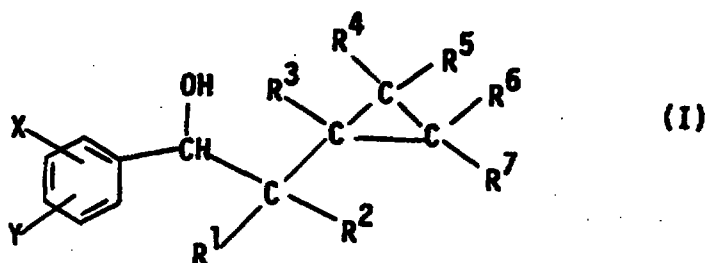


Description

The invention described herein relates to a process for preparing certain cyclopropane derivatives useful as chemical intermediates in the preparation of agricultural products. More particularly it relates to alpha-aryl-alpha-cyclopropylalkyl-1H-azolyl ethanols including the imidazolyl and 1,2,4-triazolyl ethanols known to be useful as fungicides. It also relates to certain of the cyclopropane precursors themselves which are novel compounds.

Fungicidal alpha-aryl-alpha-cyclopropylalkyl-1H-azolyl ethanols are disclosed in GB-A-2136423. One process described for making them involves starting with an aryl cyclopropylalkyl methanol. Unfortunately, such compounds are not readily prepared by conventional methods.

A common method for preparing secondary and tertiary alcohols is to treat a Grignard reagent with an aldehyde or a ketone. In applying this method to the compounds of interest difficulties arise with the cyclopropylalkyl Grignard reagent. For example, 1-cyclopropylethyl bromide rearranges to the homoallylic bromide making it difficult to prepare the Grignard reagent required for the cyclopropylethyl compound. Further, it has been found that when the cyclopropylethyl Grignard reagent is reacted with an alpha-aryl-1H-1,2,4-triazole ethanone, the unsaturated alcohol is formed in admixture with the desired product. According to the present invention there is provided a process for the preparation of a compound of the general formula (I):



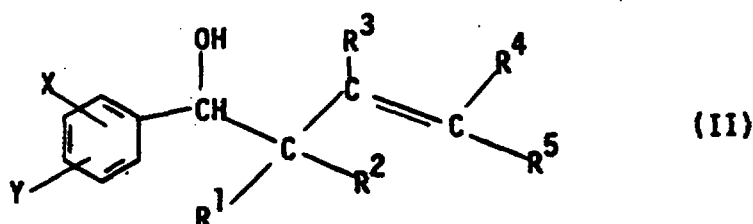
wherein

X is hydrogen, halogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted aralkyl, alkoxy or optionally substituted aryloxy,

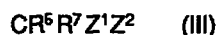
Y is halogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted aralkyl, alkoxy or optionally substituted aryloxy,

and

R¹ to R⁷ are independently hydrogen or C₁₋₆ alkyl, which comprises treating a compound of the general formula (II):



wherein X, Y and R¹ to R⁵ have the meanings given before, with a compound of the general formula (III):



wherein R⁶ and R⁷ have the meanings given before,

and Z¹ and Z², which are the same or different, are halogen in the presence of metallic zinc in an ether solvent.

Alkyl groups and the alkyl moieties of alkoxy and aralkyl groups can be in the form of straight or branched chains and contain preferably 1 to 6, more preferably 1 to 4, carbon atoms. Examples are methyl, ethyl, *n*-propyl, *n*- and *t*-butyl and moieties thereof. Examples of haloalkyl groups are trichloro- and trifluoromethyl.

Cycloalkyl groups include C₃₋₆cycloalkyl and cycloalkylalkyl groups include C₃₋₆cycloalkyl(C₁₋₄)alkyl. Examples are cyclopropyl, cyclohexyl and 1-cyclopropylethyl.

Alkenyl and alkynyl groups contain preferably 2 to 6, more preferably 2 to 4, carbon atoms in the form of straight or branched chains. Examples are ethenyl, allyl and propargyl.

Aryl groups and the aryl moieties of aralkyl and aryloxy groups are preferably phenyl which may be substituted with one or more of the following: halogen, C₁₋₄alkyl (especially methyl and ethyl), C₁₋₄-alkoxy (especially methoxy), haloalkyl (especially trifluoromethyl) and haloalkoxy (especially trifluoromethoxy).

Halogen, as a value of X and Y or as a substituent in any other value of X is preferably chlorine or fluorine. The halogen values of Z¹ and Z² are preferably selected from bromine and iodine. Usually Z¹ and Z² will be both bromine or both iodine.

The process of the invention is typically carried out in the presence of metallic zinc catalyst in an ether solvent under anhydrous conditions. The precise conditions will depend, *inter alia*, on the particular reactants involved but generally they will include those known in the literature for the Simmons-Smith reaction (see *Org. React. (NY)*, 1973, 20, 1 and *J.Org.Chem.*, 1985, 50, 4640).

Typically, the process will be carried out in the presence of a zinc-copper couple (see *J.Chem.Soc.*, 1978, p.1025). Zinc-silver, zinc-platinum, and zinc-palladium couples may be substituted for or used in conjunction with the zinc-copper couple (see *J.Org.Chem.*, 1964, 29, 2049).

Other catalysts which may be employed in the process of the invention include the art-recognized nickel and cobalt complexes. Increased yields may be realized if a Lewis acid or alkali halide is used in conjunction with these catalysts. (see *Chemistry Letters*, 1979, pp. 761-762, *Chemistry Letters*, 1981, pp. 395-396, *Bull.Chem.Soc.Jpn.*, 1983, 56, 1025-1029, and 1592-1597).

The catalyst system for the process of this invention may also comprise a zinc-based couple in the further presence of a metallo-hydride reducing agent. Suitable metallo-hydride reducing agents are described in U.S. Patent No. 4,472,313.

While members of the general class of metallo-hydride reducing agents, may be employed, such as lithium aluminium hydride, or alkali metal borohydrides, the preferred metallic hydride reducing agents (VIII) are those which are soluble in the ether medium, and more preferably organometallic hydrides of which preferred classes include those of formula (VIIIa) :



in which

A signifies an alkali metal or one equivalent of an alkaline earth metal, e.g. sodium or lithium; and each of W¹, W² and W³ is, independently, a hydrogen atom, or an alkyl or alkoxy radical of 1 to 6 carbon atoms; or an alkoxyalkoxy or alkyleneoxyalkyl radical having from 2 to 6 carbon atoms;

provided that at least one of W¹, W² and W³ is other than a hydrogen atom; or of formula (VIIIb):



in which

W⁴ and W⁵, which may be the same or different, each signify a a hydrogen atom or an alkyl radical of 1 to 6 carbon atoms;

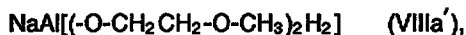
provided that at least one of W⁴ and W⁵ is alkyl.

The alkyl and alkoxy radicals mentioned above in connection with compounds of formulae (VIIIa) and (VIIIb) are understood to include as the alkyl portion thereof methyl, ethyl, propyl, butyl, amyl and hexyl, including isomers where such exist, but are preferably unbranched; and the alkylene (and alkylene portion of alkyleneoxy) radicals are understood to include methylene, ethylene, n-propylene, n-butylene, n-amylene

and n-hexylene radicals, including isomers where they exist, but are preferably unbranched.

With respect to compounds of formula (VIIIa), W^1 , W^2 and W^3 may be the same or different but are preferably the same. With respect to the compounds (VIIIb), W^4 and W^5 may be the same or different, but are preferably the same.

A suitable hydride reagent of formula (VIIIa) is sodium dihydridobis-(2-methoxyethoxy)aluminate (SDBA), which is obtainable commercially under the brand name "Vitride", and has the structure (VIIIa')



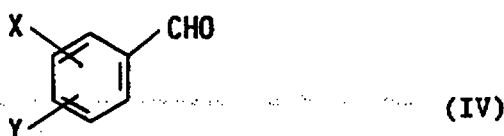
an important property of the hydride (VIIIa') is that it is soluble in a variety of solvents.

In carrying out the process it is preferred that the zinc and compound of general formula (III) each be present in molar excess, e.g. in a molar ratio of from about 2 to 6 times preferably from about 3.5 to 5 that of the compound of general formula (II). The hydride reducing agent (VIII) however, need be present only in catalytic amounts, e.g. from about 0.5% to 3%, preferably from about 1.0 to 2.0%, of the molar amount of the compound of general formula (II).

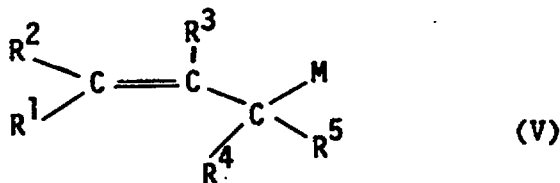
Examples of suitable solvents are diethyl ether, tetrahydrofuran dibutyl ether, dimethoxyethane, toluene, xylene, and mixtures thereof. The reaction may be facilitated by sonocation (the use of ultrasound).

The temperature at which the reaction is carried out will depend largely on the choice of solvent but it will normally be in the range of from 0°C to 150°C, more usually from 10°C to 100°C.

The compound of general formula (II) may be prepared by treating a compound of general formula (IV):



wherein X and Y are as previously defined, with an organometallic reagent of the general formula (V)



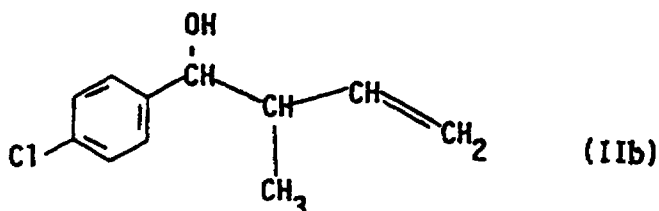
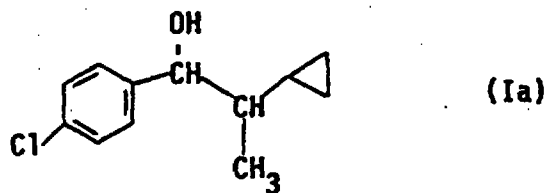
wherein R^1 to R^5 are as previously defined and M is a metal (for example, magnesium, lithium, boron, silicon, tin, chromium, aluminium or titanium). The reaction may be carried out either with or without a catalyst present using conditions described in the relevant literature for carrying out such organometallic reactions.

In particular, compounds of the general formula (II) wherein R^1 is hydrogen or methyl and R^2 to R^5 are hydrogen can be prepared by treating compounds of the general formula (IV) with allylmagnesium chloride or bromide, or crotylmagnesium chloride or bromide, respectively.

In another aspect, the invention includes, in combination, the process steps of :

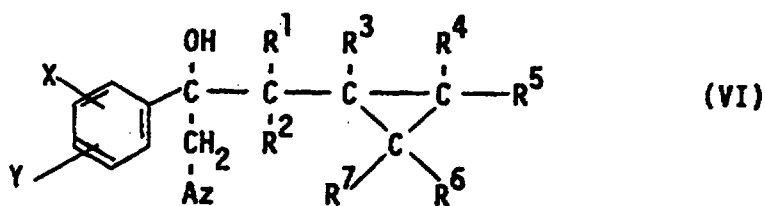
- (a) treating a compound of formula (IV) with an organometallic reagent of formula (V) to form a compound of formula (II); and
- (b) treating the compound of formula (II) with a compound of formula (III) to form a compound of formula (I).

Various compounds of formula I, as well as of formula (II) are believed to be novel and form yet another aspect of the present invention. Specifically, the invention includes the compounds having the formulae (Ia) and (IIb) :



The compounds of the general formulae (IV) and (V) can be prepared by methods described in the literature.

The compounds of the general formula (I) are useful intermediates in the preparation of agricultural products of the formula (VI) :

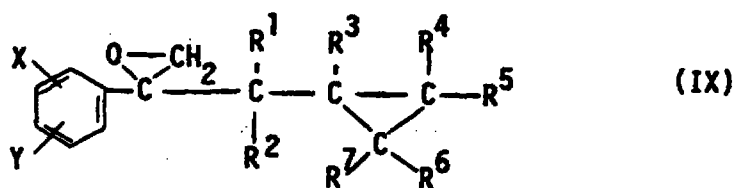


wherein X, Y and R¹ to R⁷ are as defined before, and

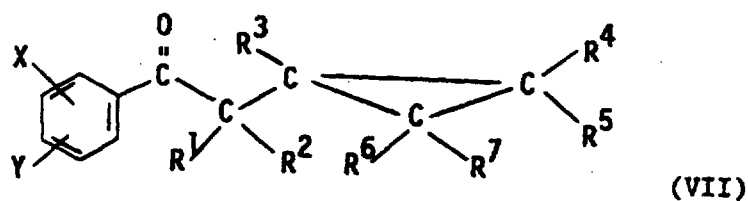
Az is 1H-azolyl.

The products in which Az is 1H-1,2,4-triazolyl or 1H-imidazolyl are known to be useful as fungicides.

The products of formula (VI) may be prepared in a known manner by the reaction, in the presence of a base, of the appropriate azole with an epoxide of the formula (IX)



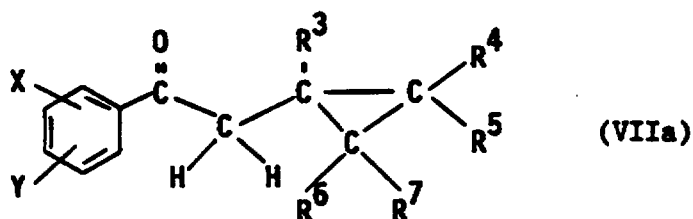
or its halohydrin derivative. The epoxide of formula (IX) and its halohydrin derivative are formed by the epoxidation of a compound of the general formula (VII) :



wherein X, Y and R¹ to R⁷ are as previously defined.

The compounds of general formula (VII) may be obtained by oxidation of the intermediates of formula (I) using a wide variety of oxidising agents, for instance, chromium trioxide in a variety of solvents, pyridinium chlorochromate and pyridinium dichromate, or by the Moffat reaction (dimethylsulphoxide, acetic anhydride and triethylamine) or one of its variations, particularly the Swern variation (dimethylsulphoxide, oxalyl chloride and triethylamine).

In an alternative procedure, compounds of general formula (VII) wherein R³ to R⁷, X and Y are as previously defined and either one or both of R¹ and R² are alkyl groups, may be prepared from compounds of general formula (VIIa) :

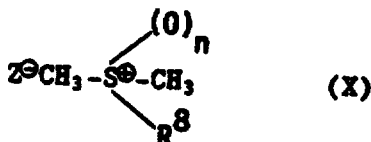


wherein R³ to R⁷ and X and Y are as previously defined,

by treatment with an appropriate base and then with a compound of the formula R¹W wherein R¹ is alkyl and W is a leaving group such as chloride, bromide, iodide, tosylate, mesylate or triflate. If R² is also alkyl the process can be repeated, treating the intermediate compound formed above first with R²W, wherein R² is alkyl and W is as previously defined.

In particular, compounds of the general formula (VII), wherein R¹ is methyl and R² to R⁷ are hydrogen, can be prepared by treating compounds of general formula (VII) wherein R¹ to R⁷ are hydrogen with an appropriate base, for example, sodium hydride or lithium diisopropylamide and then with methyl iodide or methyl bromide at low temperature.

The compounds of formula (IX) may be obtained by reacting the compound of formula (VII) with a compound of formula (X)



wherein

n is 0 or 1,

Z is halogen or methylsulfate,

R⁸ is alkyl,

in the presence of a base.

In general, the procedures for preparing compounds of the formulae (VI) and (IX) from compounds of formula (VII) are known (see, e.g. U.K. Patent 2 129 000).

The invention is illustrated by the following examples in which temperatures are expressed in degrees centigrade and percentages are by weight. The term 'ether' refers to diethyl ether; chromatography was carried out using silica gel as the solid phase; and magnesium sulphate was used to dry solutions. The following abbreviations are used throughout:

g = gramme(s)	s = singlet
mol = mole	d = doublet
mmol = millimole(s)	t = triplet
M = molar	m = multiplet
ml = millilitre(s)	q = quadruplet
IR = infrared	p = pentuplet
NMR = nuclear magnetic resonance	J = coupling constant
m/s = mass spectrograph	Hz = Hertz
CDCl ₃ = deuteriochloroform	M ⁺ = mass ion

EXAMPLE 1**15 Preparation of 1-(4-chlorophenyl)-2-cyclopropylpropan-1-one**

Crotyl chloride (154.7g, 1.71 mol) in dry tetrahydrofuran (530 ml) was added to magnesium turnings (46.0g, 1.89mol) in dry tetrahydrofuran (130 ml) at such a rate so as to maintain steady reflux. After addition was complete the mixture was heated under reflux for a further hour and then cooled to 0°C. 4-Chlorobenzaldehyde (120.0g, 0.854 mol) in dry tetrahydrofuran (780 ml) was added over a period of 2 hours. After a further hour the solution was decanted from the excess magnesium into saturated aqueous ammonium chloride solution and the magnesium washed with ether. 2M Hydrochloric acid was added to dissolve the precipitate and the mixture extracted with ether. The combined extracts were washed with water, dried and evaporated in vacuo. Partial purification was achieved by chromatography [SiO₂, hexane-ethyl acetate mixtures] to give 3-methyl-4-(4-chlorophenyl)-but-1-en-4-ol (118.45g, approximately 90% pure, approximately 64%).

3-Methyl-4-(4-chlorophenyl)but-1-en-4-ol (63.68g, approximately 90% pure, approximately 292 mmol), dibromomethane (45.5 ml, 648 mmol), zinc dust (84.75g, 1.296 mol) and copper(I) chloride (12.83g, 130 mmol) in dry ether (180 ml) were heated under reflux in a sonic bath for 3½ hours. The mixture was then filtered (celite) and the filtrate poured into 2M hydrochloric acid. The mixture was extracted with ether and the combined extracts washed with water, saturated aqueous sodium bicarbonate solution and water, dried and evaporated in vacuo. Chromatography [SiO₂, hexane-ethyl acetate (100:0) to (80:20)] gave 1-(4-chlorophenyl)-2-cyclopropylpropan-1-ol (44.72g, 73%).

Oxalyl chloride (22.2 ml, 255 mmol) was added to a stirred solution of dimethylsulphoxide (35 ml, 489 mmol) in dry dichloromethane (950ml) at -78°C under nitrogen.

After 15 minutes 1-(4-chlorophenyl)-2-cyclopropylpropan-1-ol (44.72g, 212 mmol) in dry dichloromethane (330 ml) was added over approximately 35 minutes. After 75 minutes triethylamine (154ml, 1105 mmol) was added and the mixture allowed to warm to room temperature. Hexane was added and the mixture washed with 1M hydrochloric acid, saturated aqueous sodium bicarbonate solution and water, dried and evaporated in vacuo. Chromatography [SiO₂, hexane-ethyl acetate (100:0) to (90:10)] gave 1-(4-chlorophenyl)-2-cyclopropylpropan-1-one (38.0g, 86%).

EXAMPLE 2**45 Preparation of 1-(4-chlorophenyl)-2-cyclopropylpropan-1-one**

Allyl chloride (97.88g, 1.28 mol) in dry tetrahydrofuran (500 ml) was added to a suspension of magnesium turnings (60.08g, 2.47 mol) in dry tetrahydrofuran (50 ml) at such a rate as to maintain steady reflux. The mixture was then heated under reflux for a further hour. 4-Chlorobenzaldehyde (120g, 854 mmol) in dry tetrahydrofuran (600 ml) was then added dropwise and the mixture refluxed for a further 2 hours. After being cooled to room temperature the mixture was poured into ice/water, carefully acidified with 1M sulphuric acid and extracted with ether. The combined extracts were washed with brine, dried and evaporated in vacuo to give crude 4-(4-chlorophenyl)but-1-en-4-ol (169.4g approximately 92% pure) which was used without further purification.

Crude 4-(4-chlorophenyl)but-1-en-4-ol from the previous reaction (85.37g, approximately 92% pure, approximately 430 mmol), zinc dust (121.5g, 1.86 mol), copper(I) chloride (18.69g, 187 mmol) and dibromomethane (163.6g, 936 mmol) in dry ether (250 ml) were heated under reflux for 3 hours in a sonic bath and then poured into 2M hydrochloric acid. The mixture was extracted with ether and the extract

washed with 2M hydrochloric acid and brine, dried and evaporated in vacuo. Chromatography [SiO_2 , hexane-ethyl acetate (90:10)] gave 1-(4-chlorophenyl)-2-cyclopropylethanol (37.24g, 44% from 4-chlorobenzaldehyde).

Oxalyl chloride (5.5 ml, 63 mmol) was added dropwise to a stirred solution of dimethylsulphoxide (5.5 ml, 78 mmol) in dry dichloromethane (150 ml) at -78°C . After 15 minutes 1-(4-chlorophenyl)-2-cyclopropylethanol (5.00g, 25.4 mmol) in dry dichloromethane (60 ml) was added to the mixture. After an hour triethylamine (27.5 ml, 197 mmol) was added, the mixture warmed to room temperature and poured into water. The mixture was extracted with dichloromethane and the extracts washed with water, dried and evaporated in vacuo to give crude 1-(4-chlorophenyl)-2-cyclopropylethanone which was used without further purification.

Oxalyl chloride (14.3 ml, 160 mmol) was added dropwise to a stirred solution of dimethylsulphoxide (14.3 ml, 200 mmol) in dry dichloromethane (350 ml) at -78°C . After 15 minutes 1-(4-chlorophenyl)-2-cyclopropylethanol (12.98 g, 66 mmol) in dry dichloromethane (120 ml) was added to the mixture. After an hour triethylamine (71.4 ml, 510 mmol) was added and the mixture warmed to room temperature and poured into water. The mixture was extracted with dichloromethane and the combined extracts washed with water, dried and evaporated in vacuo to give crude 1-(4-chlorophenyl)-2-cyclopropylethanone which was used without further purification.

Crude 1-(4-chlorophenyl)-2-cyclopropylethanone (from the previous reaction) in dry dimethylformamide (150 ml) was added dropwise to a stirred suspension of hexane-washed sodium hydride (4.57 g of a 60% dispersion in oil, 114 mmol) in dry dimethylformamide (35 ml) under nitrogen. After 1 hour the mixture was cooled to -30°C and iodomethane (16.2g, 114 mmol) in dry dimethylformamide (35 ml) added very slowly. The mixture was then poured into water and the resultant mixture extracted with ether. The extracts were washed with brine, dried and evaporated in vacuo. Chromatography [SiO_2 , hexane-ethyl acetate (95:5)] gave 1-(4-chlorophenyl)-2-cyclopropylpropan-1-one (7.66g, approximately 70% pure, approximately 28% based on 1-(4-chlorophenyl)-2-cyclopropylethanol).

Spectral Data

(i) 1-(4-Chlorophenyl)-2-cyclopropylpropan-1-one

IR (film): 3080, 2972, 2935, 1686, 1592, 1584, 1490, 1402, 1221, 1095, 1015, 977 and 844 cm^{-1} .
 ^1H NMR (CDCl_3 , 270 MHz): 7.86 (2H, m), 7.43 (2H, m), 2.74 (1H, dq, $J=8.7$ and 6.9 Hz), 1.28 (3H, d, $J=6.9$ Hz), 1.01 (1H, m), 0.54 (2H, m), and 0.18 (2H, m).
 m/s: 208 (15%), 141 (37), 139 (100), 111 (21), 75 (11), 69 (37) and 41 (16).

(ii) 3-Methyl-4-(4-chlorophenyl)but-1-en-4-ol

IR (film): 3430 (broad), 3083, 2980, 2883, 1642, 1600, 1496, 1416, 1098, 1020, 924 and 828 cm^{-1} .
 ^1H NMR (CDCl_3 , 270 MHz): 7.40-7.15 (4H, m), 5.76 (1H, m), 5.13 (2H, m), 4.6l and 4.13 (1H, 2 x d, $J=5.4$ and 6.9 Hz), 2.55 and 2.42 (1H, qd and p), $J=6.9$ and 5.4 Hz and 6.9 Hz), 2.16 and 1.94 (1H, 2 x broad s) and 0.98 and 0.87 (3H, 2 x d, $J=6.9$ and 6.9 Hz).
 m/s (Chemical Ionisation, ammonia): 213 (4%, $\text{M} + \text{NH}_3$) and 196 (100%, M^+)

(iii) 4-(4-Chlorophenyl)but-1-en-4-ol

^1H NMR (CDCl_3 , 270 MHz): 7.27 (4H, m), 5.76 (1H, ddt, $J=15.4$, 12.3 and 6.9 Hz), 5.12 (1H, dd, $J=15.4$ and 2 Hz), 5.11 (1H, dd, $J=12.3$ and 2 Hz), 4.67 (1H, t, $J=6.9$ Hz), 2.89 (1H, broad s), and 2.45 (2H, t, $J=6.9$ Hz).

EXAMPLE 3

Preparation of 1-(4-chlorophenyl)-2-cyclopropylpropan-1-ol using SDBA catalyst

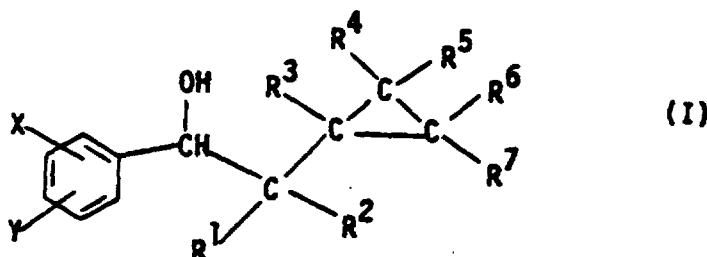
A suspension of 48 g (0.74 mol) Zn and 0.5g (0.005 mol) Cu(I)Cl in 88g toluene and 44g dimethoxyethane is prepared, and maintained at 85°C . To this suspension is added 1.8 g of a 70% solution of SDBA

in xylene. Thereafter is added 44g (39.4 g at 100% = 0.2 mol) of 3-methyl-4-(4-chlorophenyl)but-1-en-4-ol. Within one hour is added 101g (0.58 mol) dibromomethane at 95°C. When the addition is completed, 0.3g (0.003 mol) of Cu(I)Cl are added. The reaction to produce the above-titled compound is allowed to proceed for 3 hours at 95°C. The yield is 88.1%.

Claims

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

1. A process for the preparation of a compound of the general formula (I) :

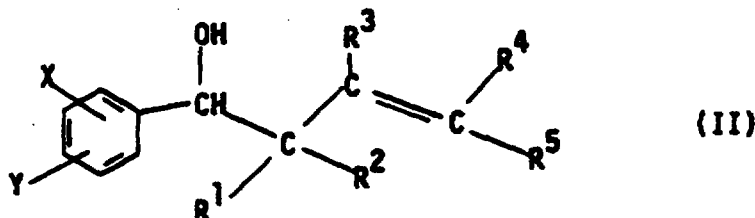


wherein

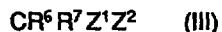
X is hydrogen, halogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted aralkyl, alkoxy or optionally substituted aryloxy,

Y is halogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted aralkyl, alkoxy or optionally substituted aryloxy, and

R¹ to R⁷ are independently hydrogen or C₁₋₆ alkyl, which comprises treating a compound of the general formula (II):



wherein X, Y and R¹ to R⁵ have the meanings given before, with a compound of the general formula (III):



wherein R⁶ and R⁷ have the meanings given before, and Z¹ and Z², which are the same or different, are halogen in the presence of metallic zinc.

2. The process of Claim 1 wherein X is hydrogen and Y is halogen.
3. The process of Claim 1 wherein X is hydrogen, Y is 4-chlorine, R¹ is methyl, and R²-R⁷ are hydrogen.
4. The process of Claim 1 wherein X is hydrogen, Y is 4-chlorine, and R¹-R⁷ are hydrogen.
5. The process of Claim 1 wherein the compound of general formula (II) is treated with the compound of general formula (III) in the further presence of a catalytic amount of a metallo-hydride reducing agent.

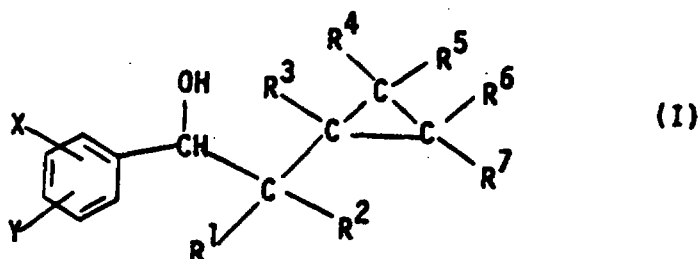


in xylene. Thereafter is added 44g (39.4 g at 100% = 0.2 mol) of 3-methyl-4-(4-chlorophenyl)but-1-en-4-ol. Within one hour is added 101g (0.58 mol) dibromomethane at 95° C. When the addition is completed, 0.3g (0.003 mol) of Cu(I)Cl are added. The reaction to produce the above-titled compound is allowed to proceed for 3 hours at 95° C. The yield is 88.1%.

Claims

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

1. A process for the preparation of a compound of the general formula (I) :

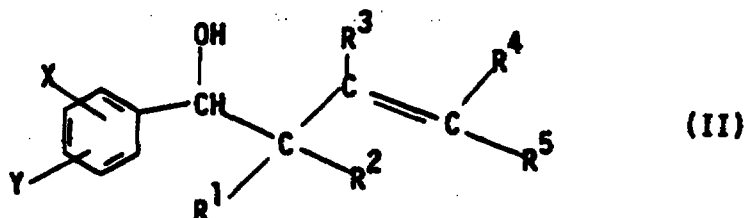


wherein

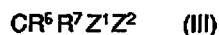
X is hydrogen, halogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted aralkyl, alkoxy or optionally substituted aryloxy,

Y is halogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted aralkyl, alkoxy or optionally substituted aryloxy, and

R¹ to R⁷ are independently hydrogen or C₁₋₆ alkyl, which comprises treating a compound of the general formula (II):



wherein X, Y and R¹ to R⁵ have the meanings given before, with a compound of the general formula (III):

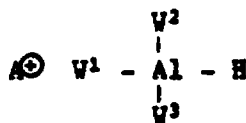


wherein R⁶ and R⁷ have the meanings given before, and Z¹ and Z², which are the same or different, are halogen in the presence of metallic zinc.

2. The process of Claim 1 wherein X is hydrogen and Y is halogen.
3. The process of Claim 1 wherein X is hydrogen, Y is 4-chlorine, R¹ is methyl, and R²-R⁷ are hydrogen.
4. The process of Claim 1 wherein X is hydrogen, Y is 4-chlorine, and R¹-R⁷ are hydrogen.
5. The process of Claim 1 wherein the compound of general formula (II) is treated with the compound of general formula (III) in the further presence of a catalytic amount of a metallo-hydride reducing agent.



6. The process of Claim 5 in which the metallo-hydride reducing agent is of the formula:



in which

A signifies an alkali metal or one equivalent of an alkaline earth metal, e.g. sodium or lithium; and each of

W^1 , W^2 and W^3 is, independently, a hydrogen atom, or an alkyl or alkoxy radical of 1 to 6 carbon atoms; or an alkoxyalkoxy or alkyleneoxyalkyl radical having from 2 to 6 carbon atoms;

provided that at least one of W^1 , W^2 and W^3 is other than a hydrogen atom; or of the formula:

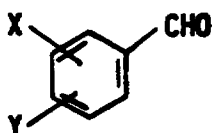


in which

W^4 and W^5 , each is, independently, a hydrogen atom or an alkyl radical of 1 to 6 carbon atoms; provided that at least one of W^4 and W^5 is alkyl.

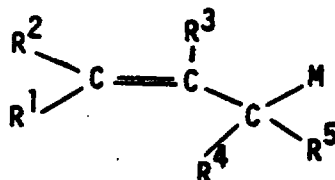
7. The process of Claim 6 in which the metallo-hydride reducing agent is sodium dihydrido-bis(2-ethoxymethoxy) aluminate.

8. A process for the preparation of a compound of the general formula (I), as defined in Claim 1, which comprises the steps of
(a) treating a compound of the general formula (IV) :



(IV)

with an organometallic reagent of the general formula (V) :



(V)

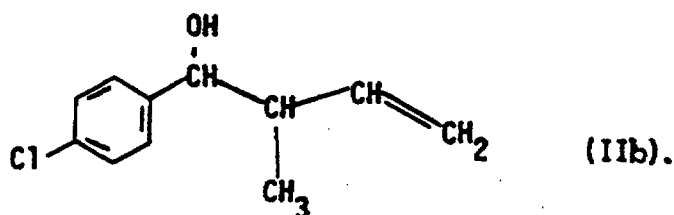
to form a compound of the general formula (II), as defined in Claim 1; and

(b) treating the compound of formula (II) with a compound of formula (III), as defined in Claim 1; X, Y and R^1 to R^7 being as defined in Claim 1 and M being a metal atom.

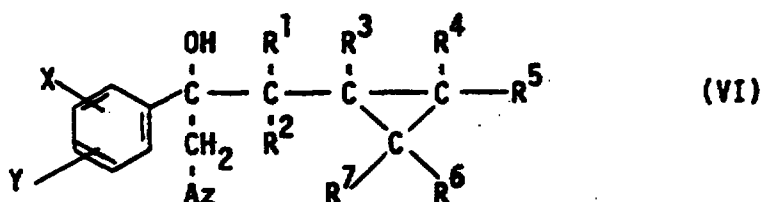
9. The compound of formula I, as stated in Claim 1, wherein X is hydrogen, Y is 4-chlorine, R^1 is methyl and R^3 to R^7 are hydrogen.



10. The compound having the formula (IIb):



11. A process of preparing a compound of formula (VI)

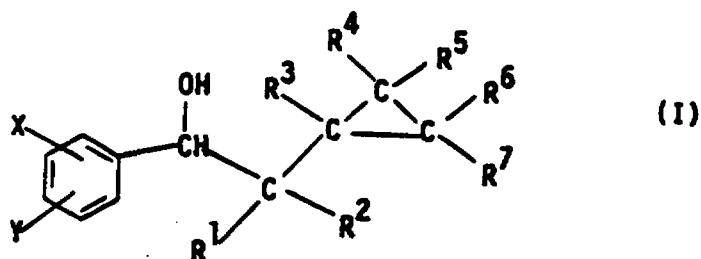


wherein X, Y and R¹ to R⁷ are as defined in Claim 1, using as intermediate a compound of formula (I) as defined in Claim 1, characterized in that the compound of formula (I) is obtained by the process of Claim 1.

12. The process of Claim 11, wherein X is hydrogen, Y is 4-chloro, R¹ is methyl, R² to R⁷ are hydrogen and Az is 1H-1,2,4-triazolyl.

Claims for the following Contracting State : ES

1. A process for the preparation of a compound of the general formula (I) :

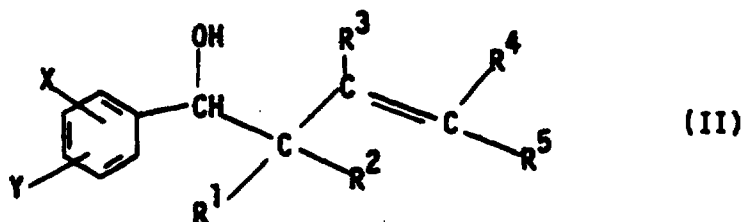


wherein

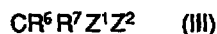
X is hydrogen, halogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted aralkyl, alkoxy or optionally substituted aryloxy,

Y is halogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted aralkyl, alkoxy or optionally substituted aryloxy, and

R¹ to R⁷ are independently hydrogen or C₁₋₆ alkyl, which comprises treating a compound of the general formula (II):

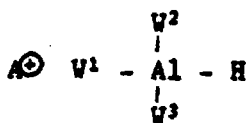


10 wherein X, Y and R¹ to R⁵ have the meanings given before, with a compound of the general formula (III):



15 wherein R⁶ and R⁷ have the meanings given before, and Z¹ and Z², which are the same or different, are halogen in the presence of metallic zinc.

2. The process of Claim 1 wherein X is hydrogen and Y is halogen.
- 20 3. The process of Claim 1 wherein X is hydrogen, Y is 4-chlorine, R¹ is methyl, and R²-R⁷ are hydrogen.
4. The process of Claim 1 wherein X is hydrogen, Y is 4-chlorine, and R¹-R⁷ are hydrogen.
5. The process of Claim 1 wherein the compound of general formula (II) is treated with the compound of general formula (III) in the further presence of a catalytic amount of a metallo-hydride reducing agent.
- 25 6. The process of Claim 5 in which the metallo-hydride reducing agent is of the formula:



35 in which

A signifies an alkali metal or one equivalent of an alkaline earth metal, e.g. sodium or lithium; and each of W¹, W² and W³ is, independently, a hydrogen atom, or an alkyl or alkoxy radical of 1 to 6 carbon atoms; or an alkoxyalkoxy or alkyleneoxyalkyl radical having from 2 to 6 carbon atoms;

provided that at least one of W¹, W² and W³ is other than a hydrogen atom; or of the formula:



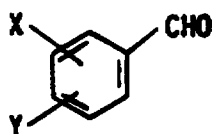
in which

50 W⁴ and W⁵, each is, independently, a hydrogen atom or an alkyl radical of 1 to 6 carbon atoms; provided that at least one of W⁴ and W⁵ is alkyl.

7. The process of Claim 6 in which the metallo-hydride reducing agent is sodium dihydrido-bis(2-ethoxymethoxy) aluminate.
- 55 8. A process for the preparation of a compound of the general formula (I), as defined in Claim 1, which comprises the steps of

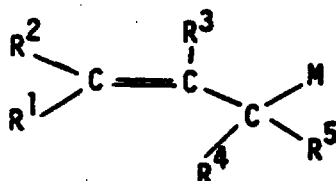


(a) treating a compound of the general formula (IV) :



(IV)

with an organometallic reagent of the general formula (V)

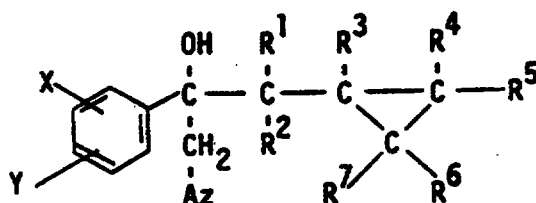


(V)

to form a compound of the general formula (II), as defined in Claim 1; and

(b) treating the compound of formula (II) with a compound of formula (III), as defined in Claim 1; X, Y and R¹ to R⁷ being as defined in Claim 1 and M being a metal atom.

9. A process of preparing a compound of formula (VI)



(VI)

wherein X, Y and R¹ to R⁷ are as defined in Claim 1,

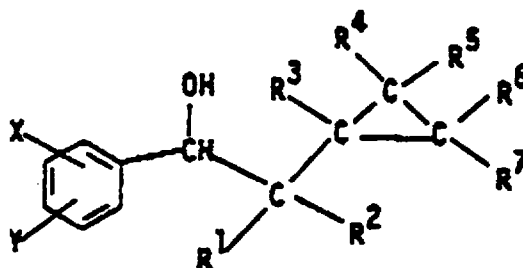
using as intermediate a compound of formula (I) as defined in Claim 1, characterized in that the compound of formula (I) is obtained by the process of Claim 1.

10. The process of Claim 9, wherein X is hydrogen, Y is 4-chloro, R¹ is methyl, R² to R⁷ are hydrogen and Az is 1H-1,2,4-triazolyl.

Patentansprüche

Patentansprüche für folgende Vertragsstaaten : AT, BE, CH, DE, FR, GB, GR, IT, LI, LU, NL, SE

1. Verfahren zur Herstellung einer Verbindung der allgemeinen Formel (I)



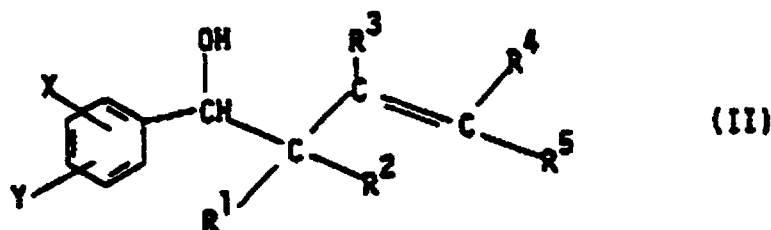
(I)

worin
X

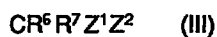
Wasserstoff, Halogen, Alkyl, Halogenalkyl, Cycloalkyl, Cycloalkylalkyl, Alkenyl, Alkynyl, gegebenenfalls substituiertes Aryl, gegebenenfalls substituiertes Aralkyl, Alkoxy oder



gegebenenfalls substituiertes Aryloxy ist,
 Y Halogen, Alkyl, Halogenalkyl, Cycloalkyl, Cycloalkylalkyl, Alkenyl, Alkynyl, gegebenenfalls substituiertes Aryl, gegebenenfalls substituiertes Aralkyl, Alkoxy oder gegebenenfalls substituiertes Aryloxy bedeutet und
 R¹ bis R⁷ unabhängig Wasserstoff oder C₁-C₆ Alkyl sind,
 dadurch gekennzeichnet, daß eine Verbindung der allgemeinen Formel (II)

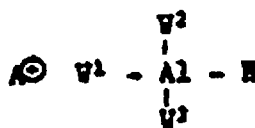


worin X, Y und R¹ bis R⁵ die oben angegebenen Bedeutungen haben, mit einer Verbindung der allgemeinen Formel (III)



worin R⁶ und R⁷ die oben angegebenen Bedeutungen haben und Z¹ und Z², die gleich oder verschieden sind, für Halogen stehen, in Gegenwart von metallischem Zink umgesetzt wird.

2. Verfahren nach Anspruch 1, worin X Wasserstoff ist und Y für Halogen steht.
3. Verfahren nach Anspruch 1, worin X Wasserstoff ist, Y für 4-Chlor steht, R¹ Methyl ist und R² bis R⁷ Wasserstoff sind.
4. Verfahren nach Anspruch 1, worin X Wasserstoff ist, Y für 4-Chlor steht und R¹ bis R⁷ Wasserstoff sind.
5. Verfahren nach Anspruch 1, worin die Verbindung der allgemeinen Formel (II) mit der Verbindung der allgemeinen Formel (III) in weiterer Gegenwart einer katalytischen Menge eines Metallhydridreduktionsmittels behandelt wird.
6. Verfahren nach Anspruch 5, worin das Metallhydridreduktionsmittel folgende Formel hat



worin

A ein Alkalimetall oder ein Äquivalent eines Erdalkalimetalls, wie Natrium oder Lithium, bedeutet und die Substituenten W¹, W² und W³ jeweils unabhängig ein Wasserstoffatom oder einen Alkyl- oder Alkoxyrest mit 1 bis 6 Kohlenstoffatomen oder einen Alkoxyalkoxy- oder Alkylenoxyalkylrest mit 2 bis 6 Kohlenstoffatomen darstellen, mit der Maßgabe, daß wenigstens einer der Substituenten W¹, W² und W³ etwas anderes als ein Wasserstoffatom ist, oder worin das Metallhydridreduktionsmittel die folgende Formel hat





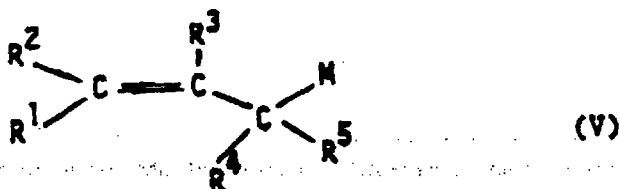
worin

W^4 und W^5 jeweils unabhängig ein Wasserstoffatom oder einen Alkylrest mit 1 bis 6 Kohlenstoffatomen bedeuten, mit der Maßgabe, daß wenigstens einer der Reste W^4 und W^5 für Alkyl steht.

7. Verfahren nach Anspruch 6, worin das Metallhydridreduktionsmittel Natriumdihydrido-bis(2-ethoxymethoxy)aluminat ist.
8. Verfahren zur Herstellung einer Verbindung der allgemeinen Formel (I) gemäß Definition von Anspruch 1, dadurch gekennzeichnet, daß
- (a) eine Verbindung der allgemeinen Formel (IV)



mit einem Organometallreagens der allgemeinen Formel (V)

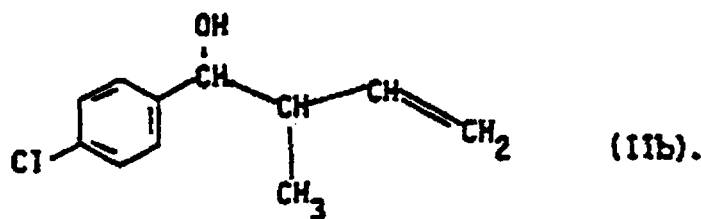


behandelt und eine Verbindung der allgemeinen Formel (II) gemäß Definition von Anspruch 1 gebildet wird und

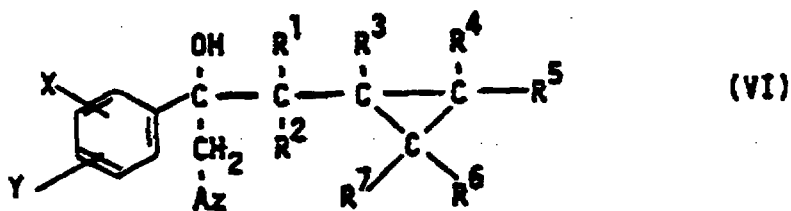
(b) die Verbindung der Formel (II) mit einer Verbindung der Formel (III) gemäß Definition von Anspruch 1 behandelt wird, wobei X, Y und R^1 bis R^7 wie im Anspruch 1 definiert sind und M ein Metallatom ist.

9. Verbindung der Formel (I) gemäß Anspruch 1, worin X Wasserstoff ist, Y für 4-Chlor steht, R^1 Methyl ist und R^2 bis R^7 Wasserstoff sind.

10. Verbindung der Formel (IIb)



11. Verfahren zur Herstellung einer Verbindung der Formel (VI)



worin X, Y und R^1 bis R^7 wie im Anspruch 1 definiert sind, unter Verwendung einer Verbindung der

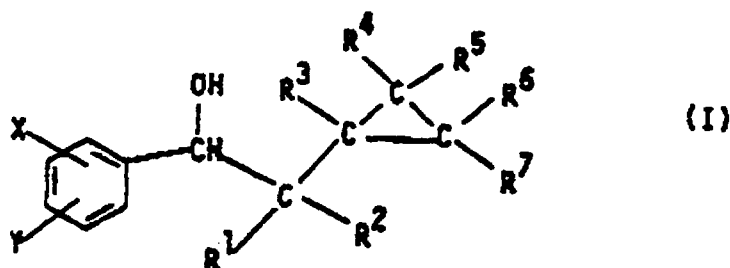


Formel (I) gemäß Definition von Anspruch 1 als Zwischenprodukt, dadurch gekennzeichnet, daß die Verbindung der Formel (I) nach dem Verfahren von Anspruch 1 erhalten wird.

12. Verfahren nach Anspruch 11, worin X Wasserstoff ist, Y für 4-Chlor steht, R¹ Methyl ist, R² bis R⁷ Wasserstoff sind und Az für 1H-1,2,4-Triazolyl steht.

Patentansprüche für folgenden Vertragsstaat : ES

1. Verfahren zur Herstellung einer Verbindung der allgemeinen Formel (I).

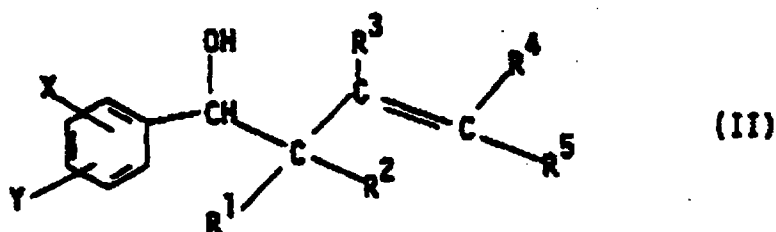


worin

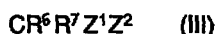
X Wasserstoff, Halogen, Alkyl, Halogenalkyl, Cycloalkyl, Cycloalkylalkyl, Alkenyl, Alkynyl, gegebenenfalls substituiertes Aryl, gegebenenfalls substituiertes Aralkyl, Alkoxy oder gegebenenfalls substituiertes Aryloxy ist,

Y Halogen, Alkyl, Halogenalkyl, Cycloalkyl, Cycloalkylalkyl, Alkenyl, Alkynyl, gegebenenfalls substituiertes Aryl, gegebenenfalls substituiertes Aralkyl, Alkoxy oder gegebenenfalls substituiertes Aryloxy bedeutet und

R¹ bis R⁷ unabhängig Wasserstoff oder C₁-C₆ Alkyl sind, dadurch gekennzeichnet, daß eine Verbindung der allgemeinen Formel (II)



worin X, Y und R¹ bis R⁵ die oben angegebenen Bedeutungen haben, mit einer Verbindung der allgemeinen Formel (III)

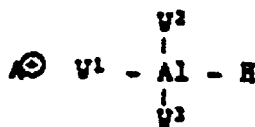


worin R⁶ und R⁷ die oben angegebenen Bedeutungen haben und Z¹ und Z², die gleich oder verschieden sind, für Halogen stehen, in Gegenwart von metallischem Zink umgesetzt wird.

2. Verfahren nach Anspruch 1, worin X Wasserstoff ist und Y für Halogen steht.
3. Verfahren nach Anspruch 1, worin X Wasserstoff ist, Y für 4-Chlor steht, R¹ Methyl ist und R² bis R⁷ Wasserstoff sind.
4. Verfahren nach Anspruch 1, worin X Wasserstoff ist, Y für 4-Chlor steht und R¹ bis R⁷ Wasserstoff sind.
5. Verfahren nach Anspruch 1, worin die Verbindung der allgemeinen Formel (II) mit der Verbindung der allgemeinen Formel (III) in weiterer Gegenwart einer katalytischen Menge eines Metallhydridreduktionsmittels behandelt wird.

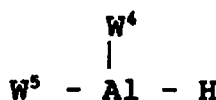


6. Verfahren nach Anspruch 5, worin das Metallhydridreduktionsmittel folgende Formel hat



worin

A ein Alkalimetall oder ein Äquivalent eines Erdalkalimetalls, wie Natrium oder Lithium, bedeutet und die Substituenten W^1 , W^2 und W^3 jeweils unabhängig ein Wasserstoffatom oder einen Alkyl- oder Alkoxyrest mit 1 bis 6 Kohlenstoffatomen oder einen Alkoxyalkoxy- oder Alkyle-noxyalkylrest mit 2 bis 6 Kohlenstoffatomen darstellen, mit der Maßgabe, daß wenigstens einer der Substituenten W^1 , W^2 und W^3 etwas anderes als ein Wasserstoffatom ist, oder worin das Metallhydridreduktionsmittel die folgende Formel hat

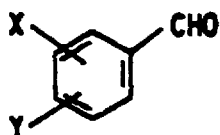


worin

W^4 und W^5 jeweils unabhängig ein Wasserstoffatom oder einen Alkylrest mit 1 bis 6 Kohlenstoffatomen bedeuten, mit der Maßgabe, daß wenigstens einer der Reste W^4 und W^5 für alkyl steht.

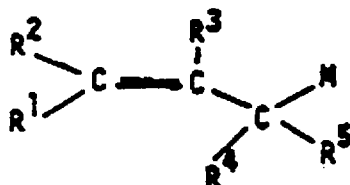
7. Verfahren nach Anspruch 6, worin das Metallhydridreduktionsmittel Natriumdihydrido-bis(2-ethoxymethoxy)aluminat ist.

8. Verfahren zur Herstellung einer Verbindung der allgemeinen Formel (I) gemäß Definition von Anspruch 1, dadurch gekennzeichnet, daß
(a) eine Verbindung der allgemeinen Formel (IV)



(IV)

mit einem Organometallreagens der allgemeinen Formel (V)



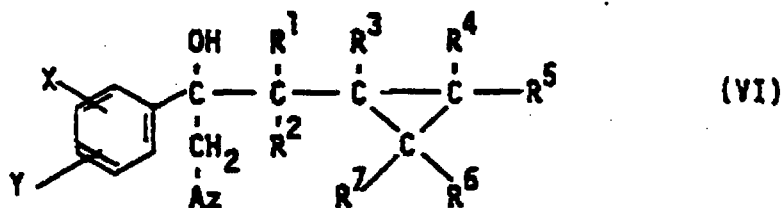
(V)

behandelt und eine Verbindung der allgemeinen Formel (II) gemäß Definition von Anspruch 1 gebildet wird und

(b) die Verbindung der Formel (II) mit einer Verbindung der Formel (III) gemäß Definition von Anspruch 1 behandelt wird, wobei X, Y und R^1 bis R^7 wie im Anspruch 1 definiert sind und M ein Metallatom ist.



9. Verfahren zur Herstellung einer Verbindung der Formel (VI)



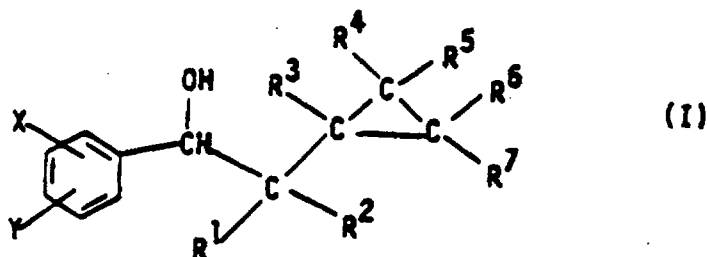
worin X, Y und R¹ bis R⁷ wie im Anspruch 1 definiert sind, unter Verwendung einer Verbindung der Formel (I) gemäß Definition von Anspruch 1 als Zwischenprodukt, dadurch gekennzeichnet, daß die Verbindung der Formel (I) nach dem Verfahren von Anspruch 1 erhalten wird.

10. Verfahren nach Anspruch 11, worin X Wasserstoff ist, Y für 4-Chlor steht, R¹ Methyl ist, R² bis R⁷ Wasserstoff sind und Az für 1H-1,2,4-Triazolyl steht.

Revendications

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

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

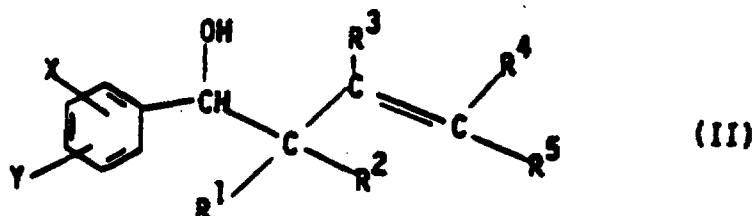


dans laquelle

X signifie l'hydrogène, un halogène ou un groupe alkyle, haloalkyle, cycloalkyle, cycloalkylalkyle, alcényle, alcynyle, aryle éventuellement substitué, aralkyle éventuellement substitué, alcoxy ou aryloxy éventuellement substitué,

Y signifie un halogène ou un groupe alkyle, haloalkyle, cycloalkyle, cycloalkylalkyle, alcényle, alcynyle, aryle éventuellement substitué, aralkyle éventuellement substitué, alcoxy ou aryloxy éventuellement substitué, et

R¹ à R⁷ signifient indépendamment l'hydrogène ou un groupe alkyle en C₁-C₆, qui comprend le traitement d'un composé de formule (II)



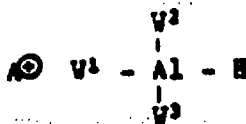
dans laquelle X, Y et R¹ à R⁵ ont les significations données ci-dessus, par un composé de formule (III)

CR⁶R⁷Z¹Z² (III)



dans laquelle R⁶ et R⁷ ont les significations données ci-dessus, et Z¹ et Z², qui sont identiques ou différents, signifient un halogène, en présence de zinc métallique.

2. Le procédé de la revendication 1, dans lequel X signifie l'hydrogène et Y signifie un halogène.
3. Le procédé de la revendication 1, dans lequel X signifie l'hydrogène, Y signifie 4-chloro, R¹ signifie un groupe méthyle et R²-R⁷ signifient l'hydrogène.
4. Le procédé de la revendication 1, dans lequel X signifie l'hydrogène, Y signifie 4-chloro et R¹-R⁷ signifient l'hydrogène.
5. Le procédé de la revendication 1, dans lequel le composé de formule (II) est traité par le composé de formule (III) également en présence d'une quantité catalytique d'un agent réducteur du groupe des métallo-hydrures.
6. Le procédé de la revendication 5, dans lequel l'agent réducteur du groupe des métallo-hydrures répond à la formule



dans laquelle

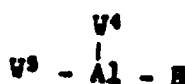
A

signifie un métal alcalin ou un équivalent d'un métal alcalino-terreux, par exemple le sodium ou le lithium, et

chaque W¹, W² et W³

signifie, indépendamment, un atome d'hydrogène ou un groupe alkyle ou alcoxy en C₁-C₆ ou un groupe alcoxyalkoxy ou alkylèneoxyalkyle en C₂-C₆,

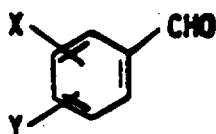
au moins un symbole W¹, W² et W³ ayant une signification autre que l'hydrogène, ou répond à la formule



dans laquelle W⁴ et W⁵ signifient chacun, indépendamment, un atome d'hydrogène ou un groupe alkyle en C₁-C₆,

au moins un symbole W⁴ et W⁵ devant signifier un groupe alkyle.

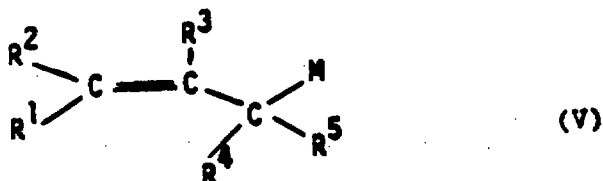
7. Le procédé de la revendication 6, dans lequel l'agent réducteur du groupe des métallo-hydrures est le dihydrido-bis(2-éthoxyméthoxy)aluminate de sodium.
8. Un procédé de préparation d'un composé de formule (I) tel que défini à la revendication 1, qui comprend les étapes
 - (a) traitement d'un composé de formule (IV)



(IV)



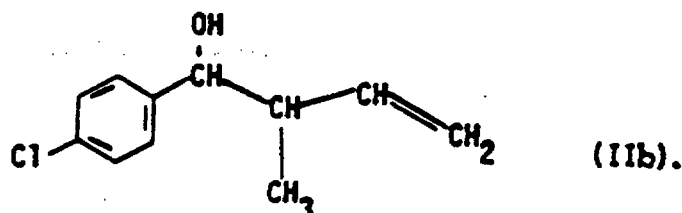
par un réactif organométallique de formule (V)



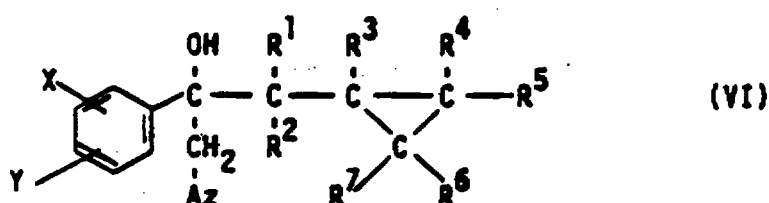
pour former un composé de formule (II) tel que défini à la revendication 1, et
(b) traitement du composé de formule (II) par un composé de formule (III) tel que défini à la revendication 1; X, Y et R¹ à R⁷ étant tels que définis à la revendication 1 et M signifiant un atome de métal.

9. Le composé de formule I tel que spécifié à la revendication 1, dans lequel X signifie l'hydrogène, Y, signifie 4-chloro, R¹ signifie un groupe méthyle et R² à R⁷ signifient l'hydrogène.

10. Le composé répondant à la formule (IIb)



11. Un procédé de préparation d'un composé de formule (VI)



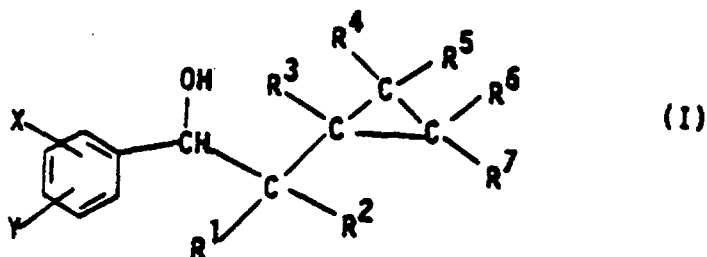
dans laquelle X, Y et R¹ à R⁷ sont tels que définis à la revendication 1, utilisant comme produit intermédiaire un composé de formule (I) tel que défini à la revendication 1, caractérisé en ce que le composé de formule (I) est obtenu selon le procédé de la revendication 1.

12. Le procédé de la revendication 11, dans lequel X signifie l'hydrogène, Y signifie 4-chloro, R¹ signifie un groupe méthyle, R² à R⁷ signifient l'hydrogène et Az signifie le groupe 1H-1,2,4-triazolyle.



Revendications pour l'Etat contractant suivant : ES

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

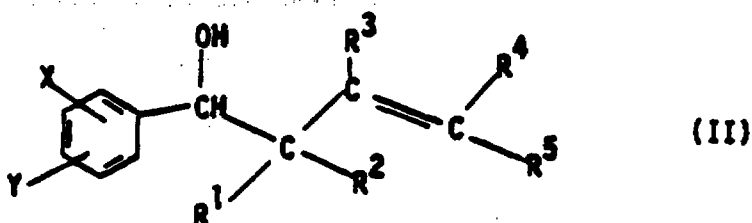


dans laquelle

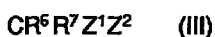
X signifie l'hydrogène, un halogène ou un groupe alkyle, haloalkyle, cycloalkyle, cycloalkylalkyle, alcényle, alcynyle, aryle éventuellement substitué, aralkyle éventuellement substitué, alcoxy ou aryloxy éventuellement substitué,

Y signifie un halogène ou un groupe alkyle, haloalkyle, cycloalkyle, cycloalkylalkyle, alcényle, alcynyle, aryle éventuellement substitué, aralkyle éventuellement substitué, alcoxy ou aryloxy éventuellement substitué, et

R¹ à R⁷ signifient indépendamment l'hydrogène ou un groupe alkyle en C₁-C₆, qui comprend le traitement d'un composé de formule (II)

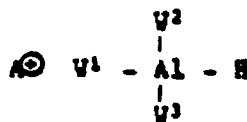


dans laquelle X, Y et R¹ à R⁵ ont les significations données ci-dessus, par un composé de formule (III)



dans laquelle R⁶ et R⁷ ont les significations données ci-dessus, et Z¹ et Z², qui sont identiques ou différents, signifient un halogène, en présence de zinc métallique.

2. Le procédé selon la revendication 1, dans lequel X signifie l'hydrogène et Y signifie un halogène.
3. Le procédé de la revendication 1, dans lequel X signifie l'hydrogène, Y signifie 4-chloro, R¹ signifie un groupe méthyle et R²-R⁷ signifient l'hydrogène.
4. Le procédé de la revendication 1, dans lequel X signifie l'hydrogène, Y signifie 4-chloro et R¹-R⁷ signifient l'hydrogène.
5. Le procédé de la revendication 1, dans lequel le composé de formule (II) est traité par le composé de formule (III) également en présence d'une quantité catalytique d'un agent réducteur du groupe des métallo-hydrures.
6. Le procédé de la revendication 5, dans lequel l'agent réducteur du groupe des métallo-hydrures répond à la formule



dans laquelle

A signifie un métal alcalin ou un équivalent d'un métal alcalino-terreux, par exemple le sodium ou le lithium, et

chaque W^1 , W^2 et W^3 signifie, indépendamment, un atome d'hydrogène ou un groupe alkyle ou alcoxy en $\text{C}_1\text{-C}_6$ ou un groupe alcoxyalcoxy ou alkylèneoxyalkyle en $\text{C}_2\text{-C}_6$,

au moins un symbole W^1 , W^2 et W^3 ayant une signification autre que l'hydrogène, ou répond à la formule



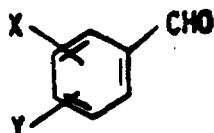
dans laquelle W^4 et W^5 signifient chacun, indépendamment, un atome d'hydrogène ou un groupe alkyle en $\text{C}_1\text{-C}_6$,

au moins un symbole W^4 et W^5 devant signifier un groupe alkyle.

7. Le procédé de la revendication 6, dans lequel l'agent réducteur du groupe des métallos-hydrures est le dihydrido-bis(2-éthoxyméthoxy)aluminate de sodium.

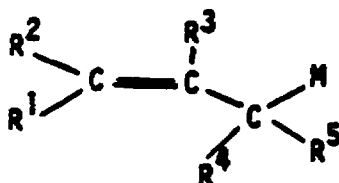
8. Un procédé de préparation d'un composé de formule (I) tel que défini à la revendication 1, caractérisé en ce qu'il comprend les étapes

(a) traitement d'un composé de formule (IV)



(IV)

par un réactif organométallique de formule (V)



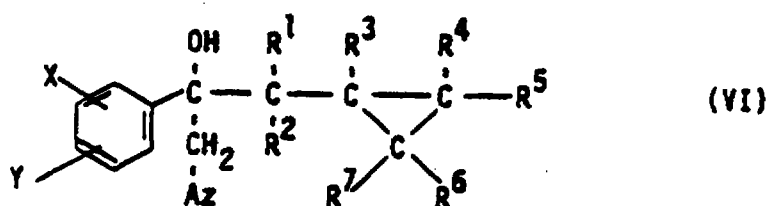
(V)

pour former un composé de formule (II) tel que défini à la revendication 1, et

(b) traitement du composé de formule (II) par un composé de formule (III) tel que défini à la revendication 1; X, Y et R^1 à R^7 étant tels que définis à la revendication 1 et M signifiant un atome de métal.



9. Un procédé de préparation d'un composé de formule (VI)



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dans laquelle X, Y et R¹ à R⁷ sont tels que définis à la revendications 1, utilisant comme produit intermédiaire un composé de formule (I) tel que défini à la revendication 1, caractérisé en ce que le composé de formule (I) est obtenu selon le procédé de la revendication 1.

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10. Le procédé de la revendication 9, dans lequel X signifie l'hydrogène, Y signifie 4-chloro, R¹ signifie un groupe méthyle, R² à R⁷ signifient l'hydrogène et Az signifie le groupe 1H-1,2,4-triazolyle.