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SYNTHESIS AND STUDY OF 2-C- AND 4-C-METHYLXANTHONES

A. C. JAIN, V. K. KHANNA and T. R. SESHADRI

Department of Chemistry, University of Delhi, Delhi-7, India

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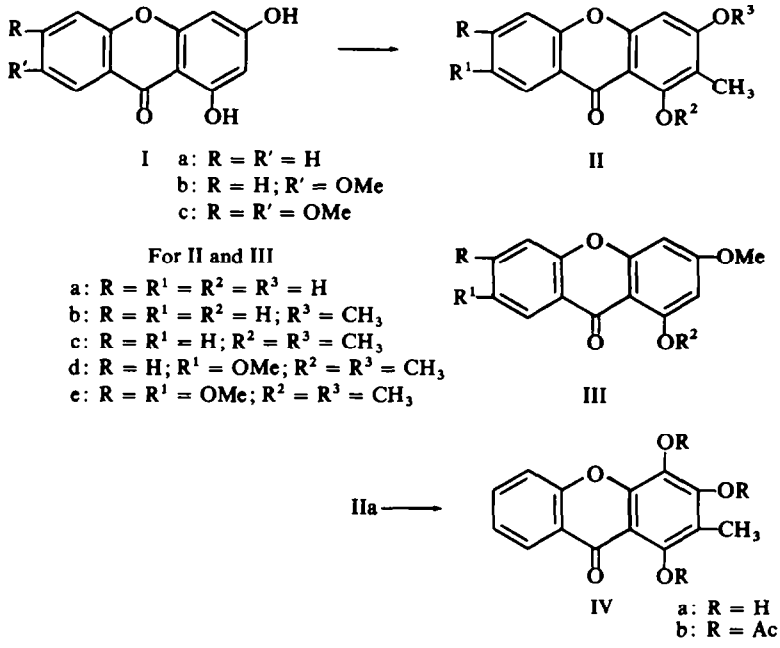
Abstract—2-C- and 4-C-methylxanthones with different oxygenation patterns have been synthesized by two methods: (1) nuclear methylation of 1,3-dihydroxyxanthones (I) to the corresponding 2-C-methyl derivatives (II) and (2) condensation of 2-methyl-(VI) and 4-methyl-(IX) 3,5-dimethoxyphenols with substituted salicylic acids. The 2-methylphenol (VI) gives 2-C-methyl-3-methoxy-1-hydroxyxanthones (VIII) and the 4-methylphenol (IX) gives 4-C-methyl isomers (XI). These observations might be of significance in understanding the mechanism of xanthone formation. C-Methylphloroglucinol (XII) yields exclusively 2-C-methyl-1,3-dihydroxyxanthones (IIa and XIV). The NMR spectra of these xanthones distinguish between 2-C- and 4-C-methylxanthones.

C-METHYLXANTHONES derived from orcinol units, known synthetically and as natural products,[1,2] carry C-Me groups either in 1- or 3-position. But 2-C and 4-C-methylxanthones which could be produced in Nature from polyhydroxy compounds by the transmethylation process either after or before the formation of the hetero-oxygen ring, are not known. However, a C-glucosylxanthone has been found; it is mangiferin which has been shown to be 2-C-glucosyl-1,3,6,7-tetrahydroxyxanthone by degradation[3–6] as well as by synthesis.[7,8] It is considered to be formed by the C-glucosylation of the tetrahydroxyxanthone. Similarly there are isopentenyl and its derived units in 2- and 4-positions in many natural xanthones.[9] This indicates the possibility of analogous C-methylxanthones also occurring in Nature. In this paper, the synthesis of such xanthones in two different ways is reported.

The first method involves the nuclear methylation of 1,3-dihydroxyxanthones with methyl iodide in the presence of methanolic alkali. In 5,7-dihydroxyflavonoids, such a reaction brings about C-methylation in the 6-position and in 2,4-dihydroxy- and 2,4,6-trihydroxy-benzoyl derivatives C-methylation in the 3-position.[10] Similarly in 1,3-dihydroxyxanthones, C-methylation can be expected to take place in the 2-position. 1,3-Dihydroxyxanthone (Ia)[11] itself has now been methylated with methyl iodide in the presence of methanolic sodium methoxide. The product is a mixture of 1-hydroxy-3-methoxyxanthone (IIIa) and 2-methyl-1,3-dihydroxyxanthone (IIa) which forms mono- and di-methyl ethers and is hydroxylated by alkaline persulphate, giving 2-C-methyl-1,3,4-trihydroxyxanthone (IVa). This compound yields a triacetate (IVb) whose structure was confirmed by its NMR spectrum. Generally the C-methylated product obtained in nuclear methylations is also partially O-methylated;[10] the absence in the present case of O-methylation lends further support to the conclusion that C-methylation precedes O-methylation, the two earlier examples being the nuclear methylation of 3-O-methylgalangin[12] and 3,2′,4′-tri-O-methylmorin.[13]

An alternative procedure uses complete O-methylation of the mixture of IIa and IIIa with dimethyl sulphate in the presence of potassium carbonate and acetone. The



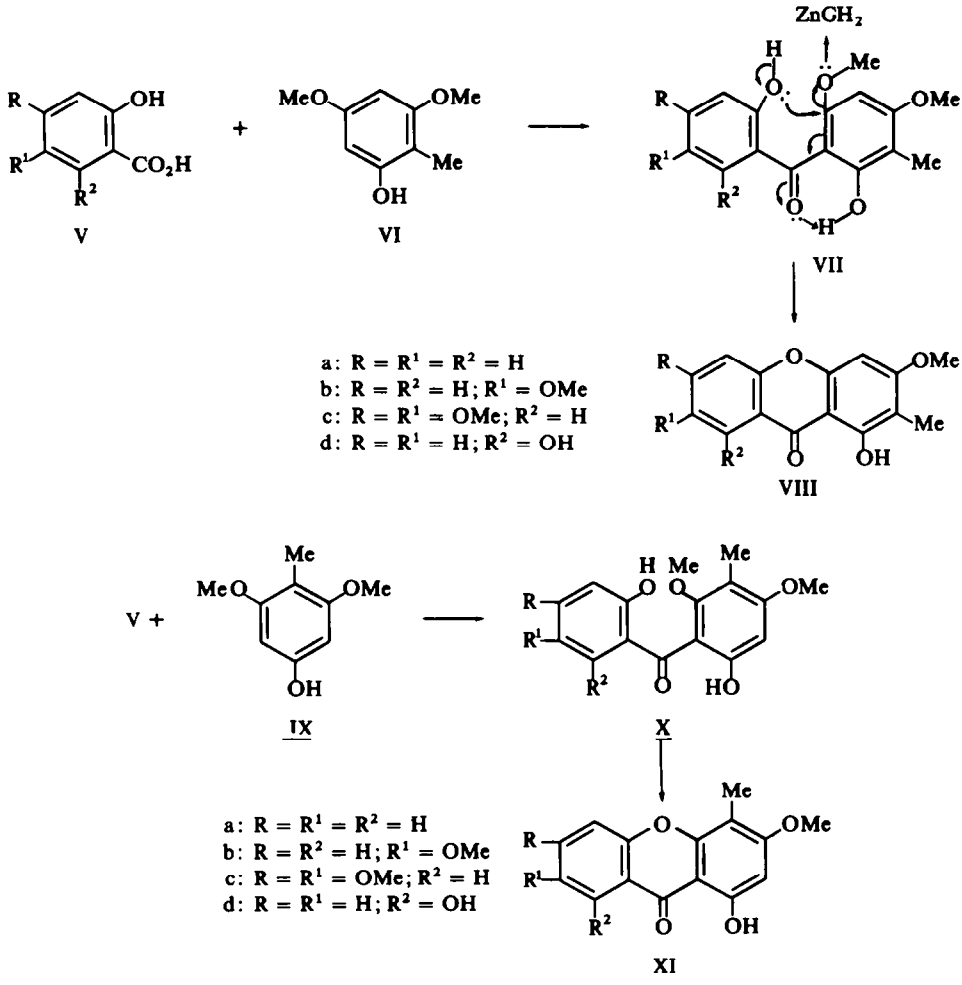
resulting 1,3-dimethoxyxanthone (IIIc) and its C-methyl derivative (IIc) differ considerably in solubility, the latter being sparingly soluble in methanol. Hence this procedure was used in the nuclear methylation of two more xanthones viz., 1,3-dihydroxy-7-methoxyxanthone (Ib)[11] and 1,3-dihydroxy-6,7-dimethoxyxanthone (Ic).[14]

In the second method, 2-methyl-3,5-dimethoxyphenol (VI) and its 4-C-methyl isomer[15] (IX) were separately condensed with salicylic acid in the presence of $POCl_3$ and $ZnCl_2$. The single product from the phenol (VI) was identical with 2-methyl-3-methoxy-1-hydroxyxanthone (IIb) prepared by the nuclear methylation method. The presence of the 3-OMe in the product would indicate that the condensation takes place by the carboxylic attack of the nuclear position *ortho* to the free phenolic OH and subsequent xanthone ring closure involves loss of a OMe (see VII). This loss does not take place before acylation since the excess of phenol is recovered unchanged. The reaction seems to involve synchronous displacement of OMe by the phenoxy group, being aided by the chelated carbonyl group as shown in formula VII.

Condensation of salicylic acid with 4-methyl-3,5-dimethyoxyphenol (IX) gave an isomeric xanthone considered to be 4-C-methyl-3-methoxy-1-hydroxyanthone (XIa). Obviously a similar process of ring closure involving synchronous displacement of OMe by phenoxy group takes place here also.

Next, the above condensations were repeated at lower temperatures in order to avoid the possibility of demethylation. But the phenols VI and IX were recovered unchanged almost completely. It appears that the temperature 70–75° is fairly critical for the above synthesis.

Parallel experiments were carried out with the phenols VI and IX separately using two other acids viz. 5-methoxy-salicylic acid (Vb), and 4,5-dimethoxysalicylic acid

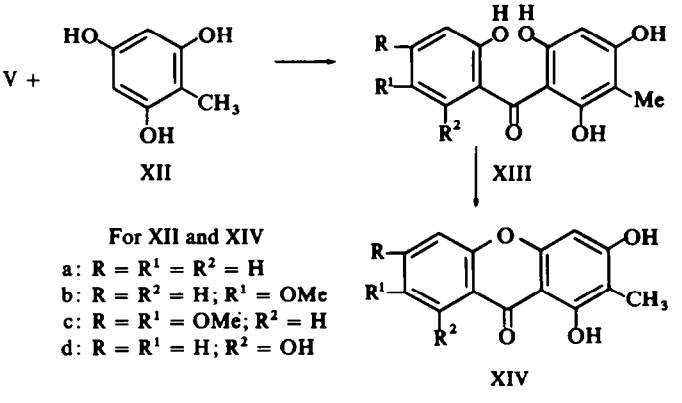


(Vc). They gave similar results i.e., the phenol (VI) gave 2-methylxanthones (VIIIb and c) and IX yielded 4-methylxanthones (XIb and c). Further γ-resorcyclic acid (Vd) was also used in the above condensations to see if it would still promote cyclization, involving loss of methanol though a free OH group is present in the other part of the molecule capable of chelation with the carbonyl group in the intermediate benzophenone (VII or X). But here also the cyclization involving loss of methanol occurred and 2-methylxanthone (VIIId) was obtained from VI and the 4-isomer (XId) from IX.

In the literature, there are several examples in which demethylated xanthones have been isolated in this condensation. The following are two such examples: phloroglucinol when condensed with 6-methoxy-2-hydroxybenzoic acid gave a mixture of 1,3,8-trihydroxy- and 1,3-dihydroxy-8-methoxyxanthones;[16] 2,6-dimethoxyquinol and γ-resorcylic acid gave a mixture of 3-methoxy-1,2,8-trihydroxy- and 3-methoxy-1,4,8-trihydroxy-xanthones.[17] At the same time, there is an example where no loss of OMe has occurred, even though it could take place. Thus phloroglucinol dimethyl ether when condensed with 2,3-dihydroxy-4-methoxybenzoic acid gave 1,3,6-trimethoxy-5-hydroxyxanthone.[23] Further it is surprising that resorcinol gives mainly

3-hydroxyxanthones by the method of Grover *et al.* while Nencki's conditions of condensation yield 1-hydroxyanthones.[11] Thus these results do not constitute uniform behaviour and these reactions require study in greater detail.

Next C-methylphloroglucinol (XII) was condensed with salicylic acid. Though there are two possibilities, only one xanthone was formed and it was identical with 2-C-methyl-1,3-dihydroxyxanthone (IIa) prepared earlier by nuclear methylation. Parallel condensations using three other salicylic acid derivatives (Vb, c and d) also gave the corresponding 2-methyl-1,3-dihydroxyxanthones (XIVb, c and d) showing that this is the normal course of the reaction. This exclusive formation of only 2-methyl isomer is remarkable because in analogous studies using 3-methyl-2,4,6-trihydroxybenzoyl compounds, generally mixtures of two isomeric C-methylflavones, flavonols, chromones[10] and isoflavones[10,18] result.



For XII and XIV

a: R = R¹ = R² = H
b: R = R² = H; R¹ = OMe
c: R = R¹ = OMe; R² = H
d: R = R¹ = H; R² = OH

NMR spectra have earlier been used for proving the presence of H-2 and H-4 protons in xanthones and reports of their resonances are conflicting. In some cases[4,20,21] the H-2 proton is considered to have higher δ values and in others[17,22,23] the reverse and explanations have been given. However, doubt exists if these proton-resonances

TABLE 1. NMR SPECTRAL DATA (δ; ppm) IN $CDCl_3$

Xanthone	2 or 4H	—OCH_3	2 or 4 —CH_3	—$OCOCH_3$
2-Methyl-3-methoxy-1-hydroxy- (IIb)	6·22(s)	3·78(s) (3H)	1·92(s) (3H)	
4-Methyl-3-methoxy-1-hydroxy- (XIa)	6·32(s)	3·85(s) (3H)	2·13(s) (3H)	
2-Methyl-3,7-dimethoxy-1-hydroxy- (VIIIb)	6·27(s)	3·82(s) (6H)	1·99(s) (3H)	
4-Methyl-3,7-dimethoxy-1-hydroxy- (XIb)	6·30(s)	3·84(s) (6H)	2·11(s) (3H)	
2-Methyl-3,6,7-trimethoxy-1-acetoxy-	6·68(s)	3·87(s), 3·90(s), 3·92(s) (9H)	2·02(s) (3H)	2·54(s) (3H)
4-Methyl-3,6,7-trimethoxy-1-acetoxy-	6·54(s)	3·84(s), 3·88(s), 3·91(s) (9H)	2·17(s) (3H)	2·37(s) (3H)
2-Methyl-3-methoxy-1,8-diacetoxy-	6·62(s)	3·82(s) (3H)	1·98(s) (3H)	2·37(s), 2·40(s) (6H)
2-Methyl-1,3,8-triacetoxy-	6·85(s)		1·97(s) (3H)	2·23(s) (3H) 2·36(s) (3H) 2·40(s) (3H)

could be used for establishing constitutions definitely. In a number of isomeric compounds we have examined, a study of H-2 and H-4 protons could be made without ambiguity. The spectral data are given in Table 1, from which it will be clear that there is no marked difference in the H-2 and H-4 signals and further H-4 proton signals are slightly upfield as compared to those of H-2 protons in the first two pairs of C-methylxanthones but the reverse happens in the third pair of xanthones. This difference may be partly due to the fact that the third pair of xanthones have an acetoxyl group in 1-position; an attempt was therefore made to examine the corresponding acetates of the first two pairs, but it failed because of lack of adequate solubility. But the signals of Me groups are more significant and uniform; 4-C-Me protons have always higher δ values than the 2-C-Me ones. This is in agreement with the recent data on analogous isoflavones.[19] Thus Me signals seem to be more dependable for establishing correct orientation.

EXPERIMENTAL

All m.ps reported are uncorrected. Unless otherwise stated, light petroleum ether had boiling range 60–80°; UV spectra were taken in MeOH soln; figures in brackets in UV data represent log ε values; IR spectra were taken using KBr disc; R_f values are given for qualitative TLC on silica gel in the following solvent systems: (A) $CHCl_3$ (B) $CHCl_3$:MeCOMe, 90:10; the plates were sprayed with 10% H_2SO_4; acetylation was carried out by refluxing with Ac_2O in the presence of pyridine for 4 hr and partial O-methylation was carried out by refluxing with calculated amount of Me_2SO_4 for 4 hr and complete O-methylation with excess of Me_2SO_4 in the presence of K_2CO_3 and acetone until negative ferric reaction.

Nuclear methylation of 1,3-*dihydroxyxanthone* (Ia)

Method 1 (*preparation of* 2-*methyl*-1,3-*dihydroxyxanthone*, IIa). To a soln of Ia,[11] (3 g) in anhyd MeOH (150 ml) was added a methanolic soln of NaOMe (5 g Na/50 ml MeOH). The mixture was cooled, treated with MeI (30 ml) in one lot and then refluxed for 3 hr during which more MeI (15 ml) was also added. After removal of the solvents, the reaction mixture was treated with water (150 ml), acidified with HCl and extracted with ether (Ether extract A). This extract was in turn extracted first with 5% Na_2CO_3 aq and then with 5% NaOH aq and finally washed with water. The ether soln gave a residue, which on TLC using solvent system (A) showed the presence of a single compound. It crystallized from MeOH as light yellow needles (1 g), m.p. 148°, green ferric reaction. These properties agree with those of IIa in m.m.p. and TLC.

The Na_2CO_3 soluble and NaOH soluble parts were acidified separately, and extracted with ether. Since the two extracts were found to be identical on TLC (solvent B; R_f 0·7), they were mixed and evaporated together and the solid thus obtained was crystallized from MeOH yielding IIa as light yellow needles (0·8 g), m.p. 248°; green ferric reaction; λ_{max} 236, 311 nm (4·54, 4·22 respectively); ν_{max} 1650 cm^{-1} (xanthone C=O). (Found: C, 68·9; H, 4·5. $C_{14}H_{10}O_4$ requires: C, 69·4; H, 4·2%).

The above IIa (0·24 g) on partial methylation gave IIb which crystallized from MeOH as light yellow needles, m.p. 172°; R_F 0·4 (solvent A); green ferric reaction; λ_{max} 240, 306 nm (4·50, 4·24 respectively); ν_{max} 1665 cm^{-1} (xanthone-C=O). Found: C, 70·2; H, 5·1. $C_{15}H_{12}O_4$ requires: C, 70·3; H, 4·7%). The acetate crystallized from EtOAc–light petroleum as colourless needles, m.p. 222°. (Found: C, 68·9; H, 5·2, $C_{17}H_{14}O_5$ requires: C, 68·5; H, 4·7%), Complete methylation of IIa yielded IIc which crystallized from MeOH as colourless needles, m.p. 156°; R_f 0·8 (solvent B); λ_{max} 238, 277, 299–300 nm (4·59, 4·03, 4·20 respectively); ν_{max} 1655 cm^{-1} (xanthone-C=O). (Found: C, 70·7; H, 5·7. $C_{16}H_{14}O_4$ requires: C, 71·1; H, 5·2%).

Method 2 (*preparation of* 2-*methyl*-1,3-*dimethoxyxanthone*, IIc). In another experiment, nuclear methylation was carried out as mentioned above. But the product (ether extract A) was directly O-methylated completely. The product was fractionally crystallized from MeOH. The sparingly soluble fraction recrystallized from MeOH as colourless needles, m.p. 156°; it was identical with IIc in m.m.p. and TLC.

2-*Methyl*-1,3,4-*triacetoxyxanthone* (IVb). To an ice-cooled and stirred soln of IIa (0·5 g) in aq. NaOH (0·4 g/8 ml) was added dropwise a saturated soln of potassium persulphate (0·5 g in 25 ml H_2O) during 2 hr and stirring continued for another 2 hr. After 24 hr at room temp the soln was acidified to congo red and the unchanged product was filtered off. The filtrate was treated with Na_2SO_3 (2 g) and conc HCl

(25 ml) and after 4 hr at room temp, IVa was filtered off, dried and was directly acetylated. Compound IVb crystallized from MeOH as colourless needles (70 mg), m.p. 211°; no ferric reaction; ν_{max} 1780 (ester—C=O) 1670 cm^{-1} (xanthone—C=O); δ (in $CDCl_3$): 2·31, 2·37, 2·46 (three —OCOC$\underline{H}_3$), 2·06 ppm (C—C$\underline{H}_3$). (Found: C, 62·7; H, 4·4. $C_{20}H_{16}O_8$ requires: C, 62·5; H, 4·2%).

Nuclear methylation of 7-*methoxy*-1,3-*dihydroxyxanthone* (Ib)

Preparation of 2-*methyl*-1,3,7-*trimethoxyxanthone*, IId. Compound Ib,[11] (1 g) was methylated with MeI (15 ml) in the presence of methanolic–NaOMe (1·7 g Na/70 ml) as described. The ether extract was directly methylated with excess of Me_2SO_4 in the presence of K_2CO_3 and acetone until it gave no ferric reaction. The product was fractionally crystallized from MeOH. The sparingly soluble fraction was recrystallized from MeOH, yielding IId as colourless needles (0·3 g), m.p. 152°; R_f 0·9 (solvent B); λ_{max} 238, 255, 282, 310 nm (4·50, 4·51, 4·61, 4·12 respectively); ν_{max} 1665 cm^{-1} (xanthone —C=O). (Found: C, 68·1; H, 5·8. $C_{17}H_{16}O_5$ requires: C, 68·0; H, 5·4%).

Nuclear methylation of 6,7-*dimethoxy*-1,3-*dihydroxyxanthone* (Ic)

Preparation of 2-*methyl*-1,3,6,7-*tetramethoxyanthone*, IIe). Compound Ic[14] (1 g) was methylated with MeI (15 ml) in the presence of methanolic NaOMe (prepared from 1·7 g Na) as described. The product was fractionally crystallized from MeOH. The sparingly soluble fraction on recrystallization from MeOH gave IIe as colourless needles (0·3 g), m.p. 184°, R_f 0·8 (solvent B); λ_{max} 250–51, 310–11 nm (4·55, 4·26 respectively); ν_{max} 1650 cm^{-1} (xanthone —C=O). (Found: C, 65·5; H, 5·9. $C_{18}H_{18}O_6$ requires: C, 65·4; H, 5·5%).

2-*Methyl* 3,5-*dimethoxyphenol* (VI). A soln of 4,6-dimethoxy-2-hydroxybenzaldehyde (4·5 g) prepared according to Jain *et al.*,[15] in glacial AcOH (20 ml) was added to ZnHg (prepared from 20 g of Zn dust), followed by 4N HCl (75 ml). The mixture was refluxed for 4 hr, filtered hot, washed with AcOH and the filtrate extracted with ether. The extract was washed with 5% $NaHCO_3$ aq and finally with water. The product crystallized from MeOH yielding 2-methyl-3,5-dimethoxyphenol (4·0 g) as yellow needles, m.p. 61° (lit.,[24] m.p. 61°).

2-*Methyl*-3-*methoxy*-1-*hydroxyxanthone* (IIb). A mixture of salicylic acid (0·5 g), 2-methyl-3,5-dimethoxyphenol (0·8 g), fused $ZnCl_2$ (3 g) and $POCl_3$ (5 ml) was heated at 70–75° for 2 hr and poured over ice. After 24 hr at room temp, it was extracted with ether and the ether extract was washed first with 2% NaOH aq and then with water. The residue showed on TLC (solvent system A) a single spot (R_f 0·4). It crystallized from $CHCl_3$–MeOH as light yellow needles (0·15 g), m.p. 173–174°; green ferric reaction; it was identical with IIb in m.m.p. and TLC.

4-*Methyl*-3-*methoxy*-1-*hydroxyxanthone* (VIIIa). A mixture of salicylic acid (0·5 g), 4-methyl-3,5-dimethoxyphenol[15] (0·8 g), fused $ZnCl_2$ (3 g) and $POCl_3$ (5 ml) was heated as described. The solid obtained after pouring the reaction mixture over ice was washed with hot water and was examined on TLC using solvent system A which showed the presence of three compounds one of which corresponded to the starting phenol. The mixture was separated by fractional crystallization from MeOH. The sparingly soluble fraction on recrystallization from MeOH yielded VIIIa as light yellow needles (0·25 g), m.p. 201–202°; green ferric reaction; R_f 0·4 (solvent A); λ_{max} 233, 258, 307–308 nm (4·44, 4·39, 4·10 respectively); ν_{max} 1665 cm^{-1} (xanthone —C=O). (Found: C, 69·8; H, 4·9. $C_{15}H_{12}O_4$ requires: C, 70·3; H, 4·7%). The acetate crystallized from EtOAc–light petroleum as colourless needles, m.p. 211°. (Found: C, 68·3; H, 4·9. $C_{17}H_{14}O_5$ requires: C, 68·5; H, 4·7%).

The methanolic mother liquor was evaporated to dryness and passed over a column of silica gel. On elution with benzene, first a light yellow solid of indefinite nature was obtained; it crystallized from EtOAc–light petroleum as light yellow needles (10 mg), m.p. 220°; ν_{max} 1660 cm^{-1} (—C=O band). The other fractions of benzene eluate gave the starting phenol (100 mg), m.p. and m.m.p. 148°; identical TLC.

2-*Methyl*-3,7-*dimethoxy*-1-*hydroxyxanthone* (VIIIb). A mixture of 5-methoxy-2-hydroxybenzoic acid (0·55 g), 2-methyl-3,5-dimethoxyphenol (0·75 g), fused $ZnCl_2$ (4 g) and $POCl_3$ (7 ml) was heated. The solid product crystallized from $CHCl_3$–MeOH yielding VIIIb as light yellow needles (0·15 g), m.p. 175°; green ferric reaction; R_f 0·5 (solvent A); λ_{max} 235, 307 nm (4·50, 4·21 respectively); ν_{max} 1660 cm^{-1} (xanthone —C=O). (Found: C, 67·4; H, 5·2. $C_{16}H_{14}O_5$ requires: C, 67·1; H, 4·9%). The acetate crystallized from EtOAc–light petroleum as colourless needles, m.p. 228–229°. (Found: C, 65·3; H, 5·3. $C_{18}H_{16}O_6$ requires: C, 65·8; H, 4·9%).

4-*Methyl*-3,7-*dimethoxy*-1-*hydroxyxanthone* (XIb). A mixture of 5-methoxy-2-hydroxybenzoic acid

(0·55 g), 4-methyl-3,5-dimethoxyphenol (0·75 g), fused $ZnCl_2$ (4 g) and $POCl_3$ (7 ml) was heated. The product crystallized from MeOH yielding XIb as light yellow needles (0·15 g), m.p. 189–191°; green ferric reaction; R_f 0·5 (solvent A); λ_{max} 232, 263, 310 nm (4·28, 4·34, 3·87 respectively) ν_{max} 1660 cm^{-1} (xanthone —C=O). (Found: C, 66·9; H, 5·3. $C_{16}H_{14}O_5$ requires: C, 67·1; H, 4·9%). The acetate crystallized from EtOAc–light petroleum as colourless needles, m.p. 214–215°. (Found: C, 65·6; H, 5·1. $C_{18}H_{16}O_6$ requires: C, 65·8; H, 4·9%).

2-*Methyl*-3,6,7-*trimethoxy*-1-*hydroxyxanthone* (VIIIc). A mixture of 4,5-dimethoxy-2-hydroxybenzoic acid (0·55 g), 2-methyl-3,5-dimethoxyphenol (0·75 g), fused $ZnCl_2$ (4 g) and $POCl_3$ (7 ml) was heated. The solid product crystallized from $CHCl_3$–MeOH yielding VIIIc as light yellow needles (0·1 g), m.p. 214°; olive green ferric reaction; R_f 0·4 (solvent A); λ_{max} 242, 318 nm (4·42, 4·23 respectively); ν_{max} 1650 cm^{-1} (xanthone —C=O). (Found: C, 64·9; H, 5·5. $C_{17}H_{16}O_6$ requires: C, 64·6; H, 5·1%). Its acetate crystallized from EtOAc–light pertroleum as colourless needles, m.p. 239°. (Foung: C, 63·4; H, 5·6. $C_{19}H_{18}O_7$ requires: C, 63·7; H, 5·1%).

4-*Methyl*-3,6,7-*trimethoxy*-1-*hydroxyanthone* (XIc). A mixture of 4,5-dimethoxy-2-hydroxybenzoic acid (0·55 g), 4-methyl 3,5-dimethoxyphenol (0·75 g), fused $ZnCl_2$ (4 g) and $POCl_3$ (7 ml) was heated. The product crystallized from $CHCl_3$–MeOH yielding XIc as light yellow needles (0·1 g), m.p. 268°; green ferric reaction; R_f 0·4 (solvent A); λ_{max} 258, 310 nm (4·45, 4·11 respectively); ν_{max} 1660 cm^{-1} (xanthone —C=O). (Found: C, 64·9; H, 5·5. $C_{17}H_{16}O_6$ requires: C, 64·6; H, 5·1%). The acetate crystallized from EtOAc–light petroleum ether as solourless needles, m.p. 242°. (Found: C, 63·7; H, 5·4. $C_{19}H_{18}O_7$ requires: C, 63·7; H, 5·1%).

2-*Methyl*-3-*methoxy*-1,8-*dihydroxyxanthone* (VIIId). A mixture of 2-methyl-3,5-dimethoxyphenol (0·8 g), γ-resorcyclic acid (0·6 g), fused $ZnCl_2$ (4 g) and $POCl_3$ (7 ml) was heated and the product was extracted with ether. The ether extract was first washed with 2% Na_2CO_3 aq followed by water and then examined on TLC using solvent system A which showed two spots one of which corresponded to the starting phenol. The residue obtained after removing ether was passed over a column of silical gel. It was first eluted with benzene which gave the starting phenol and the eluted with $CHCl_3$. This fraction crystallized from MeOH yielding VIIId as light yellow needles (0·1 g), m.p. 218°; green ferric reaction, R_f 0·9 (solvent A); λ_{max} 249, 325 nm (4·07, 3·84 respectively); ν_{max} 1650 cm^{-1} (xanthone —C=O). (Found: C, 66·0; H, 4·0. $C_{15}H_{12}O_5$ requires: C, 66·2; H, 4·4%). The acetate crystallized from EtOAc–light petroleum as colourless needles, m.p. 216–218°. (Found: C, 63·9; H, 4·6. $C_{19}H_{16}O_7$ requires: C, 64·0; H, 4·5%).

4-*Methyl*-3-*methoxy* 1,8-*dihydroxyxanthone* (XId). A mixture of γ-resorcylic acid (0·6 g), 4-methyl-3,5-dimethoxyphenol (0·8 g), fused $ZnCl_2$ (4 g) and $POCl_3$ (7 ml) was heated and the product was worked up as above. The fraction eluted with $CHCl_3$, crystallized from MeOH yielding XId as light yellow needles (50 mg), m.p. 158°; green ferric reaction; λ_{max} 230, 250, 337 nm (4·15, 4·19, 3·98 respectively); ν_{max} 1665 cm^{-1} (xanthone —C=O). (Found: C, 66·3; H, 4·9. $C_{15}H_{12}O_5$ requires: C, 66·2; H, 4·4%).

2-*Methyl*-1,3-*dihydroxyxanthone* (IIa). A mixture of salicylic acid (1·5 g) C-methylphloroglucinol (2·3 g) fused $ZnCl_2$ (5 g) and $POCl_3$ (10·5 ml) was heated at 70–75° for 2 hr, then poured over ice and after 24 hr, the solid was filtered off, and washed several times with hot water. The dried solid (2·5 g) was examined by TLC (solvent B), which showed the presence of only one mobile compound and some immobile compounds. The solid was then taken up in EtOAc and immobile components were precipitated with light petroleum. The product was filtered off and the filtrate on evaporation gave a residue (1·4 g) which crystallized from MeOH as light yellow needles, m.p. 250°; green ferric reaction. It was identical with IIa in mixed m.p. and TLC. The diacetate crystallized from EtOH as colourless needles, m.p. 182–183°; R_f 0·8 (solvent B); ν_{max} 1770 (ester —C=O), 1680 cm^{-1} (xanthone —C=O). The partial methyl ether crystallized from MeOH as light yellow needles, m.p. 173–174°; it was identical with IIb in m.m.p. and TLC. The complete methyl ether crystallized from MeOH as colourless needles, m.p. 159°; it was identical with IIc in m.m.p. and TLC.

2-*Methyl*-7-*methoxy*-1,3-*dihydroxyxanthone* (XIVb). A mixture of 5-methoxy-2-hydroxybenzoic acid (2·25 g) C-methylphloroglucinol (2.55 g), fused $ZnCl_2$ (10 g) and $POCl_3$ (27 ml) was heated as in the previous cases. The product crystallized from MeOH yielding XIVb as yellow needles (1·2 g), m.p. 275–277°; green ferric reaction; R_f 0·75 (solvent B); λ_{max} 231, 261, 312 nm (4·58, 4·49, 4·21 respectively); ν_{max} 1645 cm^{-1} (xanthone —C=O). (Found: C, 65·8; H, 4·9. $C_{15}H_{12}O_5$ requires: C, 66·2; H, 4·4%). The diacetate crystallized from EtOH as colourless needles, m.p. 205–206°; R_f 0·9 (solvent B); ν_{max} 1775 (ester —C=O), 1665 cm^{-1} (xanthone —C=O). Partial methylation of XIVb yielded a product which crystallized from MeOH as light yellow needles, m.p. 176°; green ferric reaction. It was identical with VIIIb in m.m.p. and TLC.

The xanthone XIVb was completely methylated and the product crystallized from MeOH as colourless needles, m.p. 151°; it was identical with IId, in m.m.p. and TLC.

2-Methyl-6,7-dimethoxy-1,3-dihydroxyxanthone (XIVc). A mixture of 4,5-dimethoxy-2-hydroxybenzoic acid (2·3 g); C-methylphloroglucinol (2·6 g), fused $ZnCl_2$ (14 g) and $POCl_3$ (27 ml) was heated as in the previous cases. The product crystallized from MeOH yielding XIVc as yellow needles (0·8 g), m.p. 280° (d); green ferric reaction; R_f 0·7 (solvent B); λ_{max} 241, 259, 318 nm (4·33, 4·38, 4·16 respectively); ν_{max} 1650 cm^{-1} (xanthone —C═O). (Found: C, 63·7; H, 5·2. $C_{16}H_{14}O_6$ requires: C, 63·6; H, 4·7%).

The diacetate crystallized from EtOH as colourless needles m.p. 240°; R_f 0·8 (solvent B); ν_{max} 1760 (ester —C═O) 1660 cm^{-1} (xanthone —C═O). The xanthone XIVc was partially methylated and then crystallized from $CHCl_3$–MeOH yielding VIIIc as light yellow needles, m.p. 213°; m.m.p. and TLC were identical. The xanthone XIVc was completely methylated and the product crystallized from MeOH as colourless needles, m.p. 184°; it was identical with IIe in m.m.p. and TLC.

2-Methyl-1,3,8-trihydroxyxanthone (XIVd). A mixture of γ-resorcyclic acid (2·2 g), C-methylphloroglucinol (2·5 g), fused $ZnCl_2$ (14 g) and $POCl_3$ (27 ml) was heated as in previous cases. The product crystallized from MeOH yielding XIVd as yellow needles, m.p. 255°; green ferric reaction; R_f 0·8 (solvent B); λ_{max} 248, 329 nm (4·45, 4·28 respectively); ν_{max} 1660 cm^{-1} (xanthone —C═O). (Found: C, 64·7; H, 4·2. $C_{14}H_{10}O_5$ requires: C, 65·1; H, 3·9%).

The triacetate crystallized from EtOH as colourless needles, m.p. 200–201°; R_f 0·9 (solvent B); ν_{max} 1770 (ester —C═O), 1670 cm^{-1} (xanthone —C═O).

The dimethyl ether crystallized from MeOH as light yellow needles, m.p. 225–227°; green ferric reaction; R_f 0·5 (solvent B); ν_{max} 1655 cm^{-1} (xanthone —C═O). (Found: C, 67·0; H, 4·5. $C_{16}H_{14}O_5$ requires: C, 67·1; H, 4·9%).

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