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XANTHONES FROM *CRATOXYLUM MAINGAYI*

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Key Word Index—*Cratoxylum maingayi*; Guttiferae; wood; xanthones.

Abstract—1,7-dihydroxy-, 2,8-dihydroxy-1-methoxy-, 1,7-dihydroxy-4-methoxyxanthone and the new 7-hydroxy-1,2,3,8-tetramethoxyxanthone, were isolated from the wood of *Cratoxylum maingayi*. The structure of the new xanthone was confirmed by X-ray crystallography. © 1998 Elsevier Science Ltd. All rights reserved

INTRODUCTION

Cratoxylum is a relatively small genus of tropical southeast Asian trees. The literature contains reports on the chemistry of four species, which like other members of the Guttiferae, typically produce xanthones [1–5]. Our investigation of the wood of *Cratoxylum maingayi* from Thailand has now yielded 1,7-dihydroxyxanthone (euxanthone, **1a**) a common constituent of Guttiferae [6, 7], 1,7-dihydroxy-4-methoxyxanthone (**1b**) [3], 2,8-dihydroxy-1-methoxyxanthone (**2**) [8], all three previously isolated from *C. formosanum* [5], and the new 7-hydroxy-1,2,3,8-tetramethoxyxanthone (**3a**).

RESULTS AND DISCUSSION

Structural assignment **3a** to the new xanthone was based on the following data. Mass, ^{1}H and ^{13}C NMR spectra (both in $CDCl_3$ the latter in Table 1) indicated the presence of four methoxyls and one hydroxyl group. The ^{1}H NMR spectrum exhibited no signals for bonded OH, while the ^{13}C NMR spectrum exhibited the C=O signal at δ181.7, thus indicating that the hydroxyl was not located at C-1 or C-8. The ^{1}H NMR spectrum also exhibited one singlet at δ6.65 and two mutually coupled doublets (J = 9.1 Hz) at δ7.31 and 7.10, indicating that one aromatic ring was 1,2- or 3,4-disubstituted and the other 1,2,3- or 2,3,4-trisubstituted. In the ^{13}C NMR spectrum, three of the methoxyl signals were in the range δ61.5–62.5 and only one at δ56.2, indicating that each of three of the methoxyl groups was flanked by two substituents (which included the C=O and the oxygen of the xanthone ring) and that the fourth methoxyl was adjacent to an aromatic ring proton. The chemical shift (δ6.65) of the singlet in the trisubstituted ring indicated that it could not correspond to H-1 or H-8 of a xanthone (for examples of δH-1 in 2,3,4-trisubstituted xanthones see [5, 9–14]). Consequently, the three substituents in the first ring had to be at positions 1, 2 and 3, with an –OH at C-3 and two methoxyls at C-1 and C-2, leaving two methoxyls for C-7 and C-8 of the second ring, or three methoxyls at C-1, C-2 and C-3, the hydroxyl at C-7 and the fourth methoxyl at C-8, as in **3a**.

That **3a** was the correct structure was established by HETCOR and selective INEPT experiments which allowed assignment of all carbons in the ^{13}C NMR spectra of the new xanthone and its acetate (Table 1). Thus, irradiation at the frequencies of H-4, H-5 and H-6 identified the signals of C-4, C-5 and C-6 in the ^{13}C NMR spectra of **3a** and **3b**, while similarly irradiation of the four –OMe signals identified the singlets of the C atoms to which they were attached; that singlet linked to the unencumbered methoxyl at δ56.2 remaining constant at

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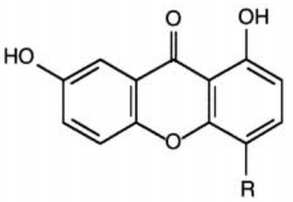

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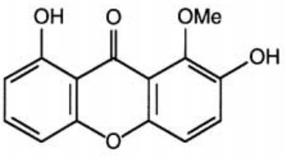

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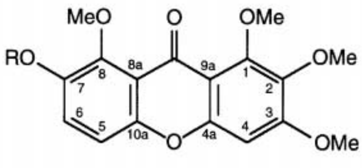

3 a R = H
b R = Ac

δ158.4. Since in contrast to the downfield shift of C-6 the chemical shift of C-4 had undergone no change on acetylation, the hydroxyl group of the new xanthone was located on C-7. The remaining ^{13}C signals of **3a,b** were assigned by selective INEPT experiments involving H-4, H-5 and H-6.

Final proof for structure **3a** of the new xanthone was provided by X-ray analysis. The result is shown in Fig. 1.

EXPERIMENTAL

Plant material

Wood of *C. maingayi* Dyer was collected in Kao Kichakoot National Park, Chantaburi, Thailand in February 1996. A voucher specimen is deposited in the herbarium of the Royal Forestry Department, Bangkok, Thailand.

Extraction and isolation

Powdered wood (2.4 kg) was percolated with MeOH at room temp. to exhaustion. Evapn of the soln at red. press. furnished the crude MeOH extract (110 g), which was dissolved in $CHCl_3$ at 40°, filtered and evaporated at red. press. to give 18 g of a gum. This was chromatographed over silica gel (450 g) and eluted with petrol–$CHCl_3$, 500 ml frs being collected as follows: frs 1–49 (petrol–$CHCl_3$, 4:1), 50–69 (petrol–$CHCl_3$, 1:1), 69–148 (petrol–$CHCl_3$, 3:7) and 149–168 (petrol–$CHCl_3$, 1:9).

Table 1. ^{13}C NMR spectra of **3a,b** ($CDCl_3$, 50 MHz)

C	**3a**	**3b**
1	153.4*s*	153.5*s*
2	139.3*s*	139.6*s*
3	158.4*s*	158.5*s*
4	95.4*d*	95.4*d*
4a	153.8*s*	153.5*s*
5	113.2*d*	112.8*d*
6	121.2*d*	128.1*d*
7	145.3*s*	139.9*s*
8	144.0*s*	154.2*s*
8a	116.3*s*	117.6*s*
9	174.9*s*	174.5*s*
9a	110.9*s*	111.1*s*
10a	149.9*s*	151.6*s*
1,2,8-OMe	62.6*q*, 62.0*q* 62.0*q*	62.4*q*, 62.0*q* 62.0*q*
3-OMe	56.2*q*	56.2*q*
Ac	–	169.4, 20.7*q*

Frs 1–69 contained nonpolar material which was not studied further. Frs 70–77 (1.3 g) were combined and purified by prep. TLC (silica gel, $CHCl_3$–Me_2CO–HCO_2H, 95:5:1) to give 19 mg of **2**. Frs 78–89 (1.0 g) on combination and purification by prep. TLC (silica gel, $CHCl_3$–Me_2CO–HCO_2H, 95:5:1) gave 8 mg of **2**. Frs 90–100 (0.48 g) on combination and purification by prep. TLC (silica gel, $CHCl_3$–Me_2CO–HCO_2H, 95:5:1) gave 15 mg of **2** and 15 mg of **1a**. Frs 101–124 (0.54 g) on purification by prep. TLC (silica gel, $CHCl_3$–Me_2CO–HCO_2H, 85:15:1) gave 17 mg of **1b**. Frs 125–168 (1.0 g) on purification in the same manner afforded 25 mg of **1b** and 45 mg of **3a**.

Acetylation of **1a** (7 mg), **1b** (12 mg), **2** (8 mg) and **3a** (10 mg) by Ac_2O–Py, followed by the usual work-up, afforded 6 mg, 10 mg and 6 mg of the diacetates of **1a**, **1b** and **2** and 8 mg of **3b**, respectively.

*1,7-Dihydroxyxanthone (**1a**)*

Physical properties and ^{1}H NMR spectra of **1a** and its acetate corresponded to those in the lit. [6, 7]. ^{13}C NMR (DMSO-d_6, 75 MHz): δ181.7 (C-9), 161.0 (C-1), 155.9 (C-3), 154.2 (C-4a), 149.4 (C-10a), 137.3 (C-3), 125.7 (C-6), 120.5 (C-8a), 119.5 (C-5), 109.7 (C-2), 108.0 (C-4), 107.9 (C-8) and 107.2 (C-9a).

*1,7-Dihydroxy-4-methoxyxanthone (**1b**)*

^{1}H NMR (DMSO-d_6, 300 MHz): δ11.99*s* (1-OH), 10.19 *brs* (7-OH), 7.59 (*d*, J = 9 Hz, H-5), 7.45 (*d*, J = 9 Hz, H-3), 7.44 (*d*, J = 2.6 Hz, H-8), 7.36 (*dd*, J = 9, 2.8 Hz, H6), 6.71 (*d*, J = 8.9 Hz, H-2), 3.88 (*s*, 3p, OMe); ^{13}C NMR (assignments by HETCOR and selective INEPT) δ 181.7 (C-9), 154.3 (C-10a), 153.3 (C-1), 145.2 (C-7), 139.9 (C-4), 125.8 (C-6), 120.5 (C-8a), 120.1 (C-3), 119.7 (C-5), 108.4 (C-9), 108.0 (C-2), 107.8 (C-8), 56.8 (OMe). ^{1}H NMR of diacetate ($CDCl_3$): δ7.95 *d* (J = 2.8 Hz, H-8), 7.61 (*d*, J = 9.0 Hz, H-5), 7.47 (*dd*, J = 9.1, 2.8 H-z, H-6), 7.23 (*d*, J = 8.8 Hz, H-2), 6.96 (*d*, J = 8.7 Hz, H-3), 4.04 (*s*, 3p, OMe), 2.47 and 2.34 (each *s* and 3p, Ac). ^{13}C NMR of diacetate (DMSO-d_6, assignments by HETCOR and selective INEPT): δ181.7 (C-9), 154.3 (C-10a), 153.3 (C-1), 149.4 (C-4a),

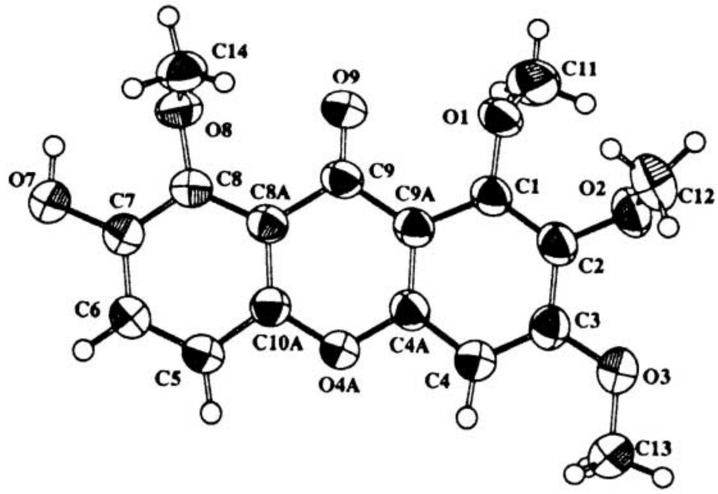

Fig. 1. Molecular structure of compound **3a** showing the atom-labelling scheme. H atoms are depicted as spheres of arbitrary radii. Displacement ellipsoids are shown at the 50% probability level.

139.9 (C-4), 125.8 (C-6), 120.5 (C-8a), 119.7 (C-5), 108.4 (C-9a), 108.0 (C-2), 107.8 (C-8), 56.8 (OMe).

2,8-*Dihydroxy*-1-*methoxyxanthone* (**2**)

The ^{1}H NMR spectra of **2** and its diacetate compared with those in the lit. [15]. ^{13}C NMR ($CDCl_3$, 75 MHz): δ182.1 (C-9), 162.0 (C-8), 155.8 (C-10a), 150.9 (C-4a), 145.5 (C-4), 144.2 (C-1), 136.6 (C-6), 123.4 (C-3), 114.8 (C-9a), 114.2 (C-2), 110.3 (C-7), 109.0 (C-8a), 106.5 (C-5), 62.8 (OMe). Assignments of multiplets were by HETCOR, others by selective INEPT.

7-*Hydroxy*-1,2,3,8-*tetramethoxyxanthone* (**3a**)

Yellow crystals, mp 218° ($CHCl_3$-petrol). EI-MS (70 eV) *m*/*z* (rel. int.) 332 ([M^+], 95), 317 (100), 299 (70), 274 (85), 259 (40), 231 (30); IR ν (cm^{-1}) (KBr) 3383 (OH), 2927, 1644, 1611, 1500, 1423, 1293, 1207, 1135, 1093. UV λ (nm, MeOH) (log ε) 359 (5.0), 307 (4.2), 283 (4.0) 259 (4.2), 241 (4.2); λ (nm, MeOH + NaOH) (log ε) 406 (3.3), 279 (4.3), 211 (4.3); λ (nm, MeOH + $AlCl_3$) (log ε) 358 (3.8), 249 (4.5). ^{1}H NMR (300 MHz, $CDCl_3$): δ7.31 (*d*, J = 9.1 Hz, H-6), 7.10 (*d*, J = 9.1 Hz, H-5), 6.65 (*s*, H-4), 4.03, 4.01, 3.96, 3.90 (all *s* and 3p, -OMe). ^{1}H NMR of monoacetate: δ7.34 (*d*, J = 9.1 Hz, H-6), 7.16 (*d*, J = 9.1 Hz, H-5), 6.67*s* (H-4), 4.01, 3.97, 3.97, 3.91 (all *s* and 3p, –OMe), 2.18 (*s* and 3p, Ac); ^{13}C NMR of **3a,b** in Table 1.

X-ray diffraction analysis of **3a**

Crystals suitable for X-ray diffraction studies were obtained by slow evapn of a satd $CHCl_3$–petrol soln. They belonged to $P2_1/c$ space group with cell dimensions a = 14.134(7) Å, c = 17.304(12) Å and β = 127.95(6); z = 4. The calculated density is $D_x = 1.41$ g cm^{-3}. Of the 14498 reflections measured, at room temp., with a Stoe IPDS image plate equipped with Mo Kα radiation, 3754 were independent reflections and 2697 were observed ($I > 2\sigma I$). The structure was solved using SHELXS86 [16] and refined with SHELXL93 [17]. Refinement of positional and anisotropic thermal parameters for all non-hydrogen atoms converged to $R[F^2 > 2\sigma(F^2)]$ = 0.05 and wR = 0.15. All hydrogen atoms except those from one methyl group were found in the difference Fourier map; therefore, the hydrogen positions around C-11 were calculated assuming the tetrahedral environment for the carbon atom and refined using the riding model. Tables containing the final fractional coordinates, temperature parameters, bond distances and bond angles will be deposited with the Cambridge Crystallographic Data Centre, Cambridge, England. The three rings in the structure define a plane with a r.m.s. deviation for the fitted atoms of 0.031 Å; the maximum deviation of the oxygen atoms not considered in the calculation of the least squares plane is 0.26 Å. A perspective view of the molecule showing the atomic numbering scheme was obtained using XPMA [18] and ORTEP [19] and is given in Fig. 1.

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