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TOVOXANTHONE FROM *TOVOMITA CHOISYANA**

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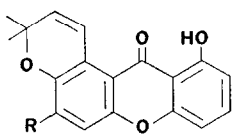
Key Word Index—*Tovomita choisyana*; Guttiferae; tovoxanthone; sitosterol; stigmasterol; betulinic acid.

Abstract—The wood of *Tovomita choisyana* Pl. et Tr. (Guttiferae) contains sitosterol, stigmasterol, betulinic acid and 1,6-dihydroxy-6′,6′-dimethylpyrano-(2′,3′:7,8)-xanthone.

Tovomita choisyana Pl. et Tr. is an arboreous Guttiferae species which occurs near Belem, at the estuary of the Amazon river. Its trunk wood contains sitosterol, stigmasterol, betulinic acid and a new compound for which elemental, MS and functional analysis led to formula $C_{18}H_{12}O_3(OH)_2$. The UV spectrum was compatible with a xanthone skeleton, indicating at the same time the *ortho* ($AlCl_3$-shift of maxima) and *para* (strong identical NaOH- and NaOAc-shifts) relationship of the hydroxyls and the carbonyl.[3,4] The existence of a chelate bridge was confirmed by the IR ($\nu_{max}^{C=O}$ 1640 cm^{-1}) and PMR (τ — 3·1, *s*, one OH) spectra. The hydroxyls cannot be situated on the same ring, since the aromatic region of the PMR spectrum contains signals typical of three vicinal protons on a C-1 oxygenated xanthone.[5] The *para*-hydroxyl must thus be located at C-6 of ring B which also supports a 2,2-dimethylchromene ring. This was characterized in the PMR spectrum by two doublets (τ 2·05 and 4·22, *J* 10·0 Hz), representing an AB system of olefinic protons, and a singlet at τ 8·51 representing the protons of two methyls. Such structural features usually give rise to bands at about τ 3·3, 4·4 and 8·5.[6] In the present case, the strong deshielding of the A proton demonstrates its closeness to the carbonyl. In confirmation, also the benzylic protons of dihydrotovoxanthone are strongly deshielded, the corresponding spectrum including two methylene triplets at τ 6·52 and 8·14. In 2,2-dimethylchroman derivatives these signals usually appear around τ 7·3 and 8·2.[6]



(Ia) R = OH
(Ib) R = OMe
(Ic) R = H

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It was desired to test the structural proposal of 1,6-dihydroxy-6′,6′-dimethylpyrano-(2′,3′:7,8)-xanthone (Ia) for tovoxanthone by synthesis. 2,2-Dimethylchromenes can be prepared easily, though in low yield, by direct interaction of a phenol with 2-methyl-but-3-yn-2-ol and $ZnCl_2$.[7] When this reaction was tried with 1,7-dihydroxyxanthone (euxanthone) as a model substrate, ring closure occurred in the required way, involving the hydroxyl at C-7 and the *peri*-carbon, leading to 1-hydroxy-6′,6′-dimethylpyrano-(2′,3′:7,8)-xanthone (Ic). Analogously, 1,7-dihydroxy-6-methoxyxanthone[8] led to a derivative (Ib), which proved to be identical with the methyl ether prepared by treatment of tovoxanthone with diazomethane. This showed a free hydroxyl at C-1 ($AlCl_3$-UV shift) and three vicinal protons at contiguous positions, providing unequivocal proof for the proposed structure.

EXPERIMENTAL

For experimental techniques see Ref. 4. All known compounds were identified by direct comparison with authentic samples.

Isolation of the constituents of Tovomita choisyana. The ground wood (4·5 kg) was extracted with benzene. The solvent was evaporated and the residue (16 g) was chromatographed on silica giving the following fractions with the indicated eluants: A (benzene), B (benzene–$CHCl_3$, 1:1), C ($CHCl_3$–MeOH, 99:1). A (1 g) was filtered through silica and recrystallized from acetone, yielding *tovoxanthone* (Ia). B (200 mg) was recrystallized from acetone yielding a mixture of *sitosterol* and *stigmasterol*. C (200 mg) was recrystallized from $CHCl_3$–MeOH yielding *betulinic acid*.

Tovoxanthone (Ia). Thick yellow needles, m.p. 219° (acetone). Found: C, 67·55; H, 4·33. $C_{18}H_{14}O_4$ requires: C, 67·49; H, 4·28%. ν_{max}^{KBr} (cm^{-1}): 3330, 1640, 1605, 1572, 1453, 1298, 1235, 1154. λ_{max}^{EtOH} (nm): 242, 265, 319 (ε 45 500, 36 750, 28 500); $\lambda_{max}^{EtOH+NaOH}$ (nm): 248, 330 inf. (ε 45 250, 17 050); $\lambda_{max}^{EtOH+NaOAc}$ (nm): 254, 327 inf. (ε 46 500, 14 250); $\lambda_{max}^{EtOH+AlCl_3}$ (nm): 243, 267, 334 (ε 46 500, 31 300, 27 150). PMR ($CDCl_3$, τ): −3·1 (*s*, O<u>H</u>), 2·05 (*d*, *J* 10·0 Hz, H-4′), 2·55 (*t*, *J* 8·0 Hz, H-3), 3·20 (*s*, H-5), 3·23 (*dd*, *J* 1· and 8·0 Hz, H-4), 3·33 (*dd*, *J* 1·5 and 8·0 Hz, H-2), 4·22 (*d*, *J* 10·0 Hz, H-5′), 8·51 (*s*, two C<u>H</u>$_3$). MS: M 310 (39%), *m/e* (%) 295 (100), 282 (17), 295/2 (16). The *monomethyl ether* (Ib) was obtained by treatment of Ia with CH_2N_2 in ether; and by synthesis according to Cardillo, *et al.*[7] 1,7-Dihydroxy-6-methoxyxanthone[8] (600 mg), 2-methylbut-3-yn-2-ol (4·8 ml) and anhydrous $ZnCl_2$ (750 mg) were heated under reflux (3 hr). The reaction mixture was cooled to room temp. and extracted repeatedly with $CHCl_3$. The $CHCl_3$ soln. was concentrated to a small volume. The precipitated 1,7-dihydroxy-6-methoxyxanthone (500 mg) was separated by filtration. The soln. was washed with N HCl, dried and chromatographed on silica. Benzene eluted the desired product (30 mg). The methyl ether of tovoxanthone and the synthetic product were shown to be identical by direct comparison. Yellow needles, m.m.p. 186–188°, co-TLC, ν_{max}^{KBr} (cm^{-1}): 1642, 1605, 1573, 1449, 1280, 1241, 827, 770. *Dihydrotovoxanthone* was obtained from tovoxanthone (H_2, Pd–C, EtOH) as yellow needles, m.p. 170–172° (EtOH). ν_{max}^{KBr} (cm^{-1}): 1645, 1605, 1575, 1480, 1455, 1295, 1235, 1155, 1055, 907, 833, 770, 709. λ_{max}^{EtOH} (nm): 244, 316, 386; $\lambda_{max}^{EtOH+NaOH}$ and $\lambda_{max}^{EtOH+NaOAc}$ (nm): 246, 368, 386. PMR $CDCl_3$ τ): 6·52 (*t*, *J* ca. 7 Hz), 8·14 (*t*, *J ca.* 7 Hz), 8·63 (*s*, two C<u>H</u>$_3$).

1-*Hydroxy*-6′,6′-*dimethylpyrano*-(2′,3′:7,8)-xanthone (Ic). Prepared from 1,7-dihydroxyxanthone under the conditions described above for Ib. Yield 7% (recovered euxanthone *ca.* 80%). M: Found 294; $C_{18}H_{14}O_4$ requires 294. Yellow needles, subl. 108°, m.p. 142–144° (acetone), ν_{max}^{KBr} (cm^{-1}): 1646, 1611, 1580, 1470, 1333, 1280, 1240, 1120, 1068, 1045, 915, 820, 758. λ_{max}^{EtOH} (nm): 239, 269, 305 (ε 39 800, 53 650, 14 450); $\lambda_{max}^{EtOH+AlCl_3}$ (nm): 242, 272, 325 (ε 26 750, 41 400, 13 500). PMR (CCl_4, τ): 1·95 (*d*, *J* 10 Hz, H-4′), 2·48 (*t*, *J* 8 Hz, H-3), 2·83 (*s*, H-5, H-6), 3·22 (*dd*, *J* 1 and 8 Hz, H-4), 3·31 (*dd*, *J* 1 and 8 Hz, H-2), 4·23 (*d*, *J* 10 Hz, H-5′), 8·52 (*s*, two C<u>H</u>$_3$).

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