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QUINONE AND XANTHONE CONSTITUENTS OF *KIELMEYERA RUPESTRIS*[1]

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Abstract—The compounds 2,6-dimethoxy-1,4-benzoquinone, 2-hydroxy-1-methoxyxanthone, 3-hydroxy-1,2-dimethoxyxanthone, 4-hydroxy-2,3-dimethoxyxanthone, 4-methoxy-2,3-methylenedioxyxanthone, 5-hydroxy-1,3-dimethoxyxanthone, 1,5-dihydroxy-3-methoxyxanthone and 3-hydroxy-1,5,6-trimethoxyxanthone were isolated from *Kielmeyera rupestris* A. P. Duarte.

THE MORPHOLOGICAL characters of *Kielmeyera rupestris* A. P. Duarte, a new species of the Guttiferae family, were recently described.[2] A phytochemical examination of its wood revealed the presence of 2,6-dimethoxy-1,4-benzoquinone, identified by direct comparison with a synthetic sample. In addition, seven xanthones were isolated. Among these, 2-hydroxy-1-methoxyxanthone,[3] 3-hydroxy-1,2-dimethoxyxanthone,[4] 4-hydroxy-2,3-dimethoxyxanthone,[3,5] 4-methoxy-2,3-methylenedioxyxanthone,[5] 5-hydroxy-1,3-dimethoxyxanthone[3,5] and 1,5-dihydroxy-3-methoxyxanthone[3,5] had already been isolated previously from *K. speciosa* St. Hil.,[3,4] *K. corymbosa* (Spr.) Mart.[5] and *K. coriacea* Mart.,[5] and were identified by direct comparison with authentic samples.

Only one compound proved to be new. Its molecular weight indicated a monohydroxy-trimethoxyxanthone structure. NMR spectrometry showed that the four substituents were located at carbons 1, 3, 5 and 6 of the xanthone skeleton,[6] which was confirmed by showing that the monomethyl ether was identical with an authentic sample of 1,3,5,6-tetramethoxyxanthone (Ia). It was easily ascertained that the hydroxyl is not either at C-1, since no u.v. spectral shift was observed upon addition of $AlCl_3$, or at C-5, since the Gibbs test curve[7] was unmistakably negative.

Both the remaining alternative structures should display the usual high acidity of 3-hydroxyxanthones[7] in view of the *para* relationship of the hydroxyl and the carbonyl groups. It was expected, however, that Ic, with its hydroxyl function *ortho* to an inductively electron-withdrawing methoxyl group, would be more highly acidic than Ib. This hypothesis was

[1] Part XVIII in the series "The Chemistry of Brazilian Guttiferae"; for Part XVII see: O. R. GOTTLIEB, A. A. LINS MESQUITA, E. MARTINS DA SILVA and M. TEIXEIRA DE MELO, *Phytochem.* **8**, 665 (1969).

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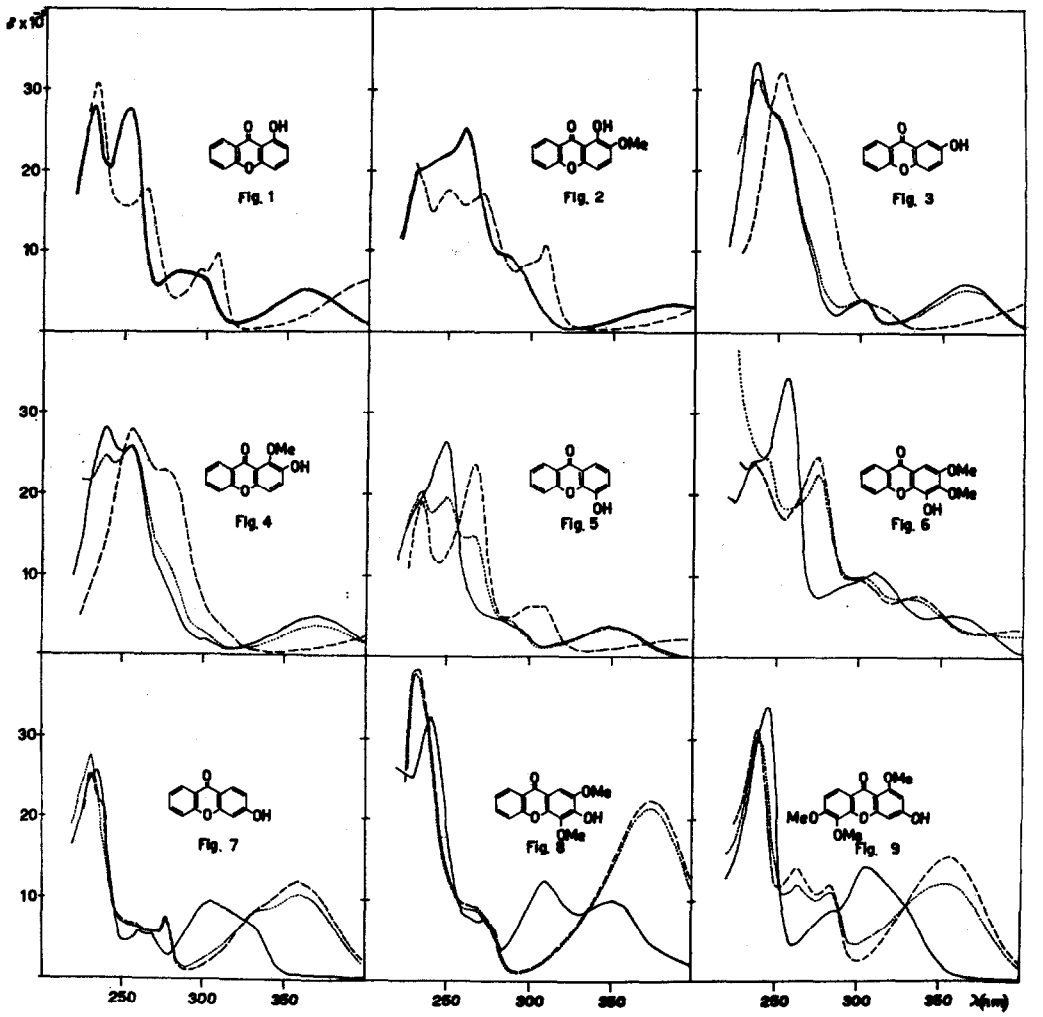
shown to be correct when tested on a series of model compounds and led to a simple analytical method for detecting the position of xanthone hydroxyl groups.

The relative acidity of the phenolic hydroxyls on one of the four different positions of the xanthone skeleton can be conveniently ascertained by comparing the u.v. absorption spectra of the substance in neutral medium with that in the presence of a weak base such as



FIGS. 1–9. ULTRAVIOLET SPECTRA OF XANTHONES IN EtOH (——), EtOH + NaOH (------) AND EtOH + NaOAc (·····).

sodium acetate.[7] Such spectra are superimposable for 1-hydroxyxanthones even when these derivatives have an additional oxygen function at the 2-position (Figs. 1 and 2). The spectra are still superimposable for 2-hydroxyxanthones which have no *ortho* substitution (Fig. 3), but when oxygen functions are present at C-1 or C-3 slight hyper- or hypochromic effects appear, as shown in Fig. 4. Similar slight effects characterize the spectra of simple 4-hydroxyxanthones (Fig. 5); when, however, these compounds are also substituted at C-3 batho-

chromic shifts of the principal maxima occur (Fig. 6). Such bathochromic shifts, usually somewhat more pronounced, are given by the 3-hydroxyxanthones (Fig. 7). It should be noted that in the NaOAc spectra of 3-methoxy-4-hydroxyxanthones and of 3-hydroxyxanthones the displaced K bands do not show enhanced intensity (Table 1). Strong hyperchromic effects are, however, typical of 3-hydroxyxanthones which sustain additional oxy groups at the 2- or 4-positions (Fig. 8, Table 1). Only one exception to this rule

TABLE 1. COMPARISON OF WAVELENGTHS AND EXTINCTION COEFFICIENTS OF THE K BANDS IN THE U.V. SPECTRA OF HYDROXYXANTHONES (IN EtOH) IN THE ABSENCE (K)* AND IN THE PRESENCE (K′) OF NaOAc

Xanthone	$\lambda_{K'} - \lambda_K$ (nm)	$\epsilon_{K'}/\epsilon_K$	Xanthone	$\lambda_{K'} - \lambda_K$ (nm)	$\epsilon_{K'}/\epsilon_K$
1-OH†	0	1·0	1,5-diOH-3-OMe[5]	0	0·7
1-OH-2-OMe†	0	1·0	Guanandin[15]‡	0	1·0
1-OH-3-OMe†	0	1·0	Isoguanandin[15]§	0	1·0
1-OH-4-OMe†	0	1·0			
1-OH-7-OMe[8]	0	1·0	4-OH-2,3-diOMe[5]	25	0·7
1-OH-3,5-diOMe[5]	0	1·0	4-OH-2,3-OCH_2O[5]	27	0·9
1-OH-7,8-diOMe[9]	0	1·0	1,5-diOH-6-OMe[16]	15	0·7
1-OH-5,6-diOMe[9]	0	1·0			
1-OH-3,4-diOMe†	0	1·0	3-OH†	55	1·1
1-OH-3,7-diOMe[10]	0	1·0	1,3-diOH†	47	1·1
1-OH-3,5,6-triOMe[11]	0	1·0	1,3-diOH-7-OMe[17]	40	1·1
			1,3,5-triOH[5]	26	1·0
2-OH†	0	0·9	3-OH-1,5,6-triOMe	50	0·9
1,7-diOH[8]	0	1·0			
1,2-diOH†	0	1·0	3-OH-2-OMe†	65	1·8
2-OH-1-OMe[12]	0	1·0	2,3-diOH†	64	1·7
2-OH-3-OMe†	0	0·9	3-OH-1,2-diOMe[4]	52	1·4
1,2-diOH-3-OMe†	0	1·0	2,3-diOH-1-OMe[4]	51	1·4
1,7-diOH-8-OMe[9]	0	1·0	3-OH-2,4-diOMe[4]	66	1·6
1,7-diOH-3,6-diOMe†	0	1·0	2,3-diOH-4-OMe†	66	1·8
			3,4-diOH-2-OMe[5]	50	1·3
4-OH[13]	0	1·0	1,6-diOH[14]	56	1·7
1,4-diOH†	0	1·0	1,6-diOH-5-OMe[16]	60	1·7
1,5-diOH[14]	0	1·0	1,5,6-triOH[16]	30	1·3
5-OH-1,3-diOMe[5]	0	1·0	1,3,8-triOH-7-OMe[18]	25	1·6

* λ_{max} in EtOH from 280 to 350 nm; ϵ 5000 to 17000.
† These compounds were synthesized in our laboratory by A. A. Lins Mesquita and G. G. de Oliveira.
‡ 1,5-Dihydroxy-6-(3,3-dimethylallyl)-xanthone.
§ 1,5-Dihydroxy-8-(3,3-dimethylallyl)-xanthone.

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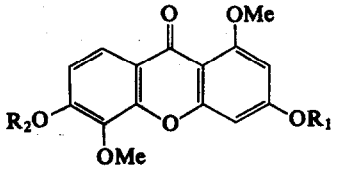
has been observed so far. Also 1,6-dihydroxyxanthones give rise to strong batho- and hyperchromic spectral shifts upon addition of sodium acetate (Table 1).

Comparison of the u.v. spectra in neutral and in sodium acetate media of the new xanthone isolated from *K. rupestris* showed a strong red shift typical of 3-hydroxyxanthones, unaccompanied by enhancement of intensity of the K band (Fig. 9). While the substance thus clearly sustains a hydroxyl which is conjugated with the carbonyl, the *ortho* positions to this hydroxyl must be free of substitution. In conjunction with the above-mentioned data, this fact is compatible only with the structure of 3-hydroxy-1,5,6-trimethoxyxanthone (Ib).

Confirmation of this proposal was obtained by comparison of the NMR spectra of Ib and its monoacetate (Id). The expected paramagnetic shift, due to the introduction of the acetyl group, affected chiefly the bands attributed to the protons at C-2 and C-4. The original hydroxyl thus must be situated at C-3.



(Ia) $R_1 = R_2 = Me$
(Ib) $R_1 = H$, $R_2 = Me$
(Ic) $R_1 = Me$, $R_2 = H$
(Id) $R_1 = Ac$, $R_2 = Me$

EXPERIMENTAL

M.ps. were determined using a Kofler hot-stage microscope and are uncorrected. Separation by column chromatography was carried out using 50 times the weight of the mixture of Merck Kieselgel 0·05–0·20 mm. TLC employed Merck Kieselgel G. i.r. spectra were determined in KBr pellets using a Perkin–Elmer Infracord model 137B spectrometer. Only major bands are quoted. U.v. spectra were determined on 95% EtOH soln., using a Beckman DU spectrophotometer. Additives (excess of $NaOAc.3H_2O$, $AlCl_3.6H_2O$, or 2 drops of 20% NaOH)were introduced in equal amounts into the cell containing the solution and the cell containing the blank. Mass spectra were obtained with an AEI instrument model MS-9, operating at an ionizing voltage of 70 eV. Only peaks with an intensity of over 15% of the base peak are quoted. NMR spectra were taken in $CDCl_3$ solution with a Varian HA-60-IL instrument.

Benzene extraction of the wood of Kielmeyera rupestris. *Isolation of β-sitosterol, 3-hydroxy-1,2-dimethoxyxanthone, 3-hydroxy-1,5,6-trimethoxyxanthone, 4-hydroxy-2,3-dimethoxyxanthone, 1,5-dihydroxy-3-methoxyxanthone, 5-hydroxy-1,3-dimethoxyxanthone, 4-methoxy-2,3-methylenedioxyxanthone, 2-hydroxy-1-methoxyxanthone.* The powered wood (8·6 kg) was continuously extracted with hot benzene. Removal of the solvent gave a residue (30 g) which was extracted with dil. Na_2CO_3. The aqueous solution was acidified and the precipitate (6·5 g) which appeared was separated by filtration, dried and chromatographed on silica, giving various fractions with the indicated eluants: $CHCl_3$ (A_1, A_2 in this order), $CHCl_3$–MeOH, 99:1 (A_3), $CHCl_3$–MeOH, 98:2 (A_4):

A_1 was separated by fractional crystallization from ethanol into 3-hydroxy-1,2-dimethoxyxanthone (10 mg) and 3-hydroxy-1,5,6-trimethoxyxanthone (8 mg): A_2 was crystallized from ethanol, yielding 4-hydroxy-2,3-dimethoxyxanthone (9 mg): A_3 was crystallized from ethanol, yielding 1,5-dihydroxy-3-methoxyxanthone (15 mg): A_4 was crystallized from ethanol, yielding 5-hydroxy-1,3-dimethoxyxanthone (30 mg).

The Na_2CO_3-insoluble portion (23·5 g) was dried and chromatographed on silica, giving various fractions with the indicated eluants: light petroleum (b.p. 60–70°)–benzene, 1:1 (B_1), benzene (B_2), benzene–$CHCl_3$ 1:1 (B_3), $CHCl_3$ (B_4).

B_1 was precipitated with methanol yielding an aliphatic aldehyde, m.p. 90–91° (50 mg): B_2 was separated by fractional crystallization from ethanol into β-sitosterol (500 mg) and 2-hydroxy-1-methoxyxanthone (42 mg); B_3 was recrystallized from ethanol, yielding 4-methoxy-2,3-methylenedioxyxanthone (10 mg): B_4 was a mass from which nothing useful could be isolated.

Ethanol extraction of the wood of K. rupestris. *Isolation of β-sitosterol, 3-hydroxy-1,2-dimethoxyxanthone,*

3-hydroxy-1,5,6-trimethoxyxanthone, *2,6-dimethoxy-1,4-benzoquinone*, *5-hydroxy-1,3-dimethoxyxanthone*. The ground wood, after extraction with benzene, was then continuously extracted with hot ethanol. Removal of the solvent gave residue (90 g), which was extracted with hot $CHCl_3$. The product (5 g) which remained after evaporation of the $CHCl_3$ was chromatographed on silica, giving various fractions with the indicated eluants: benzene–$CHCl_3$ 2:1 (C_1), 1:1 (C_2), 1:5 (C_3), $CHCl_3$ (C_4, C_5 in this order), $CHCl_3$–MeOH, 98:2 (C_6), 1:1 (C_7).

C_1 was an oil composed of aliphatic esters (2 g): C_2 was an oil composed of aliphatic esters (400 mg): C_3 was crystallized from ethanol yielding β-sitosterol (1·5 g): C_4 was separated by fractional crystallization into 3-hydroxy-1,2-dimethoxyxanthone (20 mg) and 3-hydroxy-1,5,6-trimethoxyxanthone (22 mg): C_5 was crystallized from ethanol yielding 2,6-dimethoxy-1,4-benzoquinone (15 mg): C_6 was crystallized from ethanol yielding 5-hydroxy-1,3-dimethoxyxanthone (40 mg): C_7 was washed with ether yielding an aliphatic alcohol, m.p. 288–291° (200 mg).

3-Hydroxy-1,5,6-trimethoxyxanthone was obtained as colourless crystals, m.p. 246–248°, from EtOH. U.v. spectrum: Fig. 9, not affected by addition of $AlCl_3$. Gibbs test negative. NMR spectrum: τ3·73 and 3·63, doublets, $J = 2·5$ Hz, 2-H and 4-H; τ 3·04 and 2·02, doublets, $J = 9·0$ Hz, 7-H and 8-H; τ 5·87, 6·00 and 6·05, singlets, three OCH_3. I.r. spectrum: 1621, 1600, 1575, 1460, 1295, 1209, 1153, 1110, 1070 cm^{-1}. Mass spectrum: *m/e* (%) 302 (100), 301 (58), 286 (15), 273 (42), 271 (15), 258 (21), 257 (17), 256 (29), 229 (35), 69 (17), 64 (30), 57 (18), 55 (18), 44 (100).

1,3,5,6-Tetramethoxyxanthone. 3-Hydroxy-1,5,6-trimethoxyxanthone (5 mg) was methylated with Me_2SO_4–K_2CO_3, yielding colourless crystals (3 mg), m.p. 142–144°, and mixture m.p., with an authentic sample of 1,3,5,6-tetramethoxyxanthone 142–145°.[19] U.v. spectrum: λ_{max} 245, 285 inf., 305 nm (ε resp. 38·300, 9·440, 17·140).

1,5,6-Trimethoxy-3-acetoxyxanthone. 3-Hydroxy-1,5,6-trimethoxyxanthone (10 mg) was acetylated with Ac_2O–pyridine, yielding colourless crystals (8·5 mg), m.p. 210–213°. U.v. spectrum: λ_{max} 243, 301, 335 inf. nm (ε resp. 53·300, 22·000, 8·400). NMR spectrum: τ 3·63 and 3·46, doublets, $J = 2·5$ Hz, 2-H and 4-H; τ 3·00 and 1·97, doublets, $J = 9·0$ Hz, 7-H and 8-H; τ 5·94 and 6·06, singlets, three OCH_3, τ 7·58, singlet, one $COCH_3$.

2,6-Dimethoxy-1,4-benzoquinone. Found: m.p. 248–250°. Mass spectrum; *m/e* (%) 168 (88), 138 (33), 125 (22), 97 (29), 80 (100), 69 (100). I.r. spectrum: 1695, 1645, 1633, 1595, 1319, 1258, 1215, 1102 cm^{-1}. U.v. spectrum: λ_{max} 288, 385 nm (ε resp. 12·800, 600). Required: m.p. 250°,[20] M 168.

2-Hydroxy-1-methoxyxanthone. Found: m.p. 171–172°, M 242. Required: m.p. 169–171°,[3] M 242.
3-Hydroxy-1,2-dimethoxyxanthone. Found: m.p. 235–238°, M 272. Required: m.p. 236–238°,[4] M 272.
4-Hydroxy-2,3-dimethoxyxanthone. Found: m.p. 218–220°, M 272. Required: m.p. 218–219°,[5] M 272.
4-Methoxy-2,3-methylenedioxyxanthone. Found: m.p. 234–236°, M 270. Required: m.p. 237–238°,[5] M 270. *5-Hydroxy-1,3-dimethoxyxanthone*. Found: m.p. 262–264°, M 272. Required: m.p. 263–265°.[5] M 272. *3-Methoxy-1,5-dihydroxyxanthone*. Found: m.p. 268–270°, M 258. Required: m.p. 269–271°,[5] M 258.

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