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J. Nat. Prod., **1991**, 54 (1), 127-135• DOI:
10.1021/np50073a010 • Publication Date (Web): 01 July 2004

Journal of Natural Products
Vol. 54, No. 1, pp. 127-135, Jan-Feb 1991

SYNTHESIS OF 1,3,4,8-TETRAOXYGENATED XANTHONES

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ABSTRACT.—Six 1,3,4,8-tetraoxygenated xanthones are synthesized. The possibility of a 1,3,4,8-tetraoxygenated pattern for two xanthones from *Centaurium linarifolium* is disproved. New structures are proposed for these two xanthones as 1,3,5-trihydroxy-2-methoxyxanthone, already cited in the literature, and 1,3-dihydroxy-2,5-dimethoxyxanthone, not previously cited.

During the past 30 years, a large number of xanthones have been isolated from higher plants and their natural occurrence and synthesis have gained considerable importance (1). In addition, in several cases the medical properties of plants have been attributed to their xanthone constituents, and several pharmacological studies have been done on them (2).

Centaurium linarifolium (Lamark) G. Beck (Gentianaceae), a plant commonly found in eastern Spain, has been used in folk medicine as a digestive, an antipyretic, and a blood circulation stimulant (3). Several new xanthones were isolated from this plant, and two alternative structural proposals were advanced on the basis of spectral data for two of them (4). These were 1,3,8-trihydroxy-2-methoxy- or 1,3,8-trihydroxy-4-methoxyxanthone and 3,8-dihydroxy-1,2-dimethoxy- or 3,8-dihydroxy-1,4-dimethoxyxanthone.

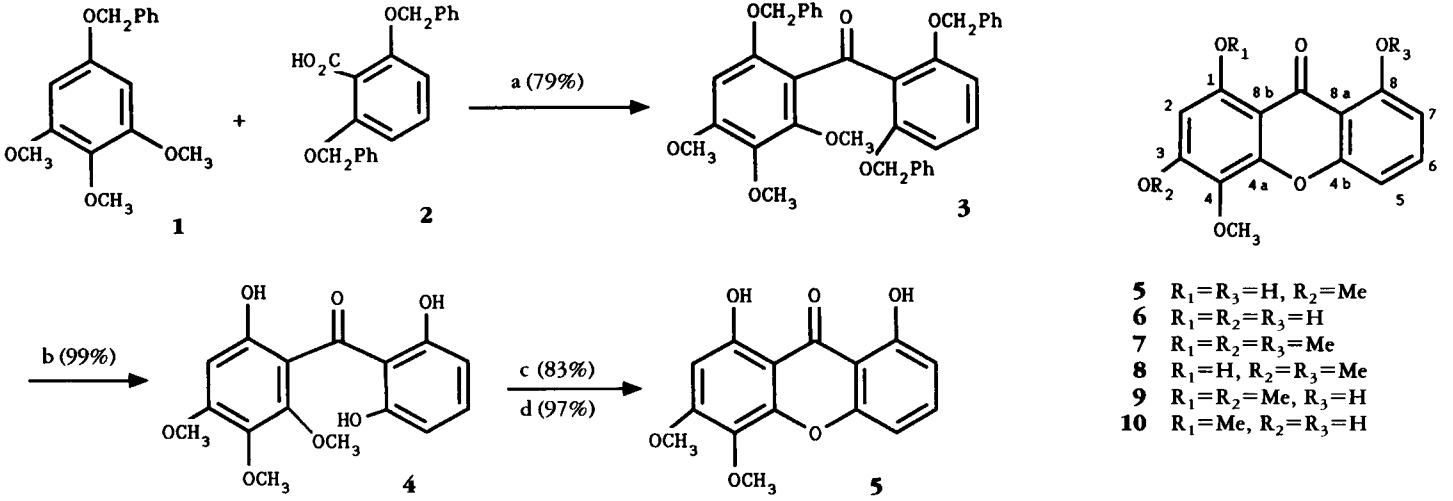
No naturally occurring 1,3,4,8-tetraoxygenated xanthones have been described before, although the synthesis of 1,4,8-trihydroxy-3-methoxy (5) and 1,3,4,8-tetramethoxyxanthone (6) has been described. In a previous report we have discarded the 1,2,3,8-tetraoxygenated pattern for the xanthones from *Centaurium linarifolium* (7), and in the present paper six 1,3,4,8-tetraoxygenated xanthones have been synthesized in order to confirm the alternative structures. A systematic study of their spectral data, summarized in Tables 1, 2, and 3, will be very valuable in the assignment of the correct structures for new 1,3,4,8-tetraoxygenated xanthones.

For unambiguous assignment of the ^{13}C-nmr signals from unsubstituted carbon atoms, ^{1}H-^{13}C correlation experiments were performed. This allowed the assignment of the ^{13}C signals for C-2, C-5, C-6, and C-7, which was confirmed by the ^{1}H-^{13}C coupled nmr spectra (J_{ipso} = 160 Hz). The rest of the aromatic ^{13}C signals were assigned by comparison with previous assignments for xanthones (8,9) and by the multiplicity and coupling constants from the ^{1}H-^{13}C coupled nmr spectra (J_{ortho} = 1–4 Hz, J_{meta} = 7–10 Hz, J_{para} too small to be accurately described).

RESULTS AND DISCUSSION

Our synthetic strategy (Scheme 1) based on our previous experience (7,10,11), consisted of the preparation of the appropriately substituted benzophenone, using TFAA as condensing agent (12), which was then cyclized to the corresponding xanthone. Benzyl ethers were used as the protective groups for all phenolic groups (13). This allowed control of the position and number of hydroxyl groups on the intermediate benzophenone, and hence, after cyclization, complete control over the xanthone structure.

Condensation of 1-benzyloxy-3,4,5-trimethoxybenzene [**1**] and 2,6-dibenzyloxybenzoic acid [**2**], using trifluoroacetic anhydride (TFAA) as condensing agent (12) (Scheme 1), led to 2,2′,6′-tribenzyloxy-4,5,6-trimethoxybenzophenone [**3**], which was hydrogenated in EtOAc, using Pd-C as catalyst (14), to 2,2′,6′-trihydroxy-4,5,6-trimethoxybenzophenone [**4**] (7). When heated with tetramethylammonium hydroxide in pyridine (6), benzophenone **4** underwent cyclization to 1,8-dihydroxy-



5 $R_1=R_3=H$, $R_2=Me$
6 $R_1=R_2=R_3=H$
7 $R_1=R_2=R_3=Me$
8 $R_1=H$, $R_2=R_3=Me$
9 $R_1=R_2=Me$, $R_3=H$
10 $R_1=Me$, $R_2=R_3=H$

a) TFAA/CH_2Cl_2 ($-14°$); b) H_2 (Pd-C)/EtOAc-HCl, room temperature
c) Me_4NOH/C_6H_5-H_2O (Δ); d) Me_2CO-H_2O (Δ)

SCHEME 1

TABLE 1. ^{1}H nmr of 1,3,4,8-Tetraoxygenated Xanthones.[a]

Proton	Compound (Solvent)							
	5 ($CDCl_3$)	**6** (DMSO-d_6)	**7** ($CDCl_3$)	**8** ($CDCl_3$)	**8-Ac**[b] ($CDCl_3$)	**9** ($CDCl_3$)	**9-Ac**[b] ($CDCl_3$)	**10** (DMSO-d_6)
H-2	6.38	6.40	6.35	6.34	6.56	6.35	6.36	6.47
H-5	6.96 md	6.93 md	7.03 md	7.08 md	7.07 md	6.88 md	7.38 md	6.94 md
H-6	7.56 t	7.57 t	7.49 t	7.58 t	7.54 t	7.47 t	7.59 t	7.57 t
H-7	6.76 md	6.79 md	6.74 md	6.77 md	6.75 md	6.70 md	6.91 md	6.68 md
-OH	11.88	11.81	—	13.11	13.11	13.05	13.05	13.37
	11.90	11.91						
-OMe	3.90	4.01	3.90	3.89	3.94	3.89	3.90	3.80
	3.95		3.94	3.92	3.96	3.97	3.95	(6H)
			3.96	4.01	(9H)	3.98	3.98	
			(12H)					
-OAc					2.46		2.46	

[a]Spectra were run on a Bruker AC-200 (200 MHz) instrument. Chemical shifts are quoted in δ ppm, signals being denoted in the usual way; md, doublet ($J = 8.3$ Hz) split further narrowly ($J = 0.7$ Hz); t, triplet ($J = 8.4$ Hz). Singlets are unmarked. Unless marked otherwise OMe signals each integrated for 3 protons and the rest for one proton.

[b]Ac stands for the corresponding peracetylated derivative.

3,4-dimethoxyxanthone **[5]** (83%). The compound was identified as a dihydroxydimethoxyxanthone ($C_{15}H_{12}O_6$) by the ^{1}H-nmr signals of its hydroxyl groups (δ 11.88 and 11.90) at low field due to double chelation with the carbonyl group (7) and by its uv spectrum in MeOH, which did not change on addition of NaOAc but showed a bathochromic shift when $AlCl_3$ was added. These facts indicated that both hydroxy groups occupy the C-1 and C-8 positions. A quantitative yield of 1,8-dihydroxy-3,4-

TABLE 2. ^{13}C nmr of 1,3,4,8-Tetraoxygenated Xanthones.[a]

Carbon	Compound					
	5[b]	**6**[c]	**7**[b]	**8**[b]	**9**[c]	**10**[b]
C-1	158.59	157.12	156.63	159.11	157.55	156.97
C-2	94.89	98.62	91.65	94.59	91.20	95.94
C-3	160.51	160.24	156.85	159.25	158.31	157.94
C-4	128.77	127.74	129.48	127.89	130.05	128.35
C-4a	149.12	149.24	150.43	148.29	151.60	151.52
C-4b	156.05	155.35	156.45	157.76	155.15	154.58
C-5	110.91	110.49	109.09	109.88	110.75	110.29
C-6	136.91	137.01	133.47	135.31	135.78	135.96
C-7	107.20	107.08	105.69	105.62	106.30	106.29
C-8	161.27	160.28	160.14	160.47	162.01	161.31
C-8a	107.51	106.53	113.10	110.48	108.69	107.99
C-8b	102.00	100.62	108.26	103.55	105.46	103.54
C=O	184.76	183.32	175.15	181.36	181.69	180.41

[a]Chemical shifts are quoted in δ ppm. In ^{13}C-^{1}H coupled spectra the following multiplicities are observed: C-1 d (J_{ortho}); C-2 d (J_{ipso}); C-3 d (J_{ortho}); C-4 d (J_{meta}); C-4a s; C-4b dd (J_{meta}, J_{ortho}); C-5 ddd (J_{ipso}, J_{meta}, J_{ortho}); C-6 dt (J_{ipso}, J_{ortho}); C-7 ddd (J_{ipso}, J_{meta}, J_{ortho}); C-8 dd (J_{meta}, J_{ortho}); C-8a t (J_{meta}); C-8b d (J_{meta}).

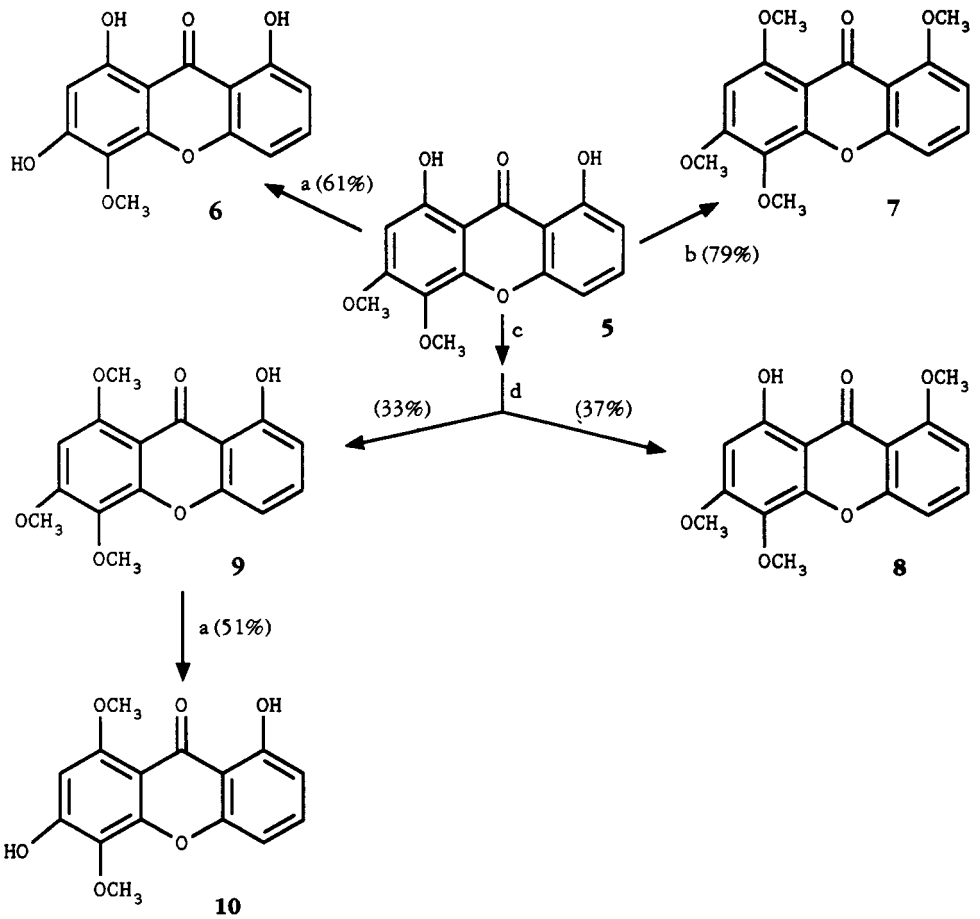
[b]In $CDCl_3$.

[c]In DMSO-d_6.

TABLE 3. Comparison of uv Absorption Maxima [λ max nm (log ε)].[a]

Compound	Solvent	Absorbance
5	(EtOH)[b]	232(4.4) 254(4.5) 258(sh) 303(sh) 338(4.2)
5	(EtOH + NaOMe)	222 240 270 300 373
5	(EtOH + $AlCl_3$)[c]	269 275 320 370 420(sh)
6	(EtOH)	230(3.9) 246(4.0) 259(4.0) 267(sh) 292(sh) 338(3.4)
6	(EtOH + NaOMe)	222 240 271 376
6	(EtOH + NaOAc)[d]	242(sh) 259(sh) 267 278 360
6	(EtOH + $AlCl_3$)[c]	271 273 321 369
7	(EtOH)[e]	209(5.1) 236(5.2) 313(4.8)
8	(EtOH)[b]	241(4.5) 256(sh) 328(4.2) 365(sh)
8	(EtOH + NaOMe)	222 239 265 274 308 321(sh) 395
8	(EtOH + $AlCl_3$)	211 222(sh) 250(sh) 271 353 425
9	(EtOH)[b]	231(4.4) 251(4.5) 332(4.1)
9	(EtOH + NaOMe)	239 271 274 308 323 394
9	(EtOH + $AlCl_3$)[c]	230 257 275(sh) 366 420(sh)
10	(EtOH)	232(sh) 246(4.5) 332(4.2)
10	(EtOH + NaOMe)	220 251 271 342
10	(EtOH + NaOAc)[d]	232 241 265 349
10	(EtOH + $AlCl_3$)	232 259 277 312 360

[a](sh) means a shoulder in the previous peak and (inf) an inflexion point.
[b]uv spectrum showed no variation when NaOAc was added.
[c]uv spectrum showed no variation when HCl was added.
[d]uv spectrum was identical to that in MeOH or EtOH when BO_3H_3 was added.
[e]uv spectrum showed no variation when $AlCl_3$ or NaOMe was added.



a) piperidine/H_2O (Δ); b) $Me_2SO_4/K_2CO_3/Me_2CO$ (Δ)
c) CH_2N_2/Et_2O room temperature; d) Chromatographic separation on Si gel

SCHEME 2

dimethoxyxanthone [**5**] was obtained when benzophenone **4** was refluxed in Me_2CO with a catalytic amount of H_2O (14).

Selective methylation and demethylation of 1,8-dihydroxy-3,4-dimethoxyxanthone [**5**] led to the preparation of five xanthones (Scheme 2) with the same oxygenation pattern. Heating 1,8-dihydroxy-3,4-dimethoxyxanthone [**5**] under reflux in aqueous piperidine (15) afforded 1,3,8-trihydroxy-4-methoxyxanthone [**6**] (61%). The substance was a trihydroxymonomethoxy xanthone ($C_{14}H_{10}O_6$), and its uv spectrum in MeOH showed a bathochromic shift when NaOAc was added, indicating acidic character. These facts indicated the presence of a hydroxyl group at C-3 besides those at C-1 or -8 (16) and confirmed that selective demethylation of methoxy groups para to a carbonyl group occurs under mild alkaline conditions (15). Confirmation of the selective demethylation at C-3 and not at C-4 was provided by the difference in physical and spectral data of **6** and those described for synthetic 1,4,8-trihydroxy-3-methoxyxanthone (5).

These physical and spectral data were different from those of the trihydroxymonomethoxyxanthone isolated from *C. linarifolium* (4). This result, in combination with that previously obtained (7), disproves both 1,3,8-trihydroxy-2-methoxy- and 1,3,8-trihydroxy-4-methoxyxanthone as possible structures for this xanthone.

Permethylation of **5** (Scheme 2) with Me_2SO_4 and K_2CO_3 in Me_2CO (17) gave 1,3,4,8-tetramethoxyxanthone [**7**]. Its physical and spectral data were identical with those described for synthetic material by Stout and Balkenhol (6). Methylation of **5** by treatment for 4 days at room temperature with an ethereal solution of CH_2N_2, followed by cc separation, led to 1-hydroxy-3,4,8-trimethoxyxanthone [**8**] (37%), 8-hydroxy-1,3,4-trimethoxyxanthone [**9**] (33%), and 25% of starting material **5**.

As both xanthones **8** and **9** have not been previously cited in the literature, their structures were elucidated by a study of the ^{1}H-nmr spectra of the corresponding acetylated derivatives. Acetylation of **8** leaves almost unchanged the chemical shifts of the ABX system but increases by 0.22 ppm the chemical shifts of the singlet signal assigned to H-2. This is consistent with the displacement expected for a proton in the ortho position to an acetoxy group and indicates that the hydroxyl group in **8** is located in the trisubstituted ring (18,19). The acetyl derivative of **9** does not show displacement of the H-2 signal but shows displacements for the signals of H-5, H-6 and H-7 (0.5, 0.1, and 0.2 ppm) that are consistent with protons placed at the ortho, meta, and para positions relative to an acetoxy group at C-8 (18,19). This confirms that the hydroxy group in **9** is in the monosubstituted ring.

Demethylation of **9** by heating under reflux in aqueous piperidine (15) afforded 3,8-dihydroxy-1,4-dimethoxyxanthone [**10**] (51%), which was identified as follows: The material is a dihydroxy-dimethoxyxanthone ($C_{15}H_{12}O_6$) and has a strong acidic character, because its uv spectrum in MeOH showed a bathochromic shift on addition of NaOAc. These facts indicated a hydroxyl group at C-3 in addition to the one at C-8 (16). Selective demethylation at C-3 (15) and not C-1 was confirmed by physical and spectral data differences between **10** and 1,8-dihydroxy-3,4-dimethoxyxanthone [**5**].

The physical and spectral data of **10** differ from those of the dihydroxy-dimethoxyxanthone isolated from *C. linarifolium* (4), and thus both the 3,8-dihydroxy-1,4-dimethoxy and 3,8-dihydroxy-1,2-dimethoxyxanthone (7) structures have to be discarded. For both naturally occurring xanthones, only a small amount of sample was isolated, which made purification difficult. In addition, preparation of derivatives was not possible. The previously incorrect structural assignment was based solely on spectral data (4).

As both the 1,2,3,8- (7) and 1,3,4,8-tetraoxygenated patterns have been discarded for the tetraoxygenated xanthones isolated from *C. linarifolium*, new assignments are needed. Lins-Mesquita *et al.* (16) claimed that for 1,3-dihydroxyxanthones, uv spectra obtained in MeOH + NaOMe and MeOH + NaOAc are not superimposable. This assumption allowed 1,3-dihydroxy structures to be discarded for the dihydroxy-dimethoxyxanthone isolated from *C. linarifolium*. We have found that, in contrast to others, the uv spectra of some 1,3-dihydroxyxanthones in MeOH + NaOMe and MeOH + NaOAc are superimposable (7,10). Consequently, 1,3-dihydroxy structures can be reconsidered for the dihydroxy-dimethoxy xanthone isolated from *C. linarifolium*. Its ^{1}H nmr showed an ABX system with ortho coupling constants; therefore, a methoxy group must be placed at C-5 and both 1,3-dihydroxy-2,5-dimethoxy or 1,3-dihydroxy-4,5-dimethoxy structures can be considered. A singlet signal (H-2 or H-4) was found at δ 6.82 in its ^{1}H nmr, which corresponds to a hydrogen at C-4, because a proton at C-2 should be found at higher field (δ <6.5) (20). The uv spectra were more consistent with a 1,2,3,5-tetraoxygenated structure (21–24). In addition, its physical and spectral data differed from those reported for 1,3-dihydroxy-4,5-dimethoxyxanthone isolated from *Frasera caroliniensis* Walt. (6).

Therefore, the dihydroxy-dimethoxyxanthone isolated from *C. linarifolium* (4) is reassigned as 1,3-dihydroxy-2,5-dimethoxyxanthone, which has not previously been described. This structure has been cited in a review by Sultanbawa (1) for a xanthone

isolated from *Kielmeyera candidissima*, but in the original paper it was assigned as 1,3-dihydroxy-2,8-dimethoxyxanthone (25). This structure has been recently disproved (7). As its spectral data are quite similar with those of the dihydroxy-dimethoxyxanthone isolated from *C. linarifolium* (4), we propose 1,3-dihydroxy-2,5-dimethoxyxanthone as the correct structure for both naturally occurring xanthones.

The trihydroxy-monomethoxyxanthone isolated from *C. linarifolium* is reassigned as 1,3,5-trihydroxy-2-methoxyxanthone because its ^{1}H-nmr and uv spectra differ from those of 1,3,4,5-tetraoxygenated xanthones and the physical and spectral data agree with those described in the literature (21–24) for naturally occurring 1,3,5-trihydroxy-2-methoxyxanthone.

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 or EtOH 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 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′,6′-TRIBENZYLOXY-4,5,6-TRIMETHOXYBENZOPHENONE [**3**].—To a stirred solution of 2,6-dibenzyloxybenzoic acid [**2**] (1.27 g, 3.0 mmol) and 1-benzyloxy-3,4,5-trimethoxybenzene [**1**] (0.82 g, 2.99 mmol) in dry CH_2Cl_2 (34 ml), under argon at 0°, TFAA (3.5 ml) was added (12). After 3 h at room temperature, the crude mixture was poured over ice (50 g) and extracted with CH_2Cl_2 (4 × 25 ml). The combined extracts were washed with saturated $NaHCO_3$ solution and brine. After crystallization from hexane/CH_2Cl_2, 2,2′,6′-tribenzyloxy-4,5,6-trimethoxybenzophenone [**3**] was obtained as colorless plates (1.4 g, 2.37 mmol, 79%): mp 157–159°, ir ν max (KBr) cm^{-1} 3200–2860, 1675, 1595, 1495, 1455, 1405, 1390, 1265, 1205, 1130, 1105, 830, 765, 750, 700; ^{1}H nmr ($CDCl_3$) δ 3.47, 3.71, and 3.82 (9H, 3s, 3 OMe), 4.66 (2H, s, OCH_2Ph), 4.88 (4H, s, 2 OCH_2Ph), 6.14 (1H, s, H-3), 6.51 (2H, d, J = 8.4 Hz, H-2′ + H-5′), 7.10–7.21 (16H, m, aromatic protons 3 BzO + H-4′); hrms *m/z* (%) $[M]^+$ 590 (20) (found 590.229 ± 0.009, calcd for $C_{37}H_{34}O_7$, 590.230), 274 (20), 273 (29), 211 (19), 210 (34), 181 (13), 91 (100).

PREPARATION OF 2,2′,6′-TRIHYDROXY-4,5,6-TRIMETHOXYBENZOPHENONE [**4**].—To a stirred solution of 2,2′,6′-tribenzyloxy-4,5,6-trimethoxybenzophenone [**3**] (1.6 g, 2.69 mmol) in EtOAc (125 ml), concentrated HCl (0.5 ml) and 5% Pd-C (30 mg) were added (14). The mixture was hydrogenated at room temperature and 1 atm of pressure for 3 h. The catalyst was filtered off, and the solution was washed with H_2O until neutral. After crystallization from hexane/Et_2O, 2,2′,6′-trihydroxy-4,5,6-trimethoxybenzophenone [**4**] (857 mg, 2.68 mmol, 99%) was obtained as orange-yellow prisms: mp 180–182°; ir ν max (KBr) cm^{-1} 3300, 3000–2800, 1615, 1575, 1490, 1470, 1450, 1400, 1350, 1285, 1260, 1210, 1140, 995, 940, 865, 810, 780, 735, 710; ^{1}H nmr ($CDCl_3$) δ 3.60, 3.73, and 3.90 (9H, 3s, 3 OMe), 6.30 (1H, s, H-2), 6.44 (2H, d, J = 8 Hz, H-2′ + H-4′), 7.21 (1H, t, H-3′), 7.48 (2H, broad s, 2 OH), 10.73 (1H, s, OH); hrms *m/z* (%) $[M]^+$ 320 (36) (found 320.087 ± 0.004, calcd for $C_{16}H_{16}O_7$, 320.089), 289 (100), 228 (15), 210 (13), 184 (63), 169 (52), 137 (35).

PREPARATION OF 1,8-DIHYDROXY-3,4-DIMETHOXYXANTHONE [**5**].—*Method A.*—To a stirred solution of 2,2′,6′-trihydroxy-4,5,6-trimethoxybenzophenone [**4**] (1.6 g, 5 mmol) in pyridine (21.6 ml) under argon, H_2O (10.9 ml) and 10% aqueous tetramethylammonium hydroxide (8 ml) were added. The mixture was refluxed for 14 h (6), poured over ice (70 g), acidified with concentrated HCl, and extracted with Et_2O (4 × 35 ml). The combined extracts were washed with $NaHCO_3$ solution and H_2O. The crude residue was crystallized (Me_2CO/H_2O) to give 1,8-dihydroxy-3,4-dimethoxyxanthone [**5**] (1.19 g, 4.13 mmol, 83%) as yellow needles, mp 198–200°. Found C 62.3, H 4.2; calcd for $C_{15}H_{12}O_6$, C 62.5, H 4.2%. Ir ν max (KBr) cm^{-1} 2980, 2930, 1655, 1625, 1610, 1580, 1515, 1475, 1365, 1290, 1230, 1210, 1150, 1115, 1070, 1055, 825, 820, 730.

Method B.—To a solution of 2,2′,6′-trihydroxy-4,5,6-trimethoxybenzophenone [**4**] (859 mg, 2.68 mmol) in Me_2CO (100 ml), H_2O (5 ml) was added. The solution was refluxed for 7 h (14). When the solution was allowed to cool to room temperature, 1,8-dihydroxy-3,4-dimethoxyxanthone [**5**] (750 mg, 2.6 mmol, 97%) crystallized.

PREPARATION OF 1,3,8-TRIHYDROXY-4-METHOXYXANTHONE [**6**].—A stirred solution of 1,8-

dihydroxy-3,4-dimethoxyxanthone [**5**] (200 mg, 0.698 mmol) in piperidine (25.4 ml) and H_2O (10.6 ml) was reluxed under argon for 44 h (15). The crude solution was poured over ice H_2O (50 ml), acidified with concentrated HCl (8 ml), and extracted with Et_2O (4 × 25 ml). The combined extracts were washed with $NaHCO_3$ solution and H_2O. The residue was crystallized from hexane/CH_2Cl_2 to give 1,3,8-trihydroxy-4-methoxyxanthone [**6**] (116 mg, 0.413 mmol, 61%) as orange-yellow prisms, mp 215–218°. Found C 61.0, H 3.8; calcd for $C_{14}H_{10}O_6$, C 61.3, H 3.7%. Ir ν max (KBr) cm^{-1} 3330, 2920, 1660, 1630, 1610, 1590, 1510, 1480, 1295, 1265, 1230, 1170, 1160, 1065, 1050, 815.

PREPARATION OF 1,3,4,8-TETRAMETHOXYXANTHONE [**7**].—To a stirred solution of 1,8-dihydroxy-3,4-dimethoxyxanthone [**5**] (200 mg, 0.694 mmol) in Me_2CO (100 ml), anhydrous K_2CO_3 (1.0 g) and Me_2SO_4 (3.15 ml) were added (17). The mixture was refluxed for 24 h, the K_2CO_3 was filtered off, and the solution was poured over 0.1 M NH_4OH (50 ml) and extracted with CH_2Cl_2 (4 × 15 ml). The combined extracts were washed with 1 M HCl (3 × 10 ml), NaHCO-saturated solution, and H_2O. 1,3,4,8-Tetramethoxyxanthone [**7**] was obtained as a white solid (174 mg, 0.55 mmol, 79%): mp 187–189° [lit. (6) 192°]; ir ν max (KBr) cm^{-1} 3060–2800, 1650, 1615, 1595, 1570, 1500, 1470, 1440, 1410, 1330, 1285, 1265, 1240, 1210, 1125, 1090, 985, 905, 850, 810, 780, 640. Its physical and spectral data were identical with those reported by Stout and Balkenhol (6).

PREPARATION OF 1-HYDROXY-3,4,8-TRIMETHOXYXANTHONE [**8**] AND 8-HYDROXY-1,3,4-TRIMETHOXYXANTHONE [**9**].—1,8-Dihydroxy-3,4-dimethoxyxanthone [**5**] (230 mg, 0.80 mmol) was added to a saturated solution of CH_2N_2 in Et_2O (10 ml). The mixture was stirred at room temperature for 44 h. The crude mixture obtained was purified by cc to give starting material [**5**] [hexane-Et_2O (8:2)] (58.7 mg, 0.20 mmol, 25%), compound **8**, and compound **9**.

1-Hydroxy-3,4,8-trimethoxyxanthone [**8**].—Compound **8** [hexane-Et_2O (7:3)] (89.6 mg, 0.30 mmol, 37%): yellow prisms (hexane/CH_2Cl_2); mp 205–207°. Found C 63.8, H 4.6; calcd for $C_{16}H_{14}O_6$, C 63.6, H 4.7%. Ir ν max (KBr) cm^{-1} 3100, 2930, 1655, 1605, 1575, 1515, 1485, 1450, 1440, 1400, 1370, 1330, 1320, 1270, 1235, 1215, 1150, 1125, 1095, 1085, 1040, 990, 980, 860, 835, 785.

8-Hydroxy-1,3,4-trimethoxyxanthone [**9**].—Compound **9** [hexane-Et_2O (6:4)] (78.1 mg, 0.26 mmol, 33%): yellow prisms (hexane/CH_2Cl_2); mp 217–220°. Found C 63.7, H 4.8; calcd for $C_{16}H_{14}O_6$, C 63.6, H 4.7%. Ir ν max (KBr) cm^{-1} 2930, 1645, 1610, 1575, 1510, 1460, 1415, 1330, 1280, 1245, 1220, 1130, 1080, 980, 860, 820, 785, 775.

PREPARATION OF 3,8-DIHYDROXY-1,4-DIMETHOXYXANTHONE [**10**].—To a stirred solution of 8-hydroxy-1,3,4-trimethoxyxanthone [**9**] (78 mg, 0.26 mmol) in piperidine (10 ml) under argon, H_2O (4.1 ml) was added, and the solution was refluxed for 24 h (15). The reaction mixture was poured over ice-H_2O (25 ml), acidified with concentrated HCl, and extracted with CH_2Cl_2 (4 × 25 ml). The combined extracts were washed with $NaHCO_3$ solution and H_2O. The crude residue was crystallized from CH_2Cl_2/hexane to give 3,8-dihydroxy-1,4-dimethoxyxanthone [**10**] (38.1 mg, 0.13 mmol, 51%) as yellow prisms, mp 233–236°. Found C 62.7, H 4.1; calcd for $C_{15}H_{12}O_6$, C 62.5, H 4.2%. Ir ν max (KBr) cm^{-1} 3500–3350, 3060–2800, 1650, 1610, 1570, 1525, 1505, 1470, 1460, 1445, 1425, 1335, 1290, 1240, 1225, 1100, 1085, 1015, 970, 815, 770, 710, 640.

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Received 14 May 1990