Tetrahedron Letters No.31, pp. 3731-3736, 1966. Pergamon Press Ltd.
Printed in Great Britain.

CAPARRAPIDIOL AND CAPARRAPITRIOL: TWO NEW ACYCLIC SESQUITERPENE ALCOHOLS.

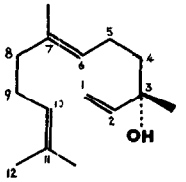
J. Borges del Castillo, C.J.W. Brooks and M.M. Campbell,
Department of Chemistry,
University of Glasgow, Glasgow, W.2.

(Received 1 June 1966)

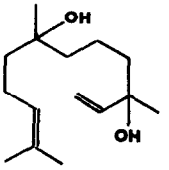
We report the isolation and characterisation of compounds which appear to be the first naturally occurring acyclic sesquiterpene diol and triol. Caparrapí oil or resin, which is obtained by incision at the base of the Colombian tree Ocotea caparrapí, was examined by Tapia (1) who reported the isolation of an alcohol, "caparrapiol", $C_{15}H_{26}O$, and an acid, $C_{15}H_{26}O_3$. We have examined a sample of caparrapí oil collected by Dr. A.Fernandez Perez: the acidic fraction was insignificant. Acidic components have, however, been observed in other samples (2).

Chromatography of the oil (3 g) on alumina (150 g Woelm, grade III) using a light petroleum-diethyl ether gradient elution, afforded the major component (2.76 g) as a colourless oil. Analysis indicated the formula $C_{15}H_{26}O$, and this fraction was shown to be (+)S-nerolidol, (I), from its infra-red, n.m.r. and mass spectra, its physical constants (n^{20}, 1.4807; $[\alpha]_D$ + 18° in EtOH) and gas-liquid chromatographic properties. Caparrapí oil appears to be the richest source of nerolidol so far described.

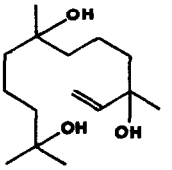
A second, more polar compound (0.29 g) was then eluted as a clear, faintly fragrant, viscous oil, $[\alpha]_D$ + 8° in $CHCl_3$, which decomposed readily on exposure to air, but which could be stored in ethanol at 0°C. Analysis indicated the composition $C_{15}H_{28}O_2$ (Found, C, 74.67%; H, 11.82%; calcd. C, 74.95%; H, 11.74%). This formula was supported by the mass spectrum (MS9) which indicated a sesquiterpene diol "caparrapidiol", (molecular ion, m/e 240). An acyclic structure was shown by hydrogenation: uptake of two moles of hydrogen was indicated by mass spectrometry of the product.



I



II



III

The infra-red spectrum (liquid film) of caparrapidiol was found to be closely similar to that of nerolidol, except for increased absorption intensity in the hydroxyl region. (FIG. 1). Strong bands near 920 and 1000 cm^{-1} indicated the presence of a vinyl group. The n.m.r. (60 Mc) spectrum confirmed this structural feature, showing typical multiplets centred on τ = 4.06 and 4.80

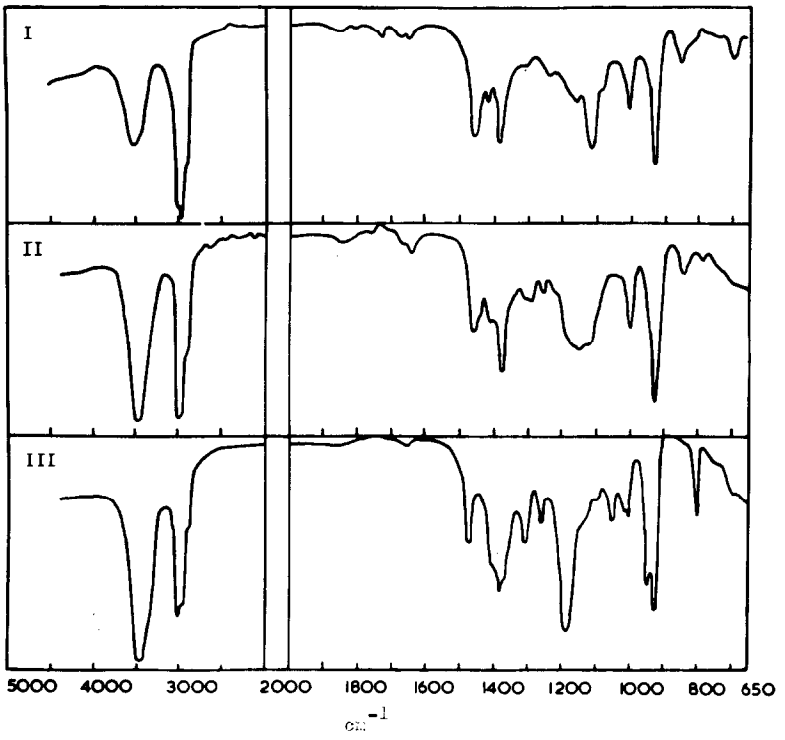


FIG. 1.

Liquid film i.r. spectra of nerolidol (I), caparrapidiol (II), and caparrapitriol (III).

which contained also the signal due to the olefinic proton of an isopropylidene grouping (τ = 8.30 and 8.36). Two unsplit peaks at τ = 8.71 and τ = 8.82 were assigned to methyl groups at tertiary alcoholic centres. A peak ascribed to two hydroxyl protons at τ = 7.95 disappeared on D_2O exchange. All assignments were supported by integration.

Caparrapidiol was found to dehydrate when left in ethanol for several days on a column of alumina: nerolidol was identified as one of the products.

Caparrapidiol bis-trimethylsilyl ether was characterised by gas chromatography-mass spectrometry (GCMS). The following ions were observed: m/e = 384 (0.5%) [parent ion]; m/e = 301 (0.5%) [loss of C_6H_{11} by cleavage at $C_{(7)}$-$C_{(8)}$]; m/e = 294 (1%) [M - $(CH_3)_3SiOH$]; m/e = 204 (1%)[M - 2 x $(CH_3)_3SiOH$]; m/e = 199 (25%)[$C_{(6)}$-$C_{(7)}$ cleavage]; m/e = 143 (100%) [$C_{(3)}$-$C_{(4)}$ cleavage].

The above evidence confirms structure (II) rather than (IV) for caparrapidiol: the relative configuration remains to be determined.

Further elution of the chromatographic column from which (I) and (II) were obtained, yielded "caparrapitriol" as a white, crystalline solid (30 mg) m.p. 96-97°C, $[\alpha]_D$ + 3° in $CHCl_3$. Analysis indicated the structure $C_{15}H_{30}O_3$ (Found, C, 69.52%; H, 11.45%; calcd. C, 69.72%; H, 11.70%). This compound was also observed to dehydrate on an alumina column, affording principally (I) and (II), as shown by comparative thin-layer and gas-liquid chromatography.

The infra-red spectrum of caparrapitriol (melted film: FIG. 1) closely resembled those of (I) and (II), but showed more intense hydroxyl absorption and diminished olefinic absorption. These results confirmed the close relationship of the three alcohols. Solutions of the triol in CCl_4 showed a sharp peak at 3610 cm^{-1} corresponding to non-bonded hydroxyls: a broad peak at 3340 cm^{-1} disappeared on dilution, indicating intermolecular hydrogen-bonding.

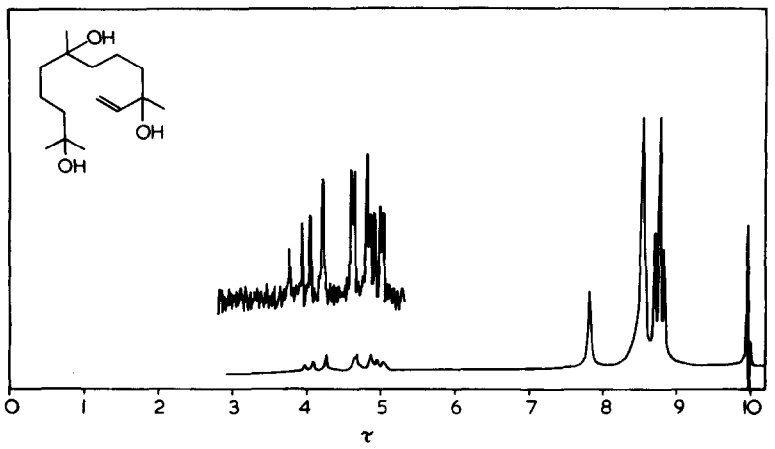
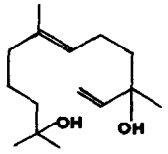


FIG. 2.

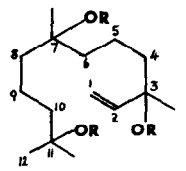
n.m.r. spectrum of caparrapitriol (III) in $CDCl_3$ at 60 Mc.

The n.m.r. spectrum confirmed structure (III), the following assignments being supported by integration: - two multiplets centred at τ = 4.06 and τ = 4.82 (vinyl); a sharp singlet at τ = 7.87 which corresponded to three hydroxyl protons, and disappeared on D_2O exchange; a diffuse peak at τ = 8.60 (methylene protons); two singlets at τ = 8.74 and 8.86 (two methyl groups at tertiary alcoholic centres), and a sharp singlet at τ = 8.81, characteristic of a gem-dimethyl attached to a tertiary alcoholic centre.

The three alcohols, (I), (II) and (III), were found to give similar mass spectra (measured on an LKB Model 9000 Gas Chromatograph-Mass Spectrometer) as a result of initial thermal dehydration to a common hydrocarbon, followed by normal fragmentation.



IV



V

$R = Si(CH_3)_3$

Caparrapitriol tri-trimethylsilyl ether (V), characterised by its gas chromatographic retention and by GCMS, afforded the following significant ions: m/e = 384 (0.5%) [M - $(CH_3)_3SiOH$]; 301 (1%) [cleavage at $C_{(7)}$-$C_{(8)}$]; 289 (3%) [cleavage at $C_{(6)}$-$C_{(7)}$]; 211 (14%) [301 - $(CH_3)_3SiOH$]; 199 (8%) [289 - $(CH_3)_3SiOH$]; 143 (100%) [cleavage at $C_{(3)}$-$C_{(4)}$]; 131 (30%) [cleavage at $C_{(10)}$-$C_{(11)}$].

The good gas chromatographic properties of trimethylsilyl ethers and their value in directing the course of mass spectral fragmentations combine to make them very suitable for structural characterisation by GCMS. Their application to steroids is well known (3), and the present results confirm their general utility.

(1) M. Tapia, Bull. Soc. Chim. France, 19, 638 (1898).

(2) H.H. Appel, C.J.W. Brooks and M.M. Campbell (to be published).

(3) P. Eneroth, K. Hellström and R. Ryhage, J. Lipid Research, 5, 245 (1964).

The sample of caparrapí oil was kindly provided by Dr. A. Fernandez Perez (Bogotá) through the helpful agency of Mr. A.G. Kenyon (Tropical Products Institute). We are greatly indebted to Dr. H.H. Appel (Valparaiso, Chile) for his kind interest. We also thank Mr. A. McCormick for recording mass spectra and assisting with their interpretation. Dr. J. Feeney (Varian Associates) kindly carried out a spin decoupling experiment.