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THE STRUCTURE OF CUPRESSENE

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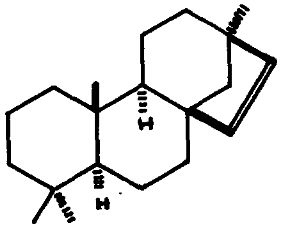
During a recent gas-liquid chromatographic (g.l.c.) survey of gymnosperms for diterpene hydrocarbons (1) it was shown that a sample of "cupressene", m.p. 74-75°, originally isolated from Cupressus macrocarpa Hartweg (2), was a mixture of isophyllocladene (32%), phyllocladene (trace), and a major diterpene hydrocarbon (67%) for which the name cupressene was retained. This survey revealed that cupressene occurred in the oils of a number of species from one of which, Podocarpus ferrugineus G. Benn., it could be obtained as a liquid in 80% purity (g.l.c.) after fractional crystallisation at low temperatures. Crystalline "cupressene", m.p. 74.5-75.5°, has again been isolated from C. macrocarpa but in all cases g.l.c. examination has shown it to be a mixture, probably a eutectic (3), of cupressene and isophyllocladene in the ratio of 2:1.

Although cupressene has yet to be isolated in a pure state further physical and chemical evidence of enriched material (85% from g.l.c.), $[\alpha]_D$ - 10°, from P. ferrugineus has led to its formulation as (I), and thus it is identical with hibaene, $[\alpha]_D$ - 50°, (4) and enantiomeric with stachene, $[\alpha]_D$ + 33° (5).

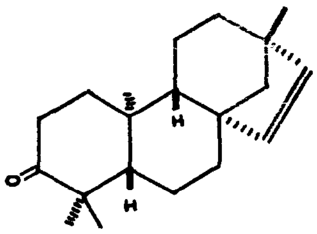


(I)

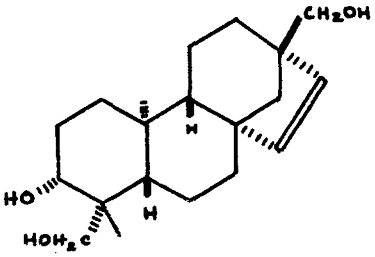
Oxidation of cupressene with osmium tetroxide gave a chromatographically pure diol, $C_{20}H_{34}O_2$, m.p. 168.5–169°, lacking peaks due to unsaturation in the infrared spectrum, while treatment with perbenzoic acid gave an epoxide, $C_{20}H_{32}O$, m.p. 125–125.5°, homogeneous by g.l.c. and saturated according to the infrared spectrum. Both derivatives have melting points considerably different from those of the corresponding derivatives from isophyllocladene (6). They are thus true derivatives of cupressene which must therefore possess only one double bond and be tetracyclic.

The infrared spectra of enriched cupressene fractions show no diminution of the 751 cm.$^{-1}$ band, previously assigned to a cis-disubstituted double bond (7), but virtual absence of the 823 cm.$^{-1}$ band, typical of isophyllocladene, which is a known impurity of "cupressene" from C. macrocarpa. Consideration of the n.m.r. spectrum of enriched cupressene and its epoxide and a comparison with those of phyllocladene, isophyllocladene, kaurene, isokaurene, 15,16-epoxyphyllocladane, and 15,16-epoxykaurane leaves little doubt that cupressene may be represented by (I). In the olefinic region the spectrum of cupressene exhibits an AB quartet (doublets at 5.41, 5.67δ, J = 5.5 c/sec.) of a cis-disubstituted double bond attached to quaternary carbon atoms. Three sharp signals assigned to quaternary C-methyl groups appear at 0.74, 0.83, and 0.86δ, at almost the same positions as those shown by isophyllocladene, and can be assigned to methyl groups with similar environments, viz. the C_4-gem dimethyl and C_{10}-methyl groups. A signal at ca. 2.6δ in the spectra of phyllocladene and kaurene, typical of an allylic bridgehead proton (8) at C_{13}, is absent in the spectrum of cupressene and is replaced by that of a further quaternary methyl group at 0.99δ.

From the above evidence and the close similarity of bands of a cis-disubstituted double bond in the infrared spectra of stachenone (9)(II) and beyerol (10) (III) at 749 and 750 cm.$^{-1}$, respectively, and the presence of



(II)



(III)

two doublet peaks at 5.43 and 5.67δ (J = 6 c./sec.) in the n.m.r. spectrum of stachenone, it appeared probable that cupressene possessed the same carbon skeleton, represented by (I) or a stereoisomer.

Assuming a trans A/B ring fusion, there are four possible structures (excluding enantiomers) with this skeleton. Those with a trans-anti-trans or trans-anti-cis backbone would be most likely (11) and from the following evidence a decision in favour of the former can be made. If cupressene possessed a trans-anti-cis backbone, acid treatment would be expected to effect a Wagner-Meerwein rearrangement to isophyllocladene analogous to the steviol-isosteviol (12) and allogibberic-gibberic acid (13) rearrangements. In confirmation of the original observations (2) cupressene was recovered unchanged (g.l.c.) after heating with p-toluene sulphonic acid in benzene solution. The infrared spectra of 17-norkaur-15-ene (14) and 17-norphylloclad-15-ene (15) with trans-anti-cis and trans-anti-trans backbones, respectively, exhibit peaks due to cis double bonds at 721 and 745 $cm.^{-1}$ respectively. The higher wave-number of the double bond of cupressene (751 $cm.^{-1}$) suggests that it also has a similar environment to that of 17-norphylloclad-15-ene, stachenone, and beyerol.

Further, as can be seen from the Table, the diamagnetic shielding of

TABLE

Effect of $C_{15(16)}$-Double Bond on the C_{10}-Methyl Resonance

Compound	Chemical shift in p.p.m. C_4-gem-dimethyl		C_{10}-methyl
Isophyllocladene	0.83	0.86	0.75
Phyllocladene	0.82	0.87	0.92
15,16-Epoxyphyllocladane	0.84	0.87	0.92
Isokaurene	0.82	0.87	1.03
Kaurene	0.82	0.87	1.03
15,16-Epoxykaurane	0.82	0.88	1.02
Cupressene	0.83	0.86	0.74
15,16-Epoxycupressane	0.83	0.87	1.04

the C_{10}-methyl group of isophyllocladene (10,16) is removed by epoxidation. In the isokaurene series, in which the olefinic centre is remote from the angular methyl group, no such shielding occurs. Since the signal of the C_{10}-methyl group in cupressene shows a considerable downfield shift on epoxidation, cupressene must also have its D-ring in close proximity to the C_{10}-methyl group and thus possess the trans-anti-trans configuration as in (I).

In recent communications enantiomeric diterpenes of structure (I) have been reported: the (-)-isomer, hibaene, from *Thujopsis dolabrata* Sieb. et Zucc. (4) and the (+)-isomer, stachene, from *Erythoxylon monogynum* Roxb. (5) of proved absolute configuration (17). In addition, oxygenated derivatives of stachene have been reported from the latter species (5,18). Through the courtesy of Professor Kitahara and Dr Murray we have been able to compare the infrared and n.m.r. spectra of hibaene and stachene with those of cupressene and, as expected, they are virtually identical. Moreover, cupressene and stachene have the same retention values on g.l.c. Since cupressene from *P. ferrugineus* possesses a negative rotation its structure and absolute configuration is represented by (I).

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