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CONSTITUTION AND BIOGENESIS OF TWO NEW SESQUITERPENES

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STRUCTURAL investigations of the two new sesquiterpenes (I and II) have provided further examples of optically inactive natural products containing asymmetric centres. The previously described geijerene[1,2] (III) also belongs to this class which requires in the biogenetic scheme, a special step leading to the formation of a racemic product.

We have isolated from gurjun balsam oil and from Dysoxylon frazeranum oil[3] a new sesquiterpene, (δ-elemene), $C_{15}H_{24}$*, b.p.$_{10}$ 107°, n_D^{25} 1.4828, d_4^{25} .8590, $[\alpha]_D \pm 0.0^\circ$ (single peak on Apiezon M at 170°), which yields a crystalline nitrosochloride, m.p. 200°, $[\alpha]_D \pm 0.0^\circ$. The infra-red and ultra-violet spectra are consistent with isolated vinyl (907, 1001 cm^{-1}) and vinylidene (894 cm^{-1}) groups and a trisubstituted double bond (818 cm^{-1}). Complete hydrogenation yields $C_{15}H_{30}$, n_D^{25} 1.4609, d_4^{25} .8399, $[\alpha]_D$-0.17°, the infra-red spectrum of which leads to a presumption of identity with elemene[4] (IV).

Ozonolysis of δ-elemene followed by treatment of the ozonide with

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* Analyses consistent with quoted formulae were obtained in all cases.

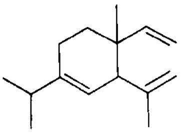
[1] M.D. Sutherland, Chem. & Ind. 1220 (1959).

[2] A.J. Birch, J. Grimshaw, A.R. Penfold, N. Sheppard and R.N. Speake, J.Chem.Soc. 2286 (1961).

[3] R.P. Hildebrand and M.D. Sutherland, Aust.J.Chem. 12, 678 (1959).

[4] V. Sykora, J. Cerny, V. Herout and F. Sorm, Coll.Czech.Chem.Comm. 19, 566 (1954).

hydrogen peroxide in acetic acid, yielded a mixture of acids, which were fractionated as methyl esters, the major product being a diketoester (V), $C_{13}H_{22}O_4$, b.p.$_5$ 145-148°, bis-2,4-dinitro-phenylhydrazone, $C_{25}H_{30}N_8O_{10}$, m.p. 138.5-139°.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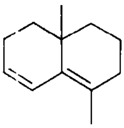
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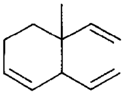
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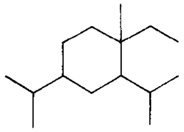
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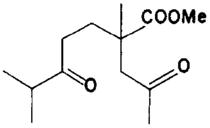
V

Hydrogenation with a deactivated Adams' catalyst in ethanol yielded a dihydro compound, $C_{15}H_{26}$, lacking the intense infra-red vinyl bands shown by δ-elemene. Ozonolysis, etc. yielded a diketone, $C_{13}H_{24}O_2$, b.p.$_5$ 122-127°, $[\alpha]_D$-1.15°, bis-dinitrophenylhydrazone, $C_{25}H_{32}N_8O_8$, m.p. 167°. Hydrogenation with palladized charcoal in ethanol gave a mixture of two tetrahydro compounds, the major product still showing a strong band at 885 cm^{-1} due to a vinylidene group. Oxidation yielded a ketone, (92% purity by gas chromatography), $C_{14}H_{26}O$, $[\alpha]_D$-1.82° (10 cm, hom.), dinitrophenylhydrazone, $C_{20}H_{30}N_4O_4$, m.p. 124-125°.

δ-Elemene was isomerized with either potassamide in liquid ammonia or potassium hydroxide[5] in methanol at 170°, to yield a conjugated hydrocarbon (ε 26,000 at λ_{max} 249 m).

These and other results are compatible only with I, which is entirely consistent with the NMR spectrum.[6] Hence δ-elemene is an isopropyl geijerene and like geijerene[1,2], it is optically inactive although containing two asymmetric centres. The small rotations recorded for non-crystalline products noted above are attributed to the presence of optically active

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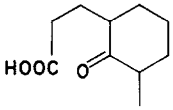
[5] L. Bateman, J.I. Cunneen and E.S. Waight, J.Chem.Soc. 1714 (1952).

[6] Our thanks are due to Dr. N. Sheppard, University Chemical Laboratory, Cambridge for the measurement and interpretation of the NMR spectrum.

impurities (observable by gas chromatography and optical rotation) in the less pure δ-elemene used for degradation.

The second hydrocarbon (cogeijerene, II) $C_{12}H_{18}$, b.p.$_{10}$ 97°, n_4^{25} 1.5298, d_4^{25} 0.9396, $[\alpha]_D +0.70^\circ$, (single peak with slight shoulder on Apiezon M at 170°), co-occurs with geijerene in the essential oil[7] of Geijera parviflora.



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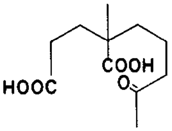
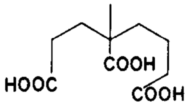


VII



VIII

Prominent spectral features include a maximum (ε 14,500) at 242 mμ, shoulders at 235 and 251 mμ and a strong infra-red band at 745 cm^{-1}. The Kuhn-Roth isopropylidene estimation yielded no acetone and the C-methyl estimation 1.01 moles of acetic acid. Hydrogenation, peracid titration and molecular refraction indicated two double bonds and two rings. Dehydrogenation over palladized charcoal yielded principally 1,4-dimethylazulene with some 1-methyl-, 1,4-dimethyl- and 1,5-dimethyl-naphthalene indicated by gas chromatography. Reduction with sodium and methanol in liquid ammonia yielded a dihydro compound $C_{12}H_{20}$, b.p.$_{10}$ 91°, d_4^{25} 0.9086, n_4^{25} 1.4962, $[\alpha]_D \pm 0.0^\circ$ with a strong band at 800 cm^{-1} instead of that at 745 cm^{-1}.

Ozonolysis, etc. of dihydrocogeijerene yielded two isomeric acids (for one, p-bromophenacyl ester, $C_{20}H_{25}O_4Br$, m.p. 125°), the methyl esters, $C_{13}H_{22}O_3$ (VI), $[\alpha]_D \pm 0.0^\circ$, of which were separated by gas chromatography. Both esters showed carbonyl absorption at 1735 and 1704 cm^{-1} indicative of a heavily substituted cyclohexanone[8]. Ozonolysis etc. of cogeijerene yielded no neutral products but principally the keto acid, VII separated as the

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[7] A.R. Penfold, J.Proc.Roy.Soc.N.S.W. 64, 264 (1930).

[8] Y. Mazur and F. Sondheimer, J.Amer.Chem.Soc. 80, 5222 (1958).

dimethyl ester, $C_{13}H_{22}O_5$, b.p.$_5$ 164° $[\alpha]_D \pm 0.0°$, dinitrophenylhydrazone, $C_{19}H_{26}N_4O_8$, m.p. 80-81°. The acid VII by treatment with alkaline hypobromite, yielded amongst other products bromoform, and the tricarboxylic acid VIII, $C_{10}H_{16}O_6$, m.p. 115°, $[\alpha]_D \pm 0$, tri-p-bromophenacyl ester $C_{34}H_{31}O_9Br_3$, m.p. 127°. An identical tricarboxylic acid was obtained by hypobromite oxidation[9] of β-(1-methyl-2-oxocyclohexyl)-propionic acid[10]. The NMR spectrum[6] of cogeijerene is entirely consistent with its formulation as II. The observed small rotations of liquid products are attributed in this case also, to the presence of optically active impurities in the cogeijerene used for degradations.

While the isolation of certain terpenes (e.g. limonene, α-pinene, δ-cadinene[3]) in approximately racemic form is commonplace, the exactly racemic nature[11] of geijerene ($[\alpha]_D \pm 0.00°$)[12], cogeijerene and δ-elemene requires a special explanation. The postulate of Ruzicka[13] in 1953 and Hendrickson[14] in 1959, that elemol (IX) results from a recyclization of a ten-ring precursor (X) can be reconciled with the optically inactive nature of our terpenoids if it is assumed that the recyclization takes place in the absence of enzymatic control. The elemol and β-elemene[15] precursors would yield optically active products as is observed, since the precursors

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[9] M.W. Farrer, J.Org.Chem. 1708 (1957).

[10] R.L. Frank and R.C. Pierle, J.Amer.Chem.Soc. 73, 724 (1951).

[11] We wish to thank Professor C. Djerassi for measurements of the optical rotatory dispersion curves of these substances. Geijerene and δ-elemene showed zero rotation from 600 to 250 mμ. In the case of cogeijerene, a rotation of approx. -11° at 325 mμ was observed and is attributed to a minor impurity.

[12] W.R. Owen and M.D. Sutherland, J.Sci. Food Agric. 1, 88 (1956).

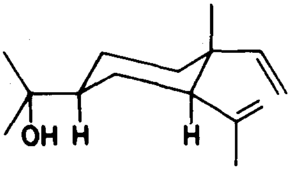
[13] L. Ruzicka, Experientia 9, 357 (1953).

[14] J.B. Hendrickson, Tetrahedron 7, 82 (1959).

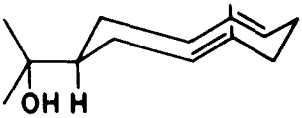
[15] V. Sykora, V. Herout and F. Sorm, Coll.Czech.Chem.Comm. 21, 267 (1956).

have already one asymmetric centre. Geijerene and δ-elemene would be inactive since such an asymmetric centre is lacking in the appropriate precursors. The same inactive precursor (XI) of geijerene could also yield optically inactive cogeijerene through non-enzymatic protonation and deprotonation.

The question as to whether these optically inactive sesquiterpenes are present in the living plant or result from the isolation procedures[16] is under investigation.



IX



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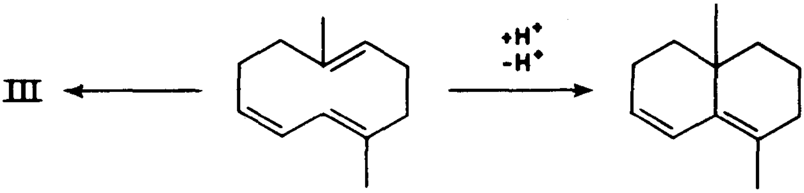

XI

II

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[16] Y-R. Naves, Bull.Soc.Chim.Fr. 1518 (1960).