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CAPARRAPI OXIDE, A SESQUITERPENOID FROM CAPARRAPI OIL

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Abstract—Caparrapi oxide, isolated from the essential oil of *Ocotea caparrapi* Nates (Dugand), has been assigned the structure 1,3,7,7-tetramethyl-3-vinyl-2-oxabicyclo [4,4,0] decane (I), formally derivable by cyclization of nerolidol.

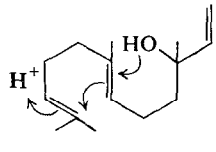
INTRODUCTION

COMPARISON of various samples of the oil from *Ocotea caparrapi* Nates (Dugand), (*Lauraceae*) by combined gas chromatography-mass spectrometry, has indicated the common presence of nerolidol and structurally related sesquiterpenoids.[1] Certain samples contained, as a major constituent, a compound (unaffected by mild acetylation) having a retention index (1% SE-30, 100°C) of 1420, and yielding in its mass spectrum main peaks at *m/e* 222 (M^+), 207, 189, 137, 124 and 109. (Accurate mass measurement of the ion at *m/e* 124 (MS9) gave a value 124·1205: calcd. for C_9H_{16}, 124·1252: for $C_8H_{12}O$, 124·0888). The unusually short retention time, together with the mass spectral data (reminiscent of bicyclofarnesol derivatives) prompted further investigation of this component, which we have named *caparrapi oxide*.

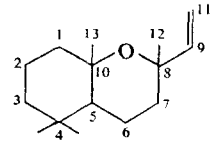
RESULTS AND DISCUSSION

Caparrapi oxide was readily isolated from the neutral fraction of the oil. GLC on three phases of graded polarity showed no indication of inhomogeneity. The i.r. spectrum (liquid film: Fig. 1) indicated the presence of a vinyl group, while bands in the C—O stretching region were attributable to a tetrahydropyran ring .[2, 3] Hydrogenation (Pd-C) afforded a dihydro-compound (M.W.224 from mass spectrometry) showing no vinyl absorption.

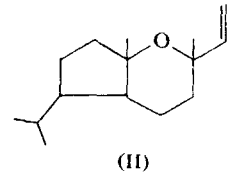
The NMR spectrum of caparrapi oxide (60 Mc/sec; Fig. 2) showed a typical vinyl multiplet, which was not further coupled, indicating an adjacent tertiary carbon atom. Four methyl groups could be distinguished by singlet peaks at τ 9·10 and 9·20 and (two superimposed) at 8·70. The absence of methylenic signals below τ 8 indicated that the ethereal oxygen atom was flanked by tertiary carbon atoms.



Nerolidol



(I)



(II)

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The above evidence suggested that caparrapi oxide possessed the gross structure I, formally derivable by cationic cyclization of nerolidol. The alternative structure (II) is inconsistent with NMR data: the separation (cps) of peaks ascribed to the geminal methyl groups was proportional to the applied frequency, and double irradiation confirmed the absence of an isopropyl group. Mass spectroscopic data [1] were also in better accord with (I).

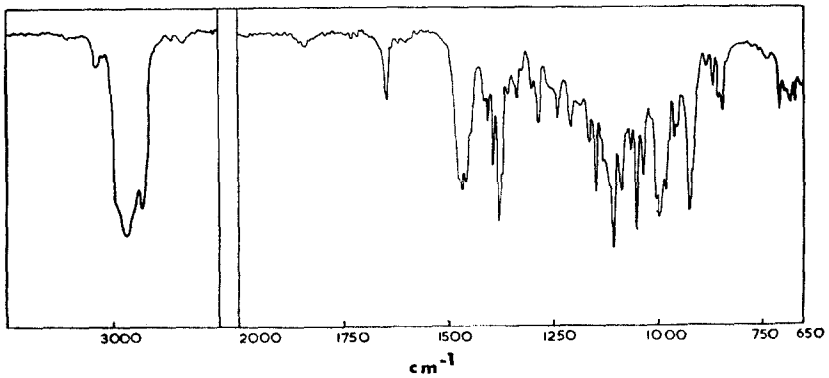


FIG. 1. I.R. SPECTRUM OF CAPARRAPI OXIDE (LIQUID FILM).

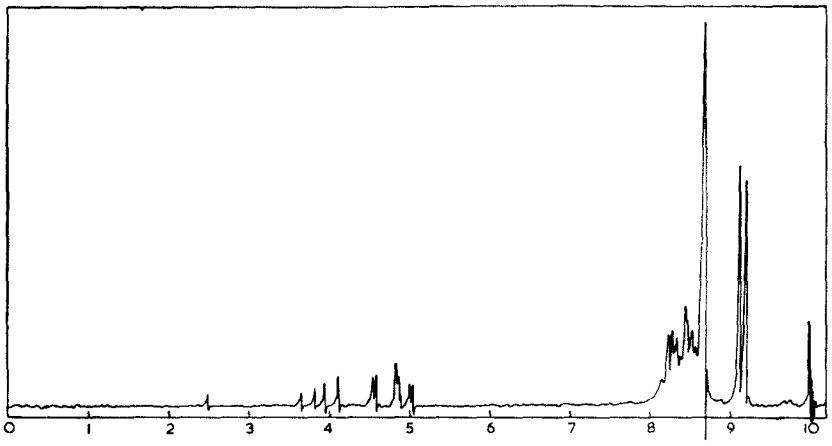
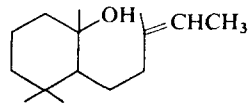


FIG. 2. NMR SPECTRUM (60 Mc) OF CAPARRAPI OXIDE ($CDCl_3$).

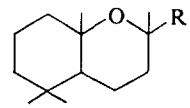
Reduction of caparrapi oxide with lithium in liquid ammonia gave mainly (*ca.* 85 per cent as judged by GLC) the expected product (III). This was not isolated in a pure state but was characterized by NMR, which indicated five methyl groups [peaks at τ 8·40 (broad), 8·44 (centre of doublet), 8·84, 9·05 and 9·19 (singlets)], a single olefinic proton (τ *ca.* 4·75, multiplet) and two allylic protons of a methylene group (τ *ca.* 7·9, multiplet). The i.r. spectrum included ν_{max} 830 and 1660 cm^{-1} $\left(>C=\!\!<^{H}\right)$.

Caparrapi oxide was converted smoothly by $OsO_4/NaIO_4$ to the *aldehyde* (IV). NMR showed singlet peaks for the *gem*-dimethyl group (τ 9·15, 9·20) and for the methyl groups flanking the ether oxygen (τ 8·70 and 8·80, consistent with the expected small difference in shielding). The aldehyde proton appeared as a sharp singlet at τ 0·42. Reduction of the

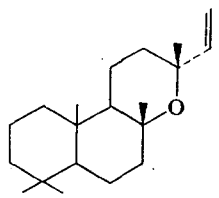
aldehyde with lithium aluminium hydride yielded the *alcohol* (V): ν_{max} (CCl_4) 3570 cm^{-1} (ϵ_a 40) unaffected by dilution [*cf.* 2-hydroxymethyltetrahydropyran, ν_{max} (CCl_4) 3597 (ϵ_a 55)[4]]. The NMR spectrum showed two well-defined doublets (CH_2OH) centred on τ 6·72 and 6·90 ($J \sim 10$ c/s), and four methyl group singlets (τ 8·72, 8·84, 9·12 and 9·24). The alcohol was further characterized as its crystalline p-*bromobenzoate*.



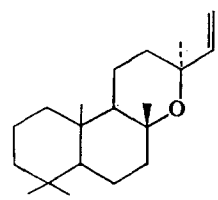
(III)



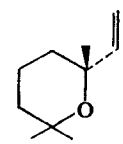
(IV) R=CHO
(V) R=CH_2OH



(VI)



(VII)



(VIII)

Structure I was further supported by comparing spectral data (i.r., MS and NMR) for caparrapi oxide with those for manoyl and epimanoyl oxide (VI, VII) and the monoterpenoid oxide (VIII). The i.r. spectrum of caparrapi oxide (Fig. 1) closely resembled those of VI[5,6] and VIII[7] in accordance with the proposed correspondence of the tetrahydropyran ring system and vinylic group. In the mass spectrum, many of the abundant ions from caparrapi oxide had their counterparts in the spectra of VI and VII.[8] The published NMR spectrum of VI[9] is closely similar to that of I, particularly in the vinylic region. Moreover, the chemical shifts of the $C_{(8)}$ and $C_{(10)}$ methyl groups of caparrapi oxide (Table 1) are almost identical to those of the methyl groups at $C_{(8)}$ and $C_{(13)}$ in manoyl oxide: the implied *cis*-configuration of these methyl groups is as expected for hypothetical cyclization of (+)S-*trans*-nerolidol in a two-chair conformation. Caparrapi oxide is thus a C_{15} homologue of the monoterpenoid oxide (VIII) isolated from distilled oil of lime.[7]

TABLE 1. CHEMICAL SHIFTS OF METHYL GROUPS ($CDCl_3$)

Manoyl oxides				Caparrapi oxide and derivatives				
Oxide	$C_{(8)}$	$C_{(13)}$	Ref.	Oxide	$C_{(8)}$	$C_{(10)}$	$C_{(4)}$	
VI	8·73,	8·73	(10)	I	8·70,	8·70	9·10,	9·20
	8·78,	8·80	(9)					
VII	8·92,	8·83	(10)	IV	8·70,	8·80	9·15,	9·20
	8·89,	8·80	(9)	V	8·72,	8·84	9·12,	9·24

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EXPERIMENTAL

Conventional techniques were used for column chromatography, TLC and GLC. Materials used included Kieselgel G (Merck) for analytical TLC and Kieselgel HF_{254} (Merck) for preparative TLC. The column packing (1% SE-30 on 100–120 mesh silanized Gas-Chrom P) most commonly used for GLC was prepared by the method of Horning *et al.*[11] Analytical GLC was carried out using the Pye Argon chromatograph or the Perkin-Elmer F-11 instrument.

M.p.s were recorded on a Kofler block and are uncorrected. Rotations were measured in $CHCl_3$ at room temperature. Routine i.r. spectra were measured on a Unicam SP200 model and high resolution spectra on the SP100 double beam spectrophotometer. Mass spectra were measured on an AEI MS9 spectrometer and gas chromatography-mass spectrometry (GLC-MS) was effected on an LKB9000 instrument. NMR spectra were determined on a Perkin-Elmer R10 instrument or on a Varian HA100 model equipped with spin decoupler.

Hydrogenations to determine olefinic unsaturation were done on the micro-scale, and the products evaluated by GLC-MS.

Isolation of Caparrapi Oxide

The neutral fraction (1 g) of sample 4 of caparrapi oil[1] was adsorbed on neutral alumina (40 g, Woelm grade III) and subjected to gradient elution, using light petroleum (0·5 l., b.p. 60–80°) and diethyl ether (0·5 l.), and collecting 50 ml aliquots. Fractions 2–4, eluted with 1% ether-light petroleum, afforded caparrapi oxide (140 mg). Preparative TLC and vacuum diffusion (40°/5 mm Hg) yielded pure caparrapi oxide as a fragrant oil, $[\alpha]_D - 18°$ (*c*, 1·0 in $CHCl_3$). Found: C, 80·97; H, 11·87. $C_{15}H_{26}O$ required: C, 81·02; H, 11·79 per cent. GLC retention data: $I^{100°}_{1\%\,SE-30}$ 1420, $I^{100°}_{1\%\,OV-1}$ 1430, $I^{100°}_{1\%\,OV-17}$ 1540, $I^{100°}_{3\%\,OV-22}$ 1570*. I.r. data: ν_{max} 3080, 1840, 980, 920 cm^{-1} (vinyl group) and ν_{max} 1047, 1080, 1120 cm^{-1} (tetrahydropyran ring).

Osmium Tetroxide Oxidation of Caparrapi Oxide

Caparrapi oxide (15 mg. 0·06 mM) was dissolved in dry tetrahydrofuran (3 ml). OsO_4 (20 mg, 0·08 mM) in dry tetrahydrofuran was added with stirring. One drop of pyridine was added, and the solution, which darkened immediately, was left overnight at room temperature. Saturated aq. $Na_2S_2O_5$ (5 ml) was added, and the solution stirred for 1 hr. Extraction with ether afforded a mixture of diastereoisomeric diols as an oil (14 mg): $I^{120°}_{1\%\,SE-30}$; 1800, 1820.

Periodate Cleavage of Diols to Aldehyde (IV)

The mixture of diastereoisomeric diols (13 mg) was dissolved in ethanol (2 ml) and saturated aq. $NaIO_4$ (2 ml) added. The solution was stirred for 4 hr and extracted with ether, yielding an oil (10 mg), which was purified by vacuum diffusion (40°/5 mm Hg). (Found: C, 74·70; H, 10·63. $C_{14}H_{24}O_2$ required: C, 74·95; H, 10·78 per cent): ν_{max} (CCl_4) 1740 cm^{-1} (ϵ_a, *ca.* 320): shoulder at 1732 cm^{-1} (ϵ_a, *ca.* 200): $I^{120°}_{1\%\,SE-30}$ 1550.

Reduction of Aldehyde (IV)

Aldehyde (IV) (38 mg, 0·14 mM) was dissolved in dry ether (4 ml) and $LiAlH_4$ (8 mg, 0·20 mM) added slowly with stirring. After 1 hr, aqueous methanol (1 ml.) was added dropwise. Ether extraction afforded an oil (36 mg) which, after preparative TLC and vacuum diffusion (40°/5 mm Hg) gave alcohol (V) (23 mg): $[\alpha]_D - 5·5°$ (*c*, 1·0 in $CHCl_3$)): (Found: C, 74·59; H, 11·81. $C_{14}H_{26}O_2$ required: C, 74·29; H, 11·58 per cent) ν_{max} (CCl_4) 3570 cm^{-1} (ϵ_a 40) unaffected by dilution; *p*-bromobenzoate, m.p. 60·5–61·5°: (Found: C, 61·48; H, 6·99. $C_{21}H_{29}BrO_3$ required: C, 61·61; H, 7·14 per cent).

Ring-opening of Caparrapi Oxide

Oxide (50 mg) in ether (2 ml) was added dropwise to Li (200 mg) in liq. NH_3 (50 ml) in a "cold-finger" reaction vessel. The deep blue solution was maintained at liquid NH_3 temperature for 1 hr and ammonium chloride (500 mg) and ethanol (10 ml.) added. The liq. NH_3 was allowed to boil off and the residue partitioned between H_2O and ether. The ethereal extract afforded a clear oil (50 mg). Preparative TLC (benzene) afforded the principal constituent as an oil (43 mg), the i.r. characteristics of which corresponded to the expected ring-opening product [ν_{max} (liquid film) 3600, 1660, 830 cm^{-1}]. GLC-MS revealed the presence of two isomeric constituents in the ratio 85:15 (Molecular ions, *m/e* 224; $I^{125°}_{1\%SE-30}$ 1545, 1555). The mixture was unresolvable in several TLC solvent systems.

Acknowledgements—We thank Dr. J. Martin for the accurate mass measurement by mass spectrometry, and Dr. K. H. Overton for NMR facilities. One of us (MMC) is indebted to the Salters' Company for a Scholarship.

* 3% OV-22 phase was kindly supplied by Dr. W. R. Supina (Supelco, Inc.)

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