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SELECTIVE REDUCTION OF THE DISTANT DOUBLE BOND(S) IN GERANYL, FARNESYL AND GERANYL GERANYL DERIVATIVES.

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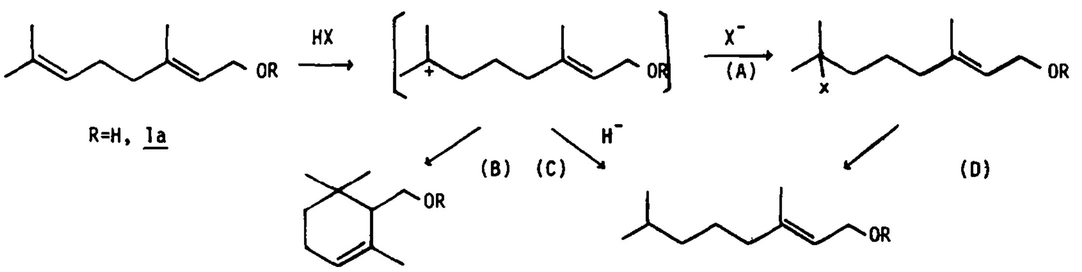
Abstract : Selective addition of hydrogen chloride on the non-proximal double bond(s) of the title compounds followed by hydrogenolysis led to selective hydrogenation of these double bond(s).

The polyprenols display considerable selectivity in the reaction of various double bonds. In presqualene or prephytoene alcohol formation, the C_2-C_3 double bond is involved[1a], whereas in the biosynthesis of phytol from geranyl geraniol[1b] it is unaffected during the reduction of the other three double bonds. This is all the more intriguing since both processes are triggered by electrophilic attack. The catalytic hydrogenation of geraniol 1a occurs preferentially at the C_2-C_3 double bond; however the selective hydrogenation of geranyl trimethylsilane and more so with geranyl isopropyldimethylsilane occurred at the distal double bond[2].

Previous work[3] had shown various factors which influence to a considerable extent the reactivity of trisubstituted double bonds towards electrophilic attack. With these results in hand the question of the regioselective reduction of the double bonds in polyprenols could be addressed. The method used involved successive reaction with a proton and a hydride ion (or their equivalents). The most direct method (see scheme I(C)) was first studied with the very efficient one pot reactant hydrogenosilane in acid conditions. Then an alternative two step process was proposed (D)



SCHEME I

The biological reduction of geranyl geraniol 3a is carried out by an NADH containing enzyme[1b]. It takes place in such important processes as the biosynthesis of tocopherol 15 and chlorophyll. Whether it occurs before or after attachment to trimethyl hydroquinone or phacophorbide is not yet clear. In some cases, the enzymatic reduction by NADH involves an essential zinc ion[1c], this might be mimicked by acid activation of the double bond followed by hydride transfer.

Ionic hydrogenation of olefins has been carried out catalytically[4], with sodium borohydride and acid[5] or with substituted silicon hydride[6]. With Et_3SiH/trifluoroacetic acid (TFA)[7] tri- and tetrasubstitued olefins are rapidly converted into the corresponding trifluoroacetates which are then reduced (see also[8,9,10]). In fact, addition of a Lewis acid such as BF_3,Et_2O[11], $LiClO_4$[12] or the use of a more polar solvent ($MeNO_2$)[12] led to a considerable acceleration of the reaction. This technique was first tried with citronellyl acetate 8b in order to avoid interference of another double bond. The results are shown in table I.

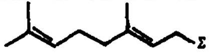
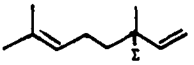
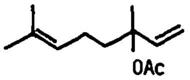
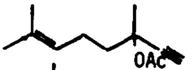
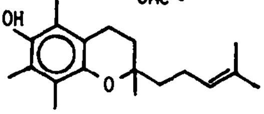
TABLE I : Reduction with ET_3SiH.

Run (a)	Substrate	$LiClO_4$ eq	T °C	t hr	Addition Product %	Reduction Product %	Cyclisation Product %
1 (h)	8b	0	80	22	9a 50	11 27	
2	"	0	80	"	" 3	" 75	
3	"	0	50	"	" 54	" 24	
4	"	0.1	50	"	" 2	" 80	
5	"	0.1	20	"	" 51	" 42	
6	"	0.2	20	"	" 29	" 60	
7	"	1	20	"	" 1	" 90	
8	"	1	20	3	" 25	" 65	
9 (b)	"	1	20	"	" 45	" 42	
10 (c)	"	1	20	48	9b 20	" 65	
11	1b	1	20	1	16a 0	4b t	17b 20
12 (d)	"	1	20	0.5	" 0	" t	" 14
13	"	0	60	10	(f)		
14 (e)	16a	0	50	78	(g)		
15 (e)	"	0	100	2		" 6	" 8
16 (e)	"	1	20	15	16c 0	" 2	" 8
17	1c	1	20	"	" 0	4c t	17c 52
18 (e)	16b	1	20	"		" t	" 40

The percentage were calculated by VPC after the usual workup and addition of an internal standard. (a) Standard condition: 1 mmol of substrate, 1 ml of $iPrNO_2$, 2.5 eq of TFA, 2 eq of Et_3SiH except for the following notes.(b) 1eq of $C_{11}H_{23}OAc$. (c) Acid 5 eq of CCl_2HCOOH. (d) Solvent: Et_3SiH (12 eq). (e) No acid. (f)Complete degradation (g) No reaction. (h) Solvent: CH_2Cl_2 1 ml. t: trace.

In dichloromethane, with Et_3SiH and TFA reduction of 8a into 11 takes place at 80°C, but considerable addition of acid to the double bond was also observed. The use of 2-nitropropane however led to a considerable increase in chemoselectivity (run 2). This must have been caused by the easier ionisation of the intermediate 9a. Lowering the temperature slowed down the reduction of the acid addition product (run 3), but this could be offset by addition of $LiClO_4$, one equivalent of which allowed the reduction to proceed at room temperature with 90% yield in 20 hours (run 7). Care should be taken not to introduce an internal standard which might "neutralise"[1a] some of the acid (run 9). Dichloroacetic acid could be used but was less efficient (run 10). However with geranyl acetate 1b under the best conditions found so far, the reaction was very rapid but only a trace of the dihydro compound could be found; some cyclogeranyl acetate 17b and polymers were formed. This could not be improved by working with an excess of Et_3SiH or at higher temperature (run 12, 13). The addition of TFA onto the distal double bond was then first carried out and the adduct 16a submitted to the reduction conditions in $iPrNO_2$ with $LiClO_4$ but with no acid present. Very low yields (2-6 %) of dihydrogeranyl acetate 4b were obtained and a lot of polymerisation products (run 15,16). Changing geranyl acetate for the corresponding 2,4-dinitrophenyl ether 1c or using the adduct 16b led to considerable cyclisation (17c) without appreciable reduction (4c)(run 17,18).

TABLE II: Miscellanous reductions with Et_3SiH(2eq).

Run	Substrate		t hr	Results
1		1d	20	Reduction 4d: 7% Cyclisation 17d: 93%
2		18b	20	Reduction 19b: 87%
3		18a	1	Degradation
4			20	Reduction 20% (a)
5		12	36	Reduction 14: 85%

Experimental conditions: Substrate:1 mmol; Solvent:$iPrNO_2$, 1 ml; Acid: TFA , 2.5eq; $LiClO_4$: leq; Temp.: 20°C.
(a) calculated by GLC-Mass. % of isolated product. Σ=SO_2ptol.

A number of related compounds (table II) were then treated as in run 7 of table I. Geranyl p-tolyl sulfone 1d underwent mostly cyclisation (17d) together with 7% reduction (4d), but the linalyl p-tolyl sulfone 18b gave a 87% yield of dihydrosulfone 19b. Linalyl acetate 18a was rapidly destroyed, but the more stable dehydrolinalyl acetate gave 20% yield of the hydrogenated compound. This technique could also be used with the chroman derivative 12[13a], the double bond of which was smoothly (85%) reduced to 14[14]. The higher isoprenolog (α-tocotrienol[13b])13 underwent mainly cyclisation. It so appeared that various reactions compete efficiently with the desired reduction. In order to use a more efficient reducing agent, a two step procedure was considered(scheme I, (A)-(D)).

The addition of hydrogen halides to acyclic terpenes has been known for a long time, although it has been mainly used on squalene [15,16]. Dry hydrogen chloride added smoothly to geranyl acetate in dichloromethane at -78°C. The acetoxy chloride 20b could be isolated by distillation (72%). A number of by-products could be identified (see experimental part). The addition of HCl to geraniol itself gave more by-products, hence the chloro alcohol 20a was preferably prepared by lithium aluminium hydride reduction of the acetate 20b. Similar additions of one mole of HCl were carried out with neryl acetate, geranyl dinitrophenyl ether(1c to give 20c), geranyl *p*-tolyl sulfone(1d to give 20d) and linalyl *p*-tolyl sulfone(18b to give 19a).

With farnesyl acetate 2b the reaction was stopped when analysis showed the substitution of the acetoxy group by chlorine. The dichlorotetrahydrofarnesyl acetate 25b could be isolated (40%) by chromatography. Geranylgeranyl acetate 3b could be efficiently (62%) hydrochlorinated at -78°C in pentane, where the addition product 27b is sparingly soluble. Addition of hydrogen bromide proved possible, but more difficult to carry out, thus the chloro derivatives were used for the reduction experiments.

The hydrogenolysis of alkyl halides can be carried out in a variety of ways ^{17}. The above haloalcohols were initially treated with the radical anion of di*t*-butyl biphenyl (LiDBB)^{18} which has been recently recommended. Chlorohydrogeraniol 20a and chlorohydronerol 21a were smoothly converted into dihydrogeraniol 4a (70%) and dihydronerol 28a (75%) respectively. The bromide 23a also gave dihydrogeraniol (45%) but elimination was also observed (17%). Dichloro tetrahydrofarnesol 25a gave a 32% yield of tetrahydrofarnesol 5a and considerable (48%) elimination. The separation proved difficult.

Preliminary experiments with tributyl tin hydride^{19a} with photoinitiation in the stoechiometric or catalytic ^{19b} mode gave impure product (hydrostannation) in low yield. With free radical (AIBN) initiation,1 eq of Bu$_3$SnH gave a high yield of the desired product (table III). A small amount of isomerisation (E to Z)^{20} of the double bond was observed. In a blind experiment (run 8), the dihydrogeraniol 4a itself was isomerised to a considerable extent. The acetate could be used directly and gave a higher yield (run 2,5,7). The catalytic mode was tried too and gave more isomerisation (more than 10%), propably because of longer reaction times (4 days).

TABLE III: Reductive dehalogenation of halohydro terpene derivatives with Bu$_3$SnH

Run	Substrate	Time mn	Bu$_3$SnH eq(a)	Products yield(E/ Z) %
1	n=1 ; X=Cl ; R=H 20a	60	1.1	4a : 91% (95/ 5)
2	" ; " ; R=Ac 20b	45	1.5	4b : 92 (95/ 5)
3	" ; X=Br ; R=H 23a	60	1.1	4a : 64 (94/ 6)
4	n=2 ; X=Cl ; R=H 25a	120	1.1	5a : 70 (90/10)
5	" ; " ; R=Ac 25b	30	1.4	5b : 98 (95/ 5)
6	n=3 ; " ; R=H 27a	90	1.1	7a : 61 (94/ 6)
7	" ; " ; R=Ac 27b	60	1.5	7b : 93 (95/ 5)
8	n=1 : X=H ; R=H 4a	60	1	4a/28a : (b) (87/13)
	"	300	"	" : (b) (70/30)

Experimental conditions: Substrate: 1 mmol; Cyclohexane: 1 ml/mmol; AIBN: 0.1 eq/Cl. (a) eq with respect to Cl to be reduced. (b) an aliquot was preleved and filtered before injection in a VPC column, no internal standard was added In other experiments the percentage is calculated for isolated products.

We next tried sodium borohydride under solvolytic conditions [21] with chloro dihydrogeraniol 20a, but we observed only substitution and elimination reaction.

With zinc borohydride[22] in ether, preliminary experiments showed that the starting material was consumed to give the desired dihydro derivative which disappeared again! It turned out that reduction of the halide gives diborane which adds to double bonds. Addition of an alkene (more reactive, in excess), such as cyclohexene, provided a diborane trap and good results could be obtained (table IV). The experimental procedure proved to be very important, in that addition to a mixture of zinc borohydride and cyclohexene of the halide in ether gave much better results than other ways of mixing the reagents. Dihydrogeraniol 4a (run 4,7) and phytol 7a and its acetate (run 13,14) could thus be obtained in good yields. Cyclisation products could not be detected, and the mechanism has not yet been elucidated (the important role of the zinc)[23].

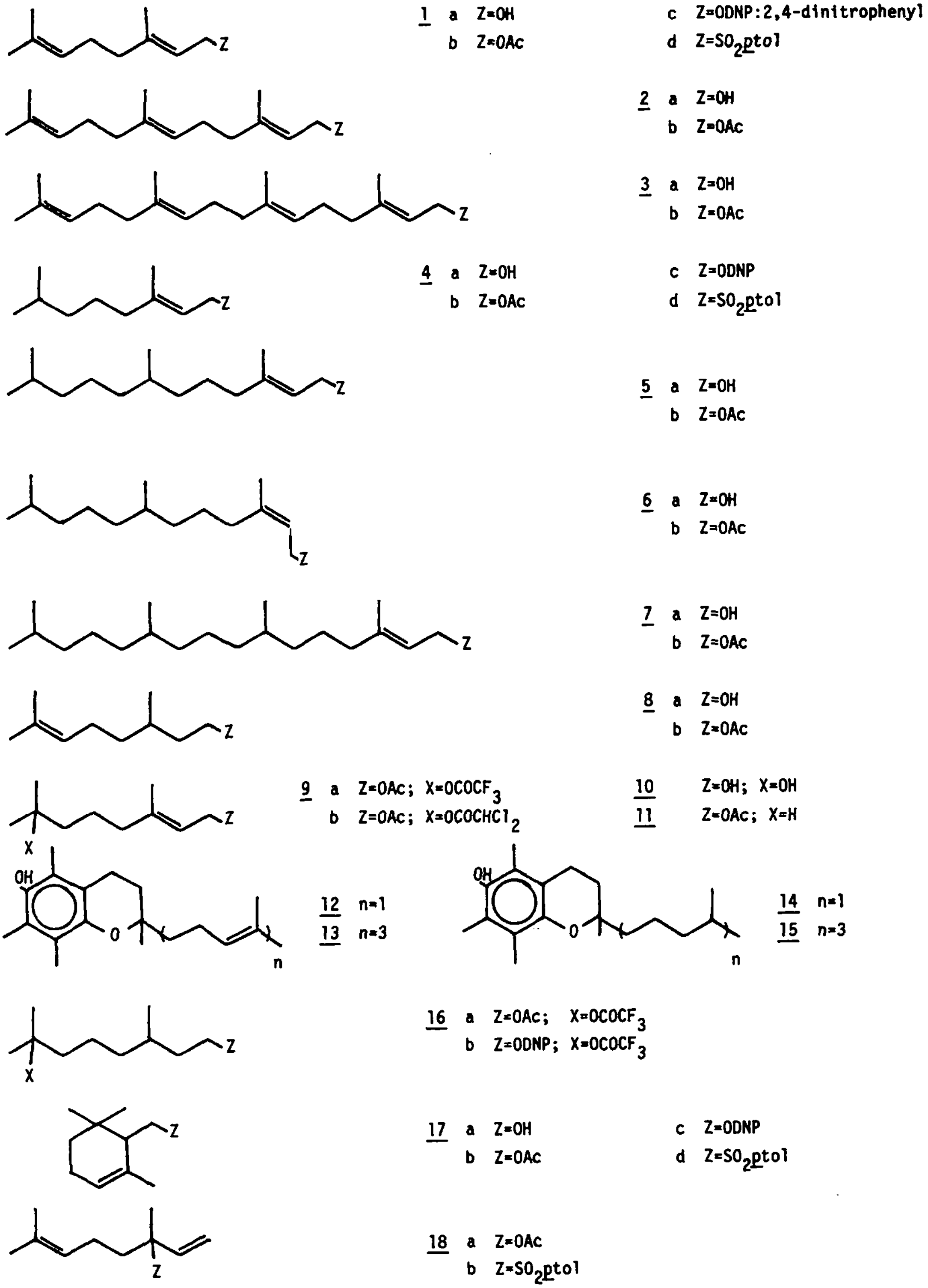
TABLE IV: Reduction with $Zn(BH_4)_2$ in ether

Run	1 Substrate /mmol	2 $Zn(BH_4)_2$ eq/ml/N	T °C	t min	3 Cyclohexene eq	Start. mat. %	Reduct. prod.%	Condition of addit.
1	n=1 ; X=Cl ; R=H ; 20a /0.5	2/4/0.25	20	12	5		4a : 53	(1+3)+2
2	"	"	"	6	"	44	" 39	"
3	"	"	"	12	"	44	" 44	1+(2+3)
4	"	"	"	"	"	0	" 80	(2+3)+1 b
5	"	"	40	6	"	0	" 78	"
6	"	1.2/2.5/.5	"	"	"	10	" 73	"
7	"	2 /2 /0.5	"	"	"	0	" 79	"
8	"	"	0	"	"	90	" 0	"
9	"	"	20	"	"	54	" 42	"
10	"	4 /2 /0.5	40	"	15	20	" 61	"
11	n=1 ; X=Cl ; R=Ac ; 20b/0.5	2 /2 /0.5	"	"	5	0	4b :74 a	"
12	n=3 ; X=Cl ; R=Ac ; 27b/0.25	6 /3 /0.5	"	"	15	0	7b :57 a	"
13	"	"	"	3	"	0	" 76	"
14	" R=H ; 27a/0.25	"	"	"	"	12	7a : 44	"
15	"	"	"	6	"	0	" 69	"

-(a) small amount of phytol -(b) dropwise. % of isolated product.

In a last series of experiments, a dihydropyridine derivative was selected as the reducing agent. It had recently been shown that 1-benzyl-3,5-dipyrrolidinocarbamoyl-1,4-dihydropyridine 29 was reasonably stable in the presence of dichloroacetic acid in acetonitrile[24]. However, when citronellyl acetate (as a model) was added to such a reaction mixture, no reduction was observed. The geranyl acetate / TFA adduct 16a was next used in nitromethane where a small amount (1.9%) of dihydrogeranyl acetate was observed. 1-benzyl-1,4-dihydronicotinamide <u>30</u> gave 2.6-3.4% yield of <u>4b</u> in the $LiClO_4$ system. It thus proved possible to carry out a biomimetic synthesis of phytol, but the yields were very low. The two step procedures above were found to be much more efficient.

SCHEME II



<u>1</u> a Z=OH b Z=OAc c Z=ODNP:2,4-dinitrophenyl d $Z=SO_2$ptol

<u>2</u> a Z=OH b Z=OAc

<u>3</u> a Z=OH b Z=OAc

<u>4</u> a Z=OH b Z=OAc c Z=ODNP d $Z=SO_2$ptol

<u>5</u> a Z=OH b Z=OAc

<u>6</u> a Z=OH b Z=OAc

<u>7</u> a Z=OH b Z=OAc

<u>8</u> a Z=OH b Z=OAc

<u>9</u> a Z=OAc; $X=OCOCF_3$ b Z=OAc; $X=OCOCHCl_2$

<u>10</u> Z=OH; X=OH

<u>11</u> Z=OAc; X=H

<u>12</u> n=1

<u>13</u> n=3

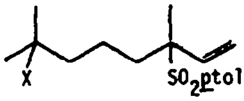
<u>14</u> n=1

<u>15</u> n=3

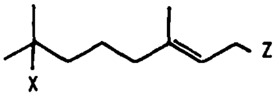
<u>16</u> a Z=OAc; $X=OCOCF_3$ b Z=ODNP; $X=OCOCF_3$

<u>17</u> a Z=OH b Z=OAc c Z=ODNP d $Z=SO_2$ptol

<u>18</u> a Z=OAc b $Z=SO_2$ptol

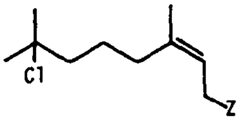


19 a X=Cl
b X=H

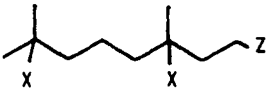


X=Cl a Z=OH d Z=SO$_2$ptol
20 b Z=OAc e Z=Cl
c Z=ODNP

X=Br a Z=OH
23 b Z=OAc
c Z=Br

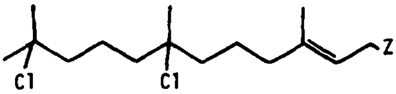


21 a Z=OH
b Z=OAc

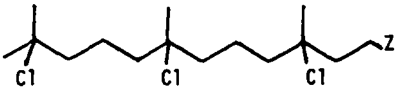


22 a Z=OAc; X=Cl
b Z=Cl; X=Cl

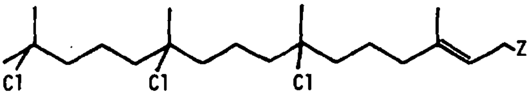
24 Z=OAc; X=Br



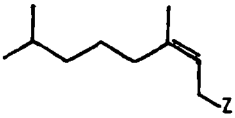
25 a Z=OH
b Z=OAc
c Z=Cl



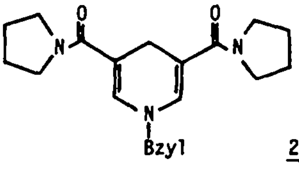
26 a Z=OAc
b Z=Cl



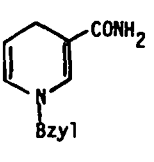
27 a Z=OH
b Z=OAc



28 a Z=OH
b Z=OAc



29



30

EXPERIMENTAL

Melting points were determined in a capillary tube and are not corrected. The spectroscopic instrumentation included ^{1}H NMR(PMR): Brucker WH 80 (80 MHz) and Cameca 250 (250 MHz), CDCl$_3$ solution with respect to Me$_4$Si unless otherwise stated. ^{13}C NMR(CMR): Brücker 90 (90 MHz), δ values are given in ppm and coupling constants in Hertz. IR: Perkin-Elmer 599, either neat or in CHCl$_3$ solution(values given in cm^{-1},S:strong, m: medium, w: weak). Mass spectra: Varian Mat CH9, and for the GLC-Mass measurement: Ribermag with capillary column; Chemical ionisation: CI; Electronic impact: EI. GLC: Varian 1740, column: OV 101 5% (4m) on Anakrom Q; Integrator: Intersmat Minigrator; Girdel 30, column: OV 101 10% (4m) or capillary column: SE 52, integrator: Hewlet Packard HP3380A; Intersmat, column: FFAP 10%. Microanalysis were carried out in the microanalytical laboratories of the Université P. et M. Curie to whom our thanks are due. Analytical TLC were carried out on Merck plates (5735, plastic sheet, silicagel 60F254, thickness 0.2mm). Flash chromatography(FC)^{25} was carried out with silica gel (Merck 7736), eluted with a mixture of pentane/ether/ethyl acetate. Some by-products were obtained in such a low yield, or were so unstable that only a partial, but unequivocal, characterisation was possible.

Geraniol and nerol were purchased from Fluka. t,t Farnesol was isolated from the mixture (Fluka) of isomers by MPLC (LOBAR Merck) with a C(440-37) Lichroprep Si 60 column (4063μm) Geranylgeraniol was a generous gift from the Kuraray Co..

Reduction with Et_3SiH.

* Dihydrocitronellyl acetate: 3,7-dimethyloctyl acetate, 11.

Trifluoroacetic acid (0.2 ml, 2.5 mmol, 2.5 eq) was slowly added to a mixture of citronellyl acetate 8a (198 mg, 1 mmol), lithium perchlorate (106 mg, 1 mmol), triethylhydrogeno silane (242 mg, 2 mmol) and 2-nitropropane (1ml) at 20°C, the mixture was allowed to stand for 22 hours. The organic solution was washed with aqueous saturated sodium bicarbonate solution followed by extraction with ether. After drying ($MgSO_4$) and filtering, the solution was evaporated. The residue was purified by FC to give 180 mg (90%) of pure dihydrocitronellyl acetate 11 identical to a sample prepared by catalytical hydrogenation of geraniol, followed by acetylation in pyridine.

* 3,7-Dimethyl-3-p-toluenesulfonyl-1-octene 19b.

By using the same procedure with the 3,7-dimethyl-3-p-toluenesulfonyl-1,6-octadiene 18b and a reaction time of 48 h, we have obtained after purification by FC 256 mg (87%) of dihydrolinalyl sulfone 19b,colourless liquid. **PMR**(250): 0.83 (d, J=6Hz,6H); 1.19(m,4H); 1.32 (s,3H); 1.85(m,2H); 2.39 (s,3H); 5.08 (d,J=17Hz,1H); 5.37 (d, J=10.5Hz,1H); 5.92 (dd, J=17&10.5Hz,1H);7.15 (d,J=8Hz,2H);7.52 (d, J=8Hz,2H). **CMR**: 16.4 (CH_3); 21.6 (CH_2+CH_3); 22.6 (2 CH_3); 27.7 (CH); 32.9 (CH_2); 39.2 (CH_2);68.2 (C); 119.8 (CH_2); 128.6 (2 CH); 130.4 (2 CH); 132.1 (C); 135.2 (CH); 144.0 (C). **IR**: 2940-2860 S;1630 w; 1590 m; 1300 S; 1150 S. **MS CI** (NH_3): 312(M+18,10). **Anal.**:calc. for $C_{17}H_{26}O_2S$, C 69.34 H 8.90; found, C 69.31 H 9.05.

* 3,7-Dimethyl-7-trifluoroacetoxy-2E-octen-1-yl acetate 16b.

To a solution of geranyl acetate 1b (11g, 56 mmol) in CH_2Cl_2 (140 ml) at 0°C was slowly added (21 ml, 280 mmol, 5eq) trifluoroacetic acid. After 100 mn the excess of acid was neutralised with a saturated aqueous solution of $NaHCO_3$. The organic layer was washed with water, dried ($MgSO_4$), filtered and evaporated to give 15 g of crude oil. After purification on 250 g of silica Merck(60) eluted with petroleum ether/ethyl acetate,we obtained (9 g, 52%) of 6b. Colourless liquid. **PMR**(80): 1.52 (m,2H); 1.55 (s,6H); 1.69 (s,3H); 1.79 (m,2H); 2.05 (m+s,5H); 4.59,J=7Hz,2H); 5.36 (t,J=7Hz,1H). **CMR**:16.1 (CH_3); 20.8 (CH_3); 21.5 (CH_2); 25.4 (2CH_3); 39.2 (CH_2); 39.8 (CH_2); 61.0 (CH_2); 88.8(C); 114.2 (CF_3,J=285Hz); 118.8(CH); 140.8 (C); 155.6 (C,J=41Hz); 170.4 (C). **IR**: 2940 S; 1770 S; 1735 S; 1660 w; 1450 S. **MS CI** (NH_3): 328 (M+18,100), 214(31). **Anal.**: calc. for $C_{14}H_{21}F_3O_4$, C 54.19 H 6.82; found, C 54.21, 6.76.

* 3,7-Dimethyl-7-trifluoroacetoxyoctyl acetate 9a.

By using the same procedure with citronellyl acetate 8b. Colorless oil. **PMR** (250): 0.91 (d, J=1.3Hz, 3H); 1.1-1.9 (m, 9H); 1.56 (s,6H); 2.03 (s,3H); 4.06 (ddd, J=14,14&5Hz,2H). **CMR**: 19.4 (CH_3); 20.9 (CH_3); 21.1 (CH_3); 25.7 (2 CH_3); 29.8 (CH); 35.6 (CH_2); 37.0 (CH_2); 40.6 (CH_2); 62.8 (CH_2); 89.1 (C); 114.0 (CF_3, J=258Hz); 155.6 (C, J=41Hz); 170.6 (C). **IR**: 2940-2870 S; 1770 S; 1735 S; 1450 m. **MS CI(NH3)**: 330 (M+18, 57); 216 (100); 199 (30). **Anal.**:calc. for $C_{14}H_{23}F_3O_4$, C 53.84 H 7.42; found, C 53.70 H 7.46.

* 3,7-Dimethyl-1-(2,4-dinitrophenoxy)-7-trifluoroacetoxy-2E-octene 16c.

In the same way as previously, 1c[26] (8 g,25mmol) gives 16c (5.1 g,47%). **PMR**(250): 1.55 (m,2H); 1.57 (s,6H); 1.79 (s,3H); 1.82 (m,2H); 2.12 (t,J=6Hz,2H); 4.74 (d,J=6.5Hz,2H); 5.48 (t,J=6.5Hz,1H); 7.18 (d,J=9.5Hz,1H); 8.38 (dd,J=9.5&2.8Hz,1H); 8.69(d,J=2.8Hz,1H). **CMR**: 16.3 (CH_3); 21.2 (CH_2); 25.3 (2CH_2); 39.0 (CH_2); 39.5 (CH_2); 67.3 (CH_2); 88.9 (C); 114.2 (CF_3,J=285Hz); 114.7 (C); 117.4 (CH); 121.2 (CH); 128.5 (CH); 138.7 (CH); 139.4 (CH); 143.1 (C);155.6(C);156.2(C). **IR**:2940 S;1770 S;1735 w;1660 w;1530 S;1490 m. **MS CI** (NH_3): 452(M+18,100). **Anal.**: calc. for $C_{18}H_{21}F_3N_2O_7$, C 49.77 H 4.87 N 6.45; found, C 50.24 H 4.88 N 6.33.

Addition of hydrogen chloride.

* Geranyl acetate: 7-chloro-3,7-dimethyl-2E-octen-1-yl acetate 20b.

A stream of dry hydrogen chloride was passed through a solution of geranyl acetate 1b (19.5 g, 0.1 mol)in CH_2Cl_2 (250 ml) at -78°C, the reaction was monitored by TLC. When the starting material was consumed, the solution was poured into water and washed with saturated aqueous $NaHCO_3$ solution. After work-up, distillation gave 20b (16.6 g, 72%),b.p. 68°C at 0.001 torr as a colourless liquid. **PMR**(80): 1.57 (s,6H); 1.71 (s,3H); 1.5-1.8 (m,4H); 2.06 (s,3H); 2.13 (t, J=6Hz,2H); 4.60 (d, J=7Hz,2H); 5.37 (t, J=7Hz,1H). **CMR**: 15.9 (CH_3); 20.6 (CH_3); 22.7 (CH_2); 32.1 (2CH_3); 39.0 (CH_2); 45.0 (CH_2); 60.7 (CH_2); 69.9 (C); 118.5 (CH); 140.6 (C); 169.7 (C).**IR**: 2980-2950 S; 1735 S; 1665 w; 1450 m.**MS CI** (NH_3): 252 (M+18,36), 250 (100). **Anal.**: calc for $C_{12}H_{21}ClO_2$, C 61.93 H 9.09; found, C 61.76 H 9.21.

* By-products: these products were isolated in very small proportions from different experiments on geraniol or geranyl acetate by flash chromatography.

\- 3,7-Dichloro-3,7-dimethyl-1-octyl acetate 22b.

Colourless liquid. **PMR**(80): 1.61 (s,9H); 1.75 (s,6H); 2.05 (s,3H); 2.12 (t, J=7Hz,2H); 4.31 (t, J=7Hz,2H). **MS CI** (NH_3): 290 (M+18,10); 288 (60); 286 (100); 252 (12); 250 (35).

\- 1,7-Dichloro-3,7-dimethyl-2E-octene 20e .

Colourless liquid. **PMR**(80): 1.57 (s,6H); 1.73 (d, J=1Hz,3H); 1.6-1.8 (m,4H); 2.07 (t, J=6Hz,2H); 4.08 (d,J=8Hz,2H); 5.51 (tq, J=8&1Hz,1H). **MS EI**: 210 (5); 208 (8); 174 (18); 172 (65); 136 (12); 121 (27).

\- 1,3,7-Trichloro-3,7-dimethyloctane 22c.

Light yellow liquid. **PMR**(80): 1.60 (s,9H); 1.75 (m,6H); 2.24 (m, J=8&2Hz,2H); 3.97 (t, J=8Hz,2H). **CMR**: 20.4 (CH_2); 29.7 (CH_3); 32.6 (2 CH_3); 40.2 (CH_2); 44.4 (CH_2); 45.8 (CH_2); 46.6 (CH_2); 70.5 (C); 72.0 (C). **MS CI** (NH_3): 266 (M+18,7); 264 (21); 262 (22); 228 (8); 192 (10); 190 (30); 174 (33); 172 (100).

* Neryl acetate: 7-chloro-3,7-dimethyl-2Z-octen-1-yl acetate 21b.

Colourless liquid (47%). **PMR**(80): 1.57 (s,6H); 1.5-1.8 (m,4H); 1.79 (s,3H); 2.05 (s,3H); 2.13 (t, J=6Hz,2H); 4.55 (d, J=7Hz,2H); 5.38 (t, J=7Hz,1H). **CMR**: 21.1 (CH_3); 23.4 (CH_3); 23.5 (CH_2); 31.8 (CH_2); 32.5 (2 CH_3); 45.5 (CH_2); 60.8 (CH_2); 70.6 (C); 119.3 (CH); 142.1 (C); 170.6 (C). **IR**: 2990-2950 S; 1740 S; 1670 w; 1460 m. **MS** CI (NH_3): 252 (M+18,23), 250 (27), 214 (88), 154 (100). **Anal.**: calc. for $C_{12}H_{21}ClO_2$, C 61.93 H 9.09; found, C 61.81 H 9.09.

* Farnesyl acetate 2b.

The reaction was carried out as for 20b on 8 g of farnesyl acetate 2b, and stopped when TLC showed the formation of less polar compounds (terminal chlorides). Purification by FC gave four fractions in the order of elution : Fraction n°1(0.1g) gave compounds 25c and 26b; fraction n°2 (4.2g) contained monochloro and cyclised products; fraction n°3 (4.2g) contained 25b and fraction n°4 (0.5g) contained 26a.

- 7,11-Dichloro-3,7,11-trimethyl-2E-dodecen-1-yl acetate 25b.

Colourless liquid. **PMR**(250): 1.52(s,3H); 1.56(s,6H); 1.5-1.9(m,10H); 2.05(s,3H); 2.09 (t,J=8Hz,2H); 4.57(d,J=8Hz,2H); 5.33(t,J=8Hz,1H). **CMR**: 16.3(CH_3); 20.4(CH_2); 21.0(CH_3); 22.5(CH_2); 29.7(CH_3); 32.3(CH_3); 32.4(CH_3); 39.3(CH_2); 43.4(CH_2); 44.0(CH_2); 45.9(CH_2); 61.0(CH_2); 70.4(C); 74.3(C); 118.5(C); 141.0(C); 170.2(C). **MS** CI (NH_3): 356(M+18,18), 354(20), 320(23), 318(38). **Anal.**: calc. for $C_{17}H_{30}Cl_2O_2$, C 60.53 H 8.96; found, C 60.52 H 9.13.

- 1,7,11-Trichloro-3,7,11-trimethyl-2E-dodecene acetate 25c.

Colourless liquid. **PMR**(80): 1.59(m,9H); 1.73(m,13H); 2.08(t,J=6Hz,2H); 4.12 (d,J=8Hz ,2H); 5.48(t,J=8Hz,1H). **MS** CI (NH_3): 324(M+18,18); 322(55); 320(54); 298(7); 296(37); 294(61); 260(24); 258(65); 222(42); 205(100).

- 3,7,11-Trichloro-3,7,11-trimethyl-1-dodecyl acetate 26a.

Colourless liquid; **PMR**(80): 1.60(m,12H); 1.75(m,12H); 2.05(s,3H); 2.12(t,J=7Hz,2H); 4.3(t,J=7Hz,2H). **MS** CI (NH_3): 394 (M+18,10), 392(25), 390(20), 356(23), 354(35), 320(42), 318(100), 282(45).

- 1,3,7,11-Tetrachloro-3,7,11-trimethyl dodecane 26b.

Colourless liquid. **PMR**(80): 1.60 (m,12H); 1.75(m,12H); 2.23(t,J=8Hz,2H); 3.7(t,J=8Hz ,2H). **MS** CI (NH_3): 372(M+18,5); 370(13); 368(25); 366(21).

* Geranylgeranyl acetate 3b: 7,11,15-trichloro-3,7,11,15-tetramethyl-2E-hexadecen-1-yl acetate 27b.

Geranylgeranyl acetate (441.5 mg, 1 mmol) in pentane (1ml) was added at -78°C to a 1.8N solution of HCl in pentane. A light brown gum separated out. After 5 min the mixture was worked up. The desired trichloroacetate 27b was isolated by FC. Colourless crystals (from pentane / ether, 283 mg, 63%), m.p. 35-37°C. **PMR**(250): 1.53(s,3H); 1.55(s,3H); 1.59(s,6H); 1.7(s,3H); 1.5-1.8(m,16H); 2.05(s,3H); 2.05(m,2H); 4.58(d,J=8Hz,2H); 5.36(t,J=8Hz,1H). **CMR**: 16.3(CH_3); 20.0(CH_2); 20.4(CH_2); 21.0(CH_3); 22.5(CH_2); 29.7(2 CH_3); 32.4(2 CH_3); 39.2(CH_2); 44.0-43.3(4 CH_2); 45.8(CH_2); 61.0(CH_2); 70.4(C); 73.9(C); 74.0(C); 118.5(CH); 141.0(C); 170.1(C). **IR**: 2940 S, 1730 S, 1660 w, 1450 m. **MS** CI (NH_3): 462(M+18,16); 460(50); 458(47); 424(15); 422(17); 388(13); 386(20); 350(80). **Anal.**: calc. for $C_{22}H_{39}Cl_3O_2$, C 59.80 H 8.90; found, C 59.62 H 9.05.

Hydrogenolysis of the hydrogen chloride adducts of the terpene acetates.

Lithium aluminium hydride (LAH)(38 mg, 1 mmol) was slowly added to a solution of the acetate (1 mmol) in anhydrous ether (5 ml) at 0°C. After standing for 4 hours the usual work-up gave the corresponding alcohol, in a yield of at least 95%.

* 7-Chloro-3,7-dimethyl-2E-octen-1-ol 20a.

Colourless oil. **PMR**(80): 1.56 (s,6H); 1.68 (s,3H); 1.7 (m,4H); 2.05 (t, J=6Hz,2H); 4.25 (d, J=7Hz,2H); 5.44 (t, J=7Hz,1H). **CMR**: 16.0 (CH_3); 22.9 (CH_2); 32.3 (2 CH_3); 39.2 (CH_2); 45.2 (CH_2); 58.7 (CH_2); 70.7 (C); 123.6 (CH); 137.8 (C). **IR**: 3320 S, 2970-2850 S, 1660 S, 1450 m. **MS** CI(NH_3): 210 (M+18,5); 208 (15); 192 (8); 190 (23); 172 (36); 154 (100). **Anal.**: calc for $C_{10}H_{19}ClO$, C 62.98 H 10.04; found, C 62.99 H 10.01. **RN**: 39847-63-7[16].

* 7-Chloro-3,7-dimethyl-2Z-octen-1-ol 21a .

Colourless oil. **PMR**(80): 1.58 (s,6H); 1.66 (s,2H); 1.7 (s,2H); 1.77 (s,3H); 2.1 (t, J=6Hz,2H); 4.13 (d, J=7Hz,2H); 5.46 (t,J=7Hz,1H). **CMR**: 23.4-23.7 (CH_2+CH_3); 31.8 (CH_2); 32.6 (2 CH_3); 45.6 (CH_2); 59.1 (CH_2); 70.8 (C);124.5 (CH);139.4 (C). **IR**:3400 m,2950-2860 S, 1650 w, 1450 m. **MS** CI(NH_3): 210 (M+18,11);208 (37);192 (16);190 (48). **Anal**:calc. for $C_{10}H_{19}ClO$, C 62.98 H 10.04; found, C 62.99 H 9.99.

* 7,11-dichloro-3,7,11-trimethyl-2E-dodecen-1-ol 25a.

Colourless oil. **PMR**(250): 1.53 (s,3H); 1.58 (s,6H); 1.6-1.8 (m,10H); 1.67 (s,3H); 2.03 (t, J=6Hz,2H); 4.14 (d, J=7Hz,2H); 5.40 (tq, J=7&1Hz,1H). **CMR**: 16.1 (CH_3); 20.4 (CH_2); 29.7 (CH_3); 32.4 (2 CH_3); 39.3 (CH_2); 43.4-43.9 (2 CH_2); 45.9 (CH_2); 58.9 (CH_2); 70.6 (C); 74.3 (C); 123.6 (CH); 138.4 (C). **IR**: 3600 m; 3440 m; 2980-2880 S; 1665 m; 1450 S. **RN**: 39847-59-1[16].

* 7,11,15-Trichloro-3,7,11,15-tetramethyl-2E-hexadecene-1-ol 27a.

Colourless crystals ,m.p. 60-65°C from ether/pentane. **PMR**(250): 1.53 (s,3H); 1.55 (s,3H); 1.59 (s,6H); 1.67 (s,3H); 1.5-1.8 (m,16H); 2.02 (t, J=6.5Hz,2H); 2.20 (s,1H); 4.11 (d,J=7Hz,2H); 5.37 (t, J=7Hz,1H). **CMR**: 16.1 (CH_3); 20.0 (CH_2); 20.4 (CH_2); 22.6 (CH_2); 29.7 (2 CH_3); 32.4 (2 CH_3); 39.3 (CH_2); 43.4-44.0 (4 CH_2); 58.9 (CH_2); 70.6 (C); 74.0 (C); 74.3 (C); 123.6 (CH); 138.2 (C). **IR**: 3600 m; 3440 m; 2960-2840 S; 1665 m; 1450 S. **MS** CI(NH_3): 420 (M+18, 33); 418 (100); 416 (95); 402 (2); 400 (5); 398 (5); 384 (10); 382 (53); 380 (80); 366 (2); 364 (7); 362 (10); 346 (17); 344 (40); 328 (7); 326 (13); 308 (37); 290 (42). **Anal.**: calc for $C_{20}H_{37}Cl_3O$, C 60.07 H 9.33; found, C 59.99 H 9.43.

Miscellanous hydrogen chloride adducts.(same procedure as for 1b).

* From geranyl 2,4-dinitrophenyl ether 1c: 7-chloro-1-(-2,4-dinitrophenoxy)-3,7-dimethyl -2E-octene 20c, 80% .

Pale brown oil. PMR(250): 1.56 (s, 6H); 1.6–1.7 (m,4H); 1.78 (s,3H); 2.12 (t, J=5.5Hz,2H); 4.85 (t, J=6.5Hz,2H); 5.49 (tq, J=6.5&1Hz,1H); 7.20 (d, J=9Hz,1H); 8.41 (dd, J=9&3Hz,1H); 8.72 (d, J=3Hz,1H). CMR: 16.8 (CH_3); 22.9 (CH_2); 32.4 (2 CH_3); 39.2 (CH_2); 45.2 (CH_2); 67.5 (CH_2); 70.9 (C); 114.7 (CH); 117.1 (CH); 121.4 (CH); 128.6 (CH); 133.7 (C); 139.5 (C); 143.6 (C); 146.3 (C). IR: 3110 m; 2980–2900 S; 1665 m; 1615 m; 1540 S; 1500 m; 1470 m. MS CI (NH_3): 376 (M+18, 33); 374 (100); 338 (15). **Anal.**: calc. for $C_{16}H_{21}ClN_2O_5$, C 53.86 H 5.93 N 7.85; found, C 53.88 H 5.88 N 8.03.

* From linalyl p-tolyl sulfone 18b: 7-chloro-3,7-dimethyl-3-(p-toluene sulfonyl)-1-octene 19a, 90%.

Colourless crystals, m.p. 96°C from ether. PMR(250): 1.35 (s,3H); 1.52 (s,6H); 1.3–2 (m,6H); 2.39 (s,3H); 5.08 (d, J=17Hz, 1H); 5.37 (d, J=10.5Hz,1H); 5.92 (dd, J=17&10.5Hz,1H); 7.15 (d, J=8Hz, 2H); 7.52 (d, J=8Hz,2H). CMR: 16.4 (CH_3); 19.6 (CH_2);21.6 (CH_3); 32.5 (2 CH_3); 32.8 (CH_2); 46.1 (CH_2); 68.1 (C); 70.4 (C); 120.2 (CH_2); 128.7 (2 CH); 130.4 (2 CH); 132 (C); 134.9 (CH); 144.1 (C). IR ($CHCl_3$): 2980–2880 S; 1590 m; 1300 S; 1150 S. MS CI(NH_3): 348 (M+18, 41); 346 (100); 310 (26). **Anal.**: calc for $C_{17}H_{25}ClO_2S$, C 62.08 H 7.66; found, C 61.95 H 7.85.

* From geranyl p-tolyl sulfone 1d: 7-chloro-3,7-dimethyl-1-(p-toluene sulfonyl)-2E-octene 20d, 80%.

Colourless crystals, m.p. 67°C from ether. PMR(250): 1.38 (s,3H); 1.56 (s, 6H); 1.5–1.6 (m,4H); 2.0 (t, J=6.5Hz, 2H); 2.43 (s,3H); 3.78 (d, J=8Hz,2H); 5.17 (t, J=8Hz,1H); 7.29 (d, J=9Hz,2H); 7.71 (d, J=9Hz, 2H). CMR: 16.0 (CH_3); 21.6 (CH_3); 22.9 (CH_2); 32.3 (2 CH_3); 39.3 (CH_2); 45.1 (CH_2); 55.9 (CH_2); 70.7 (C); 110.6 (CH); 128.0 (2 CH); 129.2 (2 CH); 135.5 (C); 144.0 (C); 145.3 (C). IR ($CHCl_3$): 2900 S; 1580 m; 1300 S; 1140 S. MS CI(NH_3): 348 (M+18, 45); 346 (100); 310 (53). **Anal.**: calc for $C_{17}H_{25}ClO_2S$, C 62.08 H 7.66; found, C 61.95 H 7.85.

Addition of hydrogen bromide to geranyl acetate.

* A stream of dry hydrogen bromide is passed through a solution of geranyl acetate 1b (3.92g, 20mmol) in methylene chloride (50ml) at -78°C until the substitution products appear on TLC. The usual work-up gives after FC: fraction n°1, 23c (0.5g, 9%); fraction n°2, 1b (0.7g, 18%); fraction n°3, 23b (2.4g, 50%); fraction n°4, 24 (0.07g, 1%).

\- 1,7-Dibromo-3,7-dimethyl-2E-octene 23c.

Unstable colourless oil.PMR(80): 1.6–1.8 (m,4H); 1.77 (s,9H); 2.08 (t, J=6Hz,2H); 3.99 (d, J=8Hz,2H); 5.57 (t, J=8Hz, 1H).

\- 7-Bromo-3,7-dimethyl-2E-octen-1-yl acetate 23b.

Colourless oil. PMR(250): 1.73 (s, 3H); 1.77 (s,6H); 1.7–1.8 (m,4H); 2.05 (s,3H); 2.06 (m,2H); 4.60 (d,J=7Hz,2H); 5.37 (t, J=7Hz,1H). CMR: 16.3 (CH_3); 21.0 (CH_3); 24.1 (CH_2); 34.2 (2 CH_3); 39.1 (CH_2); 46.7 (CH_2); 61.0 (CH_2); 67.6 (C); 118.5 (CH); 141.0 (C). IR: 2930 S; 1730 S; 1660 w; 1440 m. MS CI(NH_3): 296 (M+18, 30); 294 (27); 214 (100). **Anal.**: calc for $C_{12}H_{21}BrO_2$, C 51.99 H 7.63; found C 51.84 H 7.74.

\- 3,7-Dibromo-3,7-dimethyl-1-octyl acetate 24.

Unstable colourless oil. PMR (80): 1.6–1.8 (m,6H); 1.78 (s,9H); 2.06 (s,3H); 2.13 (t, J=8Hz,2H); 4.33 (t, J=8Hz,2H). MS CI(NH_3): 378 (M+18, 13); 376 (26); 296 (100); 294 (100); 214 (92).

* 7-Bromo-3,7-dimethyl-2E-octene-1-ol 23a.

Reduction with $LiAlH_4$ of the bromoacetate 23b (1.9g) as above gave the bromoalcohol 23a (98%). Unstable colourless oil. PMR (80): 1.69 (s,3H); 1.75 (s,6H); 1.6–1.8 (m,4H); 1.89 (s,1H); 2.06 (t, J=6Hz,2H); 4.14 (d, J=7Hz,2H); 5.40 (t, J=7Hz,1H). CMR: 16.1 (CH_3); 24.2 (CH_2); 34.2 (2 CH_3); 39.1 (CH_2); 46.7 (CH_2); 58.8 (CH_2); 68.0 (C); 123.6 (CH); 137.8 (C).IR: 3420 S; 2960–2850 S; 1660 m; 1440 S.

Reduction with Li/DBB.

* Under a dry atmosphere (Ar + a magnetic stirrer covered with glass) were added successively at 0°C, freshly distilled THF (60 ml), lithium (630 mg, 90 mmol, 3 eq) and dit-butyl biphenyl[18] (1.6 g, 6 mmol, 0.2 eq). After stirring for a night at 0°C, a deep blue colour appeared. 7-Chloro-3,7-dimethyl-2E-octene-1-ol 20a (5.9 g, 31 mmol) in THF (20 ml) was added in two portion. After standing for 24 hours, for the reappearence of the blue colour, the solution was filtered and hydrolysed. Most of the solvent was evaporated and the usual work-up gave 5.7 g of crude oil. Distillation (45°C/0.003 mmHg) gave 6,7-dihydrogeraniol 4a (3.2 g, 61%) identical to a sample supplied by BASF.PMR(80): 0.87 (d, J=6Hz,6H); 1–1.7 (m,5H); 1.39 (s,1H); 1.66 (s,3H); 2.0 (t, J=7Hz,2H); 4.15 (d, J=7Hz,2H); 5.40 (t, J=7Hz,1H). CMR: 16.2 (CH_3); 22.6 (2 CH_3); 25.5 (CH_2); 27.9 (CH); 38.6 (CH_2); 39.8 (CH_2); 59.0 (CH_2); 123.1 (CH); 139.1 (C). RN: 1461-04-72.

\- Dihydronerol: 3,7-dimethyl-2Z-octen-1-ol 28a.

By the same procedure as above ,dihydronerol (75% from 21a) was prepared, identical to the sample supplied by BASF. PMR(80): 0.86 (d, J=6Hz,6H); 1–1.7 (m,5H); 1.39 (s,1H); 1.77 (s,3H); 2.07 (t, J=7Hz,2H); 4.13 (d, J=7Hz,2H); 5.43 (t, J=7Hz,1H). CMR: 22.7 (CH_3); 22.9 (CH_3); 23.5 (CH_3); 26.1 (CH_3); 27.9 (CH); 32.2 (CH_3); 38.8 (CH_3); 58.8 (CH_3); 123.9 (CH); 139.6 (C). RN: 18530-67-1.

* The corresponding acetates were prepared by acetylation in pyridine of the authentique sample suppliad by BASF.

\- Dihydrogeranyl acetate: 3,7-dimethyl-2E-octen-1-yl 4b.

PMR(80): 0.87 (d, J=6Hz,6H); 1-1.7 (m,5H); 1.70 (s,3H); 2.04 (t, J=7Hz, 2H); 2.05 (s,3H); 4.59 (d, J=7Hz,2H); 5.36 (t, J=7Hz,1H).CMR: 16.5 (CH_3); 21.1 (CH_3); 22.7 (2 CH_3); 25.5 (CH_2); 28.0 (CH); 38.7 (CH_2); 39.8 (CH_2); 61.4 (CH_2); 118.0 (CH); 142.3 (C); 170.6 (C). **RN**: 70795-75-4.

- Dihydroneryl acetate: 3,7-dimethyl-2Z-octen-1-yl acetate 28b.

PMR(250): 0.87 (d, J=6.8Hz,6H); 1.13 (m,2H); 1.39 (m,2H); 1.52 (m,1H); 1.75 (s,3H); 2.04 (s,3H); 2.08 (t, J=8Hz,2H); 4.53 (d, J=7Hz,2H); 5.32 (t, J=7Hz,1H). CMR: 21.1 (CH_3); 22.7 (2 CH_3); 23.6 (CH_3); 26.0 (CH_2); 28.0 (CH); 32.3 (CH_2); 38.7 (CH_2); 61.0 (CH_2); 118.6 (CH); 142.7 (C).**RN**: 70795-76-5.

Reduction with Bu_3SnH.

* Dihydrogeraniol: 3,7-dimethyl-2E-octene-1-ol 4a.

Azoisobutyronitrile (AIBN)(22 mg, 0.1 mmol) and tributyltin hydride[19a] (0.32 ml, 1.2 mmol) were added to a solution of 7-chloro-3,7-dimethyl-2E,octene-1-ol (20a)(192mg, 1mmol) and the mixture heated at 75°C for 2 hours. Most of the solvent was evaporated and the residue was flash chromatographed (petroleum ether/CH_2Cl_2,then ether) to give 4a (102 mg, 70%), identical to the product of the preceding reaction.

* 3,7,11-Trimethyl-2E-dodecen-1-yl acetate 5b,and alcohol 5a.

By the same procedure on 25b we obtained 5b (98%:trans/cis=96/4). Colourless oil. PMR(250): 0.85 (d, J=6.5Hz,3H); 0.87 (d, J=6.5Hz,3H); 1-1.7 (m,12H); 1.69 (s,3H); 2.02 (t, J=7Hz,2H); 2.06 (s,3H); 4.59 (d, J=7Hz,2H); 5.36 (tq, J=7&1Hz,1H). CMR: 16.5 (CH_3); 19.8 (CH_3); 21.1 (CH_3); 22.8 (2 CH_3); 24.9 (CH_2); 25.2 (CH_2); 28.1 (CH); 32.8 (CH); 36.8 (CH_2); 37.4 (CH_2); 39.5 (CH_2); 39.9 (CH_2); 61.4 (CH_2); 117.9 (CH); 142.2 (C); 170.5 (C). IR: 2930-2860 S; 1735 S; 1660 w; 1450 S. MS CI(NH_3): 286 (M+18,10); 226 (100).

The corresponding alcohol 5a could be isolated either by hydrogenolysis of 25a (70%: trans/cis=90/10) or hydrolysis of 5b. Colourless oil. PMR(250): 0.85 (d, J=6.5Hz,3H); 0.87 (d, J=6.5Hz,3H); 1-1.7 (m,12H); 1.67 (s,3H); 2.02 (t, J=7Hz,2H); 4.15 (d, J=7Hz,2H); 5.40 (tq, J=7&1Hz,1H). CMR: 16.2 (CH_3); 19.8 (CH_3); 22.7 (2 CH_3); 24.9 (CH_2); 25.2 (CH_2); 28.0 (CH); 32.8 (CH); 37.0 (CH_2); 37.3 (CH_2); 39.4 (CH_2); 39.9 (CH_2); 59.2 (CH_2); 123.0 (CH); 139.4 (C). MS EI: 227 (4); 226 (7); 208 (1); 140 (1); 137 (2); 126 (6); 123 (31); 111 (6); 109 (7); 97 (12); 95 (24). **RN**: 61252-24-2[27].

* 3,7,11-Trimethyl-2Z-dodecen-1-yl acetate 6b, and alcohol 6a.

The acetate 6b Was isolated in small quantities from preceding hydrogenolysis experiments. Colorless oil. PMR(250): 0.85 (d, J=6.5Hz,3H); 0.87 (d, J=6.5Hz,3H); 1-1.7 (m,12H); 1.75 (s, 3H); 2.05 (s,3H); 2.07 (t, J=7Hz, 2H); 4.56 (d, J=7Hz,2H); 5.34 (t, J=7Hz,1H). CMR: 19.8 (CH_3); 21.1 (CH_3); 22.8 (2 CH_3); 23.6 (CH_3); 24.9 (CH_2); 25.7 (CH_2); 28.1 (CH); 32.4 (CH_2); 32.8 (CH); 36.8 (CH_2); 37.4 (CH_2); 39.5 (CH_2); 61.0 (CH_2); 118.7 (CH); 142.8 (C); 170.5 (C). IR: 2930-2860 S; 1735 S; 1660 w; 1450 S. MS CI(NH_3): 286 (M+18,10); 226 (100).

The corresponding alcohol 6a could be isolated in small proportions either by hydrogenolysis of 25a or hydrolysis of 6b. Colourless oil. PMR(250): 0.85 (d, J=6.5Hz;3H); 0.87 (d, J=6.5Hz,3H); 1-1.7 (m,12H); 1.74 (s,3H); 2.06 (t, J=7Hz,2H); 4.13 (d, J=7Hz,2H); 5.40 (t, J=7Hz,1H). CMR: 19.8 (CH_3); 22.7 (2 CH_3); 23.5 (CH_3); 24.9 (CH_2); 25.8 (CH_2); 28.0 (CH); 32.3 (CH_2); 32.8 (CH); 37.0 (CH_2); 37.3 (CH_2); 39.4 (CH_2); 58.9 (CH_2); 123.9 (CH); 139.7 (C).IR: 2930-2860 S; 1735 S; 1670 w; 1450 S. **RN**: 64354-69-4[27].

* The reduction of hexahydrotrichlorogeranyl geraniol 27a(E) and its acetate 27b gave in high yield (61 and 93% respectively) the corresponding dehalogenated product: phytol and phytyl acetate as a 95/5 mixture of E/Z isomers.

Reduction with zinc borohydride.

* Dihydrogeranyl acetate 4b.

A solution of 7-chloro-3,7-dimethyl-2E-octen-1-yl acetate 20b (115 mg, 0.5 mmol) in dry ether (0.5 ml) was slowly added to a 0.5 M solution of zinc borohydride[22] in ether (3 ml) containing cyclohexene (0.5 ml) at 40°C. After 6 min the mixture was hydrolysed and worked up. Dihydrogeranyl acetate 4b (72 mg, 74%) was isolated by FC and found identical to a sample obtained by acetylation of dihydrogeraniol.

* Phytyl acetate 7b (76%) was obtained in a similar way as a colourless oil, identical to a sample obtained by acetylation in pyridine of phytol. PMR(250): 0.85 (d, J=6.5Hz, 6H); 0.87 (d, J=6.5Hz,6H); 1-1.7 (m,19H); 1.7 (s,3H); 2.02 (t, J=7.5Hz,2H); 2.06 (s,3H); 4.6 (d, J=7Hz,2H); 5.36 (tq, J=7&1Hz, 1H). **RN**: 76337-16-1.

* Phytol itself was obtained in a yield of 69% as a colourless oil identical to a sample supplied by Merck.PMR(250): 0.85 (d, J=6.5Hz,6H); 0.87 (d, J=6.5Hz,6H); 1-1.7 (m,19H); 1.67 (s, 3H); 1.99 (t, J=7.5Hz, 2H); 4.14 (d, J=7Hz,2H); 5.40 (tq; J=7&1Hz,1H). **RN**: 7541-49-3.

Reduction with a NADH analogue.

* 1,7-Dimethyl-7-trifluoroacetoxy-2E-octene-1-yl acetate (310 mg, 1 mmol) was diluted in degassed $MeNO_2$ (1 ml). $LiClO_4$ (106 mg, 1mmol), then dihydronicotinamide 30[28] (1mmol) were added under dry atmosphere (Ar). After 4 hours at 80°C, the reaction was stopped and the usual work-up gave a crude oil which was rapidly chromatographed. The fraction containing the mixture of intermediate products (acetates) was analysed by GLC after addition of an internal reference (undecenyl acetate), to give a yield of 3.4% in dihydrogeranyl acetate.

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