

CCCLXXIII.—*The Chemistry of Cadinene. Part II.*
Compounds related to Cadinene.

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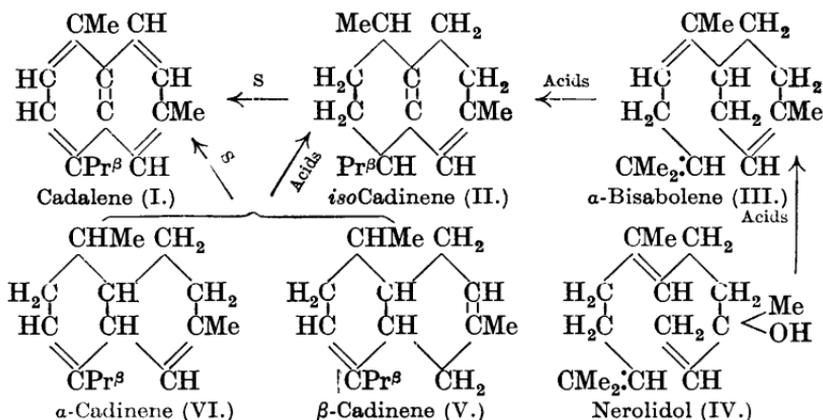
A. Hydrocarbons related to Cadinene.

IN the present paper, it is shown that (a) the *isocadinene* described by Henderson and A. Robertson (J., 1924, **125**, 1992) and (b) the sesquiterpene isolated from cade oil by Tröger and Feldmann (*Arch. Pharm.*, 1898, **236**, 692) and subsequently investigated by Lepeschkin (*J. Russ. Phys. Chem. Soc.*, 1908, **40**, 126) are probably identical and differ from *cadinene* only in the positions of the double bonds. Both sesquiterpenes must be hexahydrocandalenes, since they yield *cadalene* on dehydrogenation by Ruzicka's method (*Helv. Chim. Acta*, 1921, **4**, 505).

From a comparison of the physical and chemical properties, it seems reasonable to suggest that *isocadinene* may be represented by (II), which is the formula provisionally assigned by Ruzicka and Capato (*Helv. Chim. Acta*, 1925, **8**, 259) to the hexahydrocandalene synthesised by them from *nerolidol* (IV) and *bisabolene* (III) by the action of acid reagents. A comparison of the physical properties of *isocadinene*, the cade oil sesquiterpene, and Ruzicka and Capato's synthetic hexahydrocandalene is given below :

	B. p. /11—12 mm.	<i>d.</i>	<i>n_D</i> .
<i>iso</i> Cadinene	124—126°	0.914	1.515
Cade oil sesquiterpene	124—128	0.918	1.515
Synthetic hexahydrocadalene	125—126	0.916	1.509

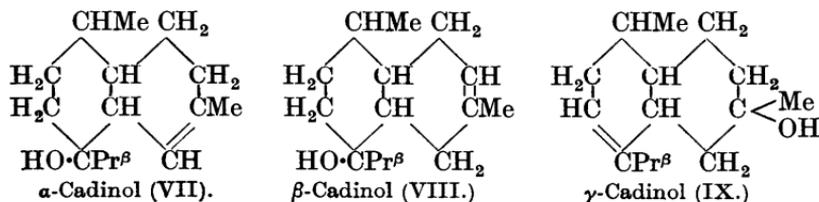
The close similarity of these compounds is evident. Further, they all give liquid addition products with the halogen acids, and by heating with sulphur, a good yield of cadalene. As *isocadinene* and Ruzicka and Capato's compound are both produced by the prolonged action of acids on the hexahydrocadalene framework, it is probable that (II) represents the end-product to which the hexahydrocadalenes are transformed by the action of acid reagents. The exact position of the double bonds in this molecule, however, is not known with certainty.



These considerations also afford an explanation of Ruzicka and Capato's failure to synthesise cadinene (V and VI) by the continued action of acid reagents upon the nerolidol and bisabolene structures (*loc. cit.*).

B. Some Dicyclic Alcohols associated with Cadinene.

It is a remarkable fact that although cadinene is so widely distributed in nature, yet the cadinol alcohols, of which three isomeric forms (VII, VIII, and IX) are obviously possible, have hitherto been discovered in only one plant source, *viz.*, galbanum oil.



Recently, while examining the higher-boiling fractions of oil of false cubebs, we observed that a good yield of cadinene dihydrochloride could be obtained from the alcoholic fraction. The presence of an alcohol of the type VII, VIII, or IX was thus indicated. An extensive fractionation of the oil under diminished pressure revealed the presence of several distinct though closely similar compounds. The rotatory power-b. p. curve for the various fractions showed two distinct breaks, indicating the presence of at least two compounds. Further work led to the isolation of a constant-boiling mixture of isomeric, unsaturated, dicyclic sesquiterpene alcohols, $C_{15}H_{25}(OH)$, the principal constituent of which proved to be a *l-cadinol*, which is identical in all its physical and chemical properties excepting the optical rotation with Semmler's *d-cadinol* from galbanum oil, as the following figures show :

	B. p.	<i>d.</i>	n_D .	$[R_L]_D$.	
<i>l</i> -Cadinol	153—155°/10 mm.	0.9727	1.508	68.00	$[\alpha]_{5461}^{15} - 54^\circ$
<i>d</i> -Cadinol from galbanum oil	155—165/12 mm.	0.9720	1.507	67.97	$\alpha_D + 22^\circ$

From the alcohol fraction of oil of false cubebs we have isolated an apparently new dicyclic *sesquiterpene alcohol*, $C_{15}H_{25}(OH)$, which does not form a stable hydrochloride and therefore cannot be regarded as a cadinene derivative. The new alcohol, for which we propose the name *cubebol*,* is crystalline in a pure state, but owing to its extreme solubility in all ordinary organic solvents and in *cadinol* it cannot be isolated directly from the oil. We have obtained it in a pure form by the hydrolysis of its *phenylurethane* derivative. This derivative, and the α -*naphthylurethane*, also prepared, should serve definitely to characterise the alcohol. The dicyclic structure of *cubebol* has been established (*a*) by the formation of a *dibromide*, $C_{15}H_{25}OBr_2 \cdot CO \cdot NH \cdot C_6H_5$, from the phenylurethane derivative and (*b*) by the unsaturation of the alcohol itself, which forms an unstable, oily *dibromide*, $C_{15}H_{26}OBr_2$. The quantity of this alcohol so far available has not permitted a more complete examination of its structure, but preliminary experiments indicate that it does not dehydrogenate to either *cadalene* or *eudalene*, and therefore does not appear to belong to the hydrated hexahydrocadalene series, as might at first be supposed from its association with *cadinol* in nature.

EXPERIMENTAL.

Sesquiterpene from Oil of Cade.—This sesquiterpene, isolated as previously described and purified by vacuum distillation, had b. p.

* "Cubeb camphor," described in the early literature, appears to differ from *cubebol* in its higher m. p., lower solubility, etc.

124—128°/12 mm., d_4^{20} 0.9181, n_D^{20} 1.5150, $[R_L]_D$ 67.0 (calc. for a dicyclic sesquiterpene, 66.2). The large exaltation appears to be characteristic of this compound and of *isocadinene*, and may indicate a system of conjugated bonds (compare II) or, less probably, the admixture of a monocyclic component (compare Semmler and Jakubowicz, *Ber.*, 1914, 47, 2252) (Found: C, 87.9; H, 11.7. Calc. for $C_{15}H_{24}$: C, 88.2; H, 11.8%).

The sesquiterpene (2.8 g.) was mixed with finely-powdered sulphur (1.2 g.) and heated at 200°; evolution of hydrogen sulphide then began. The temperature was gradually raised to 250° during 1 hour. The product, isolated by vacuum distillation, consisted principally of a mobile oil, b. p. 130—150°/10 mm., which was repeatedly distilled over sodium. This oil gave with a concentrated alcoholic solution of picric acid a good yield of cadalene picrate which, alone or mixed with a specimen prepared from cadalene obtained by the dehydrogenation of pure *cadinene*, melted at 114°.

isoCadinene was prepared from pure *cadinene* (regenerated from the dihydrochloride) by the action of glacial acetic acid in sealed tubes at 230—240°. It is difficult to convert *cadinene* completely by this method into its isomeric form, and the product often contains small amounts of unchanged *cadinene* which may be removed by conversion into the dihydrochloride.

isoCadinene (2.4 g.) was dehydrogenated by heating with sulphur as described above, and the product identified as cadalene (picrate, m. p. 114°). Yield, 40%.

Fractionation of Oil of False Cubebs.—The oil was fractionally distilled under reduced pressure. The principal sesquiterpene fractions were (a) a small fraction, b. p. 116—128°/10 mm., containing a little *cadinene*; (b) a fraction, b. p. 130—148°/10 mm., which gave a good yield of *cadinene* dihydrochloride when treated with hydrogen chloride in glacial acetic acid solution. The liquid portion of the hydrochloride was regenerated by heating with sodium acetate in glacial acetic acid solution, and the product consisted of a sesquiterpene, b. p. 120—124°/10 mm., which, however, still contained a small quantity of *cadinene* and resembled fraction (a) in its properties. The next fraction (c) was alcoholic, b. p. 148—160°/10 mm., and consisted of a bluish-green, viscous liquid. This liquid (120 g.) was hydrolysed by heating with methyl-alcoholic potash (25 g. of KOH in 400 c.c. of alcohol), the alcohol distilled off, water added, and the product extracted with ether and dried. After removal of the ether, the product was redistilled under reduced pressure. The larger part (80 g.) consisted of a bluish-green liquid, b. p. 153—155°/10 mm., d_4^{15} 0.9727, n_D^{15} 1.508, $[\alpha]_{561}^{15}$ —54°, $[R_L]_D$ 68.0 (calc. for a dicyclic sesquiterpene alcohol,

68·12) (Found: C, 81·3; H, 11·6. $C_{15}H_{26}O$ requires C, 81·1; H, 11·7%). The fraction was unsaturated and gave a 30% yield of cadinene dihydrochloride, m. p. 118°, $[\alpha]_{5461}^{65} - 43·7°$ in 2·380% chloroform solution, when treated in glacial acetic acid solution with dry hydrogen chloride.

Cubebol Phenylurethane.—The alcohol fraction (20 g.) and phenylcarbimide (10 g.) were heated together for 15 hours at 80–100°. On cooling, diphenylcarbamide, m. p. 238°, crystallised. The dark oily residue, isolated by means of anhydrous ether, in which diphenylcarbamide is nearly insoluble, was dissolved in alcohol, and water added to the point of precipitation. The *phenylurethane*, which slowly crystallised at 0° in well-defined needles, was repeatedly extracted with anhydrous ether and recrystallised from alcohol, in which it was moderately easily soluble; it then melted at 186° and had $[\alpha]_{5461}^{19} + 58·9°$ in 5% chloroform solution (Found: C, 77·0; H, 9·4; N, 4·4. $C_{22}H_{31}O_2N$ requires C, 77·4; H, 9·2; N, 4·1%). The yield (about 4%) could be somewhat increased by steam-distilling the alcoholic solution after no more crystals would separate from it; the distillate consisted of hydrocarbons and unattacked alcohol and from the residue a further quantity of the phenylurethane could be crystallised.

A *dibromide* was prepared from the phenylurethane by treating an alcoholic solution with excess of bromine at a low temperature. A solid compound separated on the addition of a little water. It was rather unstable, decomposing at 76–80°, and could not be satisfactorily purified owing to the small quantity available (Found: Br, 36·4. $C_{22}H_{31}O_2NBr_2$ requires Br, 32·0%).

Cubebol α -Naphthylurethane.—This was prepared from the cadinol fraction by a method similar to that described above, but it was more difficult to separate from the dinaphthylcarbamide, m. p. 284°, produced. It crystallised from alcohol, in which solvent and in ether it is less soluble than the phenylurethane derivative, as a mass of minute needles, m. p. 197–198·5° (Found: C, 80·7; H, 8·2. $C_{26}H_{33}O_2N$ requires C, 79·8; H, 8·5%).

Cubebol.—The phenylurethane was unattacked by boiling dilute methyl- or ethyl-alcoholic potassium hydroxide, or by acids, but was hydrolysed (1 g.) by heating with ethyl-alcoholic potassium hydroxide (1 g. in 12 c.c.) in sealed tubes for 2–3 hours, finally at 186°. After cooling, the product was diluted with water, neutralised with carbon dioxide, and repeatedly extracted with ether. The ethereal extracts were washed with dilute sulphuric acid (to remove aniline), then with dilute sodium carbonate solution, and dried. On removing the ether, a crystalline product was obtained which was extremely soluble in all ordinary organic

solvents, the vapour of ether or ligroin being sufficient to liquefy it. The substance was purified by vacuum sublimation and had m. p. 61—62° (Found : C, 80.7; H, 11.2. $C_{15}H_{26}O$ requires C, 81.1; H, 11.7%).

When the alcohol is treated with hydrogen chloride in ethereal or glacial acetic acid solution at 0°, a characteristic red coloration is produced, but no stable hydrochloride is formed; the product contains less than one atom of chlorine (Found : Cl, 9.6. $C_{15}H_{26}OCl$ requires Cl, 13.7%).

Cubebol Dibromide.—When the alcohol was gradually treated with bromine, both being in chloroform solution at 0°, addition and, to a small extent, substitution took place, accompanied by a deep blue coloration. On removing the chloroform, an unstable oil was obtained, which decomposed very quickly on exposure to light (Found : Br, 42.2. $C_{15}H_{26}OBr_2$ requires Br, 41.8%).

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