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LEIAXANTHONE, A 1,3,5,6-TETRAOXYGENATED XANTHONE FROM *HAPLOCLATHRA LEIANTHA*

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Key Word Index—*Haploclathra leiantha*; Guttiferae; trunk wood; 1,3-dihydroxy-5,6-dimethoxyxanthone; leiaxanthone.

Abstract—A new xanthone was isolated from the trunk wood of *Haploclatha leiantha* and its structure determined by UV, IR and mass spectrometry as 1,3-dihydroxy-5,6-dimethoxyxanthone.

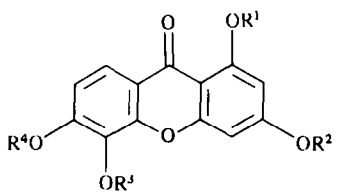
INTRODUCTION

Haploclathra leiantha (Benth) Benth., a native of the Amazonia region, is a tree which grows up to a height of 15 m. The plant was collected in the region of the lower Rio Negro-Rio Jafari, from a specimen identified by the botanist Klaus Kubitzki, Dept. of Botany, Hamburg University (Herb. no. 58569, Instituto Nacional de Pesquisas da Amazonia, INPA, Brazil).

Only one species of this genus (*H. verticillata*) has been investigated before [1]. Investigation of the trunk wood of *H. leiantha* has yielded besides previously known compounds (see Experimental) a new 1,3,5,6-tetraoxygenated xanthone, for which we give the trivial name leiaxanthone. We report its structure as **1**; the isolation and identification of this xanthone constitute the subject of the present paper.

RESULTS AND DISCUSSION

Leiaxanthone (**1**), obtained from the chloroform–methanol fractions by chromatography of ethanol extract of the trunk wood, showed mp 205–207°. On the basis of elementary analysis and mass spectrometry, the molecular formula was assigned as $C_{15}H_{12}O_6$. The xanthone (**1**) formed a monomethyl ether (**2**) with diazomethane and a dimethylether (**3**) with dimethyl sulphate–potassium carbonate. Hence the compound was a dihydroxydimethoxyxanthone in which one of the hydroxyl groups is chelated.



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

The UV spectrum of **1** showed λ^{max}_{EtOH} 246, 285, 318 nm (ε resp. 28 000, 7500, 15 300) is characteristic of a 1,3,5,6-tetraoxygenated xanthone [2]. The aluminium chloride shift also proves the presence of a hydroxyl group at the *ortho*-position relative to the carbonyl [3]. The presence of the 1,3,5,6-tetraoxygenated system was confirmed by methylation of **1** with diazomethane. The monomethyl ether of the xanthone (**2**) was found to be identical with 1-hydroxy-3,5,6-trimethoxyxanthone [2]. Exhaustive methylation with dimethyl sulphate–potassium carbonate yielded a dimethyl ether derivative (**3**) which was found to be identical with 1,3,5,6-tetramethoxyxanthone [4] in all aspects.

Besides the transformation into derivatives, the 1,3,5,6-tetraoxygenated system of **1**, was confirmed by the presence of one pair of *ortho*-coupled and *meta*-coupled protons in two different aromatic rings evidenced by the ^{1}H NMR spectrum.

The other hydroxyl group could be located at C-3, C-5 or C-6. The use of sodium acetate as an additive in the UV spectrum provides selective information. Being a weaker base it ionizes only the hydroxyl at C-3 to much the same extent that sodium hydroxide does. Accordingly, 3-hydroxyxanthones give rise to identical bathochromic shifts of the UV maxima in the presence of either sodium hydroxide or sodium acetate. The same phenomenon is observed with 1,6-dihydroxyxanthone. The 1,3-dihydroxy system, however, is less acidic since the curves in the presence of the two additives are not quite superimposable [3] as in this case. Furthermore the suggestion of 1,6-dihydroxy-3,5-dimethoxy xanthone for compound **1** can be ruled out by comparing mp, UV and IR data with those in the literature [2, 5].

The remaining alternative structures could both be considered now by putting the hydroxyl group at C-3 or C-5. The correct position can be conveniently ascertained by comparing wavelengths and extinction coeficients of the K bands in the UV spectra of hydroxyxanthones in the absence and in the presence of sodium acetate. [6]. Whilst 1,5-dihydroxyxanthone does not show any bathochromic shift in its K band (λ EtOH + NaOAc − λ EtOH and the extinction coefficient (ε EtOH + NaOAc/ε EtOH) is equal to 1, and the values found for 1,3-dihydroxyxanthone are

respectively 47 nm and 1.1, close to the values of 52 and 1.1, found for the xanthone (1). Thus, the hydroxyl group must be located at the C-3 position, leaving the C-5 and C-6 positions for the additional two methoxy groups. The data for the mp and the UV spectrum of the xanthone (1) also do not agree with the literature [7] values for 1,5-dihydroxy-3,6-dimetoxyxanthone.

The mass spectrum showed a dominant $[M]^+$ peak at *m/z* 288 (100%), as well as significant ion peaks of fragments at *m/z* 273 $[M-Me]^+$ (12%), 259 $[M-CHO]^+$ (21%), 145 $[M-C_2H_3O]^+$ (68%) and 130 $[M-CO]^{2+}$ which are in accordance with the proposed structure. On the basis of these studies and biogenetic considerations [8] we propose the structure 1,3-dihydroxy-5,6-dimethoxyxanthone for compound 1.

EXPERIMENTAL

Mps are uncorr. Separation by CC was carried out using Merck Kieselgel 0.063–0.200 mm and Merck Macherey Nagel and CO polyamide CC6 (< 0.07 mm). TLC employed Merck Kieselgel 60 G and spots were visualized with I_2 vapour and UV fluorescence. IR spectra were determined in KBr pellets; only major bands are quoted. UV spectra were determined in 90% EtOH soln and additives (excess $NaOAc \cdot 3H_2O$, $AlCl_3 \cdot 6H_2O$ or drops of 20% NaOH) were introduced in equal amounts into the cell containing the soln and the cell containing the blank. Only MS peaks with a rel. int. above 10% are quoted.

Isolation and purification of constituents. Powdered trunk wood of *H. leiantha* (6 kg) was continuously extracted with hot EtOH in a Soxhlet apparatus. Removal of solvent gave a residue (247.3 g). Part (118 g) was chromatographed on silica gel (620.0 g) using C_6H_6, $CHCl_3$ and MeOH as eluents. Several fractions were collected and separated into three groups (A_1–A_3) by TLC.

A_1 (4.610 g) was repeatedly chromatographed on silica gel giving lupeol (1.3 g), sitosterol (0.2 g), hexanoic acid (0.1 g) and friedelin (0.05 g), all being identified by comparison with authentic samples (TLC, mp, mmp, IR and MS). A_2 (5.140 g) was repeatedly chromatographed on silica gel and separated by fractional crystallization from EtOH into 2,8-dihydroxy-1-methoxyxanthone (0.5 g) and 1,5-dihydroxy-3-methoxyxanthone (0.03 g). A_3 (13.077 g) was chromatographed on silica gel (90 g) using C_6H_6, EtOAc and MeOH as eluents. Several fractions were collected and separated into nine groups (B_1 to B_9) by TLC. B_1 (0.7 g) was recrystallized from EtOH giving an additional amount of 2,8-dihydroxy-1-methoxyxanthone (0.2 g). B_2 (1.1 g) was recrystallized from EtOH giving 2,8-dihydroxy-1,6-dimethoxyxanthone (0.5 g). B_3 (0.13 g) was recrystallized from EtOH giving an additional amount of 1,5-dihydroxy-3-methoxyxanthone (0.03 g). B_4 (2.2 g) was chromatographed on silica gel (25 g) using *n*-hexane, EtOAc and MeOH as eluents. Repeated TLC of the EtOAc fraction yielded the xanthone 1 (0.15 g). B_7 (0.8 g) after isolation by TLC yielded 1,3,5-trihydroxy-6-methoxyxanthone (0.1 g). B_8 (2.4 g) was chromatographed on polyamide CC6, giving 3-hydroxy-1,5,6-trimethoxyxanthone as the major product, after washing with Et_2O and sublimation (0.06 g). B_9 (1.1 g) after washing with MeOH and sublimation yielded 1,3-dimethoxy-5,6-dihydroxyxanthone (0.05 g) known as ferrxanthone. The other groups of the fractions will be studied in the future. All of the known xanthones had their structures confirmed by mp, TLC, IR, MS, and NMR, agreeing with lit. values. They were also converted into derivatives (partial methylation with CH_2N_2 and total methylation with Me_2SO_4–K_2CO_3) and compared with authentic samples available in our laboratory.

1,3-Dihydroxy-5,6-dimethoxyxanthone (1). Yellow crystals, mp 205–207°. UV λ_{max}^{EtOH} nm: 246, 285, 318 (ε resp. 28 000, 7500, 15 300); $\lambda_{max}^{EtOH+NaOH}$ nm: 246, 264, 286 sh, 374 (ε resp. 21 000, 16 100, 6300, 14 700) acidification restored the spectrum in EtOH; $\lambda_{max}^{EtOH+NaOAC}$ nm: 243, 266, 285, 370 (ε resp. 20 700, 15 000, 10 000, 17 000); $\lambda_{max}^{EtOH+NaOAC+H_3BO_3}$ nm: identical to the spectrum in EtOH; $\lambda_{max}^{EtOH+AlCl_3}$ nm: 238, 253, 265 sh, 285 sh, 329 (ε resp. 16 700, 18 400, 15 300, 7200, 15 300); IR ν_{max}^{KBr} cm^{-1}: 3480–3260, 1655, 1600, 1575, 1505, 1160, 1100, 960, 800, 690. ^1H NMR (DMSO-d_6): δ 12.70 (1H, *s*, OH), 3.95 (3H, *s*, OMe), 3.98 (3H, *s*, OMe), 6.30 (1H, *d*, *J* = 2.5 Hz, C-2), 6.45 (1H, *d*, *J* = 2.5 Hz, C-4), 6.90 (1H, *d*, *J* = 8.5 Hz, C-7), 7.70 (1H, *J* = 8.5 Hz, C-8). MS *m/z* (rel. int): 288 $[M]^+$ (100), 273 $[M-Me]^+$ (12), 259 $[M-CHO]^+$, (21), 245 $[M-CO-Me]^+$ (68) and 130 $[M-CO]^{2+}$ (23). (Found: C, 62.25; H, 4.12, $C_{15}H_{12}O_6$ requires C, 62.58; H, 4.20%.)

1-Hydroxy-3,5,6-trimethoxyxanthone (2). A soln of 1 (50 mg) was methylated with CH_2N_2 in Et_2O soln, giving 2 as yellow needles, mp 185–187° (lit. [9] 181–183°). UV λ_{max}^{EtOH} nm: 245, 280 sh, 315, 340 (ε resp. 46 500, 10 500, 23 200, 9300); IR ν_{max}^{KBr} cm^{-1}: 3500–3200, 1655, 1600, 1565, 1505, 1150, 1110, 960, 800, 695; ^1H NMR ($CDCl_3$): δ 12.70 (1H, *s*, OH), 3.88 (3H, *s*, OMe) 3.98 (3H, *s*, OMe), 4.00 (3H, *s*, OMe), 3.70 (1H, *d*, *J* = 2.5 Hz, C-2), 3.50 (1H, *d*, *J* = 2.5 Hz, C-4), 3.05 (1H, *d*, *J* = 8.5 Hz, H-7) 2.05 (1H, *d*, *J* = 8.5 Hz, C-8). MS *m/z* (rel. int.): 302 $[M]^+$ (100), 287 ($[M-Me]^+$ (20), 273 $[M-CHO]^+$ (21), 272 $[M-CH_2O]^+$ (12), 259 ($[M-CO-Me]^+$ (67).

1,3,5,6-Tetramethoxyxanthone (3). A soln of 1 (50 mg) in dry Me_2CO was methylated with Me_2SO_4–K_2CO_3, yielding 3 as colourless crystals, mp 141–143°, (lit. [10] 142–145°). UV λ_{max}^{EtOH} nm: 245, 285 sh, 305 (ε resp. 38 300, 9400, 17 100); IR ν_{max}^{KBr} cm^{-1} : 2940, 1620, 1595, 1565, 1505, 1485, 1215, 1200, 1120, 975, 790, 700. ^1H NMR ($CDCl_3$): δ 3.98–4.10 (All *s*, 12H, 4 × OMe), 6.40 (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).

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