Spirans. Part IX.[1] Dimers and Trimers of *o*-Quinone Methides

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Weak aqueous bases transform 2-chloromethyl-4,6-dimethylphenol mainly into the well-known trimer (IV), a xanthenspirochromanone, but to a small extent into a novel type of dimer with the methylenexanthenone structure (X). When heated, this dimer dissociates into an *o*-quinone methide (II) which adds to cyclo-octa-1,5-diene, to give a cyclo-octa[*b*][1]benzopyran derivative (XI), or to the dimer, to give a new trimer (XII) isomeric with (IV).

Weak aqueous bases convert 2-chloromethylphenol into a polymer $(C_7H_6O)_{12}$. A relation between this polymer and the dimer (X) is pointed out. The trimerisation of *o*-quinone methides is analysed as a sequence of two steps of which the first is relatively slow.

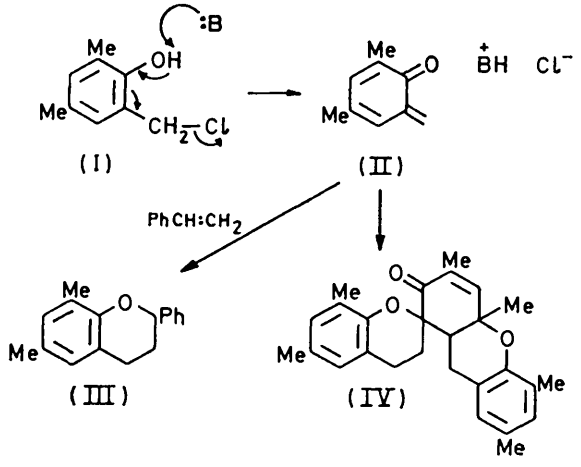
When 2-chloromethyl-4,6-dimethylphenol (I) is treated with base it is believed to give an *o*-quinone methide[2] (II) that can be trapped by styrene as the chroman derivative[3] (III) but, left to itself, rapidly forms the trimer[4-6] (IV) (Scheme 1). We have examined these reactions again for two reasons: first, the lower homologue 2-chloromethylphenol behaves in a different way (though trimerisation is general[7,8]) and, second, the results of the trapping experiments were not those we expected.

Gardner and his colleagues[4] have prepared the *o*-quinone methide (II) using a different technique and preserved it for study at low temperatures. Above −20° it rapidly trimerised giving the trimer (IV), the structure of which they support[4-6] with full degradative and spectroscopic evidence. Two routes suggest themselves for trimer formation, depending on which of two dimers, (V) and (VI), is thought the more probable (Scheme 2). Although *o*-quinone methides often give spiro-compounds,[9] and (V) has been made by another route,[7] neither dimer has been obtained from the *o*-quinone methide (II) despite a number of trapping experiments with various alkenes.[3,10] A chroman derivative such as (III) has always resulted and any *o*-quinone methide not so trapped has completed trimerisation. Thus the alkene seems to interfere effectively only with the dimerisation, as if the quinone methide added more quickly to the dimer than it does to itself or to the added alkene.

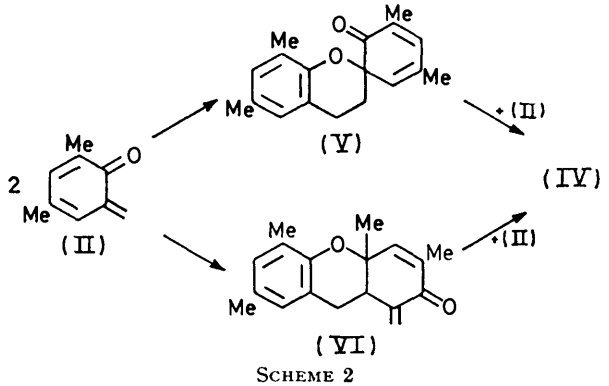
Other considerations lead to the same conclusion. The development of benzenoid aromaticity favours the operation of an *o*-quinone methide as the 'diene' component in 1,4-cycloadditions. In the dimerisations considered here, however, the *o*-quinone methide also provides the 'ene' component, a function that must be

[1] Part VIII, M. S. Chauhan, F. M. Dean, D. Matkin, and M. L. Robinson, *J.C.S. Perkin I*, 1973, 120.
[2] A. B. Turner, *Quart. Rev.*, 1964, **18**, 347.
[3] M. Wakselman and M. Vilkas, *Compt. rend.*, 1964, **258**, 1526.
[4] P. D. Gardner, H. Sarrafizadeh, and L. Rand, *J. Amer. Chem. Soc.*, 1959, **81**, 3364.
[5] S. B. Cavitt, H. Sarrafizadeh, and P. D. Gardner, *J. Org. Chem.*, 1962, **27**, 1211.
[6] A. Merijan, B. A. Shoulders, and P. D. Gardner, *J. Org. Chem.*, 1963, **28**, 2148.
[7] K. Fries and E. Brandes, *Annalen*, 1939, **542**, 48.
[8] K. Hultzsch, *J. prakt. Chem.*, 1941, **159**, 180.
[9] W. W. Sullivan, D. Ullman, and H. Schechter, *Tetrahedron Letters*, 1969, 457; C. L. Cook and L. C. Butler, *J. Org. Chem.*, 1969, **34**, 227; J. Brugidou and H. Christol, *Bull. Soc. chim. France*, 1966, 1693; R. Pummerer, G. Schmidutz, and H. Seifert, *Chem. Ber.*, 1952, **85**, 535.
[10] D. A. Bolon, *J. Org. Chem.*, 1970, **35**, 715, 3666.

opposed by the considerable aromatic character possessed by *o*-quinone methides themselves but which must be lost almost entirely; hence dimerisation should be less

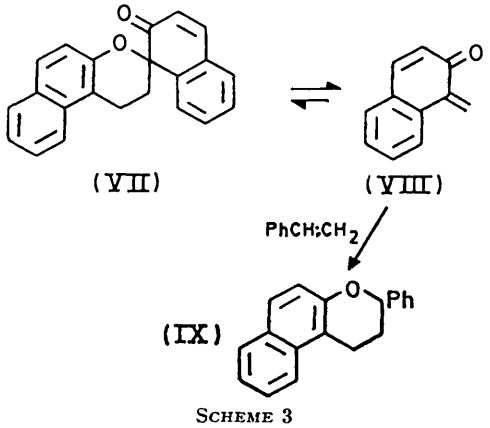


SCHEME 1



SCHEME 2

favoured than addition to a simple alkene derivative. Evidence for this comes from a demonstration of the converse case, in which the dimer (VII) dissociates into the quinone methide (VIII) at temperatures at which the chroman derivative (IX) is stable.[1]



SCHEME 3

Nevertheless, the survival of small amounts of a dimer seemed a reasonable expectation, so we repeated the treatment of the phenol (I) with base in the presence of a large excess of styrene and searched for such species. We encountered the trimer (IV) and the chroman (III) as described, and succeeded in isolating a small quantity of a dimer as well. It proved to have the entirely unexpected structure (X).

The i.r. spectrum showed the new dimer to be an unsaturated ketone lacking hydroxy-groups. The angular methyl group resonated as a sharp singlet at τ 8·81 and the aromatic methyl groups as a band at 7·83. The vinylic methyl group produced a doublet (J 2 Hz) at τ 8·19 and the associated vinylic proton a quartet at 3·45 overlaid by one aromatic resonance (the other aromatic proton resonated at 3·26). A broadened two-proton singlet at τ 7·49 is particularly important for orientational purposes since it has to be assigned to the ring methylene group in (X) and thus helps to exclude the similar structure (VI) which must have generated an ABM pattern instead. The exocyclic methylene protons resonate at widely different fields because of the adjacent carbonyl group;[11] one band appears at τ 3·91 and the other at 4·18 with splitting owing to geminal interaction and also to allylic coupling (J *ca.* 1 Hz) with the angular proton (τ 5·31), thus confirming the orientation shown. The mass spectrum revealed a parent ion at *m/e* 268 that loses one methyl group, presumably the angular one. By far the most important fragmentation, however, is into ions *m/e* 134 indicative of a retrograde cycloaddition regenerating the quinone methide (II).

That a purely thermal fission of this kind does occur is shown by heating the dimer in cyclo-octa-1,5-diene, when it affords the chroman derivative (XI). A second product, and the only one in the absence of a trapping alkene, is a trimer with structure (XII) resulting from an addition of the quinone methide (II) to the dimer (X). The new trimer is very like the old (IV), but the n.m.r. spectra distinguish clearly between them (Table). In

N.m.r. spectra [a] of the trimers (IV) and (XII)

Assignment		Trimer (IV)			Trimer [b] (XII)		
			Mult.	J/Hz		Mult.	J/Hz
Angular CH_3		8·34	s		8·46	s	
CH_3·C=CH		8·19	d	2	8·21	d	1·5
Aromatic	(i)	7·82	s		7·90	s	
CH_3	(ii)	7·82	s		7·83	s	
	(iii)	7·82	s		7·75	s	
	(iv)	7·82	s		7·75	s	
$ArCH_2$·CH_2		7·0 to 8·0	m		7·58	t [b]	6
$ArCH_2$·CH_2					7·12	t [b]	6
$ArCH_2$·CH							
$ArCH_2$·CMe					7·29	d [b]	4
ArO·CH					5·65	d	2
MeC=CH		3·58	q	2	3·64	q	1·5
ArH	(i)	3·41	m [b]		3·32	m [b]	
	(ii)	3·32	m		3·23	m	
	(iii)	3·26	m		3·23	m	
	(iv)	3·26	m		3·23	m	

[a] In $CDCl_3$. [b] Unsharp.

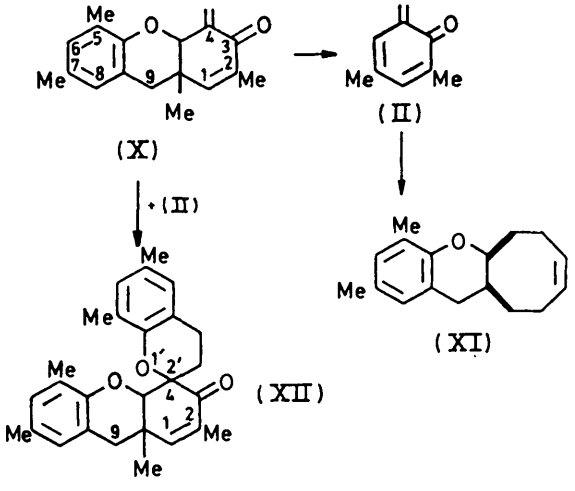
particular, the new trimer resonates at τ 5·65 because of its isolated angular proton adjacent to ether oxygen, and the small splitting (<2 Hz) is believed to reflect long-range coupling with a methylenic proton such as we have noted in related chroman derivatives.[1] Con-

[11] Z. Sanek, *Tetrahedron Letters*, 1970, 671.

versely, the old trimer (IV) has no such band but possesses a more complex splitting pattern near τ 7 because of its ABM segment (though overlapping bands prevented a detailed analysis in this region).

The thermal dissociation of the dimer (X) but of neither trimer accords entirely with the views already expressed. Since the quinone methide (II) is relatively stable in the thermodynamic sense it would be trapped out by dimer (X) instead of reacting with itself to produce the old trimer (IV) which was neither expected nor found in the reaction mixture.

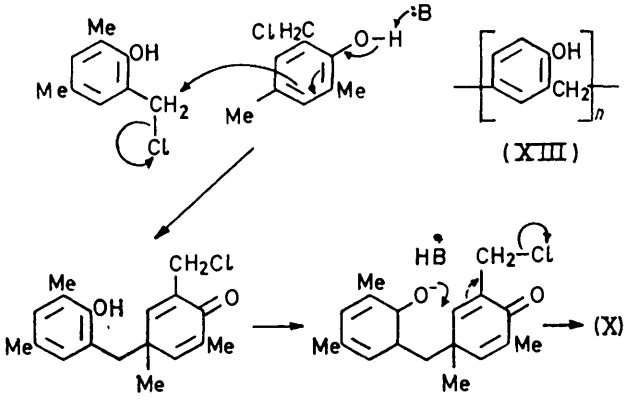
It seems very unlikely that dimer (X) is formed directly from the *o*-quinone methide (II). There is no precedent for such a process. Dimer (X) could hardly resist conversion into trimer (XII) while the isomers (V) and (VI) are being wholly converted into trimer (IV). Moreover, the dimer was difficult to detect immediately the main reaction was complete but easily detected after the lapse of time and particularly easily detected in the initial precipitate (mainly triethylammonium chloride) after treatment with water. Hence



SCHEME 4

we suggest that dimer (X) is formed by a coupling reaction (shown as S_N2 in type but S_N1 is equally acceptable) followed by a cyclisation which is slower and may occur in a salt-like intermediate (Scheme 5).

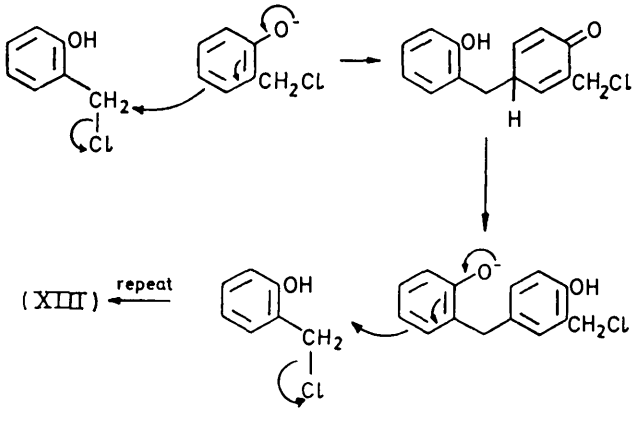
The coupling reaction has a close precedent. In 1931 Freudenberg and his colleagues[12] treated 2-chloromethylphenol with base and obtained a polymer they represented as (XIII; $n = 18$). We have prepared this polymer similarly and confirmed its nature spectroscopically. Acetylation affected all the oxygen atoms, which are therefore all hydroxylic, and the product gave an n.m.r. spectrum possessing three broad areas of resonance: (i) τ 7·9 (3H, Ac), (ii) 3·1 (3H, ArH), and (iii) 6·2 (2H). This last band can only be attributed to a methylene group connecting two aromatic residues and structure (XIII) follows, except that some di-*ortho*-substituted residues might be present and the value of n has to be decided. The mass spectra suggested, by peaks at m/e 592 and 444, that the polymer might be



SCHEME 5

only a tetramer or a mixture of that with a trimer, cyclic polymers of this type having been described.[13,14] But vapour phase osmometry gave for the acetate in benzene values of n close to 12, and we accept this value and attribute the mass spectral results to thermal collapse of the polymer in the ion source, low volatility preventing the appearance of the parent ion.

Polymer (XIII) would be produced by coupling reactions like that already suggested but with aromatisation at each stage (Scheme 6). The methyl groups in the higher homologue would prevent aromatisation and also tend to obstruct the coupling process for steric reasons. Since methyl groups stabilise quinones they should also stabilise quinone methides, so a change of reaction course between the two homologues is not surprising. While 2-chloromethylphenol might give small amounts of the *o*-quinone methide (XIV) and thence the known trimer[5] related to (IV), we did not

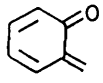


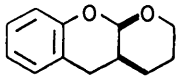
SCHEME 6

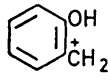
observe this. Polymerisation was not reduced in the presence of dihydropyran which, being a vinylic ether, is an excellent trapping agent for quinone methides,[1,10] and only a small amount of the adduct (XV) was

[12] K. Freudenberg, F. Sohns, W. Dürr, and C. Niemann, *Cellulosechemie*, 1931, **12**, 263; *Chem. Zentr.*, 1931, II, 2143.
[13] A. Zincke and E. Ziegler, *Ber.*, 1944, **77**, 264.
[14] J. B. Niederl and H. J. Vogel, *J. Amer. Chem. Soc.*, 1940, **62**, 2512.

obtained. Even this may have arisen from the carbonium ion (XVI); recent work [3,15] has shown that such ions are capable of undergoing the stereospecific cycloaddition reactions formerly thought to be confined to the quinonoid species. Thus we also obtained the chroman (XI) by treating cyclo-octa-1,5-diene with 2-hydroxymethyl-4,6-dimethylphenol and perchloric acid.


(XIV)


(XV)


(XVI)

EXPERIMENTAL

N.m.r. spectra were obtained for solutions in deuteriochloroform. The light petroleum used had b.p. 60—80°. Molecular weights other than that of the polymer were determined mass spectroscopically.

6,8-*Dimethyl*-2-*phenyl*-5-(1-*phenylethyl*)*chroman*.— To styrene (10·4 g) and 2-hydroxymethyl-4,6-dimethylphenol (1·5 g) in dichloromethane (150 ml) was added perchloric acid (5 ml). After 20 h the dichloromethane and styrene were removed under reduced pressure and the residue was chromatographed on silica from benzene–light petroleum (1 : 1), giving much polymeric material (rejected) and a fraction that afforded the 5-(1-*phenylethyl*)*chroman* (0·45 g), m.p. 151° (from light petroleum) (Found: C, 87·6; H, 7·8%; *M*, 342. $C_{25}H_{26}O$ requires C, 87·7; H, 7·7%; *M*, 342), τ 8·34 (d, *J* 7 Hz, CH·C*H*$_3$), 8·00 (s, 6-CH$_3$), 7·82 (s, 8-CH$_3$), 7·2—7·9 (m, CH$_2$·CH$_2$), 5·45 (q, *J* 7 Hz, C*H*Me), 5·03 (dd, *J* 3 and 10 Hz, O·C*H*·CH$_2$), 3·12br (7-H), and 2·8 (m, C_6H_5).

A similar experiment using less perchloric acid (0·5 ml) in acetic acid (10 ml) as described by Wakselman and Vilkas [3] gave 6,8-dimethyl-2-phenylchroman (2 g). Chromatography on silica of the crude product furnished a small amount of the 5-(1-phenylethyl)chroman, m.p. and mixed m.p. 150°.

4,4a,9,9a-*Tetrahydro*-2,5,7,9a-*tetramethyl*-4-*methylenexanthen*-3-*one* (X).—Solutions of triethylamine (1 g) in benzene (300 ml) and of 2-chloromethyl-4,6-dimethylphenol [16] (0·8 g) in benzene (350 ml) were added, dropwise and simultaneously, to styrene (50 g) in stirred benzene (100 ml). Addition was complete in about 7 h but stirring was continued for 12 h more and the solution filtered. The residue was kept with water (400 ml) for 18 h giving a solid that, purified from light petroleum, gave the methylenexanthenone as a crystalline powder (70 mg), m.p. 106—107°, $\nu_{max.}$ (KBr) 2960 (ArH), 2920, 2860 (CH$_3$), 1667 (dienone C:O), and 1635 cm^{-1} (aromatic and ethylenic) (Found: C, 80·6; H, 7·8%; *M*, 268. $C_{18}H_{20}O_2$ requires C, 80·6; H, 7·5%; *M*, 268).

The filtered benzene solution was washed with water, dried (MgSO$_4$), and evaporated to a gum that was purified by chromatography on silica from light petroleum giving the known trimer [4,7] (IV) (0·33 g), m.p. and mixed m.p. 199—200°, along with 6,8-dimethyl-2-phenylchroman (III), identified mass spectroscopically with an authentic specimen (see before).

4,4a,9,9a-*Tetrahydro*-2,5,6′,7,8′,9a-*hexamethylxanthen*-4-*spiro*-2′-*chroman*-3-*one* (XII).—The 4-methylenexanthen-3-one (0·7 g) was heated in refluxing mesitylene (20 ml) under nitrogen for 6 h and the product recovered by evaporating the solvent under reduced pressure. Chromatography on silica from benzene–light petroleum (1 : 1) gave the starting material (15 mg) and the *xanthenespirochromanone*, which separated from benzene–light petroleum as tiny prisms (40 mg), m.p. 165°, $\nu_{max.}$ (KBr) 1670 (conj. C:O), 1642 (C:C), and 1605 cm^{-1} (aromatic) (Found: C, 80·3; H, 7·5%; *M*, 402. $C_{27}H_{30}O_3$ requires C, 80·6; H, 7·5%; *M*, 402).

cis-6,7,10,11,11a,12-*Hexahydro*-2,4-*dimethyl*-5aH-*cyclo-octa*[b][1]*benzopyran* (XI).—(i) To 2-hydroxymethyl-4,6-dimethylphenol (1 g) in dichloromethane (150 ml) was added cyclo-octa-1,5-diene (70 g) and then perchloric acid (0·5 ml) in acetic acid (10 ml). After 16 h, volatile materials were removed under reduced pressure and the residue was chromatographed on silica from benzene–light petroleum giving, as one fraction, the *cyclo-octabenzopyran* as a thick liquid (1 g), devoid of hydroxylic or carbonyl absorption, and having τ 7·89 (s, ArCH$_3$), 7·84 (s, ArCH$_3$), 7·0—8·5 (m, CH$_2$·CH$_2$ and CH$_2$·CH), 5·7 (m, O·CH), 4·49 (t, *J* 5 Hz, CH=CH), 3·40br (ArH), and 3·33br (ArH) (Found: C, 84·1; H, 9·5%; *M*, 242. $C_{17}H_{22}O$ requires C, 84·3; H, 9·2%; *M*, 242).

(ii) The methylenexanthenone (X) (0·1 g) was heated in refluxing cyclo-octadiene (20 ml) under nitrogen for 7 h. The alkene was removed by distillation and the residue chromatographed on silica from benzene–light petroleum (1 : 1) giving three main fractions: (*a*) unchanged methylenexanthenone (trace), (*b*) the xanthenspirochromanone (XII) (30 mg), and (*c*) the cyclo-octabenzopyran, identical (i.r. and mass spectra) with a sample prepared as in (i).

Action of Bases on 2-*Chloromethylphenol*.—Saligenin (2-hydroxymethylphenol) (1·0 g) was ground with concentrated hydrochloric acid (25 ml) at −10° for 10 min; the product was extracted into ether (200 ml) and washed with a small amount of ice–water. This method [17] gave a solution containing about 0·8 g of the desired halide, t.l.c. indicating the presence of a little impurity (not identified). To it was slowly added a saturated solution (10 ml) of sodium hydrogen carbonate in water; each addition produced a yellow colour that faded rapidly as a colourless precipitate formed. A little more of the base was added and the absence of the colouration was taken as indicating complete reaction. The precipitate was collected, washed with water, and dried in air and then *in vacuo*. It formed a powder (0·6 g) insoluble in light petroleum, chloroform, or benzene but soluble in warm ethanol from which it separated in a form indistinguishable from the original, m.p. *ca.* 120°. Chromatography on silica from chloroform containing ethanol suggested that the material was more or less homogeneous but trailing could not be eliminated entirely. This material is considered to be essentially the dodecamer (XIII; $n = 12$), but it resisted the complete drying required for analysis or it resinified further. The acetate was made by treatment with acetic anhydride and triethylamine at 100° for 20 min and separated from ethanol, in which it is sparingly soluble, as a microcrystalline solid, m.p. 113—114°, $\nu_{max.}$ 1750 cm^{-1}, readily soluble in benzene and chloroform (Found: C, 72·85, 72·85; H, 5·6, 5·7. Calc. for $C_{36}H_{32}O_8$: C, 73·0; H, 5·4%).

A similar experiment was carried out using triethylamine (1·5 ml) in moist ether (50 ml) instead of sodium hydrogen carbonate solution. The reaction proceeded in the same

[15] R. R. Schmidt, *Tetrahedron Letters*, 1969, 5279.
[16] E. Ziegler, H. M. Muella, and J. Simmler, *Ber.*, 1943, **76**, 664.
[17] E. Ziegler, *Monatsh.*, 1948, **78**, 334.

way and the product was indistinguishable from that obtained before.

cis-3,4,4a,10a-*Tetrahydro*-2H,5H-*pyrano*[2,3-b][1]*benzopyran* (XV).—An ethereal solution (40 ml) of 2-chloromethylphenol [17] [prepared from saligenin (1 g) and concentrated hydrochloric acid (25 ml)] was stirred with dihydropyran (50 g) and saturated aqueous sodium hydrogen carbonate was added until no further colouration was noted. The precipitated polymer was removed and the ether solution was washed with water, dried ($MgSO_4$), and evaporated to a gum which was chromatographed on silica from benzene–light petroleum (1 : 4). One fraction gave the *pyranobenzopyran* as a syrup (50 mg), τ 8·35 (4H, m, O·CH_2·CH_2·CH_2·CH), 7·41 and 7·10 (two dd, J 22 and 4·5 Hz, ArCH_2·CH), *ca.* 6·2 (2H, m, O·CH_2·CH_2), 4·73 (d, J 2 Hz, O·CH·C in *cis*-fused system), and *ca.* 3·1 (4H, m, ArH) (Found: C, 75·6; H, 7·1%; M, 190. $C_{12}H_{14}O_2$ requires C, 75·8; H, 7·4%; M, 190). In the mass spectrometer, this pyranopyran gives a parent ion that collapses to another ion m/e 131 (m^* 90·3) corresponding to *o*-quinone methide; however, a more important fragmentation is that giving an ion m/e 158 (m^* 131·3), considered to be the benzypyrylium ion.

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