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ISOLATION AND STRUCTURE OF MACARANGONOL, A DITERPENE KETOL FROM *MACARANGA TANARIUS*[*]

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Abstract-The light petroleum extract of the stems of *Macaranga tanarius* (Euphorbiaceae) yielded-in addition to several other terpenoids a new diterpene ketol, macarangonol, to which we assign structure I.

A new diterpene ketol, macarangonol, has been isolated from the light petroleum extracts of *Macaranga tanarius* Muell.-Arg. (Euphorbiaceae).

MACARANGONOL, m.p. 210–211°, $[\alpha]_D -142°$, has the molecular formula of $C_{20}H_{30}O_2$, M^+ at *m/e* 302.2200 (calc. 302.2244). It gave a positive Liebermann-Burchardt test (violet → brown → green), and a pale yellow colour with tetranitromethane.

The NMR spectrum (see Fig. 1) showed the presence of four methyl singlets, one axial carbinyl proton coupled to one axial and one equatorial proton, and four olefinic protons. Three of the olefinic peaks constituted an ABC system (confirmed by decoupling) while one was isolated and weakly coupled; the olefinic proton region was very similar to those

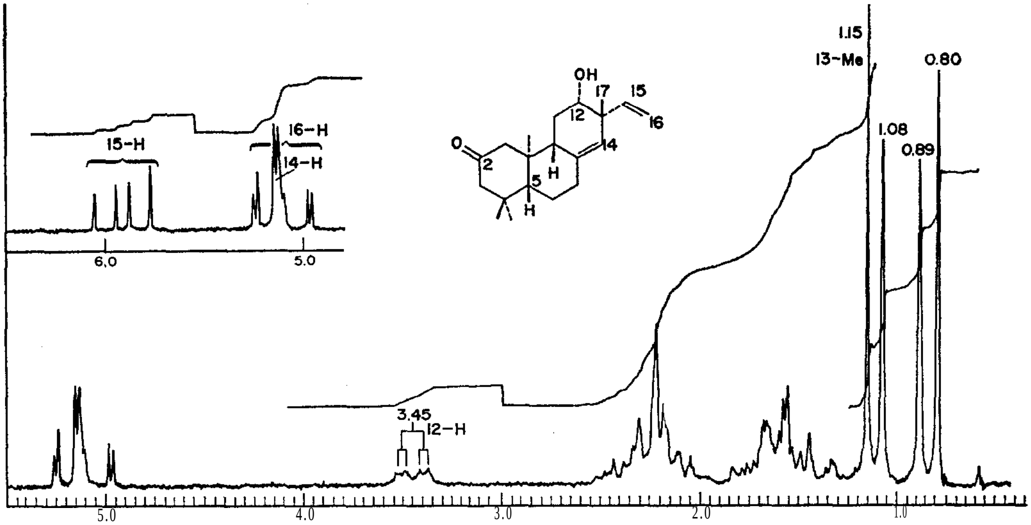

FIG. 1. NMR SPECTRUM OF MACARANGONOL I IN $CDCl_3$, 100 MHz (VARIAN HA-100).

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[*] Part IX in the series "An Examination of the Euphorbiaceae of Hong Kong"; for Part VIII, see W. H. Hui and W. K. Lee, *J. Chem. Soc.* (in press).

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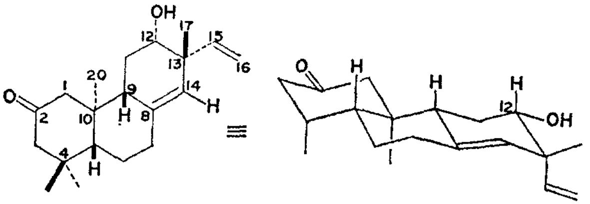
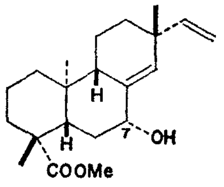
generally encountered in the 8 (14), 15-pimaradiene and 8 (14), 15-isopimaradiene (epimeric at C-13) classes of diterpenoids.[1] The i.r. spectrum (KBr disk) exhibited absorptions due to hydroxyl (3410, 1069 cm-‘), saturated carbonyl (1690 cm^{-1}; 1714 cm^{-1} in chloroform), monosubstituted double bond (1008,924 cm^{-1}) and trisubstituted double bond (840 cm-‘).

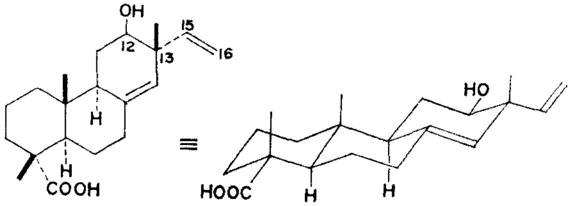
The O-H stretching region indicated that the hydroxyl group was involved in a weak intramolecular n-hydrogen bonding with the double bond. Namely, the spectrum in chloroform (the solubility in carbon tetrachloride was not sufficient) had bands at 3605 (free), 3492 (intramol. H-bonding) and 3424 cm^{-1} (intermol. H-bond).



I



II



III

The carbonyl group was isolated from the double bonds as shown by the u.v. maximum at 290 nm (ε 21·1) and the corresponding CD Cotton effect (290 nm, Δε—1·66) (both in methanol). The low intensities of the u.v. maximum and Cotton effect, and absence of NMR methylene peaks in the region lower than 2·5 ppm also excluded the presence of a β,γ-unsaturated enone moiety. Deuteration of macarangonol I by refluxing in D_2O with Na/EtOD and subsequent cooling gave crystals of the pentadeuterio derivative (M^+ at *m/e* 307), which when treated with light water was converted into the tetradeuterio derivative (M+ at *m/e* 306). The carbonyl group is thus flanked by two methylene groups.

The evidence cited above indicates that macarangonol I is a keto alcohol belonging to the 8(14), 15-pimaradiene or 8(14), 15-isopimaradiene type of diterpenes. The carbonyl is at C-2, which is the only location to account for the incorporation of four D atoms upon deuteration (followed by H_2O treatment). The negative sign and amplitude (a: -67 in ORD) of the Cotton effect establishes the configuration at C-5 and C-IO as being β and a, respectively.[2]

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[1] See for example: E. WENKERT and P. BEAK, *J. Am. Chem. Soc.* 83,998 (1961). However, for correct structure of rimuene see R. E. IRELAND and L. N. MANDER, *Tetrahedron Letters* 3453 (1964).

[2] P. K. GRANT and R. HODGES, *Chem. & Ind.* 1300 (1960).

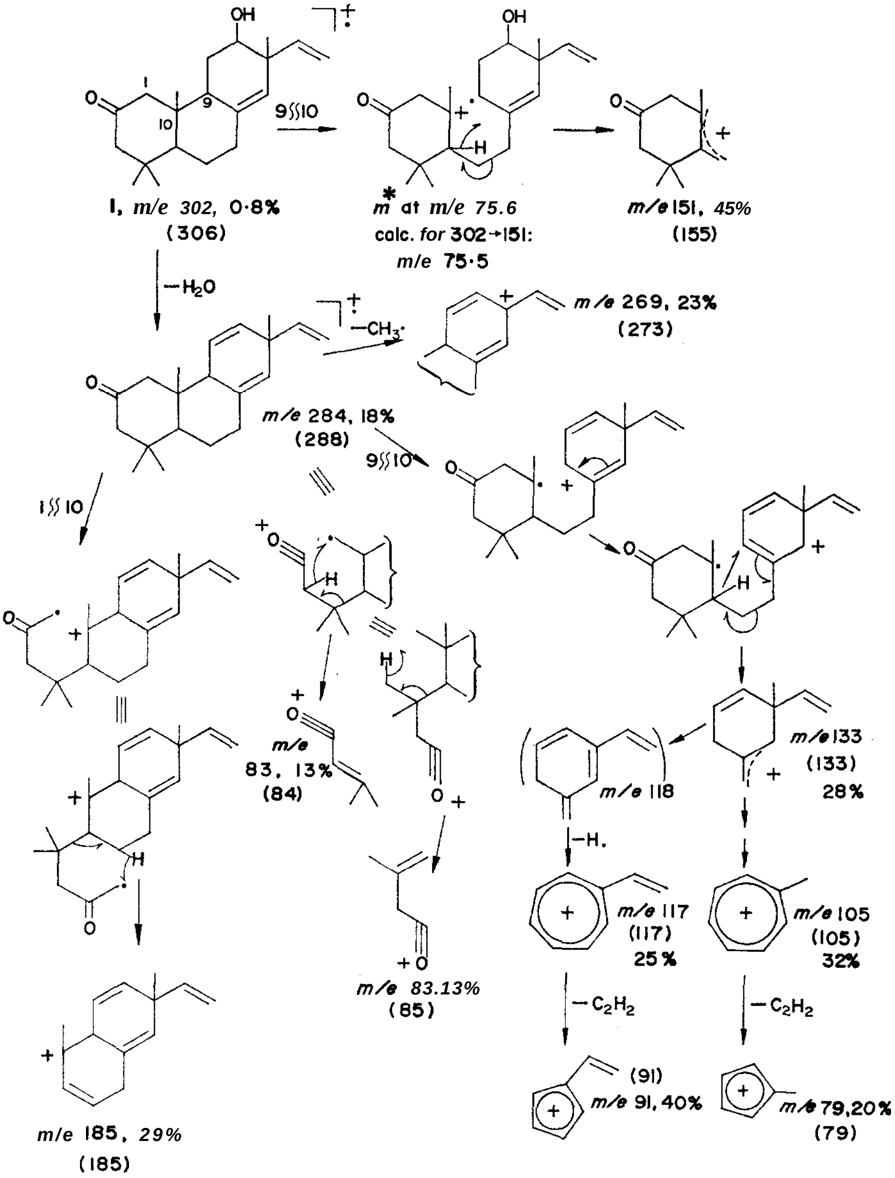

FIG. 2. PRINCIPAL MASS FRAGMENTATIONS OF MACARANGONOL I. INTENSITIES ARE RELATIVE TO THE BASE PEAK AT *m/e* 28. NUMERALS IN PARENTHESES ARE MASS PEAKS FOR THE 1,1,3,3-TETRADEUTERIO DERIVATIVE.

The secondary hydroxyl group was placed at C-12 and assigned an equatorial configuration on the following basis: (i) the 12-H at 3·45 ppm has *J* 11 and *J* 4Hz; (ii) the p-axial carbinyl proton at C-7 in the related pimaradiene II appears as an octet at the lower field of 3·92 ppm (*J* 12·0, 6·5, 2·0 Hz);[3] (iii) the hydroxyl group is intramolecularly hydrogen bonded to a double bond; (iv) the MS showed a series of prominent peaks, the genesis of which is well accounted for by the cation at *m/e* 284 (Fig. 2).

[3] S. MIHASHI, I. YANAGISAWA, O. TANAKA and S. SHIBATA, *Tetrahedron Letters 1683 (1969).*

The remaining point to be determined is the configuration at C-13. It has been reported[4] that the 8(14),15-pimaradiene and 8(14),15-isopimaradiene diterpenes can be differentiated by virtue of the molecular rotation (Φ) at *ca.* 225 nm. Namely, the former class has strongly positive values (Φ ca. +29,000) whereas the latter class is characterized by weaker negative values (Φ *ca.* -4000). However, these results were not applicable to the present case (Φ_{230} -7000) because the suspected hydrogen-bonding between the 15-ene and hydroxyl group would alter the distribution of electrons in the homo-diene. A comparison of shifts in the 13-methyl and 13-vinyl NMR signals induced upon derivatization of the 12-hydroxyl group is also not feasible as the latter bisects the two C-13 substituents (see I). However, a *cis*-relation between the 12-hydroxyl and the 13-vinyl groups was finally assigned by comparing the olefinic NMR peaks with those of the methyl ester of '6β-hydroxysandaracopimaric acid' III[5] (= 12β-hydroxy-8(14), 15-isopimaradien-18-oic acid),* for which a *trans*-relation has been established. The A B portions of the ABC system in I and III (both measured in $CDCl_3$)† differed greatly, and hence unlike III, the 12-hydroxyl group should be *cis* to the 13-vinyl group. This establishes the structure of macarangonol as I, or ent.- 8(14),15-pimaradien-12β-ol-2-one.

EXPERIMENTAL

M.p. was taken on a Kofler hot stage apparatus and is uncorrected. Alumina for chromatography was B.D.H. analytical grade; light petroleum had b.p. 60–80°. NMR spectra and CD/ORD spectra were recorded with a Varian HA-100 spectrometer and JASCO-ORD/UV-5 spectropolarimeter.

Extraction *of material.* Milled air-dried stems of *Macaranga tanarius* (36 kg) were extracted twice with light petroleum (60 l.) at room temp. for 7 days. The combined extract was distilled to a small volume, and chromatographed on alumina (2 kg). Elution with light petroleum-benzene mixture yielded several compounds (to be reported elsewhere). Further elution with $CHCl_3$–benzene (1:1), afforded macarangonol (50 mg), m.p. 210–211°, $[\alpha]_D$ -142" ($CHCl_3$). (Found: C, 79.38; H, 9.88%. $C_{20}H_{30}O_2$ requires C, 79.42; H, 10·00%.)

Deuteration of macaranganol I. Sodium (10 mg) was dissolved in 0·5 ml of deuterio-ethanol, and 5·4 mg of macaranganol was added immediately after the evolution of D_2 had subdued. The solution was heated to boiling, and 0·2 ml of D_2O was added. After refluxing the solution for 1·5 hr, it was cooled to room temp., and needles of pentadeuterio-macaranganol were collected by filtration, washed with a few drops of D_2O and air-dried, yield 5·3 mg.

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* According to systematic nomenclature of cyclic diterpenes (third revision, October 1968) proposed to IUPAC by J. W. Rowe, USDA, Madison, Wisconsin 53705.

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[4] C. R. ENZELL and S. R. WALLIS, *Tetrahedron Letters 243* (1966).

[5] J. W. AP SIMON and O. E. EDWARDS, *Can. J. Chem.* **39,** 2543 (1961).