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STUDIES IN THE XANTHONE SERIES—VI*

CLAISEN REARRANGEMENTS, SELECTIVE DEMETHYLATIONS AND SYNTHESIS OF DIHYDROISOJACAREUBIN[1] AND ALVAXANTHONE TRIMETHYL ETHER‡

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Abstract—The Claisen rearrangements of 3',3'-dimethyllallyl ethers of 1-hydroxy-3,5,6-trimethoxyxanthone (IIIb), 1,5-dihydroxy-3,6-dimethoxyxanthone (XV) and 0,0-dimethylphloracetophenone (VIIa) gave both *ortho* and *para* rearrangement products in each case, and led to the synthesis of dihydroisojacareubin (IIa, 3' and 4' = 2H), and alvaxanthone trimethyl ether (XXb).

Selective demethylation of methylated 1,3,5,6-tetrahydroxyxanthones occurs with acidic reagents at the 5-position and has been attributed to the presence of a pyrogallol-2-methyl ether moiety.

The Gibbs colour reaction is discussed.

THE elegant degradative studies of King *et al.*[2] showed that jacareubin an extractive from *Calophyllum brasiliense* (Guttiferae) can have either the linear (Ia) or angular (IIa) pyranoxanthone structure. The linear structure (Ia) was favoured by application of the Gibbs reaction to jacareubin dimethyl ether.[3] More recently, however, it has been reported that a Gibbs test can be misleading[4] unless the results are compared with those of known reference compounds.[5] Since the recent synthesis[6] of dihydrojacareubin does not distinguish between the linear and angular structures further experimental evidence is desirable to confirm the structure of jacareubin. We thus extended our studies[7] of Claisen allylation reactions in xanthones to prepare key intermediates for the synthesis of linear (Ia) and angular (IIa) pyranoxanthones. Attempts to C-allylate the sodium salt of 1-hydroxy-3,5,6-trimethoxyxanthone (IIIa) with 3,3-dimethylallyl bromide in benzene enabled us to isolate only the ether (IIIb).[8] This product was

* Part V: F. Scheinmann, *Tetrahedron* **18**, 853 (1962).

‡ See note added in proof.

[1] Preliminary accounts of parts of this work have appeared previously: E. D. Burling and F. Scheinmann, *Chem. & Ind.* 1756 (1962); E. D. Burling (in part), A. Jefferson and F. Scheinmann, *Tetrahedron Letters* No. 12, 599 (1964); P. Golborn, A. Jefferson and F. Scheinmann, *International Symposium on Organic Reaction Mechanisms.* Cork, Ireland, July (1964).

[2] F. E. King, T. J. King and L. C. Manning *J. Chem. Soc.* 3932 (1953).

[3] F. E. King, T. J. King and L. C. Manning *J. Chem. Soc.* 563 (1957).

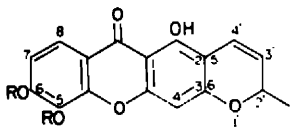
[4] H. Inouye, Y. Kanaya and Y. Murata, *Chem. Pharm. Bull. Japan* **7**, 573 (1959); K. Murai, *J. Pharm. Soc. Japan* **81**, 231 (1961); L. H. Briggs, R. H. Locker, *J. Chem. Soc.* 3131 (1951); V. Anger, H. Mitterman and F. Feigl, *Talanta* II, 662 (1964); C. A. Henrick and P. R. Jeffries, *Austr. J. Chem.* **17**, 934 (1964).

[5] L. Crombie and R. Peace, *J. Chem. Soc.* 5445 (1961).

[6] H. B. Bhat and K. Venkataraman, *Tetrahedron* **19**, 77 (1963).

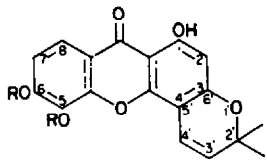
[7] F. Scheinmann and H. Suschitzky, *Tetrahedron* **7**, 31 (1959).

[8] The presence of a crystalline sodium phenoxide is a necessary condition for a heterogeneous reaction leading to exclusive carbon allylation but it has been recognized that even under these conditions a homogeneous reaction leading to oxygen allylation may compete see footnote (10), N. Kornblum, P. J. Berrigan and W. J. Le Noble, *J. Amer. Chem. Soc.* **85**, 1141 (1963).



I

(a) R=H
(b) R=Me



II

(a) R = H
(b) R = Me

more readily prepared by reaction of the hydroxyxanthone (IIIa) in acetone in the presence of potassium carbonate. Rearrangement of the ether (IIIb) in boiling dimethylaniline was complex and chromatography of the reaction mixture gave 1-hydroxy-3,5,6-trimethoxyxanthone and three new products, A, B and C. The major product A was shown to be a 1-hydroxy-3,5,6-trimethoxyxanthone with a 3,3-dimethylallyl side chain by its characteristic NMR spectrum (Table 1).[9] The presence of two *ortho* aromatic protons due to H-7 and H-8 (J 9 c/s) proved that no migration occurred to the other aromatic ring, but it was not possible to decide whether the side chain was in the 2- or 4- position of the xanthone nucleus from spectra, and the Gibbs reaction using photomeric control was inconclusive (Figs. 1, 2). The orientation of the side chain in the 4-position (IIIc) follows from formation with formic acid and with hydrogen bromide, of adducts (IIId and IIIe) and not the pyrano xanthone (IV) which would be expected if there was a free hydroxyl group adjacent to the side chain. This was confirmed by ozonolysis which yields acetone and xanthylacetaldehyde (IIIf) different from the 2-xanthylaldehyde (IIIg). Compound B was shown to be the expected Claisen rearrangement product (IIIh) by the NMR spectrum (Table 1) which shows the dimethylallyl residue as three vinyl protons with an ABX system (τ = 3·82, 5·24, 5·30) J(AX) 17·8, J(BX) 10·3) linked to a tertiary carbon containing two methyl groups which give a sharp singlet (8·44 τ).[10] Treatment with dimethylaniline under the conditions of the rearrangement or with formic acid yields compound C whose NMR spectrum is consistent with the furanoxanthone (V). In a repeat experiment of this Claisen rearrangement a trace amount of the 2,4-di-(3′,3′-dimethylallyl)-xanthone (IIIi) was also isolated and characterized by its NMR spectrum.

Although Claisen rearrangements to a *para* position are not often reported when there is a vacant *ortho* site,[11] it has been suggested that migration to the *para* position may occur by prior rearrangement to the blocked *ortho* position.[12] Thus both *ortho* and *para* products may be also expected from the rearrangement of 1-allyloxy-3,5,6-trimethoxyxanthone (IIIj). However only the *ortho* rearrangement product (IIIk) was obtained since ozonolysis of the product yields formaldehyde and the 2-xanthyl acetaldehyde (IIIg) which cyclizes in polyphosphoric acid to give the furanoxanthone (VI). These results suggest that the 3,3-dimethyl groups on the allyl ether (IIIb) are

[9] e.g. G. H. Stout, V. F. Stout and M. J. Welsh *Tetrahedron* **19**, 667 (1963).

[10] e.g. M. L. Wolfrom, F. Komitsky, G. Fraenkel, J. H. Looker, E. E. Dickey, P. McWain, A. Thompson, P. M. Mundell and O. M. Windrath *Tetrahedron Letters* No. 12, 749 (1963).

[11] D. S. Tarbell, The Claisen Rearrangement in R. Adams, *Organic Reactions* Vol. II; Chap. 1. J. Wiley, New York (1944); H. Schmid, *Gazzetta* **92**, 968 (1962).

[12] S. J. Rhoads, Rearrangements Proceeding through "No Mechanism" Pathways, in P. de Mayo *Molecular Rearrangements* Vol. I; Chap. 11; p. 655, Interscience, New York (1963).

largely responsible for formation of the *para* product (IIIc) since *meta* substituents alone do not appreciably influence a Claisen rearrangement.[13] Furthermore this rearrangement is not specific to xanthone systems because we have shown that the 3′,3′-dimethylallyl ether of O,O-dimethylphloroacetophenone (VIIa) also yields *ortho*

TABLE 1—PROTON MAGNETIC RESONANCE ABSORPTIONS, τ(ppm) AND J(c/s) IN $CDCl_3$ AND CCl_4 USING TETRAMETHYLSILANE AS INTERNAL REFERENCE EXCEPT FOR (IIa 3′ AND 4′ = 2H) WHICH WAS MEASURED IN CF_3COOH.

AROMATIC, METHOXYL AND HYDROXYL PROTONS

Compound	H-2	H-4	H-7	H-8	J H-7/H-8	Methoxyl	Hydroxyl
IIIa	3·72s	3·55s	3·07d	2·09d	9·0	(6·12, 6·02, 6·00)s	−2·68s
IIIj	3·75s	3·49s	3·10d	2·05d	9·0	(6·14, 6·04, 6·02)s	—
IIIk	—	3·55s	3·12d	2·14d	9·0	(6·08, 6·02*)s	−2·81s
IIIb	3·73s	3·47s	3·09d	2·00d	9·0	(6·16, 6·07, 6·05)s	—
IIIc	3·68s	—	3·06d	2·08d	9·0	(6·08, 6·03, 6·01)s	−2·87s
IIIh	—	3·63s	3·15d	2·12d	9·0	(6·17, 6·10, 6·05)s	−2·18s
V	—	3·63s	3·20d	2·16d	9·0	(6·12, 6·09, 6·06)s	—
IIIi	—	—	3·10d	2·10d	9·0	(6·12, 6·07, 6·00)s	−2·93s
IIIg	—	3·42s	2·97d	2·00d	9·0	(6·27, 6.08, 6·00)s	−3·14s
IIIf	3·64s	—	3·05d	2·08d	9·0	(6·07*, 6·00)s	−2·97s
VI	—	3·26s	3·11d	2·00d	9·0	(6·03, 6·01, 5·98)s	—
IIa(3′ and 4′ = 2H)	3·29s	—	2·66d	1·93d	9·0	—	†
XVI	3·64s	—	3·26s	—	—	(6·15, 5·98)s	−3·48
XVIIa	—	3·21a	2·93s	—	—	(5·92, 5·85)s	

Compound	H-3	H-5				Methoxyl	
VIIc	—	4·04s	—	—	—	6·09s*	†
VIIb	3·98s	—	—	—	—	(6·09, 6·00)s	†

ALLYLIC SIDE CHAIN PROTONS

Compound	.CH_2	.CH: X	:CH_2 A	B	:$C(CH_3)_2$	$C(CH_3)_2$	J(AX)	J(BX)
IIIj	5·35d	3·83c	4·29d, 4·65d		—	—	15·7	9·8
IIIk	6·62d	4·12c	5·03d, 5·07d		—	—	17·6	7·8
IIIb	5·38d	4·41t	—		8·24s, 8·19s	—		
IIIc	6·51d	4·78t	—		8·34s, 8·14s	—		
IIIi	6·64, 6·46d	4·74t	—		8·31s,* 8·21s 8·14s	—		
IIIh	—	3·82q	5·24d, 5·30d		—	8·44s	17·8	10·3
XVI	6·52d, 5·98d	4·73t 4·65t	—		8·31s, 8·25s 8·16s	—		
XVIIa	5·88d, 5·70d	4·28t	—		8·19s, 8·16s	—		
VIIc	6·75d	4·82t	—		8.32s, 8·22s	—		
VIIb	—	3·64q	5·20q, 5·68q		—	8·47s*	18·7	10·2

† No measurements were made after 1 kc from tetramethylsilane. s = singlet d = doublet t = triplet q = quartet c = complex

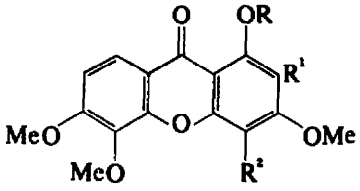
* double intensity signifying two methyl groups.

[13] W. N. White and C. D. Slater, *J. Org. Chem.* **26**, 3631 (1961); D. S. Tarbell and S. S. Stradling, *J. Org. Chem.* **27**, 2724 (1962).

TABLE 1 (*continued*)

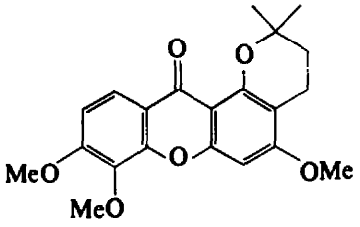
FURANO AND PYRANO RING AND SUBSTITUENT PROTONS

Compound	.CH_2	.CH	.CH:	.CH_3	$C(CH_3)_2$
V	—	5·52q	—	8·54d	(8·86, 8·61)s
VI	—	—	3·21d, 2·31d J = 2·0	—	—
IIa (3′ and 4′ = 2H)	7·94t, 6·85t	—	—	—	8·48s*
XVII a	—	5·16q	—	8·45d	(8·77, 8·52)s

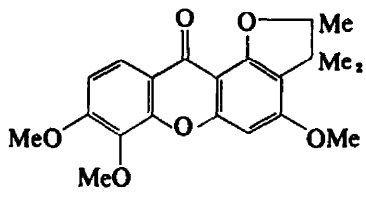


III

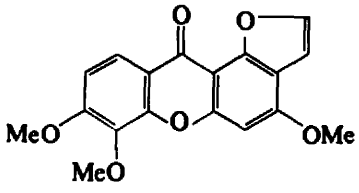
(a) R = R^1 = R^2 = H
(b) R = CH_2·CH:CMe_2, R^1 = R^2 = H
(c) R = R^1 = H, R^2 = CH_2·CH:CMe_2
(d) R = R^1 = H, R^2 = CH_2·$CH_2C(Br)Me_2$
(e) R = R^1 = H, R^2 = CH_2·$CH_2C(O_2CH)Me_2$
(f) R = R^1 = H, R^2 = CH_2·CHO
(g) R = R^2 = H, R^1 = CH_2CHO
(h) R = R^2 = H, R^1 = CMe_2·CH:CH_2
(i) R = H, R^1 = R^2 = CH_2·CH:CMe_2
(j) R = CH_2·CH:CH_2, R^1 = R^2 = H
(k) R = R^2 = H, R^1 = CH_2·CH:CH_2
(l) R = R^2 = H, R^1 = CH_2·CH:CMe_2



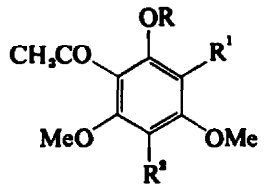
IV



V



VI

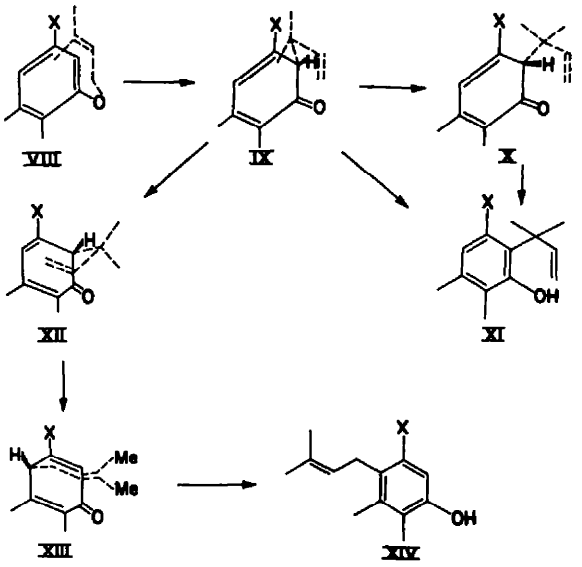


VII

(a) R^1 = R^2 = H, R = CH_2·CH:CMe_2
(b) R = R^2 = H, R^1 = CMe_2·CH:CH_2
(c) R = R^1 = H, R^2 = CH_2·CH:CMe_2

(VIIb) and *para* (VIIc) rearrangement products, and very recently Schmid *et al.* reported similar experimental results with 3′-phenylallyl and 3′-methylallyl *meta* substituted phenyl ethers.

For formation of the *para* rearrangement product two mechanisms are possible. In one mechanism the reaction proceeds by two intramolecular migrations similar to those which occur when both *ortho* positions are substituted. In the other mechanism



formation of the *para* product occurs by an intermolecular migration due to formation of solvent separated ion-pairs.

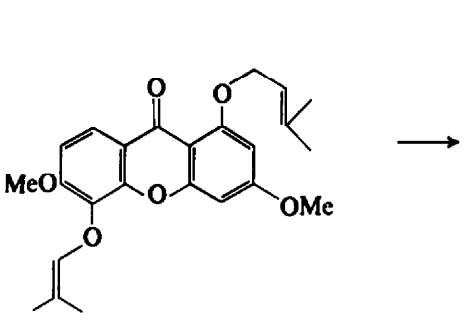
We favour that both *ortho* and *para* Claisen rearrangement products have been formed from the same *o*-dienone intermediate (IX) and that the presence of the methyl substituents on the allyl side chain in the intermediate (IX) hinders enolization to such an extent that rearrangement to the *para* position becomes a competitive reaction. Thus if rearrangement to an *ortho* dienone occurs in the accepted stereochemical pathway[12] the side chain will be attached in a pseudo-axial conformation on to the cyclohexadienone (IX). Interaction of the methyl groups on the side chain in the *ortho* dienone (IX) with neighbouring groups on the ring will hinder formation of the pseudo-equatorial conformer (X) and also hinder enolization to the *o*-allyl phenol phenol (XI) which may be autocatalytic or catalysed by solvent. Free rotation of the side chain in the pseudo-axial conformation (IX) gives a conformer (XII) which has the correct orientation for a Cope rearrangement to yield the thermodynamically more stable *p*-dienone (XIII) and hence the *p*-phenol (XIV). In the rearrangement of 1-allyloxy-3,5,6-trimethoxyxanthone (IIIj) enolization of the *o*-dienone intermediate is not hindered by steric factors and thus the 2-allylxanthone (IIIk) is the only product. Schmid *et al.*[14] have shown that the solvent does significantly influence the rearrangement of meta substituted aryl crotyl ethers because polar solvents which favour enolization favour formation of the *ortho* product while replacement of hydrogens at *ortho* and *para* positions by deuterium gives increased yield of *p*-crotyl phenols. The Swiss workers also described[14] an allyl phenol rearrangement but our attempts to

[14] J. Borgulya, H. J. Hansen, R. Barner and H. Schmid, *Helv. Chem. Acta* **46**, 2444 (1963). H. Schmid, *Oesterr. Chemiker-Ztg.* **65** (4), 109–116 (1964) has given a similar mechanism for rearrangement of e.g. *meta* substituted aryl crotyl ethers.
It has recently been reported by E. N. Marvell, B. Richardson, R. Anderson, J. L. Stephenson and T. Crandall, *J. Org. Chem.* **30**, 1032 (1965) that both *ortho* (~90%) and *para* (~10%) rearrangement products are given from allyl 2-alkylphenyl ethers. This does not affect our mechanism in the xanthone series because with the allyl ether (IIIj) only the *ortho* product (IIIk) is obtained (see also Ref. 7) whereas the dimethylallyl ether (IIIb) gives mainly the *para* product (IIIi).

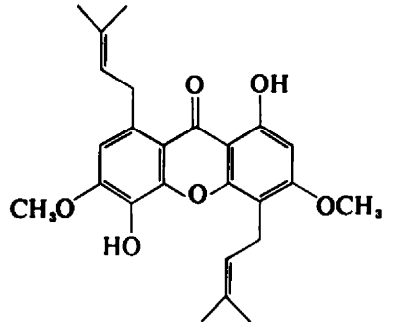
convert the 2-(1′-,1′dimethylallylxanthone (IIIh) into the 4-(3′,3′-dimethylallyl)-xanthone (IIIc) were unsuccessful because of preferential cyclization to the furanoxanthone (V).

The formation of 1-hydroxy-3,5,6-trimethoxy-4(3′,3′-dimethylallyl)-xanthone (IIIc) afforded the opportunity to prepare the angular pyranoxanthone (IIa; 2H at C-3′ and C-4′) by demethylation and cyclization with hydriodic acid. The product was not identical with dihydrojacareubin and was thus named dihydroisojacareubin. The linear pyranoxanthone structure (Ia) for jacaerubin has now been confirmed by an unambiguous synthesis of dihydrojacareubin (Ia; 2H at C-3′ and C-4′).[15]

Natural xanthones have been isolated recently containing two isoprene units.[16] The structure of alvaxanthone has still not been fully elucidated but the data suggests that it is a 1,3,5,6-tetrahydroxyxanthone with two isoprene units. We thus synthesized 1,3,5,6-oxygenated xanthones with one isoprene unit in each ring. The reaction of 1,5-dihydroxy-3,6-dimethoxyxanthone with 3,3-dimethylallylbromide gave the ether (XV) which rearranged to give two xanthones (XVI and XVIIa) whose structures are unambiguously assigned on basis of their NMR spectra (Table 1). Thus each product has two isolated aromatic protons as singlets while the absence of a peak in the region of 2τ confirms that C-8 is substituted (by a 3,3-dimethylallyl side chain). Migration in the other ring occurs as expected to give the *ortho* product, which was isolated as the furanoxanthone (XVIIa), and in addition the *para* isomer (XVI).



XV



XVI

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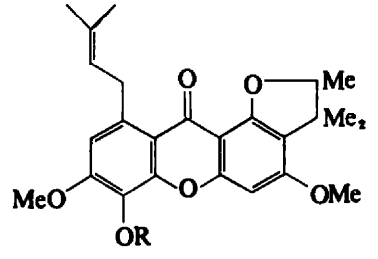


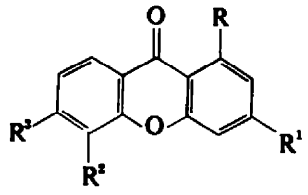
XVII

(a) R = H

(b) R = Me

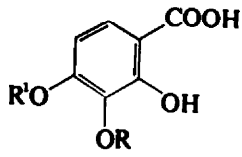
[15] A. Jefferson and F. Scheinmann, *Tetrahedron Letters* No. 20, 1289 (1964).

[16] M. L. Wolfrom, F. Komitsky, G. Fraenkel, J. H. Looker, E. E. Dickey, P. McWain, A. Thompson, P. Mundell and O. M. Windrath, *J. Org. Chem.* **29**, 689 (1964).



XVIII

(a) $R = R^1 = OH$, $R^2 = R^3 = OMe$
(b) $R = R^1 = R^2 = OH$, $R^3 = OMe$
(c) $R = R^1 = R^3 = OH$, $R^2 = OMe$
(d) $R = R^1 = R^2 = R^3 = OH$
(e) $R = R^1 = OH$, $R^2 = OMe$, $R^3 = H$
(f) $R = OH$, $R^1 = Me$, $R^2 = OMe$, $R^3 = H$
(g) $R = R^1 = R^2 = R^3 = OMe$
(h) $R = OH$, $R^1 = R^2 = R^3 = OMe$
(i) $R = R^1 = R^3 = OMe$, $R^2 = OH$
(j) $R = R^1 = R^3 = OMe$, $R^2 = OAc$
(k) $R = R^3 = OH$, $R^1 = R^2 = OMe$
(l) $R = OH$, $R^1 = R^2 = OMe$, $R^3 = OAc$



XIX

(a) $R = R^1 = Me$
(b) $R^1 = Me$, $R = H$
(c) $R = Me$, $R^1 = H$

Methylation of the furanoxanthone (XVIIa) gave the trimethyl ether (XVIIb) which is different from alvaxanthone trimethyl ether.[16]

In another synthetic route to natural xanthones 1,3-dihydroxy-5,6-dimethoxyxanthone (XVIIIa) was required. Attempts to prepare the dimethoxyxanthone (XVIIIa) by condensation of 2-hydroxy-3,4-dimethoxybenzoic acid (XIXa) with phloroglucinol in presence of phosphorus oxychloride and zinc chloride at 75° yields a monomethoxyxanthone which forms a triacetate and with diazomethane gives 1-hydroxy-3,5,6-trimethoxyxanthone. The product was shown to be 1,3,5-trihydroxy 6-methoxyxanthone (XVIIIb) by its synthesis from condensation of 2,3-dihydroxy-4-methoxybenzoic acid (XIXb) with phloroglucinol. The isomeric 1,3,6-trihydroxy-5-methoxyxanthone (XVIIIc) could not be prepared from condensation of 2,4-dihydroxy-3-methoxybenzoic acid (XIXc) with phloroglucinol under similar conditions because demethylation occurred and only 1,3,5,6-tetrahydroxyxanthone (XVIIId) was isolated. These results were unexpected since 5-methoxyxanthones, e.g. 1,3-dihydroxy-5-methoxyxanthone (XVIIIe) and 1-hydroxy-5-methoxy-3-methylxanthone (XVIIIf), have been synthesized previously by the Grover *et al.* method.[17] We attributed selective demethylation by acidic reagents to the presence of a pyrogallol 2-methyl ether moiety and this is supported by other examples. Thus with sulphuric acid, 3,4,5-trimethoxybenzoic acid[18] and 3,4,5-trimethoxy-benzaldehyde[19] are demethylated at the 4-position; 2-hydroxy-3,4-dimethoxy-benzoic acid demethylates at the 3-position,[20] and we have shown that pyrogallol 2-methyl ether and pyrogallol trimethyl ether are demethylated by phosphorus oxychloride and fused zinc chloride at the 2-position.

[17] V. V. Kane, A. B. Kulkani and R. C. Shah, *J. Sci. Ind. Res., India* **18 B**, 28 (1959).
[18] R. L. Alimchand and A. N. Meldrum, *J. Chem. Soc.* **117**, 964 (1920).
[19] I. A. Pearl and D. L. Beyer, *J. Amer. Chem. Soc.* **74**, 4262 (1952).
[20] T. A. Geismann and W. Moje, *J. Amer. Chem. Soc.* **73**, 5765 (1951).

Further demethylation studies with polymethoxyxanthones provide additional evidence that the pyrogallol 2-methyl ether moiety is most susceptible to acid catalysed ether cleavage. Thus both 1,3,5,6-tetramethoxyxanthone (XVIIIg) and 1-hydroxy-3,5,6-trimethoxyxanthone (XVIIIh) demethylate selectively at the 5-position in the presence of sulphuric acid at 50–55°.

It is noteworthy that the 1-methoxyl group does not also demethylate under these conditions and in xanthone synthesis[21] because by analogy with 5-methoxyflavones, demethylation is expected when a methoxyl group is adjacent to a ring carbonyl function.[22]

The structure of 5-hydroxy-1,3,6-trimethoxyxanthone (XVIIIi) was proved by unambiguous synthesis from condensation of 2,3-dihydroxy-4-methoxybenzoic acid (XIXb) with phloroglucinol dimethyl ether in presence of phosphorus oxychloride and zinc chloride. 1,5-dihydroxy-3,6-dimethoxyxanthone (XVIIIk) was converted to 5-hydroxy-1,3,6-trimethoxyxanthone (XVIIIi) by first forming 5-acetoxy-1-hydroxy-3,6-dimethoxy xanthone (XVIIIl) by acetylation with boroacetic anhydride, followed by methylation and hydrolysis.

The experimental observations of selective demethylation can be rationalized by assuming that in a pyrogallol 2-methyl ether system the central oxygen atom is not coplanar with the benzene ring due to non-bonded interaction with the adjacent oxygen functions. The steric inhibition of mesomerism causes the central oxygen atom to be more electronegative than its neighbours and hence more susceptible to reaction with acidic reagents.

The Gibbs Colour Test. The Gibbs colour test[3] with photometric control, although useful in structure determination of jacareubin was found misleading when applied to related synthetic xanthones. Using the qualitative procedure[3] both 2-allyl-1-hydroxy-3,5,6-trimethoxy-xanthone (IIIk) and 1-hydroxy-3,5,6-trimethoxy-4-(3′,3′-dimethylallyl)-xanthone (IIIc) gave results which appear positive (Fig. 1). However by contrast with 1-hydroxy-3,5,6-trimethoxyxanthone (IIIa) these results appear negative (Fig. 2). The quantitative procedure[3] was applied to 1-hydroxy-3,5,6-trimethoxy-2-(3′,3′-dimethylallyl)-xanthone (IIII)[15] and to the 4-isomer (IIIc). Since the 4-isomer (IIIc) has a lower molar extinction coefficient it may be regarded as giving a negative Gibbs test if the criterium of Crombie and Peace[5] is adopted.

EXPERIMENTAL

M.ps are uncorrected. Elements analyses are by Drs. Weiler and Strauss, Oxford. UV spectra in MeOH, were measured on an automatic recording Optica Spectrophotometer (No. CF4DRN1A), IR spectra in $CHCl_3$ were measured on the Perkin-Elmer Infracord 137, and NMR spectra were measured on the Varian HR100. Except where stated otherwise, analytical thin layer chromatography (tlc) was on silica gel G by Stahl (Merck) and preparative TLC on silica gel HF 254 (Merck).

Preparation of Methyl Ethers of 1,3,5,6-*Tetrahydroxyxanthone*

1-*Hydroxy*-3,5,6-*trimethoxyxanthone* (IIIa)

This product m.p. 185°, was prepared essentially by the method of Shah and Shah.[23] It was unnecessary to purify the 1,3,5,6-tetrahydroxyxanthone intermediate since impurities were readily

[21] J. C. Roberts and J. G. Underwood, *J. Chem. Soc.* 2060 (1962).

[22] F. Sondheimer and A. Meisels, *Tetrahedron* **9**, 139 (1960); S. Wawzonek, *Heterocyclic Compounds* (Edited by R. C. Elderfield) Vol. 2; p. 265. J. Wiley, New York.

[23] G. D. Shah and R. C. Shah, *J. Sci. Ind. Res. India.* **15 B**, 630 (1956).

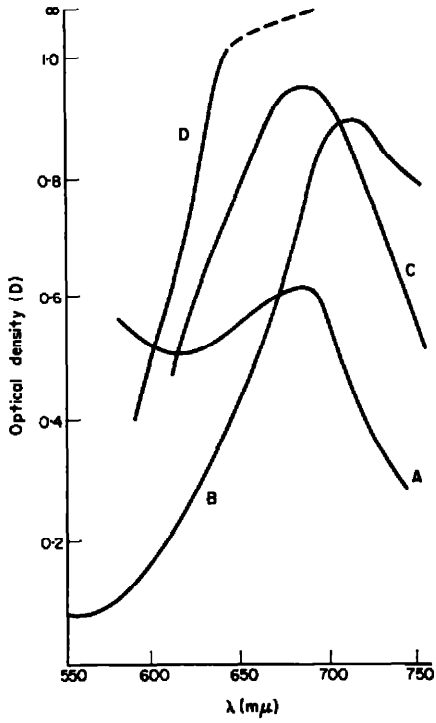


FIG. 1. The Gibbs test by the qualitative procedure. Concentration of each phenol = 0·1 g/l. Optical density measured 20 mins after mixing the phenol with reagent.

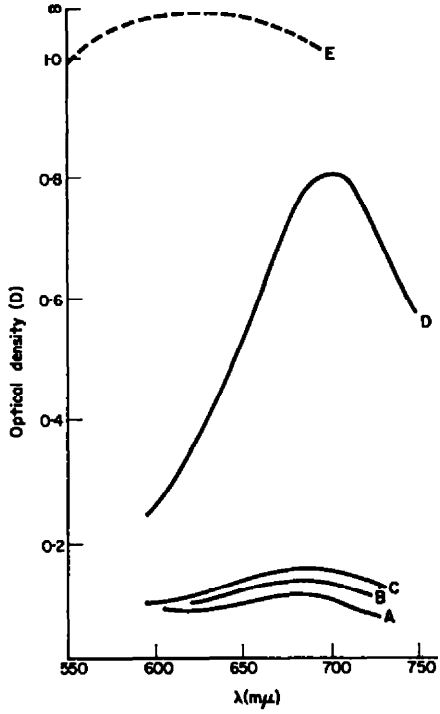


FIG. 2. The Gibbs test by the qualitative procedure. Concentration of each phenol = 0·02 g/l. Optical density measured 20 min after mixing the phenol with reagent.

A = *p*-Cresol
B = 2-Allyl-1-hydroxy-3,5,6-trimethoxyxanthone (IIIk),
C = 1-Hydroxy-3,5,6-trimethoxy-4-(3′,3′-dimethylallyl)-xanthone (IIIc),
D = 1-Hydroxy-3,5,6-trimethoxyxanthone (IIIa),
E = Phenol.

removed in the final stage by isolation of 1-hydroxy-3,5,6-trimethoxyxanthone as its insoluble sodium salt.

1,3,5-*Trihydroxy-6-methoxyxanthone* (XVIIIb)

(a) Compound XIXb (1·13 g) and anhydrous phloroglucinol (1·13 g) in $POCl_3$ (15 ml) containing $ZnCl_2$ (7 g) were heated at 70–75° for 2 hr. The deep red viscous oil was cooled and poured onto ice. The orange solid which separated was filtered off washed with water and dried. Sublimation at 150–190°/0·1 mm gave 1,3,5-*trihydroxy-6-methoxyxanthone* (500 mg), mp 280–285°(dec). (Found: C, 61·16; H, 3·49; OMe, 12·18. $C_{14}H_{10}O_6$ requires: C, 61·45; H, 3·67; OMe, 11·32%.) λ_{max} mμ (log ε): 248(4·70), 266(4·46), 338(4·24). The triacetate recrystallizes from EtOH as needles, m.p. 191–192°. (Found: C, 60·23; H, 4·51; OMe, 7·84. $C_{20}H_{18}O_9$ requires: C, 60·01; H, 4·03; OMe, 7·76%.) λ_{max} mμ (log ε): 235(4·56), 276(4·19), 345(4·32).

(b) The reaction between 2-hydroxy-3,4-dimethoxybenzoic acid (XIXa) and phloroglucinol under conditions similar to those described in (a) gave 1,3,5-trihydroxy-6-methoxyxanthone as pale yellow needles from aqueous EtOH, m.p. 281–284°. The product and its triacetate were identical with the corresponding xanthones obtained by method (a).

Methylation of 1,3,5-trihydroxy-6-methoxyxanthone with diazomethane in ether gave a pale yellow solid, m.p. 180–182°, undepressed on admixture with an authentic sample of 1-hydroxy-3,5,6-trimethoxyxanthone.

1,5-*Dihydroxy*-3,6-*dimethoxyxanthone* (XVIIIk)

Compound IIIa (1/g) in conc. H_2SO_4 (10 ml) was heated at 50° for 40 hr. The brown solution was poured onto ice, and the clear aqueous solution was refluxed for 2 hr. The beige precipitate was filtered off, dried, and recrystallized from methyl ethyl ketone to give 1,5-*dihydroxy*-3,6-*dimethoxyxanthone* (0·6 g) as yellow needles, m.p. 272–274°. (Found: C, 62·28; H, 3·94. $C_{15}H_{12}O_6$ requires: C, 62·50; H, 4·16%.) λ_{max} mμ (log ε): 247(4·64), 287(4·05), 326(4·27). IR: 1660, 1630, 1600, 1575 cm^{-1}. The diacetyl derivative recrystallizes from aqueous EtOH as colourless needles m.p. 201°. (Found: C, 61·10; H, 4·32. $C_{19}H_{16}O_8$ requires: C, 61·28; H, 4·30%.)

5-*Acetoxy*-1-*hydroxy*-3,6-*dimethoxyxanthone* (XVIIII)

Compound XVIIIk (650 mg), boroacetic anhydride (800 mg) in acetic anhydride (5 ml) was refluxed for 5 min. Ether was added to the cooled solution, and the mixture was allowed to stand at 0° for 2 hr. The bright yellow solid complex was filtered off, washed with ether and decomposed by boiling water. Crystallization from EtOH and then methyl ethyl ketone gave 5-*acetoxy*-1-*hydroxy*-3,6-*dimethoxyxanthone* (560 mg) was pale yellow needles m.p. 210–211°. (Found: C, 61·90; H, 4·31. $C_{17}H_{14}O_7$ requires: C, 61·81; H, 4·24%.) λ_{max} mμ (log ε): 241(4·62), 278(3·77), 311(4·37), 340(3·77). IR: 1770, 1650, 1630, 1600, 1570 cm^{-1}.

5-*Acetoxy*-1,3,6-*trimethoxyxanthone* (XVIIIj)

Compound XVIII1 (130 mg) and dimethylsulphate (60 mg) in acetone (40 ml) containing K_2CO_3 (60 mg) was heated at reflux for 9 hr. The solvent was removed from the filtered solution, and the residue recrystallized from aqueous MeOH to give 5-*acetoxy*-1,3,6-*trimethoxyxanthone* (90 mg) as colourless needles m.p. 230–232° identical (mixed m.p. and IR) with an authentic sample. λ_{max} mμ (log ε): 243(4·59), 278(shoulder) (3·90), 303(4·26), 321(shoulder) (4·03); IR: 1765, 1650, 1625, 1600, 1570 cm^{-1}.

5-*Hydroxy*-1,3,6-*trimethoxyxanthone* (XVIIIi)

(a) Compound XIXb (1·3 g) and phloroglucinol dimethyl ether (1·3 g) were condensed together under Grover *et al.*[24] conditions as described above. The crude product was purified by preparative talc by developing the plate with ethyl acetate–$CHCl_3$ (30:70). The main band was scraped off the plate, placed in a column and eluted with ethyl acetate. Removal of the solvent and recrystallization from aqueous EtOH gave 5-*hydroxy*-1,3,6-*trimethoxyxanthone* as colourless needles m.p. 250–252°. λ_{max} mμ (log ε): 248(4·61), 285(4·07), 311(4·25). IR: 1600, 1575, 1460 cm^{-1}.

(b) Compound XVIIIg (630 mg) in conc. H_2SO_4 (5 ml) was heated at 55° for 16 hr. The light brown solution was poured onto ice and the precipitate filtered off and washed with water. The precipitate was dissolved in ethyl acetate, and extracted with 2 N NaOH. The bright yellow insoluble sodium salt was filtered off, washed with ethyl acetate and acidified with 2 N HCl. The beige precipitate was recrystallized twice from aqueous EtOH and yields colourless needles of 5-*hydroxy*-1,3,6-*trimethoxyxanthone* (340 mg) m.p. 252–254° (dec) identical (mixed m.p. and IR) with the authentic sample prepared by the Grover *et al.* method.[24] (Found: C, 63·24; H, 4·78. $C_{16}H_{14}O_7$ requires: C, 63·57; H, 4·56%.) The acetyl derivative recrystallizes from aqueous MeOH as needles m.p. 232–234°. (Found: C, 62·88; H, 4·56. $C_{18}H_{16}O_7$ requires: C, 62·80; H, 4·65%.)

(c) Compound XVIIIj (50 mg) was triturated with conc. H_2SO_4 (1 ml) for 30 min. After pouring onto ice water a white precipitate separated, which was recrystallized from aqueous EtOH to give 5-*hydroxy*-1,3,6-*trimethoxyxanthone* (30 mg) m.p. 252–254° identical (mixed m.p. and IR) with the sample prepared previously.

Attempted preparation of 1,3,6-*trihydroxy*-5-*methoxyxanthone* (XVIIIc)

Compound XIXc (2·0 g) and anhydrous phloroglucinol (2·0 g) were condensed with $ZnCl_2$ (12 g) and $POCl_3$ (25 ml) under Grover *et al.* conditions.[24] The crude product was sublimed at 150–180°/0·1 mm to give a solid (0·9 g) m.p. 310–315° (dec). The tetra-acetyl derivative recrystallizes from

[24] P. K. Grover, G. D. Shah and R. C. Shah, *J. Chem. Soc.* 3982 (1955).

aqueous acetic acid, m.p. 240–242° identical (m.p. and IR) with an authentic sample of 1,3,5,6-tetra-acetoxyxanthone.

Demethylation of pyrogallol methyl ethers

(a) *Pyrogallol-2-methyl ether.* (2·5 g) and anhydrous $ZnCl_2$ (15·0 g) in $POCl_3$ (31 ml) were heated at 70–75° for 2 hr and then poured onto ice. The ether extract was dried and the solvent removed to give pyrogallol (2·25 g) m.p. 130–133°; confirmed by mixed m.p. and formation of its triacetate, m.p. 172–173°.

(b) *Pyrogallol trimethyl ether* (2·5 g) as in method (a) gave 2,6-dimethoxyphenol (1·83 g). A pure sample was obtained by chromatography, eluting with $CHCl_3$–cyclohexane (70–30). The benzoyl derivative recrystallizes from MeOH–water as needles m.p. 117–118°. (lit. m.p. 116–117°.[35])

Preparation of allyl ethers

1-*Allyloxy*-3,5,6-*trimethoxyxanthone* (IIIj)

A mixture of 1-hydroxy-3,5,6-trimethoxyxanthone (IIIa) (15 g), allyl chloride (4·1 g), KI (9·9 g), K_2CO_3 (13·7 g) in dry acetone (1 l.) was refluxed for 20 hr.

Further amounts of KI (4·5 g), K_2CO_3 (6·9 g) and allyl chloride (2·1 g) were added and heating was continued for 15 hr, until a test sample gave no colouration with $FeCl_3$. Evaporation of the filtered solution and recrystallization from pet. ether (b.p. 100–120°) gave 1-*allyloxy*-3,5,6-*trimethoxy-xanthone* (9 g) as colourless needles, m.p. 143–144°. (Found: C, 66·56; H, 5·20. $C_{19}H_{18}O_6$ requires: C, 66·66; H, 5·26%.) λ_{max} mμ (log ε): 246(4·69), 291(shoulder) (3·93), 305(4·28). IR: 1645, 1610, 1595, 1565 cm^{-1}.

3,5,6-*Trimethoxy*-1-(3′3′-*dimethylallyloxy*)-*xanthone* (IIIb)

Compound IIIa (4 g) and 3,3-dimethylallyl bromide (2·4 g) in acetone (80 ml) containing K_2CO_3 (3·7 g) were refluxed for 30 hr. More 3,3-dimethylallyl bromide (1·2 g) was added, and refluxing was continued 15 hr. Evaporation of the solvent from the filtered solution and crystallization of the residue from pet. ether gave the product (3·5 gm) as colourless needles m.p. 139–140°. Column chromatography on alumina (Grade H, Peter Spence) and elution with $CHCl_3$, followed by removal of the solvent and recrystallization of the residue from pet. ether (b.p. 100–120°) gave 3,5,6-*trimethoxy*-1-(3′3′-*dimethylallyloxy*)-*xanthone* m.p. 142°. (Found: C, 68·01; H, 6·11. $C_{21}H_{22}O_6$ requires: C, 68·11; H, 5·94%.) λ_{max} mμ (log ε): 246(4·66), 291(shoulder) (3·91), 305(4·28). IR: 1645, 1620, 1600, 1565 cm^{-1}.

3,6-*Dimethoxy*-1,5 *di*(3′3′-*dimethylallyloxy*)-*xanthone* (XV)

1,5-Dihydroxy-3,6-dimethoxyxanthone (560 mg), K_2CO_3 (0·64 g), and 3,3 dimethylallyl bromide (0·76 g) in acetone (150 ml) were refluxed for 20 hr. Further amounts of 3,3 dimethylallyl bromide (0·38 g) and K_2CO_3 (0·32 g) were added and refluxing was continued for 15 hr. The solvent was removed from the filtered solution, and the residue recrystallized twice from pet. ether to give 3,6-*dimethoxy*-1,5 *di*(3′3′-*dimethylallyloxy*)-*xanthone* (425 mg) as long colourless needles, m.p. 112°. (Found: C, 70·74; H, 6·51. $C_{28}H_{32}O_6$ requires: C, 70·73; H, 6·60%.) λ_{max} mμ (log ε): 247(4·80), 287(shoulder) (4·22), 307(4·44). IR: 1640, 1605, 1595, 1565 cm^{-1}.

2,4-*Dimethoxy*-6-(3′3′-*dimethylallyloxy*)-*acetophenone* (VIIa)

2,4-Dimethoxy-6-hydroxyacetophenone (9·3 g) and 3,3-dimethyl allyl bromide (8·5 g) in acetone (200 ml) containing K_2CO_3 (12 g) was heated at reflux for 48 hr. The solvent was removed from the filtered solution and the residue distilled at 150–155°/0·2 mm to give a pale yellow oil. Low temp. recrystallization from pet. ether (b.p. 40–60°) gave colourless needles (5 g) of 2,4-*dimethoxy*-6-(3′3′-*dimethyllallyloxy*)-*acetophenone*, m.p. 39°. (Found: C, 68·29; H, 7·61. $C_{15}H_{20}O_4$ requires: C, 68·19; H, 7·58%.) λ_{max} mμ (log ε) 224(4·11), 279(3·69). IR: 1675, 1600, 1595 cm^{-1}.

[35] C. D. Hurd and H. E. Winberg, *J. Amer. Chem. Soc.* **64**, 2085 (1942).

Claisen rearrangements

Rearrangement of 1-*allyloxy*-3,5,6-*trimethoxyxanthone* (IIIj)

Compound IIIj (8 g) in dimethylaniline (60 ml) was refluxed for 4 hr. The solution was cooled and acidified with 2 N HCl. The beige precipitate was filtered off, dried and recrystallized from acetone to give 2-*allyl*-1-*hydroxy*-3,5,6-*trimethoxyxanthone* (IIIk; 4.6 g) as pale yellow needles, m.p. 194°. (Found: C, 66·70; H, 5·41. $C_{19}H_{18}O_6$ requires: C, 66·66; H, 5·26%.) λ_{max} mμ (log ε): 251(4·47), 284(4·06), 323(4·40). IR: 1645, 1600, 1565 cm^{-1}. Thin layer chromatography of the crude reaction mixture showed that a trace of 1-hydroxy-3,5,6-trimethoxyxanthone was the only other product. The acetyl derivative, m.p. 163°, recrystallizes from aqueous acetone. (Found: C, 65·95; H, 5·18. $C_{21}H_{20}O_7$ requires: C, 65·63; H, 5·27%.) The methoxy derivative, m.p. 132°, recrystallizes from pet. ether (b.p. 100–120°). (Found: C, 67·63; H, 5·79. $C_{20}H_{20}O_6$ requires: C, 67·41; H, 5·62%.)

Rearrangement of 3,5,6-*trimethoxy*-1(3′,3′-*dimethylallyloxy*)-*xanthone* (IIIb)

3,5,6-Trimethoxy-1-(3′,3′-dimethylallyloxy)-xanthone (3 g) in dimethylaniline (90 ml) was refluxed for 8 hr. The solution was acidified with 2 N HCl. The beige precipitate was extracted with $CHCl_3$, and the organic layer was washed with water and dried ($MgSO_4$). Removal of the solvent and crystallization of the residue from pet. ether (b.p. 100–120°) gave crude 1-*hydroxy*-3,5,6-*trimethoxy*-4-(3′,3′-*dimethylallyl*)-*xanthone* (IIIc) (1·5 g), m.p. 155–156°. A pure sample obtained by column chromatography, and elution with a solvent mixture of $CHCl_3$–benzene (30:70) has m.p. 162°. (Found: C, 68·35; H, 6·18. $C_{21}H_{22}O_6$ requires: C, 68·11; H, 5·94%.) λ_{max} mμ (log ε): 244(4·58), 283(3·89), 316(4·27), 400(3·80). IR: 1645, 1615, 1600, 1565 cm^{-1}. The acetyl derivative was recrystallized from aqueous EtOH, m.p. 129–130°. (Found: C, 66·95; H, 5·94. $C_{23}H_{24}O_7$ requires: C, 67·00; H, 5·83%.) The pet. ether was removed from the filtrate from crystallization of IIIc to give a yellow oil which was chromatographed on silica gel, and eluted with benzene. Crystallization from pet. ether (b.p. 60–80°) gave 1-*hydroxy*-3,5,6-*trimethoxy*-2-(1′,1′-*dimethylallyl*)-*xanthone* (IIIh; 0·7 g) as yellow needles m.p. 122°. (Found: C, 67·87; H, 5·95. $C_{21}H_{22}O_6$ requires: C, 68·11; H, 5·95%.) λ_{max} mμ (log ε): 246(4·61), 282(4·01), 317(4·25). IR: 1645, 1600, 1585 cm^{-1}. The 1-*methoxy* derivative was prepared by refluxing with dimethyl sulphate in acetone in presence of K_2CO_3 and recrystallizes from pet. ether (b.p. 80–100°) to give white plates, m.p. 124°. (Found: C, 68·43; H, 6·22. $C_{22}H_{24}O_6$ requires: C, 68·23; H, 6·25%.)

Trace amounts of 3,5,6-*trimethoxy*-4′5′-*dihydro*-4′4′5′ *trimethyl*-*furano*-(2′,3′-1,2)-*xanthone* (V) and 1-*hydroxy*-3,5,6-*trimethoxyxanthone* (IIIa) were shown to be present in the crude reaction mixture by tlc, by developing with benzene–$CHCl_3$ 70:30.

In another experiment, chromatography of the crude reaction mixture on silica gel, and eluting from the column with benzene, followed by recrystallization from pet. ether (b.p. 40–60°) gave 1-*hydroxy*-3,5,6-*trimethoxy*-2,4-*di*-(3′,3′-*dimethylallyl*)-*xanthone* (IIIi; 40 mg) as yellow needles m.p. 120°. (Found: C, 70·93; H, 6·89. $C_{26}H_{30}O_6$ requires: C, 71·10; H, 7·01%.) λ_{max} mμ (log ε): 245(4·57), 316(4·24), 430(4·0). IR: 1645, 1600, 1575.

Hydrogen bromide adduct of IIIc

1-Hydroxy-3,5,6-trimethoxy-4-(3′,3′-dimethylallyl)-xanthone (2·79 g) in glacial acetic acid (500 cc) was saturated with HBr gas in the presence of a trace amount of diphenylamine, and then allowed to stand at room temp for 5 days. The solvent was removed and the residue was dissolved in ether and methylated with diazomethane. The ether was removed, and the residue recrystallized from pet. ether (b.p. 100–120°) to give the HBr adduct (IIId) as yellow needles m.p. 152–153°. (Found: C, 55·98; H, 5·24; Br, 18·10. $C_{21}H_{23}O_6Br$ requires; C, 55·90; H, 5·10; Br, 17·74%.) IR: 1590, 1565, 1510 cm^{-1}.

Formic acid adduct of IIIc

1-Hydroxy-3,5,6-trimethoxy-4-(3′3′-dimethylallyl)-xanthone (60 mg) in formic acid (1 ml) was heated at 100° for 2 hr, cooled and poured into water. The IR spectrum of the formic acid adduct (IIIe) had a very strong carbonyl band at 1710 cm^{-1} (C=O).[26]

[26] P. Yates and G. H. Stout, *J. Amer. Chem. Soc.* **80**, 1691 (1958).

Rearrangement of 3,6-*dimethoxy*-1,5-*di*(3',3'-*dimethylallyloxy*)*xanthone* (XV)

3,6-dimethoxy-1,5-di-(3',3'-dimethylallyloxy)-xanthone (1 g) in dimethylaniline (50 ml) was refluxed for 5 hr. The solution was acidified with 2 N HCl and the precipitate was filtered off and dried. The crude product, in a small amount of $CHCl_3$ was introduced onto a silica gel column made up in a solution of equal parts of $CHCl_3$ and cyclohexane, and then the solvent of elution was gradually changed to pure $CHCl_3$. The initial fractions were combined, and the solvent was removed. The solid (650 mg) in $CHCl_3$ was applied to 10 preparative tlc plates (1 mm), which were then developed with $CHCl_3$. The orange band in UV light (R_f.80) was removed, extracted with ethyl acetate, and the solvent was evaporated. Crystallization from methyl ethyl ketone, and then pet. ether (b.p. 100–120°) gave 1,5-*dihydroxy*-3,6-*dimethoxy*-4,8-*di*-(3',3'-*dimethylallyl*)-*xanthone* (XVI; 150 mg) as yellow needles m.p. 200° (dec). (Found: C, 70·97; H, 6·50. $C_{32}H_{32}O_8$ requires: C, 70·75; H, 6·60%.) λ_{max} mμ (log ε): 242(shoulder) (4·48), 258(4·67), 286(3·86), 335(4·30). IR: (Nujol): 1630, 1605, 1595, 1560 cm^{-1}. The grey band in UV light (R_f.50) was eluted with ethyl acetate, and then the solvent evaporated. Recrystallization of the residue from $CHCl_3$–pet. ether (b.p. 100–120°) gave pale yellow needles of 5-*hydroxy*-3,6-*dimethoxy*-8-(3',3'-*dimethylallyl*)-4',5'-*dihydro*-4',4',5'-*trimethylfurano*-(2',3'-1,2) *xanthone* (XVIIa; 200 mg), m.p. 238–239° (dec). (Found: C, 70·68; H, 6·69. $C_{28}H_{28}O_6$ requires: C, 70·75; H, 6·60%.) λ_{max} mμ (log ε): 257(4·69), 276(4·06), 314(4·29). IR: (Nujol): 3300, 1605, 1600, 1560 cm^{-1}. The methyl ether derivative (XVIIb) recrystallizes from pet. ether (b.p. 100–120°) as colourless needles m.p. 118°. (Found: C, 71·02; H, 6·51. $C_{26}H_{30}O_6$ requires: C, 71·24; H, 6·85%.) IR: 1640, 1625, 1600, 1575 cm^{-1}.

Rearrangement of 2,4-*dimethoxy*-6(3',3'-*dimethylallyloxy*)*acetophenone* (VIIa)

2,4-Dimethoxy-6-(3',3'-dimethylallyloxy)-acetophenone (4 g) in dimethylaniline (40 ml) was refluxed for 5 hr. The solution was cooled, acidified with 2 N HCl and extracted with benzene. The benzene layer was washed with water, dried ($MgSO_4$), and then the solvent was removed to yield an oil, b.p. 150–160°/0·5 mm (3·1 g). The yellow oil (1 g) was dissolved in $CHCl_3$, and introduced onto a silica gel column made up in cyclohexane, and then the $CHCl_3$ concentration in the eluting solvent was slowly increased. The first fractions were combined, and the solvent removed. The yellow oil was dissolved in $CHCl_3$, and applied to alumina G preparative tlc plates, which were then developed with $CHCl_3$–cyclohexane (40:60). The material close to the solvent front was removed and eluted with ethyl acetate in a column. The ethyl acetate was removed and the residue recrystallized from pet. ether (b.p. 40–60°) to give 6-*hydroxy*-2,4-*dimethoxy*-5-(1',1'-*dimethylallyl*)-*acetophenone* (VIIb) as yellow needles (100 mg), m.p. 103–104°. (Found: C, 68·05; H, 7·78. $C_{15}H_{20}O_4$ requires: C, 68·19; H, 7·58%.) λ_{max} mμ (log ε): 294(4·30), 334(shoulder) (3·49). IR: 1600, 1560, 1455 cm^{-1}. The middle fractions were combined, and the solvent removed to give a pale yellow crystalline solid. Recrystallization from pet. ether (b.p. 60–80°) gave 6-*hydroxy*-2,4-*dimethoxy*-3-(3',3'-*dimethylallyl*)-*acetophenone* (VIIb; 120 mg) as pale yellow needles, m.p. 102–104°. (Found: C, 68·82; H, 7·87. $C_{15}H_{20}O_4$ requires: C, 68·19; H, 7·58%.) λ_{max} mμ (log ε): 294(4·30), 326(shoulder) (3·61). IR: 1605, 1590, 1455 cm^{-1}.

Ozonolysis of allyl side chains

The rate of ozone formation was determined by the standard method.[27] A stream of ozonized O_2 was passed through a cooled (−10°) solution of the allyl xanthone (150 mg) in ethyl acetate (50 ml) until the theoretical amount of O_2 had been generated. The solution was allowed to warm up to room temp (½ hr) and then it was hydrogenated at atm press. in the presence of 5% Pd–C until the rapid uptake of H_2 ceased. The Pd–C was filtered off and the solvent was distilled into dimedone or 2:4 dinitrophenylhydrazine. The pale yellow residue was recrystallized from acetone to give the xanthylacetaldehyde as pale yellow needles (75 mg). Identification of acetone or formaldehyde was carried out by either tlc of the 2:4 dinitrophenylhydrazone derivative on alumina G[28] or by the mixed m.p. of the derivative with an authentic sample.

[27] R. P. Linstead, J. Elvidge and M. Whalley, *A Course in Modern Techniques of Organic Chemistry*. Butterworth's, London (1955).

[28] G. Urbach, *J. Chromat.* 12, 196 (1963).

SAMPLE XANTHYLACETALDEHYDE		Found		Required			
		%C	%H	%C	%H	M.P°	VOLATILE fraction
IIIk	IIIg	62·73	4·72	62·78	4·65	224–226	Formaldehyde
IIIc	IIIf	62·72	4·73	62·78	4·65	214–216	Acetone

1-*Hydroxy*-3,5,6-*trimethoxy*-2-*xanthylacetaldehyde* (IIIg) has UV spectrum with λ_{max} mμ (log ε): 246(4·58), 283(3·88), 316(4·26). IR: 1720, 1645, 1600, 1575 cm^{-1}. The 2:4 dinitrophenylhydrazone derivative recrystallizes from dimethylformamide, m.p. 256° (dec). (Found: C, 54·96; H, 4·00; N, 10·02. $C_{34}H_{30}N_4O_{10}$ requires: C, 54·96; H, 3·82; N, 10·69%.)

1-*Hydroxy*-3,5,6-*trimethoxy*-4-*xanthylacetaldehyde* (IIIf) has UV spectrum with λ_{max} mμ (log ε): 244(4·59), 283(3·89), 318(4·29). IR: 1720, 1645, 1600, 1575 cm^{-1}. The 2:4 dinitrophenylhydrazone derivative recrystallizes from dimethylformamide m.p. 266–268° (dec). (Found: C, 54·63; H, 4·05; N, 10·68. $C_{34}H_{30}N_4O_{10}$ requires: C, 54·96: H, 3·82; N, 10·69%.)

Preparation of Furano and Pyranoxanthones

1,5,6-*Trihydroxy*-5′,6′-*dihydro*-6′,6′-*dimethylpyrano*(2′,3′-3,4)*xanthone* (*Dihydroisojacareubin*) (IIa 2H at both C-3′ and C-4′)

Compound IIIc (300 mg) in 55% w/w HI (7 ml) and acetic acid (14 ml) was refluxed for 3 hr. The solution was cooled and poured onto ice-water, to give an orange precipitate, which was filtered off, washed with water and dried. The crude product was sublimed at 200–220°/1·0 × 10^{-4} mm and then crystallized from aqueous MeOH to give 1,5,6-*trihydroxy*-5′,6′-*dihydro*-6′,6′-*dimethylpyrano*-(2′,3′-3,4)-*xanthone* (100 mg) as pale yellow needles m.p. 288° different from dihydrojacareubin (mixed m.p. and IR spectrum). (Found: C, 65·56; H, 4·84. $C_{18}H_{16}O_4$ requires: C, 65·84; H, 4·88%.) λ_{max} mμ (log ε): 251(4·63), 285(4·05), 326(4·34). IR: (Nujol) 3200, 1650, 1600, 1575 cm^{-1}.

1-*Hydroxy*-5,6-*dimethoxy*-5′,6′-*dihydro*-6′,6′-*dimethylpyrano*(2′,3′-3,4)*xanthone* (IIb; C-3′ and C-4′ = 2H)

An excess of diazomethane in ether was added to a solution of dihydroisojacareubin (60 mg) dissolved in MeOH (3 ml) at 0°. After allowing the solution to stand at 0° for 2 hr, the excess diazomethane was reacted with acetic acid. The solvents were removed, the oily residue dissolved in benzene and shaken with Claisens alkali. The bright yellow precipitate was filtered off, washed with benzene, dried and acidified with 2 N HCl. The beige precipitate was recrystallized from aqueous MeOH to give 1-*hydroxy*-5,6-*dimethoxy*-5′,6′-*dihydro*-6′.6′-*dimethylpyrano*-(2′,3′-3,4)-*xanthone* (45 mg) as pale yellow needles m.p. 148°. (Found: C, 67·70; H, 5·41. $C_{20}H_{20}O_6$ requires: C, 67·41; H, 5·26%.) λ_{max} mμ (log ε): 246(4·60), 284(3·93), 321(4·32).

3,5,6-*Trimethoxy*-*furano*(2′,3′-1,2) *xanthone* (VI)

1-Hydroxy-3,5,6-trimethoxy-2-xanthylacetaldehyde (170 mg) in polyphosphoric acid (5 cc) was stirred vigorously at 85–90° for 50 min, and then the cooled reaction mixture was poured onto water. The $CHCl_3$ extract was dried ($MgSO_4$) and then chromatographed on activated alumina (Type H-Peter Spence). Elution with $CHCl_3$ and recrystallization of the product from aqueous acetic acid and then ethyl acetate yields 3,5,6-*trimethoxy*-*furano*-(2′,3′-1,2)-*xanthone* as colourless needles m.p. 245°. (Found: C, 66·15; H, 4·21. $C_{18}H_{14}O_6$ requires: C, 66·30; H, 4·21%.) λ_{max} mμ (log ε): 254(4·58), 263(4·60), 281(4·14), 315(4·25). IR: 1645, 1610, 1600, 1575, 1060 cm^{-1}.

3,5,6-*Trimethoxy*-4′,5′-*dihydro*-4′,4′,5′-*trimethylfurano*(2′,3′-1,2)*xanthone* (V)

(a) 3,5,6-Trimethoxy-1-(3′,3′-dimethylallyloxy)-xanthone (3 g) in dimethylaniline (50 ml) was refluxed for 3 days. The cooled solution was acidified with 2 N HCl and the crude product was filtered off and dried. Column chromatography on alumina (Grade H-Peter Spence), and elution with $CHCl_3$–benzene (70:30), followed by removal of the solvent and crystallization of the solid from

pet. ether (b.p. 100–120°) gave 3,5,6-*trimethoxy*-4′,5′-*dihydro*-4′4′,5′-*trimethylfurano*-(2′,3′-1,2)-*xanthone* (1·5 g) as colourless rods, m.p. 155–156°. (Found: C, 68·17; H, 6·06. $C_{21}H_{22}O_6$ requires: C, 68·11; H, 5·94%.) λ_{max} mμ. (log ε): 248(4·66), 285(shoulder) (4·04), 299(4·39). IR: 1650, 1610, 1600, 1575 cm^{-1}.

(b) Compound IIIh (100 mg) in formic acid (5 ml) was heated on a steam bath for 2 hr. The solution was poured into water, and the product isolated as in the preceding experiment (a). This product was identical (m.p. and IR) with that obtained by method (a).

(c) Compound IIIh (100 mg) in dimethylaniline (10 ml) was heated under reflux for 24 hr. The product, isolated as above (a) was identical with V as shown by mixed m.p. and IR.

Gibbs Tests

(a) *Qualitative procedure.*[8] The weighed sample (2 mg) in "analaR" pyridine (1 ml) was treated with a solution of freshly prepared 2,6-dichlorobenzoquinone chloromide in pyridine (5 ml of 0·2% solution), and diluted to 20 ml with sodium borate buffer (pH 9·2). The absorption spectrum was determined 20 min. after mixing, against a cell containing the reagent system without the sample. Any necessary dilution was carried out using the aqueous buffer solution.

(b) *Quantitative procedure.*[8] The variation of ε_{max} with time was investigated for IIIl and the 4-isomer (IIIc), the solutions being prepared as in method (a) and being diluted to 60 ml with aqueous borate solution.

Sample	λ_{max} mμ	ε_{max} 20 min	40 min	60 min	80 min	100 min
III c	690	1400	2800	4600	4900	4400
III l	687	3000	4700	7200	6010	5200

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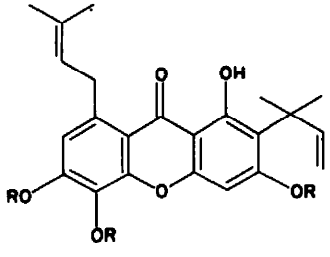
NOTE ADDED IN PROOF

THE STRUCTURE OF ALVAXANTHONE AND PREPARATION OF ITS TRIMETHYL ETHER

A. JEFFERSON and F. SCHEINMANN

After our paper had been accepted for publication the structure of alvaxanthone was reported as XXa and alvaxanthone trimethyl ether as XXb.[29]



XX

a; R = H
b; R = Me

[29] M. L. Wolfrom, F. Komitsky, Jr. and P. M. Mundell, *J. Org. Chem.* **30**, 1088 (1965).

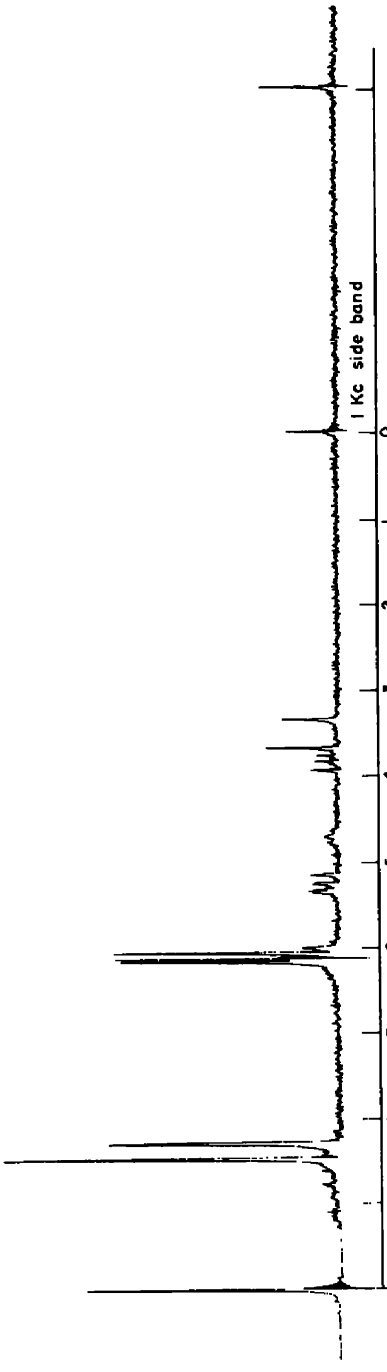


FIG. 3 NMR spectrum of alvaxanthone trimethyl ether (XXb) in carbon tetrachloride, with 1 k.c. standardization sideband from tetramethylsilane, the internal reference (varian HR 100 spectrometer).

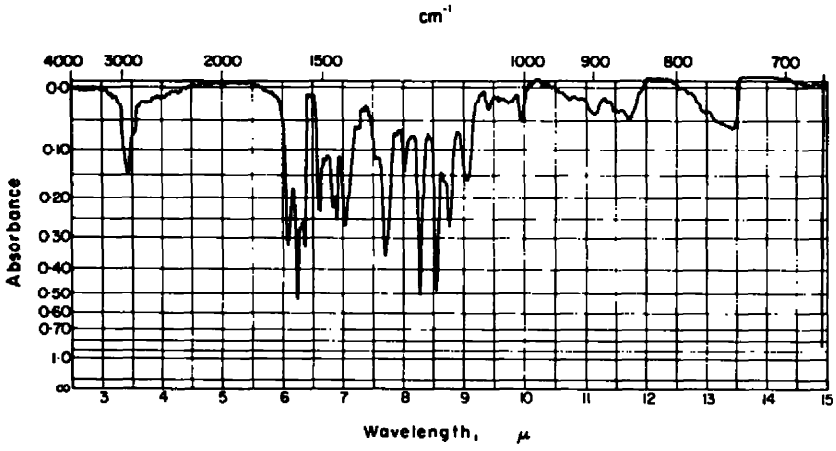


FIG. 4 Infrared spectrum of alvaxanthone trimethyl ether (XXb) in carbon tetrachloride.

We thus re-investigated the Claisen rearrangement of the dimethylallyl ether (XV) and shortened the reaction time so that alvaxanthone methyl ether could be isolated in addition to the furanoxanthone (XVII). Refluxing the reaction mixture for 2 hr followed by methylation with diazo methane and separation by TLC gave the trimethyl ether (XXb). Its structure follows from its NMR spectrum (Fig. 3), which is very similar to that obtained by Wolfrom *et al.*[29] for alvaxanthone triacetate, except for the signals due to the acetoxy and methyl ether groups, and from cyclization to the furanoxanthone (XXb) which can be achieved on the chromatography plate. Although an authentic sample was not available for direct comparison, our product (XXb) has the same m.p. as alvaxanthone trimethyl ether and thus provides synthetic evidence for the structure of alvaxanthone proposed by Wolfrom *et al.*[29]

EXPERIMENTAL

Compound XV (200 mg) in dimethylaniline (5 ml) was refluxed for 2 hr, and after cooling, the solution was carefully neutralized with 2 N HCl. The beige solid was filtered off, dried, dissolved in MeOH, and methylated with diazomethane in ether. The ether was removed *in vacuo*, and the residue dissolved in $CHCl_3$ was applied to 10 preparative TLC plates which were developed with $CHCl_3$–petroleum ether (b.p. 60–80°) (70:30). The band ($R_f = 0{\cdot}80$) which was black when viewed under UV light, was scraped off and eluted with ethyl acetate. The ethyl acetate was removed, and the residue recrystallized from pet. ether (b.p. 60–80°) to give 1 *hydroxy*-2-(1′,1′-*dimethylallyl*)-8-(3′,3′-*dimethylallyl*)-3,5,6-*trimethoxyxanthone* (10 mg) as yellow needles m.p. 151–154° (lit.[16] m.p. 151–152). The IR spectrum of synthetic alvaxanthone trimethyl ether (XXb) in CCl_4 is shown in Fig 4.