SESQUITERPENOIDS FROM THE ESSENTIAL
OIL OF CYPERUS ROTUNDUS

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A recent publication[1] on cyperolone, a constituent of the essential oil of Cyperus rotundus Linn. of Japanese origin, prompts us to place on record our work, todate, on this oil of Indian origin. This work is in extension of our earlier investigations[2].

The essential oil contains at least 27 components (GLC), comprising of sesquiterpene hydrocarbons (25%, ~10 components), sesquiterpene epoxides (12%, ~3 components), sesquiterpene ketones (20%, ~4 components), mono-terpene and aliphatic alcohols (25%, ~4 components) and, unidentified. It is the purpose of this communication to report on the structures of some new sesquiterpenoids, one of which appears to be identical with cyperolone.

(+)-Copadiene

Copadiene (RRT*, 1.81), b.p. 130-140°(bath)/1 mm, n_D^{30} 1.5089, $[\alpha]_D$ +17.3 (CHCl$_3$), analyses for $C_{15}H_{22}$ and, is obviously a conjugated diene: λ_{max}^{EtOH} 245 mµ, є 14,750. It shows the following structural features: three methyls (PMR[3]: 3H signals at 44, 47 and 53 c/s; the 44 c/s signal is clearly due to a quaternary methyl, whereas the other two signals could be arising from an isopropyl group), one vinylidene group (IR: 3060, 1755, 1650, 878 cm^{-1}. PMR: 2H singlet at 256 c/s) and a cis-disubstituted ethylenic linkage (IR:

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*Throughout this paper, RRT refers to relative retention time with respect to copaene, under the following conditions: 20% diethyleneglycol polysuccinate on Chromosorb W; 1.5 meter x 6 mm; 50 ml of H$_2$/min; temp. 80-200°, 6°/min.

775, 685 cm^{-1}. PMR: a 2H multiplet located between 342-374 c/s, the pattern is clearly the AB part of an ABX system). The methyl signals and the well-separated methylene groups envelope (located between 85-107 c/s) in the PMR spectrum, were suggestive of the new hydrocarbon being closely related to copaene (I)[2,4], which has similar features in its PMR spectrum[2] and, is also a constituent of the oil.

The above data are interpreted in favour of structure II for the new sesquiterpene. This formulation appeared all the more attractive, as it can explain its UV absorption, which shows a considerable bathochromic shift as compared to, say β-phellandrene (III) (λ_{max} 232 mμ, log є 4.3)[5], which has

I   II   III

IV   V   VI
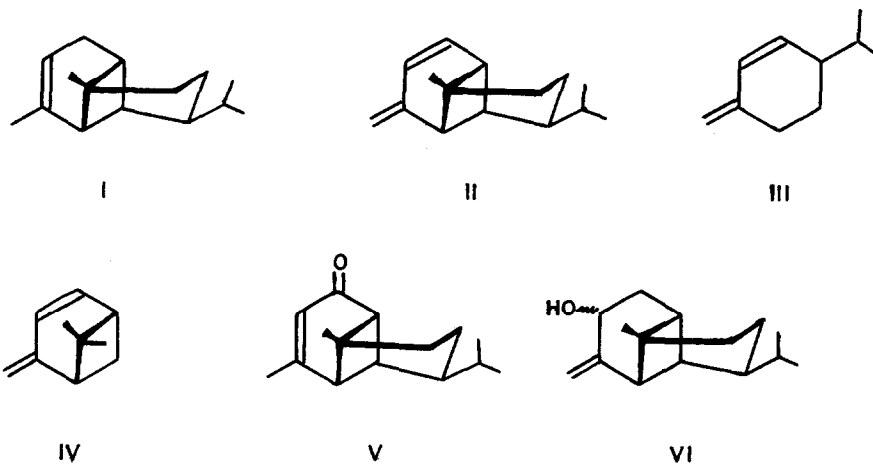
the same chromophore. This bathochromic shift of ca. 13 mμ is consistent with the location of the chromophore in a strained bicyclo [3,1,1] heptane system[2] and the position of λ_{max} is close to that of verbenene (IV)[6] (λ_{max} 245.5 mμ), as required by the formulation II.

The above structure has been confirmed by its direct correlation with (±)-mustakone (V)[2]. Mustakone on reduction by LiAlH$_4$ gave an epimeric mixture of alcohols (IR: OH 3300, 1018, 1045 cm^{-1}. PMR: CHOH, 1H broad singlet at 258 c/s; C=CH-, 1H broad singlet at 320 c/s). This product on

dehydration with alumina[7], furnished a hydrocarbon, identified (GLC, IR) as copadiene.

An attempted correlation with (+)-copaene (I) through VI failed, as all attempts at dehydration furnished only the corresponding ketone by proto-tropy. However, on account of its co-occurrence with (+)-copaene (I) in the essential oil, copadiene is considered[8] to have the absolute stereochemistry depicted in II.

(+)-Epoxyguaiene

Of the three epoxides present in the essential oil, two (RRT, 3.93 and 4.43) have been obtained pure. Structure of one of these (RRT, 3.93) has been finalised and the compound has been named epoxyguaiene, in view of its structure.

Epoxyguaiene, b.p. 102-104°/1 mm, n_D^{30} 1.4948, $[\alpha]_D$ +11.0, analyses for $C_{15}H_{24}O$ and does not show any absorption for OH or C=O in the IR, and hence must be an ether. In its PMR spectrum it shows signals for: two CH_3-CH (two 3H doublets centred at 53 and 63.5 c/s, with J = 6 and 7 c/s respectively), one vinylic methyl (100 c/s) and $-\overset{|}{C}=CH_2$ (2H broad singlet at 276 c/s). Since, (-)-α-guaiene (VII)[9], with its characteristic two secondary methyl groups (which occur centred at 55.5 and 62.5 c/s) is a constituent of the essential oil, it was suspected[8] that the naturally occurring epoxide may be VIII. This

VII   VIII   IX
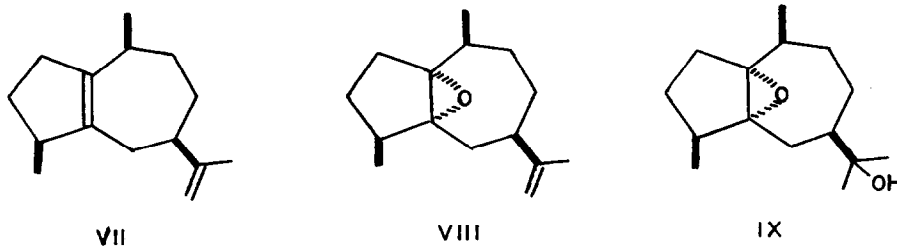
was easily established by the action of perbenzoic acid (C_6H_6) on (-)-α-guaiene[10] when a mixture of two epoxides (~1:1) was produced; one of these (higher

retention time, polyester column) was shown to be identical ($[\alpha]_D$, GLC, IR, PMR) with the naturally occurring epoxide.

The above experiments do not establish the stereochemistry of the epoxide ring. While, the above work was in progress, Pesnelle[12] described the preparation of IX, the stereochemistry of the epoxide ring being based on its resistance to attack by $LiAlH_4$. The dehydration of IX with $SOCl_2$-pyridine has been reported[12] to give VIII, the described PMR spectrum of which is essentially identical with that of our product. This defines (+)-epoxyguaiene as VIII.

(-)-Rotundone

Rotundone (RRT, 7.06), b.p. 128-129°/1 mm, n_D^{30} 1.5118, $[\alpha]_D$ -92.7 ($CHCl_3$), analyses for $C_{15}H_{22}O$ and has the following UV and IR characteristics: λ_{max}^{EtOH} 239 mμ (ε 11,990); C=O 1710 cm^{-1}; C=C 1660, 895 cm^{-1} ($E_{c=o}/E_{c=c}$ = 1.2). On quantitative hydrogenation over Pd-$CaCO_3$ catalyst in EtOH, it yielded a dihydroderivative ($[\alpha]_D$ -35.5°), which does not have any significant absorption $\sim$ 890 cm^{-1} in its IR spectrum, but still shows the characteristics of an $\alpha\beta$-unsaturated ketone: λ_{max}^{EtOH} 239 mμ (ε 9,500); C=O 1710 cm^{-1}; C=C 1660 cm^{-1} ($E_{c=o}/E_{c=c}$ = 1.4). Thus, a vinylidene group has been reduced during hydrogenation and this group must be isolated. The dihydroderivative on further hydrogenation (PtO_2 catalyst, AcOH) furnished tetrahydro-rotundone: no UV maximum between 215-270 mμ; $\nu^{C=O}$ 1745 cm^{-1}. These results require that rotundone should be an $\alpha\beta$-unsaturated bicyclic ketone, with the carbonyl located in a 5-membered ring and having one more isolated olefinic linkage (-C=CH_2).

In its PMR spectrum, rotundone shows signals for: two secondary methyls (3H doublets centred at 58.5 and 67.5 c/s, each with J = 7 c/s), one vinylic methyl (3H doublet centred at 108 c/s, J = 1 c/s) and one vinylidene group (2H, somewhat broad singlet at 283 c/s). These data suggested that rotundone may have the guaiene (VII) skeleton, with its characteristic two secondary methyls. This possibility appeared all the more attractive[8], as (-)-α-guaiene (VII) is one of the hydrocarbons present in the essential

oil, and rotundone gives the characteristic proazulene test $(Br_2\text{-}AcOH)$[13].
Three structures (X, XI, XII) come up for consideration and of these clearly
XI and XII are less likely on biogenetic considerations and the observed
λ_{max} of rotundone. The PMR spectrum of dihydro-rotundone shows the presence
of: two secondary methyls (3H doublets centred at 56.5 and 66.5 c/s, each
with J = 7 c/s; at 46.5 and 60.5 c/s in C_6H_6 solution), and one isopropyl
group (6H, unsymmetrical doublet centred at 54 c/s, J = 6.5 c/s; 46.5 c/s
in C_6H_6 solution). These results clearly rule out XI and XII.
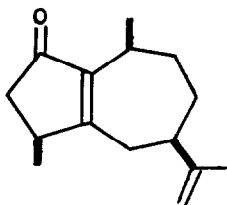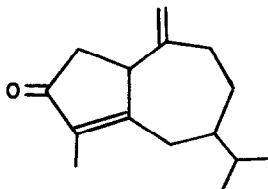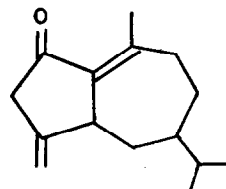
X   XI   XII

Final proof for the structure X, which also establishes its absolute
stereochemistry as shown in X, was obtained by a direct correlation with
(-)-α-guaiene (VII). Dihydroguaiene prepared by selective hydrogenation[11] of
VII was oxidised with tert-butyl chromate to give as one of the products a
liquid ($[\alpha]_D$ -39.1), identified (TLC, GLC, IR, PMR) as (-)-dihydro-rotundone.

A hydroxyketone (cyperolone)

This compound (RRT, 8.50), b.p. 120°(bath)/0.1 mm (slowly solidified,
m.p. 38-39°), $[\alpha]_D$ +52°, was obtained as a very minor component. The compound
has the following structural features: one quaternary methyl (PMR: 57 c/s),
one vinylic methyl (PMR: 3H doublet at 107 c/s, J = 1.5 c/s), CH_3-C=O (IR:
1695 cm^{-1}. PMR: 3H singlet at 127 c/s), a secondary OH (IR: 3570, 1080 cm^{-1}.
PMR: 1H multiplet centred at 263 c/s) and a vinylidene group (IR: 3030, 1645,
890 cm^{-1}. PMR: 2H singlet at 288 c/s). The mass spectrum shows M^+ at m/e =
236, which is consistent with the compound being $C_{15}H_{24}O_2$.

On biogenetic considerations we had adopted XIII, as the working structure, which could also explain the rather low value for acetyl absorption (IR) as being due to intramolecular chelation, when the publication of
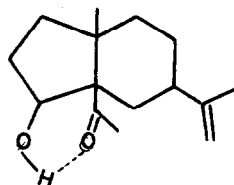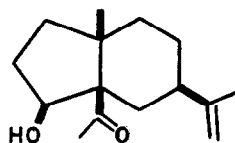
XIII   XIV

Hikino et al.[1] reached us. It is clear from the reported spectral data that our compound is only cyperolone (XIV). Further work was, then, abandoned.

Biogenetic considerations[14]

The essential oil from the rhizomes of Cyperus rotundus has been the subject of study by several workers[1,2,15] and the isolation of no less than fifteen components, new and known, has been reported. It is significant to note that the basic skeletons (copane, selinane and guiane) known to occur todate in the essential oil, all require as the initial step a 1,10-cyclisation of trans-farnesol in their projected biogenesis[16] and all the compounds isolated so far have the same absolute configuration (R chirality) at C_{10} (farnesol numbering).

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REFERENCES

1   H. Hikino, K. Aota, Y. Maebayashi and T. Takemoto, Chem. Pharm. Bull.
     14, 1439 (1966); H. Hikino, N. Suzuki and T. Takemoto, ibid. 14, 1441
     (1966). Also see: H. Hikino, K. Aota and T. Takemoto, Tetrahedron 23,
     2169 (1967).

2   V.H. Kapadia, B.A. Nagasampagi, V.G. Naik and Sukh Dev, Tetrahedron 21,
     607 (1965).

3   All PMR spectra were taken in CCl_4, unless stated otherwise, on a
     Varian A-60 spectrometer; the signals are recorded in c/s from
     tetramethylsilane as zero.

4   P de Mayo, R.E. Williams, G. Buchi and S.H. Feairheller, Tetrahedron 21,
     619 (1965).

5   J.B. Davenport, M.D. Sutherland and T.F. West, J. Appl. Chem. 1, 527
     (1951).

6   R.N. Moore and G.S. Fischer, J. Amer. Chem. Soc. 78, 4362 (1956).

7   E. von Rudloff, Can. J. Chem. 39, 1860 (1961).

8   A.H. Kapadi, R.R. Sobti and Sukh Dev, Tetrahedron Letters 2729 (1965).

9   E.J. Eisenbraun, T. George, B. Riniker and C. Djerassi, J.Amer.Chem.Soc.
     82, 3648 (1960); L. Dolejs, A. Mironov and F. Sorm, Tetrahedron Letters
     No.11, 18 (1960); K. Takeda and H. Minato, ibid. No.22, 32 (1960);
     H. Minato, Tetrahedron 18, 365 (1962).

10   This was conveniently obtained by dehydration of (-)-α-guaiol with
     pyridine-treated Al_2O_3[7], to give directly VII in ~ 98% purity, in
     contrast to previously reported methods[11] which give substantial quan-
     tities of the isopropylidene isomer.

11   e.g. cf. K. Takeda, H. Minato and S. Nosaka, Tetrahedron 13, 308 (1961).

12   P. Pesnelle, Recherches 15, 34 (1966).

13   S. Sabetay and H. Sabetay, Compt. rend. 199, 313 (1934).

14   cf. Ref.8.

15   B. Trivedi, O. Motl, V. Herout and F. Sorm, Coll. Czech. Chem. Comm. 29,
     1675 (1964).

16   For a recent summary see: J.H. Richards and J.B. Hendrickson, The
     Biosynthesis of Steroids, Terpenes and Acetogenins pp.225-239. Benjamin,
     New York (1964).