# *Carissone.*

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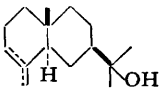
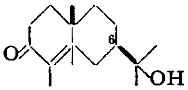
Eudesmol has been transformed into carissone which establishes the absolute stereochemistry of the latter compound as well as that of the cyperones.

KLYNE (*J.*, 1953, 3072), who applied the method of molecular-rotation differences to the sesquiterpenes, showed that the stereochemistry at the quaternary carbon atoms of eudesmol (I), selinene, and the cyperones are identical and the same as that at $C_{(10)}$ in the steroids. Riniker, Kalvoda, Arigoni, Fürst, Jeger, Gold, and Woodward (*J. Amer. Chem. Soc.*, 1954, **76**, 314) confirmed this by the synthesis of a derivative of eudesmol from a compound whose absolute stereochemistry is known. Barton and Tarlton (*J.*, 1954, 3492) showed that carissone (Mohr, Schindler, and Reichstein, *Helv. Chim. Acta*, 1954, **37**, 462) must have structure (II) by converting it into α- and β-cyperone by dehydration under different conditions; however, the stereochemistry at $C_{(6)}$ remained undetermined We have now transformed eudesmol into carissone which establishes the absolute stereochemistry of the latter and proves experimentally the relation between the cyperone and the eudesmol group deduced by Klyne. Another proof of the stereochemistry of the cyperones has been given by McQuillin (*J.*, 1955, 528) from a consideration of the mechanism of their synthesis from (—)-dihydrocarvone.

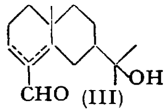
Reaction of eudesmol with nitrosyl chloride, followed by treatment with a base, gave the αβ-unsaturated ketone oxime which after conversion into its 2 : 4-dinitrophenylhydrazone was indistinguishable from the authentic derivative of carissone kindly provided by Professor D. H. R. Barton. Oxidation of the crude alcoholic fraction obtained by the action of selenium dioxide on eudesmol also gave carissone, but by the action of peracetic acid on the sesquiterpene alcohol, followed by hydrolysis and oxidation, an isomeric ketone was formed. Its 2 : 4-dinitrophenylhydrazone with $\lambda_{max.}$ 380 mμ is consistent with the structure (III) but because of the low yield it has not been further investigated. These results show that the eudesmol used in this work was a mixture of *exo*- and *endo*-double-bond isomerides although chromatographed material was used.



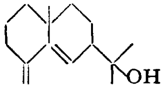
(I)



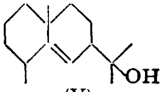
(II)



(III)



(IV)



(V)

Among the products of the selenium dioxide oxidation was a crystalline diene which was stable to chromic oxide in pyridine and did not react with maleic anhydride. Its ultraviolet absorption maximum at 240 mμ and an infrared band at 870 cm.$^{-1}$ indicated the formula (IV) for the diene, and the resistance to attack by maleic anhydride is ascribed to steric hindrance by the neighbouring *iso*propyl group. On catalytic hydrogenation the diene took up one mol. of hydrogen and the band at 870 cm.$^{-1}$ disappeared; the product had an ultraviolet absorption spectrum typical of a trisubstituted double bond and therefore has structure (V).

[*Added July 15th,* 1955.]—Carissone 2 : 4-dinitrophenylhydrazone can be converted in good yield into carissone by Demaecker and Martin's method (*Nature*, 1954, **173**, 266).

## EXPERIMENTAL

*Carissone from Eudesmol Nitrosochloride.*—Saturated methanolic hydrogen chloride (12 ml.) was added slowly with stirring to an ice-cold solution of eudesmol (3·5 g.) and ethyl nitrite (7 ml.) in methanol (10 ml.), then after 0·5 hr. the green solution was concentrated *in vacuo*, water was added and the whole extracted with ether, to give the crude nitrosochloride. This derivative in absolute ethanol (40 ml.) in which sodium (0·5 g.) was dissolved was refluxed for 0·5 hr., then diluted with water and neutralised with gaseous carbon dioxide, and the crude oxime (3·2 g.) extracted with ether. After chromatography over alumina, the oxime (0·5 g.; $\lambda_{max.}$ 243 mμ, ε 7000) was obtained in a purer state from the ether–methanol (20 : 1) eluate. Since the oxime did not crystallise it was hydrolysed by boiling ethanolic hydrochloric acid, and the resulting product converted into its 2 : 4-dinitrophenylhydrazone which after 4 crystallisations from chloroform–ethanol gave carissone 2 : 4-dinitrophenylhydrazone (0·2 g.), m. p. and mixed m. p. 176—177° which resolidified and melted again at 203—205°, $[\alpha]_D$ +450° (*c*, 0·04 in $CHCl_3$) (Found: N, 13·0. Calc. for $C_{21}H_{28}O_5N_4$: N, 13·4%). The ultraviolet absorption spectrum in EtOH had $\lambda_{max.}$ 390 mμ (ε 24,000), and the infrared spectrum was identical with that of an authentic sample.

*Carissone by Selenium Dioxide Oxidation of Eudesmol.*—Eudesmol (10 g.) and selenium dioxide (6 g.) in benzene (100 ml.) were stirred vigorously and refluxed for 4 hr., then filtered hot. The solvent was removed. The residue (12·6 g.) was chromatographed over alumina and from the benzene–light petroleum (b. p. 60—80°) eluate a solid (3·8 g.) was isolated which after crystallisation from ethanol–water or acetone–water gave the pure *diene* (IV), m. p. 108—109°, $\lambda_{max.}$ 240 mμ (ε 24,000) (Found: C, 81·5; H, 11·2. $C_{15}H_{24}O$ requires C, 81·8; H, 11·0%). Further elution of the column with benzene–methanol gave a low-melting glass (5 g.) which was treated with chromic oxide (1·5 g.) in pyridine (40 ml.). The solution was kept at room temperature for 4 hr. After addition of water, the crude oxidation product was isolated by extraction with ether and converted into the 2 : 4-dinitrophenylhydrazone in the usual way. The derivative was purified by chromatography over alumina and eluted with benzene–chloroform (1 : 1), to afford carissone 2 : 4-dinitrophenylhydrazone (750 mg.), m. p. 170°, raised after one crystallisation from chloroform–ethanol to constant m. p. 176—177° (Found: N, 13·4%).

*Peracetic Acid Oxidation of Eudesmol.*—To eudesmol (15 g.) in acetic acid (85 ml.) containing concentrated sulphuric acid (1 ml.), 30% hydrogen peroxide (8 ml.) was slowly added during 0·5 hr. The mixture was cooled during the addition with water, then warmed to 40° for 4 hr. Next morning the solution was poured into water containing ferrous sulphate, and an ether extract, after being washed with water, was concentrated. The residue was refluxed with 10% ethanolic potassium hydroxide for 1 hr., then extracted once again into ether, washed with water, dried, and distilled. The fraction (3·3 g.), b. p. 105—115°/0·1 mm., was treated with chromic oxide (1·6 g.) in pyridine (17 ml.) at room temperatrure for 3 hr. The crude oxidation product (2·6 g.) was converted into its 2 : 4-dinitrophenylhydrazone which was purified by chromatography over alumina. The chloroform–methanol eluate gave material of m. p. 80—85°, whence the pure *derivative* (40 mg.) was obtained after 7 recrystallisations from methanol and ethanol; it had m. p. 116—118° with softening at 102°, $\lambda_{max.}$ 380 mμ (ε 23,700) (Found: C, 60·3; H, 6·9; N, 13·5. $C_{21}H_{28}O_5N_4$ requires C, 60·6; H, 6·8; N, 13·4%).

*Hydrogenation of the Diene.*—The diene (IV) took up 1 mol. of hydrogen in ethanol in the presence of Adams catalyst, and the resulting *monoene* (V) was obtained pure (m. p. 76—78°) after several crystallisations from ethanol–water (Found: C, 81·0; H, 11·5. $C_{15}H_{26}O$ requires C, 81·0; H, 11·8%). The infrared spectrum was different from that of eudesmol and its ultraviolet absorption spectrum had at 220, 210, 205, and 200 mμ ε 835, 2700, 3880, and 4500 respectively (cf. Bladon *et al.*, *J.*, 1952, 2737).

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