Journal of Natural Products
Vol. 52, No. 4, pp. 852-857, Jul-Aug 1989

THE SYNTHESIS OF 1,8-DIHYDROXY-2,3,4,6-TETRAMETHOXY-XANTHONE AND 1,6-DIHYDROXY-3,5,7,8-TETRAMETHOXY-XANTHONE, A CONFIRMATION OF STRUCTURE

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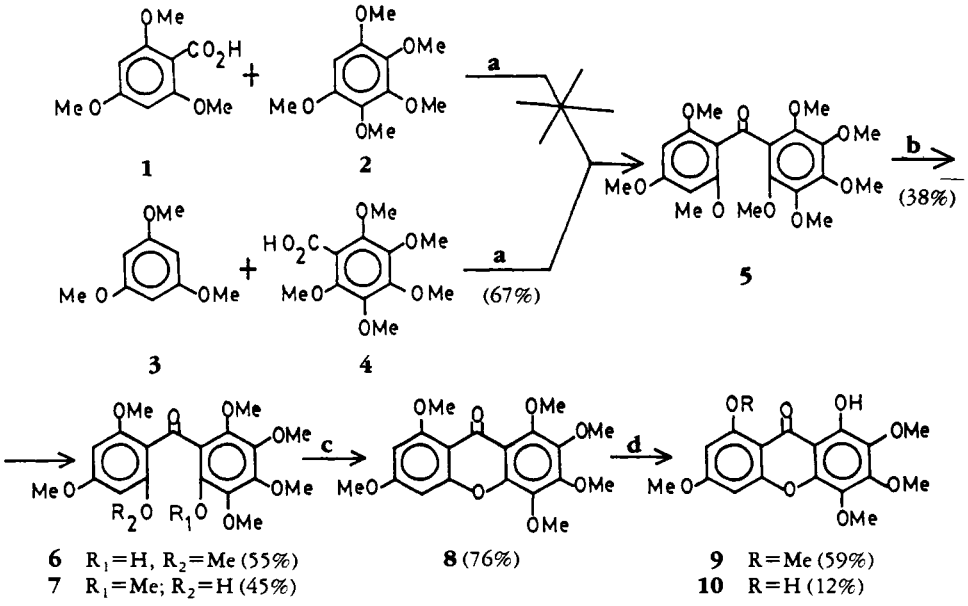
ABSTRACT.—1,8-Dihydroxy-2,3,4,6-tetramethoxyxanthone [**10**] has been synthesized by trifluoroacetic anhidride (TFAA) condensation. 1-6-Dihydroxy-3,5,7,8-tetramethoxyxanthone [**18**] has been synthesized by Friedel-Crafts acylation. Both xanthones were identical to the natural xanthones isolated from *C. linarifolium*.

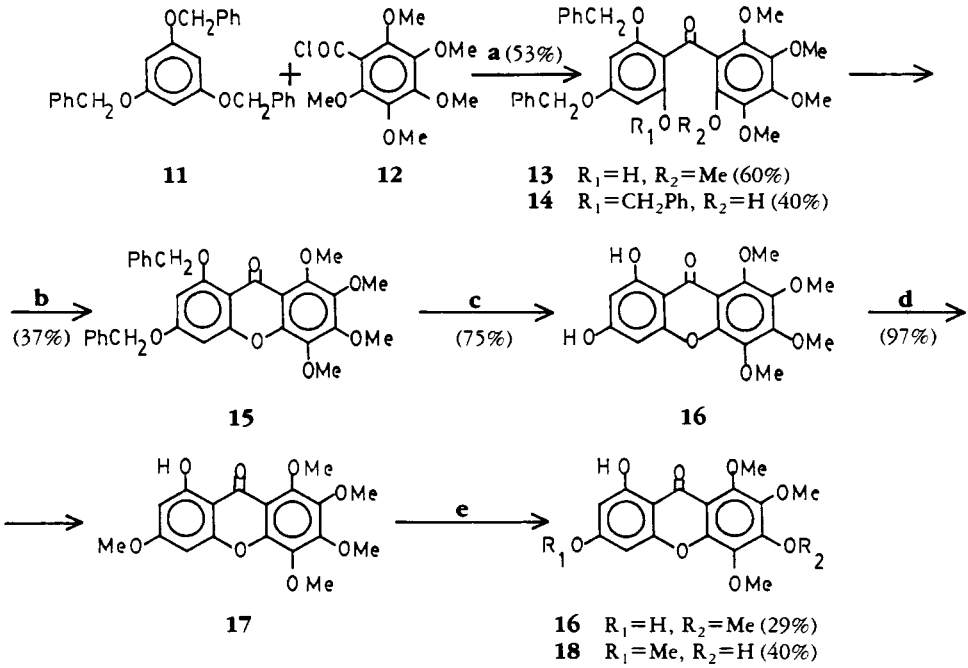
Centaurium linarifolium (Lamark) G. Beck (Gentianaceae), is a plant used in folk medicine as a digestive, an antipyretic, and a drug helpful in increasing blood circulation (1). From this plant several new xanthones were isolated; two were identified as 1,8-dihydroxy-2,3,4,6-tetramethoxyxanthone [**10**] and 1,6-dihydroxy-3,5,7,8-tetramethoxyxanthone [**18**] on the basis of their spectral data (2). The present paper describes the synthesis of compounds **10** and **18**, performed to confirm the assigned structures.

In our previous reports (3,4) we obtained highly oxygenated xanthones by cyclization of the appropriate benzophenones with elimination of H_2O, MeOH, or $PhCH_2OH$. The benzophenones can be prepared by Friedel-Crafts acylation (5) or by trifluoroacetic anhydride (TFAA) condensation (6) of suitably substituted benzene compounds, which can be synthesized by conventional methods.

In the present paper we have used both possibilities to obtain unambiguous syntheses of compounds **10** and **18**. TFAA condensation led to the best yield in Scheme 1, but we find it inadequate for the method outlined in Scheme 2 as is the case in the synthesis of related xanthones (4).



SCHEME 1. **a**: TFAA/CH_2Cl_2 (−14°); **b**: $AlCl_3/CH_3CN$ (Δ); **c**: Me_4NOH/C_5H_5N-H_2O (Δ); **d**: BCl_3/CH_2Cl_2 (room temperature).



SCHEME 2. **a**: $AlCl_3/Et_2O$ (room temperature); **b**: Me_4NOH/C_5H_5N-H_2O (Δ); **c**: H_2(Pd/C)/EtOAc-HCl (room temperature); **d**: CH_2N_2/Et_2O (room temperature); **e**: piperidine-H_2O (Δ).

As we have reported previously (3,4), Friedel-Crafts acylation occurs with simultaneous *O*-deprotection of ortho benzyloxy and methoxy groups. This deprotection is observed with both the acylating and the substrate molecules and to a larger extent for benzyl than for methyl groups; thus, in Scheme 2 compound **13** was the main product, but an appreciable amount of **14** was obtained.

The first attempt to obtain 2,2′,3,4,4′,5,6,6′-octamethoxybenzophenone [**5**] was from 2,4,6-trimethoxybenzoic acid [**1**] and pentamethoxybenzene [**2**]. Pentamethoxybenzene [**2**] was obtained by methylation of 2,3,4,6-tetramethoxyphenol, prepared from 1,3,5-trimethoxybenzene by consecutive Vilsmeier-Haack formylation (7) and acid-catalyzed oxidation with H_2O_2 in MeOH (8) with better yield than the conventional Baeyer-Villiger oxidation with *m*-chloroperbenzoic acid (9–11). Condensation of **1** and **2** using TFAA as condensing agent, however, gave no reaction at shorter reaction times and polymeric products at longer reaction times. Compound **5** was finally prepared from 1,3,5-trimethoxybenzene [**3**] and pentamethoxybenzoic acid [**4**] obtained by formylation and oxidation of pentamethoxybenzene [**2**] (11), using TFAA as condensing agent (6) (Scheme 1).

Demethylation of **5** with $AlCl_3$ in MeCN (12) yielded a mixture of 2-hydroxy-2′,3,4,4′,5,6,6′-heptamethoxybenzophenone [**6**] and 2-hydroxy-2′,3′,4,4′,5′,6,6′-heptamethoxybenzophenone [**7**] in 55% and 45% yield, respectively, as determined by ^{1}H-nmr spectroscopy. The crude mixture of benzophenones was then refluxed with tetramethylammonium hydroxide in pyridine (13) to afford 1,2,3,4,6,8-hexamethoxyxanthone [**8**].

Selective demethylation of **8** using low concentrations of BCl_3 in CH_2Cl_2 and a short reaction time, in order to minimize unwanted demethylations (14), afforded a mixture of 1,8-dihydroxy-2,3,4,6-tetramethoxyxanthone [**10**] (12%) and 1-hydroxy-2,3,4,6,8-pentamethoxyxanthone [**9**] (59%). The struc-

ture of 1-hydroxy-2,3,4,6,8-pentamethoxyxanthone [**9**] was confirmed by spectral analysis and comparison with the alternative structure **17** synthesized according to Scheme 2. The results showed that the most sterically hindered and therefore electronegative methoxy group situated ortho to the xanthone carbonyl group undergoes selective demethylation (15). With prolonged reaction time a mixture of mono- and polydemethylated xanthones was obtained. Purification on preparative tlc finally afforded 1,8-dihydroxy-2,3,4,6-tetramethoxyxanthone [**10**], identical to the xanthone isolated from *C. linarifolium* (2) (mp, ir, uv, ^{1}H nmr, ms).

Selective demethylation of positions 1 and 6 in **8**, in order to obtain 1,6-dihydroxy-3,5,7,8-tetramethoxyxanthone [**18**], should also lead to demethylation of positions 3 and 8, so the synthesis of **18** was performed using the benzyloxy group as hydroxyl protecting group (16) (Scheme 2).

The benzophenone precursors were prepared by Friedel-Crafts acylation of 1,3,5-tribenzyloxybenzene [**11**] (17) with pentamethoxybenzoyl chloride [**12**], generated in situ from pentamethoxybenzoic acid [**4**] (5). This acylation yielded a mixture of 4,6-dibenzyloxy-2-hydroxy-2′,3′,4′,5′,6′-pentamethoxybenzophenone [**13**] (60%) and 2-hydroxy-3,4,5,6-tetramethoxy-2′,4′,6′-tribenzyloxybenzophenone [**14**] (40%), as determined by ^{1}H-nmr spectroscopy.

As both benzophenones **13** and **14** should lead to the same xanthone on cyclization, the crude mixture was refluxed with tetramethylammonium hydroxide in pyridine (13) to afford 1,3-dibenzyloxy-5,6,7,8-tetramethoxyxanthone [**15**]. Surprisingly, most of the 4,6-dibenzyloxy-2-hydroxy-2′,3′,4′,5′,6′-pentamethoxybenzophenone [**13**] was recovered, and prolongation of the reaction time led to lower yields of **15**.

Hydrogenolysis of 1,3-dibenzyloxy-5,6,7,8-tetramethoxyxanthone [**15**] with Pd/C as catalyst (18) afforded 1,3-dihydroxy-5,6,7,8-tetramethoxyxanthone [**16**]. Methylation of **16** with an ethereal solution of CH_2N_2 afforded 1-hydroxy-3,5,6,7,8-pentamethoxyxanthone [**17**]. Its physical and spectral data were identical with those of the naturally occurring xanthone from *Eustoma grandiflora* (19) and *C. linarifolium* (20), thus confirming the proposed structure for it.

When heated under reflux in aqueous piperidine (21), 1-hydroxy-3,5,6,7,8-pentamethoxyxanthone [**17**] afforded a mixture of 1,3-dihydroxy-5,6,7,8 -tetramethoxyxanthone [**16**] (29%), and 1,6-dihydroxy-3,5,7,8-tetramethoxyxanthone [**18**] (40%), together with some starting material **17**. Selective demethylation of a methoxy group para to a carbonyl function occurs under mild alkaline conditions (5). This is not unexpected because oxygen atoms para to a carbonyl group are less basic. Purification on preparative tlc finally afforded 1,6-dihydroxy-3,5,7,8-tetramethoxyxanthone [**18**], identical to the xanthone isolated from *C. linarifolium* (2) (mp, ir, uv, ^{1}H nmr, ms).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—All melting points were determined with a Reichert apparatus and are uncorrected. Uv spectra were determined with a Perkin-Elmer Lambda 9 spectrophotometer in MeOH solution. Ir spectra were determined with a Perkin-Elmer model 281 recording spectrophotometer for KBr or NaCl pellets. ^{1}H-nmr spectra were recorded in the stated solvents with a Bruker AC-200 (200 MHz) instrument; chemical shifts are reported as δ values with TMS as internal standard. Low and high resolution mass spectra were taken with a Varian-166 mass spectrometer. Si gel Merck 60 (0.06–0.20 mm) was used for cc and Si gel 60 $HF_{254-360}$ for tlc.

PREPARATION OF 2,2′,3,4,4′,5,6,6′-OCTAMETHOXYBENZOPHENONE [**5**].—Pentamethoxybenzoic acid [**4**] (11) (174 mg, 0.63 mmol) and 1,3,5-trimethoxybenzene [**3**] (300 mg, 1.75 mmol) were dissolved in anhydrous CH_2Cl_2 (6 ml), and the solution was kept in an ice-NaCl bath, under Ar. Trichloroacetic anhydride (0.9 ml) was added (6), and the solution was stirred for 15 min at −14°. Afterwards, the solution was poured into ice-H_2O and extracted with CH_2Cl_2. The organic layers were washed with aqueous $NaHCO_3$ and H_2O. After purification of

the crude product on cc [hexane-Et_2O (5:5)], 179 mg (0.42 mmol, 67%) of 2,2',3,4,4',5,6,6'-octamethoxybenzophenone [**5**] was obtained as a waxy product: ir ν max (KBr) cm^{-1} 2910, 1655 (C=O of benzophenone), 1580, 1445, 1395, 1350, 1325, 1275, 1215, 1145, 1110, 1050, 1020, 995, 965, 940, 905, 870, 800; ^1H nmr ($CDCl_3$) δ 3.60, 3.61, 3.64, 3.77, 3.80, 3.92 (24H, 6s, 8 × OMe), 6.05 (2H, s, H-3', H-5'); ^{13}C nmr ($CDCl_3$) δ 55.2, 56.0, 61.0, 61.3, 61.5, 91.0, 114.6, 128.0, 142.6, 146.9, 148.4, 160.3, 162.9, 190.5 (several signals are superimposed); uv λ max (MeOH) nm 210, 230 (sh), 290; hrms *m/z* (%) $[M]^+$ 422 (100) (found 422.153 ± 0.005, calcd for $C_{21}H_{26}O_9$, 422.157), 391 (14), 255 (10), 241 (68), 195 (97), 181 (37).

PREPARATION OF 2-HYDROXY-2',3,4,4',5,6,6'-HEPTAMETHOXYBENZOPHENONE [**6**] AND 2-HYDROXY-2',3',4,4',5',6,6'-HEPTAMETHOXYBENZOPHENONE [**7**].—The above benzophenone [**5**] (165 mg, 0.39 mmol) was dissolved in dry MeCN (9 ml), and $AlCl_3$ (300 mg) was added (12). After 1 h at room temperature the mixture was refluxed for 50 min, poured over 1 M aqueous HCl, and extracted with CH_2Cl_2 to give a crude product which after purification on preparative tlc [CH_2Cl_2-Me_2CO-HOAc (90:10:0.2)] yielded a yellow solid (60 mg, 38%); ir ν max (KBr) cm^{-1} 1640–1560 (br, C=O of benzophenone); ^1H nmr ($CDCl_3$) δ 3.33 (s, OMe of **7**), 3.42 (s, OMe of **6**), 3.71, 3.81, 3.82, 3.85, 3.88 (5s, 10 × OMe of **6** and **7**), 3.95 (s, OMe of **6**), 4.07 (s, OMe of **7**), 5.79 (d, J = 2.2 Hz, H-3 of **7**), 6.10 (s + d, H-5 of **7** and H-3' + H-5' of **6**), 13.11 and 13.66 (2s, OH-2 of **6** and **7**). Integration of the signals followed the molar ratio: **6** = 0.55 and **7** = 0.45.

PREPARATION OF 1,2,3,4,6,8-HEXAMETHOXYXANTHONE [**8**].—To the previous solid (54 mg) in pyridine (4 ml), H_2O (2 ml) and aqueous 10% tetramethylammonium hydroxide (2 ml) were added (13). The solution was refluxed 17 h, poured into ice, acidified with HCl, and extracted with CH_2Cl_2, yielding a solid which after purification on preparative tlc [hexane-Et_2O (2:8)] and crystallization from MeOH yielded white plates, 44 mg (0.12 mmol, 76%), mp 154–157°. Its tlc, uv, ir, and ^1H nmr were identical with those of the product obtained from total methylation of the naturally occurring 1,2,3,4,6,8-hexaoxygenated xanthones from *C. linarifolium* (2).

PREPARATION OF 1-HYDROXY-2,3,4,6,8-PENTAMETHOXYXANTHONE [**9**] AND 1,8-DIHYDROXY-2,3,4,6-TETRAMETHOXYXANTHONE [**10**].—Compound **8** (34 mg, 0.09 mmol) in dry CH_2Cl_2 (4 ml) was stirred at −70° (solid CO_2-Me_2CO bath) under an Ar atmosphere. BCl_3 (0.2 ml) was added, and the mixture was stirred at room temperature for 20 min (15). Afterwards, EtOH (0.4 ml) was added in order to destroy any excess of BCl_3, and the red complex was poured into aqueous $NaHCO_3$ solution (50 ml) containing CH_2Cl_2 and stirred until a clear yellow solution was obtained (2 h). Evaporation of the dried organic layer gave a yellow solid, which was purified on preparative tlc [hexane-Et_2O (3:7)] to give two bands. The most polar one gave, after crystallization from hexane/Et_2O, 19 mg (0.053 mmol, 59%) of yellow plates of 1-hydroxy-2,3,4,6,8-pentamethoxyxanthone [**9**]: mp 140–142°; ir ν max (KBr) cm^{-1} 2930, 1640 (C=O of xanthone), 1610, 1580, 1570, 1465, 1420, 1390, 1320, 1305, 1245, 1220, 1205, 1130, 1105, 1065, 1050, 1035, 980, 820; ^1H nmr ($CDCl_3$) δ 3.90 (6H, s, 2 × OMe), 3.92, 3.96, 4.09 (9H, 3s, 3 × OMe), 6.32, 6.54 (2H, 2d, J = 2.3 Hz, H-5 and H-7), 13.13 (1H, s, OH-1); uv λ max (MeOH) nm (log ϵ) 242 (sh), 249 (4.08), 263 (sh), 320 (3.93), 360 (sh) (uv spectra showed no variation when NaOAc was added); λ max (MeOH + NaOMe) 239, 274, 307, 405; λ max (MeOH + $AlCl_3$) 250, 280, 348, 420 (uv spectra showed no variation when HCl was added).

The least polar band gave, after crystallization from Me_2CO, 4 mg (0.012 mmol, 13%) of yellow plates, mp 170–173°, of 1,8-dihydroxy-2,3,4,6-tetramethoxyxanthone [**10**]: ir ν max (KBr) cm^{-1} 3100, 2850, 1655 (C=O of xanthone), 1615, 1595, 1565, 1470, 1465, 1370, 1330, 1270, 1240, 1210, 1185, 1130, 1090, 1055, 1040, 1020, 980, 955, 935, 850, 810, 775; ^1H nmr ($CDCl_3$) δ 3.88, 3.91, 3.92, 4.12 (12H, 4s, 4 × OMe), 6.33 and 6.48 (2H, 2d, J = 2.2 Hz, H-5 and H-7), 11.87, 11.95 (2H, 2s, OH-1 and OH-8); ^{13}C nmr ($CDCl_3$) δ 55.9, 61.2, 61.6, 62.1, 93.1, 97.6, 102.1, 103.5, 132.5, 135.6, 145.5, 150.4, 154.3, 157.5, 162.7, 167.1, 183.9; uv λ max (MeOH) nm (log ϵ) 232 (sh), 258 (4.05), 333 (4.16), 378 (sh) (uv spectra showed no variation when NaOAc was added); λ max (MeOH + NaOMe) 245, 270, 338, 390 (sh); λ max (MeOH + $AlCl_3$) 276, 332 (sh), 373 (uv spectra showed no variation when HCl was added); hrms *m/z* (%) $[M]^+$ 348 (86) (found 348.081 ± 0.005, calcd for $C_{17}H_{16}O_8$, 348.084), 333 (100), 318 (31), 303 (53), 288 (50), 273 (31), 245 (53).

The tlc, uv, ir, and ^1H nmr of **10** were identical with those of naturally occurring 1,8-dihydroxy-2,3,4,6-tetramethoxyxanthone [**10**] isolated from *C. linarifolim* (2). An mmp of this product with authentic **10** showed no depression.

PREPARATION OF 4,6-DIBENZYLOXY-2-HYDROXY-2',3',4',5',6'-PENTAMETHOXYBENZOPHENONE [**13**] AND 2',4',6'-TRIBENZYLOXY-2-HYDROXY-3,4,5,6-TETRAMETHOXYBENZOPHENONE [**14**].—Pentamethoxybenzoic acid [**4**] (228 mg, 0.84 mmol) in dry C_6H_6 (4 ml) was

treated under Ar with good stirring at room temperature with 0.4 ml of oxalyl chloride (5). After 1 h the solvent and excess reagent were removed under reduced pressure. The residue was dissolved in anhydrous Et_2O (8 ml), and 1,3,5-tribenzyloxybenzene [**11**] (17) (332 mg, 0.84 mmol) and $AlCl_3$ (350 mg) were added (5). After stirring 3 h at room temperature, the mixture was hydrolyzed with ice-H_2O (50 ml) containing concentrated HCl (5 ml) and extracted with Et_2O to give a crude product (470 mg) that was purified by cc [hexane-Et_2O (9:1)] to yield an oil (260 mg, 53%): ir ν max cm^{-1} 1620 (br, C=O of benzophenone); ^1H nmr ($CDCl_3$) δ 3.73, 3.74, 3.75, 3.88 (4s, 9 × OMe of **13** and **14**), 4.78, 5.09, 5.31 (3s, 3 × CH_2 of BzO of **14**), 4.82, 5.11 (2s, 2 × CH_2 of BzO of **13**), 6.04 (s, H-3′ + H-5′ of **14**), 6.08 (d, J = 2.2 Hz, H-5 of **13**), 6.27 (d, J = 2.2 Hz, H-3 of **13**), 6.97–7.44 (m, aromatic protons of **13** and **14**), 13.84 (s, OH-2 of **13** and **14**). Integration of the signals follows the molar ratio: **13** = 0.6 and **14** = 0.4.

PREPARATION OF 1,3-DIBENZYLOXY-5,6,7,8-TETRAMETHOXYXANTHONE [**15**].—The previous oil (260 mg) was treated with pyridine (3 ml), H_2O (2 ml), and aqueous 10% tetramethylammonium hydroxide (1.2 ml) (13). The mixture was refluxed 15 h, poured into ice, acidified with HCl, and extracted with Et_2O, yielding an oil which was purified on cc.

From hexane-Et_2O (9:1), 109 mg (0.20 mmol, 45%) of 4,6-dibenzyloxy-2-hydroxy-2′,3′,4′,6′-pentamethoxybenzophenone [**13**] was obtained as a yellow oil: ir ν max (KBr) cm^{-1} 2940, 1620 (C=O of benzophenone), 1590, 1470, 1415, 1380, 1300, 1175, 1110, 1070, 745, 705; ^1H nmr ($CDCl_3$) δ 3.68, 3.70, 3.83 (15H, 3s, 5 × OMe), 4.77, 5.06 (4H, 2s, 2 × CH_2 of BzO), 6.04 (1H, d, J = 2.2 Hz, H-5), 6.23 (1H, d, J = 2.2 Hz, H-3), 6.93–7.38 (10H, m, aromatic protons), 13.80 (1H, s, OH-2); ^{13}C nmr ($CDCl_3$) δ 60.9, 61.3, 61.4, 70.3, 70.7, 92.6, 94.7, 104.1, 107.5, 125.4, 127.1, 127.2, 127.6, 128.0, 128.3, 128.5, 128.6, 135.2, 135.7, 142.5, 144.6, 147.7, 161.8, 164.0, 165.9, 167.8, 195.4 (several signals are superimposed).

From hexane-Et_2O (8:2), 84 mg (0.16 mmol, 73%) of 1,3-dibenzyloxy-5,6,7,8-tetramethoxyxanthone [**15**] was obtained as a white waxy product: ir ν max (KBr) cm^{-1} 2900, 1645 (C=O of xanthone), 1605, 1575, 1455, 1400, 1300, 1185, 1125, 1095, 1065, 980, 810, 730, 695; ^1H nmr ($CDCl_3$) δ 3.91, 3.97, 3.98, 4.07, (12H, 4s, 4 × OMe), 5.07, 5.25 (4H, 2s, 2 × CH_2 of BzO), 6.41, 6.57 (2H, 2d, J = 2.2 Hz, H-2 and H-4), 7.23–7.55 (10H, m, aromatic protons); uv λ max (MeOH) nm (log ϵ) 252 (4.53), 308 (4.27), 340 (sh) (uv spectra showed no variation when NaOMe was added).

PREPARATION OF 1,3-DIHYDROXY-5,6,7,8-TETRAMETHOXYXANTHONE [**16**].—Compound **15** (81 mg, 0.15 mmol) was dissolved in 4 ml of EtOAc, Pd/C (5%) (10 mg) and concentrated HCl (0.1 ml) were added, and the mixture was hydrogenated at room temperature for 4 h under 1 atm of pressure (18). After filtration of the catalyst, purification by cc [C_6H_6-EtOAc (9:1)] and crystallization from hexane/C_6H_6, compound **16** (39 mg, 0.112 mmol, 75%) was obtained as yellow plates: mp 210–213°; ir ν max (KBr) cm^{-1} 3600–3150, 2920, 1645, 1610, 1595, 1560, 1465, 1410, 1295, 1170, 1065, 810; ^1H nmr (Me_2CO-d_6) δ 3.91, 3.95, 3.96, 4.10 (12H, 4s, 4 × OMe), 6.04 (1H, s broad, OH-3), 6.23, 6.39 (2H, 2d, J = 2.3 Hz, H-2 and H-4), 13.28 (1H, s, OH-1); uv λ max (EtOH) nm (log ϵ) 248 (4.52), 317 (4.28), 355 (sh); λ max (EtOH + NaOMe) 252, 282, 363; λ max (EtOH + NaOAc) 244, 250 (sh), 353; λ max (EtOH + $AlCl_3$) 292, 343 (uv spectra showed no variation when HCl was added); hrms *m/z* (%) $[M]^+$ 348 (60) (found 348.083 ± 0.005, calcd for $C_{17}H_{16}O_8$, 348.084), 333 (100), 305 (38), 290 (32), 289 (22), 275 (24), 273 (14), 272 (15), 247 (47), 245 (10), 244 (16), 219 (20), 191 (25).

PREPARATION OF 1-HYDROXY-3,5,6,7,8-PENTAMETHOXYXANTHONE [**17**].—Compound **16** (35 mg, 0.099 mmol) was treated overnight with ethereal solution of CH_2N_2, yielding, after crystallization from MeOH, 35 mg (0.096 mmol, 97%) of 1-hydroxy-3,5,6,7,8-pentamethoxyxanthone [**17**] as yellow plates, mp 114–115°.

Its physical and spectral data were identical with those of the naturally occurring xanthone from *E. grandiflora* (19) and *C. linarifolium* (20).

PREPARATION OF 1,6-DIHYDROXY-3,5,7,8-TETRAMETHOXYXANTHONE [**18**].—To 32 mg (0.087 mmol) of **17** dissolved in piperidine (4 ml), 1.7 ml of H_2O was added, and the mixture was refluxed for 22 h (21). The reaction mixture was poured into ice-H_2O (50 ml) containing HCl (5 ml) and extracted with CH_2Cl_2. The organic layers were washed with aqueous $NaHCO_3$ and H_2O, dried, evaporated, and purified by preparative tlc [hexane-Et_2O (3:7)].

The least polar band yielded 8.9 mg (0.026 mmol, 29%) of 1,3-dihydroxy-5,6,7,8-tetramethoxyxanthone [**16**], mp 208–211°.

The most polar band yielded, after crystallization from hexane/CH_2Cl_2, 12.2 mg (0.035 mmol, 40%) of 1,6-dihydroxy-3,5,7,8-tetramethoxyxanthone [**18**] as yellow plates: mp 180–181°; ν max (KBr) cm^{-1} 3240, 2840, 1655 (C=O of xanthone), 1600, 1565, 1555, 1490, 1460, 1320, 1300, 1210, 1190, 1160, 1130, 1050, 900, 810, 800, 755; ^1H nmr ($CDCl_3$) δ 3.85, 3.95, 3.99, 4.01 (12H, 4s, 4 × OMe),

6.29 (1H, d, J = 1.8 Hz, H-2), 6.40 (1H, d, J = 1.8 Hz, H-4), 6.48 (1H, broad s, OH-6), 13.30 (1H, s, OH-1); ^{13}C nmr (Me_2CO-d_6) δ 56.4, 61.7, 62.2, 92.7, 97.8, 104.1, 132.9, 139.8, 148.4, 150.0, 151.5, 157.7, 164.6, 167.1, 181.0 (several signals are superimposed); uv λ max (MeOH) nm (log ε) 211 (sh), 252 (4.12), 278 (sh), 320 (4.23), 358 (sh); λ max (MeOH + NaOMe) 217, 244, 263 (sh), 367; λ max (MeOH + NaOAc) 232, 244 (sh) 368, max (MeOH + $AlCl_3$) 206, 225 (sh), 265, 284 (sh), 349, 404 (sh) (uv spectra showed no variation when HCl was added); hrms *m/z* (%) $[M]^+$ 348 (58) (found 348.086 ± 0.005, calcd for $C_{17}H_{16}O_8$, 348.085), 333 (100), 305 (40), 290 (51), 288 (19), 273 (15), 245 (15).

The tlc, uv, ir and ^{1}H nmr of **18** were identical with those of naturally occurring 1,6-dihydroxy-3,5,7,8-tetramethoxyxanthone [**18**] isolated from *C. linarifolium* (2). An mmp of this product with authentic **18** also showed no depression.

ACKNOWLEDGMENTS

One of us (M.J.A.) acknowledges a grant by Conselleria de Cultura, Educació i Ciencia de la Generalitat Valenciana.

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Received 4 November 1988