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# TERPENOIDS—LVI

## ABSOLUTE CONFIGURATION OF ELEMOL*

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**Abstract**—The absolute configuration of elemol has been decided on the basis of its direct conversion to tetrahydrosaussurea-lactone. It is also shown that the lactone afforded by the formic acid treatment of the hydroxy acid obtained by ozonisation of dihydro elemol is a $\gamma$-lactone and not a $\delta$-lactone as previously assumed.

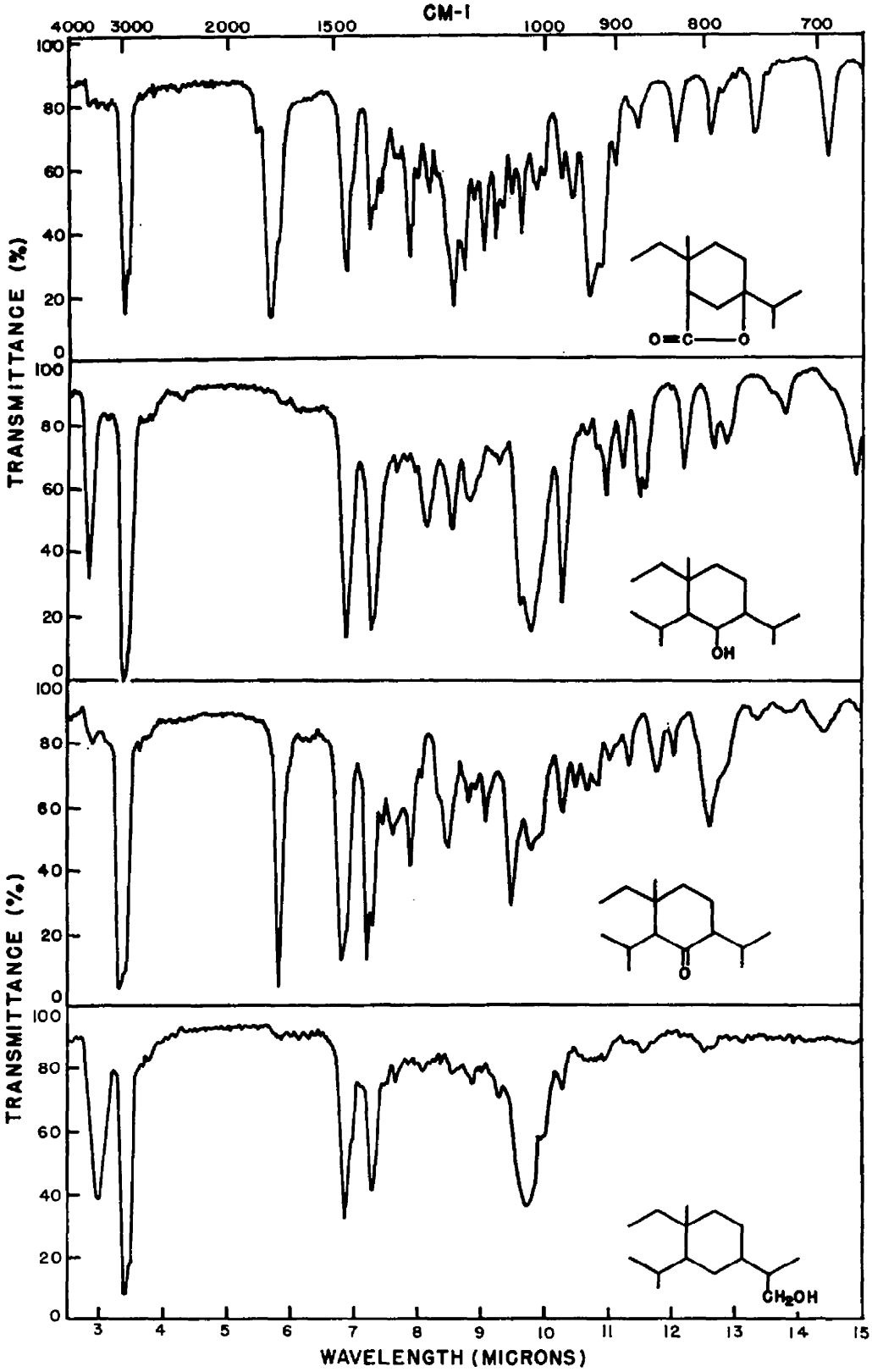
THE crystalline monocyclic alcohol, elemol, $C_{15}H_{26}O$, m.p. 52–53°, occurs naturally in the *Manila elemi* oil[1] and the tail fractions of *Java citronella* oil.[2] It has been shown to be represented by the structure (I).[3–5] On the basis of analogy, but without adequate experimental evidence, it has been sometimes assumed to be represented by the stereoformula XXVI.

On hydrogenation under controlled conditions, it is converted to dihydroelemol (II), which on ozonisation gives a mixture of the hydroxy methyl ketone (III) and the hydroxy acid (IV). The latter on treatment with formic acid is converted to a lactone,[6] on the basis of which, it has been assumed that the carboxyl group and the hydroxy-isopropyl group in IV are in *cis*-disposition[7] and the lactone formed is represented by the $\delta$-lactone structure (V).

We now present IR and NMR spectral evidence to show that the lactone obtained from IV is actually a $\gamma$-lactone and is represented by the structure VII. The IR spectrum (Fig. I) shows bands at 1770 $cm^{-1}$ characteristic of $\gamma$-lactone and doublet at 1360, 1380 $cm^{-1}$ in the methyl bending region indicating the presence of an isopropyl group. The NMR spectrum (Fig. II) of the $\gamma$-lactone (VII) shows signals at 0·81, 0·86, 0·91, 0·93, 1·0, 1·02 $\delta$ (12H) due to four methyl groups at $C_2$, $C_{11}$, $C_{12}$ and $C_{13}$, and at 1·8, 1·85 $\delta$ (2H) due to two protons at $C_5$ and at 2·2 $\delta$ (1H) due to one proton at $C_3$. It is, apparently, not formed by simple lactonization of the carboxyl and the hydroxyl group in IV but through an intermediate (VI) obtained via dehydration of the hydroxyl group followed by migration[8] of the resultant double bond to the ring and subsequent cyclization.

* Contribution No. 695 from the National Chemical Laboratory, Poona-8, India.

[1] A. M. Clover, *Phillipine J. Sci.* **2**, A, (1907); Ref. in Ber. Schimmel & Co., II, 21 (1907).
[2] K. Kafuku, T. Ikeda and Y. Fujita, *J. Chem. Soc., Japan* **53**, 636 (1932).
[3] L. Ruzicka and M. Pfeiffer, *Helv. Chim. Acta* **9**, 841 (1926).
[4] V. Sykora, V. Herout, J. Pliva and F. Sorm, *Coll. Czech. Chem. Comm.* **19**, 124 (1954).
[5] V. Sykora, J. Cerny, V. Herout and F. Sorm, *Coll. Czech. Chem. Comm.* **19**, 566 (1954).
[6] L. Ruzicka, A. G. van Veen, *Liebig's Ann.*, **476**, 70 (1929).
[7] V. Sykora, V. Herout and F. Sorm, *Coll. Czech. Chem. Comm.* **20**, 220 (1955).
[8] S. K. Paknikar and S. C. Bhattacharyya, *Tetrahedron* **18**, 1509 (1962).


CM-1
4000
3000
2000
1500
1000
900
800
700
TRANSMITTANCE (%)
100
80
60
40
20
0
O=C—O
OH
CH2OH
3
4
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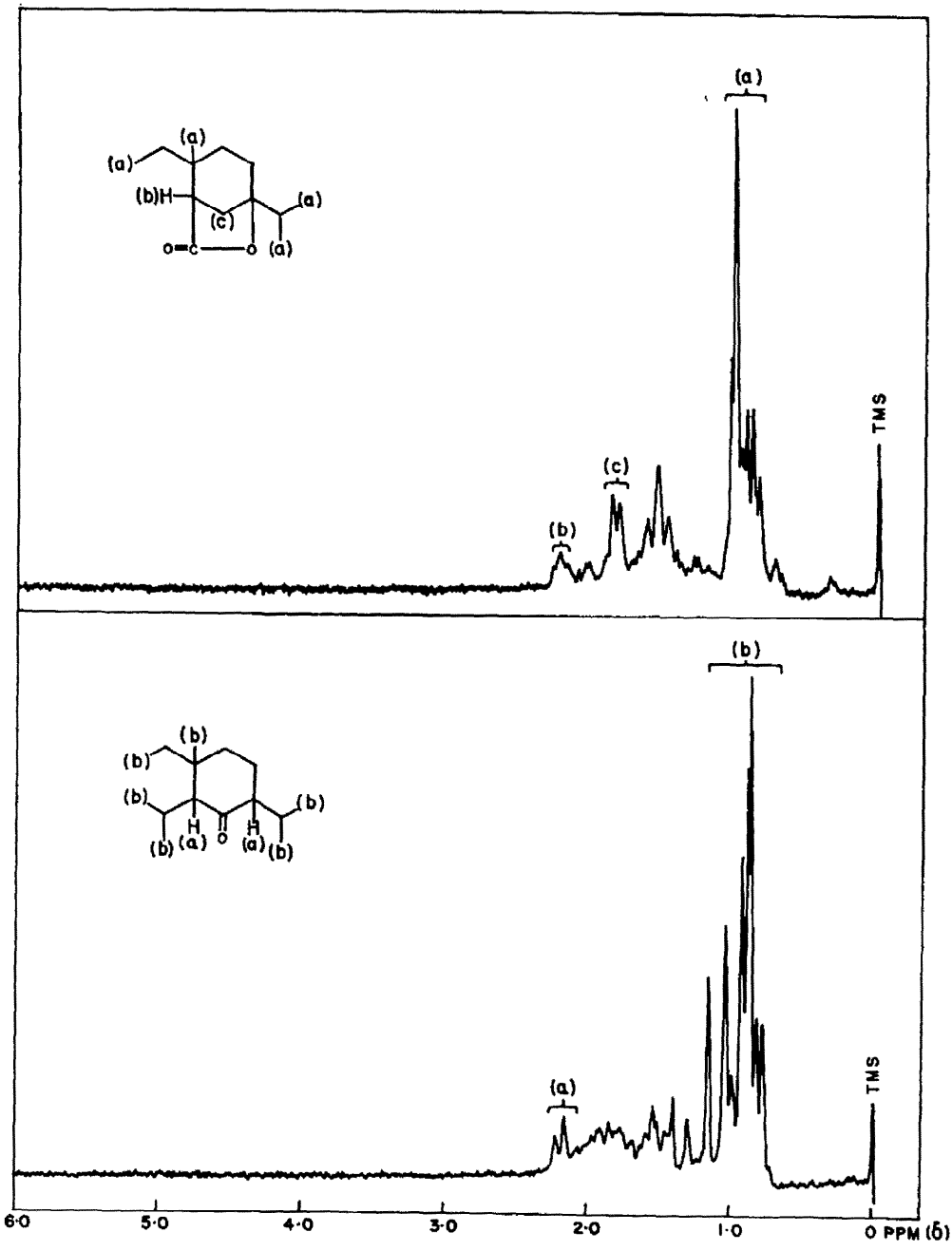
6
7
8
9
10
11
12
13
14
15
WAVELENGTH (MICRONS)


(a)
(a)
(b)H
(c)
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o
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TMS
(b)
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(b)
(b)
(b)
H
(b)
(a)
o
H
(a)
(b)
(b)
(a)
TMS
6·0
5·0
4·0
3·0
2·0
1·0
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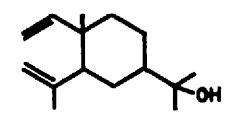
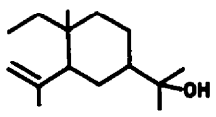
FIG. II

Simple and unambiguous synthetic evidence is also given to show that the absolute configuration of elemol is represented by the structure* XXVI.




I

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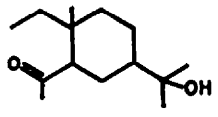
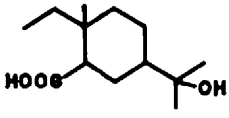
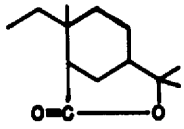


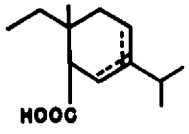

III



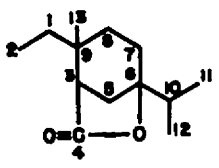

IV



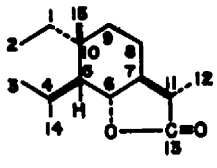

V



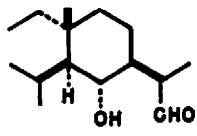

VI



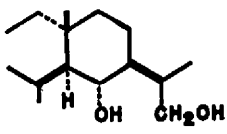

VII



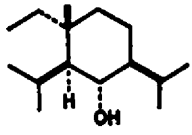

VIII



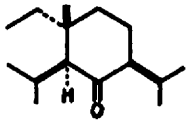

IX




X




XI




XII

For this purpose, tetrahydrosaussurea lactone of known stereochemistry (VIII)[9,10] was first used. Tetrahydrosaussurea lactone, on controlled reduction with lithium aluminium hydride,[11] affords the hydroxy aldehyde (IX) along with the diol (X). Wolf-Kishner reduction of this mixture followed by chromatography affords the pure crystalline monol (XI) which has previously been obtained in our laboratory by the metal-amine reduction of costunolide derivatives.[12] On oxidation with chromic acid, it is converted to the ketone (XII). The structures of the alcohol and the ketone are also fully supported by spectral evidence (IR spectra, Fig. I). The NMR spectrum

* T. G. Halsall, D. W. Theobald and K. B. Walshaw, in a recent communication [*J. Chem. Soc.* 1029 (1964)] has arrived at the same conclusion by correlating elemol with (+) *epi*-α-cyperone by an elaborate series of experiments.

[9] A. Somasekar Rao, G. R. Kelkar and S. C. Bhattacharyya, *Tetrahedron* **13**, 319 (1961).

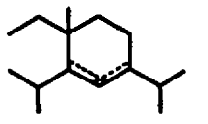
[10] D. M. Simonovic', A. Somasekar Rao and S. C. Bhattacharyya, *Tetrahedron* **19**, 1061 (1963).

[11] A. M. Shaligram, A. S. Rao and S. C. Bhattacharyya, *Tetrahedron* **18**, 969 (1962).

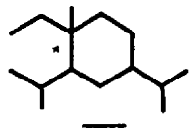
[12] G. H. Kulkarni, G. R. Kelkar and S. C. Bhattacharyya, *Tetrahedron* **20**, 1301 (1964).

(Fig. II) of the ketone (XII) shows signals at 0·80, 0·82, 0·86, 0·90, 0·92, 1·05, 1·17 $\delta$ (18 H) due to six methyl groups and at 2·16, 2·24 $\delta$ (2H) due to protons adjacent to the carbonyl group. The alcohol (XI) forms a benzoyl derivative pyrolysis of which affords a hydrocarbon (XIII), which is converted on hydrogenation to the saturated hydrocarbon, elemane (XIV). A similar hydrocarbon (XIVa) can also be prepared by hydrogenation of pure tetrahydroelemene (XV), obtained via pyrolysis of tetrahydroelemol benzoate[3,8] (XVI, R = $-CO\cdot C_6H_5$). The purity is ensured because of its very method of preparation from XV (GLC 98%). Though the hydrocarbon XIV obtained from XIII shows identical physical properties and IR spectrum with that of XIVa and a single peak on mixed GLC analysis, their NMR spectra show some differences suggesting that XIV is possibly a mixture of stereoisomers formed during hydrogenation of XIII.

Since, the stereochemistry of elemol is not clear from the above experiments,

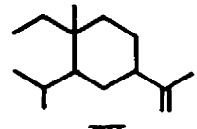


XIII

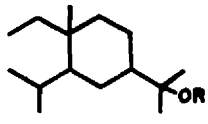


XIV

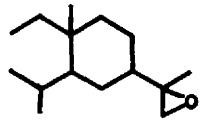
XIVa, via XV



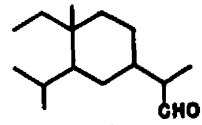
XV



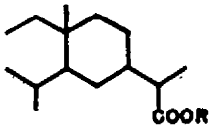

XVI R=H, R=-CO·C$_6$H$_5$



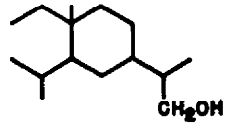

XVII



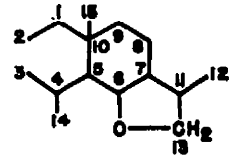

XVIII



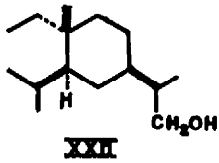

XIX R=H, R=CH$_3$



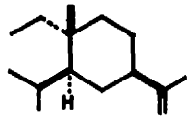

XX



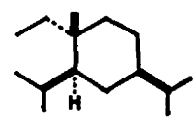

XXI



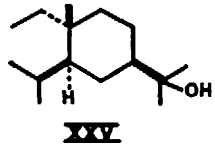

XXII



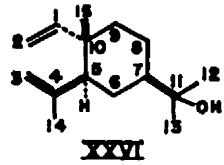

XXIII




XIV




XXV




XXVI

elemol was converted to tetrahydrosaussurea lactone (VIII), which is a product of definite stereochemistry, high m.p. and good rotation.

On treatment with perbenzoic acid the hydrocarbon (XV) gives an epoxide (XVII), isomerization of which with boron trifluoride ethereate under controlled conditions affords the aldehyde (XVIII). This aldehyde is oxidized to the corresponding acid (XIX, R = H) with potassium permanganate or silver oxide, the methyl ester (XIX, R = $CH_3$) of which is reduced to the alcohol (XX) with lithium aluminium hydride. This alcohol (IR spectrum, Fig. I) is more conveniently obtained by hydroboration[13,14] of XV. The alcohol (XX), on refluxing in benzene solution with lead tetra-acetate[15,16] under a nitrogen atmosphere, is converted to the oxide (XXI), which (from GLC analysis) is composed of two isomers in nearly equal proportions (probably epimeric around $C_6$). Careful chromatography followed by chromic acid oxidation of suitable fractions (decided on the basis of IR spectra and GLC analysis) affords tetrahydrosaussurea lactone (VIII), the identity of which was proved by comparison of m.p., mixed m.p., optical rotation and superimposable IR spectrum with an authentic sample.

Since the stereochemistry of tetrahydrosaussurea lactone is thoroughly established on the basis of degradative and synthetic experiments, it is clear that the stereoformulae of the alcohol (XX), tetrahydroelemene (XV), elemane (XIVa), tetrahydroelemol (XVI; R = H) and elemol (I) can be represented by the formulae XXII, XXIII, XXIV, XXV and XXVI respectively.

## EXPERIMENTAL

Mps. are uncorrected. Specific rotations were determined in $CHCl_3$ solution. IR spectra were measured with a Perkin–Elmer (Model 137b) Infracord spectrophotometer by Mr. Gopinath and Mr. Deshpande. GLC analyses were taken with the Griffin VPC Apparatus MK IIA by Dr. Ghatge and Mr. Bapat. Microanalyses were carried out by Mr. Pansare and colleagues.

*Isolation of elemol* (I). The tail fractions of *Java citronella* oil were used for isolation of elemol, m.p. 52–53°, $(\alpha)_D$ −5·82° (*c*, 3·4). IR spectrum showed complete identity with the spectrum of authentic elemol.

*Hydrogenation of elemol to dihydroelemol* (II). A solution of elemol (4·35 g) in ethanol (75 ml) was partially hydrogenated over Pd-C (1·25 g, 5%), until the absorption corresponded to one mole $H_2$. After filtering off the catalyst the filtrate afforded dihydroelemol (4·1 g) which was purified by sublimation *in vacuo*, m.p. 45–46°, $(\alpha)_D$ −1·53° (*c*, 1·96). IR spectrum (in Nujol), bands at: 3400 1639, 1300, 1176, 1124, 1090, 1010, 961, 910, 892 $cm^{-1}$. (Found: C, 80·30; H, 12·53. $C_{15}H_{28}O$ requires: C, 80·29; H, 12·58%).

*Ozonolysis of dihydroelemol* (II) *to hydroxy-methyl-ketone* (III) *and hydroxy acid* (IV). Dihydroelemol (4·1 g) was ozonized in $CHCl_3$ solution (in 4 batches) at −10°. The combined ozonide after removal of $CHCl_3$ *in vacuo*, was decomposed with water and extracted with ether. The organic material was then separated into neutral (3·5 g) and acidic portions (0·51 g). The neutral portion was hydroxy-methyl ketone (III). The crystalline hydroxy acid (IV) obtained from acidic portion was crystallized twice from pet ether, m.p. 143–44°, $(\alpha)_D$ +28·57° (*c*, 0·7). IR spectrum (in Nujol), bands at: 3400 $cm^{-1}$ (hydroxyl group), 2640, 1681 $cm^{-1}$ (carboxyl group). (Found: C, 68·48; H, 10·62. $C_{15}H_{24}O_3$ requires: C, 68·38; H, 10·59%).

*Cyclization of hydroxy acid* (IV) *to γ-lactone* (VII). The hydroxy acid (400 mg) in formic acid (5 ml) was heated on a water bath for 2 hr. After cooling to room temp, it was diluted with water and

[13] H. C. Brown and P. A. Tierney, *J. Amer. Chem. Soc.* **80**, 1552 (1958).
[14] H. C. Brown and G. Zweifel, *J. Amer. Chem. Soc.* **81**, 247 (1959).
[15] G. Cainelli, M. Lj. Mihailovic, D. Arigoni and O. Jeger, *Helv. Chim. Acta* **42**, 1124 (1959).
[16] V. M. Mic'ovic', R. I. Mamuzic', D. Jeremic' and M. Lj. Mihailovic', *Tetrahedron Letters* No. 29, 2091 (1963).

extracted with ether. The organic layer washed free from formic acid, yielded the lactone (0·32 g) which was purified by chromatography over alumina and then distilled *in vacuo*, b.p.128–130° (bath)/1 mm, $(\alpha)_D$ + 17·18° (*c*, 3·61). IR spectrum (Fig. I, in liquid film), bands at: 1770 $cm^{-1}$ ($\gamma$-lactone), 1360, 1380 $cm^{-1}$ (isopropyl group). NMR spectrum is described in Fig. II. (Found: C, 74·33; H, 10·59. $C_{13}H_{22}O_2$ requires: C, 74·24; H, 10·54%).

*Conversion of tetrahydrosaussurea lactone* (VIII) *to the alcohol* (XI). To a stirred solution of tetrahydrosaussurea lactone (3 g) in dry ether (30 ml) was added at −5° over a period of 30 min. an ethereal solution of $LiAlH_4$ (21·4 ml, 1 ml ≡ 5·63 mg $LiAlH_4$). After addition the solution was stirred for 1 hr at −5° and then allowed to come to room temp. The reaction mixture was carefully decomposed by adding small quantity of water and extracted with ether. Removal of ether furnished a product (2·3 g) which gave a positive Fehling's test The above partially reduced product (2·3 g) was dissolved in freshly distilled diethylene glycol (20 ml) and hydrazine hydrate (3 ml, 100%) by heating on a steam bath for 2 mins. The solution was kept at room temp for 30 min with occasional shaking, KOH (3·5 g) was added and the mixture refluxed at 110–115° for 2 hr in a $N_2$ atm. The water was removed by raising the temp to 190° and the reaction mixture was then refluxed at 190° for further 4 hr. The viscous reaction product was cooled, diluted with water (50 ml) and repeatedly extracted with ether. Ethereal layer washed with water and dried. Removal of ether gave viscous mass (1·5 g).

The combined reaction product (5·1 g) from 4 batches was chromatographed over neutral alumina (grade IV, 100 g) and eluted with pet ether (2·8 g, mainly XI) and ether (2·2 g, mainly diol X, characterized through its IR spectrum). Pet ether eluted fraction (2·8 g) was then rechromatographed on alumina (grade II, 60 g). Elution with pet ether–benzene(1:1) gave the monol (XI, 2·3 g), which was purified by distillation and sublimation, b.p. 105–108° (bath)/0·5 mm, m.p. 36–37°, $(\alpha)_D$ +1·842° (*c*, 6·516); GLC analysis showed a single peak. IR spectrum (Fig. I, in Nujol), bands at: 3497, 1227, 1177, 1136, 1040, 1020, 970, 909, 892, 871, 862, 820, 790, 777 $cm^{-1}$. (Found: C, 79·91; H, 13·47. $C_{15}H_{30}O$ requires: C, 79·57; H, 13·36%).

*Oxidation of the monol* (XI) *to the ketone* (XII). The monol (0·15 g) was dissolved in pure acetone (25 ml). Jones' reagent[17,18] (2 ml) was added dropwise into it until a persistent orange colour was formed. After 10 min, the product was diluted with water (50 ml) and extracted with ether. Removal of ether *in vacuo*, afforded the ketone (0·14 g) which after elution of the chromatographic column (grade II, 20 g) with pet ether, was further purified by distillation *in vacuo*, b.p. 90° (bath)/0·4 mm, $n_D^{25}$ 1·4655, $(\alpha)_D$ + 60·84° (*c*, 6·509); GLC analysis gave a single peak. IR spectrum (Fig. I, in liquid film), bands at: 1706, 1380, 1359, 1333, 1307, 1258, 1171, 1130, 1096, 1049, 1016, 966, 952, 934, 921, 906, 882, 847, 830, 797 $cm^{-1}$. NMR spectrum is described in Fig. II. (Found: C, 80·32; H, 12·64. $C_{15}H_{28}O$ requires: C, 80·29; H, 12·58%).

*Benzoyl derivative of the alcohol* (XI) *and pyrolysis of the benzoate to the hydrocarbon* (XIII). The alcohol (2·1 g) was dissolved in dry pyridine (15 ml) and benzoyl chloride (5 ml) was added. The mixture was shaken thoroughly and left at the room temp for 48 hr after which it was worked up in the usual way to furnish benzoate of the alcohol; IR spectrum (in liquid film), bands at: 1706, 1258 and 704 $cm^{-1}$.

The benzoate (2 g) was heated in a distillation flask at 210–230° (bath temp) *in vacuo* (100 mm). The distillate was taken up in ether and freed from benzoic acid by washing with $NaHCO_3$aq. The ethereal extract containing the neutral portion, was washed with water, dried and solvent evaporated. The hydrocarbon (0·45 g) obtained was further purified by chromatography over alumina (grade I, 20 g) and distilled *in vacuo* over Na, b.p. 110–115° (bath)/2 mm, $n_D^{28}$ 1·4676, $(\alpha)_D$ −30·42° (*c*, 4·24). IR spectrum (liquid film), bands at: 1380, 1360, 1325, 1290, 1198, 1163, 1136, 1111, 1081, 1015, 885, 854 $cm^{-1}$ (Found: C, 86·32; H, 13·67. $C_{15}H_{28}$ requires: C, 86·46; H, 13·54%).

*Hydrogenation of hydrocarbon* (XIII) *to elemane* (XIV). A solution of the hydrocarbon (0·19 g) in ethyl acetate (20 ml) was hydrogenated over Adams catalyst (80 mg) until 2 moles $H_2$ were absorbed. The product (0·17 g) obtained was purified by chromatography over alumina (grade I, 20 g) and distilled *in vacuo* over Na, b.p. 120–25° (bath)/6·5 mm, $n_D^{25}$ 1·4630, $(\alpha)_D$ +0°. GLC analysis showed a single peak. The IR spectrum was identical with that of elemane described in the literature.[19]

[17] R. H. Bible, Jr., *Tetrahedron* **11**, 22 (1960).

[18] K. Bowden, I. M. Heilbron, E. R. H. Jones and B. C. L. Weedon, *J. Chem. Soc.* 39 (1946).

[19] F. Sorm, M. Holub, V. Sykora, J. Mleziva, M. Streibl, J. Pliva, B. Schneider and V. Herout, *Coll. Czech. Chem. Comm.* **18**, 512 (1953).

*Tetrahydroelemol benzoate* (XVI, R = $CO.C_6H_5$). Tetrahydroelemol benzoate was prepared via hydrogenation of elemol benzoate,[8] IR bands at: 1710, 1280, 712 $cm^{-1}$.

*Tetrahydroelemene* (XV). The hydrocarbon was prepared by pyrolysis of the benzoate according to the procedure previously followed in this laboratory.[8] It had the following properties, b.p. 128–130°/9 mm, $n_D^{25}$ 1·4748. GLC analysis indicated 98% purity.

*Hydroboration of tetrahydro elemene* (XV) *to alcohol* (XX). Through a solution of the hydrocarbon (XV, 2 g) dissolved in dry tetrahydrofuran (25 ml) diborane gas $B_2H_6$, was passed at 0° for 1 hr and then for a further 1 hr at room temp. The diborane gas was prepared separately by adding slowly a solution of $NaBH_4$ (1·5 g) in pure dry diglyme (20 ml) to a mixture of freshly distilled $BF_3$–ethereate (10 ml) in dry diglyme (10 ml). Nitrogen was used as the carrier-gas. Excess of diborane in the reaction flask was decomposed by adding small pieces of ice. The mixture was cooled in the ice-bath, 3N KOH (25 ml) was added followed by slow addition of $H_2O_2$ (25 ml, 30%, 1 hr). After a further period of 1 hr at room temp, the upper layer was separated; the aqueous layer was extracted with ether and the combined extracts dried ($Na_2SO_4$). Removal of solvent gave the alcohol (1·5 g) which was purified by chromatography and distillation *in vacuo*, b.p. 140° (bath)/0·7 mm, $n_D^{25}$ 1·4770, $(\alpha)_D$ −3·836° (*c*, 3·91); GLC analysis showed a single peak. The IR spectrum (Fig. I, in liquid film) showed bands at: 3350, 1380, 1360, 1299, 1235, 1130, 1075, 1031, 1000, 970 $cm^{-1}$. (Found: C, 79·97; H, 13·10. $C_{15}H_{30}O$ requires: C, 79·57; H, 13·36%).

*Lead tetra-acetate oxidation of the alcohol* (XX) *to the oxide* (XXI). A mixture of the alcohol (3·8 g), freshly prepared dry lead tetra-acetate (6 g, 1 mole) and anhydrous benzene (75 ml) was refluxed on a water bath for 1 hr with mechanical stirring in a $N_2$ atm. After cooling to room temp, the lead tetra-acetate was filtered off. The filtrate on processing afforded the oxide (1·1 g) which was purified by chromatography over alumina (grade I, 50 g) and distilled *in vacuo*, b.p. 90–92° (bath)/1mm, $n_D^{30}$ 1·4718, $(\alpha)_D$ −2·7° (*c*, 3·7). GLC analysis showed two peaks of equal proportion. IR spectrum (in liquid film), bands at: 1031 $cm^{-1}$ (oxide), 1450, 1370, 1345, 1325, 1277, 1198, 1178, 1176, 1149. 1136, 1112, 1087, 1051, 1004, 986, 961, 926, 911, 866, 833, 816, 781, $cm^{-1}$ (Found: C, 79·73; H, 12·26, $C_{15}H_{28}O$ requires: C, 80·29, H, 12·58%).

This oxide (1 g) was rechromatographed on alumina (grade I, 50 g) and 25 fractions (5 ml each) with pet ether were collected. Fractions 4–14 were combined on the basis of GLC analysis and IR spectrum to give the oxide (0·48 g) suitable for oxidation.

*Chromic acid oxidation of the oxide* (XXI) *to tetrahydrosaussurea lactone* (VIII). The oxide (0·48 g) in acetic acid (12 ml) was oxidized with chromic acid (0·507 g) dissolved in water (2 ml) and acetic acid (10 ml). The mixture was heated on a water bath at 70–80° for 15 min, cooled and methyl alcohol (3 ml) was added. After dilution with water (100 ml), the mixture was extracted with ether and the extract washed with $Na_2CO_3$ aq and water. The residue obtained after removal of ether was saponified by refluxing with alcoholic KOH (12 ml, 10%; 1 hr). The alcohol was then removed and the residue diluted with water (20 ml) and extracted with ether. The aqueous solution on acidification gave white crystals (60 mg) of tetrahydrosaussurea lactone which was crystallized from pet ether, had m.p. and mixed m.p. with an authentic sample 122–23°; $(\alpha)_D$ +40·14° (*c*, 2·018) (Found: C, 75·60; H, 11·45. $C_{15}H_{26}O_2$ requires: C, 75·58; H, 11·0%). The IR spectrum was superimposable with that of an authentic sample.