

Synthesis of New Trioxygenated Xanthenes of *Tovomita excelsa*

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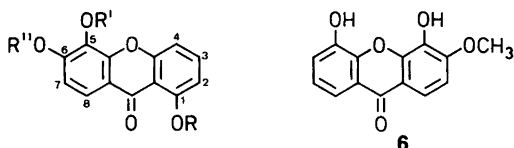
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De Oliveira *et al.*¹ reported the isolation of two new isomeric xanthenes from the trunk wood of *Tovomita excelsa* Andrade-Lima *et G. Mariz*. Based on their spectral characteristics they were assigned the structures 1,5-dihydroxy-6-methoxyxanthone (**1**) and 5,6-dihydroxy-1-methoxyxanthone (**2**), respectively. Herein we report the synthesis of these in order to verify the proposed structures.

1,5,6-Trihydroxyxanthone (**3**),² the key intermediate in both syntheses, was prepared by the condensation of 2,6-dihydroxybenzoic acid³ and pyrogallol in the presence of zinc chloride and phosphorus oxychloride at 70–80°C. Partial methylation of **3** using 1 mol of dimethyl sulfate gave 1,5-dihydroxy-6-methoxyxanthone (**1**) as the major product. The ¹H NMR spectrum of **1** showed a singlet at δ 3.98 (3H) indicating the presence of a methoxy group. The UV spectrum of **1** showed a bathochromic shift of 28 nm in the presence of AlCl₃/HCl shift reagent, thus indicating the presence of the chelated hydroxy group⁴ at C-1. With the shift reagent NaOAc the UV spectrum of **1** did not exhibit any bathochromic shift, thus indicating the absence of a free hydroxy group at the conjugated C-6 position.⁴ The m.p. and the spectral data of synthetic **1** agreed well with those reported¹ for the natural sample, thus confirming its structure.

Partial benzoylation of **3**, using 2.2 mol of benzyl chloride, followed by methylation furnished the hitherto unknown compounds 5,6-dibenzyl-oxy-1-hydroxyxanthone (**4**) and 5,6-dibenzyl-oxy-1-methoxy-xanthone (**5**). The ¹H NMR spectrum of **4** displayed two singlets (2H each) for the two benzylic groups at δ 5.16 and 5.24 ppm. The UV spectrum showed a bathochromic shift of 71 nm with the AlCl₃/HCl shift reagent, thus indicating the presence of a chelated hydroxy group⁴ at C-1 in **4**. Furthermore, **4** did not exhibit any bathochromic shift in its UV spectrum in the presence of NaOAc/H₃BO₃ shift reagent, thereby showing that the *ortho*-dihydroxy system (i.e. 5,6-dihydroxy groups) in **3** has been blocked. Catalytic de-benzoylation using Pd/C (5%) yielded 5,6-dihydroxy-1-methoxyxanthone (**2**), the m.p. and the spectral data of which are not consistent with those reported¹ for the natural sample. Compound **2** crystallized from methanol as colourless needles which melted at 258–260°C, while the m.p. reported for the natural sample is 218–223°C. The IR spectrum of **2** showed bands for hydroxy and carbonyl functions at 3300 cm⁻¹ and 1640 cm⁻¹, respectively, whereas they have been reported at 3380 cm⁻¹ and 1648 cm⁻¹ for the natural sample. The UV absorption maxima of **2** are observed at 316, 290 and 236 nm, whereas the natural sample showed bands at 275, 290, 243 and

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- 1: R=R'=H, R''=CH₃
- 2: R=CH₃, R'=R''=H
- 3: R=R'=R''=H
- 4: R=H, R'=R''=CH₂C₆H₅
- 5: R=CH₃, R'=R''=CH₂C₆H₅

238 nm. A bathochromic shift of 14 nm was observed with the NaOAc/H₃BO₃ shift reagent for the synthetic sample, while the spectrum of the natural sample exhibited no shift with this reagent.¹ Such a bathochromic shift in UV absorption maxima of polyphenolic compounds is characteristic of an *ortho*-dihydroxy system in the structure of the compound.⁴ The presence of this system in **2** was further confirmed by a shift of 20 nm with AlCl₃ shift reagent which disappeared on addition of HCl. The MS and ¹H NMR spectra of **2** also showed marked differences from those reported¹ for the natural sample: the mass spectrum of **2** exhibited peaks at *m/z* 241 (*M*-OH)⁺ and *m/z* 240 (*M*-H₂O)⁺ which are characteristic for such compounds because of the "ortho effect".⁵ However, the natural sample did not show any peaks due to these characteristic fragments. A direct comparison of the synthetic sample and the natural sample could not be made due to the non-availability of the latter to us. In view of the marked discrepancies in the m.p. and the spectral characteristics of the synthetic and natural samples, the proposed structure of the latter needs revision. On the basis of the data reported¹ for the natural sample, its most probable structure is 4,5-dihydroxy-3-methoxyxanthone (**6**), which to our knowledge is unknown in the literature. Further studies to establish the constitution of the natural material are in progress.

Experimental

Melting points were determined on a Nalge micro melting point apparatus and are uncorrected. UV spectra (λ_{\max} in nm) were recorded on a Beckmann UV-5260 spectrophotometer using methanol as solvent, IR spectra (ν_{\max} in cm⁻¹) of nujol

mulis on a Perkin-Elmer model 137 instrument, mass spectra [reported as *m/z* (% rel. int.)] on a Varian 311 A instrument and ¹H NMR spectra on a Jeol FX-200 FT-NMR instrument using DMSO-*d*₆ as solvent (unless otherwise stated). The NMR chemical shifts are expressed in δ (ppm) downfield from TMS as internal standard.

1,5-Dihydroxy-6-methoxyxanthone (1). To a solution of **3**² (200 mg) in dry acetone (20 ml) were added dimethyl sulfate (0.04 ml) and anhydrous K₂CO₃ (1 g) and the mixture was heated under reflux for 1 h. On normal work-up the product crystallized from aqueous methanol as colourless needles (50 mg), m.p. 247–248 °C; lit.⁶ m.p. 245–248 °C. The compound gave a green colour with ferric chloride. IR: 3250, 1680, 1460, 1400, 1280, 1210, 1190, 1080, 1060, 780. UV: 322, 246; +AlCl₃: 362, 312, 261, 232; +AlCl₃+HCl: 350, 310; +NaOAc: 322, 246; +NaOAc+H₃BO₃: 320, 246; +NaOMe: 342, 300, 268, 242. ¹H NMR: 3.98 (3H, s, -OCH₃), 6.78 (1H, d, *J*=8Hz, H-2), 7.06 (1H, d, *J*=8Hz, H-4), 7.22 (1H, d, *J*=8Hz, H-7), 7.66 (1H, d, *J*=8Hz, H-8), 7.70 (1H, m, H-3), 9.70 (1H, s, D₂O-exchangeable, -OH), 12.5 (1H, s, D₂O-exchangeable, -OH). MS: 259 (16, *M*+1), 258 (100, *M*), 243 (10), 229 (2), 216 (3), 215 (19), 187 (12), 186 (2), 131 (4), 129 (4), 115 (3).

5,6-Dibenzoyloxy-1-hydroxyxanthone (4). To a solution of **3**² (0.7 g) in dry acetone (50 ml) were added benzyl chloride (0.63 ml), potassium iodide (1 g) and anhydrous K₂CO₃ (5 g) and the mixture was heated under reflux for 6 h. Normal work-up gave a solid which crystallized from chloroform-petroleum ether as cream-yellow plates, m.p. 180–181 °C. Anal. C₂₇H₂₀O₅: C, H. IR: 3350(br), 1640, 1600, 1450, 1280, 1200, 1080, 1060, 790, 730. UV: 358, 306, 266, 242; +AlCl₃: 420, 340, 278(sh), 252, 230; +AlCl₃+HCl: 429, 336, 310, 278, 250, 230; +NaOAc: 358, 306, 266, 242; +NaOAc+H₃BO₃: 360, 306, 246, 242; +NaOMe: 400, 292, 236. ¹H NMR: 5.16 (2H, s, -OCH₂C₆H₅), 5.24 (2H, s, -OCH₂C₆H₅), 6.44 (1H, d, *J*=8Hz, H-2), 6.88 (1H, d, *J*=8Hz, H-7), 7.02 (1H, d, *J*=8Hz, H-4), 7.40 (1H, m, H-3), 7.44 (10H, m, 2 × -OCH₂C₆H₅), 7.92 (1H, d, *J*=8Hz, H-8), 12.74 (1H, s, D₂O-exchangeable, -OH).

5,6-Dibenzoyloxy-1-methoxyxanthone (5). To a solution of **4** (0.5 g) in dry acetone (20 ml) were added dimethyl sulfate (0.1 ml) and anhydrous K_2CO_3 (2 g) and the mixture was heated under reflux for 72 h. Normal work-up gave a cream-coloured solid which crystallized from chloroform as colourless needles (0.5 g), m.p. 138–139°C. Anal. $C_{28}H_{22}O_5$: C, H. IR: 2900, 1740, 1650, 1600, 1440, 1390, 1290, 1270, 1230, 1100, 1060, 960, 780, 730. 1H NMR($CDCl_3$): 4.00 (3H, s, $-OCH_3$), 5.16 (2H, s, $-OCH_2C_6H_5$), 5.22 (2H, s, $-OCH_2C_6H_5$), 6.69 (1H, d, $J=8$ Hz, H-7), 6.93 (1H, m, H-3), 7.40 (12H, m, H-2, H-4, $2 \times -OCH_2C_6H_5$), 7.96 (1H, d, $J=8$ Hz, H-8). MS: 439 (2, $M+1$), 438 (8, M), 348 (4), 347 (14), 92 (7), 91 (100, $C_6H_5CH_2$), 65 (4).

5,6-Dihydroxy-1-methoxyxanthone (2). To a solution of **5** (0.4 g) in ethyl acetate (16 ml) was added Pd/C (0.1 g, 5%) and the mixture was hydrogenated for 2 h with continuous stirring. The product crystallized from methanol as colourless needles, m.p. 258–260°C. Anal. $C_{14}H_{10}O_5$: C, H. IR: 3300, 1640, 1580, 1460, 1250, 1180, 1100, 1050, 790. UV: 316, 290, 236; $+AlCl_3$: 336, 296, 262, 236; $+AlCl_3+HCl$: 314, 292, 236; $+NaOAc$: 336, 292, 264, 236; $+NaOAc+H_3BO_3$: 330, 292,

256, 236; $+NaOMe$: 342, 292, 268, 236. 1H NMR: 3.84 (3H, s, $-OCH_3$), 6.80 (1H, d, $J=8$ Hz, H-7), 6.88 (1H, d, $J=8$ Hz, H-4), 7.08 (1H, d, $J=8$ Hz, H-2), 7.34 (1H, m, H-3), 7.58 (1H, d, $J=8$ Hz, H-8). MS: 259 (15, $M+1$), 258 (100, M), 257 (36, $M-1$), 241 (13, $M-OH$), 240 (10, $M-H_2O$), 229 (44), 228 (19), 213 (7), 212 (40), 200 (4), 171 (4), 129 (4), 115 (6), 100 (5).

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