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STRUCTURE OF MUSTAKONE AND COPAENE*

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A new sesquiterpene ketone, $C_{15}H_{22}O$, (semicarbazone, m.p. 198-99°) having b.p. 128-29°/1 mm, $[\alpha]_D$ +0.34 ($CHCl_3$; c, 2.6%), has been isolated from the essential oil of Cyperus rotundus Linn. (Sanskrit, mustaka) and has been named mustakone. On catalytic hydrogenation (Pt/acetic acid) it took up one mole of hydrogen to give a saturated ketone, $C_{15}H_{24}O$, n_D^{30} 1.4921, $[\alpha]_D$ +0.14 ($CHCl_3$; c, 2.6%). Mustakone, $C_{15}H_{22}O$, is thus, mono-olefinic and hence should be tricyclic.

The dihydroketone displayed its $\nu^{c=o}$ at 1712 cm^{-1} and hence the ketone function must be located in a six-membered ring. Mustakone showed λ_{max}^{EtOH} 255 mμ (ε 5700),

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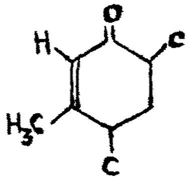
[*] Delivered as a lecture at the Department of Organic Chemistry, Indian Institute of Science, Bangalore, on Aug.24, 1963. After this paper had been prepared for communication, a short paper by G.Büchi, S.H.Feairheller, P.de Mayo and R.E.Williams [Proc. Chem. Soc. 214 (1963)] on the structure of copaene appeared (the above issue of this journal was received in our library on Sept.20, 1963). These authors propose the same structure for copaene.

$\nu^{c=o}$ 1685 cm^{-1}, $\nu^{c=c}$ 1628 cm^{-1}, and therefore, it must be an αβ-unsaturated ketone. Its proton magnetic resonance (PMR) spectrum[1] recorded signals for an isopropyl group (50, 56 cps), one quaternary methyl (sharp signal at 58 cps) and a methyl on a trisubstituted olefinic linkage (doublet centred at 119 cps, J = 2 cps); an absorption (AB_3 multiplet, J = 2 cps) at 335 cps accounted for one vinyl proton, which should be α to the carbonyl. This information, taken along with the fact that mustakone does not exhibit any infrared absorption between 1400-1430 cm^{-1} (absence of methylene groups α to the carbonyl[2] or γ to an αβ-unsaturated ketone[3]; the dihydro derivative had δ^{CH_2} at 1418 cm^{-1}) leads to the partial formula (I):



I

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[1] All PMR spectra were taken on 10-20% solutions in CCl_4 on a Varian A-60 spectrometer; the signals are recorded in cps from tetramethylsilane as zero.

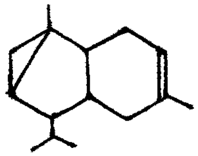
[2] R.N.Jones and A.R.H.Cole, *J.Amer.Chem.Soc*. **74**, 5648 (1952); R.N.Jones, A.R.H.Cole and B.Nolin, *ibid*. **74**, 5662 (1952).

[3] e.g. see: P. de Mayo and H.Takeshita, *Canad.J.Chem.* **41**, 440 (1963).

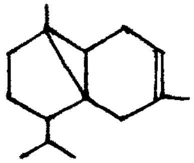
A comparison of the PMR spectrum of mustakone with a number of tricyclic sesquiterpenoid PMR spectra revealed significant similarity with that of copaene. When the dihydroketone was subjected to Wolff-Kishner reduction, a hydrocarbon, identified as dihydrocopaene (Copane) , by a comparison of their infrared spectra, was obtained. The new sesquiterpenoid, thus, must possess the same skeleton as copaene, a hydrocarbon also occuring in the essential oil of *Cyperus rotundus*.

The structure of copaene, currently in vogue is (II)[4,5] though this and the related structure (III)[4] have been criticised[6] and alternatives like (IV) and (V) have been

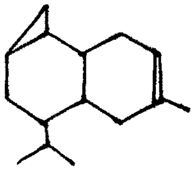
II



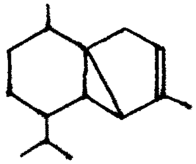
III



IV



V



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[4] L.H.Briggs and W.I.Taylor, *J.Chem. Soc.* 1338 (1947).

[5] F.Vonasek, V.Herout and F.Sorm, *Collec. Czech. Chem. Communs.* **25**, 919 (1960).

[6] P. de Mayo, *Perfum. essent. oil Rec.* **49**, 238 (1958)

considered. However, these alternatives are readily ruled out on the basis of PMR spectrum of copaene, which clearly showed a total of four methyl groups (isopropyl methyls, 48, 54 cps; quaternary methyl, 48 cps and, a methyl on an olefinic bond, doublet centred at 99 cps) one of which is quaternary. It has already been pointed out that mustakone showed its λ_{max} at 255 mμ, a value which is considerably higher than that (~ 240 mμ) expected for an unstrained β-substituted cyclohexenone. On the basis of structure (II) or (III) for copaene, it is not possible to derive an expression for mustakone, which would answer this property (or incorporate the part structure I). This made us suspect that copaene, in fact, may not contain a three-membered ring at all, a possibility first pointed out by Birch[7] in 1951. In full support of this, it was found that copane (b.p. 105°/5 mm, n_D^{30} 1.4830, α_D -2.3; prepared by the catalytic hydrogenation of copaene, which was isolated from the wood of *Cedrela toona* Roxb. and had: b.p. 112-14°/8 mm, n_D^{30} 1.4864; $[\alpha]_D$ -6.5, $CHCl_3$) was recovered unchanged after attempted hydrogenation over prereduced PtO_2 in acetic acid containing perchloric acid, even at 50°, or after treatment with hydrochloric acid gas in ether at 0° or after digestion with 98% formic acid at 100° for 4 hrs.

While looking for an alternative[8] formulation for

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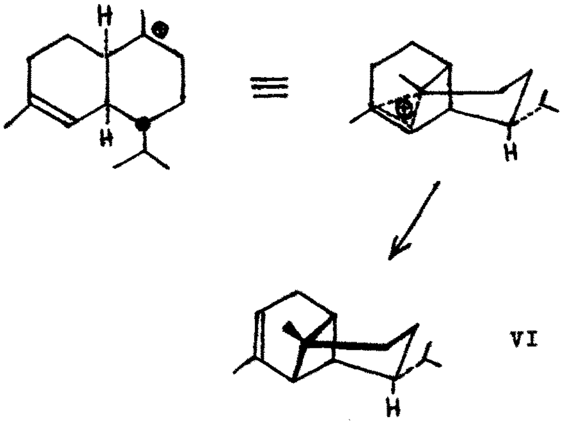
[7] A.J.Birch, *Rep. Progr. Chem*. **47**, 195 (1951).

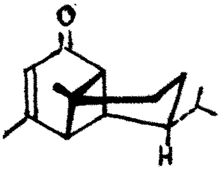
[8] Though the expression, considered by Birch, for copaene does not incorporate a cyclopropane ring, it is untenable on the basis of PMR spectrum of copaene.

copaene, the possibility (VI) derivable as indicated,



VI

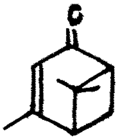
looked attractive, as it can, not only, explain all the known reactions of copaene, but also uniquely meets the requirements of mustakone, which becomes (VII) and hence should exhibit, ultraviolet absorption characteristics similar to verbenone (VIII)[9], as indeed is the case.



VII

λ_{max} 255 mμ

ε 5,700



VIII

λ_{max} 253 mμ

ε 6,840

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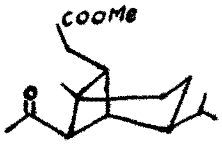
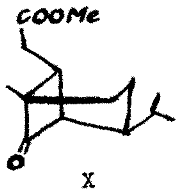
[9] R.N.Moore and G.S.Fisher, J.Amer.Chem.Soc. 78, 4632 (1956).

Experimental evidence in favour of (VI) was obtained as follows: Oxidative ozonolysis of copaene yielded the keto acid (IX), which was purified *via* its semicarbazone (m.p. 220-22° dec.); its methyl ester ($\nu^{C=O}$ 1704, 1743 cm^{-1}; PMR: -COOC$\underline{H}_3$217, $-\overset{O}{\overset{\|}{C}}-\underline{CH_3}$ 116 cps) was treated with perbenzoic acid in chloroform containing some p-toluene sulphonic acid, for 7 days at ~ 25°. The product on alkaline hydrolysis, followed by chromatography of its methyl ester yielded an alcohol ester ($\nu^{C=O}$ 1736 cm^{-1}, ν^{OH} 3475 cm^{-1}), which on oxidation furnished the cyclobutanone derivative (X) ($\nu^{C=O}$ 1780, 1748 cm^{-1}; no band in the 1400-1430 region).



IX



X

The above evidence, together with the fact[10]

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[10] This has been re-checked experimentally.(-)-Copaene furnished 25% yield of (-)-cadinene hydrochloride. However, the mother liquor on work up yielded a liquid dihydrochloride with $[\alpha]_D$ -16.0 ($CHCl_3$; c, 1.2%) and having infrared absorption completely different from that of cadinene dihydrochloride.

that (-)-copaene yields (-)-cadinene dihydrochloride (of established absolute stereochemistry[11]) on treatment with hydrochloric acid gas, suffice to fix the structure and stereochemistry of copaene and mustakone as (VI) and (VII) respectively. Structure (VI) on ring cleavage with hydrochloric acid gas would lead to (+)-cadinene dihydrochloride and hence the absolute configuration of (-)-copaene would be represented by mirror-image of (VI).

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[11] V.Sykora, V.Herout and F.Sorm, Collec. Czech. Chem. Communs. **23**, 2181 (1958).