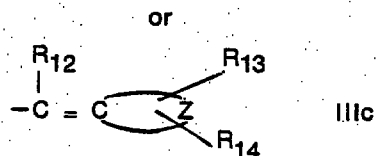
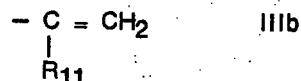
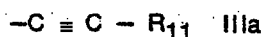
t is 2, 3 or 4, and

v is 3, 4, 5 or 6;

R_3 and R_5 represent, independently, hydrogen or lower alkyl, and

R_4 represents C_{1-6} alkyl or C_{3-6} cycloalkyl- (C_{1-6}) -alkyl; and

R_6 represents a group of formula



wherein

R_{11} represents hydrogen, optionally α -hydroxy substituted alkyl; alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, phenyl, phenalkyl or thienyl,

R_{12} , R_{13} and R_{14} represent, independently, hydrogen or lower alkyl, and

$\begin{array}{c} \text{---}C \\ \diagup \end{array} Z$ represents a C_{5-8} cycloalkylidene radical optionally containing a double bond; or

b) R_1 represents a group of formula IIa to IIg as defined under a),

R_2 represents hydrogen or lower alkyl,

R_3 and R_4 together form a group $-(CH_2)_u-$, wherein u is an integer of 1 to 8, and

R_5 and R_6 have the meanings given under a).

Any lower alkyl or lower alkoxy radical has 1 to 4 carbon atoms, especially 2 or 1 carbon atoms.

Alkyl moieties have 1 to 12 carbon atoms especially 2 to 8 carbon atoms, particularly 2 to 6 carbon atoms and most preferably 2 to 4 carbon atoms and if bridging 1 to 4 particularly 1 or 2 carbon atoms. Any alkenyl or alkynyl radical has 3 to 6 carbon atoms, especially 3 or 4 carbon atoms, e.g. allyl, propenyl or propynyl. Such alkyl, alkoxy, alkenyl and alkynyl groups can be straight-chain or branched.

A preferred cycloalkylidene radical is cyclohexylidene. The term cycloalkyl is to be understood as including polycyclo groups such as bornyl or adamantyl but is preferably cyclohexyl or cyclopentyl.

Conveniently R_7 and R_8 are identical and are both hydrogen. Conveniently R_9 is hydrogen or halogen. In IIb and IIc the bond to the carbon atom to which R_2 and R_3 are attached is conveniently attached meta to X and para to the ring nitrogen, respectively. X is conveniently sulphur, imino or lower alkylamino. R_1 is preferably a radical of formula IIb, IIc or IId, or especially IIa. R_2 is preferably hydrogen. R_3 is preferably hydrogen and R_4 is conveniently alkyl. R_5 is conveniently hydrogen.

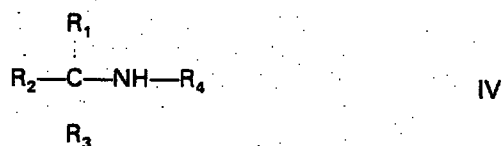
The values of p , r , s , t , u and v are conveniently chosen to produce a seven- preferably a five- or six-membered ring.

The double bond between R_6 and the nitrogen atom preferably has the trans-configuration.

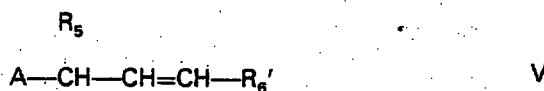
Halogen stands for fluorine, chlorine or bromine, preferably chlorine or bromine.

The present invention also provides a process for the production of a compound of formula I, which comprises

a) when R_6 represents a group of formula IIIa, as defined above, (compound Ia), reacting a compound of formula IV,

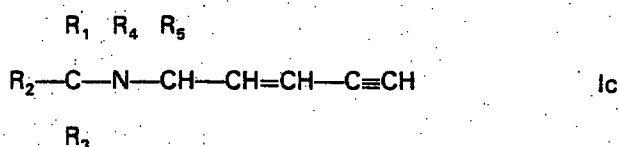


wherein R_1 to R_4 are as defined above, with a compound of formula V,



wherein A is a leaving group, R_5 is as defined above, and R_6' stands for a group of formula IIIa, as defined above, or

b) when R_6 represents a group of formula IIIa, wherein R_{11} represents α -hydroxyalkyl (compounds Ib), reacting a metalated compound of formula Ic,



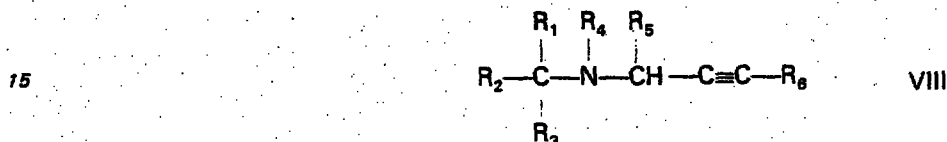
22

wherein R_1 to R_5 are as defined above, with a carbonyl compound of formula VII,



wherein R_{15} , R_{16} and R_{17} represent independently hydrogen or lower alkyl, or

c) when the double bond between R_6 and the nitrogen atom is in trans configuration (compounds Id) reducing a compound of formula VIII,

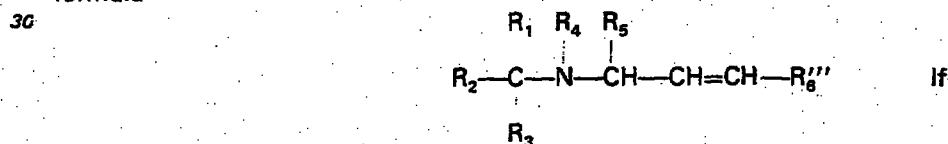


wherein R_1 to R_6 are as defined above, with diisobutylaluminum hydride, or

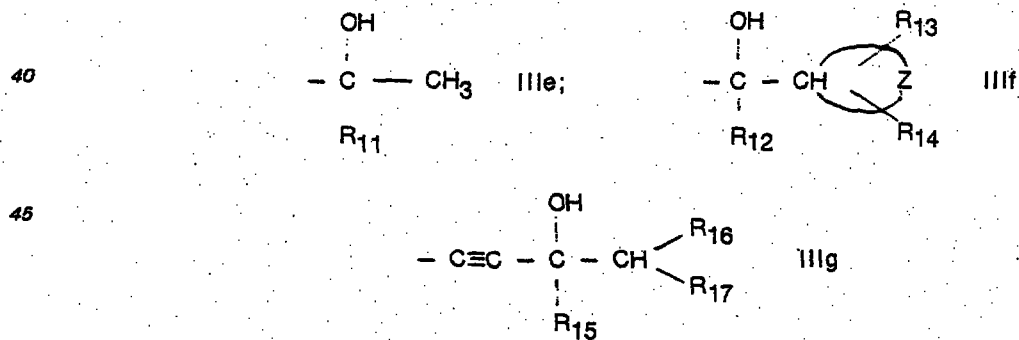
d) when R_6 represents a group of IIIb or IIIc as defined above or a group of formula IIId,



wherein R_{15} , R_{16} and R_{17} are as defined above (compounds Ie) splitting off water from a compound of formula

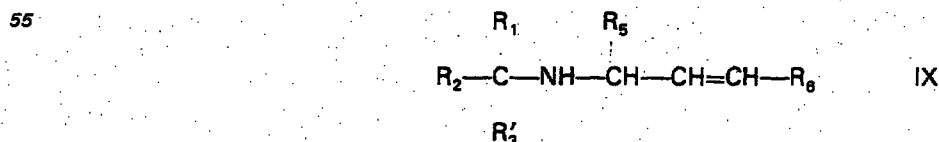


wherein R_1 to R_5 are as defined above, and R_6''' represents a group of formula IIIe, IIIf, or IIIg,



wherein R_{11} to R_{17} and Z are as defined above, or

e) when R_3 represents hydrogen or lower alkyl and R_4 represents C_{1-6} alkyl or C_{3-8} cycloalkyl- (C_{1-6}) -alkyl (compounds Ig), introducing the group R_4' into a compound of formula IX,



wherein

R_1 , R_2 , R_5 and R_6 are as defined above,

R_3 represents hydrogen or lower alkyl, and

R_4' represents C_{1-6} alkyl or C_{3-8} cycloalkyl- (C_{1-6}) -alkyl.

Process a) may be effected in conventional manner for the production of tertiary amines by condensation from analogous starting materials. The process may be effected in an inert solvent such

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as a lower alkanol, e.g. ethanol, optionally in aqueous admixture, an aromatic hydrocarbon solvent, e.g. benzene or toluene, a cyclic ether, e.g. dioxane or a carboxylic acid dialkylamide solvent, e.g. dimethylformamide. The reaction temperature is conveniently from room temperature to the boiling temperature of the reaction mixture, preferably room temperature. The reaction is conveniently effected in the presence of an acid binding agent, such as an alkali metal carbonate, e.g. sodium carbonate. The leaving group A is conveniently iodine or preferably chlorine or bromine, or an organic sulphonyloxy group having 1 to 10 carbon atoms, e.g. alkylsulphonyloxy, preferably having 1 to 4 carbon atoms such as mesyloxy, or alkylphenylsulphonyloxy preferably having 7 to 10 carbon atoms such as tosyloxy.

Process b) may be effected in conventional manner, for example by metalating the compound of formula Ic, e.g. with butyllithium in an inert solvent such as an ether e.g. tetrahydrofuran and subsequently reacting the metalated compound of formula Ic, thus obtained, preferably without isolation with a compound of formula VII.

The reduction with diisobutylaluminium hydride (DIBAH) according to process c) is preferably carried out in an inert solvent e.g. in an aromatic hydrocarbon such as toluene or benzene and at room temperature or raised temperature e.g. 35 to 40°C.

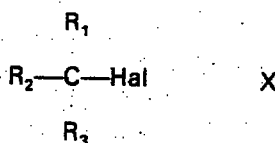
The splitting-off of water according to process d) can be carried out with a suitable agent such as an inorganic acid, e.g. hydrochloric or sulphuric acid, an organic acid, e.g. methanesulphonic acid, benzenesulphonic acid or *p*-toluenesulphonic acid or an inorganic or organic acid anhydride or -halide e.g. POCl₃ in an inert solvent. An excess of an acid halide if used can act as reaction medium whereby the reaction is carried out in the presence of an acid binding agent such as a tertiary amine, e.g. a trialkylamine or a tertiary amine, e.g. a trialkylamine or pyridine. Reaction temperatures vary according to reaction conditions and lie for example between -10 and 180°C. The splitting-off of water can also be carried out with the help of polyphosphoric acid at temperatures between 80 and 120°C whereby inorganic acids such as phosphoric acid, organic acids such as acetic acid or an excess of polyphosphoric acid can serve as solvent.

Process e) may be effected in manner conventional for the "alkylation" of secondary amines (the term "alkylation" being used here to denote introduction of any of the hydrocarbyl groups R₄), for example by direct "alkylation" with an "alkylating" agent, for example a halide or sulphate, or by reductive alkylation, in particular by reaction with an appropriate aldehyde and subsequent or simultaneous reduction. Reductive "alkylation" is suitably effected by reacting a compound of formula IX in an inert organic solvent, such as a lower alkanol, e.g. methanol and at an elevated temperature, in particular at the boiling temperature of the reaction mixture with the corresponding aldehyde. The subsequent reduction may be effected with, for example, a complex metal hydride reducing agent, e.g. NaBH₄ or LiAlH₄. The reduction may also be effected simultaneously to the alkylation, for example by use of formic acid which may serve both as reducing agent and as a reaction medium. The reaction is preferably carried out at raised temperature, in particular at the boiling point of the reaction mixture.

Free base forms of the compounds of formula I may be converted into salt forms and vice versa. Suitable acid addition salts are e.g. hydrochloride, hydrogen fumarate or naphthalene-1,5-disulphonate.

The compounds of the formula I and their intermediates can be obtained in the form of isomeric mixtures of the various *cis/trans* isomers which can be separated according to established methods. Alternatively, isomers of the compounds can be obtained by using the appropriate isomer of the starting material. Unless otherwise stated the compounds are always to be understood as being mixtures of these isomers.

The starting materials of formula IV are in part new and can be prepared by reacting in conventional manner a compound of formula X,

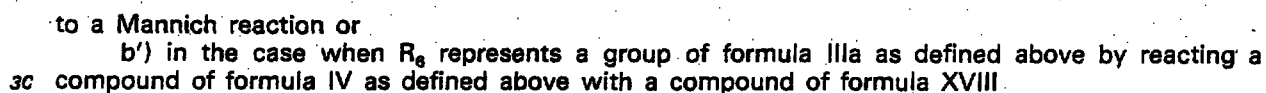
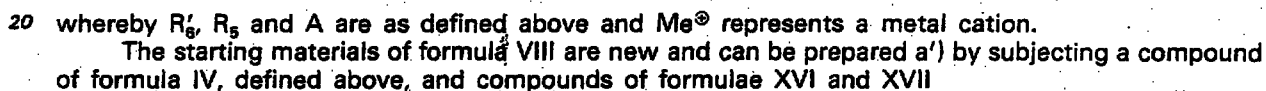


with a compound of formula XI,



wherein in the formula X and XI R₁ to R₄ are as defined above and Hal stands for halogen.

⁵ according to the following scheme

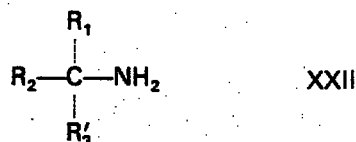


	R'_6 Hal	XX
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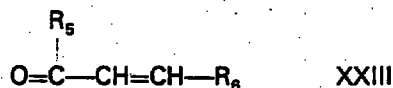
$$\begin{array}{ccccccc}
 & R_1 & R_4 & R_5 & & OH & \\
 & | & | & | & & | & \\
 R_2 - & C & - N - & CH - & C \equiv C - & C - CH_3 & \\
 & | & & & & | & \\
 & R_3 & & & & R_{11} &
 \end{array}
 \quad \text{XXI}$$

whereby in the formulae XVI to XXI R_1 to R_8 , R'_8 , R_{11} , A and Hal are as defined above.

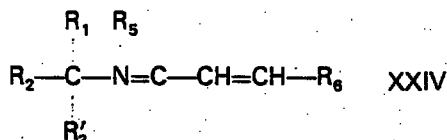
The starting materials of formula IX are new and can be prepared for example by reacting a compound of formula XXII,



with a compound of formula XXIII



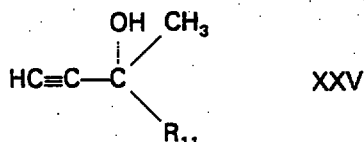
to give a compound of formula XXIV



and reducing this e.g. with a complex hydride such as $NaBH_4$, whereby in the formulae XXII to XXIV R_1 , R_2 , R_3' , R_5 and R_6 are as defined above.

Compounds of formula XXI can be prepared

a'') by subjecting a compound of formula IV as defined above, a compound of formula XVII as defined above, and a compound of formula XXV,



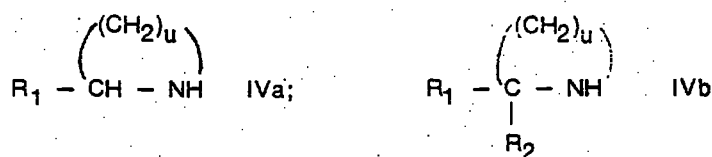
to a Mannich reaction, or

b'') metalating a compound of formula XIX, as defined above, and reacting the metal compound thus obtained with a carbonyl compound of formula XXVI,

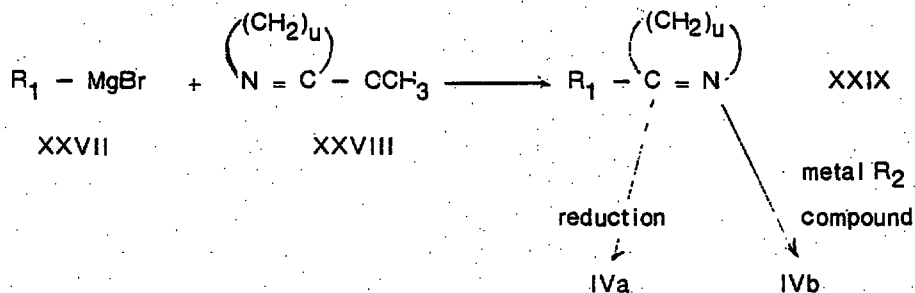


whereby in the formulae XXV and XXVI R_{11} is as defined above.

The compounds of formulae IVa and IVb



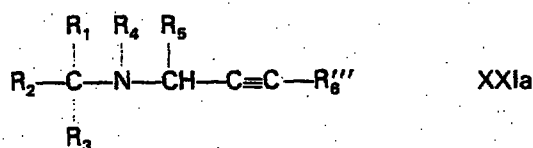
can be prepared according to the following scheme



whereby in the formulae IVa, IVb and XXVII to XXIX R_1 , R_2 and u are as defined above.

The starting materials of formula If wherein R_6'' represents a group of formula IIIe or IIIf as

defined above are new and can be prepared by reduction with LiAlH_4 of a compound of formula XXla,



wherein R_1 to R_5 are as defined above and R_6''' represents a group of formula IIIe or IIIf as defined above.

Compounds of formula XX are in part new and can be prepared by reacting a compound of formula XII, as defined above, with butyllithium and a halogen.

The new compounds of formulae IV, V, VII, IX, XX and I also form part of the invention. The remaining intermediate compounds are either known or can be prepared according to known methods or as hereinbefore described.

The compounds of formula I exhibit chemotherapeutic activity. In particular, they exhibit anti-mycotic activity, as indicated *in vitro* in various families and types of mycetes, including *Trichophyton* spp, *Aspergillus* spp, *Microsporum* spp and *Sporotrichium schenkii* and *Candida* spp at concentrations of, for example 0.01 to 100 $\mu\text{g/ml}$, and *in vivo* in the experimental skin mycosis model in guinea pigs. In this model, guinea pigs are infected by subcutaneous applications of *Trichophyton Quinckeanum*. The test substance is administered daily for 7 days beginning 24 hours after the infection either by local application by rubbing the test substance (taken up in polyethylene glycol) on the skin surface, or perorally or sub-cutaneously, the test substance being administered as a suspension. The activity is shown on local application at concentrations of for example 0.01 to 5%. The oral activity is shown *in vivo* in the guinea-pig — *Trichophytosis* model at dosages of, for example 2 to 70 mg/kg.

The compounds are therefore indicated for use as anti-mycotic agents in particular against dermatophytes. An indicated daily dose is from 70 to 2000 mg. If desired, this may be administered in divided doses 2 to 4 times a day in unit dosage form containing from about 17.5 mg to about 1000 mg or in sustained release form. The invention therefore also concerns compounds of formula I for use as chemotherapeutic agents e.g. as antimycotic agents.

The compounds may be used in free base form or in the form of chemotherapeutically acceptable acid addition salts. Such salt forms exhibit the same order of activity as the free base forms. Suitable salt forms are e.g. hydrochloride, hydrogen fumarate or naphthalene-1,5-disulphonate.

The compounds may be admixed with conventional chemotherapeutically acceptable diluents and carriers, and, optionally, other excipients and administered in such forms as tablets or capsules. The compounds may alternatively be administered topically in such conventional forms as ointments or creams or parenterally. The concentrations of the active substance will of course vary depending on the compound employed, the treatment desired and the nature of the form etc. In general, however, satisfactory results are obtained e.g. in topical application forms at concentrations of from 0.05 to 5, in particular 0.1 to 1 wt%.

Such compositions also form part of the invention.

Examples of preferred compound groups are

(i) compounds of formula I wherein R_1 represents alkyl, alkenyl, alkynyl, cycloalkylalkyl, phenyl or phenalkyl and all other substituents are as defined under formula I;

(ii) compounds of formula I wherein

a) R_1 represents a group of the formula IIa, IIb, IIc,

R_2 represents hydrogen,

R_3 represents hydrogen,

R_4 represents lower alkyl,

R_5 represents hydrogen or lower alkyl,

or R_3 and R_4 together form a group $-(\text{CH}_2)_n-$ or

a) wherein R_1 and R_2 together represent a group of the formula IIh,

R_3 represents hydrogen,

R_4 represents lower alkyl,

R_5 represents lower alkyl and

R_6 is as hereinbefore defined,

whereby within these groups R_6 is preferably a group of formula IIIa as hereinbefore defined and/or R_1 is preferably a group of formula IIa.

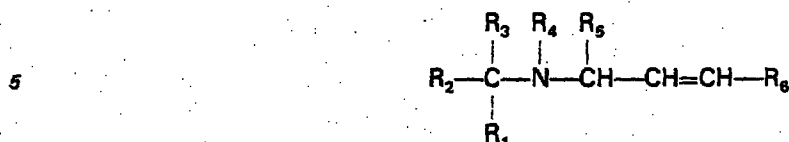
Preferred meanings of the substituents in the compounds of the formula I are such as set out hereinbefore.

Compounds of formula I are generally preferred wherein the double bond between R_6 and the nitrogen atom is in *trans*-configuration.

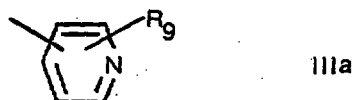
Particularly preferred individual compounds are:

N-methyl-N-(1-naphthylmethyl)-non-2(*trans*)-en-4-ynyl-1-amine and N-methyl-N-(1-naphthylmethyl)-6,6-dimethyl-hept-2(*trans*)-en-4-ynyl-1-amine, and their hydrochlorides.

EP—A—0000896 discloses compounds of formula



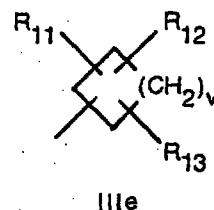
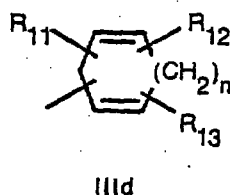
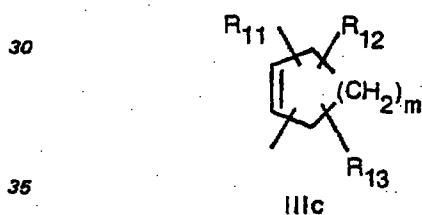
wherein R_1 represents a radical of formula IIa, IIb, IIc, IId and IIe as defined above, R_2 , R_3 and R_5 are as defined above, R_4 is alkyl(C_{1-6}), alkenyl(C_{3-12}), alkynyl(C_{3-12}), cycloalkyl(C_{3-8})alkyl(C_{1-6}) and R_6 is (i) an aromatic, five-membered heterocycle containing one oxygen, sulphur or nitrogen hetero-ring atom and optionally an additional one or two nitrogen hetero-ring atoms and being optionally substituted on a carbon ring atom by halogen of atomic number from 9 to 53, hydroxy, lower alkyl or lower alkoxy, and any nitrogen ring atom present being optionally substituted when possible, by lower alkyl, (ii) a radical of formula IIIa,



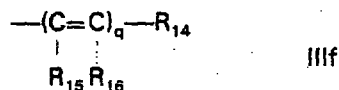
20 wherein R_9 is as defined above, (iii) a radical of formula IIIb,



25 wherein R_{10} is alkyl (C_{1-12}), alkenyl(C_{3-12}), alkynyl(C_{3-12})cycloalkyl(C_{3-8})alkyl(C_{1-6}), phenyl-alkyl (C_{7-12}), phenyl, phenylalkoxy(C_{7-18}), or aminoalkyl(C_{1-12});
(iv) a radical of formula IIIc, IId or IIe,



wherein R_{11} , R_{12} and R_{13} , independently, are hydrogen or lower alkyl, m is a whole number from 1 to 4, n is a whole number from 0 to 3, and v is a whole number from 0 to 5, (v) a radical of formula IIIf,



45 wherein R_{14} is lower alkyl, alkoxy (C_{1-12})-carbonyl, alkenyl, (C_{3-12}), alkynyl(C_{3-12}), phenylalkyl(C_{7-12}) or phenyl, R_{15} and R_{16} , independently, are hydrogen or lower alkyl, and q is a whole number from 0 to 5, or
(vi) a radical of formula IIIg



55 wherein R_{17} and R_{18} , independently, are hydrogen, halogen of atomic number from 9 to 53, trifluoromethyl, hydroxy, nitro, lower alkyl or lower alkoxy, with the proviso that one of R_{17} and R_{18} is other than hydrogen, and with the general proviso that R_1 is not a radical of formula IIa when R_6 is a radical of formula IIIg or phenyl, R_2 is hydrogen and R_3 is hydrogen or lower alkyl, exhibiting chemotherapeutic activity, in particular antimycotic activity.

60 The following Examples illustrate the invention whereby all temperatures are in degrees centigrade.

Example 1:

trans-N-(3-Benzo[b]thiophenemethyl)-N-methyl-non-2-en-ynyl-1-amine and cis-N-(3-Benzo[b]thiophenemethyl)-N-methyl-non-2-en-ynyl-1-amino [process a]]

12 g 1-Bromo-2-nonen-4-yne (cis/trans mixture) are added dropwise to a mixture of 10.5 g N-(3-Benzo[b]thiophenemethyl)-N-methylamine, 8.2 g K_2CO_3 and 100 ml dimethylformamide and stirred overnight. The reaction mixture is filtered and the solvent removed under vacuum. The residue is partitioned between ether and saturated aqueous $NaHCO_3$, the organic phase dried, concentrated under vacuum and chromatographed over kieselgel using toluene/ethylacetate 4:1 as eluant. The trans isomer is eluted first followed by the cis isomer. Both are oils.

Example 2:

trans-N-Methyl-N-(1-naphthylmethyl)-6-hydroxy-6-methyl-hept-2-en-4-ynyl-1-amino [process b]]

10.7 ml of a 15% butyllithium solution in hexane are added dropwise to 3 g of trans N-methyl-N-(1-naphthylmethyl)pent-2-en-4-ynyl-1-amine in absolute tetrahydrofuran and reacted after 30 minutes with a solution of 1.79 g of acetone. The reaction mixture is stirred for 24 hours at room temperature, poured into ice and extracted with chloroform. The organic phase is washed, dried and concentrated under vacuum. After chromatography over kieselgel (eluant toluene/ethyl acetate 4:1) the title compound is obtained as an oil.

Example 3

a) trans-N-Methyl-N-(1-naphthylmethyl)-non-2-en-4-ynyl-1-amine [process c]]

72 ml of a 1.2 M solution of DIBALH in toluene are added dropwise to a solution of 5 g N-methyl-N-(1-naphthylmethyl)-2,4-nonadiynyl-1-amine in dry toluene and the resulting mixture stirred under protective gas overnight at 40° and then for 24 hours at room temperature.

The excess reagent is broken down with 2N NaOH under cooling and the reaction mixture extracted with ether. The organic phase is dried, concentrated under vacuum and chromatographed over kieselgel (eluant — toluene/ethylacetate 95:5). The title substance is isolated as an oil.

b) Hydrochloride salt

The compound from a) is converted to its hydrochloride in conventional manner e.g. by treating with 4N ethanolic HCl and melts after recrystallisation at 118—121°C.

Example 4:

N-Methyl-N-(1-naphthylmethyl)-deca-2(trans), 6(cis)-dien-4-ynyl-1-amine

1 g trans-N-Methyl-N-(1-naphthylmethyl)-6-hydroxy-dec-2-en-4-ynyl-1-amine are refluxed under a water separator with 570 mg *p*-toluenesulphonic acid (monohydrate) in benzene. The mixture is cooled after 2 hours, the organic phase shaken a number of times with saturated aqueous $NaHCO_3$, dried and concentrated under vacuum. The residue is chromatographed over kieselgel (eluant — toluene/ethylacetate 9:1) to give the title product.

Example 5:

N-Methyl-N-(1-naphthylmethyl)-4-cyclohexyl-2-(trans)-4-pentadienyl-1-amine (A) and N-Methyl-N-(1-naphthylmethyl)-4-cyclohexylidenyl-2-(trans)-pentenyl-1-amine (B)

1 g N-Methyl-N-(1-naphthylmethyl)-4-hydroxy-4-cyclohexyl-2-pentenyl-1-amine is refluxed under a water separator with 570 mg *p*-toluenesulphonic acid (monohydrate) in benzene. The mixture is cooled after 2 hours, the organic phase shaken a number of times with saturated aqueous $NaHCO_3$, dried and concentrated under vacuum. The residue is chromatographed over kieselgel (eluant — toluene/ethyl acetate 9:1) to obtain first title product (A) followed by title product (B) as oils.

Example 6:

trans-N-Methyl-N-(1-naphthylmethyl)-4-cyclohexylidenyl-2-buten-yl-amine [process e)]

3 g (1-Naphthylmethyl)methylamine and 2.86 g 4-cyclohexylidenyl-2-butenal are stirred in ether together with a 4Å molecular sieve. The reaction mixture is filtered and concentrated under vacuum. The residue is taken up in methanol, treated with 800 mg $NaBH_4$ and stirred for 2 hours at room temperature.

The reaction mixture containing the secondary amine thus obtained is taken directly for reductive methylation. 8ml 37% aqueous formaldehyde solution are added and refluxed for 1 hour. The mixture is then treated under ice-cooling with 3.6 g $NaBH_4$ and stirred for 16 hours at room temperature. The resulting mixture is concentrated under vacuum, the residue partitioned between saturated $NaHCO_3$ and ethyl acetate and the organic phase dried and concentrated. The title substance is obtained by chromatography over kieselgel (eluant — toluene/ethyl acetate 4:1) as an oil.

The following compounds of formula I can be obtained in an analogous manner.

TABLE I

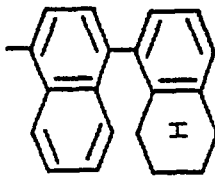
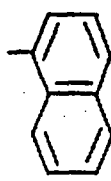
Example	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	Conf.	Physical data	Proc.
7		H	H	CH ₃	H	$-\text{C}::\text{C}-(\text{CH}_2)_3-\text{CH}_3$	trans	oil	c, e
8	—	H	H	CH ₃	H	—	cis	oil	e
9		H	H	CH ₃	H	—	cis	oil	a, e
10		H	H	CH ₃	H	—	trans	oil	a, c, e
11	—	H	H	CH ₃	H	—	cis	oil	a, e
12		H	H	CH ₃	H	—	trans	oil	a, c, e
13	—	H	H	CH ₃	H	—	cis	oil	a, e
14		H	H	CH ₃	H	$-\text{C}::\text{CH}$	trans	m.p. (hydrochloride) 150–155°	a, c, e

TABLE I (Continued)

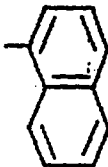
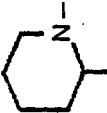
Example	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	Conf.	Physical data	Proc.
15		H	R ₃ , R ₄ , N 		H	-C≡CH	trans	m.p. (hydrochloride) 150-155°	a, c
16	— " —	H	H	CH ₃	H	-C≡C-C(CH ₃) ₃	trans	m.p. (hydrochloride) 199-202° (crystal inversion above 135°)	a, c, e
17	— " —	H	H	CH ₃	H	— " —	cis	oil	a, e
18	— " —	H	H	CH ₃	H	-C≡C-C ₆ H ₅	trans	oil	a, c, e
19	— " —	H	H	CH ₃	H	— " —	cis	oil	a, e
20	— " —	H	H	CH ₃	H	-C≡C-CH(CH ₃)-C ₂ H ₅	trans	m.p. (hydrochloride) 160-162°	a, c, e
21	— " —	H	H	CH ₃	H	— " —	cis	oil	a, e
22	— " —	H	H	CH ₃	H	-C≡C-CH ₂ -CH(CH ₃) ₂	trans	m.p. (hydrochloride) 124-126°	a, c, e
23	— " —	H	H	CH ₃	H	— " —	cis	oil	a, e
24	— " —	H	H	CH ₃	H	-C≡C- 	trans	oil	a, c, e

TABLE I (Continued)

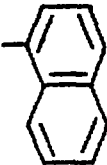
Example	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	Conf.	Physical data	Proc.
25		H	H	CH ₃	H	$\begin{array}{c} \text{OH} \\ \\ -\text{C}\equiv\text{C}-\text{C}-\text{CH}_3 \\ \\ \text{CH}_3 \end{array}$	trans	oil	c, e
26	—	H	H	CH ₃	H	$\begin{array}{c} \text{OH} \\ \\ -\text{C}\equiv\text{C}-\text{C}-\text{C}_2\text{H}_5 \\ \\ \text{C}_2\text{H}_5 \end{array}$	trans	oil	b, c, e
27	—	H	H	CH ₃	H	$\begin{array}{c} \text{OH} \\ \\ -\text{C}\equiv\text{C}-\text{CH}-(\text{CH}_2)_3-\text{CH}_3 \end{array}$	trans	oil	b, c, e
28	—	H	H	CH ₃	H	$\begin{array}{c} \text{OH} \\ \\ -\text{C}\equiv\text{C}-\text{C}-\text{CH}_3 \\ \\ \text{C}_2\text{H}_5 \end{array}$	trans	oil	b, c, e
29	—	H	H	CH ₃	H	$\begin{array}{c} \text{OH} \\ \\ -\text{C}\equiv\text{C}-\text{C}-\text{CH}_3 \\ \\ \text{C}(\text{CH}_3)_3 \end{array}$	trans	oil	b, c, e
30	—	H	H	CH ₃	H	$-\text{C}\equiv\text{C}-(\text{CH}_2)_3-\text{CH}_3$	trans	m.p. (hydrochloride) 118–121°	a, e
31	—	H	H	CH ₃	H	$-\text{C}\equiv\text{C}-(\text{CH}_2)_2-\text{CH}_3$	trans	oil	a, c, e

TABLE I (Continued)

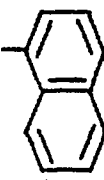
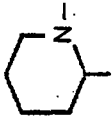
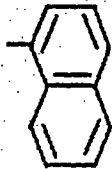
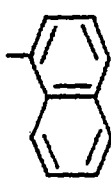
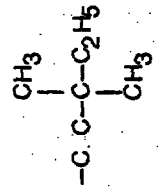
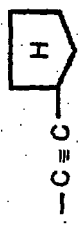
Example	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	Conf.	Physical data	Proc.
32		H	H	CH ₃	H	-C≡C-(CH ₂) ₄ -CH ₃	trans	oil	a, c, e
33	— " —	H	H	CH ₃	H	-C≡C-(CH ₂) ₅ -CH ₃	trans	oil	a, c, e
34	— " —	H	R ₃ , R ₄ , N 		H	-C≡C-(CH ₂) ₂ -CH ₃	trans	oil	a, c
35	— " —	H	— " —		H	-C≡C-(CH ₂) ₃ -CH	trans	oil	a, c
36	— " —	H	H	CH ₃	H	-C≡C-CH=CH-(CH ₂) ₂ -CH ₃	trans	oil	a, c, e
37	— " —	H	H	CH ₃	H	-C≡C-C=CH.CH ₃ C ₂ H ₅	trans	oil	a, c, d, e
38	— " —	H	H	CH ₃	H	-C≡C-C=CH.CH ₃ CH ₃	trans	oil	a, c, d, e
39	— " —	H	H	CH ₃	H	-C≡C-C=CH ₂ C(CH ₃) ₃	trans	oil	a, c, d, e
40	— " —	H	H	CH ₃	H	-C=CH ₂ C ₆ H ₅	trans	oil	c, d, e

TABLE I (Continued)

Example	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	Conf.	Physical data	Proc.
41		H	H	CH ₃	H	$\begin{array}{c} \text{---C=CH}_2 \\ \\ \text{CH}_2\text{---CH} \begin{array}{l} \text{---CH}_3 \\ \text{---CH}_3 \end{array} \end{array}$	trans	oil	c, d, e
42	---	H	H	CH ₃	H	$\begin{array}{c} \text{---C---CH}_2 \\ \\ (\text{CH}_2)_3\text{---CH}_3 \end{array}$	trans	oil	c, d, e
43	---	H	H	CH ₃	H	$\begin{array}{c} \text{---C---CH}_2 \\ \\ \text{C}(\text{CH}_3)_3 \end{array}$	trans	oil	c, d, e
44	---	H	H	CH ₃	H	$\left\{ \begin{array}{l} \text{CH}_3 \\ \\ \text{---C=CH} \end{array} \right. \begin{array}{c} \text{---CH}_2 \\ \\ \text{---C---} \end{array} \begin{array}{c} \text{---CH} \\ \\ \text{---CH}_2 \end{array} \begin{array}{c} \text{---CH}_3 \\ \\ \text{---CH}_3 \end{array}$	trans	oil	c, e
45	---	H	H	CH ₃	H	$\begin{array}{c} \text{---CH=CH} \\ \\ \text{---CH}_2 \end{array}$	trans	oil	c, d
46	---	H	H	CH ₃	H	$\text{---C}\equiv\text{C---CH}_2\text{OH}$	trans	oil	b, c, e

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TABLE I (Continued)

Example	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	Conf.	Physical data	Proc.
47		H	H	CH ₃	CH ₃	-C C-(CH ₂) ₃ -CH ₃	trans	oil	a, c, e
48	---	H	H	CH ₃	CH ₃	---	cis	oil	a, e
49	---	H	H	CH ₃	H		trans	oil	a, c, e
50	---	H	H	CH ₃	H	---	cis	oil	a, e
51	---	H	H	CH ₃	H		trans	oil	a, c, e
52	---	H	H	CH ₃	H	---	cis	oil	a, e
53	---	H	H	CH ₃	H		trans	oil	a, c, e
54	---	H	H	CH ₃	H	---	cis	oil	a, e

35

TABLE I (Continued)

Example	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	Conf.	Physical data	Proc.
55		H	H	CH ₃	H		trans	oil	c, d, e
56		H	H	CH ₃	H	-C≡C-C(CH ₃) ₃	cis	oil	a, c, e
57	— " —	H	H	CH ₃	H	-C≡C-C(CH ₃) ₃	cis	oil	a, e
58		H	H	CH ₃	H		trans	oil	c, d, e
59	— " —	H	H	CH ₃	H	-C≡C-C(CH ₃) ₃	trans	oil	a, c, e



In the following table NMR data are given. Data comprises peaks in ppm relative to TMS as standard in CDCl_3 . Types of peaks are

5	m = multiplet
	dt = double triplet
	dm = double multiplet
10	s = singlet
	d = doublet
	t = triplet
15	ps.t = pseudo triplet
	dd = double doublet
20	dbr = double broad
	br = broad
25	qua = quartet
	mbr = multiple broad
	sext = sextuplet
30	ddd = double double doublet
	sbr = single broad

35

40

45

50

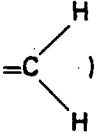
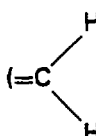
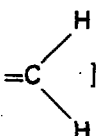
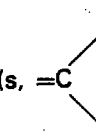
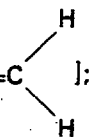
55

60

65

Example	Isomer	Spectrum
1,7	trans	$\delta = 7.7-8.0$ (m, 2H); 7.15—7.45 (m, 4H); 6.14 (dt, $J = 16$ and 2×6.5 Hz, 1 olef. H); 6.65 (dm, $J = 16$ Hz, 1 olef. H); 3.72 (s, 2H); 3.10 (d, $J = 6.5$ Hz, 2H); 2.3 (m, 2H); 2.24 (s, 3H); 1.2—1.7 (m, 4H); 0.9 (ps.t., 3H).
1,8	cis	$\delta = 7.7-8.0$ (m, 2H); 7.15—7.45 (m, 4H); 6.0 (dt, $J = 11$ and 2×6.5 Hz, 1 olef. H); 5.64 (dm, $J = 11$ Hz, 1 olef. H); 3.66 (s, 2H); 3.35 (d, $J = 6.5$ Hz, 2H); 2.34 (m, 2H); 2.28 (s, 3H); 1.2—1.7 (m, 4H); 0.9 (ps.t., 3H).
9	cis	$\delta = 8.2-8.4$ (m, 1H); 7.7—7.9 (m, 2H); 7.3—7.6 (m, 4H); 6.05 (dt, $J = 10.8 + 2 \times 7$ Hz, 1 olef. H); 5.65 (dm, $J = 10.8$ Hz, 1 olef. H); 3.92 (s, 2H); 3.38 (dd, $J = 7$ u. 1.5 Hz, 2H); 2.34 (m, 2H); 2.25 (s, 3H); 1.2—1.8 (m, 4H); 0.94 (m, 3H).
10	trans	$\delta = 6.9-7.2$ (m, 3H); 6.12 (dt, $J = 16$ and 2×6.5 Hz, 1 olef. H); 5.64 (dm, $J = 16$ Hz, 1 olef. H); 3.4 (s, 2H); 3.05 (d, $J = 6.5$ Hz, 2H); 2.7—2.9 (m, 4H); 2.2—2.4 (m, 2H); 2.18 (s, 3H); 1.65—1.9 (m, 4H); 1.3—1.7 (m, 4H); 0.92 (m, 3H).
11	cis	$\delta = 6.85-7.2$ (m, 3H); 5.97 (dt, $J = 11$ and 6.5 Hz, 1 olef. H); 5.60 (dm, $J = 11$ Hz, 1 olef. H); 3.45 (s, 2H); 3.30 (d, $J = 6.5$ Hz, 2H); 2.7—2.9 (m, 4H); 2.2—2.4 (m, 2H); 2.22 (s, 3H); 1.7—1.9 (m, 4H); 1.3—1.7 (m, 4H); 0.95 (m, 3H).
12	trans	$\delta = 7.1-7.8$ (m, 5H); 6.14 (dt, $J = 16$ and 2×6.5 Hz, 1 olef. H); 5.65 (dm, $J = 16$ Hz, 1 olef. H); 3.63 (s, 2H); 3.1 (d, $J = 6.5$ Hz, 2H); 2.2—2.4 (m, 2H); 2.25 (s, 3H); 1.2—1.7 (m, 4H); 0.9 (m, 3H).
13	cis	$\delta = 7.1-7.8$ (m, 5H); 6.0 (dt, $J = 11$ and 2×6.5 Hz, 1 olef. H); 5.64 (dm, $J = 11$ Hz, 1 olef. H); 3.66 (s, 2H); 3.35 (d, $J = 6.5$ Hz, 2H); 2.2—2.4 (m, 2H); 2.30 (s, 3H); 1.2—1.7 (m, 4H); 0.9 (m, 3H).
16	trans	$\delta = 8.2-8.35$ (m, 1H); 7.7—7.9 (m, 2H); 7.3—7.6 (m, 4H); 6.18 (dt, $J = 17$ and 2×7 Hz); 5.65 (dm, $J = 17$ Hz, 1H); 3.9 (s, 2H); 3.12 (dd, $J = 7$ u. 1 Hz, 2H); 2.22 (s, 3H); 1.25 (s, 9H).
17	cis	$\delta = 8.2-8.35$ (m, 1H); 7.7—7.9 (m, 2H); 7.3—7.6 (m, 4H); 6.03 (dt, $J = 11$ and 2×6.5 Hz, 1H); 5.65 (dbr, $J = 11$ Hz, 1H); 3.92 (s, 2H); 3.38 (d, $J = 6.5$ Hz, 2H); 2.26 (s, 3H); 1.27 (s, 9H).
18	trans	$\delta = 8.2-8.35$ (m, 1H); 7.7—7.9 (m, 2H); 7.2—7.6 (m, 9H); 6.36 (dt, $J = 16$ and 2×6.5 Hz, 1H); 5.9 (dm, $J = 16$ Hz, 1H); 3.94 (s, 2H); 3.22 (d, $J = 6.5$ Hz, 2H); 2.28 (s, 3H).
19	cis	$\delta = 8.2-8.4$ (m, 1H); 7.7—7.9 (m, 2H); 7.2—7.6 (m, 9H); 6.20 (dt, $J = 11$ and 2×6.5 Hz, 1H); 5.85 (d, $J = 11$ Hz, 1H); 3.98 (s, 2H); 3.50 (d, $J = 6.5$ Hz, 2H); 2.30 (s, 3H).
20	trans	$\delta = 8.2-8.4$ (m, 1H); 7.7—7.9 (m, 2H); 7.3—7.6 (m, 4H); 6.20 (dt, $J = 16$ and 2×6.5 Hz, 1H); 5.80 (dm, $J = 16$ Hz, 1H); 3.90 (s, 2H); 3.14 (d, $J = 6.5$ Hz, 2H); 2.5 (m, 1H); 2.24 (s, 3H); 1.2—1.7 (m, 2H); 1.18 (d, $J = 7$ Hz, 3H); 1.0 (t, $J = 7$ Hz, 3H).
21	cis	$\delta = 8.2-8.4$ (m, 1H); 7.7—7.9 (m, 2H); 7.3—7.6 (m, 4H); 6.05 (dt, $J = 11$ and 2×6.5 Hz, 1H); 5.67 (dm, $J = 11$ Hz, 1H); 3.94 (s, 2H); 3.40 (d, $J = 6.5$ Hz, 2H); 2.55 (m, 1H); 2.28 (s, 3H); 1.2—1.8 (m, 2H); 1.20 (d, $J = 7$ Hz, 3H); 1.02 (t, $J = 7$ Hz, 3H).
22	trans	$\delta = 8.2-8.35$ (m, 1H); 7.65—7.9 (m, 2H); 7.3—7.6 (m, 4H); 6.20 (dt, $J = 16$ and 2×6.5 Hz, 1H); 5.68 (dm, $J = 16$ Hz, 1H); 3.88 (s, 2H); 3.13 (d, $J = 6.5$ Hz, 2H); 2.22 (s, 3H); 2.2 (m, 2H); 1.6—2.1 (m, 1H); 1.0 (d, $J = 7$ Hz, 6H).

Example	Isomer	Spectrum
23	cis	$\delta = 8.2-8.4$ (m, 1H); 7.7—7.9 (m, 2H); 7.3—7.6 (m, 4H); 6.04 (dt, $J = 12$ and 2×7 Hz, 1H); 5.65 (dbr, $J = 12$ Hz, 1H); 3.90 (s, 2H); 3.38 (d, $J = 7$ Hz, 2H); 2.24 (s, 3H); 2.2 (m, 2H); 1.6—2.0 (m, 1H); 1.0 (d, $J = 7$ Hz, 6H).
24	trans	$\delta = 8.2-8.4$ (m, 1H); 7.65—7.9 (m, 2H); 7.3—7.6 (m, 4H); 7.15—7.3 (m, 2H); 6.95 (m, 1H); 6.36 (dt, $J = 16$ u. 2×6 Hz, 1H); 5.9 (dbr, $J = 16$ Hz, 1H); 3.92 (s, 2H); 3.20 (d, $J = 6$ Hz, 2H); 2.28 (s, 3H).
2,25	trans	$\delta = 8.15-8.35$ (m, 1H); 7.6—7.9 (m, 2H); 7.3—7.6 (m, 4H); 6.22 (dt, $J = 16$ and 2×6.5 Hz, 1H); 5.67 (dt, $J = 16$ and 2×1.5 Hz, 1H); 3.88 (s, 2H); 3.13 (dd, $J = 6.5$ u. 1.5 Hz); 2.22 (s, 3H); 2.15 (br. —OH); 1.5 (s, 6H).
26	trans	identical with Ex. 2,25 except $\delta = 1.8$ (br, OH); 1.65 (qua, $J = 8$ Hz, 4H); 1.0 (t, $J = 8$ Hz, 6H).
27	trans	$\delta = 8.2-8.35$ (m, 1H); 7.6—7.9 (m, 2H); 7.3—7.6 (m, 4H); 6.26 (dt, $J = 16$ and 2×6 Hz, 1H); 5.7 (dm, $J = 16$ Hz, 1H); 4.46 (mbr, 1H); 3.90 (s, 2H); 3.15 (d, $J = 6$ Hz, 2H); 2.25 (s, 3H); 2.0 (br, OH); 1.2—1.8 (m, 6H); 0.9 (m, 3H).
28	trans	$\delta = 8.15-8.35$ (m, 1H); 7.7—7.9 (m, 2H); 7.3—7.6 (m, 4H); 6.25 (dt, $J = 16$ and 2×6.5 Hz, 1 olef. H); 5.70 (dbr, $J = 16$ Hz, 1H); 3.9 (s, 2H); 3.14 (d, $J = 6.5$ Hz, 2H); 2.24 (s, 3H); 2.1 (br, OH); 1.72 (qua, $J = 7$ Hz, 2H); 1.50 (s, 3H); 1.04 (t, $J = 7$ Hz, 3H).
29	trans	$\delta = 8.15-8.35$ (m, 1H); 7.7—7.9 (m, 2H); 7.3—7.6 (m, 4H); 6.22 (dt, $J = 16$ and 2×6.5 Hz, 1H); 5.70 (dm, $J = 16$ Hz, 1H); 3.9 (s, 2H); 3.14 (d, $J = 6.5$ Hz, 2H); 2.24 (s, 3H); 1.95 (m, OH); 1.46 (s, 3H); 1.06 (s, 9H).
3,30	trans	$\delta = 8.2-8.35$ (1 arom. H); 7.7—7.9 (2 arom. H); 7.3—7.6 (4 arom. H); 6.17 (dt, 1 olef. H, $J = 16 + 2 \times 6.5$ Hz); 5.67 (d, 1 olef. H, $J = 16$ Hz); 3.89 (s, 2H); 3.13 (d, 2H, $J = 6.5$ Hz); 2.21 (s, 3H); 2.2—2.4 (m, 2H); 1.2—1.8 (4H); 0.8—1.05 (m, 3H).
31	trans	identical with Ex. 3,30 except: $\delta = 2.28$ (t, 2H); 1.55 (sext., 2H); 1.0 (t, 3H).
32	trans	identical with Ex. 3,30 except: $\delta = 1.2-1.8$ (m, 6H).
33	trans	identical with Ex. 3,30 except: $\delta = 1.2-1.8$ (m, 8H).
34	trans	$\delta = 8.5$ (br, 1H); 7.3—7.9 (m, 6H); 6.02 (ddd, $J = 5, 8 + 16$ Hz, 1H); 5.46 (dbr, $J = 16$ Hz, 1H); 3.80 (br, 1H); 3.1—3.35 (m, 2H); 2.52 (dd, $8 + 14$ Hz, 1H); 2.0—2.35 (m, 3H); 1.6—2.0 (m, 6H); 1.54 (sext., $J = 7$ Hz, 2H); 0.97 (t, $J = 7$ Hz, 3H).
35	trans	identical with Ex. 34 except: $\delta = 1.3-1.7$ (m, 4H); 0.9 (ps.t, 3H).
4,36	trans	$\delta = 8.2-8.35$ (m, 1H); 7.7—7.9 (m, 2H); 7.3—7.6 (m, 4H); 6.26 (dt, $J = 15.5 + 2 \times 6.5$ Hz, 1H); 5.9 (dt, $J = 11 + 2 \times 7$ Hz); 5.85 (d, $J = 15.5$ Hz, 1H); 5.58 (dbr, $J = 11$ Hz); 3.92 (s, 2H); 3.18 (d, $J = 6.5$ Hz, 2H); 2.35 (t, 2H); 2.26 (s, 3H); 1.2—1.7 (m, 2H); 0.95 (ps.t, 3H).
37	trans	$\delta = 8.15-8.35$ (m, 1H); 7.7—7.9 (m, 2H); 7.3—7.6 (m, 4H); 6.25 (dt, $J = 16 + 6$ Hz, 1H); 5.86 (d, $J = 16$ Hz, 1H); 5.70 (t, $J = 7$ Hz, 1H); 3.94 (s, 2H); 3.20 (d, $J = 6$ Hz, 2H); 2.26 (s, 3H); 2.16 (qua, $J = 8$ Hz, 2H); [1.8 (d, $J = 7$ Hz) und 1.7 (d, $J = 7$ Hz); Σ 3H, in ratio 6/1]; 1.06 (t, 3H).
38	trans	$\delta = 8.2-8.35$ (m, 1H); 7.7—7.9 (m, 2H); 7.3—7.6 (m, 4H); 6.30 (dt, $J = 16 + 2 \times 6$ Hz, 1H); 5.86 (d, $J = 16$ Hz, 1H); 5.75 (m, 1H); 3.92 (s, 2H); 3.18 (d, $J = 6$ Hz, 2H); 2.26 (s, 3H); 1.87 (s, 3H); 1.8 u. 1.7 (2 d, 3H).

Example	Isomer	Spectrum
39	trans	$\delta = 8.2-8.4$ (m, 1H); $7.7-7.9$ (m, 2H); $7.3-7.6$ (m, 4H) 6.28 (dt, $J = 16 + 2 \times 6.5$ Hz, 1H); 5.84 (dm, $J = 16$ Hz, 1H); 5.30 (m, ); 3.92 (s, 2H); 3.18 (d, $J = 6.5$ Hz, 2H); 2.26 (s, 3H); 1.18 (s, 9H).
5,44 A	trans	$\delta = 8.2-8.35$ (1 arom. H); $7.7-7.9$ (2 arom. H); $7.3-7.6$ (4 arom. H); 6.22 (d, 1 olef. H, $J = 16$ Hz); 5.93 (dt, 1 olef. H, $J = 16 + 2 \times 6.5$ Hz); 4.87 u. 4.83 ); 3.90 (s, 2H); 3.19 (d, 2H, $J = 6.5$ Hz); 2.25 (s, 3H); 1.0-2.4 (11 H, Cyclohexyl).
B	trans	$\delta = 8.2-8.35$ (1 arom. H); $7.7-7.9$ (2 arom. H); $7.3-7.6$ (4 arom. H); 6.79 (d, 1 olef. H, $J = 16$ Hz); 5.80 (dt, 1 olef. H, $J = 16 + 2 \times 6.5$ Hz); 3.92 (s, 2H); 3.24 (d, 2H, $J = 6.5$ Hz); 2.2-2.5 (m, 4H); 2.26 (s, 3H); 1.88 (s, 3H), 1.58 (br, 6H).
40	trans	$\delta = 8.15-8.30$ (m, 1H); $7.7-7.9$ (m, 2H); $7.3-7.6$ (m, 9H); 6.51 (d, $J = 18$ Hz, 1H); 5.82 (dt, $J = 18 + 2 \times 7.5$ Hz, 1H); [5.26 (sbr, 1H) + 5.14 (d, $J = 2$ Hz, 1H) ]; 3.88 (s, 2H); 3.20 (d, $J = 7.5$ Hz, 2H); 2.22 (s, 3H).
41	trans	$\delta = 8.2-8.35$ (m, 1H); $7.7-7.9$ (m, 2H); $7.3-7.6$ (m, 4H); 6.24 (d, $J = 16$ Hz, 1 olef. H); 5.85 (dt, $J = 16 + 2 \times 6.5$ Hz, 1 olef. H); 4.95 (dd, $J = 11 + 2$ Hz, 2 olef. H); 3.9 (s, 2H); 3.18 (d, $J = 6.5$ Hz, 2H); 2.24 (s, 2H); 2.13 (d, $J = 6.5$ Hz, 2H); 1.6-2.1 (m, 1H); 0.9 (d, $J = 6.5$ Hz, 6H).
42	trans	$\delta = 8.2-8.35$ (m, 1H); $7.65-7.9$ (m, 2H); $7.3-7.6$ (m, 4H); 6.26 (d, $J = 16$ Hz, 1H); 5.86 (dt, $J = 16 + 2 \times 6.5$ Hz, 1H); 4.95 ); 3.90 (s, 2H); 3.18 (d, $J = 6.5$ Hz, 2H); 2.24 (s, 3H); 2.15-2.35 (m, 2H); 1.1-1.7 (m, 4H); 0.9 (ps.t, 3H).
43	trans	$\delta = 8.2-8.35$ (m, 1H); $7.7-7.9$ (m, 2H); $7.3-7.6$ (m, 4H); 6.30 (d, $J = 15.5$ Hz, 1H); 6.02 (dt, $J = 15.5$ Hz + 2×6.5 Hz, 1H); [5.07 (sbr, 1H) + 4.80 (d, $J = 2$ Hz, 1H), ]; 3.9 (s, 2H); 3.16 (d, 2H); 2.25 (s, 3H); 1.1 (s, 9H).

Example	Isomer	Spectrum
6,45	trans	$\delta = 8.2\text{--}8.35$ (1 arom. H); 7.7—7.9 (2 arom. H); 7.3—7.6 (4 arom. H); 6.52 (dd, 1 olef. H, $J = 15$ u. 10 Hz); 5.86 (d, 1 olef. H, $J = 10$ Hz); 5.79 (dt, 1 olef. H, $J = 15 + 2 \times 6.5$ Hz); 3.92 (s, 2H); 3.20 (d, $J = 6.5$ Hz, 2H); 2.25 (s, 3H); 2.1—2.4 (m, 4H); 1.6 (br, 6H).
46	trans	$\delta = 8.15\text{--}8.35$ (m, 1H); 7.7—7.9 (m, 2H); 7.3—7.6 (m, 4H); 6.3 (dt, $J = 16 + 2 \times 6.5$ Hz, 1H); 5.7 (dm, $J = 16$ Hz, 1H); 4.34 (d, $J = 2$ Hz, 2H); 3.9 (s, 2H); 3.16 (d, $J = 6.5$ Hz, 2H); 2.24 (s, 3H); 2.2 (OH).
47	trans	$\delta = 8.2\text{--}8.35$ (m, 1H); 7.65—7.9 (m, 2H); 7.3—7.5 (m, 4H); 6.17 (dd, $J = 16 + 7$ Hz, 1H); 5.58 (dm, $J = 16$ Hz, 1H); 3.9 (AB-System, 2H); 3.25 (m, 1H); 2.1—2.3 (m, 2H); 2.14 (s, 3H); 1.3—1.6 (m, 4H); 1.18 (d, $J = 7$ Hz, 3H); 0.85 (m, 3H).
48	cis	$\delta = 8.2\text{--}8.35$ (m, 1H); 7.6—7.9 (m, 2H); 7.3—7.6 (m, 4H); 5.98 (dd, $J = 11 + 9$ Hz, 1H); 5.6 (dm, $J = 11$ Hz, 1H); 3.96 (AB-System, 2H); 3.8; (m, 1H); 2.1—2.3 (m, 2H); 2.16 (s, 3H); 1.2—1.6 (m, 4H); 1.26 (d, $J = 7$ Hz, 3H); 0.82 (m, 3H).
49	trans	$\delta = 8.15\text{--}8.35$ (m, 1H); 7.6—7.9 (m, 2H); 7.3—7.6 (m, 4H); 6.14 (dt, $J = 16 + 2 \times 6.5$ Hz, 1H); 5.66 (dm, $J = 16$ Hz, 1H); 3.86 (s, 2H); 3.10 (d, $J = 6.5$ Hz, 2H); 2.2 (s, 3H); 1.4 (qua, $J = 7$ Hz, 2H); 1.15 (s, 6H); 0.9 (t, $J = 7$ Hz, 3H).
50	cis	$\delta = 8.2\text{--}8.35$ (m, 1H); 7.6—7.9 (m, 2H); 7.3—7.6 (m, 4H); 6.0 (dt, $J = 11 + 2 \times 6.5$ Hz, 1H); 5.64 (dm, $J = 11$ Hz, 1H); 3.9 (s, 2H); 3.35 (d, $J = 6.5$ Hz, 2H); 2.22 (s, 3H); 1.45 (qua, $J = 7$ Hz, 2H); 1.18 (s, 6H); 0.95 (t, $J = 7$ Hz, 3H).
51	trans	$\delta = 8.15\text{--}8.35$ (m, 1H); 7.6—7.9 (m, 2H); 7.3—7.6 (m, 4H); 6.16 (dt, $J = 16 + 2 \times 6.5$ Hz, 1H); 5.66 (dm, $J = 16$ Hz, 1H); 3.86 (s, 2H); 3.10 (d, $J = 6.5$ Hz, 2H); 2.7 (br, 1H); 2.2 (s, 3H); 1.4—2.1 (m, 8H).
52	cis	$\delta = 8.15\text{--}8.35$ (m, 1H); 7.6—7.9 (m, 2H); 7.3—7.6 (m, 4H); 6.0 (dt, $J = 11 + 2 \times 6.5$ Hz, 1H); 5.64 (dm, $J = 11$ Hz, 1H); 3.9 (s, 2H); 3.36 (d, $J = 6.5$ Hz, 2H); 2.75 (br, 1H); 2.22 (s, 3H); 1.4—2.1 (m, 8H).
55	trans	$\delta = 7.8\text{--}8.1$ (m, 2H); 7.25—7.5 (m, 3H); 6.50 (dd, $J = 17 + 12$ Hz, 1H); 5.85 (d, $J = 12$ Hz, 1H); 5.74 (dt, $J = 17$ u. 2×7 Hz, 1H); 3.77 (s, 2H); 3.14 (d, $J = 7$ Hz, 2H); 2.0—2.4 (m, 4H); 2.25 (s, 3H); 1.55 (sbr, 6H).
56	trans	$\delta = 8.2\text{--}8.4$ (m, 2H); 7.25—7.7 (m, 3H); 6.74 (d, $J = 8$ Hz, 1H); 6.2 (dt, $J = 18 + 2 \times 7$ Hz, 1H); 5.67 (dt, $J = 18$ u. 2×15 Hz, 1H); 4.0 (s, 3H); 3.82 (s, 2H); 3.10 (dd, $J = 7$ u. 1.5 Hz); 2.2 (s, 3H); 1.24 (s, 9H).
57	cis	$\delta = 8.2\text{--}8.4$ (m, 2H); 7.25—7.7 (m, 3H); 6.74 (d, $J = 8$ Hz, 1H); 6.05 (dt, $J = 12 \times 2 \times 7.5$ Hz, 1H); 5.65 (dt, $J = 12$ u. 2×1.5 Hz, 1H); 4.0 (s, 3H); 3.85 (s, 2H); 3.35 (dd, $J = 7.5$ u. 1.5 Hz, 2H); 2.24 (s, 3H); 1.26 (s, 9H).
58	trans	$\delta = 7.2\text{--}7.8$ (m, 6H); 6.44 (dd, $J = 17 + 12$ Hz, 1H); 5.80 (d, $J = 12$ Hz, 1H); 5.66 (dt, $J = 17 + 2 \times 7$ Hz, 1H); 5.0 (t, $J = 6$ Hz, 1H); 3.33 (d, $J = 6$ Hz, 2H); 3.14 (d, $J = 7$ Hz, 2H); 2.0—2.4 (m, 4H); 2.12 (s, 3H); 1.5 (sbr, 6H).
59	trans	$\delta = 7.1\text{--}7.7$ (m, 6H); 6.04 (dt, $J = 16 + 2 \times 6.5$ Hz, 1H); 5.6 (dm, $J = 16$ Hz, 1H); 4.9 (t, $J = 6$ Hz, 1H); 3.22 (d, $J = 6$ Hz, 2H); 3.0 (d, $J = 6.5$ Hz, 2H); 2.1 (s, 3H); 1.18 (s, 9H).
53	trans	$\delta = 8.15\text{--}8.35$ (m, 1H); 7.6—7.9 (m, 2H); 7.3—7.6 (m, 4H); 6.15 (dt, $J = 16 + 2 \times 6.5$ Hz, 1H); 5.65 (dm, $J = 16$ Hz, 1H); 3.85 (s, 2H); 3.10 (d, $J = 6.5$ Hz, 2H); 2.2 (s, 3H); 1.8—2.1 (br, 9H); 1.6—1.8 (br, 6H).

The required starting materials can be obtained e.g. as follows.

1. *Compounds of formula IV:*

5 A) (3-Benzo[b]thiophenemethyl)methylamine (for Ex. 1)

3-Chloromethylbenzo[B]thiophene is dissolved in benzene, added dropwise to a ca. 10-fold excess of methylamine in ethanol at 0—5° and then stirred for 16 hours at room temperature. The crude mixture is concentrated under vacuum, the residue partitioned between methylenechloride and 1N NaOH and the organic phase dried and evaporated under vacuum. The purified product is obtained by vacuum distillation b.p. 90—94°/1,33 Pa.

B) (3-Benzo[B]furanmethyl)methylamine (for Ex. 12 and 13)

Obtained analogously to Example A) b.p. 105—110°/5.3 Pa.

15 C) 2-(1-Naphthyl)piperidine (for Ex. 15, 34 and 35)

A Grignard complex is prepared by adding 43.4 g of 1-bromonaphthalene in absolute ether dropwise to 5.1 g of magnesium in 50 ml of absolute ether. The ether is removed from the reaction mixture and replaced by absolute benzene. 8 g 6-Methoxy-2,3,4,5-tetrahydropyridine are added to the boiling reaction mixture. After a further 8 hours the mixture is cooled, treated with saturated aqueous ammoniumchloride solution and the reaction product removed from the organic phase by shaking with aqueous HCl-solution. After neutralisation and working up the 2-(1-naphthyl)-3,4,5,6-tetrahydropyridine is dissolved directly in methanol and reduced with NaBH₄. After normal working up the product is converted with alcoholic HCl solution to its hydrochloride. M.p. 287—289° (after intensive drying under high vacuum 328—329°).

25 2. *Compounds of formula V:*

D) 1-Bromo-6,6-dimethyl-2-hepten-4-yne (for Ex. 16, 17, 56, 57 and 59)

30 (a) 6,6-Dimethyl-1-hepten-4-yn-3-ol

38 ml 3,3-Dimethyl-1-butyne are dissolved in abs. tetrahydrofuran and 172 ml of a 20% solution of n-butyl-lithium added dropwise under protective gas at a temperature of -20°. The reaction mixture is then cooled to -75° and 19.3 g acrolein in 20 ml of tetrahydrofuran added dropwise. The mixture is warmed to room temperature, reacted with saturated aqueous NH₄Cl and extracted a number of times with ether. The organic phase is dried, concentrated and the purified product obtained by vacuum distillation, b.p. 70—72°/1600 Pa.

b) 1-Bromo-6,6-dimethyl-2-hepten-4-yne

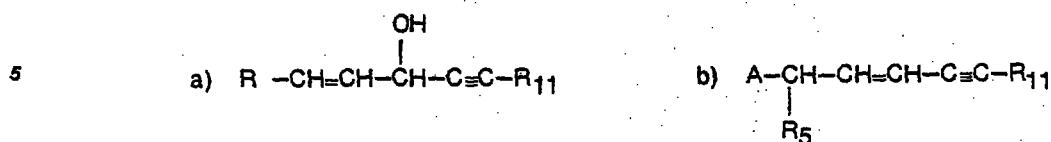
50 ml 48% HBr and 10 g PBr₄ are stirred at 40° until a homogeneous mixture is obtained. An alcoholic solution of 13.5 g 6,6-dimethyl-1-hepten-4-yn-3-ol are added dropwise at 10° and stirred for 1½ hours at room temperature. The reaction mixture is poured onto ice and extracted a number of times with hexane. The organic phase is washed a number of times with aqueous NaCl, dried and concentrated. NMR-spectrography shows that the oily product comprises a 3:1 mixture of trans- and cis-1-bromo-6,6-dimethyl-2-hepten-4-yne and is taken directly for alkylation.

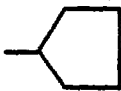
45 NMR: δ x 5.5—6.4 (m, 2 olef. H), [4.15 (d, J = 8Hz) and 3.95 (d, J = 8Hz) in ratio 1:3, 2H, = CH—CH₂Br], 1.20 (m, 9H).

Analogously to D) above the following compounds of formula V can be obtained.

TABLE II

(42)



10		R_{11}	R_5	A	Physical data	for Ex.
15	E) a b	$\left. \begin{array}{l} \text{CH}_3 \\ -\text{CH} \\ \text{C}_2\text{H}_5 \end{array} \right\}$	H	- Br	b.p. 75–80°/1460 Pa oil	20, 21
20	F) a b	$\left. \begin{array}{l} \text{CH}_3 \\ -\text{CH}_2\text{CH} \\ \text{CH}_3 \end{array} \right\}$	H	- Br	b.p. 87–91°/1730 Pa oil	22, 23
25	G) a b	$\left. \begin{array}{l} \text{CH}_3 \\ \\ -\text{C}-\text{C}_2\text{H}_5 \\ \\ \text{CH}_3 \end{array} \right\}$	H	- Br	b.p. 90°/1460 Pa oil	49, 50
30	H) a b		H	- Br	b.p. 94–96°/800 Pa oil	51, 52
35	I) a b	$\left. \begin{array}{l} -(\text{CH}_2)_3-\text{CH}_3 \end{array} \right\}$	CH_3	- Br	b.p. 92–93°/530 Pa oil	47, 48

40

The remaining compounds of formula V can be obtained analogously to D) above.

3. Compounds of formula VIII

45 M) N-Methyl-N-(1-naphthylmethyl)octa-2,4-diynyl-1-amine (for Ex. 31)

9 g 1,3-Heptadiyne, 16 g N-methyl-(1-naphthylmethyl)amine, 2.8 g paraformaldehyde and 1.3 g ZnCl_2 (anhydrous) are heated for 3 hours at 100° in absolute dioxane. After cooling the solvent is removed under vacuum, the residue partitioned between chloroform and aqueous NaHCO_3 -solution and the organic phase dried and concentrated. The purified product is obtained by chromatography over
50 kieselgel (toluene/ethyl acetate 9:1) as an oil.

N) N-Methyl-N-(1-naphthylmethyl)-2,4-nonadiynyl-1-amine (for Ex. 3)

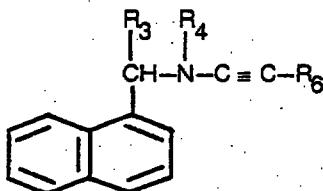
8.25 g 1-Bromohexyne are added dropwise to a mixture of 16 g N-methyl-N-(1-naphthylmethyl)-propargylamine, 0.5 g $\text{NH}_2\text{OH}\cdot\text{HCl}$, 0.25 g CuCl and 20 ml 70% ethylamine. The reaction mixture is stirred overnight at room temperature, treated with an aqueous solution of 1 g KCN and extracted a number of times with ether. The organic phase is washed with saturated aqueous NaCl, dried and evaporated. The title substance is obtained as an oil after chromatography over Kieselgel (eluant toluene/ethyl acetate 95:5).
55

60 O) N-Methyl-N-(1-naphthylmethyl)-4-t-butyl-pent-2-yn-4-enyl-1-amine (for Ex. 43)

933 mg N-Methyl-N-(1-naphthylmethyl)-4-hydroxy-4,5,5-trimethyl-2-hexynyl-1-amine are dissolved in abs. pyridine, warmed to 50° and 0.4 ml POCl_3 added. Stirring is carried out for one hour at 90°, the mixture poured onto ice and the reaction product isolated as an oil by extraction with ether and chromatography over kieselgel (eluant toluene/ethyl acetate 9:1).

65 Analogously to M), N) and O) above, the following compounds of formula VIII may be obtained.

TABLE III



	R ₃	R ₄	R ₆	Physical data	For Ex.
P)	H	CH ₃	-C≡C-(CH ₂) ₄ -CH ₃	oil	32
Q)	H	CH ₃	-C≡C-(CH ₂) ₅ -CH ₃	oil	33
R)	H	CH ₃	-C≡C-C(CH ₃) ₃	oil	16
S)	R ₃ + R ₄ + N		-C≡C-(CH ₂) ₂ -CH ₃	oil	34
T)			-C≡C-(CH ₂) ₃ -CH ₃	oil	35

The remaining compounds of formula VIII can be prepared analogously to M), N) and O) above.

4. Compounds of formula If

U) N-Methyl-N-(1-naphthylmethyl)-4-hydroxy-4-cyclohexyl-2-pentenyl-1-amine (for Ex. 5)

a) N-Methyl-N-(1-naphthylmethyl)-4-hydroxy-4-cyclohexylpent-2-ynyl-1-amine

10.7 ml of a 15% solution of BuLi in hexane are added dropwise to 3 g N-methyl-N-(1-naphthylmethyl)propargyl amine in absolute tetrahydrofuran and after 30 minutes reacted with a solution of 1.79 g cyclohexylmethyl ketone. Stirring is continued for 24 hours at room temperature and the mixture poured onto ice and extracted with ether. The organic phase is washed, dried and concentrated under vacuum. Chromatography over kieselgel (eluant toluene/ethylacetate 4:1) yields the title product as an oil.

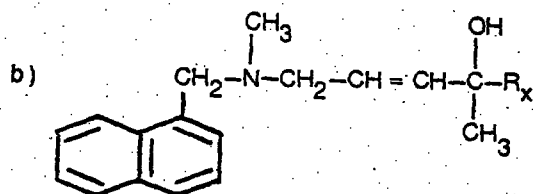
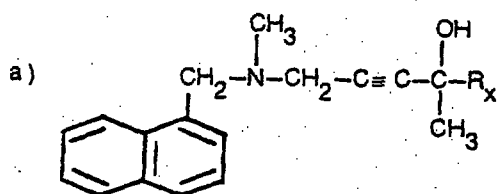
b) N-Methyl-N-(1-naphthylmethyl)-4-hydroxy-4-cyclohexyl-2-pentenyl-1-amine

10 g of the substance obtained under a) are dissolved in tetrahydrofuran and added dropwise to a suspension of 1.4 g LiAlH₄ in abs. tetrahydrofuran and the mixture refluxed for 3 hours. Excess reagent is destroyed with ethyl acetate/H₂O. After extraction with ether, drying and evaporation under vacuum followed by chromatography over kieselgel (eluant CHCl₃/C₂H₅OH 95:5) the title product is obtained as an oil.

Analogously to U) above the following compounds can be obtained.

TABLE IV

44



		R_x	physical data [a) and b)]	For Ex.
V)	}	$-\text{CH}_2-\text{CH} \begin{matrix} \text{CH}_3 \\ \text{CH}_3 \end{matrix}$	oil	41
a) b)				
W)	}	$-(\text{CH}_2)_3-\text{CH}_3$	oil	42
a) b)				
X)	}	$-\text{C}(\text{CH}_3)_3$	oil	43
a) b)				
Y)	}	$-\text{C}_6\text{H}_5$	oil	40
a) b)				

Compounds of formula IX can be prepared analogously to Example 6 above and are preferably taken directly without further purification or isolation for the final step.

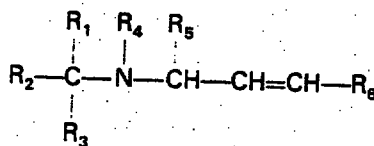
Example		Spectrum
N)		$\delta = 8.2-8.35$ (1 arom. H); $7.7-7.9$ (2 arom. H); $7.3-7.6$ (4 arom. H); 3.97 (s, 2H); 3.37 (s, 2H); 2.40 (s, 3H); $2.2-2.4$ (m, 2H); $1.2-1.8$ (4H); $0.8-1.05$ (m, 3H).
M)		identical with N) except: $\delta = 2.28$ (t, 2H); 1.58 (sext., 2H); 1.0 (t, 3H).
P)		identical with N) except: $\delta = 1.2-1.8$ (m, 6H).
Q)		identical with N) except: $\delta = 1.2-1.8$ (m, 8H).
R)		$\delta = 8.1-8.25$ (m, 1H); $7.6-7.85$ (m, 2H); $7.2-7.5$ (m, 4H); 3.92 (s, 2H); 3.33 (s, 2H); 2.35 (s, 3H); 1.22 (s, 9H).
S)		$\delta = 8.5$ (br, 1H); $7.3-7.9$ (m, 6H); 4.05 (br, 1H); 3.24 (s, 2H); 3.12 (m, 1H); $2.5-2.8$ (m, 1H); 2.26 (t, $J = 6.5$ Hz, 2H); $1.6-2.0$ (m, 6H); 1.56 (sext., $J = 7$ Hz, 2H); 0.99 (t, $J = 7$ Hz, 3H).
T)		identical with S) except: $\delta = 2.28$ (ps.t, 2H); $1.3-1.7$ (m, 4H); 0.91 (ps.t, 3H).
U)	a)	$\delta = 8.2-8.35$ (1 arom. H); $7.7-7.9$ (2 arom. H); $7.3-7.6$ (4 arom. H); 4.0 (s, 2H); 3.37 (s, 2H); 2.38 (s, 3H); 1.52 (s, 3H); $1.0-2.2$ (11H).
	b)	$\delta = 8.2-8.35$ (1 arom. H); $7.7-7.9$ (2 arom. H); $7.3-7.6$ (4 arom. H); 5.76 (m, 2 olef. H); 3.91 (s, 2H); 3.13 (m, 2H); 2.25 (s, 3H); 1.23 (s, 3H); $0.8-2.0$ (11H).
V)	a)	$\delta = 8.15-8.35$ (m, 1H); $7.7-7.9$ (m, 2H); $7.3-7.6$ (m, 4H); 3.95 (s, 2H); 3.34 (s, 2H); 2.35 (s, 3H); $1.8-2.3$ (m, 1H); 2.0 (s, OH); 1.62 (d, $J = 6.5$ Hz, 2H); 1.53 (s, 3H); 1.04 u. 1.02 (2 d, $J = 6.5$ Hz, Σ 6H).
	b)	$\delta = 8.2-8.4$ (m, 1H); $7.7-7.9$ (m, 2H); $7.3-7.6$ (m, 4H); 5.78 (AB-portion of an ABX_2 -system, 2 olef. H); 3.90 (s, 2H); 3.12 (m, 2H); 2.22 (s, 3H); $1.3-2.0$ (m, 1H); 1.5 (s, OH); 1.4 (d, 2H); 1.3 (s, 3H); 0.92 u. 0.90 (2 d, $J = 7$ Hz, Σ 6H).
W)	a)	$\delta = 8.2-8.35$ (m, 1H); $7.7-7.9$ (m, 2H); $7.3-7.6$ (m, 4H); 3.98 (s, 2H); 3.36 (s, 2H); 2.38 (s, 3H); 2.1 (br, OH); $1.2-1.9$ (m, 6H); 1.56 (s, 3H); 0.95 (ps.t., 3H).
	b)	$\delta = 8.2-8.35$ (m, 1H); $7.7-7.9$ (m, 2H); $7.3-7.6$ (m, 4H); 5.85 (AB-portion of an ABX_2 -system, 2H); 3.90 (s, 2H); 3.12 (m, 2H); 2.25 (s, 3H); $1.2-1.7$ (m, 6H + OH); 1.28 (s, 3H); 0.9 (ps.t., 3H).
X)	a)	$\delta = 8.2-8.35$ (m, 1H); $7.7-7.9$ (m, 2H); $7.3-7.6$ (m, 4H); 4.0 (s, 2H); 3.38 (s, 2H); 2.4 (s, 3H); 1.96 (br, OH); 1.54 (s, 3H); 1.14 (s, 9H).
	b)	$\delta = 8.2-8.4$ (m, 1H); $7.65-7.9$ (m, 2H); $7.3-7.6$ (m, 4H); $5.6-6.1$ (AB-portion of an ABX_2 -system, $J = 15 + 2 \times 5.5$ Hz, 2H); 3.92 (s, 2H); 3.16 (d, 2H; $J = 5.5$ Hz); 2.25 (s, 3H); 1.4 (br, OH); 1.26 (s, 3H); 0.96 (s, 9H).
Y)	a)	$\alpha = 8.2-8.35$ (m, 1H); $7.6-7.9$ (m, 4H); $7.2-7.6$ (m, 7H); 4.0 (s, 2H); 3.4 (s, 2H); 2.65 (br, OH); 2.4 (s, 3H); 1.85 (s, 3H).
	b)	$8.15-8.35$ (m, 1H); $7.65-7.9$ (m, 2H); $7.2-7.6$ (m, 9H); $5.6-6.1$ (AB-portion of an ABX_2 -system, $J = 15$ Hz + 2×5.5 Hz, 2H); 3.88 (s, 2H); 3.13 (d, $J = 5.5$ Hz, 2H); 2.24 (s, 3H); 2.0 (s, OH); 1.65 (s, 3H).



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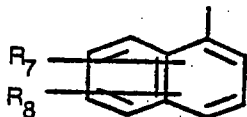
Claims for the Contracting States: BE CH DE FR GB IT LI LU NL SE

1. A compound of formula I,



wherein

a) R_1 represents a group of formula



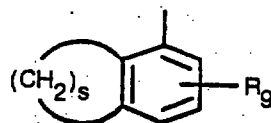
IIa



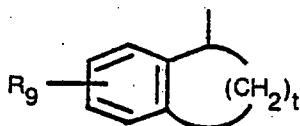
IIb



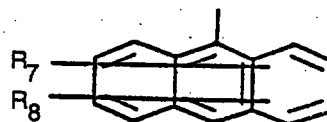
IIc



IIId

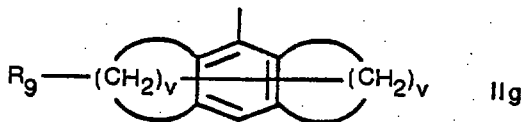


IIe



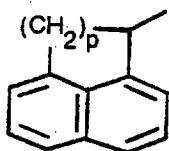
IIIf

or

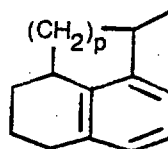


IIg

and R_2 represents hydrogen or C_1-C_4 alkyl, or R_1 and R_2 together represent a group of formula



IIh



III

whereby in the formula IIa to III,

R_7 and R_8 represent, independently, hydrogen, fluorine, chlorine, bromine, trifluoromethyl, hydroxy, nitro, C_1-C_4 alkyl or C_1-C_4 alkoxy,

R_9 represents hydrogen, fluorine, chlorine, bromine, hydroxy, C_1-C_4 alkyl or C_1-C_4 alkoxy,

X represents oxygen, sulphur, imino, C_1-C_4 alkyl imino or a radical of formula $-(CH_2)_r-$,

p is 1, 2 or 3,

r is 1, 2 or 3,

s is 3, 4 or 5,

t is 2, 3 or 4, and

v is 3, 4, 5 or 6;

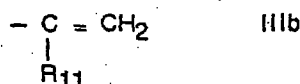
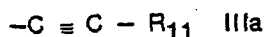
R_3 and R_5 represent, independently, hydrogen or C_1-C_4 alkyl, and

R_4 represents C_1-C_8 alkyl or C_3-C_8 cycloalkyl- (C_1-C_6) -alkyl; and

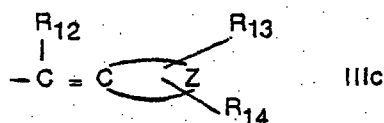


(57)

R_6 represents a group of formula



or



wherein

R_{11} represents hydrogen, optionally α -hydroxy substituted C_{1-12} alkyl; C_{3-6} alkenyl, C_{3-6} alkynyl, cycloalkyl, cycloalkylalkyl, phenyl, phenalkyl or thienyl,

R_{12} , R_{13} and R_{14} represent, independently, hydrogen or C_{1-4} alkyl; and

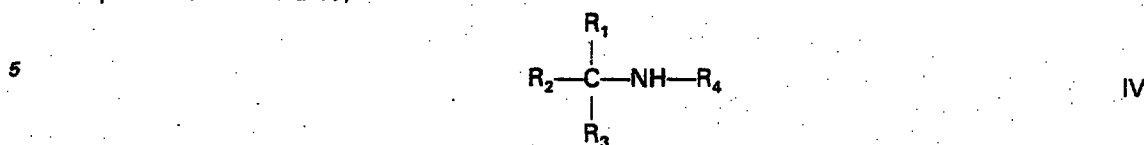
$=C \begin{array}{l} \nearrow \\ \searrow \end{array} Z$ represents a C_{5-8} cycloalkylidene radical optionally containing a double bond; or

- b) R_1 represents a group of formula IIa to IIg as defined under a),
- R_2 represents hydrogen or C_{1-4} alkyl,
- R_3 and R_4 together form a group $-(CH_2)_u-$, wherein u is an integer of 1 to 8, and R_5 and R_6 have the meanings given under a).
2. A compound as claimed in Claim 1 wherein
- a) R_1 represents a group of the formula IIa, IIb, IIc,
- R_2 represents hydrogen,
- R_3 represents hydrogen,
- R_4 represents C_{1-4} alkyl,
- R_5 represents hydrogen or C_{1-4} alkyl, or
- R_3 and R_4 together form a group $-(CH_2)_u-$ or
- b) wherein R_1 and R_2 together represent a group of the formula IIh,
- R_3 represents hydrogen,
- R_4 represents C_{1-4} alkyl,
- R_5 represents C_{1-4} alkyl and
- R_6 is as defined in Claim 1.
3. A compound as claimed in Claim 1 or Claim 2 wherein R_6 represents a group of formula IIIa as defined in Claim 1.
4. A compound as claimed in any one of Claims 1 to 3 wherein R_1 represents a group of formula IIa as defined in Claim 1.
5. A compound as claimed in any one of Claims 1 to 4 wherein the double bond between the group R_6 and the nitrogen atom is in the trans configuration.
6. A compound as claimed in any one of Claims 1 to 5 wherein R_{11} represents C_{1-12} alkyl, C_{3-6} alkenyl, C_{3-6} alkynyl, cycloalkylalkyl, phenyl or phenalkyl and all other substituents are as defined in Claim 1.
7. A compound as claimed in any one of Claims 1 to 5 wherein R_{11} represents C_{2-4} alkyl, C_{3-4} alkenyl, C_{3-4} alkynyl, cyclopentyl, cyclohexyl, cyclopentyl(C_{1-2})alkyl, cyclohexyl(C_{1-2})alkyl, phenyl, phenyl(C_{1-2})alkyl or thienyl.
8. N-Methyl-N-(1-naphthylmethyl)-non-2(trans)-en-4-ynyl-1-amine.
9. N-Methyl-N-(1-naphthylmethyl)-6,6-dimethylhept-2(trans)-en-4-ynyl-1-amine.
10. A compound as claimed in any one of Claims 1 to 9 in the form of an acid addition salt thereof.
11. A compound as claimed in any one of Claims 1 to 9 in the form of its hydrochloride.
12. A chemotherapeutical composition comprising a compound as claimed in any one of Claims 1 to 9 or a chemotherapeutically acceptable acid addition salt thereof in admixture with a chemotherapeutically acceptable diluent or carrier.
13. A compound as claimed in any one of Claims 1 to 9 or a chemotherapeutically acceptable acid addition salt thereof for use as a chemotherapeutic agent.
14. A compound as claimed in any one of Claims 1 to 9 or a chemotherapeutically acceptable acid addition salt thereof for use as an antimycotic agent.
15. A process for the production of compounds of formula I as defined in Claim 1 which comprises



48

a) when R_6 represents a group of formula IIIa, as defined above, (compound Ia), reacting a compound of formula IV,

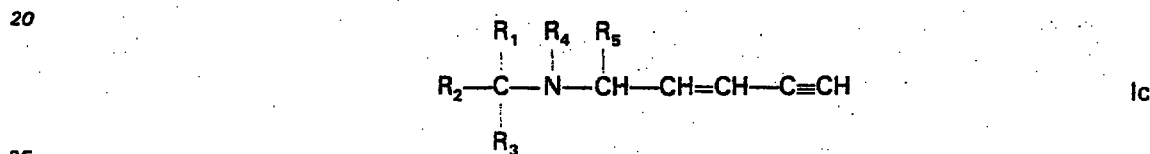


10 wherein R_1 to R_4 are as defined above, with a compound of formula V,

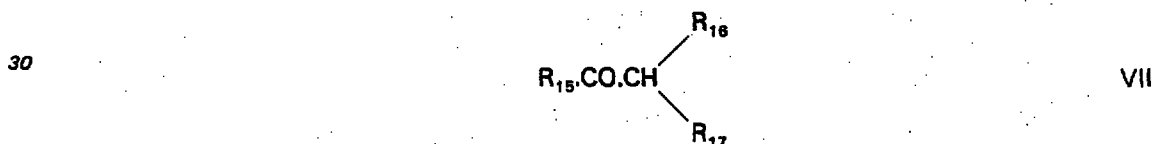


15 wherein A is a leaving group, R_5 is as defined above, and R_6' stands for a group of formula IIIa, as defined above, or

b) when R_6 represents a group of formula IIIa, wherein R_{11} represents $C_{1-12}\alpha$ -hydroxyalkyl (compounds Ib), reacting a metalated compound of formula Ic,

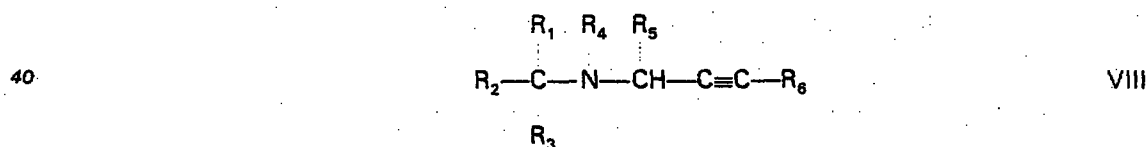


wherein R_1 to R_5 are as defined above, with a carbonyl compound of formula VII,



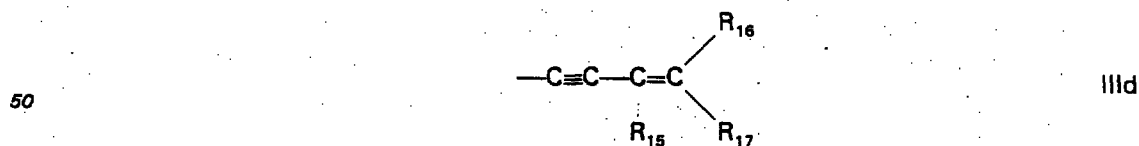
wherein R_{15} , R_{16} and R_{17} represent independently hydrogen or C_{1-4} alkyl, or

35 c) when the double bond between R_5 and the nitrogen atom is in trans configuration (compounds Id) reducing a compound of formula VIII,

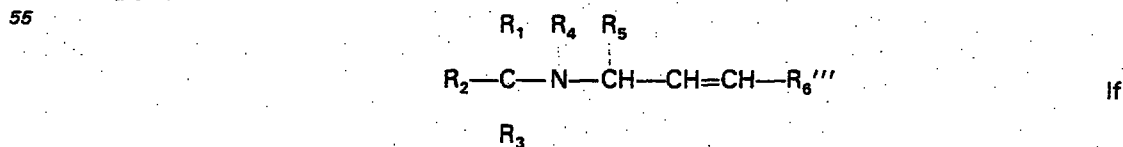


wherein R_1 to R_6 are as defined above, with diisobutylaluminiumhydride, or

45 d) when R_6 represents a group of IIIb or IIIc as defined above or a group of formula IIId,



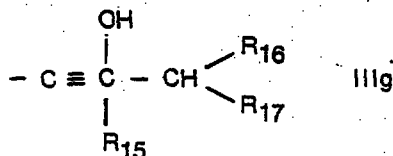
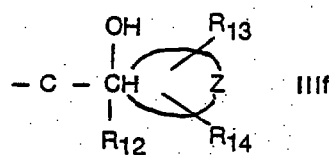
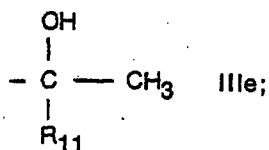
wherein R_{15} , R_{16} and R_{17} are as defined above (compounds Ie) splitting off water from a compound of formula If





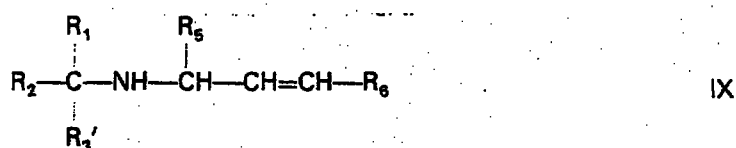
99

wherein R_1 to R_5 are as defined above, and R_6''' represents a group of formula IIIe, IIIf, or IIIg,



wherein R_{11} to R_{17} and Z are as defined above, or

e) when R_3 represents hydrogen or C_{1-4} alkyl and R_4 represents C_{1-6} alkyl or C_{3-8} cycloalkyl- (C_{1-6}) alkyl (compounds Ig), introducing, in manner conventional for the hydrocarbonylation of secondary amines, the group R_4' into a compound of formula IX,



wherein

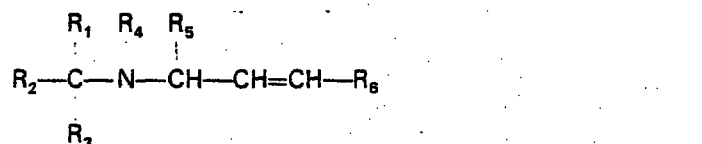
R_1 , R_2 , R_5 and R_6 are as defined above,

$R_{3'}$ represents hydrogen or C_{1-4} alkyl, and

R_4' represents C_{1-6} alkyl or C_{3-8} cycloalkyl- (C_{1-6}) alkyl.

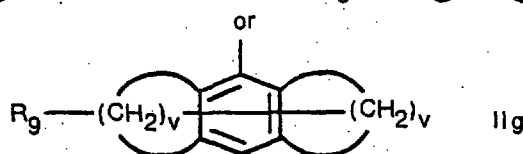
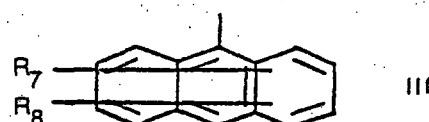
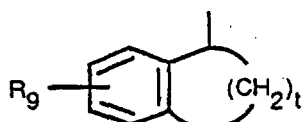
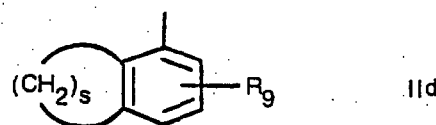
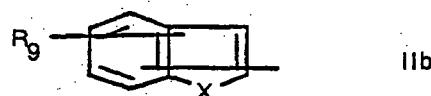
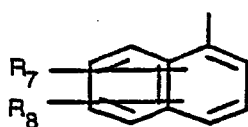
Claims for the Contracting State: AT

1. A process for preparing a compound of formula I



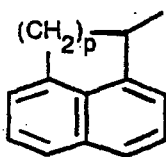
wherein

a) R_1 represents a group of formula

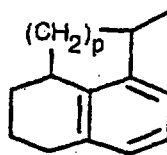




and R_2 represents hydrogen or C_1-C_4 alkyl, or R_1 and R_2 together represent a group of formula



IIh



III

10 whereby in the formulae IIa to III,

R_7 and R_8 represent, independently, hydrogen, fluorine, chlorine, bromine, trifluoromethyl, hydroxy, nitro, C_{1-4} alkyl or C_{1-4} alkoxy,

R_9 represents hydrogen, fluorine, chlorine, bromine, hydroxy, C_{1-4} alkyl or C_{1-4} alkoxy,

X represents oxygen, sulphur, imino, C_{1-4} alkyl imino or a radical of formula $-(CH_2)_r-$,

15 p is 1, 2 or 3,

r is 1, 2 or 3,

s is 3, 4 or 5,

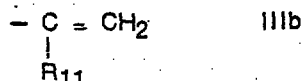
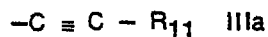
t is 2, 3 or 4, and

v is 3, 4, 5 or 6;

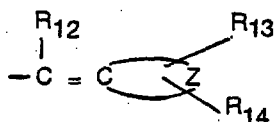
20 R_3 and R_5 represent, independently, hydrogen or C_{1-4} alkyl, and

R_4 represents C_{1-6} alkyl or C_{3-6} cycloalkyl- (C_{1-6}) -alkyl; and

R_6 represents a group of formula



or



wherein

35 R_{11} represents hydrogen, optionally α -hydroxy substituted C_{1-12} alkyl; C_{3-6} alkenyl, C_{3-6} alkynyl, cycloalkyl, cycloalkylalkyl, phenyl, phenalkyl or thienyl,

R_{12} , R_{13} and R_{14} represent, independently, hydrogen or C_{1-4} alkyl, and

$=C \text{---} Z$ represents a C_{5-6} cycloalkylidene radical optionally containing a double bond; or

b) R_1 represents a group of formula IIa to IIg as defined under a),

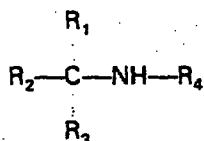
40 R_2 represents hydrogen or C_{1-4} alkyl,

R_3 and R_4 together form a group $-(CH_2)_u-$, wherein u is an integer of 1 to 8, and

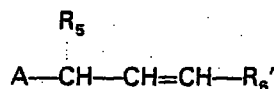
R_5 and R_6 have the meanings given under a),

which comprises

45 a) when R_6 represents a group of formula IIIa, as defined above, (compound Ia), reacting a compound of formula IV,



wherein R_1 to R_4 are as defined above, with a compound of formula V,

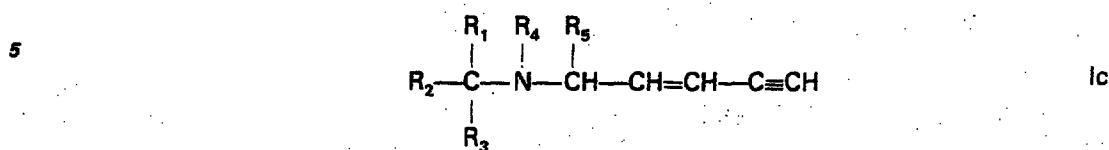


wherein A is a leaving group, R_5 is as defined above, and R_6' stands for a group of formula IIIa, as defined above, or

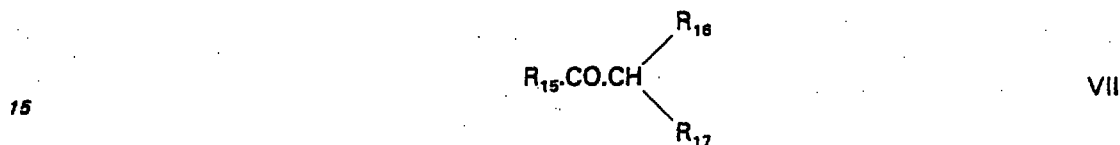


51

b) when R_6 represents a group of formula IIIa, wherein R_{11} represents $C_{1-12}\alpha$ -hydroxyalkyl (compounds Ib), reacting a metalated compound of formula Ic,

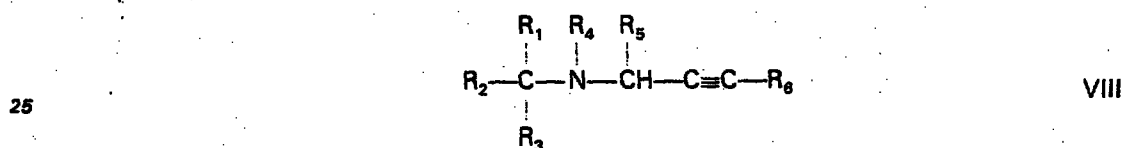


10 wherein R_1 to R_5 are as defined above, with a carbonyl compound of formula VII,



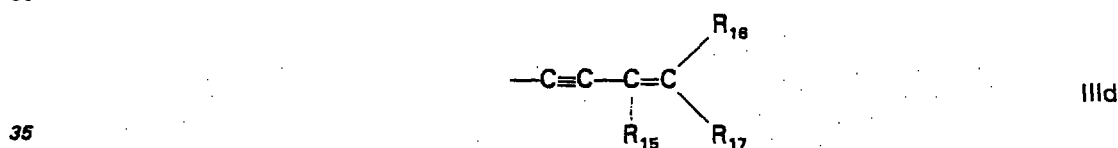
wherein R_{15} , R_{16} and R_{17} represent independently hydrogen or C_{1-4} alkyl, or

c) when the double bond between R_6 and the nitrogen atom is in trans configuration (compounds 20 Id) reducing a compound of formula VIII,

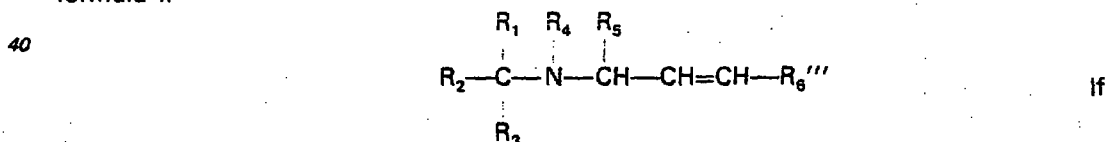


wherein R_1 to R_6 are as defined above, with diisobutylaluminiumhydride, or

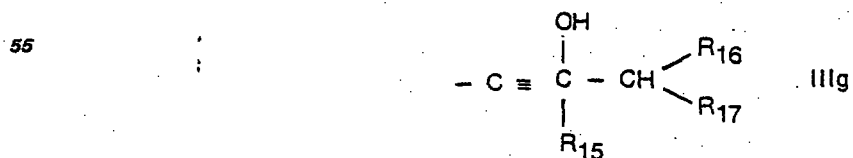
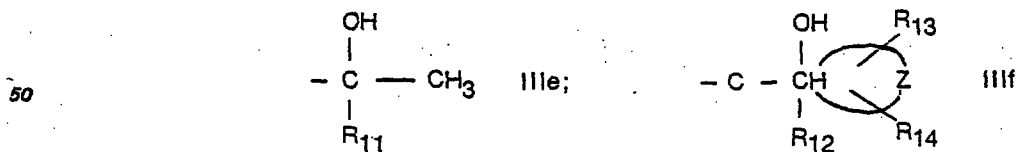
d) when R_6 represents a group of IIIb or IIIc as defined above or a group of formula IIId, 30



wherein R_{15} , R_{16} and R_{17} are as defined above (compounds Ie) splitting off water from a compound of formula If



45 wherein R_1 to R_5 are as defined above, and R_6''' represents a group of formula IIIe, IIIf, or IIIg,



60 wherein R_{11} to R_{17} and Z are as defined above, or

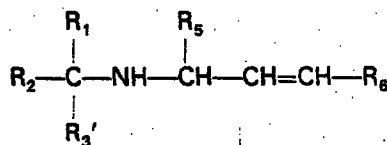
e) when R_3 represents hydrogen or C_{1-4} alkyl and R_4 represents C_{1-6} alkyl or C_{3-8} cycloalkyl-

65



(C₁₋₈)alkyl (compounds Ig), introducing, in manner conventional for the hydrocarbonylation of secondary amines, the group R₄' into a compound of formula IX,

5



IX

10 wherein

R₁, R₂, R₅ and R₆ are as defined above,
R₃' represents hydrogen or C₁₋₄alkyl, and
R₄' represents C₁₋₆alkyl or C₃₋₈cycloalkyl(C₁₋₈)alkyl.

2. A process according to Claim 1, wherein

15 a) R₁ represents a group of the formula IIa, IIb, IIc,

R₂ represents hydrogen,

R₃ represents hydrogen,

R₄ represents C₁₋₄alkyl,

R₅ represents hydrogen or C₁₋₄alkyl, or

20 R₃ and R₄ together form a group —(CH₂)_u— or

b) wherein R₁ and R₂ together represent a group of the formula IIh,

R₃ represents hydrogen,

R₄ represents C₁₋₄alkyl,

R₅ represents C₁₋₄alkyl and

25 R₆ is as defined in Claim 1.

3. A process according to Claim 1 or Claim 2 wherein R₆ represents a group of formula IIIa as defined in Claim 1.

4. A process according to any one of Claims 1 to 3 wherein R₁ represents a group of formula IIa as defined in Claim 1.

30 5. A process according to any one of Claims 1 to 4 wherein the double bond between the group R₆ and the nitrogen atom is in the trans configuration.

6. A process according to any one of Claims 1 to 5 wherein R₁₁ represents C₁₋₁₂alkyl, C₃₋₆alkenyl, C₃₋₈alkynyl, cycloalkylalkyl, phenyl or phenalkyl and all other substituents are as defined in Claim 1.

35 7. A process according to any one of Claims 1 to 5 wherein R₁₁ represents C₂₋₄alkyl, C₃₋₄alkenyl, C₃₋₄alkynyl, cyclopentyl, cyclohexyl, cyclopentyl(C₁₋₂)alkyl, cyclohexyl(C₁₋₂)alkyl, phenyl, phenyl(C₁₋₂)alkyl or thienyl.

8. A process according to Claim 1, wherein the compound obtained is N-methyl-N-(1-naphthylmethyl)-non-2(trans)-en-4-ynyl-1-amine.

40 9. A process according to Claim 1 wherein the compound obtained is N-methyl-N-(1-naphthylmethyl)-6,6-dimethyl-hept-2(trans)-en-4-ynyl-1-amine.

10. A process according to any one of Claims 1 to 9 wherein the product is obtained in the form of an acid addition salt thereof.

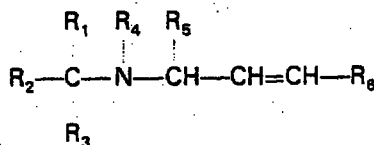
11. A process according to any one of Claims 1 to 9 wherein the compound is obtained in the form of its hydrochloride.

45 12. A compound of formula I defined in Claim 1, whenever prepared by a process according to any one of Claims 1 to 11.

13. A chemotherapeutical composition comprising a compound according to Claim 12 or a chemotherapeutically acceptable acid addition salt thereof in admixture with a chemotherapeutically acceptable diluent or carrier.

50 14. A process for preparing a chemotherapeutic composition which comprises admixing a compound of formula I

55



I

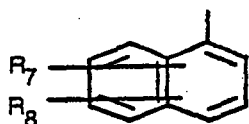
wherein

60

65



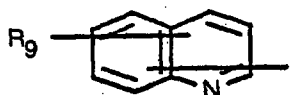
a) R_1 represents a group of formula



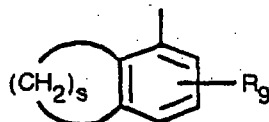
IIa



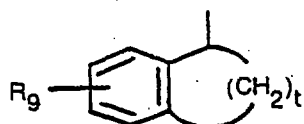
IIb



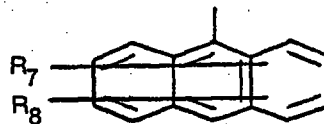
IIc



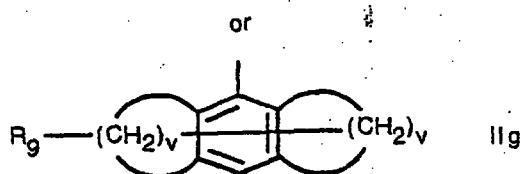
IIId



IIe

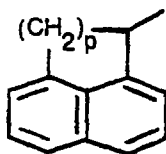


IIIf

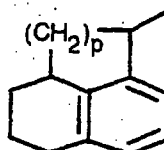


IIg

and R_2 represents hydrogen or C_1-C_4 alkyl, or R_1 and R_2 together represent a group of formula



IIh



IIIi

whereby in the formulae IIa to IIIi,

R_7 and R_8 represent, independently, hydrogen, fluorine, chlorine, bromine, trifluoromethyl, hydroxy, nitro, C_1-C_4 alkyl or C_1-C_4 alkoxy,

R_9 represents hydrogen, fluorine, chlorine, bromine, hydroxy, C_1-C_4 alkyl or C_1-C_4 alkoxy,

X represents oxygen, sulphur, imino, C_1-C_4 alkyl imino or a radical of formula $-(CH_2)_r-$,

p is 1, 2 or 3,

r is 1, 2 or 3,

s is 3, 4 or 5,

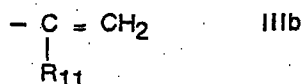
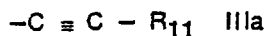
t is 2, 3 or 4, and

v is 3, 4, 5 or 6;

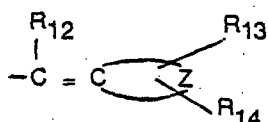
R_3 and R_5 represent, independently, hydrogen or C_1-C_4 alkyl, and

R_4 represents C_1-C_6 alkyl or C_3-C_8 cycloalkyl- (C_1-C_6) -alkyl; and

R_6 represents a group of formula



or



IIIc

wherein

R_{11} represents hydrogen, optionally α -hydroxy substituted C_1-C_{12} alkyl; C_3-C_6 alkenyl, C_3-C_6 alkynyl, cycloalkyl, cycloalkylalkyl, phenyl, phenalkyl or thienyl,



R_{12} , R_{13} and R_{14} represent, independently, hydrogen or C_{1-4} alkyl, and

$\text{=C} \begin{array}{c} \text{---} \end{array} \text{Z}$ represents a C_{5-8} cycloalkylidene radical optionally containing a double bond; or

5 b) R_1 represents a group of formula IIa to IIg as defined under a),

R_2 represents hydrogen or C_{1-4} alkyl,

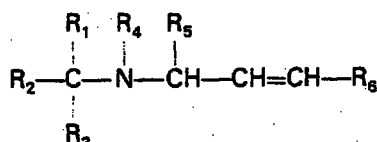
R_3 and R_4 together form a group $-(CH_2)_u-$, wherein u is an integer of 1 to 8, and

R_5 and R_6 have the meanings given under a),

10 in free base form or in the form of a chemotherapeutically acceptable acid-addition together with a chemotherapeutically acceptable diluent or carrier.

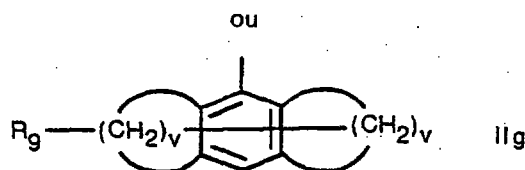
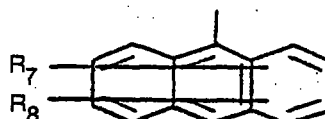
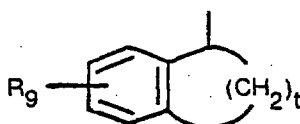
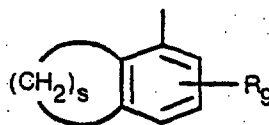
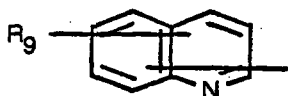
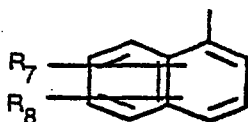
Revendications pour les Etats contractants: BE CH DE FR GB IT LI LU NL SE

15 1. Un composé de formule I,

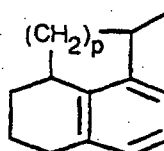
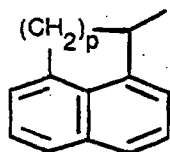


dans laquelle

a) R_1 représente un groupe de formule



50 et R_2 représente l'hydrogène ou C_{1-4} -alkyle,
ou R_1 et R_2 représentent ensemble un groupe de formule



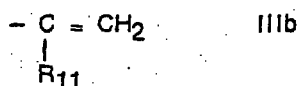
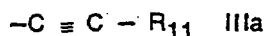
60 dans les formules IIa à III,

R_7 et R_8 représentant, indépendamment, l'hydrogène, le fluor, le chlore, le brome, trifluorométhyle, hydroxy, nitro, C_{1-4} -alkyle ou C_{1-4} -alcoxy,

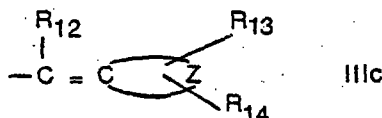
65 R_9 représentant l'hydrogène, le fluor, le chlore, le brome, hydroxy, C_{1-4} -alkyle ou C_{1-4} -alcoxy,



X représentant l'oxygène, le soufre, imino, C₁₋₄-alkyl-imino ou un radical de formule $-(CH_2)_p-$,
 p signifiant 1, 2 ou 3,
 r signifiant 1, 2 ou 3,
 signifiant 3, 4 ou 5,
 5 t signifiant 2, 3 ou 4, et
 v signifiant 3, 4, 5 ou 6,
 R₃ et R₅ représentent, indépendamment, l'hydrogène ou C₁₋₄-alkyle, et
 R₄ représente C₁₋₆-alkyle ou C₃₋₈-cycloalkyl-(C₁₋₆)-alkyle, et
 R₆ représente un groupe de formule



ou



20 dans lesquelles

R₁₁ représente l'hydrogène, C₁₋₁₂-alkyle éventuellement substitué en α par hydroxy, C₃₋₈-alcényle, C₃₋₆-alcynyle, cycloalkyle, cycloalkylalkyle, phényle, phénalkyle ou thiényl,

R₁₂, R₁₃ et R₁₄ représentent, indépendamment, l'hydrogène ou C₁₋₄-alkyle, et

25 $=C \begin{array}{c} \diagup \\ Z \\ \diagdown \end{array}$ représente un radical C₅₋₈-cycloalkylidène contenant éventuellement une double liaison, ou

b) R¹ représente un groupe de formule IIa à IIg tel que défini sous a),

R₂ représente l'hydrogène ou C₁₋₄-alkyle,

R₃ et R₄ forment ensemble un groupe $-(CH_2)_u-$, dans lequel u est un nombre entier de 1 à 8, et

30 R₅ et R₆ ont les significations données sous a).

2. Un composé tel que revendiqué à la revendication 1, dans lequel

a) R₁ représente un groupe de formule IIa, IIb, IIc,

R₂ représente l'hydrogène,

R₃ représente l'hydrogène,

35 R₄ représente C₁₋₄-alkyle,

R₅ représente l'hydrogène ou C₁₋₄-alkyle, ou

R₃ et R₄ forment ensemble un groupe $-(CH_2)_u-$ ou

b) R₁ et R₂ représentent ensemble un groupe de formule IIh,

R₃ représente l'hydrogène,

40 R₄ représente C₁₋₄-alkyle,

R₅ représente C₁₋₄-alkyle et

R₆ est tel que défini à la revendication 1.

3. Un composé tel que revendiqué à la revendication 1 ou 2, dans lequel R₆ représente un groupe de formule IIIa tel que défini à la revendication 1.

45 4. Un composé tel que revendiqué à l'une quelconque des revendications 1 à 3, dans lequel R₁ représente un groupe de formule IIa tel que défini à la revendication 1.

5. Un composé tel que revendiqué à l'une quelconque des revendications 1 à 4, dans lequel la double liaison entre le groupe R₆ et l'atome d'azote est de configuration trans.

6. Un composé tel que revendiqué à l'une quelconque des revendications 1 à 5, dans lequel R₁₁ représente C₁₋₁₂-alkyle, C₃₋₈-alcényle, C₃₋₆-alcynyle, cycloalkylalkyle, phényle ou phénalkyle et tous les autres substituants sont tels que définis à la revendication 1.

7. Un composé tel que revendiqué à l'une quelconque des revendications 1 à 5, dans lequel R₁₁ représente C₂₋₄-alkyle, C₃₋₄-alcényle, C₃₋₄-alcynyle, cyclopentyle, cyclohexyle, cyclopentyl(C₁₋₂)alkyle, cyclohexyl(C₁₋₂)alkyle, phényle, phényl(C₁₋₂)alkyle ou thiényl.

55 8. La N-méthyl-N-(1-naphtylméthyl)-non-2-(trans)-ène-4-ynyl-1-amine.

9. La N-méthyl-N-(1-naphtylméthyl)-6,6-diméthyl-hept-2(trans)-ène-4-ynyl-1-amine.

10. Un composé tel que revendiqué à l'une quelconque des revendications 1 à 9 sous forme d'un sel d'addition d'acide de ce composé.

60 11. Un composé tel que revendiqué à l'une quelconque des revendications 1 à 9 sous forme de son chlorhydrate.

12. Une composition chimiothérapeutique comprenant un composé tel que revendiqué à l'une quelconque des revendications 1 à 9 ou un sel d'addition d'acide chimiothérapeutiquement acceptable de ce composé, en mélange avec un diluant ou véhicule chimiothérapeutiquement acceptable.

65 13. Un composé tel que revendiqué à l'une quelconque des revendications 1 à 9 ou un sel

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R_1 à R_4 sont que définis plus haut, avec un composé de formule V,



25



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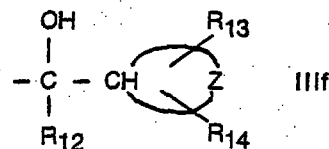
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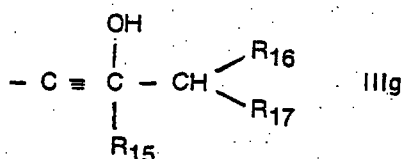
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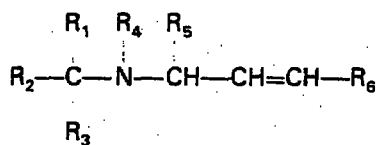


R_1 , R_2 , R_5 et R_6 sont tels que définis plus haut,
 R_3' représente l'hydrogène ou C_{1-4} -alkyle, et
 R_4' représente C_{1-6} -alkyle ou C_{3-8} -cycloalkyl- (C_{1-6}) alkyle.

40

1. Un procédé de préparation d'un composé de formule I

45



50

a) R_1 représente un groupe de formule

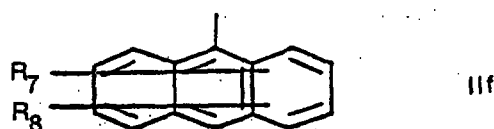
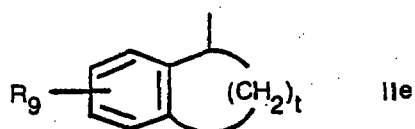
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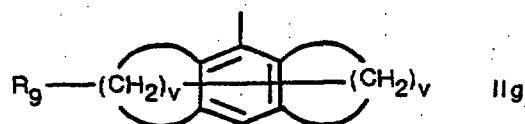


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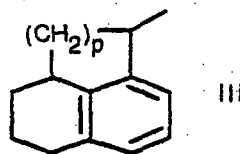
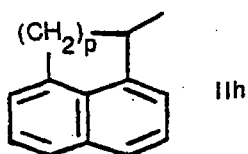
ou

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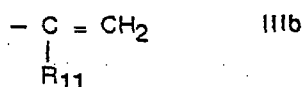
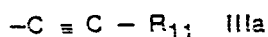
et R₂ représente l'hydrogène ou C₁₋₄-alkyle,
15 ou R₁ et R₂ représentent ensemble un groupe de formule

20



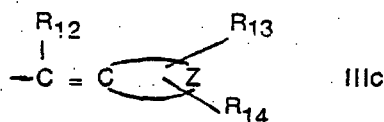
dans les formules IIa à III,

- 25 R₇ et R₈ représentant, indépendamment, l'hydrogène, le fluor, le chlore, le brome, trifluoro-
méthyle, hydroxy, nitro, C₁₋₄-alkyle ou C₁₋₄-alcoxy,
R₉ représentant l'hydrogène, le fluor, le chlore, le brome, hydroxy, C₁₋₄-alkyle ou C₁₋₄-alcoxy,
X représentant l'oxygène, le soufre, imino, C₁₋₄-alkyl-imino ou un radical de formule $-(CH_2)_r-$,
30 p signifiant 1, 2 ou 3,
r signifiant 1, 2 ou 3,
s signifiant 3, 4 ou 5,
t signifiant 2, 3 ou 4, et
v signifiant 3, 4, 5 ou 6,
35 R₃ et R₅ représentant, indépendamment, l'hydrogène ou C₁₋₄-alkyle, et
R₄ représente C₁₋₆-alkyle ou C₃₋₈-cycloalkyl-(C₁₋₆)-alkyle, et
R₆ représente un groupe de formule



ou

45



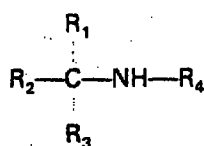
dans lesquelles

- 50 R₁₁ représente l'hydrogène, C₁₋₁₂-alkyle éventuellement substitué en α par hydroxy, C₃₋₈-alcényle,
C₃₋₈-alcynyle, cycloalkyle, cycloalkylalkyle, phényle, phénalkyle ou thiényle,
R₁₂, R₁₃ et R₁₄ représentent, indépendamment, l'hydrogène ou C₁₋₄-alkyle, et

$=C \text{---} Z$ représente un radical C₅₋₈-cycloalkylidène contenant éventuellement une double liaison, ou

- b) R₁ représente un groupe de formule IIa à IIg tel que défini sous a),
55 R₂ représente l'hydrogène ou C₁₋₄-alkyle,
R₃ et R₄ forment ensemble un groupe $-(CH_2)_u-$, dans lequel u est un nombre entier de 1 à 8, et
R₅ et R₆ ont les significations données sous a),
qui comprend

- a) lorsque R₆ représente un groupe de formule IIIa, tel que défini plus haut, (composé Ia) la
60 réaction d'un composé de formule IV,



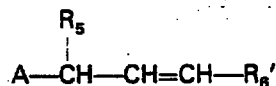
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dans laquelle

R_1 à R_4 sont que définis plus haut, avec un composé de formule V,

5



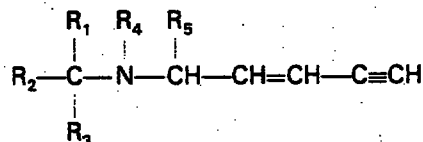
V

dans laquelle

A est un groupe éliminable, R_5 est tel que défini plus haut, et R_6' signifie un groupe de formule IIIa, tel que défini plus haut, ou

b) lorsque R_6 représente un groupe de formule IIIa, dans laquelle R_{11} représente C_{1-12} - α -hydroxyalkyle (composés Ib), la réaction d'un composé résultant de la métallation d'un composé de formule Ic,

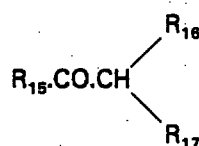
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Ic

20 dans laquelle R_1 à R_5 sont tels que définis plus haut, avec un composé carbonylé de formule VII,

25

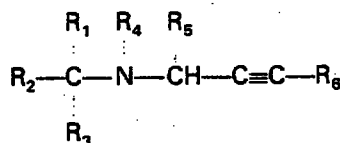


VII

dans laquelle R_{15} , R_{16} et R_{17} représentent indépendamment l'hydrogène ou C_{1-4} -alkyle, ou

30 c) lorsque la double liaison entre R_6 et l'atome d'azote est de configuration trans (composés Id), la réduction d'un composé de formule VIII,

35

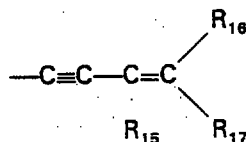


VIII

dans laquelle R_1 à R_6 sont tels que définis plus haut, avec l'hydrure de diisobutylaluminium, ou

40 d) lorsque R_6 représente un groupe de formule IIIb ou IIIc tel que défini plus haut ou un groupe de formule IIId,

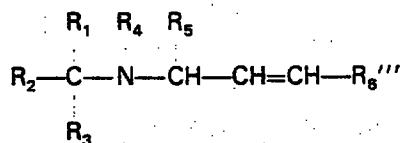
45



IIId

dans laquelle R_{15} , R_{16} et R_{17} sont tels que définis plus haut (composés Ie), l'élimination d'eau à partir d'un composé de formule If

50



If

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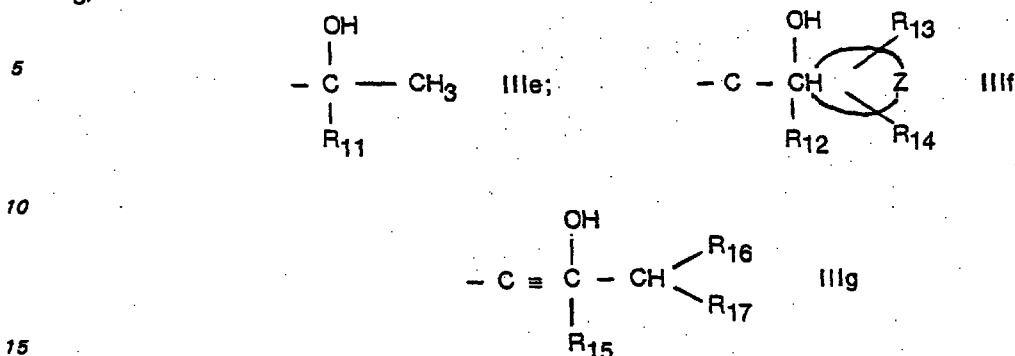
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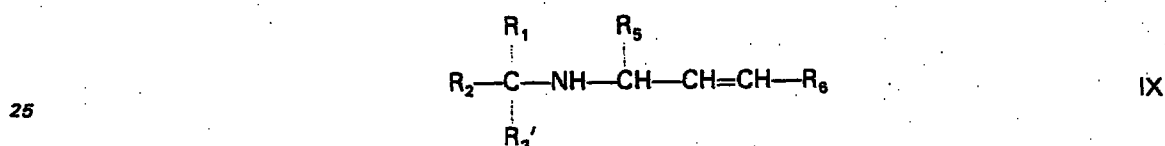
dans laquelle R_1 à R_5 sont tels que définis plus haut, et R_6''' représente un groupe de formule IIIe, IIIf, ou IIIg,



dans lesquelles R_{11} à R_{17} et Z sont tels que définis plus haut, ou

e) lorsque R_3 représente l'hydrogène ou C_{1-4} -alkyle et R_4 représente C_{1-8} -alkyle ou C_{3-8} -cycloalkyl- (C_{1-8}) alkyle (composés Ig) l'introduction, selon les méthodes habituelles pour l'hydrocarburation

20 d'amines secondaires, du groupe R_4' dans un composé de formule IX,



dans laquelle

R_1 , R_2 , R_5 et R_6 sont tels que définis plus haut,

R_3' représente l'hydrogène ou C_{1-4} -alkyle, et

R_4' représente C_{1-8} -alkyle ou C_{3-8} -cycloalkyl- (C_{1-8}) alkyle.

2. Un procédé selon la revendication 1, dans lequel

a) R_1 représente un groupe de formule IIa, IIb, IIc,

R_2 représente l'hydrogène,

R_3 représente l'hydrogène,

R_4 représente C_{1-4} -alkyle,

R_5 représente l'hydrogène ou C_{1-4} -alkyle, ou

R_3 et R_4 forment ensemble un groupe $-(CH_2)_n-$ ou

b) R_1 et R_2 représentent ensemble un groupe de formule IIh,

R_3 représente l'hydrogène,

R_4 représente C_{1-4} -alkyle,

R_5 représente C_{1-4} -alkyle et

R_6 est tel que défini à la revendication 1.

3. Un procédé selon la revendication 1 ou 2, dans lequel R_6 représente un groupe de formule IIIa tel que défini à la revendication 1.

4. Un procédé selon l'une quelconque des revendications 1 à 3, dans lequel R_1 représente un groupe de formule IIa tel que défini à la revendication 1.

5. Un procédé selon l'une quelconque des revendications 1 à 4, dans lequel la double liaison entre le groupe R_6 et l'atome d'azote est de configuration trans.

6. Un composé selon l'une quelconque des revendications 1 à 5, dans lequel R_{11} représente C_{1-12} -alkyle, C_{3-8} -alcényle, C_{3-8} -alcynyle, cycloalkylalkyle, phényle ou phénaalkyle et tous les autres substituants sont tels que définis à la revendication 1.

7. Un composé selon l'une quelconque des revendications 1 à 5, dans lequel R_{11} représente C_{2-4} -alkyle, C_{3-4} -alcényle, C_{3-4} -alcynyle, cyclopentyle, cyclohexyle, cyclopentyl- (C_{1-2}) alkyle, cyclohexyl- (C_{1-2}) alkyle, phényle, phényl- (C_{1-2}) alkyle ou thiényl.

8. Un procédé selon la revendication 1, dans lequel le composé obtenu est la N-méthyl-N-(1-naphtylméthyl)-non-2(trans)-ène-4-ynyl-1-amine.

9. Un procédé selon la revendication 1, dans lequel le composé obtenu est la N-méthyl-N-(1-naphtylméthyl)-6,6-diméthylhept-2(trans)-ène-4-ynyl-1-amine.

10. Un procédé selon l'une quelconque des revendications 1 à 9, dans lequel le produit obtenu est sous forme d'un sel d'addition d'acide de ce composé.

11. Un procédé selon l'une quelconque des revendications 1 à 9, dans lequel le composé est obtenu sous forme de son chlorhydrate.

12. Un composé de formule I défini à la revendication 1, préparé par un procédé selon l'une quelconque des revendications 1 à 11.

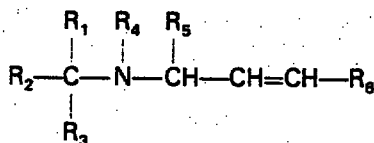
13. Une composition chimiothérapeutique comprenant un composé selon la revendication 12 ou



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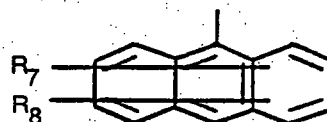
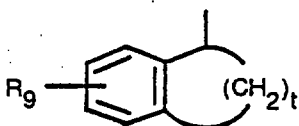
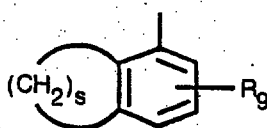
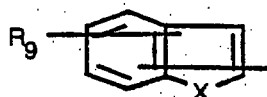
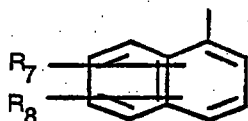
un sel d'addition d'acide chimiothérapeutiquement acceptable de ce composé, en mélange avec un diluant ou véhicule chimiothérapeutiquement acceptable.

14. Un procédé de préparation d'une composition chimiothérapeutique qui comprend l'admixtion d'un composé de formule I

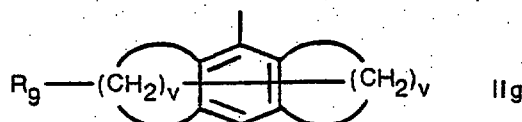


dans laquelle

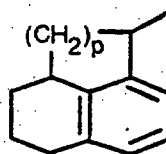
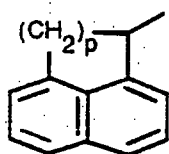
a) R_1 représente un groupe de formule



ou



et R_2 représente l'hydrogène ou C_{1-4} -alkyle,
ou R_1 et R_2 représentent ensemble un groupe de formule



dans les formules IIa à III,

R_7 et R_8 représentant, indépendamment, l'hydrogène, le fluor, le chlore, le brome, trifluorométhyle, hydroxy, nitro, C_{1-4} -alkyle ou C_{1-4} -alcoxy,

R_9 représentant l'hydrogène, le fluor, le chlore, le brome, hydroxy, C_{1-4} -alkyle ou C_{1-4} -alcoxy,

X représentant l'oxygène, le soufre, imino, C_{1-4} -alkyl-imino ou un radical de formule $-(CH_2)_r-$,

p signifiant 1, 2 ou 3,

r signifiant 1, 2 ou 3,

s signifiant 3, 4 ou 5,

t signifiant 2, 3 ou 4, et

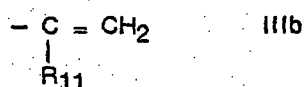
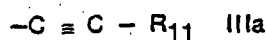
v signifiant 3, 4, 5 ou 6,

R_3 et R_5 représentant, indépendamment, l'hydrogène ou C_{1-4} -alkyle, et

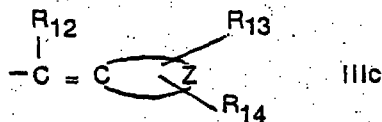
R_4 représente C_{1-6} -alkyle ou C_{3-6} -cycloalkyl- (C_{1-6}) alkyle, et



R₆ représente un groupe de formule



ou



dans lesquelles

R₁₁ représente l'hydrogène, C₁₋₁₂-alkyle éventuellement substitué en α par hydroxy, C₃₋₆-alcényle, C₃₋₆-alcynyle, cycloalkyle, cycloalkylalkyle, phényle, phénalkyle ou thiényl,

R₁₂, R₁₃ et R₁₄ représentent, indépendamment, l'hydrogène ou C₁₋₄-alkyle, et

Z représente un radical C₅₋₈-cycloalkylidène contenant éventuellement une double liaison, ou

b) R₁ représente un groupe de formule IIa à IIg tel que défini sous a),

R₂ représente l'hydrogène ou C₁₋₄-alkyle,

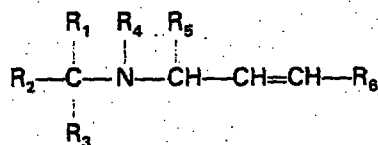
R₃ et R₄ forment ensemble un groupe $-(CH_2)_u-$, dans lequel u est un nombre entier de 1 à 8, et

R₅ et R₆ ont les significations données sous a),

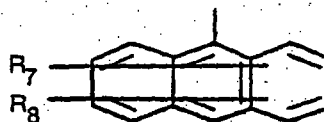
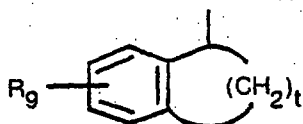
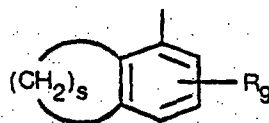
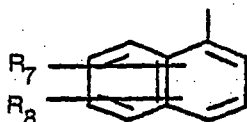
sous forme de base libre ou sous forme d'un sel d'addition d'acide chimiothérapeutiquement acceptable, ensemble avec un diluant ou véhicule chimiothérapeutiquement acceptable.

Patentansprüche für die Vertragsstaaten: BE CH DE FR GB IT LI LU NL SE

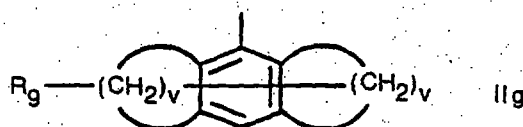
1. Eine Verbindung der Formel I



worin a) R₁ eine Gruppe der Formel



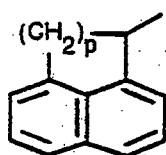
oder



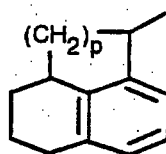


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darstellt und R_2 Wasserstoff oder C_{1-4} Alkyl darstellt, oder R_1 und R_2 zusammen eine Gruppe der Formel



IIh



III

10 darstellen, wobei in den Formeln IIa bis II:

R_7 und R_8 unabhängig Wasserstoff, Fluor, Chlor, Brom, Trifluormethyl, Hydroxy, Nitro, C_{1-4} Alkyl oder C_{1-4} Alkoxy darstellen,

R_9 Wasserstoff, Fluor, Chlor, Brom, Hydroxy, C_{1-4} Alkyl oder C_{1-4} Alkoxy darstellt,

X Sauerstoff, Schwefel, Imino, C_{1-4} Alkylimino oder einen Rest der Formel $-(CH_2)_r-$ darstellt,

15 p ist 1, 2 oder 3,

r ist 1, 2 oder 3,

s ist 3, 4 oder 5,

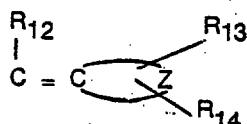
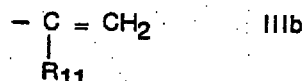
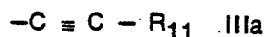
t ist 2, 3 oder 4, und

v ist 3, 4, 5 oder 6;

20 R_3 und R_5 unabhängig Wasserstoff oder C_{1-4} Alkyl darstellen, und

R_4 C_{1-6} Alkyl oder C_{3-6} Cycloalkyl- (C_{1-6}) -Alkyl; darstellt und

R_6 eine Gruppe der Formel



IIIc

darstellt, worin

35 R_{11} Wasserstoff, gegebenenfalls α -Hydroxy substituiertes C_{1-12} Alkyl; C_{3-6} Alkenyl, C_{3-6} Alkynyl, Cycloalkyl, Cycloalkylalkyl, Phenyl, Phenalkyl oder Thienyl,

R_{12} , R_{13} und R_{14} unabhängig Wasserstoff oder C_{1-4} Alkyl und

$=C \begin{array}{c} \diagup \\ \diagdown \end{array} Z$ einen C_{5-8} Cycloalkylidenrest darstellt der gegebenenfalls eine Doppelbindung enthält oder

40 b) R_1 eine Gruppe der Formel IIa bis IIg wie unter a) definiert darstellt,

R_2 Wasserstoff oder C_{1-4} Alkyl darstellt,

R_3 und R_4 zusammen ein $-(CH_2)_u$ -Gruppe bilden, worin u eine ganze Zahl von 1 bis 8 ist und R_5 und R_6 die unter a) aufgeführten Bedeutungen haben.

2. Eine Verbindung wie im Anspruch 1 beansprucht, worin

45 a) R_1 eine Gruppe der Formel IIa, IIb, IIc, darstellt,

R_2 Wasserstoff darstellt,

R_3 Wasserstoff darstellt,

R_4 C_{1-4} Alkyl darstellt,

50 R_5 Wasserstoff oder C_{1-4} Alkyl darstellt, oder

R_3 und R_4 zusammen eine $-(CH_2)_u$ -Gruppe bilden oder

b) worin R_1 und R_2 zusammen eine Gruppe der Formel IIh darstellen

R_3 Wasserstoff darstellt,

R_4 C_{1-4} Alkyl darstellt,

R_5 C_{1-4} Alkyl darstellt und

55 R_6 wie im Anspruch 1 definiert ist.

3. Eine Verbindung wie im Anspruch 1 oder Anspruch 2 beansprucht, worin R_6 eine Gruppe der Formel IIIa wie im Anspruch 1 definiert darstellt.

4. Eine Verbindung wie in einem der Ansprüche 1 bis 3 beansprucht, worin R_1 eine Gruppe der Formel IIa wie im Anspruch 1 definiert darstellt.

60 5. Eine Verbindung wie in einem der Ansprüche 1 bis 4 beansprucht, worin die Doppelbindung zwischen der Gruppe R_6 und dem Stickstoffatom in Trans-Konfiguration ist.

6. Eine Verbindung wie in einem der Ansprüche 1 bis 5 beansprucht, worin R_{11} C_{1-12} Alkyl, C_{3-6} Alkenyl, C_{3-6} Alkynyl, Cycloalkylalkyl, Phenyl oder Phenalkyl darstellt und alle anderen Substituenten wie im Anspruch 1 definiert sind.

65 7. Eine Verbindung wie in einem der Ansprüche 1 bis 5 beansprucht, worin R_{11} C_{2-4} Alkyl,

WA

9. N-Methyl-N-(1-naphthylmethyl)-6,6-dimethyl-hept-2(trans)-en-4-ynyl-1-amin.

11. Eine Verbindung wie in einem der Ansprüche 1 bis 9 in Form ihres Hydrochlorids.

10 schung mit einem chemotherapeutisch annehmbaren Verdünner oder Träger.

14. Eine Verbindung wie in einem der Ansprüche 1 bis 9 beansprucht oder ein chemotherapeutisch annehmbares Salz derselben zur Verwendung als antimycotisches Mittel.

a) wenn R_6 eine Gruppe der Formel IIIa wie oben definiert darstellt (Verbindung Ia), Umsetzung einer Verbindung der Formel IV:



V

b) wenn R_6 eine Gruppe der Formel IIa darstellt worin R_{11} $C_{1-12}\alpha$ -Hydroxyalkyl (Verbindungen Ib) darstellt, Umsetzung einer metallierten Verbindung der Formel Ic

lc

vii

c) wenn die Doppelbindung zwischen R₆ und dem Stickstoffatom in Trans-Konfiguration ist (Verbindungen Id), Reduzierung einer Verbindung der Formel VIII

viii

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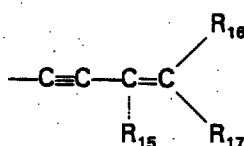


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0 024 587

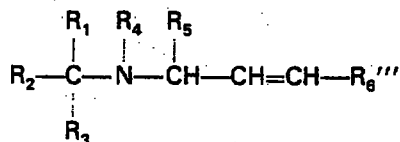
d) wenn R_6 eine Gruppe der Formel IIIb oder IIIc wie oben definiert oder eine Gruppe der Formel IIId darstellt

5



III d

10 worin R_{15} , R_{16} und R_{17} wie oben definiert sind, (Verbindungen Ie), Abspaltung vom Wasser aus einer Verbindung der Formel If

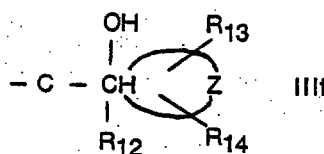
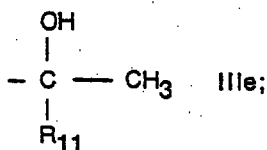


If

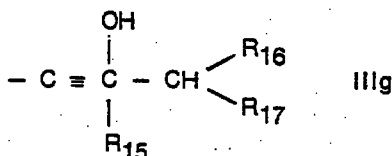
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worin R_1 bis R_5 wie oben definiert sind und R_6''' eine Gruppe der Formel IIIe, IIIf, oder IIIg, darstellt

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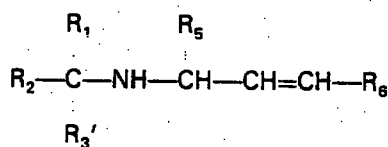


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worin R_{11} bis R_{17} und Z wie oben definiert sind, oder

35 e) wenn R_3 Wasserstoff oder C_{1-4} Alkyl und R_4 C_{1-6} Alkyl oder C_{3-8} Cycloalkyl- (C_{1-6}) alkyl (Verbindungen Ig) darstellt, Einführung, auf eine für die Hydrocarbylierung von sekundären Aminen übliche Weise, der Gruppe R_4' in eine Verbindung der Formel IX

40



IX

worin

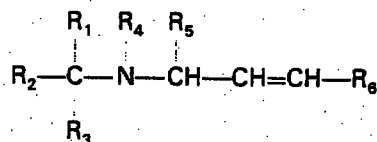
45 R_1 , R_2 , R_5 und R_6 wie oben definiert sind,
 R_3' Wasserstoff oder C_{1-4} Alkyl, darstellt und
 R_4' C_{1-6} Alkyl oder C_{3-8} Cycloalkyl- (C_{1-6}) alkyl, darstellt.

Patentansprüche für den Vertragsstaat: AT

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1. Ein Verfahren zur Herstellung einer Verbindung der Formel I

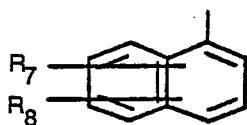
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I

worin a) R_1 eine Gruppe der Formel

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II a

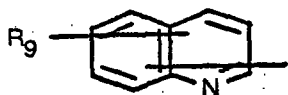
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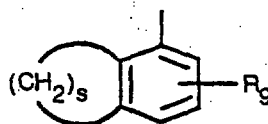
II b



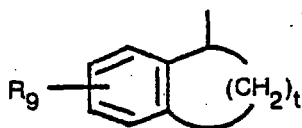
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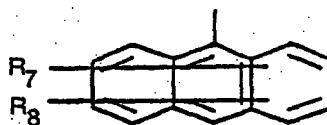
IIc



IIId

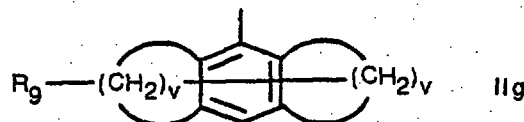


IIe



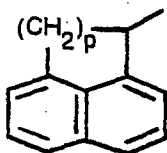
IIIf

oder

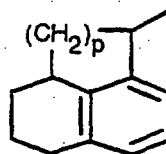


IIg

darstellt und R_2 Wasserstoff oder C_{1-4} Alkyl darstellt, oder R_1 und R_2 zusammen eine Gruppe der Formel



IIh



IIi

30 darstellen, wobei in den Formeln IIa bis IIi:

R_7 und R_8 unabhängig Wasserstoff, Fluor, Chlor, Brom, Trifluormethyl, Hydroxy, Nitro, C_{1-4} Alkyl oder C_{1-4} Alkoxy darstellen,

R_9 Wasserstoff, Fluor, Chlor, Brom, Hydroxy, C_{1-4} Alkyl oder C_{1-4} Alkoxy darstellt,

X Sauerstoff, Schwefel, Imino, C_{1-4} Alkylimino oder einen Rest der Formel $-(CH_2)_r-$ darstellt,

35 p ist 1, 2 oder 3,

r ist 1, 2 oder 3,

s ist 3, 4 oder 5,

t ist 2, 3 oder 4, und

v ist 3, 4, 5 oder 6;

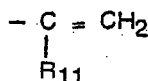
40 R_3 und R_5 unabhängig Wasserstoff oder C_{1-4} Alkyl darstellen, und

R_4 C_{1-8} Alkyl oder C_{3-8} Cycloalkyl- (C_{1-6}) -Alkyl; darstellt und

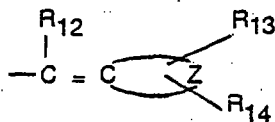
R_6 eine Gruppe der Formel



IIIa



IIIb



IIIc

darstellt, worin

55 R_{11} Wasserstoff, gegebenenfalls α -Hydroxy substituiertes C_{1-12} Alkyl; C_{3-6} Alkenyl, C_{3-8} Alkynyl, Cycloalkyl, Cycloalkylalkyl, Phenyl, Phenalkyl oder Thienyl,

R_{12} , R_{13} und R_{14} unabhängig Wasserstoff oder C_{1-4} Alkyl und

$=C \text{---} Z$ einen C_{5-8} Cycloalkylenrest darstellt der gegebenenfalls eine Doppelbindung enthält oder

60 b) R_1 eine Gruppe der Formel IIa bis IIg wie unter a) definiert darstellt,

R_2 Wasserstoff oder C_{1-4} Alkyl darstellt,

R_3 und R_4 zusammen ein $-(CH_2)_u$ -Gruppe bilden, worin u eine ganze Zahl von 1 bis 8 ist und

R_5 und R_6 die unter a) aufgeführten Bedeutungen haben,

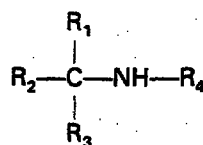
bestehend aus



67

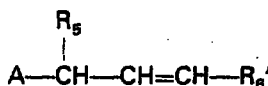
a) wenn R_6 eine Gruppe der Formel IIIa wie oben definiert darstellt (Verbindung Ia), Umsetzung einer Verbindung der Formel IV

5



IV

10 worin R_1 bis R_4 wie oben definiert sind mit einer Verbindung der Formel V



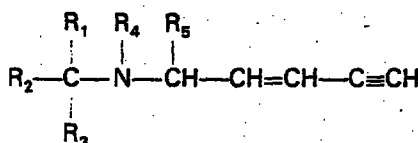
V

15

worin A eine abspaltbare Gruppe ist, R_5 wie oben definiert ist und R_6' für eine Gruppe der Formel IIIa wie oben definiert, steht, oder

b) wenn R_6 eine Gruppe der Formel IIa darstellt worin R_{11} $C_{1-12}\alpha$ -Hydroxyalkyl (Verbindungen Ib) darstellt, Umsetzung einer metallierten Verbindung der Formel Ic

20

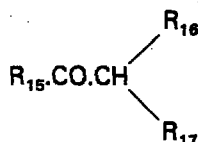


Ic

25

worin R_1 bis R_5 wie oben definiert sind, mit einer Carbonylverbindung der Formel VII

30

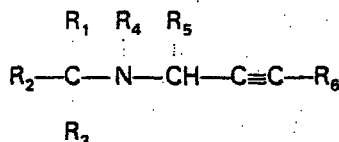


VII

35 worin R_{15} , R_{16} und R_{17} unabhängig Wasserstoff oder C_{1-4} Alkyl darstellen, oder

c) wenn die Doppelbindung zwischen R_6 und dem Stickstoffatom in Trans-Konfiguration ist (Verbindungen Id), Reduzierung einer Verbindung der Formel VIII

40

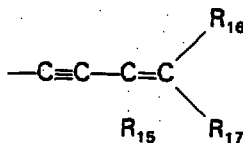


VIII

45 worin R_1 bis R_6 wie oben definiert sind mit Diisobutylaluminiumhydrid, oder

d) wenn R_6 eine Gruppe der Formel IIIb oder IIIc wie oben definiert oder eine Gruppe der Formel IIId darstellt

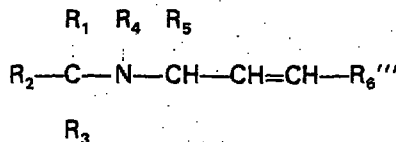
50



IIId

55 worin R_{15} , R_{16} und R_{17} wie oben definiert sind, (Verbindungen Ie), Abspaltung vom Wasser aus einer Verbindung der Formel If

60



If

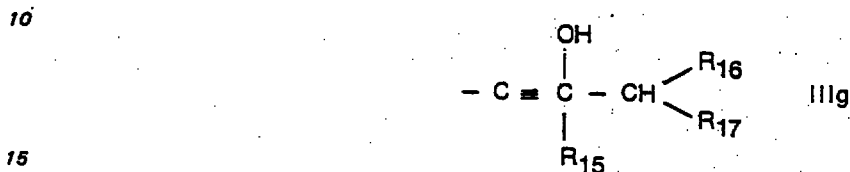
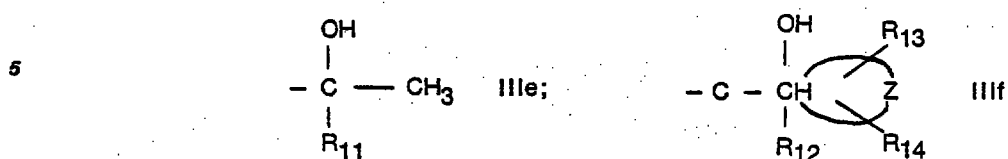
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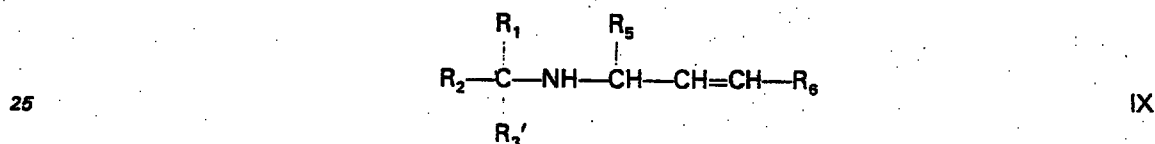
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worin R_1 bis R_5 wie oben definiert sind und R_6''' eine Gruppe der Formel IIIe, IIIf, oder IIIg, darstellt



worin R_{11} bis R_{17} und Z wie oben definiert sind, oder
e) wenn R_3 Wasserstoff oder C_{1-4} Alkyl und R_4 C_{1-8} Alkyl oder C_{3-8} Cycloalkyl- (C_{1-6}) alkyl (Verbindungen Ig) darstellt, Einführung, auf eine für die Hydrocarbonylierung von sekundären Aminen übliche
20 Weise, der Gruppe R_4' in eine Verbindung der Formel IX



worin

30 R_1, R_2, R_5 und R_6 wie oben definiert sind,
 R_3' Wasserstoff oder C_{1-4} Alkyl, darstellt und
 R_4' C_{1-6} Alkyl oder C_{3-8} Cycloalkyl- (C_{1-6}) alkyl, darstellt.

2. Ein Verfahren gemäss Anspruch 1 worin

a) R_1 eine Gruppe der Formel IIa, IIb, IIc, darstellt,

R_2 Wasserstoff darstellt,

35 R_3 Wasserstoff darstellt,

R_4 C_{1-4} Alkyl darstellt,

R_5 Wasserstoff oder C_{1-4} Alkyl darstellt, oder

R_3 und R_4 zusammen eine $-(CH_2)_n$ -Gruppe bilden oder

b) worin R_1 und R_2 zusammen eine Gruppe der Formel IIh darstellen

40 R_3 Wasserstoff darstellt,

R_4 C_{1-4} Alkyl darstellt,

R_5 C_{1-4} Alkyl darstellt und

R_6 wie im Anspruch 1 definiert ist.

3. Ein Verfahren gemäss Anspruch 1 oder Anspruch 2 beansprucht, worin R_6 eine Gruppe der
45 Formel IIIa wie im Anspruch 1 definiert darstellt.

4. Ein Verfahren gemäss einem der Ansprüche 1 bis 3 beansprucht, worin R_1 eine Gruppe der
Formel IIa wie im Anspruch 1 definiert darstellt.

5. Ein Verfahren gemäss einem der Ansprüche 1 bis 4 beansprucht, worin die Doppelbindung
zwischen der Gruppe R_6 und dem Stickstoffatom in Trans-Konfiguration ist.

50 6. Ein Verfahren gemäss einem der Ansprüche 1 bis 5 beansprucht, worin R_{11} C_{1-12} Alkyl,
 C_{3-6} Alkenyl, C_{3-6} Alkynyl, Cycloalkylalkyl, Phenyl oder Phenalkyl darstellt und alle anderen Substituenten
wie im Anspruch 1 definiert sind.

7. Ein Verfahren gemäss einem der Ansprüche 1 bis 5 beansprucht, worin R_{11} C_{2-4} Alkyl,
 C_{3-4} Alkenyl, C_{3-4} Alkynyl, Cyclopentyl, Cyclohexyl, Cyclopentyl- (C_{1-2}) alkyl, Cyclohexyl- (C_{1-2}) alkyl, Phenyl,
55 Phenyl- (C_{1-2}) alkyl oder Thienyl, darstellt.

8. Ein Verfahren gemäss Anspruch 1, worin die erhaltene Verbindung N-Methyl-N-(1-naphthylmethyl)-non-2(trans)-en-4-ynyl-1-amin ist.

9. Ein Verfahren gemäss Anspruch 1, worin die erhaltene Verbindung N-Methyl-N-(1-naphthylmethyl)-6,6-dimethylhept-2(trans)-en-4-ynyl-1-amin ist.

60 10. Ein Verfahren gemäss einem der Ansprüche 1 bis 9 worin das Produkt in Form eines Säureadditionssalzes derselben erhalten wird.

11. Ein Verfahren gemäss einem der Ansprüche 1 bis 9 worin die Verbindung in Form deren Hydrochlorid erhalten wird.

12. Ein Verbindung der Formel I wie im Anspruch 1 definiert wenn nach einem Verfahren gemäss
65 einem der Ansprüche 1 bis 11 hergestellt.

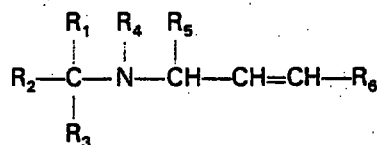


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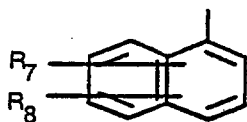
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13. Eine chemotherapeutische Zusammensetzung enthaltend eine Verbindung gemäss Anspruch 12 oder ein chemotherapeutisch annehmbares Salz derselben in Beimischung mit einem chemotherapeutisch annehmbaren Verdünner oder Träger.

14. Ein Verfahren zur Herstellung einer chemotherapeutischen Zusammensetzung bestehend aus die Beimischung einer Verbindung der Formel I



worin a) R_1 eine Gruppe der Formel



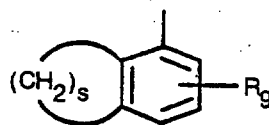
IIa



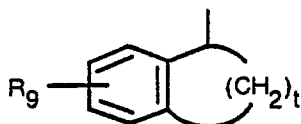
IIb



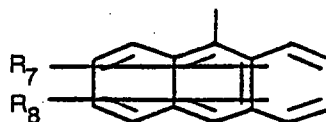
IIc



IIId

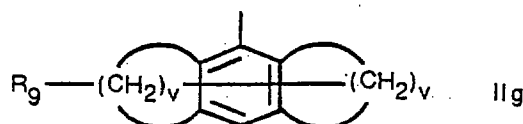


IIe



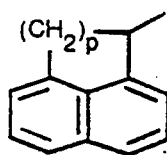
IIIf

oder

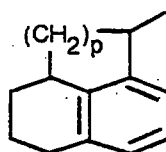


IIg

darstellt und R_2 Wasserstoff oder C_{1-4} Alkyl darstellt, oder R_1 und R_2 zusammen eine Gruppe der Formel



IIh



IIi

darstellen, wobei in den Formeln IIa bis IIi:

R_7 und R_8 unabhängig Wasserstoff, Fluor, Chlor, Brom, Trifluormethyl, Hydroxy, Nitro, C_{1-4} alkyl oder C_{1-4} Alkoxy darstellen,

R_9 Wasserstoff, Fluor, Chlor, Brom, Hydroxy, C_{1-4} Alkyl oder C_{1-4} Alkoxy darstellt,

X Sauerstoff, Schwefel, Imino, C_{1-4} Alkylimino oder einen Rest der Formel $-(CH_2)_r-$ darstellt,

p ist 1, 2 oder 3,

r ist 1, 2 oder 3,

s ist 3, 4 oder 5,

t ist 2, 3 oder 4, und

v ist 3, 4, 5 oder 6;

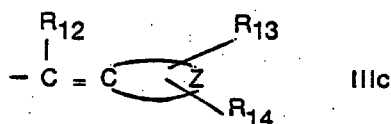
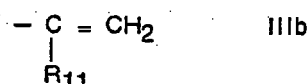
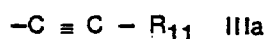
R_3 und R_5 unabhängig Wasserstoff oder C_{1-4} Alkyl darstellen, und

R_4 C_{1-6} Alkyl oder C_{3-6} Cycloalkyl- (C_{1-6}) -Alkyl; darstellt und



(16)

R_6 eine Gruppe der Formel



darstellt, worin

R_{11} Wasserstoff, gegebenenfalls α -Hydroxy substituiertes C_{1-12} Alkyl; C_{3-6} Alkenyl, C_{3-6} Alkynyl, Cycloalkyl, Cycloalkylalkyl, Phenyl, Phenalkyl oder Thienyl,

R_{12} , R_{13} und R_{14} unabhängig Wasserstoff oder C_{1-4} Alkyl und

$=C \text{---} Z$ einen C_{5-8} Cycloalkylidenrest darstellt der gegebenenfalls eine Doppelbindung enthält oder

b) R_1 eine Gruppe der Formel IIa bis IIg wie unter a) definiert darstellt,

R_2 Wasserstoff oder C_{1-4} Alkyl darstellt,

R_3 und R_4 zusammen ein $-(CH_2)_u$ -Gruppe bilden, worin u eine ganze Zahl von 1 bis 8 ist und R_5 und R_6 die unter a) aufgeführten Bedeutungen haben,

in Form der freien Base oder in Form eines chemotherapeutisch annehmbaren Säureadditionssalzes zusammen mit einem chemotherapeutisch annehmbaren Verdünner oder Träger.