DITERPENOIDS*

XIII.[†] SATURATED HYDROCHLORIDES FROM LINALOOL, GERANIOL, NEROLIDOL, FARNESOL, AND PHYTOL

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As part of a study of the hydrochlorination products obtained in the labdane series of diterpenoids,¹ the reaction between hydrogen chloride and allylic alcohols has been examined. The reactions of hydrogen chloride with linalool (I), geraniol (II), geranyl acetate (III), geranyl chloride (IV), nerolidol (V), farnesol (VI), and phytol (VII) are reported in this paper.

Discussion and Results

The synthesis of mono- and di-chloro derivatives of monoterpenoids in the myrcene series is well documented in the literature.^{2,3} Geranyl chloride (IV) (8-chloro-2,6-dimethylocta-2,6-diene) has been obtained by hydrochlorination of geraniol (II) at either $0^{\circ 4}$ or in refluxing toluene,^{5,6} and the same monochloride is formed from geraniol with phosphorus trichloride,⁷ or from linalool (I) by allylic rearrangement with hydrogen chloride.⁵ (+)-Linalool with phosphorus trichloride is reported⁸ to give (-)-linalyl chloride (VIII). However, despite the considerable work done in this field,³ no saturated trichloro acyclic monoterpenoids have been reported. We now report that gaseous hydrogen chloride adds smoothly to (\pm)-linalool in ethereal solution to give 1,3,7-trichloro-3,7-dimethyloctane (IX). The same trihydrochloride is formed under similar conditions from (+)-linalool, geraniol (II), geranyl acetate (III), and geranyl chloride (IV).

A crystalline tetrahydrochloride from (\pm) -nerolidol has been described by Ruzicka,⁹ but no structure was assigned to the compound. This preparation has been repeated and the derivative, which can also be prepared from (+)-nerolidol

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- † Part XII, Aust. J. Chem., 1967, 20, 193.
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- ² Bain, J. P., U.S. Pat. 3,062,875; U.S. Pat. 3,060,237 (Chem. Abstr., 1937, 58, 9149, 9150).
- ³ Sully, B. D., Chemy Ind., 1964, 263.
- ⁴ Carroll, M. F., J. chem. Soc., 1940, 705.
- ⁵ Simonsen, J., and Barton, D. H. R., "The Terpenes." 2nd Edn, Vol. I, p. 63. (Cambridge University Press 1961.)
- ⁶ Barnard, D., Bateman, L., Harding, A. J., Koch, H. P., Sheppard, N., and Sutherland, G. B. B. M., *J. chem. Soc.*, 1950, 915.
- ⁷ Tiemann, F., and Schmidt, R., Ber. dt. chem. Ges., 1896, 29, 921.
- ⁸ Vanin, I. I., and Chernoyarova, A. A., Zh. obshch. Khim., 1937, 7, 887 (Chem. Abstr., 1937, 31, 5757).
- ⁹ Ruzicka, L., and Capato, E., Helv. chim. Acta, 1925, 8, 273.

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and from farnesol (VI), is now assigned the structure (X) (1,3,7,11-tetrachloro-3,7,11-trimethyldodecane).



The diterpenoid allylic alcohol phytol¹⁰ (VII) can also be smoothly hydrochlorinated to give the saturated dihydrochloride (XI) (1,3-dichloro-3,7R,11R,15tetramethylhexadecane), presumably as a mixture of two isomers diastereoisomeric at C3.

The structures of compounds (IX), (X), and (XI) are indicated by the p.m.r. spectra. In each spectrum the partial structure (XII) is clearly apparent (Table 1).

¹⁰ Burrell, J. W. K., Jackman, L. M., and Weedon, B. C. L., Proc. chem. Soc., 1959, 263.

A two-proton four-line system at $6\cdot 3-6\cdot 5 \tau$ assignable to a chloromethyl group is coupled to an adjacent methylene which occurs, also as a four-line system, between 7·7 and 7·9 τ . These protons form an A_2B_2 system with $J_{AB}/\delta_{AB} \simeq 0.083$ and $J_{AB} \simeq 7$ c/s. In addition the spectrum of compound (IX) shows three methyl groups bonded to carbon atoms bearing chlorine atoms, compound (X) shows four such methyl groups, and compound (XI) shows one.

The products (IX), (X), and (XI) are formed in high yield. Their chemical structure, together with the complete loss of asymmetry when optically active linalool or nerolidol is treated with hydrogen chloride, indicates that an early step in this reaction sequence is the formation of either the optically inactive allylic carbonium ion (XIII) or the optically inactive monochloro derivative (XIV).¹¹ This step is subsequently followed by Markownikoff addition to the remaining double bonds.

TABLE 1

P.M.R. SPECTRA OF THE PARTIAL STRUCTURE (XII) PRESENT IN COMPOUNDS (IX), (X), AND (XI)

Compound	H 1	H 2	CH ₃ -C-Cl	${J}_{1,2}~({ m c/s})$
(IX)	$6 \cdot 37$	7.79	8.46	7
(X)	$6 \cdot 34$	7.82	$8 \cdot 46$	7
(XI)	$6 \cdot 37$	7.79	$8 \cdot 47$	7

 τ values. (X) in conc. CCl₄ solution, others neat

Experimental

Geranyl Acetate (III)

Geraniol in pyridine was acetylated with acetic anhydride at 5° in the normal manner. The product after elution from neutral alumina with n-hexane was distilled at $128^{\circ}/15$ mm to give the colourless acetate, n_{20}^{20} 1.4624, d_{4}^{15} 0.9160 (lit.^{12,13} b.p. 127.8°/14 mm, n_{20}^{20} 1.4624, d_{4}^{15} 0.9163) (Found: C, 73.4; H, 10.25. Calc. for $C_{12}H_{20}O_2$: C, 73.4; H, 10.3%). ν_{max} (film) 3095w, 2960s, 2920s, 2853s, 1746s, 1673m, 1445s, 1386s, 1370s, 1232s, 1110m, 1029s, 959s, 913m, 839m cm⁻¹.

Geranyl Chloride (IV)

Geraniol (10 g) in pyridine (8 ml) and anhydrous ether (20 ml) was treated with thionyl chloride (8.5 g) at 0°. The mixture was allowed to come to room temperature and worked up in the normal manner. Chromatography over neutral alumina followed by distillation gave geranyl chloride, b.p. $90-100^{\circ}/11 \text{ mm}$, n_{D}^{20} 1.4765 (lit.¹⁴ b.p. $85-105^{\circ}/11 \text{ mm}$, n_{D}^{20} 1.4728–1.4790) (Found: C, 69.3; H, 9.8; Cl, 20.25. Calc. for $C_{10}H_{17}Cl$: C, 69.5; H, 9.9; Cl, 20.5%). ν_{max} (film) 1664s, 1646m, 1452s, 1416w, 1375s, 991w, 926w, 899m, 890m, 845s, 830s, 745m cm⁻¹.

1,3,7.Trichloro-3,7-dimethyloctane (IX)

(1) (\pm)-Linalool (5 g) in anhydrous ether (20 ml) was treated with a stream of dry hydrogen chloride for 48 hr at 0°. The dark-coloured solution was washed with cold water, dried over sodium

¹¹ Dewolfe, R. H., and Young, W. G., Chem. Rev., 1956, 56, 753.

¹² Miiler, A., Ber. dt. chem. Ges., 1921, 54, 1466.

¹³ Tromp, S. T. J., Recl Trav. chim. Pays-Bas Belg., 1922, **41**, 285 (Chem. Abstr., 1923, **16**, 3059).

¹⁴ Barnard, D., and Bateman, L., J. chem. Soc., 1950, 926.

sulphate, and evaporated to dryness at room temperature. The product was chromatographed over alumina (type H) from n-hexane to give 1,3,7-trichloro-3,7-dimethyloctane (4.55 g) as a colourless oil; n_{20}^{20} 1.4785, d_{25}^{25} 1.088 (Found: C, 49.1; H, 7.9; Cl, 43.3. C₁₀H₁₉Cl₃ requires C, 48.9; H, 7.8; Cl, 43.3%). ν_{max} (film) 2953vs, 2912s, 2861s, 2826s, 1463s, 1453s, 1385s, 1363s, 1348m, 1303m, 1263s, 1233m, 1207m, 1178m, 1148s, 1118s, 1065s, 1018m, 983m, 928m, 865m, 823m, 810s, 768m, 737s cm⁻¹. P.m.r. spectrum (neat): 8.46 (9-proton singlet; CH₃-C-Cl), 8.32 (6 protons, broad singlet; $-CH_2$ -D, 7.79 (2-proton quartet; Cl-C-CH₂-C-Cl), 6.37 (2-proton quartet; $-CH_2$ Cl, $J \simeq 7$ c/s) τ .

(2) (+)-Linalool $(a_{\rm D} + 19 \cdot 9^{\circ};$ neat) was treated with dry hydrogen chloride as described in (1) above to give racemic 1,3,7-trichloro-3,7-dimethyloctane; $[a]_{\rm D} \pm 0^{\circ}$ (neat), with an infrared spectrum superimposable upon that recorded above.

(3) Geraniol (5 g) was treated with dry hydrogen chloride as described above to give the same trichloride (4.39 g) with superimposable infrared and p.m.r. spectra; $n_{\rm D}^{30} 1.4785$, $d_{25}^{25} 1.087$ (Found: C, 49.1; H, 7.9; Cl, 43.4%).

(4) Geranyl chloride (5 g) in anhydrous ether was treated as described above to give the trichloride (4.9 g), n_D^{20} 1.4784, d_{23}^{25} 1.087 (Found: C, 49.0; H, 7.9; Cl, 43.4%). The infrared and p.m.r. spectra were superimposable upon those described in (a) above.

(5) Geranyl acetate (5 g) under the same conditions gave the trichloride ($3 \cdot 89$ g), $n_2^{90} 1 \cdot 4785$, $d_{25}^{25} 1 \cdot 088$ (Found: C, $49 \cdot 1$; H, $7 \cdot 9$; Cl, $43 \cdot 3\%$). The infrared and p.m.r. spectra were superimposable upon those described above.

1.3.7.11-Tetrachloro-3,7,11-trimethyldodecane (X) (Farnesene Tetrahydrochloride⁹)

(1) (±)-Nerolidol (5 g) in anhydrous ether (20 ml) was treated with a stream of dry hydrogen chloride at 0° for 48 hr. Work-up as described above gave farnesene tetrahydrochloride (4 \cdot 7 g) as needles, m.p. 48–49° (lit.⁹ m.p. 50–51°) (Found: C, 51 \cdot 4; H, 8 \cdot 4; Cl, 40 \cdot 4. Calc. for C₁₅H₂₈Cl₄: C, 51 \cdot 5; H, 8 \cdot 0; Cl, 40 \cdot 4%). ν_{max} (Nujol) 1310s, 1273m, 1240m, 1215m, 1163s, 1148s, 1133s, 871s, 751 cm⁻¹. P.m.r. spectrum (CCl₄): 8 \cdot 46 (12-proton singlet; CH₃-C-Cl), 8 \cdot 32 (12 methylene protons), 7 \cdot 82 (2-proton quartet; Cl-C-CH₂-C-Cl), 6 \cdot 34 (2-proton quartet; -CH₂Cl, $J \simeq 7$ c/s) τ .

(2) (+)-Nerolidol ($[a]_{\rm D}$ +15.9°; neat) when treated with hydrogen chloride gave racemic farnesene tetrahydrochloride, m.p. 48–49°, $[a]_{\rm D} \pm 0.0^{\circ}$ (c, 0.8 in n-hexane).

(3) Farnesol (3 g) in ether was treated with hydrogen chloride as described above to give the tetrachloride $(2 \cdot 6 \text{ g})$, m.p. $48-49^{\circ}$, with infrared and p.m.r. spectra superimposable upon those described above.

1,3-Dichloro-3,7,11,15-tetramethylhexadecane (XI)

Phytol (practical grade, $a_{\rm D} + 0.11^{\circ}$) (3.5 g) in anhydrous ether (25 ml) was treated with dry hydrogen chloride and the reaction worked up in the normal manner to give 1,3-dichloro-3,7R,11R,15-tetramethylhexadecane (3.48 g) as a colourless mobile oil, $n_{\rm D}^{25}$ 1.4633, $d_{\rm z}^{25}$ 0.901, $[a]_{\rm D} = 0.10^{\circ}$ (neat) (Found: C, 68.3; H, 11.5; Cl, 20.15. $C_{20}H_{40}Cl_2$ requires C, 68.3; H, 11.5; Cl, 20.2%). $\nu_{\rm max}$ (film) 2907s, 2847s, 1461s, 1348m, 1258m, 1208w, 1153m, 1068m, 735s, 662m cm⁻¹. P.m.r. spectrum (neat): 9.15–9.06 (12 protons, 4 methyls), 8.73 (16 methylene protons), 8.47 (3-proton singlet; CH₃-C-Cl), 8.38 (broadened 3-proton system; -CH-), 7.79 (2-proton quartet; Cl-C-CH₂-C-Cl), 6.37 (2-proton quartet; -CH₂-Cl, $J \simeq 7$ c/s) τ .