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SESQUITERPENE HYDROCARBONS FROM THE OIL OF CUBEB
α-CUBEBENE AND β-CUBEBENE

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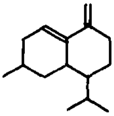
According to the reports of several investigators, the oil of cubeb (Piper cubeba L.) contains a few sesquiterpene hydrocarbons of mother skeleton of cadinane type, i.e., δ-cadinene (1), copaene (2), and a cadinene-like compound (I) (2).
In this communication, we wish to report isolation and structural determination of two sesquiterpene hydrocarbons, named α-cubebene and β-cubebene by us, both of which have the same mother skeleton.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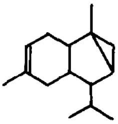
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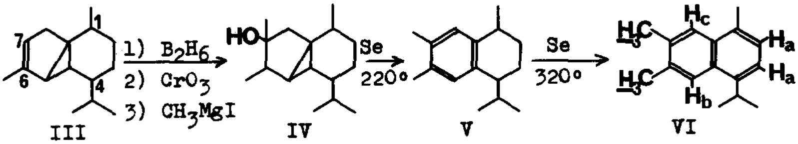
Šorm and his colleagues previously isolated a compound named "copaene" from false cubeb oil and gave it a formula II (3). However, recently, the structure of copaene isolated from Cedrela toona Roxb. was elucidated by de Mayo (4) and Sukh Dev (5). The "copaene" reported by Šorm showed a different IR spectrum from that of the one isolated from Cedrela toona.

In the course of our studies, it was revealed that two hydrocarbons (III and IX) isolated from commercial cubeb oil had cadinane carbon skeleton and one of them, α-cubebene (III), showed the identical IR spectrum with that of the compound "copaene" erroneously reported by Šorm.

α-Cubebene (III), $C_{15}H_{24}$, $[\alpha]_D^{30}$ -20.0°(c, 0.874 in chloroform) shows signals of two cyclopropane protons at 0.21 and 1.10ppm (in δ-value). Conjugation between a double bond and a cyclopropane ring is expected based on UV spectrum: λ_{max}208mμ (ε, 4,260). Its IR spectrum is shown in FIG.1.
It was hydrogenated to a dihydro derivative with platinum oxide in acetic acid, MS: M^+ion m/e 206 ; IR: the absorption bands at 3050, 1645, 825 and 780cm^{-1} disappeared ; NMR: signals of two cyclopropane protons at 0.5-0.7ppm.

These results indicate that α-cubebene is a tricyclic sesquiterpene hydrocarbon. On saturation with gaseous hydrogen chloride in dry ether solution, it was converted to (-)-cadinene dihydrochloride, m.p.114-115°; $[\alpha]_D^{30}$ -41.3°(c, 0.208 in chloroform).

In an attempt of chromatographic purification on a silica gel column, α-cubebene was isomerized to a hydrocarbon which shows close resemblance to δ-cadinene in regard to IR spectrum, MS pattern and Rt in GLC. 7-Methyl cadalene (VI) was derived from α-cubebene (III) through the following reactions:



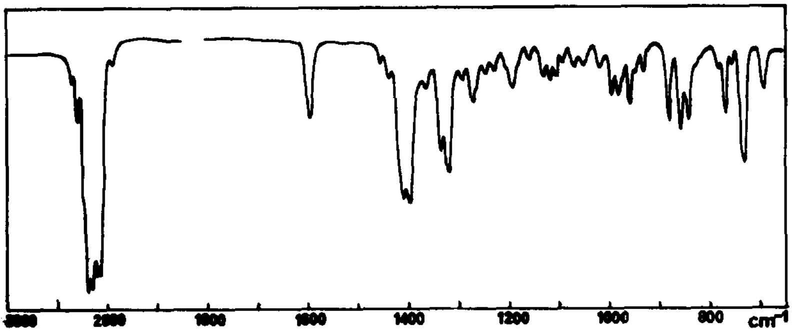
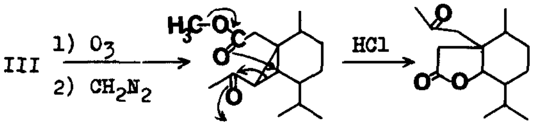


FIG.1 IR Spectrum of α-Cubebene

The picrate of VI, m.p. 121.5-122°, was identical with that of 7-methyl cadalene derived from copaene by Briggs and Taylor (6). Thus, NMR spectrum of VI well accounts for this structure, 1.36 (6H d.), 2.42 (6H s. $C_{(6)}$-CH_3 and $C_{(7)}$-CH_3), 2.58 (3H s.), 7.13 (2H s. H_a), 7.69 (1H, H_c) and 7.84ppm (1H, H_b), and the double bond in α-cubebene was proved to be at C 6-7.

The location of cyclopropane ring was proved by the following reactions. Ozonolysis of III, followed by treatment with diazomethane, gave a ketoester (VII): M^+ion m/e 266 by electron impact ; IR: 1690 and 1740cm^{-1} ; NMR: 2.20 (3H s. $C\underline{H}_3CO$-), 2.41 (2H s. -$C\underline{H}_2COO$-), 3.63ppm (3H s. $C\underline{H}_3OCO$-). The structure (VII), given to this ketoester, was supported by its NMR and MS spectra. A singlet peak (2H) in a region of δ 2.0-2.5ppm means that there is only one methylene group adjacent to carbonyl or methoxycarbonyl group and no proton on β-carbon atom to carbonyl group. The remarkably abundant ion species, M-73 (m/e 193) and M-43 (m/e 223), suggest the presence of carbomethoxy methylene group and acetyl group, respectively.



VII VIII

On treatment with conc. hydrochloric acid, this ketoester yielded a ketolactone (VIII) as a result of the cleavage of the three membered ring, IR: 1770cm^{-1}(γ-lactone) and 1720cm^{-1} (aliphatic ketone) ; MS: M^+ion m/e 252, base peak m/e 43 and an ion m/e 194 (elimination of acetone molecule) with nearly equal abundance to base peak ; NMR: 4.63ppm (broad singlet, one hydrogen on the carbon atom which carries oxide linkage).

β-Cubebene, $C_{15}H_{24}$, was isolated by preparative gas chromatography. Its IR spectrum is shown in FIG.2. The compound has a terminal methylene group conjugated with a cyclopropane ring and no methyl group attached to C=C double bond,

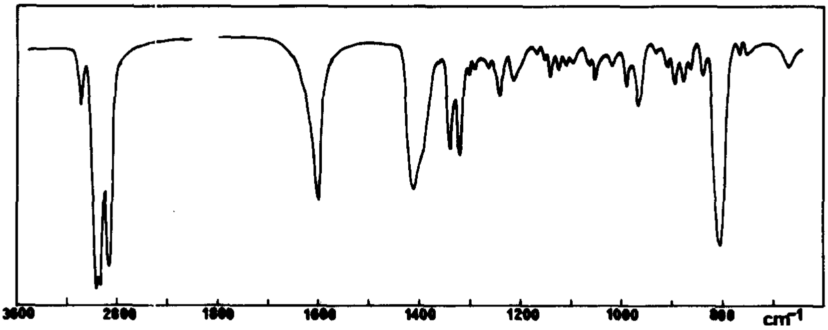


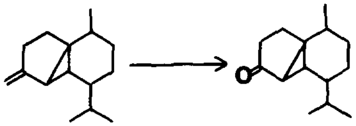
FIG.2 IR Spectrum of β-Cubebene

NMR: signals of three methyl groups (δ 0.8-1.0ppm), signals of terminal methylene protons (4.71, 1H and 4.52, 1H) ; IR: 3080, 1650 and 860cm^{-1}; UV: λ_{max}210mμ (ε, 4,340).

Based on the following evidences, β-cubebene was concluded to be an isomer of α-cubebene concerning the position of double bond: (1) On saturation with gaseous hydrogen chloride in dry ether, it also gave cadinene dihydrochloride, m.p. 114.5-115.5°. (2) When passed through a half-exhausted capillary column coated with polypropylene glycol at 150°, it was partially isomerized to α-cubebene. (3) By passing through a column packed with silica gel, it was readily isomerized to the same product from α-cubebene. (4) On hydrogenation with platinum oxide in ethanol, it yielded two dihydro derivatives, both of which showed identical MS spectra, and one of them was identical with dihydro α-cubebene.

The fact No.2 suggests that the terminal double bond is at C-6 rather than at C-1 of cadinane carbon skeleton.

On ozonolysis, β-cubebene yielded a ketone (X), m.p. 58.5-59.5°, which showed molecular ion m/e 206, $C_{14}H_{22}O$, by electron impact. As it showed λ_{max}209mμ (ε, 2,210) in UV, conjugation of carbonyl group with cyclopropane ring, and ν_{max}1715cm^{-1} in IR, a five membered cyclic ketone conjugated with a cyclopropane ring, it was concluded that the position of the terminal double bond in original hydrocarbon was at C-6.



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