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FERRXANTHONE, A 1,3,5,6-TETRAOXYGENATED XANTHONE FROM *MESUA FERREA*

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Key Word Index—*Mesua ferrea*; Guttiferae; heartwood; 1,3-dimethoxy-5,6-dihydroxyxanthone; ferrxanthone.

Abstract—A new xanthone was isolated from the heartwood of *Mesua ferrea* and its structure determined by UV, IR, NMR and mass spectrometry as 1,3-dimethoxy-5,6-dihydroxyxanthone.

INTRODUCTION

Mesua ferrea, a plant containing a variety of medicinal and biocidal compounds, has been subjected to intensive chemical investigations [1–5]. In the course of our search for new biocidal compounds, a reinvestigation of the heartwood of *M. ferrea* has now yielded besides the known compounds a new 1,3,5,6-tetraoxygenated xanthone, for which we give the trivial name 'ferrxanthone', from the more polar fractions. It also occurs in the bark. In this communication, we report its structure as **1** which to our knowledge is the first report of the occurrence of a tetraoxygenated xanthone from this source.

RESULTS AND DISCUSSION

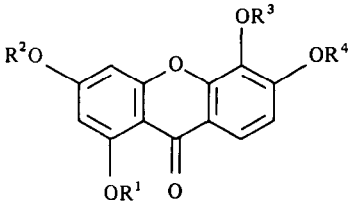
Ferrxanthone (**1**), obtained from the polar fractions by *n*-butanol extractions and chromatography was crystallized from pyridine–methanol mp 294–295°. On the basis of elementary analysis and mass spectrometry, the molecular formula was assigned as $C_{15}H_{12}O_6$.

The xanthone (**1**) gave a blue colour with alcoholic ferric chloride. It formed a diacetate (**4**) with acetic anhydride–pyridine, a dimethyl ether (**2**) with dimethyl sulphate–potassium carbonate and a monomethyl ether (**3**) with methyl iodide–potassium carbonate. Hence the compound was a dihydroxydimethoxy xanthone in which the two hydroxyl groups were not chelated (^{1}H NMR spectrum). Since its monomethyl ether (**3**) also did not give any colour with alcoholic ferric chloride, the possibility of the presence of a chelated-hydroxyl group was further ruled out.

The UV spectrum of **1** showing λ_{max} at 244, 282, 312 nm is characteristic of a 1,3,5,6-tetraoxygenated xanthone [6]. The xanthone was soluble in dilute sodium carbonate solution and showed a strong bathochromic shift of the K band on addition of sodium acetate typical of 3-hydroxyxanthones [7]. The presence of an *ortho* dihydroxy group in the molecule is indicated by a positive Tollen's test and by a bathochromic shift of 12 and 48 nm induced by sodium acetate–boric acid and aluminium chloride, respectively. Regeneration of the ethanol spectrum on the addition of hydrochloric acid further confirmed the presence of two hydroxyl groups *ortho* to each other at the C-5 and C-6 positions.

The presence of one pair each of *ortho*-coupled and *meta*-coupled protons in two different aromatic rings is evident from the ^{1}H NMR of **1** which showed four aromatic protons exhibiting *meta* and *ortho* split doublets at 6.53, 6.72 (J = 2.5 Hz) and 6.90, 7.50 (J = 8.5 Hz). Since the ^{1}H NMR signal of H-2 always appears at somewhat higher field than that of H-4 for a given set of hydroxyl or methoxyl substituents [8], the singlets at 6.53 and 6.72 were assigned to H-2 and H-4, respectively. Similarly of the two *ortho* coupled protons, a low field doublet was assigned to the C-8 hydrogen because such protons resonate at lower field due to an anisotropic effect of the carbonyl group. Acetylation of **1** caused a 0.16 ppm downfield shift [9, 10] of the H-7 and H-8 signals in the ^{1}H NMR spectrum (related to its position in the permethyl ether). However, *meta* coupled protons remain unaffected. Thus the two hydroxyl groups must be situated at the C-5 and C-6 positions.

In the mass spectrum of **1**, apart from the dominant $[M]^+$ peak at m/z 288 significant fragment ion peaks appeared from the loss of H, OH and H_2O ions which is due to the operation of an *ortho*-effect caused by the OMe substituent at C-1. The most intense peak was observed when CHO was lost from the $[M]^+$. The appearance of a characteristic doubly charged ion peak corresponding to $[M-CO]^{2+}$ at m/z 130 along with $[M-CO]^+$ and $[M-C_2H_3O]^+$ confirm the existence of a second methoxyl



1 $R^1 = R^2 = Me$, $R^3 = R^4 = H$
2 $R^1 = R^2 = R^3 = R^4 = Me$
3 $R^1 = R^2 = R^4 = Me$, $R^3 = H$
4 $R^1 = R^2 = Me$, $R^3 = R^4 = Ac$

*Contribution No. 234.

group at C-3. These findings are in accordance with similar observations made for xanthones having methoxyl substituents at C-1 and C-3 [11]. On the basis of these studies, ferrxanthone was assigned the structure 1,3-dimethoxy-5,6-dihydroxyxanthone (**1**) which is also supported by biogenetic considerations [12].

EXPERIMENTAL

Mps are uncorr. UV spectra were recorded in EtOH soln. IR spectra were determined in KBr or Nujol. MS were recorded at 70 eV. ^{1}H NMR were measured at 90 MHz in $CDCl_3$–DMSO-d_6 and chemical shifts are given in δ (ppm) scale relative to TMS. Silica gel was used for TLC and spots were visualised with I_2 vapours and UV fluorescence.

Isolation and purification. Finely chipped heartwood of *M. ferrea* L. procured from Kerala (South India) was extracted successively with *n*-hexane, $CHCl_3$ and EtOH. The $CHCl_3$ extract after silica gel chromatography (petrol–$CHCl_3$) yielded besides β-sitosterol and stigmasterol, six known xanthones which were identified as 2-methoxyxanthone, 1,7-dihydroxyxanthone, 1,5-dihydroxyxanthone, 1-hydroxy-7-methoxyxanthone, 1,5,6-trihydroxyxanthone and 1,5-dihydroxy-3-methoxyxanthone (mp, TLC and MS). The EtOH extract was concd under red. pres. to give a residue which was partitioned between *n*-BuOH and H_2O. The organic layer was evapd *in vacuo* and the residue was repeatedly chromatographed by silica gel CC using $CHCl_3$–MeOH (2:1) as eluent to give xanthone (**1**).

1,3-*Dimethoxy*-5,6-*dihydroxyxanthone* (**1**). Crystallised from pyridine–MeOH as colourless fine needles, mp 294–295°. UV λ_{max}^{EtOH} nm (log ε): 244 (4.71), 282 (4.41), 312 (4.50); $\lambda_{max}^{EtOH-NaOAc}$ nm (log ε): 244 (4.71), 284 (4.42), 337 (4.60); $\lambda_{max}^{AlCl_3}$ nm (log ε): 244 (4.75), 315 (4.20), 3.60 (3.66); $\lambda_{max}^{AlCl_3-HCl}$ nm (log ε): 244 (4.83), 282 (4.40); 312 (4.49); $\lambda_{max}^{NaOAc-H_3BO_3}$ nm (log ε): 254 (4.75), 282 (4.55), 324 (4.57). IR ν_{max}^{KBr} cm^{-1}: 3250–3450 (OH), 1750, 1600 (>C=O). ^{1}H NMR (DMSO-d_6): δ3.92 (3H, *s*, OMe), 3.98 (3H, *s*, OMe), 6.53 (1H, *d*, *J* = 2.5 Hz, C-2), 6.72 (1H, *d*, *J* = 2.5 Hz, C-4), 6.9 (1H, *d*, *J* = 8.5 Hz, C-7), 7.50 (1H, *d*, *J* = 8.5 Hz, C-8). MS *m/z* (rel. int.): 288 ([M]$^+$, 100), 287 ([M − H]$^+$, 55), 271 ([M − OH]$^+$, 19), 270 ([M − H_2O]$^+$, 7), 260 ([M − CO]$^+$, 13), 259 ([M − CHO]$^+$, 90), 258 ([M − CH_2O]$^+$, 47), 257 ([M − OMe]$^+$, 32), 245 ([M − CO − Me]$^+$, 14), 243 ([M − CO − OH]$^+$, 15), 242 ([M − H_2O − CO]$^+$, 54) and 130 ([M − CO]$^{2+}$, 15.8). (Found: C, 62.0; H, 4.2, $C_{15}H_{12}O_6$ requires C, 62.3; H, 4.2%.)

1,3,5,6-*Tetramethoxyxanthone* (**2**). A soln of **1** (50 mg) in dry Me_2CO was refluxed for 48 hr with Me_2SO_4–K_2CO_3 to yield a product which crystallized from $CHCl_3$–hexane as colourless fine needles, mp 142–144° (lit. [13] mp 146–147°). ^{1}H NMR ($CDCl_3$): δ3.98, 4.05, 4.09 (All *s*, 12H, 4 × OMe), 6.41 (1H, *d*, *J* = 2.5 Hz, C-2), 6.67 (1H, *d*, *J* = 2.5 Hz, C-4), 7.05 (1H, *d*, *J* = 8.5 Hz, C-7), 8.10 (1H, *d*, *J* = 8.5 Hz, C-8). (Found: C, 64.1; H, 4.9, $C_{17}H_{16}O_6$ requires C, 64.5; H, 5.1%.)

1,3,6-*Trimethoxy*-5-*hydroxyxanthone* (**3**). Compound **1** (50 mg) on methylation with K_2CO_3–MeI in dry Me_2CO at room temp. afforded **3** as white fine needles from MeOH, mp 251–252° (lit. [14], mp 254–255°. ^{1}H NMR ($CDCl_3$): δ3.90, 3.95, 4.0 (all *s*, 9H, 3 × OMe), 6.25 (1H, *d*, *J* = 2.5 Hz, C-2), 6.50 (1H, *d*, *J* = 2.5 Hz, C-4), 6.85 (1H, *d*, J = 8.5 Hz, C-7), 7.92 (1H, *d*, *J* = 8.5 Hz, C-8). (Found: C, 63.4; H, 4.2. $C_{16}H_{14}O_6$ requires C, 63.6; H, 4.6%.)

1,3-*Dimethoxy*-5,6-*diacetoxyxanthone* (**4**). Treatment of **1** (50 mg) with Ac_2O–pyridine at room temp. for 24 hr yielded the diacetate (**4**) (40 mg) which was crystallized from MeOH as fine needles, mp 214–215°. ^{1}H NMR ($CDCl_3$): δ2.4 (3H, *s*, OAc), 2.5 (3H, *s*, OAc), 3.95 (3H, *s*, OMe), 4.20 (3H, *s*, OMe), 6.44 (1H, *d*, *J* = 2.5 Hz, C-2), 6.51 (1H, *d*, *J* = 2.5 Hz, C-4), 7.20 (1H, *d*, *J* = 8.5 Hz, C-7), 8.26 (1H, *d*, *J* = 8.5 Hz, C-8). MS *m/z* (rel. int. %): 372 ([M]$^+$, 85). (Found: C, 61.6; H, 4.5. $C_{19}H_{16}O_8$ requires C, 61.3; H, 4.3%.)

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