

## STUDIES IN SESQUITERPENES—XXII\* STRUCTURE OF MUSTAKONE AND COPAENE†‡

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(Received 22 October 1964)

**Abstract**—In connection with the structure determination of mustakone, a sesquiterpene ketone from *Cyperus rotundus* Linn., it became apparent that the currently accepted structure of copaene, a tricyclic sesquiterpene hydrocarbon, first isolated in 1914, was untenable. Evidence is now presented which permits the derivation of the absolute stereostructures of copaene and mustakone.

FROM the essential oil of *Cyperus rotundus* Linn.,<sup>1</sup> the source for the sesquiterpene ketone, cyperone, a new ketone has been isolated and has been named *mustakone* after the local name of the plant (Sanskrit, *Mustaka*: Hindi, *Motha*).

Mustakone analyses for  $C_{15}H_{22}O$  and displays  $\lambda_{\max}^{EtOH}$  255  $m\mu$  ( $\epsilon$  5700) in the UV.

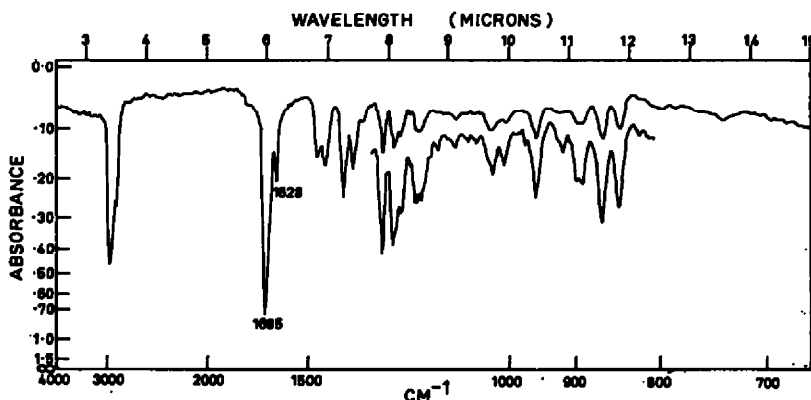


FIG. 1. IR spectrum of mustakone.

From this and its IR spectrum (Fig. 1) it is clear that mustakone is an  $\alpha\beta$ -unsaturated ketone. On quantitative catalytic hydrogenation it yields a dihydroderivative, which is saturated, hence mustakone must be tricyclic. The dihydroketone displays its  $\nu^{C=O}$

\* Part XXI: *Tetrahedron* 19, 2293 (1963).

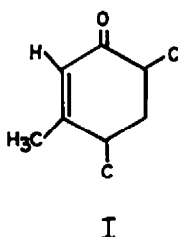
† Communication No. 736, National Chemical Laboratory, Poona.

‡ A preliminary communication appeared in *Tetrahedron Letters* 1933 (1963).

<sup>1</sup> For earlier studies of the chemistry of the essential oil, see: B. S. Rao, P. B. Panicker and J. J. Sudborough, *J. Indian Inst. Sci.* 8A, 39 (1925); B. J. Hegde and B. S. Rao, *J. Soc. Chem. Ind.* 54, 387T (1935); E. Gildmeister and F. Hoffmann, *Die Atherischen Öle* (4th Edition revised by W. Triebs and K. Bournot) Vol. IV, p. 425. Akademie Verlag, Berlin (1956). In the present re-investigation of the material the presence of a number of new compounds is indicated and these will be discussed in subsequent publications. Recently an investigation of the essential oil of Chinese origin has appeared: B. Trivedi, O. Motl, V. Herout and F. Sorm, *Coll. Czech. Chem. Comm.* 29, 1675 (1964).

at  $1712\text{ cm}^{-1}$ , therefore the ketone function should be located in a six-membered ring; moreover, from the ratio (5) of the integrated band intensities of the carbonyl and the C=C stretching vibrations (Fig. 1) in mustakone it follows that the carbonyl and the ethylenic functions should be in *s-trans* configuration.<sup>2,3</sup>

The PMR spectrum (Fig. 2) of mustakone records signals for an isopropyl group (3H signals at 50 and 56 c/s), one quaternary methyl (3H, 58 c/s) and a methyl on a trisubstituted olefinic linkage (3H doublet centred at 119 c/s,  $J = 2\text{ c/s}$ ; 1H multiplet centred at 335 c/s,  $J = 2\text{ c/s}$ ); the position of the vinyl proton signal suggests that it should be  $\alpha$  to the carbonyl. This information, taken along with the fact that mustakone does not exhibit any IR absorption between  $1400\text{--}1430\text{ cm}^{-1}$  (absence of methylene groups  $\alpha$  to the carbonyl<sup>4,5</sup> or  $\gamma$  to an  $\alpha\beta$ -unsaturated ketone;<sup>6</sup> the dihydroketone has  $\text{CH}_2$   $1418\text{ cm}^{-1}$ ) leads to the partial formula I:



However, it should be noted that the value of UV  $\lambda_{\text{max}}$  calculated<sup>7</sup> for the chromophore in I would be  $239\text{ m}\mu$  in contrast to the observed value of  $\lambda_{\text{max}} 255\text{ m}\mu$ . Thus, the other structural features in mustakone should be such as to be consistent with this bathochromic shift.

In an attempt to correlate the mustakone skeleton to one already known in sesquiterpenoid chemistry, the PMR spectrum was compared with the PMR spectra of a number of tricyclic sesquiterpenes, and significant similarities were observed in the spectra of mustakone and copaene (Fig. 3). The suspected relationship was confirmed, when it was found that the Wolff-Kishner reduction of dihydromustakone furnishes a hydrocarbon,  $\text{C}_{15}\text{H}_{28}$ , identified (IR) as dihydrocopaene (copane). The new sesquiterpenoid, thus, must possess the same skeleton as copaene, a hydrocarbon also found to occur in the essential oil of *Cyperus rotundus*.

The structure of copaene, currently in vogue is II<sup>8,9</sup> and since the structural requirements of mustakone, deduced earlier, cannot be met within the framework of formula II, the structure of copaene became a suspect and a reinvestigation was undertaken.

<sup>2</sup> D. H. R. Barton and C. R. Narayanan, *J. Chem. Soc.* 963 (1958).

<sup>3</sup> R. L. Erskine and E. S. Waight, *J. Chem. Soc.* 3425 (1960).

<sup>4</sup> R. N. Jones and A. R. H. Cole, *J. Amer. Chem. Soc.* 74, 5648 (1952).

<sup>5</sup> R. N. Jones, A. R. H. Cole and B. Nolin, *J. Amer. Chem. Soc.* 74, 5662 (1952).

<sup>6</sup> P. de Mayo and H. Takeshita, *Canad. J. Chem.* 41, 440 (1963).

<sup>7</sup> R. B. Woodward, *J. Amer. Chem. Soc.* 63, 1123 (1941); 64, 76 (1942); L. Dorfman, *Chem. Rev.* 53, 60 (1953).

<sup>8</sup> L. H. Briggs and W. I. Taylor, *J. Chem. Soc.* 1338 (1947).

<sup>9</sup> F. Vonasek, V. Herout and F. Sorm, *Coll. Czech. Chem. Comm.* 25, 919 (1960); V. Herout and V. Sykora, *Tetrahedron* 4, 246 (1958).

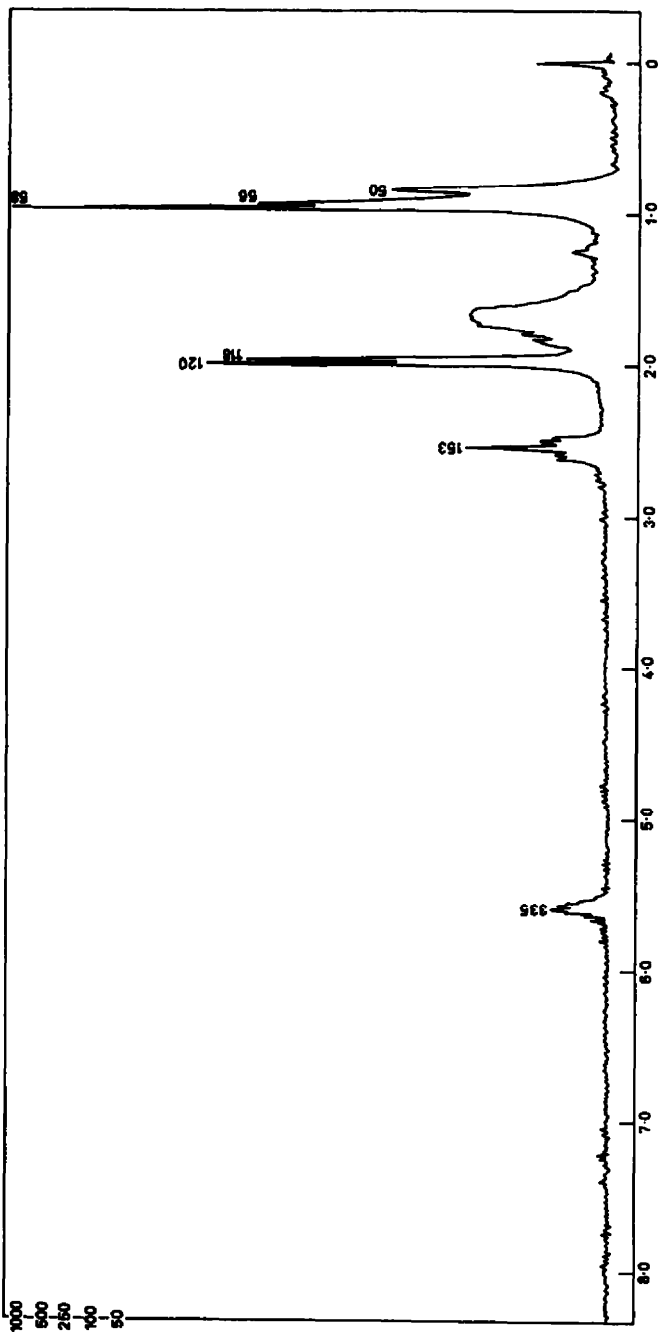


FIG. 2. PMR spectrum of mustakone.

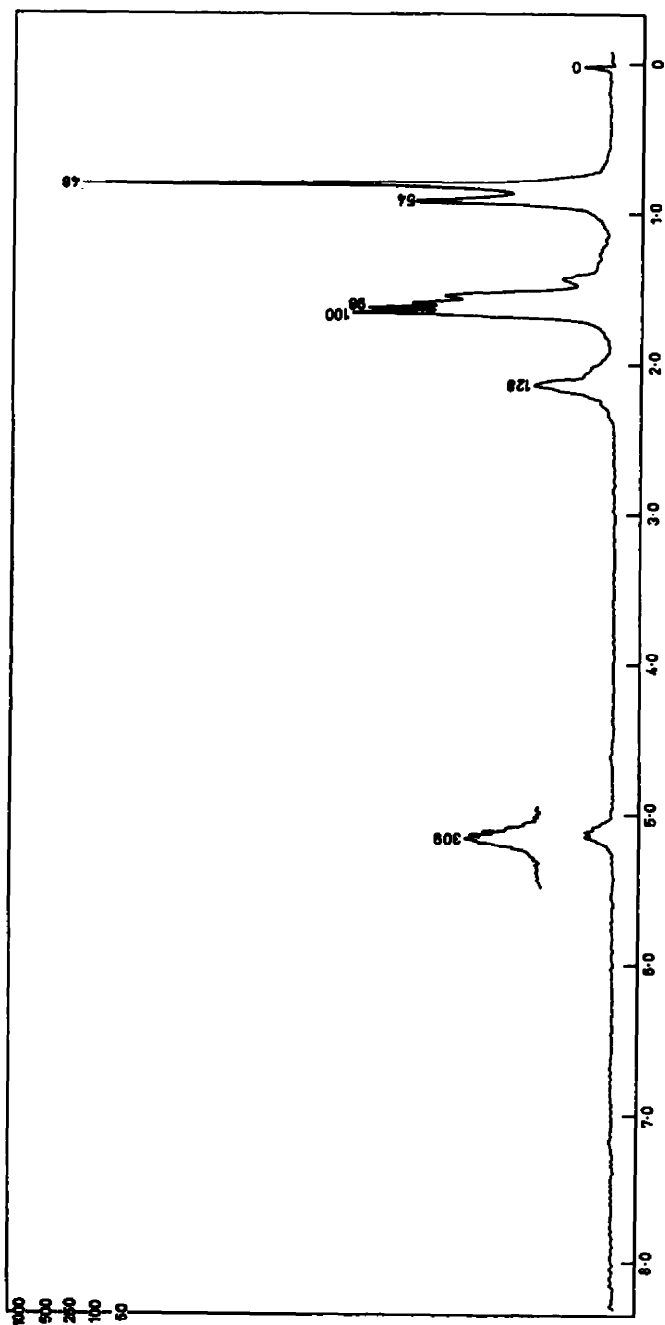
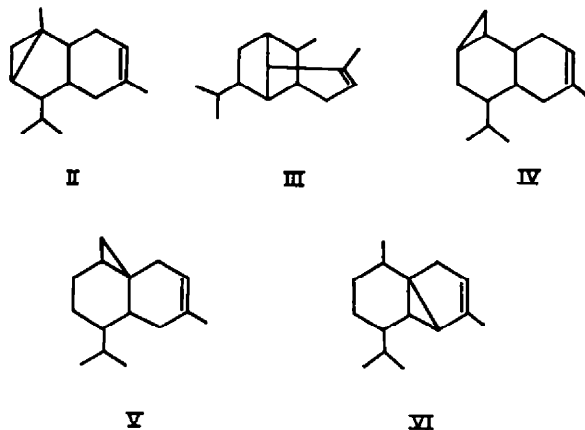


FIG. 3. PMR spectrum of copaene.

*Structure of copaene*<sup>10</sup>

Copaene was first isolated in 1914 from African copaiba balsam oil,<sup>11</sup> it is tricyclic and on treatment with hydrochloric acid gas gives cadinene dihydrochloride.<sup>12</sup> In a reinvestigation of the problem, Briggs and Taylor<sup>8</sup> put forward structure II for copaene and this has been accepted<sup>9</sup> although this structure has been criticized at least twice. Thus, Birch<sup>13</sup> in 1951 pointed out that since there is no direct evidence



for the presence of a cyclopropane ring in copaene, a structure like III cannot be ruled out on the existing evidence. de Mayo<sup>14</sup> in a general discussion on cyclopropane ring cleavage in terpenoids, reported that since there is no reason why a non-Markownikoff cyclopropane ring cleavage should occur in II, the structure is suspect and, proposed structures IV, V or VI as preferable.

The PMR spectrum of copaene (Fig. 3) clearly shows the presence of an isopropyl group (signals at 48 and 54 c/s), one quaternary methyl (48 c/s) and a methyl on a trisubstituted olefinic bond (3H doublet centred at 99 c/s,  $J = 2$  c/s; 1H unresolved multiplet centred at 309 c/s). These data are inconsistent with the formulations III–VI and since, structure II is not compatible with the structural requirements of mustakone, a new structure for copaene is essential.

It was suspected that copaene, as first pointed out by Birch,<sup>13</sup> may not contain a three-membered ring. In full support of this it was found that copaene is recovered unchanged after attempted hydrogenation over pre-reduced  $\text{PtO}_2$  in acetic acid containing perchloric acid, even at 50°, or after treatment with hydrogen chloride in ether at 0° or after digestion with 98% formic acid at 100° for 4 hr.

Formula VIII, which may be derived<sup>15</sup> as indicated, not only explains all the known reactions of copaene, but also uniquely meets the requirements of mustakone.

<sup>10</sup> Also see: G. Büchi, S. H. Fairheller, P. de Mayo and R. E. Williams, *Proc. Chem. Soc.* 214 (1963).

<sup>11</sup> Schimmel and Co., *Ber. Schimmel* p. 48. April (1914).

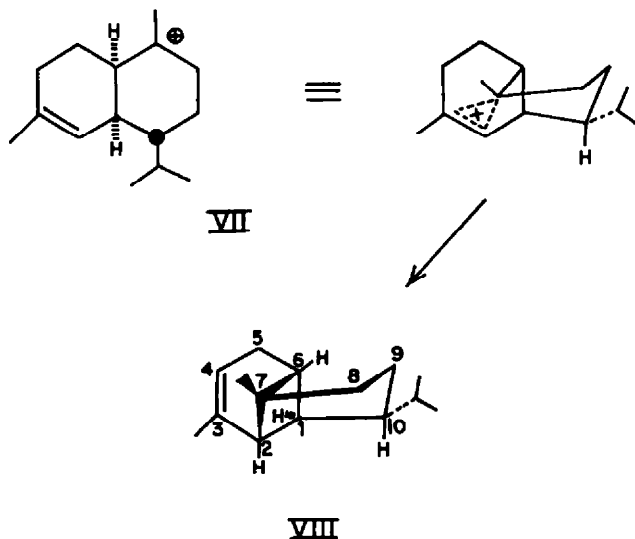
<sup>12</sup> F. W. Semmler and H. Stenzel, *Ber. Dtsch. Chem. Ges.* 47, 2555 (1914).

<sup>13</sup> A. J. Birch, *Rep. Progr. Chem.* 47, 195 (1951).

<sup>14</sup> P. de Mayo, *Perfum. essent. Oil Rec.* 49, 238 (1958).

<sup>15</sup> The genesis of VII from farnesyl cation has been discussed by P. de Mayo, J. R. Robinson, E. Y. Spencer and R. W. White [*Experientia* 18, 359 (1962)] and its role in the biogenesis of the novel sesquiterpenoid, helminthosporal established by tracer studies. The recently discovered muurolenes,<sup>20</sup> the 'cadinenes with *cis*-ring-fusion', would arise directly from VII.

Furthermore, copaene shows in the IR spectrum a strong absorption at  $788\text{ cm}^{-1}$  which disappears on hydrogenation; this is compatible with VIII as due to the strain



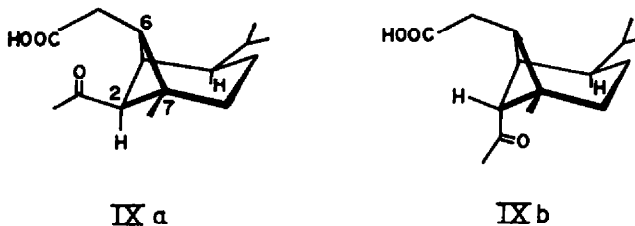
in the bicyclo [3,1,1] heptene system the CH out-of-plane deformation would occur at lower frequencies.<sup>16</sup>

Chemical evidence in favour of VIII was obtained as follows: Ozonolysis followed by alkaline hydrogen peroxide oxidation yields the keto acid,  $\text{C}_{15}\text{H}_{24}\text{O}_3$ , of Semmler and Stenzel<sup>12,17</sup> and which, now can be formulated as IX. Its methyl ester

<sup>16</sup> L. J. Bellamy, *The Infrared Spectra of Complex Molecules* pp. 387-389. Methuen, London (1958);  $\alpha$ -pinene displays its  $\delta=\text{CH}$  at  $786\text{ cm}^{-1}$ .

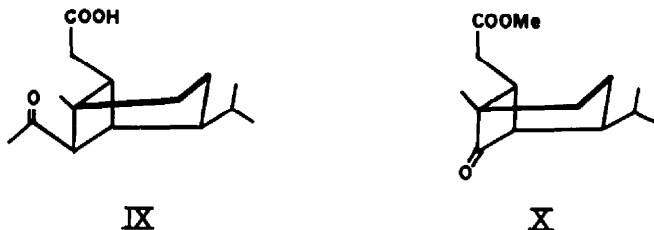
<sup>17</sup> The product is best characterized as its semicarbazone (m.p.  $220-222^\circ$ ). However, when the oxidative cleavage of the ozonide is carried out with  $\text{H}_2\text{O}_2$  in acetic acid and the acidic product converted into the semicarbazone, a mixture of semicarbazones (m.p.  $165-210^\circ$ ) is obtained, from which a small amount of a new semicarbazone (m.p.  $183-185^\circ$ ) can be isolated; this also analysed for  $\text{C}_{15}\text{H}_{27}\text{O}_2\text{N}_2$ , i.e. for the semicarbazone corresponding to the keto acid IX. The two semicarbazones, on regeneration yielded keto acids, the methyl esters of which, though having almost identical IR spectra, showed significant differences in the PMR spectra; thus, for example, the signal for the  $\text{CH}_2\text{CO}-$  occurred at 123 c/s in the sample from the lower melting semicarbazone and at 115 c/s in the other sample. That the two compounds were epimeric at  $\text{C}_1$  was established by the base-catalysed isomerization of the material from the lower melting semicarbazone to the other product.

Since, the initial oxidation product from VIII, must have the configuration IXa, this must be unstable relative to its epimer IXb, the product of base equilibration. This preference of the



bulkier acetyl group (at  $\text{C}_2$ ) to move into the axial conformation, must be attributed to the 1,3-diaxial-type interaction, between the  $-\text{COCH}_3$  and the  $-\text{CH}_2\text{COOH}$  groups on  $\text{C}_2$  and  $\text{C}_4$  respectively, in IXa and, this is expected to outweigh the resulting 1,3-diaxial interactions in IXb.

on treatment with perbenzoic acid in chloroform containing some *p*-toluenesulphonic acid yields the corresponding acetate. The product was hydrolysed and the methyl ester of the resulting hydroxy acid on  $\text{CrO}_3$ -pyridine oxidation yields the keto ester, which as required on the basis of VIII, should be a cyclobutanone (X), a fact borne



out by its IR spectrum:  $\nu^{\text{C=O}}$   $1780\text{ cm}^{-1}$  (Fig. 4). This degradation, along with its known conversion to cadinene dihydrochloride on reaction with hydrogen chloride, suffices to establish the structure VIII for copaene.

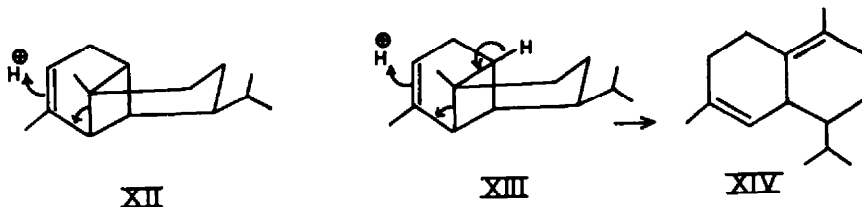
### Stereochemistry

Because of the bridged structure for copaene, the only points of stereochemical interest are the configuration at  $\text{C}_{10}$  and the absolute stereochemistry. Both of these are settled uniquely by the fact that (–)-copaene, on treatment with hydrogen chloride, furnishes (–)-cadinene dihydrochloride (XI) of established absolute stereochemistry.<sup>18</sup> Since configurations at  $\text{C}_1$  and  $\text{C}_{10}$  are not involved in the cleavage reaction,<sup>18</sup> structure VIII should furnish (+)-cadinene dihydrochloride after ring-opening

<sup>18</sup> V. Sykora, V. Herout and F. Sorm, *Coll. Czech. Chem. Comm.* **23**, 2181 (1958).

<sup>19</sup> Because of the key importance of this reaction, it has been re-checked with pure (–)-copaene, when a 25% yield of crystalline (–)-cadinene dihydrochloride was obtained. The mother liquors yielded a product  $[\alpha]_{\text{D}} -16.0$ , which analyses essentially for a dihydrochloride and, from its IR spectrum consists chiefly of a dihydrochloride different from cadinene dihydrochloride.

The ring-cleavage reaction, if operating as shown XII, should give mostly a dihydrochloride with the two rings *cis*-locked (muurolene dihydrochloride, ?<sup>20</sup>), while the formation of cadinene dihydrochloride would require either epimerization at  $\text{C}_4$  during the course of reaction (which is quite feasible) or else the direct opening (XIII) of copaene to XIV. Since muurolenes<sup>20</sup> give only



muurolene dihydrochloride, a concerted one-step formation of XIV (the hydrogen at  $\text{C}_4$  and the  $\text{C}_2$ – $\text{C}_7$  bond have the required anti-parallel geometry), may be the preferred route to cadinene dihydrochloride. This may also explain the absence of formation of any secondary monohydrochloride (in the PMR spectrum, the hydrochloride from the mother liquor failed to show any

absorption in the range expected for  $\text{>C} \begin{pmatrix} \text{H} \\ \text{Cl} \end{pmatrix}$  in the reaction, which is in direct contrast to the

behaviour of  $\alpha$ -pinene, and the closely analogous  $\alpha$ -longipinene.<sup>21</sup>

<sup>20</sup> L. Westfelt, *Acta Chem. Scand.* **18**, 572 (1964).

<sup>21</sup> H. Erdtman and L. Westfelt, *Acta Chem. Scand.* **17**, 2351 (1963).

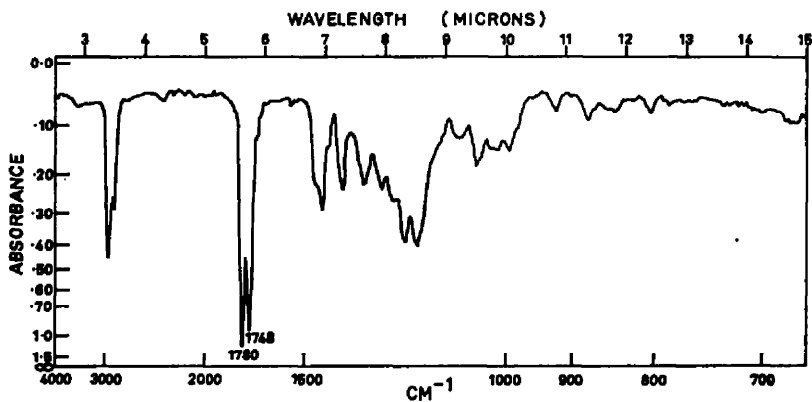


FIG. 4. IR spectrum of keto ester X.

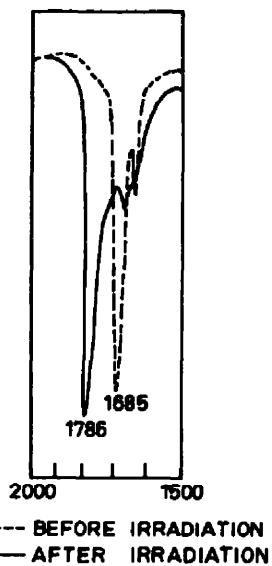
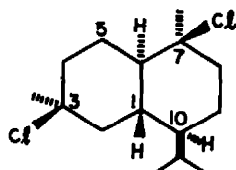


FIG. 5. Photoisomerisation of mustakone.



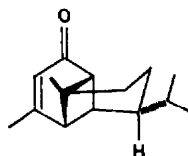
and hence the absolute configuration of (–)-copaene would be represented by the mirror-image of VIII.



XI

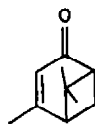
### Structure of mustakone

As mentioned previously, the structural features of mustakone fit eminently in the new framework of copaene (VIII), whence mustakone becomes XV. As can be seen, the strain due to the bicyclo [3,1,1] heptane system would account for the observed bathochromic shift in the UV absorption;<sup>22</sup> as can be expected on the basis



XV

$\lambda_{\max} 255 \text{ m}\mu$   
 $\epsilon 5,700$



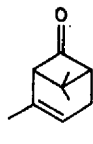
XVI

$\lambda_{\max} 253 \text{ m}\mu$   
 $\epsilon 6,840$

of XV, mustakone and verbenone (XVI)<sup>23</sup> should have very similar UV spectra, as indeed is the case.

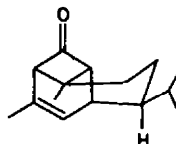
A direct conversion of (–)-copaene to (–)-mustakone<sup>24</sup> has also been achieved. Oxidation of copaene with *t*-butyl chromate yields amongst other products ~15% of mustakone, which was identified by spectral methods (IR, UV).

Finally, another, independent proof for the presence of a four-membered ring in mustakone (and hence in copaene) has been obtained. Based on the photochemical isomerization of verbenone (XVI) to chrysanthene (XVII),<sup>25</sup> irradiation of mustakone under the same conditions was carried out. The progress of the reaction was



$\nu_{\text{C=O}} 1780 \text{ cm}^{-1}$

XVII



$\nu_{\text{C=O}} 1786 \text{ cm}^{-1}$

XVIII

<sup>22</sup> See Refs cited in: U.R. Nayak, T. S. Santhanakrishnan and Sukh Dev, *Tetrahedron* **19**, 2281 (1963).

<sup>23</sup> R. N. Moore and G. S. Fischer, *J. Amer. Chem. Soc.* **78**, 4632 (1956).

<sup>24</sup> The mustakone obtained by this method has  $[\alpha]_D -54.59^\circ$  and this implies that the ketone isolated from *Cyperus rotundus*, with its  $[\alpha]_D +0.34$ , is essentially racemic. It may also be noted that the copaene isolated from the same source is also weakly dextrorotatory.

<sup>25</sup> J. J. Hurst and G. H. Whitham, *J. Chem. Soc.* 2864 (1960).

followed by measuring the IR spectrum of aliquot samples; the  $\nu^{C=O}$  at 1685 was steadily replaced by another absorption at 1786  $\text{cm}^{-1}$  and after 2½–3 hr exposure, absorption at 1786  $\text{cm}^{-1}$  predominated (Fig. 5). This is in accord with its photoisomerization to XVIII.

#### EXPERIMENTAL

All m.ps and b.ps are uncorrected. Pet. ether refers to the fraction b.p. 40–60°. Optical rotations were taken in  $\text{CHCl}_3$ . IR spectra were taken on a Perkin-Elmer Infracord, model 137 E, either as smears (liquids) or in nujol (solids). UV spectra were taken on a Perkin-Elmer Spectrophotometer, model 350, in 95% ethanol. All PMR spectra were taken in 10–20% solution in  $\text{CCl}_4$  with tetramethylsilane as the internal standard, on a Varian Associates A-60 spectrometer; peaks are reported in c/s from tetramethylsilane.

Alumina used for chromatography was made neutral by the  $\text{HNO}_3$  method and standardized according to Brockmann. Thin-layer chromatography (TLC) was carried out on silica-gel containing 15% gypsum using equipment and procedure described elsewhere;<sup>28</sup> visualization of the spots, after development, was done by spraying with 33% chlorosulphonic acid in acetic acid and warming. GLC was done on Perkin-Elmer Vapour Fractometer, model 154D, using  $\text{H}_2$  as the carrier gas and a 2-meter column (external diameter ¼") packed with 20% diethylene glycol succinate on Chromosorb W.

#### Copaene

This was isolated from the essential oil from the wood of *Cedrela toona*<sup>27</sup> by precise fractionation. The pure (GLC) material had: b.p. 112–113°/7.5 mm,  $n_D^{20}$  1.4885,  $d_4^{20}$  0.9055,  $M_D$  64.98 (Calc.  $\text{C}_{11}\text{H}_{14}$ , 64.43),  $[\alpha]_D^{20}$  –6.53 (c, 2.3%). IR spectrum:  $\text{C}=\text{C}$  3010, 1660, 788  $\text{cm}^{-1}$ .

*Action of hydrogen chloride on copaene.* Copaene (0.2 g) in dry ether (4 ml) was saturated with HCl gas at –10° and left as such at 0° overnight (15 hr). The solvent was removed (suction) and the residue taken up in pet. ether and the crystals collected after cooling at –15° for ½ hr; the product after recrystallization from ethyl acetate had m.p. 114–115°,  $[\alpha]_D$  –40.6°, mixed m.p. with an authentic sample (m.p. 116–117°) was undepressed, yield ~25%.

The solvent was removed from the original mother liquors and the residue distilled: b.p. (bath temp) 180–200°/3 mm,  $[\alpha]_D$  –15.6° (c, 1.2%). (Found: Cl 21.35%.  $\text{C}_{11}\text{H}_{14}\text{Cl}_2$  requires: Cl 25.68%).

*Dihydrocopaene (copane).* Copaene (0.5 g) was hydrogenated over pre-reduced  $\text{PtO}_2$  catalyst (50 mg) in gl. AcOH (10 ml) at 25°/715 mm; hydrogenation was complete after the uptake of 0.98 mole  $\text{H}_2$  (½ hr). Usual work up and distillation gave the product as an oil, b.p. 105–106°/5 mm,  $n_D^{20}$  1.4830  $[\alpha]_D^{20}$  = –2.31° (c, 2.2%). PMR spectrum:  $-\text{CH}(\text{Me}_2)$  48, 53 c/s;  $-\text{CHMe}$  doublet centred at 60 c/s,  $J$  = 6 c/s, quaternary methyl 60 c/s.

#### Ozonolysis of copaene to ketocarboxylic acid

(i) *Cleavage of the ozonide with alkaline hydrogen-peroxide.* Copaene (5 g) in ethyl acetate (40 ml) was ozonized at –10° till  $\text{O}_3$  passed freely (3 hr; over ozonization must be avoided). The solvent was removed under suction at room temp and the residual syrup treated with water (25 ml),  $\text{Na}_2\text{CO}_3$  (2.5 g) and  $\text{H}_2\text{O}_2$  (30%, 5 + 5 ml) first at room temp (1 hr) and later on a steam bath (2 hr). The product was separated into acidic (2.5 g) and neutral (2.5 g) portions. The acidic part was converted into its semicarbazone (pyridine method), m.p. 208–220° dec, yield 2.0 g; recrystallization from EtOH gave a product, m.p. 220–222° dec (Lit.,<sup>18</sup> m.p. 221°), yield 0.9 g.

The keto acid was regenerated from the above semicarbazone (1.9 g, m.p. 217–219°) by refluxing with oxalic acid (7 g), water (18 ml) and heptane (20 ml), with stirring for 3 hr. The product was worked up by extraction with benzene (30 ml × 4), washing and drying; solvent removal gave the required keto acid (1.61 g). The crude acid was converted into its methyl ester ( $\text{CH}_3\text{N}_2$ ), which was distilled: b.p. 130–132°/0.5 mm,  $n_D^{20}$  1.4750,  $[\alpha]_D^{20}$  +61.5° (c, 6.0%). IR spectrum:  $>=\text{O}$  1743, 1704  $\text{cm}^{-1}$ . PMR spectrum:  $\text{COOCH}_3$  218 c/s;  $\text{COCH}_3$  115 c/s; quaternary methyl 57 c/s; isopropyl methyl signals centred at 54 c/s. (Found: C, 72.60; H, 10.03.  $\text{C}_{11}\text{H}_{18}\text{O}_2$  requires: C, 72.18; H, 9.77%).

<sup>28</sup> A. S. Gupta and Sukh Dev, *J. Chromatography* **12**, 189 (1963).

<sup>27</sup> P. P. Pillai and B. S. Rao, *J. Soc. Chem. Ind.* **50**, 220T (1931).

(ii) *Cleavage of the ozonide with hydrogen peroxide in acetic acid.* When the decomposition of the above ozonide (from 1 g copaene) was carried out with  $H_2O_2$  (10%, 10 ml) in acetic acid (5 ml), first at room temp (1 hr), later at 60° (1 hr) and finally on steam-bath (2.5 hr), and then worked up as above, 0.67 g crude acid was obtained, which was converted into the semicarbazone (0.52 g), m.p. 165–206. Repeated recrystallization (ethanol) of this material, finally gave 100 mg of a material m.p. 183–185°. (Found: C, 62.23; H, 8.45.  $C_{18}H_{27}O_2N_2$  requires: C, 62.13; H, 8.73%.)

The keto acid was regenerated from this semicarbazone by the above procedure and the product esterified ( $CH_2N_2$ ) and distilled:  $[\alpha]_D^{25} +36.1^\circ$  (c, 0.35%). IR spectrum:  $>=O$  1743, 1700  $cm^{-1}$ . PMR spectrum:  $COOCH_3$  218 c/s;  $COCH_3$  123 c/s; quaternary methyl 58 c/s; isopropyl methyls centred at 54 c/s.

The above keto acid (67 mg), after being refluxed with  $Na_2CO_3$  aq (10%, 1 ml) for 4 hr, was converted into its methyl ester, which was identified by its PMR spectrum as the product from (i). The isomerized keto acid gave the semicarbazone of m.p. 217–219°.

#### *Baeyer-Villiger oxidation of the methyl ester*

The above keto ester (methyl ester of the keto acid regenerated from the semicarbazone m.p. 217–219°; 0.503 g) in  $CHCl_3$  (8 ml) was treated with perbenzoic acid in  $CHCl_3$  (7.35 ml containing 0.39 g  $\equiv$  1.5 mole per acid) and after adding *p*-toluenesulphonic acid (0.1 g), was left aside in the dark at room temp ( $\sim 30^\circ$ ). After 24 hr (in some experiments the reaction mixture had been allowed to stand for 7 days, without any adverse effect) it was found that one mole equiv. of the peracid had been used. The reaction mixture was worked up by washing it with  $Na_2CO_3$  aq (5%, 10 ml  $\times$  8), water (10 ml  $\times$  3), brine and drying ( $Na_2SO_4$ ). The solvent was flashed off to yield 0.559 g of a product, which was hydrolysed by refluxing with methanolic KOH (10%, 10 ml) for 2 hr. The solvent was completely removed and the residual K salt taken up in water (20 ml), acidified with  $H_3PO_4$  and extracted with ether (30 ml  $\times$  3). The extracts were washed with brine, dried and the solvent removed. The resulting crude hydroxy acid (0.477 g) was esterified ( $CH_2N_2$ ) and the product distilled: b.p. 120–125°/0.5 mm, yield 0.34 g.

TLC (solvent system: 10% acetone in hexane) of the above product showed essentially two spots (starting material and product). The material (0.34 g) was chromatographed over  $Al_2O_3/II$  (15 cm  $\times$  1 cm), while monitoring the eluates with TLC:

Frac. 1: Pet. ether 8 $\times$ 20 ml	35 mg of starting material
Frac. 2: Pet. ether–25% benzene 7 $\times$ 20 ml	64 mg of mostly starting material
Frac. 3: Pet. ether–50% benzene 5 $\times$ 20 ml	20 mg ?
Frac. 4: Benzene 11 $\times$ 20 ml	105 mg of required compd.
Frac. 5: Benzene–1% MeOH 5 $\times$ 20 ml	50 mg of required compd.

Fractions 4 and 5, which were identical, as revealed by TLC and IR spectrum ( $OH$  3410, 1100  $cm^{-1}$ ;  $-COOMe$  1735  $cm^{-1}$ ) were mixed and had  $[\alpha]_D^{20} +55.96^\circ$  (c, 0.6%). The product was used as such for the next step.

#### *Bis-nor keto ester (X)*

To  $CrO_3$ -pyridine complex<sup>28</sup> ( $CrO_3$  0.187 g, pyridine 2 ml) at 25° the above hydroxy ester (0.150 g) in 2.5 ml pyridine was added and the reaction mixture set aside as such for 16 hr. The product was diluted with water (10 ml) and extracted with benzene-ether (1:1; 10 ml  $\times$  4). The combined extracts were washed with water,  $NaHCO_3$  aq (5%), water (10 ml  $\times$  2) and finally with brine. After drying, the solvent was removed and the product distilled: b.p. (bath temp) 150–160°/0.5 mm,  $n_D^{20}$  1.4718,  $[\alpha]_D^{21} +38.4^\circ$  (c, 0.38%). PMR spectrum: quaternary methyl 53 c/s; isopropyl, a pair of doublets centred at 54 and 56 c/s, each with  $J = 6$  c/s;  $-COOMe$  220 c/s. (Found: C, 70.33; H, 9.34.  $C_{14}H_{20}O_2$  requires: C, 70.59; H, 9.24%.)

#### *Isolation of mustakone*

The essential oil<sup>29</sup> of *Cyperus rotundus* (440 g) was carefully fractionated twice over a spinning band column<sup>30</sup> and a cut (35 g) of b.p. 126–30°/1 mm collected separately. This was shown by GLC

<sup>28</sup> G. I. Poos, G. E. Arth, R. E. Beyler and L. H. Sarett, *J. Amer. Chem. Soc.* **75**, 425 (1953).

<sup>29</sup> Supplied by S. H. Kelkar and Co., Bombay.

<sup>30</sup> Manufactured by Nester and Faust, USA; theoretical plates 45.

to be essentially a mixture of  $\alpha$ -cyperone ( $\sim 40\%$ ) and a new compound ( $\sim 40\%$ ). By precise refractionations (total reflux), a material ( $\sim 5$  g), b.p. 113–115°/0.4 mm and free from  $\alpha$ -cyperone could be obtained. The product though showing a single peak in GLC, was shown by TLC (solvent system 10% EtOAc in toluene) to be a mixture of at least two ketones. However, mustakone could be separated from this through its semicarbazone.

The above material (2.0 g) on treatment with semicarbazide HCl (4 g) and NaOAc·2H<sub>2</sub>O (8 g) in aq alcohol ( $\sim 50$  ml) yielded a solid (1 g) (m.p. 192–196°) after 5 days at room temp, which was recrystallized (alcohol), m.p. 198–199°, yield 0.8 g. (Found: C, 70.06; H, 9.31. C<sub>18</sub>H<sub>22</sub>ON<sub>2</sub> requires: C, 69.8; H, 9.1%).

The ketone was regenerated from its semicarbazone (0.41 g) by the oxalic acid–heptane method (see above) and the product distilled: b.p. 128–129°/1 mm,  $n_D^{20}$  1.5061,  $[\alpha]_D +0.34$  (c, 2.6%). (Found: C, 82.50; H, 10.36. C<sub>18</sub>H<sub>22</sub>O requires: C, 82.51; H, 10.10%).

*Dihydromustakone.* Hydrogenation of mustakone (140 mg) over pre-reduced PtO<sub>2</sub> catalyst (25 mg) in acetic acid (5 ml) at room temp and press. was discontinued after the uptake of almost 1 molar equiv H<sub>2</sub>, when it was worked up to yield a colourless liquid: b.p. (bath temp) 130–35°/1.5 mm,  $n_D^{20}$  1.4921,  $[\alpha]_D +0.14$ , yield 128 mg; negative tetranitromethane test.

#### *Wolff-Kishner reduction of dihydromustakone to copaene*

Dihydromustakone (45 mg) was added to a solution of KOH (100 mg) in diethylene glycol (2 + 2 ml). After adding hydrazine hydrate (100%, 0.6 ml), the reaction mixture was heated in a bath at 155–160° for 2 hr, and later at 200–215° for another 2.5 hr. The reaction mixture was cooled and worked up by dilution with water and extraction with pet. ether; the solvent was removed and the product distilled to give 23 mg of a compound, identified (GLC, IR) as dihydrocopaene.

#### *Oxidation of copaene to mustakone*

This was patterned after the procedure of M. Badoche, *Bull. Soc. Chim. Fr.* 764 (1953), but using benzene in place of CCl<sub>4</sub>.

Copaene (1.1 g) in benzene (10 ml) was cooled in ice-water and a solution of t-butyl chromate (from t-BuOH 3 ml, CrO<sub>3</sub> 1.3 g and benzene 15 ml) containing AcOH (1 ml) was added slowly with stirring (1 hr). After standing for 14 days at room temp, the reaction mixture was cautiously treated with aq. oxalic acid (19 g in 180 ml water) and extracted with benzene (40 ml  $\times$  4). The combined extracts were washed with water, 5% Na<sub>2</sub>CO<sub>3</sub> aq, brine and dried. Solvent was removed to yield 0.79 g of material, which was chromatographed over Al<sub>2</sub>O<sub>3</sub>/I (23 cm  $\times$  0.8 cm), while following the separation by TLC (solvent system: 15% EtOAc in benzene):

Frac. 1	Pet. ether	25 ml	350 mg
Frac. 2	Pet. ether	25 ml	50 mg of required product.
Frac. 3	Benzene	25 ml	155 mg of required product.
Frac. 4	Benzene	25 ml	9 mg ?

Fraction 2, 3 were mixed, converted into its semicarbazone, which was obtained only as an amorphous powder (160 mg). This on treatment with oxalic acid gave a product having its IR spectrum superimposable on that of mustakone:  $n_D^{20}$  1.5065,  $[\alpha]_D -54.59$  (c, 4%),  $\lambda_{max}$  255 m $\mu$   $\epsilon$  5220, yield, 102 mg. (Found: C, 81.94; H, 10.27. C<sub>18</sub>H<sub>22</sub>O requires: C, 82.51; H, 10.16%).

#### *Ultraviolet irradiation of mustakone*

Mustakone (189 mg) in purified cyclohexane (20 ml) was placed in a quartz tube (attached to an air condenser and a guard tube) and exposed to UV radiation<sup>21</sup> externally. The reaction mixture gently refluxed. The progress of reaction was followed by withdrawal of aliquots and checking the IR spectrum. The expected isomerization appeared to be maximal after 3 hr, when the reaction was stopped. The crude product could not be purified as it, apparently, decomposed on a column of Al<sub>2</sub>O<sub>3</sub>/I.

*Acknowledgements*—The authors thank Mr. V. S. Pansare and his colleagues for the microanalyses and M/s. R. G. Bhandari, I. S. Mulla, and V. K. Bhalerao for the spectral measurements.

<sup>21</sup> Hanovia Utility Model Lamp.