

### 416. *The Constitution of Lanceol.*

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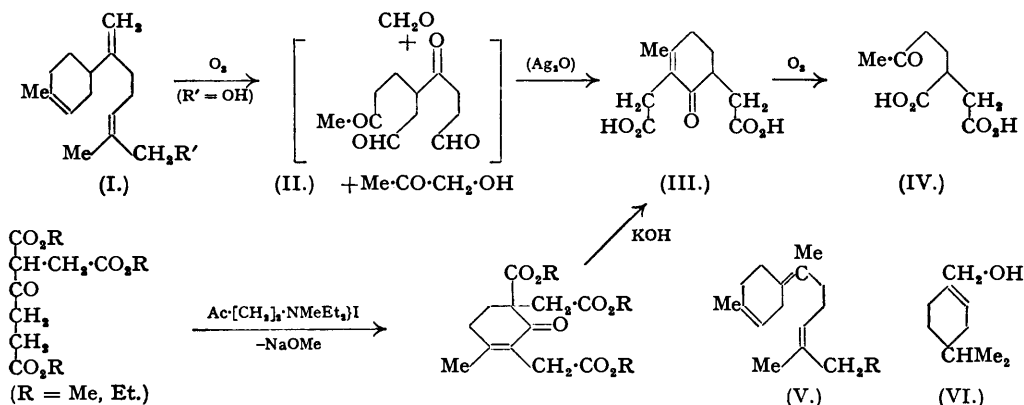
The formula (I;  $R' = OH$ ) is assigned to the chief constituent of lanceol on the basis of its known reactions and of its reduction to  $\beta$ -bisabolene (I;  $R' = H$ ) with sodium and ethanol in liquid ammonia; the structure (III) for its principal ozonolysis product is confirmed by synthesis.

PUBLISHED evidence (cf. *Ann. Reports*, 1950, **47**, 194) can be used to deduce structure (I;  $R' = OH$ ) for the sesquiterpene alcohol lanceol. Through the kindness of Professor Sir John Simonsen, F.R.S., and Dr. L. N. Owen it has been possible to confirm this formula experimentally.

Lanceol,  $C_{15}H_{24}O$ , is known (Bradfield, Francis, Penfold, and Simonsen, *J.*, 1936, 1619; Owen, *J.*, 1949, 1582), to be a primary alcohol containing the group  $\cdot CMe \cdot CH_2 \cdot OH$  because ozonolysis gives rise to hydroxyacetone; the allylic nature of the alcohol is further attested by a considerable loss of oxygen on mild catalytic hydrogenation. The other products of ozonolysis are formaldehyde (indicative of a  $\cdot CH_2$  group which has now been further confirmed by the presence of very marked infra-red absorption bands at 6.06 and 11.25  $\mu$ .) and an acid,  $C_{11}H_{14}O_5$ , to which no certain formula could be assigned. This acid is dibasic and contains a hindered carbonyl group conjugated with a double bond; the absorption at  $\lambda_{max}$ , 239  $m\mu$ , is consistent with  $\alpha\beta$ -substituents on the double bond. Further ozonolysis leads to the known acid (IV), and the formula (III) best accords with its properties, including the optical inactivity which results from the position of the original asymmetric centre adjacent to the carbonyl group. The unstable anhydride obtained by Simonsen *et al.* is probably the dilactone corresponding to the hydrated form of the carbonyl group. The acid (III) must result, under the alkaline conditions of oxidation, from the acid formed from the primary ozonolysis product (II). The formula (III) has been confirmed by the synthesis shown below, the direction assumed for the cyclisation in the course of the Robinson-Mannich reaction being based on a number of known analogies.

The formula (I;  $R' = OH$ ), containing the usual skeleton of the monocyclic sesquiterpenes, is thus established for lanceol with a high degree of probability, but on the evidence thus far available the residues giving rise to formaldehyde and hydroxyacetone in the ozonolysis might conceivably be interchanged (though this would involve breaking the isoprene rule). This possibility has been ruled out by reduction of lanceol to  $\beta$ -bisabolene (I;  $R' = H$ ), identified by conversion into bisabolene trihydrochloride. The strong infra-red absorption bands at

6.06 and 11.25  $\mu$ ., together with the high optical rotation of the hydrocarbon, indicates that isomerisation to  $\gamma$ -bisabolene (V; R = H) has not taken place during the reduction, although the trihydrochloride is optically inactive. This racemisation shows that caution must be exercised in drawing conclusions as to the nature of the bisabolene in an essential oil from the inactivity



of the derivative. That lanceol may contain some of (V; R = OH) is suggested by the formation of some lævulic acid during ozonolysis (Simonsen *et al.*, *loc. cit.*); the question could be settled by the use of Raman spectra to detect the tetrasubstituted double bond. It is noteworthy that lanceol, from *Santalum lanceolatum*, is more closely related to the santalols of true sandalwoods (*e.g.*, *S. album*) than was originally supposed.

The reduction of lanceol to bisabolene was carried out by sodium and ethanol in liquid ammonia, which have been shown to remove reductively the hydroxyl group from several allyl alcohols containing a CH<sub>2</sub> group at one or other end of the allyl system; *e.g.*, geraniol, C<sub>6</sub>H<sub>11</sub>·CMe·CH·CH<sub>2</sub>·OH  $\rightarrow$  methylgeraniolene, C<sub>6</sub>H<sub>11</sub>·CMe·CHMe (Birch, *J.*, 1945, 809). In order to test further the applicability of the method a commercial mixture of  $\alpha$ - and  $\beta$ -santalol has been reduced to a mixture of  $\alpha$ - and  $\beta$ -santalene. It is noteworthy, however, that phellandrol (VI) could not be reduced and the structural factors involved have evidently not been completely recognised. The mixture of betulenols from birch-bud oil, if correctly formulated as allyl alcohols derived from  $\beta$ -caryophyllene (*e.g.*, Treibs, *Ber.*, 1938, 71, 612; Kipping, *Ann. Reports*, 1938, 35, 279), should give rise to the latter hydrocarbon. The advantage of the method over that involving reduction of the halide is that the reagents used are unlikely to alter the bond or ring-structures in an unpredictable manner.

#### EXPERIMENTAL.

**Reduction of Lanceol.**—The lanceol ( $\alpha_D -65.6^\circ$ ) was part of a specimen originally isolated by Mr. A. R. Penfold of the Sydney Technological Museum and presented to the authors by Professor Sir John Simonsen and Dr. L. N. Owen. Lanceol (16 g.) in ethanol (50 c.c.) and ammonia (500 c.c.) was reduced by the action of sodium (15 g.) during 3 hours. Water (250 c.c.) was then cautiously added, and the oil taken up in ether, washed with water, dried, and distilled over sodium. The  $\beta$ -bisabolene so obtained was an oil (12 g.) having very little odour and b. p. 148°/18 mm.,  $n_D^{15} 1.4893$ ,  $\alpha_D^{15} -67^\circ$  (Found: C, 88.2; H, 12.0. Calc. for C<sub>15</sub>H<sub>24</sub>: C, 88.2; H, 11.8%). The hydrocarbon (2 g.) in ether (10 c.c.) was cooled in water and saturated with hydrogen chloride. After 3 hours in the refrigerator, the ether was partly removed, and the crystals removed by filtration and recrystallised from a little light petroleum (b. p. 40–60°), giving bisabolene trihydrochloride (1.4 g.), m. p. 79–80°, undepressed by an authentic specimen kindly provided by Dr. L. N. Owen and originally prepared from lemon oil by Dr. W. F. Short. The trihydrochloride (1.48 g.), dissolved in chloroform (total volume, 5 c.c.), had  $\alpha_D 0.0^\circ$ . For comparison with samples of natural bisabolene the chief infra-red bands are recorded: strong bands at 3.44, 6.06, 6.94, 7.25, 11.25, 12.5  $\mu$ .; medium bands at 8.65, 8.7, 9.03, 9.79, 10.92, 12.05  $\mu$ .; weak bands at 1.7, 2.3, 5.6, 7.43, 7.52, 7.63, 8.05, 9.52, 10.14, 10.45, 13.15  $\mu$ .; side-bands at 3.25, 3.67, 5.95  $\mu$ .

The reduction, as above, of a commercial sample of mixed santalols gave a hydrocarbon fraction, b. p. 137–139°/18 mm.,  $n_D^{15} 1.4895$ ,  $\alpha_D -21.6^\circ$ . Phellandrol under the same conditions was recovered unchanged.

**2:6-Dicarboxymethyl-3-methylcyclohex-2-ene.**—Dimethyl 3-ketoadipate (3.46 g.), ethyl chloroacetate (3.5 g.), and sodium (0.6 g.) in ethanol (12 c.c.) were refluxed for 4.5 hours, most of the ethanol was removed under reduced pressure, and the residue acidified to Congo-paper. Ether-extraction and distillation gave an oil (1.9 g.), b. p. 160–166°/0.3 mm., which probably consists of a mixture of methyl and ethyl esters. This fraction (2.3 g.) in benzene (12 c.c.) was added to a solution of sodium (0.23 g.) in methanol (10 c.c.), followed by a solution in methanol (12 c.c.) of the methiodide from 4-diethyl-

aminobutan-2-one (3 g.). The solution was left for 20 hours and then refluxed for 1 hour. Water was then added, and the product extracted with ether and distilled (1.2 g.; b. p. 190—196°/1 mm.). This product (1.59 g.) was refluxed under nitrogen for 13 hours with aqueous potassium hydroxide (20 c.c.; 10%). The solution was then evaporated under reduced pressure to about 10 c.c., then acidified with hydrochloric acid, the precipitated potassium chloride removed by filtration, and the solution submitted to continuous ether-extraction for 5 hours. The extract was crude 2:6-dicarboxymethyl-3-methylcyclohex-2-enone (0.5 g.) which was purified by washing it with ether and crystallising it from water (charcoal). It then formed colourless prisms, m. p. 173°, which did not depress the m. p. (171—173°) of the acid obtained by ozonolysis, etc., of lanceol. The constitution assigned is supported by the analysis (Found: C, 58.7; H, 6.4. Calc. for  $C_{11}H_{14}O_6$ : C, 58.4; H, 6.2%) and by its absorption at  $\lambda_{max}$ . 243 m $\mu$ . ( $\epsilon_{max}$ . 10,000 in chloroform).

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