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STRUCTURAL FEATURES CONTROLLING CATION-RADICAL LINE-BROADENING IN THE ^{1}H-NMR SPECTRA OF PHENOL DERIVATIVES IN ACID MEDIA

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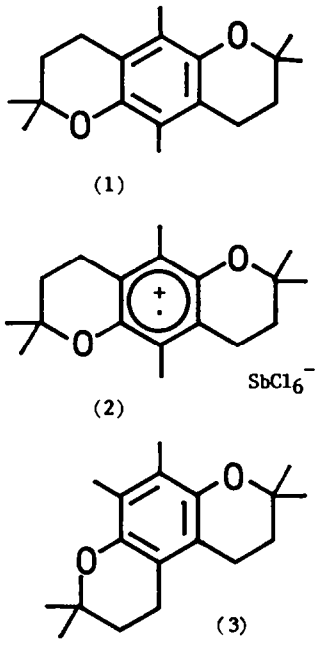
Abstract - The hexachloroantimonates of cation radicals from 2,3,4,7-8,9-hexahydro-2,2,5,7,7,10-hexamethylbenzo[1,2-*b*;4,5-*b*']dipyran (1) and the isomeric benzo[1,2-*b*;4,3-*b*']dipyran (3) have been characterised. The production of cation radical from (1) in acid media is limited by acid concentration for weak acids and also by the presence of oxygen for strong acids. The cation radical species ($Ar^{\ddagger}$) is considered to originate from substrate (Ar) via protonation then electron-transfer from neutral substrate (Ar); only when this transfer is structurally favourable do phenol derivatives exhibit line broadening in their ^{1}H-nmr spectra. Stereochemical effects greatly reduce sensitivity to acid, and in derivatives of benzene-1,2,4-triol the presence of two oxygen atoms in one ring is extremely disadvantageous. Since phenolic cation radicals are rather strong acids, their behaviour in weakly acid media is best studied (by oxidising agents or by cyclic voltammetry) through the ethers.

Earlier we showed that tocopherols and similar derivatives of 6-hydroxychroman are sensitive to acids (e.g. trifluoroacetic acid) which appear to promote the formation of cation radicals and consequently induce extensive line broadening of the bands in the ^{1}H-nmr spectra.[1-3] A similar effect is seen when certain polycyclic aromatic compounds including anthracene, thianthrene, and perylene, are treated with acid, especially sulphuric acid, and there has been discussion about the role played by acid in what seems to be a one-electron oxidation.[4-6] We have considered this again in connection with the benzodipyran derivatives after expanding earlier results and extending them to heterocyclic systems containing more than one oxygen atom.

Because cation radicals from phenols are not sufficiently stable we began with a study of the benzodipyran derivative (1) which, with antimony(V) chloride, affords a dark solid analysing to the salt (2). Based upon the organic component, the yield is excellent; reduction of the salt with any common, mild reducing agent regenerates the benzodipyran, again in high yield. The mass spectrum (EI^+) of the salt is almost the same as that of the parent heterocycle apart from relative intensities Though the salt is readily soluble in suitable solvents no proton signals could be obtained in the nmr spectrometer; however, the electron spin resonance spectrum has been extensively studied by our colleagues[7] and, although it is complex and also temperature dependent, it confirms structure (2).

The salt (2) dissolves in polar solvents and in trifluoroacetic acid it seems to be stable indefinitely. In neutral solvents it deteriorates, slowly in dichloromethane or trichloromethane, within a few hours in acetonitrile or nitromethane. It is unstable in the presence of water or alcohols. The characteristic absorption in the



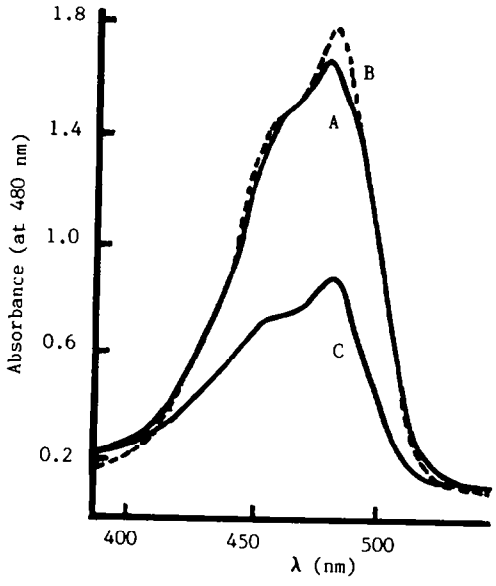


Figure 1. Spectra of cation radical salts
A, Hexachloroantimonate (2).
B, Hexachloroantimonate from (3).
C, Benzodipyran (1) in CH_2Cl_2 with F_3CCO_2H (0.65 M)(after 3 h in air).
(all heterocycles 0.29×10^{-3} M)

visible region (Fig. 1) is the same in acetonitrile as in dichloromethane and Beer's Law is obeyed at concentrations important in this study (i.e. up to about 0.2×10^{-2}M) indicating that radical dimerisation is not extensive under these conditions. The visible absorption is also unaffected by the presence of the neutral benzodipyran (1) so that charge-transfer association is not important. On the other hand, the addition of small amounts of the salt (2) to solutions of the neutral benzodipyran causes instant line broadening in the ^1H nmr spectrum indicating that electron exchange is rapid.

The hexachloroantimonate of the isomeric cation radical from the angular benzodipyran (3) has also been prepared and characterised in the same way and its spectrum (Fig. 1) and other properties found to be almost identical with those of the linear salt.

In dichloromethane the isomeric benzodipyrans (1) and (3) are stable indefinitely, but if a strong acid alone, or a weak acid with an oxidising agent (such as nitrous acid, halogens, hydrogen peroxide etc.), is added, the solution becomes more or less yellow and the characteristic absorption spectrum (Fig. 1) is observed. Stoicheimetric reactions with benzoyl peroxide in trifluoroacetic acid, or with tris-4-bromophenyliminium hexachloroantimonate, show that the spectrum corresponds to the loss of one electron. Cyclic voltammetry also indicates this.

In dichloromethane the benzodipyran (1) generates the cation radical with acid alone if this is strong enough; trifluoroacetic acid is sufficient and Fig. 1 includes a curve for it. The lower limit seems to be reached with monochloroacetic acid, which has only a slight effect. As in other examples, the cation radical is stable only if a stronger acid is present; with dichloroacetic acid, for example, there is little broadening in the nmr spectrum if (damp) air is present, and if the system is purged of air and sealed, the broadening occurs only to disappear in the course of several hours leaving a sharply defined spectrum again. Below we suggest that the cation radical may be destroyed by the water produced in its own formation.

In trifluoroacetic acid there is no regression in the broadening, only a steady increase. The enhanced stability of other cation radicals in trifluoroacetic acid has been noted previously and attributed to a reduced nucleophilicity in the solvent (including any water present) or to specific solvation effects.[6,8,9] As disclosed by the electronic spectrum, there is almost no formation of cation radical even in trifluoroacetic acid if the reactants and solvents are rid of oxygen as far as possible by vacuum line techniques and it may be that dissolved oxygen is important if it is not removed. However, there is still some line broadening which might be due to traces of oxygen still remaining or to reactions of the kind suggested by Carrington, Dravnieks, and Symonds[5] who considered the following equilibria for a susceptible aromatic substrate Ar and an acid HX:

$$Ar + HX \rightleftharpoons ArH^+ + X^- \quad \text{.....Equation 1.}$$

$$ArH^+ + Ar \rightleftharpoons ArH^{\cdot} + ArH^+_{\cdot} \quad \text{.....Equation 2.}$$

The cation radical species is produced in the second reaction at a concentration that is determined by the equilibria and might be very small. For Carrington *et al.* the concentration was increased by the acid, sulphuric acid, that was thought to oxidise the simple radical $ArH^{\cdot}$ and disturb the equilibrium. In our experiment, the radical would have to be removed by dimerisation or dismutation in the absence of oxygen; in the presence of oxygen, peroxides could be formed from the radical leading to a very efficient oxidation and an overall stoicheiometry as follows:

$$Ar + 4HX + O_2 \longrightarrow 4ArH^+_{\cdot} + 4X^- + 2H_2O \quad \text{.....Equation 3.}$$

It may be the water formed in this way that is partly responsible for the loss of cation radical species in the absence of a strong acid or at least an excess of a weak one.

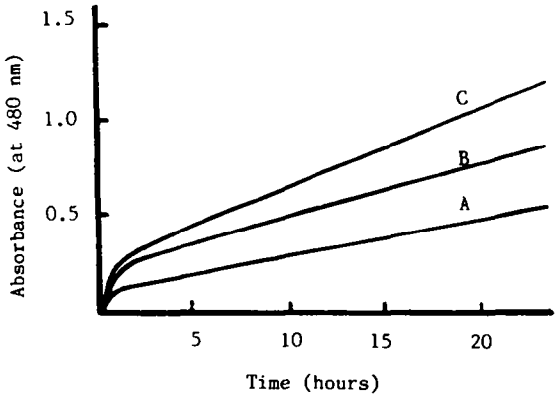


Figure 2. Effect of acid concentration and time upon cation radical formation from (1) (0.16×10^{-3}M) in CH_2Cl_2 containing F_3CCO_2H at concentrations (M): A, 0.216; B, 0.432, and C, 0.648.

When the benzodipyran (1) in dichloromethane is treated with trifluoroacetic acid in air and the development of the cation radical is followed by the visible spectrum (Fig. 2) one sees first a rapid but limited rise followed by a slower but steady rise that continues for some hours. The initial rapid rise might be attributed to a phase in which the equilibria are being set up and in which adventitious oxidants are being consumed. The slow, steady rise can be attributed to the steady-state operation of Equations 1-3 where the rate is controlled by the concentration of acid but is not much affected by air or by bubbling oxygen through the solution.

If so, then protonation will be the limiting step. Accordingly, experiments with weaker acids such as trichloroacetic acid yield essentially the same results, while stronger acids (trifluoroacetic acid containing boron fluoride) provide a different picture. The rates are higher (Fig. 3) and are increased by oxygenation which can now be the limiting process; thoroughly degassed solutions still show a steady rise, however so that oxygen, though helpful, is still not essential. Equations 1-3 suffice for these observations although for other substrates and acids certain modifications have been favoured.[4,10,11] The oxidising ability of sulphuric acid is now widely accepted,[12] whereas trifluoroacetic acid has usually been thought not to be an oxidant in these circumstances. However, now that trifluoroacetic anhydride is known to oxidise tertiary amines[13] (and be reduced to trifluoroacetaldehyde) this assumption may not be valid.

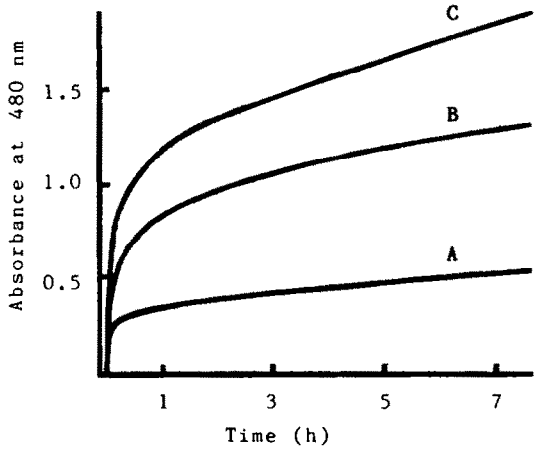
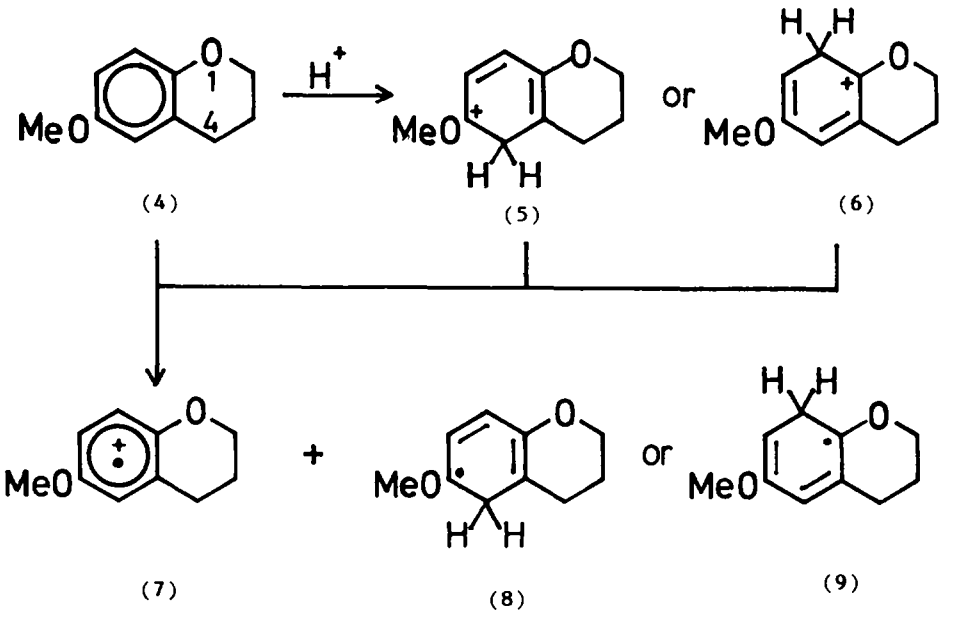


Figure 3. Effect of F_3CCO_2H/BF_3 and oxygen upon cation radical formation. Benzodipyran (1)(10^{-2}M) with acid (0.3M) in CH_2Cl_2; monitored
A, after degassing at 10^{-2}mm/Hg,
B, without degassing, and
C, after saturation with oxygen.

The protonation required as the first stage in cation radical formation is well known in phenols.[14] Scheme 1 shows two ways in which 6-methxoychroman (4) can accept a proton; in species (5) the charge in mainly stabilised on the methoxy oxygen atom, in (6) mainly upon the ring oxygen atom. In no such structures can the charge be stabilised by both oxygen atoms at the same time. In the next step (which corresponds to Eq. 2) an electron moves from a neutral molecule to a protonated molecule converting the former into the cation radical (7) and the latter into simple radicals such as (8) or (9). It is important that in the cation radical (7) the two oxygen atoms can assist in stabilising the positive charge at the same time because this is no longer restricted to one set of atoms; without this factor there would be no energy gain to set aginst the transformation of a rather well-stabilised cation (5) or (6) into a relatively ill-stabilised radical (8) or (9). With this point in mind we investigated the effect of having further oxygen atoms present in the system.

6,7-Dimethoxychroman (10) is considerably more sensitive to acid than is the methoxychroman (4). Protonation now leads to some species such as (11) in which two oxygen atoms can share the charge to start with, but then to a cation radical (12) in which three oxygen atoms can share. Thus both the initial protonation and the subsequent electron transfer are promoted. Relative broadening within cation radical (12) somewhat favours position 8 (Table 1). We explain this be extending an earlier argument;[3] in effect, three 'oxygen effects' are superimposed. Since an oxygen substituent



Scheme 1

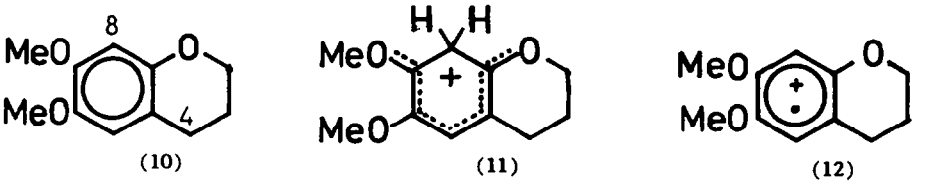
Table 1. Acid-induced line broadenings[a] in ^{1}H-nmr spectra.[b]

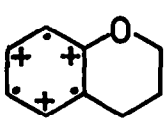
Compound	OMe	OCH_2	$ArCH_2$ (ring)	$ArCH_2CH_2$	ArH	CH_2Me	CH_2Me	ArMe
(1)			7.2	0.6				7.8
(10)	vb	vb	vb	19.6	0.13[c] 1.8[d]			
(16)	1.0		2.3	0.0	1.0[c,d]			
(18)	0.0	1.6	1.8	0.0	0.5			0.5
(19a)	vb	2.1[e] vb[f]			0.4[c] 1.2[d]	vb	0.0	
(19b)		0.9[e,f?]			0.4[c] 0.5[d]	0.0	0.0	
(20a)	0.0	0.0			0.0			
(20b)		0.0			0.0			

[a] Difference (Hz) in half-height widths for 0.3M solutions in $CDCl_3$ alone and for solutions 0.3M in both substrate and F_3CCO_2H. Broadening too wide to be estimated is indicated as vb.

[b] At 220 MHz and probe temperature.

[c] Position 5. [d] Position 8. [e] Position 2. [f] Position 3.





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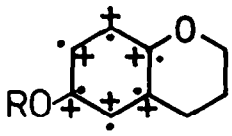

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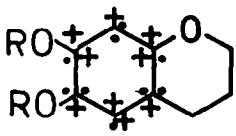
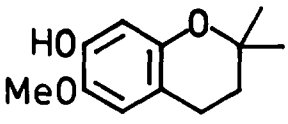


(15)

stabilises a positive centre much more than a radical centre, it will strongly bias charge around the benzene ring as depicted in diagram (13) (it is only the bias that is indicated; the signs total only one positive charge and one unpaired spin). The second oxygen atom in diagram (14) acts similarly so that the system is now more or less symmetrical. The third oxygen atom in diagram (15) adds its own bias and the result is that there will be more unpaired spin at position 8 than at position 5. The benzylic methylene group also has some effect as explained previously, but this will always be smaller than the oxygen effect.



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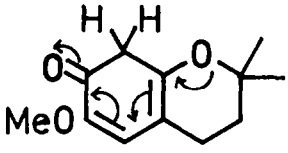

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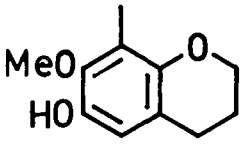


(18)

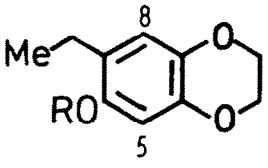
In marked contrast, the introduction of an hydroxy group instead of methoxy at position 7 converts chroman (4) into phenol (16) with much less sensitivity to acid (Table 1). As before, protonation must lead to a species similar to (11) but which will now be a protic acid able to release a proton (from OH) leaving an internally well-stabilised structure as indicated in diagram (17). The process is of course merely the tautomerism characteristic of phenols related to benzene-1,3-diol.[15] The result would be a substantial reduction in the standing concentration of the cation and so in the concentration of cation radical.

The phenol (18) was also found to be rather insensitive to acid (Table 1) even though it contains the extra methoxy group. However, this group is pinned by two *ortho* substituents and will therefore not lie in plane nor assist in delocalisation of charge; instead, it will exert only its electron-attractive effect and so reduce the ability of the system to take up a positive centre. In confirmation, the methoxy group in this molecule shows no broadening whereas in all other substrates it is their methoxy groups that are the most sensitive parts.

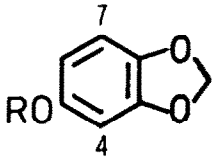
Another way of modifying the system is to have two oxygen atoms in a ring and only one outside it as in the dihydrobenzo-1,4-dioxin derivative (19a). Again significant stereochemical differences appear. For diagram (15) to apply, all three ether groups must be able to retain co-planarity with the benzene ring, and models show that this is not possible if two oxygen atoms are included in one ring as in (19a). The methoxy oxygen atom and that at position 1 have to be in-plane for any sensitivity whatever to appear, but the oxygen at position 4 must rotate to some extent and should therefore reduce the sensitivity in comparison with that of the dimethoxychroman (10)(Table 1). The corresponding phenol (19b) is much less sensitive again for the reasons already advanced in connection with phenol (16).

Finally we examined the benzodioxole derivatives (20) and found them both to be remarkably insensitive to acid-induced broadening. The ether (20a) was unaffected at the usual acid concentrations although it did respond to the concentrated acid; the phenol (20b) was scarcely affected even by neat acid. Such resistance to broadening

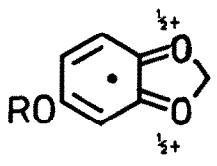
cannot be attributed to a failure of the initial protonation because protodetritiation rates show that acids react about as readily with the benzodioxole nucleus as with 1,2-dimethoxybenzene.[16] Nor can it easily be attributed to a failure of the normally rapid exchange of electrons between the cation radical and the neutral species as no reason, such as steric hindrance to association, seems to be present. It remains to consider the actual formation of the cation radicals, i.e. Equation 2. Molecular dimensions suggest that, when a ring oxygen atom adopts the sp^2 state order to engage in delocalisation with charge in the benzene ring, the five-membered ring is forced to accomodate angles to which it is not well adapted; if two oxygen atoms are present, the angle strain becomes considerable. Diagram (21) illustrates the extreme situation. Such angle strain can be reduced at the expense of increasing



(19a) R = Me
(19b) R = H



(20a) R = Me
(20b) R = H



(21)

the p component of the oxygen hybrid towards the sp^3 state but this reduces both the extent of delocatisation within the $p\pi$ system and and the extent to which the sp^2 lone pair can be delocalised into the σ framework. Hence the cation radical state is relatively unfavourable, the equilibrium (Eq. 2) moves to the left, and the broadening dwindles.

In principle the formation of cation radicals can be examined independently of protonation by using a neutral, non-nucleophilic solvent and a suitable oxidising agent; in practice the the cation radicals are often too unstable for reliable measurements to be made, and if acid is added to stabilise them the acid itself can make a dominant contribution to broadening. However, we oxidised selected substrates with tris-(4-bromophenyl)iminium hexafluoroantimonate[17] and dichloro- or trichloromethane as solvents and within the limits discussed previously[2] the results

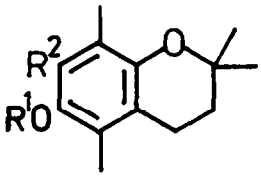
Table 2. Iminium salt induced line broadenings[a] in ^{1}H-nmr spectra.[b]

Structure	OMe	OCH_2	ArMe	ring $ArC\underline{H}_2$	$ArCH_2C\underline{H}_2$	ArH posn.5	ArH posn.8	salt concn.[c]
(1)			vb	vb	4.5			0.6
(10)	3.5	vb[d]		2.8	1.0	0.1	0.5	0.5
(22a)			7.5	21.0	0.6			2.5
(16)	vb			vb	1.1	1.4	1.3	2.9

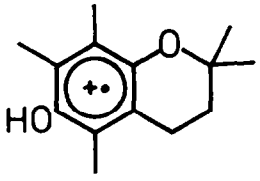
[a] Tris-(4-bromophenyl)iminium hexachloroantimonate in chloracetic acid was added to a 0.4 M solution of the substrate in $CDCl_3$.
[b] At 220 MHz and probe temperature.
[c] 10^{-3}M (approx.); final concentration obtained by adding 0.05 M salt in monochloroacetic acid.
[d] Overlaid by solvent peak.

Phenolic cation radicals are particularly troublesome in this respect. Although the earliest estimates[18] of their acidities ranged as high as pK_a -5, later work has indicated lower values about -1.3 for monohydric phenols and -0.8 for 1,4-dihydroxy-

benzene,[19] Evidently the stabilising effect of trifluoroacetic acid upon cation-radical species as noted above is more a function of solvation effects than of the suppression of ionisation - indeed, at these acidities some carboxylic acids might act as bases. A solution of the chromanol (22a) containing monochloroacetic acid (pK_a 2.9 in H_2O) showed no broadening until the iminium salt was added in sufficient quantity just to broaden beyond measurement all signals except those from the *gem*-dimethyl groups. It was kept in the usual stoppered nmr tube and monitored from time to time; after about 2 hours the spectrum was restored and the peaks nearly as sharp as they were originally.



(22a) R^1 = H; R^2 = Me
(22b) R^1 = Me; R^2 = H
(22c) R^1 = R^2 = Me



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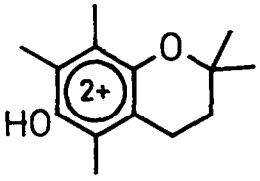


(24)

A similar problem besets the conversion of chromanols into their cation radicals by electrolysis. Parker and his colleagues[8] studied the cyclic voltammetry of the chromanol (22a) and found it impossible to obtain true reversible oxidation-reduction waves when dichloromethane was the solvent unless some trifluoroacetic acid was added when the removal of one electron at 0.8 V (*vs.* SCE) was observed. The removal of a second electron could also be observed, at 1.34 V, but only after the further addition of trifluoroacetic anhydride. Loss of the first electron was shown to give the cation radical (23), and loss of the second was considered to give the dication (24). When acetonitrile was the major solvent the cyclic voltammogram consisted in the main of a single oxidation-reduction wave the spacing between the components depending upon sweep rate and nature and concentration of added acid. The wave corresponded to a two-electron process occurring at about 0.8 V and was assigned to the formation of (24) coupled with the loss of the hydroxylic proton.

While accepting these interpretations, we remained puzzled as to why the dication (24) should lose a proton so readily in acetonitrile but not in dichloromethane containing acid, and why there was no sign in this work of the fact that the acidic solutions contain cation radical and other species before any electrolysis has taken place. We repeated some of the work of the earlier authors and found that the chromanol (22a) in dichloromethane alone gives an irregular wave indicative of a mixture of processes (Fig. 4). The addition of trifluoroacetic acid, however, caused a general collapse with the oxidation peak prominent at much lower potentials (around 0.5 V). With the further addition of trifluoroacetic anhydride the cyclic voltammogram changed again to give what seems to be the two-electron wave near 0.7 V characteristic of the earlier results with acetonitrile as solvent. A trace remains of the second oxidation step near 1.3 V (Fig. 4). This is what we had expected, since the dication (24) could well be 6 pK units more strongly acid than cation radical (23) and able to donate a proton to a carboxylic acid or anhydride. We found no conditions in which a clear second oxidation-reduction wave

could be observed in a discrete step.

In order to avoid the problem of the ionising hydroxy group we used a methyl ether. Derivative (22c) of the chromanol itself cannot be used because its methoxy group is hindered and rotated out of the aromatic plane; hence it is not a true electronic analogue of the phenol and its nmr spectrum is accordingly not sensitive to acid.[3] However, the lower homologue (22b) is satisfactory. In neat dichloromethane this ether exhibited at 1.0 V a one-electron oxidation-reduction wave that approaches reversibility, and a second oxidation step near 1.5 V which, however, is not reversible (Figure 5). This is the expected behaviour, and when appropriate

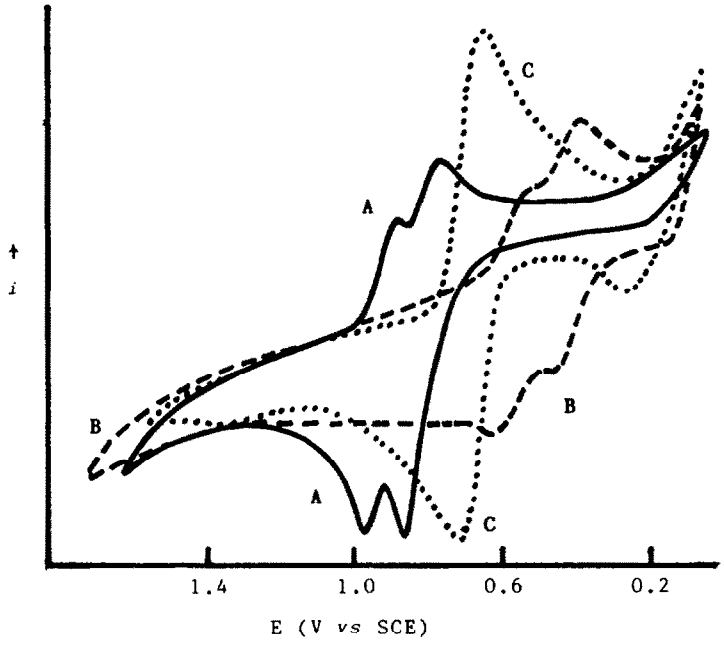


Figure 4. Cyclic voltammograms of chromanol (22a)(2×10^{-3}M) in A, CH_2Cl_2; B, F_3CCO_2H; and C, CH_2Cl_2/F_3CCO_2H (9:1 by vol.) with anhydride.

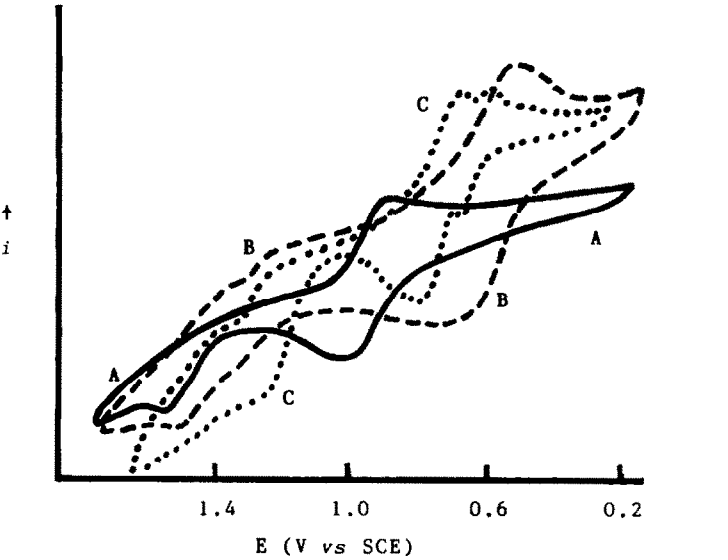


Figure 5. Cyclic voltammograms of chroman (22b)(2×10^{-3}M) in A, CH_2Cl_2; B, CH_2Cl_2/TFA(9:1) with TFAn; and C, MeCN/TFA (9:1).

allowance is made for the small structural difference, this behaviour is very close to that recorded by Parker for the parent chromanol (**22a**) and confirms his conclusions. Yet Parker was using an acid medium, whereas we find that acid makes substanial alterations to the voltammogram of the methoxychroman (Fig. 5) and, although the further addition of trifluoroacetic anhydride restores the discrete steps there remain rather large solvent (?) shifts and some small irregularities. Nevertheless, the fact that the ether displays two one-electron waves in conditions where the chromanol displays a single two-electron wave is acceptable evidence that the oxidation of the chromanol to the dication (**24**) is combined with the loss of the hydroxylic proton.

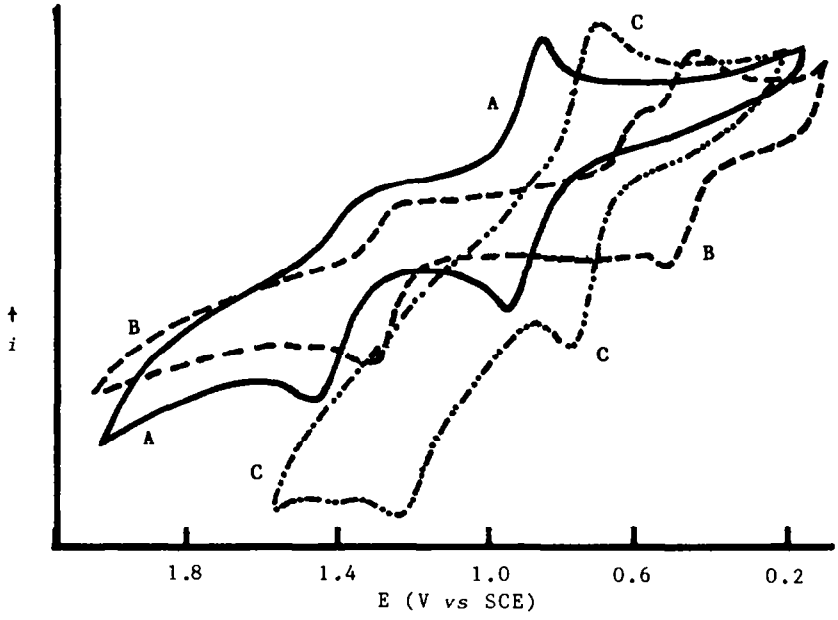


Figure 6. Cyclic voltammograms of benzodipyran isomers (**1**) and (**3**) (2×10^{-3}M) in A, CH_2Cl_2; B, CH_2Cl_2/F_3CCO_2H (9:1 by vol.) with added anhydride, and C, $MeCN/F_3CCO_2H$ (9:1 by vol.).

There remains the question of whether the shifts and other features reflect phenomena related to the nmr signal broadenings in acid. If so, these shifts should be greater for the benzodipyrans (**1**) and (**3**) because such compounds are much more sensitive in the nmr experiment. These isomers gave virtually indistinguishable cyclic voltammograms; the improved stability of the cation radical and dication in neutral dichloromethane was evident in ths fully reversible first wave and a second wave which was not fully reversible but much more nearly so than for the methoxychroman (**22b**)(Fig. 6). Despite this increased stability, there is very little difference in the positions of the oxidation peaks (Table 3). We also examined the radical cation salt (**2**); by starting the anionic sweep at 1.1 V just the second wave can be observed and it has the same properties as in the dipyran voltammogram which is reproduced in full by allowing the cycling to extend to 0.4 V thus confirming the assignments.

The presence of trifluoroacetic acid (with the anhydride) substantially modifies these results, especially the oxidation peak of the first wave (Table 3). The shifts are smaller when acetonitrile is the solvent, and whatever the nature of the medium the separation between the two oxidation peaks stays almost the same

when the methoxychroman and the benzodipyran are compared (Table 3). In solvent dichloromethane, the major shift caused by acid is in the first wave in agreement with the proposal that protonation is coupled in some way to the formation of the cation radical but not to the formation of the dication, which can only be obtained by removing an electron from the cation radical already formed. Undoubtedly general

Table. Oxidation peaks[a] of dipyran (1), salt (2), and chroman (22b)

Compound	Solvent	1st peak (V)	2nd peak (V)	Peak separation (V)
Benzodipyran (1)	(a) CH_2Cl_2	0.93	1.46	0.53
	(b) CH_2Cl_2/TFA/TFAA	0.52	1.31	0.79
	(c) MeCN/TFA	0.77	1.22	0.45
	Acid shift (a) - (b)	0.41	0.15	
Cation radical salt (2)	(a) CH_2Cl_2	0.92	1.44	0.52
	(b) CH_2Cl_2/TFA/TFAA	0.50	1.29	0.79
	Acid shift (a) - (b)	0.42	0.15	
Methoxy-chroman (22b)	(a) CH_2Cl_2	1.00	1.49	0.49
	(b) CH_2Cl_2/TFA/TFAA	0.71	1.44	0.73
	(c) MeCN/TFA	0.80	1.27	0.47
	Acid shift (a) - (b)	0.29	0.05	

[a] With tetrabutylammonium fluoroborate as supporting electrolyte in CH_2Cl_2 and sodium perchlorate in MeCN; scan rate 86 mVs^{-1}. Substrate concentration 2×10^{-3} M throughout. All runs conducted under nitrogen.

solvation and perhaps salt effects are also implicated but protonation appears to be dominant since the induced shift in the first oxidation peak increases as the acid concentration is increased; however, we found no simple proportionality between the two variables.

EXPERIMENTAL

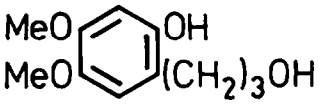
Electronic spectra were determined by means of a Unicam SP800 spectrophotometer and solutions about 10^{-3} M in ethanol unless another solvent is specified. Infrared spectra were determined by means of a Perkin Elmer 21B spectrophotometer and using mulls in paraffin except for salts, which were examined as KBr discs on a Mattson Alpha Centauri FT IR 13 apparatus. Proton magnetic spectra were obtained on a Perkin Elmer R34 machine operating at 220 MHz with Me_4Si as internal standard for the purpose of characterising new compounds and a PE A60 machine operating at 60 MHz for the purpose of measuring line broadenings. Molecular weights were determined by mass spectrometry on an AEI MS12 spectrometer; detailed mass spectra were recorded using a VG Analytical 7070E spectrometer.

Cyclic voltammetry was conducted with a Chemical Electronic potentiostat TR70/3A with a waveform generator type RB2, a Keithly 168 autoranging DMM voltmeter and a Watanabe 431 X-Y recorder. General procedure and operating conditions were modelled upon those of Parker *et al*,[8] and calibrations were effected with 1,4-dimethoxybenzene as standard and with the saturated calomel electrode as reference. Nitrogen for screening voltammetric solutions was scrubbed with Fieser's solution and dried (H_2SO_4). Sweep rates between 86 and 124 mVs^{-1} were examined.

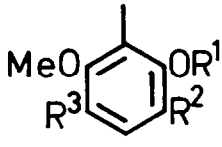
Light petroleum refers to the fraction b.p. 60 - 80 °C. Dichloromethane was dried over calcium hydride and distilled immediately before use. Trifluoroacetic anhydride was distilled immediately before use. Acetonitrile was dried over calcium hydride, kept over molecular sieve 4A, and distilled immediately before use.

Reduction of 3,4-*Dihydro*-6,7-*dimethoxy*-2H-1-*benzopyran*-2-*one*. - (i) *Diborane*. Diborane was generated by adding sodium borohydride (850 mg) in di-2-methoxyethyl ether (20 ml) to stirred boron trifluoride etherate (4.47 g) in the same solvent (13 ml) and passed into a solution of the title benzopyrone (208 mg) in tetrahydrofuran (100 ml) at 0 °C under nitrogen. Residual diborane was removed by a stream of nitrogen and the mixture was refluxed for an hour. Methanol (5 ml) was added and the solvents were removed by evaporation leaving a residue that was taken into ether, washed with water, dried ($MgSO_4$), and recovered as an oil that crystallised from ether-light petroleum giving 2-*hydroxy*-4,5-*dimethoxybenzenepropanol* (**25**) as prisms, (164 mg; 77%), m.p. 110-111 °C, $\nu_{max.}$ 3 450 and 3 210 (OH), 1 615 (aromatic), 1 373, 1 195, 1 110, and 922 cm^{-1}, δ(d_4-MeOH) 6.69 and 6.46 (each 1H, s, ArH), 3.75 and 3.73 (each 3H, s, OMe), 3.56 (2H, t, *J* 7.5 Hz, CH_2OH), 2.59 (2H, t, *J* 7.5 Hz, $ArCH_2$), and 1.79 (2H, m, $CH_2CH_2CH_2$)(Found: C, 62.0; H, 7.6%; *M*, 212. $C_{11}H_{16}O_4$ requires C, 62.3; H, 7.5%; *M*, 212).

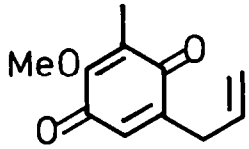
(ii) *Catalytic hydrogenation*. The title benzopyrone (2.1 g) in acetic acid (50 ml) was shaken with platinum oxide 90.5 g) under hydrogen (1 atm) for 5 h and the product was isolated in the usual way. The resulting oil solidified when kept then separated from light petroleum giving 3,4-dihydro-6,7-dimethoxy-2*H*-1-benzopyran (**10**) as prisms (1.6 g; 84%), m.p. 88-89 °C (lit.[20] 51.5 - 52°), $\nu_{max.}$ 1 621, 1 524, 1 289, 1 225, and 1 140 cm^{-1}, δ($CDCl_3$) 6.53 and 6.37 (each 1H, s, ArH), 4.12 (2H,t, *J* 6 Hz, OCH_2), 3.80 (6H, s, OMe), 2.70 (2H, t, *J* 6 Hz, $ArCH_2$), and 1.97 (2H, m, $ArCH_2CH_2CH_2$)(Found *M*, 194.09411. Calc. for $C_{11}H_{14}O_3$: *M*, 194.09418).



(25)



(26a) R^1= C_3H_5; R^2=R^3=H
(26b) R^1=R^3=H; R^2= C_3H_5
(26c) R^1=R^2=H; R^3= C_3H_5



(27)

3-*Methoxy*-2-*methyl*-6-(*prop*-2-*enyl*)*phenol* (**26b**). - 3-Methoxy-2-methylphenol (17 g), 3-bromo-1-propene (25 g), and potassium carbonate (51 g) were heated together in acetone (150 ml) for 20 h; the solids were removed by filtration and the volatile materials by means of a rotary evaporator. The residue distilled at 122 °C/15 mm giving 3-*methoxy*-2-*methyl*-1-(*prop*-2-*enyloxy*)*benzene* (**26a**) as an oil (20.5 g; 93%), $\nu_{max.}$ (film) 1 602, 1 482, 1 262, and 1 130 cm^{-1}, δ($CDCl_3$) 7.13 (1H, t, *J* 8.5 Hz; ArH-5), 6.57 (2H, d, *J* 8.5; ArH-4 and ArH-6), *ca.* 6.1 (1H, m, vinylic =CH_2), 4.57 (2H, d, *J* 5 Hz; OCH_2), 3.39 (3H, s, OMe), and 2.17 (3H, s, ArMe) (Found: C, 74.1; H, 7.8%; *M*, 178. $C_{11}H_{14}O_2$ requires C, 74.2; H, 7.9%; *M*, 178).

A mixture of the propenyl ether (14 g) and di-*N*-ethylbenzeneamine (15 g) was refluxed for 4.5 h and then cooled, diluted with light petroleum (100 ml),and washed successively with sulphuric acid (10%), water, and sodium hydroxide solution (13%; 3 x 60 ml). The alkaline extracts were acidified and the products extracted into ether which, when removed, left an oil that was chromatographed on silica and eluted by ether-light petroleum (1:10, v/v) giving the *propenylphenol* as an oil (6.5 g; 46%), $\nu_{max.}$ (film) 3 570, 1,618, 1 608, 1 505, and 1 120 cm^{-1}, δ($CDCl_3$) 6.93 (1H, d, *J* 10 Hz, ArH-4), 6.46 (1H, d, *J* 10 Hz; ArH-5), *ca.* 6.0 (1H, m, vinylic =CH), *ca.* 5.0 (2H, m, vinylic =CH), 4.98 (1H, s, removed by D_2O; OH), 3.71 (3H, s, OMe), 3.36 (2H, d, *J* 7 Hz; $ArCH_2$), and 2.17 (3H, s, ArMe)(Found C, 73.9;H, 7.9%;*M*, 178. $C_{11}H_{14}O_2$ requires C, 74.15; H, 7.9%; *M*, 178).

Later eluates supplied the isomer, 3-*methoxy*-2-*methyl*-4-(*prop*-2-*enyl*)*phenol* (**26c**) as an oil (2.63 g; 18%), $\nu_{max.}$ 3 410, 1 640, 1 608, 1 468, and 1 284 cm^{-1}, δ($CDCl_3$) 6.90 (1H, d, *J* 10 Hz; ArH-6), 6.55 (1H, d, *J* 10 Hz; ArH-5), *ca.* 6.0 (1H, m, vinylic =CH), *ca.* 5.0 (2H, m, vinylic =CH), 4.98 (1H, s, removed by D_2O; OH), 3.71 (3H, s, OMe), 3.36 (2H, d, *J* 7 Hz; $ArCH_2$), and 2.17 (3H, s, ArMe)(Found C, 73.9;H, 7.9%;*M*, 178. $C_{11}H_{14}O_2$ requires C, 74.15; H, 7.9%; *M*, 178).

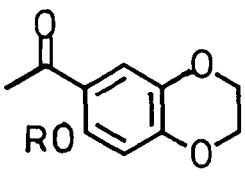
3,4-*Dihydro*-7-*methoxy*-8-*methyl*-2H-1-*benzopyran*-6-*ol* (**18**). - The 6-propenylphenol (2.5 g) in methanol (50 ml) was oxidised byadding a solution of potassium nitrosodisulphonate (11.2 g) and sodium acetate (8.4 g) in water (500 ml) and stirring the mixture in the dark for 2 h at room temperature. The organic products were extracted into dichloromethane (3 x 100 ml) and phenols were removed by a rapid washing with aqueous sodium hydroxide (5%) and then water. The non-phenolic fraction consisted of 3-*methoxy*-2-*methyl*-6-(2-*propenyl*)*benzene*-1,4-*dione* (**27**) which formed an unstable yellow oil (2.25 g; 83%), $\nu_{max.}$ 1 679, 1 321, and 1 203 cm^{-1}, δ($CDCl_3$) 6.37 (1H, s, ring CH), *ca.* 5.8 (1H, m. vinylic =CH), *ca.* 5.1 (2H, m, vinylic CH_2), 3.97 (3H, s, OMe), 3.15 (2H, d, *J* 7 Hz; $-CH_2-$), 1.91 (3H, s, 2-Me)(Found: *M*, 192. $C_{11}H_{12}O_3$ requires *M*, 192).

This dione (2 g) was kept in pyridine (dried over calcium hydride and distilled before use) at 80 °C under nitrogen for 2 h. The residue left from evaporation of the solvent under vacuum was dissolved in ethanol (50 ml) and shaken under hydrogen (at 1 atm) with platinum oxide (0.1 g) for 16 h. The product was isolated in the

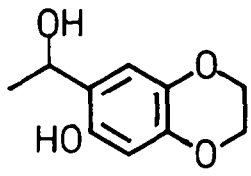
usual manner and purified on a column of silica (150 g) with elution by ether-light petroleum (1:4, v/v) giving the *benzopyranol* which crystallised from light petroleum as needles (1.1 g; 54%), m.p. 55-56 °C, $\nu_{max.}$ 3 240, 1 610, 1 365, and 1 173 cm^{-1}, $\delta(CDCl_3)$ 6.46 (1H, s; ArH), 5.20 (1H, s, removed by D_2O; OH), 4.11 (2H, t, *J* 6 Hz;OCH_2), 3.71 (3H, s; OMe), 2.49 (2H, t, *J* 6 Hz, $ArCH_2$), 2.08 (3H, s, ArMe), and 1.91 (2H, m, *J* 6 Hz; $ArCH_2CH_2CH_2O$)(Found C, 67.8; H, 7.2%; *M*, 194. $C_{11}H_{14}O_3$ requires C, 67.1; H, 7.3%; *M*,194).

3,4-*Dihydro*-6-*methoxy*-2,2-*dimethyl*-2H-1-*benzopyran*-7-*ol* (**16**). - 7-Benzyloxy-6-methoxy-2*H*-1-benzopyran-2-one (4.3 g) in acetic acid (30 ml) was shaken with platinum oxide (0.5 g) under hydrogen (at 1 atm.) for 3 h at room temperature; ethanol (30 ml) was added to the mixture which was then filtered. Evaporation of the solvent from the filtrate left a solid that crystallised from benzene to give 3,4-*dihydro*-7-*hydroxy*-6-*methoxy*-2H-1-*benzopyran*-2-*one* (**28**) as prisms (2.8 g; 95%), m.p. 152-153 °C, $\nu_{max.}$ 3 385, 1 730, 1 621, 1 520, 1 382, and 1 220 cm^{-1}, $\delta(CDCl_3)$ 6.62 (2H, s; ArH), 5.69 (1H, s, removed by D_2O;OH), 3.81 (3H, s; 5-OMe), and 2.76 (4H, m, $ArCH_2CH_2$)(Found: C, 62.1; H,5.0%; *M*, 194. $C_{10}H_{10}O_4$ requires C, 61.85; H, 5.15%; *M*, 194).

Methylmagnesium iodide was prepared by dissolving magnesium (1.9 g) in ether (18 ml) and benzene (18 ml) containing an excess of iodomethane. To this reagent was added the benzopyranone (0.88 g) in benzene (50 ml) over a period of 1 h during which time the temperature was kept at 0 °C. After removal of the ether by distillation the benzene solution was refluxed for 2 h, cooled, and washed with concentrated hydrochloric acid containing ice and then with water alone. The product was isolated from the benzene as a brown oil (0.75 g) that slowly solidified and was then purifies on a column of silica from ether-light petroleum (1:5, v/v) to give the *benzopyranol* which formed prisms (from light petroleum)(0.64 g; 61%), m.p. 119-120 °C, $\nu_{max.}$ 3 340, 1 605, 1 518, 1 370, 1 168, and 1 125 cm^{-1}, $\delta(CDCl_3)$ 6.51 and 6.39 (each 1H, s; ArH), 5.46 (1H, s, removed by D_2O; OH), 4.02 (3H, s; OMe), 2.66 (2H, t, *J* 6.5 Hz; $ArCH_2$), 1.75 (2H, t, *J* 6.5 Hz; $ArCH_2CH_2$), and 1.27 (6H, s; Me_2) (Found: C, 69.5; H, 7.9%; *M*, 208. $C_{12}H_{16}O_3$ requires C, 69.2; H, 7.7%; *M*, 208).



(**29a**) R = H
(**29b**) R = Ac



(**30**)

7-*Ethyl*-2,3-*dihydro*-1,4-*benzodioxin*-6-*ol* (**19b**). - To lithium aluminium hydride (0.2 g) in ether (sodium-dry; 15 ml) was added dropwise a solution of 2',3'-dihydro-7'-hydroxy-1',4'-benzodioxin-6'-ethanone (**29a**) (0.2 g) in benzene (sodium-dry; 6 ml) The mixture was refluxed for 18 h then quenched with aqueous ammonium chloride (20%; 10 ml). Isolated by means of ether, the organic product crystallised from ether-light petroleum giving 2,3-*dihydro*-7-(1'-*hydroxyethyl*)-1,4-*benzodioxin*-6-*ol* (**30**) as prisms (0.12 g; 60%), m.p. 132-134 °C, $\nu_{max.}$ 3 485(OH), 3 220(OH), 1 630, and 1 610 (aromatic), 1 520, 1 508, and 1 380 cm^{-1}, $\delta(CDCl_3)$ 7.5 (1H, s) and 2.84 (1H, d, *J* 5 Hz)(both removed by D_2O; phenolic and alcoholic OH, respectively), 6.50 and 6.41 (each 1H; aromatic), 4.97 (1H, m; CHOH), 4.19 (4H, s, dioxan methylene), and 1.55 (3H, d, *J* 7 Hz: Me)(Found: C, 61.45; H, 6.3%; *M*,196. $C_{10}H_{12}O_4$ requires C, 61.2; H, 6.1%; *M*, 196).

With acetic anhydride/pyridine the ketone (**29a**) gave the *acetate* (**29b**) which separated from light petroleum as needles (72 %), m.p. 71-72 °C, δ 7.36 (1H, s; ArH-8), 6.59 (1H, s; ArH-5), 4.26 (4H, m, dioxan methylene), 2.45 (3H, s; MeCOAr), 2.29 (3H, s; MeCOO)(Found: C, 61.1; H, 5.3%; *M*, 236. $C_{12}H_{12}O_5$ requires C, 61.4; H, 5.1%; *M*, 236). Sodium borohydride (40 mg) in water (1 ml) was added to a stirred solution of the acetate (114 mg) in tetrahydrofuran (10 ml) at 0 °C. After 35 min., residual borohydride was destroyed by acetic acid (3 drops) and the mixture was poured into water. Isolated by means of ether and purified by elution from a column of silica by means of hexane-ether (4:1, v/v), the product crystallised from light petroleum giving the ethylbenzodioxinol as needles (63 mg; 70%), m.p. 48 °C (lit.[21] 49-50°), δ 6.63 and 6.33 (each 1H,s; ArH), 4.48 (1H, s, removed by D_2O;OH), 4.18 (4H, s, dioxan methylene), 2.49 (2H, q, *J* 7.5 Hz; CH_2Me), and 1.14 (3H, t, *J* 7.5 Hz; CH_2Me).

Methylation of the ethylbenzodioxinol with methyl sulphate/potassium carbonate in acetone supplied the *methyl ether* (**19a**) which, after purification from hexane-ether (10:1, v/v) on silica formed an oil (81%), δ ($CDCl_3$) 6.72 and 6.46 (each 1H, s; ArH), 4.27 (4H, s; dioxan methylene), 3.79 (3H,s; OMe) 2.58 (2H, q, *J* 7.5 Hz; $ArCH_2$), and 1.18 (3H, t, *J* 7.5 Hz; $ArCH_2Me$)(Found: *M*, 194.09477. $C_{11}H_{14}O_3$ requires *M*, 194.09418).

2,3,4,7,8,9-*Hexahydro*-2,2,5,7,7,10-*hexamethylbenzo*[1,2-b:4,5-b']-*dipyran Radical Cation Hexachloroantimonate* (*2*). - *(i) Using* $SbCl_5$. Antimony pentachloride (redistilled)

(*ca.* 150 mg) in dichloromethane (2 ml) was introduced over a solution of the benzodipyran (1))100 mg) in the minimum volume of the same solvent with minimal mixing. At the interface there was animmediate change of colour and in the course of some hours a very dark precipitate formed. This product decomposed when attempts were made to recrystallise it, but purification was achieved by adding dichloromethane to concentrated solution in acetonitrile at room temperature, washing the precipitate with dichloromethane, and drying it *in vacuo* at room temperature overnight. Thus made, the *radical cation hexachloroantimonate* formed tiny prisms (180 mg) that were brown-red or greenish by reflected light and yellow brown by transmitted light and had m.p. *ca.* 124 °C (decomp.), $\lambda_{max.}$ (MeCN) 480 and sh458 nm (log ε 3.72 and 3.60), $\nu_{max.}$ 2 984, 2 929, 1 430, 1 398, 1 375, 1 330, 1 228, 1 155, 1 104, 1 086, 1 023, 976, 884, 858, 708, and 629 cm^{-1}(Found C, 35.7; H, 4.6. $C_{18}H_{26}Cl_6O_2Sb$ requires C, 35.5; H, 4.3%). No nmr spectrum could be obtained from this compound because of the extreme line broadening. Mass spectrometry (EI at 180 °C) disclosed a range of fragment ions like that from the parent benzodipyran (1) but with an exceptionally intense base peak at *m/e* 274 which corresponds to the cation in (2)($C_{18}H_{26}O_2$ requires *m/e* 274); some very weak peaks above it suggested that, under these operating conditions, the anion can chlorinate the cation to some extent.

(ii) (With Ulku Oyman). *Using iminium salt.* The cation radical salt (2) was more easily obtained pure by gradual mixing of equimolar amounts of the benzodipyran in dichloromethane with powdered tris-(4-bromophenyl)iminium hexachloroantimonate[17] which, although not normally soluble in this solvent, readily dissolves in the presence of the benzodipyran. The dark colour of the iminium salt immediately changes to brown-red and greenish crystals of the product separate soon after. When precipitation is completed by the addition of a little ether the yield is nearly quantitative. A slower precipitation and better crystals are obtained by using acetonitrile instead of dichloromethane but the yield falls to about 50%.

(With Ulku Oyman) 2,3,4,5,6,7-*Hexahydro*-2,2,7,7,9,10-*hexamethylbenzo*[1,2-b:4,3-b']-*dipyran Radical Cation Hexachloroantimonate.* - Obtained by the iminium salt method from (3), this *cation radical hexachloroantimonate* formed tiny greenish por brown prisms, m.p. *ca.* 124 °C (decomp.), $\nu_{max.}$ 2 977, 1 470, 1 435, 1 401, 1 371, 1 331, 1 230, 1 153, 1 099, 959, 937, 868, 841, and 678 cm^{-1}(Found: C, 35.8; H, 4.5. $C_{18}H_{26}Cl_6O_2Sb$ requires C, 35.5; H, 4.3%). The mass spectrum had the same general features as that of the isomeric salt; indeed, the two compounds were very similar in many respects and only the ir spectrum provided a clear distinction. This salt is, however, more soluble in acetonitrile than the isomer and the yields of pure material did not exceed about 30%.

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