Reactions of γ-arylalkanols *via* aryl radical cation and alkoxyl radical intermediates. Part 3.[1,2] Reactions of 3-arylprop-1-yl hydroperoxides with iron(II) in the presence of copper(II)

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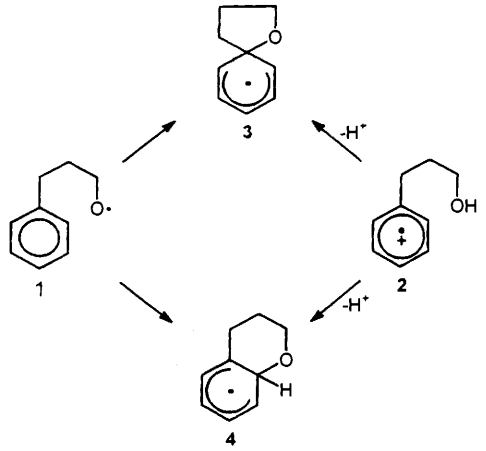
A strategy for comparing the 1,5- and 1,6-cyclisation reactions of 3-phenylpropan-1-oxyl radicals is described. Iron(II)-catalysed reduction of 3-(*p*-methylphenyl)prop-1-yl hydroperoxide and its *para*-chloro and *para*-methoxy-substituted analogues, carried out in the presence of copper(II), has been found to give in each case the appropriate *para*-substituted 3-phenylpropan-1-ol, 3-phenylpropanal and a low yield of a mixture of isomeric 6- and 7-substituted chromans. The alcohols are proposed to form *via* reduction of either the hydroperoxide or the resulting alkoxyl radical or its cyclised intermediates, and the aldehydes as a result of rearrangement of the alkoxyl radical to an α-hydroxy alkyl radical which subsequently undergoes oxidation. The 7-substituted chromans, which arise directly from 1,6-cyclisation of the alkoxyl radical, were found to dominate the 6-substituted isomers which result from rearrangement of 1,5-cyclised intermediates. This effect is attributed to inefficient interception of the 1,5-cyclised radical intermediate which permits equilibration to the thermodynamically more stable 1,6-cyclised radical isomer to occur. The effect of pH on the reactions has been investigated and although no products typical of the intermediacy of aryl radical cations were detected (even under highly acidic conditions), the formation of such intermediates cannot be excluded. Semiempirical MO calculations have been carried out (at the PM3 level of approximation) on a series of model compounds, yielding results which have clarified our understanding of the effect of substituents on the stabilities of the various intermediates arising from the cyclisation reactions of 3-phenylpropan-1-oxyl radicals. Furthermore, these calculations have supported our assumptions regarding the probability and specificity of rearrangements of the spirodienyl intermediates.

The cyclisation and related reactions which arylalkanols undergo *via* their alkoxyl radical and aryl radical cation intermediates are currently under investigation in these laboratories.[1,2]

Our interest stems from the realisation that the cyclised intermediates **3** and **4** obtained when the alkoxyl radical **1** reacts intramolecularly with the aryl ring, are identical to those which result when the aryl radical cation **2** undergoes ring-closure as a result of nucleophilic attack on the ring by the side-chain hydroxyl group (Scheme 1). However, the transition



Scheme 1

states for these two cyclisation processes are likely to differ since, in the first instance, addition of an electrophilic radical to a neutral aromatic ring is involved while in the second, nucleophilic attack by the hydroxyl group on a charged system takes place. Consequently, the regioselectivities for cyclisation might be expected to differ in the two cases. A similar effect has been postulated elsewhere[3] to account for the formation of 1,6-cyclised products observed when pent-4-en-1-ol was treated with $S_2O_8^{2-}$ in the presence of silver(I).

The main objective of this study has been to convert a series of γ-arylalkanols to their respective alkoxyl radical and aryl radical cation intermediates under comparable reaction conditions, and then to determine from their cyclisation products whether any differences in their regioselectivities could be discerned. Although earlier work[1] involving 3-phenylpropan-1-ol had revealed the formation of exclusively 1,6-cyclised products, the possibility that 1,5-cyclised intermediates could in fact form, but subsequently rearrange to their 1,6-analogues through migration of either carbon or oxygen, was recognised.

It was therefore necessary to devise a strategy which would allow us to discriminate between the direct and indirect pathways for the formation of the 1,6-cyclised products. This was accomplished through incorporating a series of *para*-substituents into the 3-phenylpropan-1-ol system. While it was anticipated that direct 1,6-cyclisation would afford exclusively the appropriate 7-substituted chroman **13**, it was argued that 1,5-ring closure followed by rearrangement would result in the 6-substituted isomer **10**, provided migration of carbon took place in preference to oxygen in one of the spirodienyl intermediates **6** or **8**; the latter supposition seems reasonable on energetic grounds, particularly in the case of the carbocation **8** (Scheme 2). In principle, the relative extents of 1,5- and 1,6-cyclisation could then be gauged by comparing the yields of the two chroman isomers **10** and **13**. The feasibility of this approach

Table 1 Reaction of 3-(*p*-methylphenyl)prop-1-yl hydroperoxide **14b** with Fe^{II}–Cu^{II}: effect of pH on product yields

		Product (% yield)					
pH_i[a]	pH_f[b]	**15b**	**16b**	**10b**	**13b**	**10b + 13b**	Ratio **13b**:**10b**
0.5	0.8	47	2	0.5	1.4	1.9	2.8
1.4	1.7	40	13	4.3	11.6	15.9	2.7
2.1	2.2	37	31	6.9	16.7	23.6	2.4
3.3	2.8	32	40	6.1	14.1	20.2	2.3
4.9	3.4	32	40	4.2	17.0	21.2	4.0
6.0	5.0	33	41	1.8	12.9	14.7	7.2

[a] pH of the initial reaction mixture, prior to the addition of the Fe^{II} solution whose pH was *ca.* 3.1. [b] pH of the final reaction mixture, 2 h after completion of addition of the Fe^{II} solution.

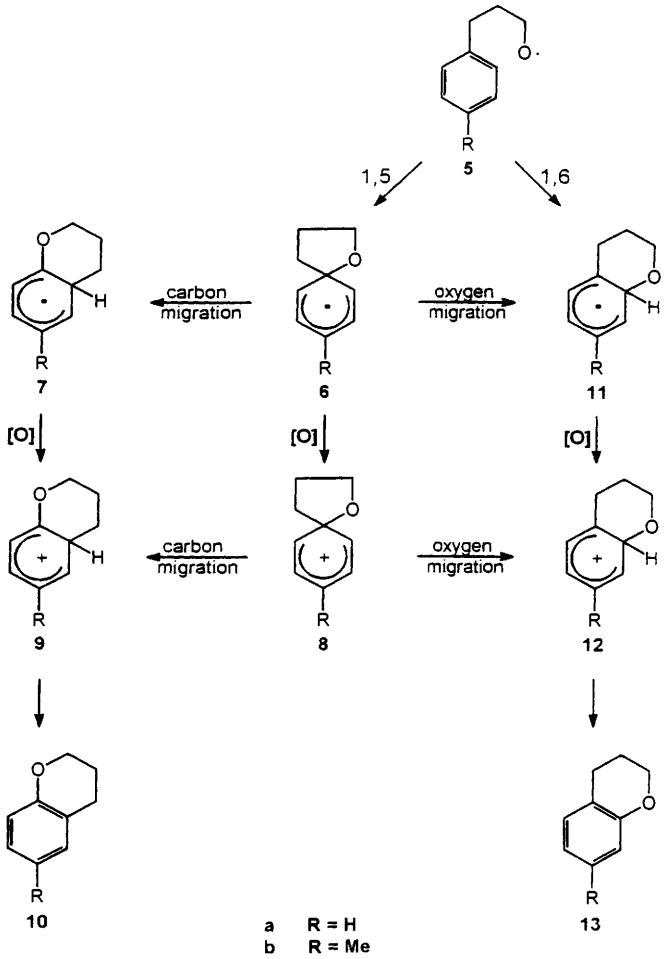
has recently been demonstrated in the case of 3-(*p*-methylphenyl)propan-1-ol.[2]

However, a potential complication lurks in the possibility that interconversion of the radical cation and alkoxyl radical intermediates could take place. It is reasonable to suppose that the cyclised radical intermediates formed from the alkoxyl radical **1** could undergo acid-catalysed ring opening to the radical cation **2**, since analogous reactions have been widely implicated in the formation of aryl radical cations from the addition of $HO^{\bullet}$ to aromatic systems at low pH.[1,4] Another possibility is that protonation of the alkoxyl radical could occur at low pH.[5] The resulting species would be expected to induce electron transfer from the aromatic ring, thereby generating an aryl radical cation (*cf.* ionisation potentials[6] for toluene and ethanol of 8.82 and 10.48 eV, respectively).

Furthermore, the possibility that the radical cation **2** could convert *via* the cyclised intermediates to the alkoxyl radical **1** can also not be excluded; ring-opening of the spirodienyl radical **3** to the alkoxyl radical **1** seems feasible in view of our earlier observation that 1,5-cyclisations of 2-phenoxyethoxy radicals take place reversibly,[7] and there is also evidence[8] that hydroxyl radicals result from the reaction of aryl radical cations with water.

Clearly, if equilibration of the aryl radical cation and alkoxyl radical were to occur, our method for determining differences in their cyclisation regioselectivities by comparing cyclised product isomer ratios could be invalidated. A vital aspect of this study has therefore been to ascertain whether such interconversions take place under our reaction conditions. Our approach in this regard has been to determine as fully as possible the products arising from the reactions of related alkoxyl radicals and radical cations, in the hope of discovering products which were unique to each intermediate; these could then serve as probes for determining whether interconversion was occurring or not.

In this report we describe the reactions which three *para*-substituted 3-phenylpropan-1-ols have been found to undergo *via* their alkoxyl radical intermediates. In particular, the influence of both the ring substituent and the reaction conditions upon the nature of the products and their distributions have been investigated. Furthermore, semi-empirical molecular orbital calculations have been performed on a series of model compounds in order to gain further insights into the influence of the ring substituents upon the stabilities of the various intermediates proposed to be involved in the cyclisation reactions.



Scheme 2

Results and discussion

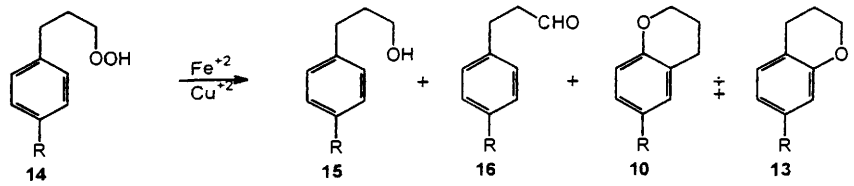
Redox decomposition of 3-arylprop-1-yl hydroperoxides

The alkoxyl radicals **5b–d** were generated as described previously[1] by reduction of the appropriate 3-arylprop-1-yl hydroperoxides **14b–d**, respectively, with iron(II) in aqueous acetonitrile [eqn. (1)]. In addition, copper(II) was included in

$$RO_2H + Fe^{II} \longrightarrow RO^{\bullet} + HO^{-} + Fe^{III} \quad (1)$$

the reaction mixtures since we have observed earlier[1] that only very low yields of cyclised products are obtained in its absence. The function of the copper(II) is evidently to promote oxidation of the intermediate cyclised radicals.

The main products (and the effect of pH on their yields) obtained from the reactions of 3-(*p*-methylphenyl)prop-1-yl hydroperoxide **14b** and its *para*-chloro- and *para*-methoxy-substituted analogues **14c** and **14d**, respectively, with iron(II) in the presence of copper(II) are given in Scheme 3 and Tables 1–3.



Scheme 3

Table 2 Reaction of 3-(*p*-chlorophenyl)prop-1-yl hydroperoxide **14c** with Fe^{II}–Cu^{II}: effect of pH on product yields

		Product (% yield)					Ratio
pH_i[a]	pH_f[b]	**15c**	**16c**	**10c**	**13c**	**10c + 13c**	**13c:10c**
0.6	1.0	45	33	0.4	1.8	2.2	4.5
1.2	1.9	18	26	0.8	2.2	3.0	2.8
2.7	2.6	20	32	0.6	3.0	3.6	5.0
4.2	3.9	24	39	0.1	1.2	1.3	12.0
5.3	3.8	54	33	0.2	0.3	0.5	1.4
6.4	5.3	30	33	trace	0.2	0.2	*c*

[a] pH of the initial reaction mixture, prior to the addition of the Fe^{II} solution whose pH was *ca.* 3.1. [b] pH of the final reaction mixture, 2 h after completion of addition of the Fe^{II} solution. [c] Not determined.

Table 3 Reaction of 3-(*p*-methoxyphenyl)prop-1-yl hydroperoxide **14d** with Fe^{II}–Cu^{II}: effect of pH on product yields

		Product (% yield)					Ratio
pH_i[a]	pH_f[b]	**15d**	**16d**	**10d**	**13d**	**10d + 13d**	**13d:10d**
0.5	0.9	66	21	0.03	0.06	0.09	2.0
1.2	1.8	61	21	0.09	0.25	0.34	2.8
2.6	2.0	59	23	0.07	0.36	0.43	5.1
4.2	3.4	51	25	0.08	2.1	2.18	26.3
5.2	3.8	48	28	0.06	2.6	2.66	43.3
6.4	4.6	29	34	0	2.3	2.3	*c*

[a] pH of the initial reaction mixture, prior to the addition of the Fe^{II} solution whose pH was *ca.* 3.1. [b] pH of the final reaction mixture, 2 h after completion of addition of the Fe^{II} solution. [c] Not determined.

In all three cases the alcohol **15** and aldehyde **16** constitute the major products. There is a tendency for the yield of the alcohol to increase and that of the aldehyde to decrease as the pH of the reaction mixture is lowered. The principal source of the alcohol is probably reduction of either the hydroperoxide directly, or the alkoxyl radical or even the cyclised radical intermediates. The aldehyde is suggested to arise directly from the alkoxyl radical as a result of its arrangement to an α-hydroxy alkyl radical[9] which subsequently undergoes oxidation. However, it is possible that acid- or base-catalysed elimination of water from the hydroperoxide could also contribute to its formation.

The yields of the 6- and 7-substituted chromans **10** and **13** ranged from moderate in the case of the methyl-substituted peroxide **14b** to low for its *para*-chloro and *para*-methoxy analogues **14c** and **14d**, respectively. The lower yield of chroman resulting from **14c** relative to that accruing from **14b** may reflect a reduced rate of cyclisation by the electrophilic alkoxyl radical onto a ring which is mildly deactivated by the chloro group. By the same token, a methoxy substitution would be expected to facilitate the cyclisation process,† but the converse is in fact observed. This anomalous behaviour is also mirrored in the failure of 3-(*p*-methoxyphenyl)propan-1-ol to react to any significant extent *via* its aryl radical cation intermediate.[11] The latter result is attributed to a substantial enhancement of the stability of the aryl radical cation by the methoxy group (*vide infra*), which reduces its reactivity. We therefore propose that in the case of the peroxide **14d**, cyclisation *via* the alkoxyl radical takes place as expected, but the resulting cyclised intermediates then rapidly undergo acid-catalysed ring-opening to the stabilised methoxy-substituted aryl radical cation which is ultimately reduced to the alcohol **15d**; it is significant that the yield of alcohol increases steadily as the pH is reduced. An implication of this proposal is that the rate of oxidation of the cyclised radical intermediates **6d** and **11d** by copper(II) is slow in comparison with their rates of acid-catalysed ring opening.

This mechanism is supported by the effect of pH on the combined yields of the chromans **10d** and **13d** (Fig. 1). The combined yield reaches a maximum at pH *ca.* 5 and then tails off as the pH is reduced further, presumably reflecting an increasing rate of acid-catalysed conversion of the cyclised radical intermediates **6d** and **11d** to aryl radical cation. The methyl- and chloro-substituted chromans display similar pH profiles (the latter is also shown for comparison in Fig. 1), except that the tailing-off of their yields is manifested at a lower pH (*ca.* 3–2), which presumably reflects the lower stabilities of

† Good yields of 1,5-cyclised products have been obtained previously from a reaction of 3-(*p*-methoxyphenyl)propan-1-ol **15d** when irradiated in the presence of HgO–I_2.[10]

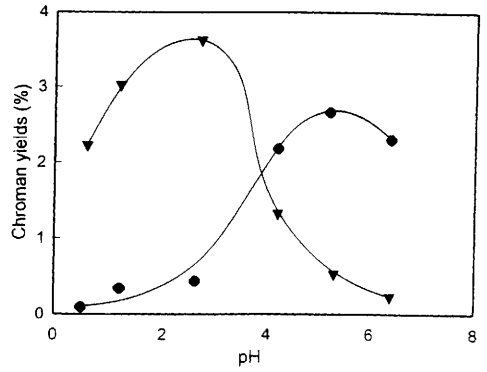


Fig. 1 Effect of pH on chroman yields: (▼) chromans **10c** + **13c**; (●) **10d** + **13d**

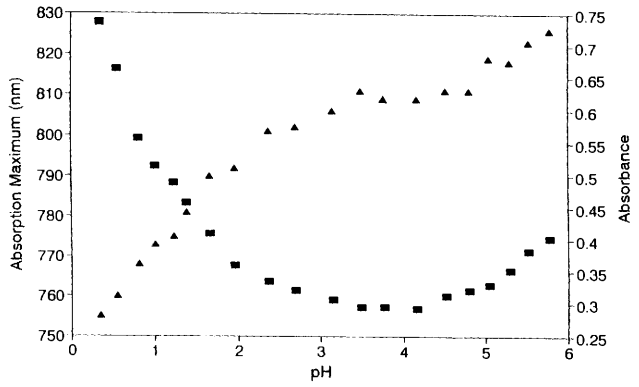


Fig. 2 Effect of pH on absorption spectrum of copper(II) acetate: (■) absorbance; (▲) absorbance maximum

the methyl- and chloro-substituted aryl radical cations relative to their methoxy-substituted counterpart (*vide infra*).

If the decline in chroman yields with pH is indeed due to acid-catalysed conversion of the cyclised radical intermediates **6** *and* **11** to the appropriate aryl radical cations, it is significant that no products typical of the latter intermediates are observed. This would suggest that under these reaction conditions, the aryl radical cations are reduced more rapidly than they are able to undergo reactions such as benzylic deprotonation.

All three substrates produce more of their respective 7- than 6-substituted chromans, with some variations in the isomer ratio with pH being observed. Although the variations are somewhat haphazard in the case of the chloro-substituted peroxide **14c**, a general tendency for the proportion of 7-substituted chroman to increase with pH may be discerned. This effect may reflect changes in the nature of the copper(II) species responsible for oxidising the cyclised radical intermediates **6** and **11**. We suggest that the oxidising species present at low pH is more effective at oxidising the 1,5-cyclised intermediate **6** than is the species present at the upper end of the pH range. As the pH is raised, the rate at which the spirodienyl radical **6** is oxidised decreases, permitting it to equilibrate *via* the alkoxyl radical to the thermodynamically-favoured intermediate **11**. Our proposal that the nature of the ancillary oxidant varies with pH was supported by the changes observed in both λ_{max} and its absorbance for an aqueous acetonitrile solution of $Cu(OAc)_2$ when its pH was varied through the addition of concentrated HCl (Fig. 2).

Thermal decomposition of 3-(*p*-methylphenyl)prop-1-yl hydroperoxide 14b

Peroxides frequently display instability towards heat and usually decompose to give alkoxyl radicals.[12] Thermal decomposition of the hydroperoxide **14b** was therefore attempted both in the presence and absence of $Cu(OAc)_2$ (Table 4). Little difference was observed between the reactions and in both cases, an even higher conversion to the alcohol **15b** was observed relative to the iron(II)-catalysed reactions, while the yields of cyclised products were lower. The chroman isomer ratio was similar to that observed earlier in the redox reaction.

Table 4 Thermal decomposition of 3-(*p*-methylphenyl)prop-1-yl hydroperoxide **14b**: effect of $Cu(OAc)_2$ on products and yields

	Product (% yield)				
$[Cu(OAc)_2]$/[**14b**]	**15b**	**16b**	**10b**	**13b**	Ratio **13**:**10b**
0.0	64	31	0.1	0.3	3.0
3.0	64	27	0.3	1.0	3.3

Semiempirical MO calculations

It is likely that ring-closure of the alkoxyl radical **1** will be subject to stereoelectronic constraints similar to those proposed by Beckwith to account for the high regioselectivity observed for cyclisation of the hex-5-enyl and related radicals.[13] According to Beckwith's hypothesis, more favourable overlap between the SOMO of the radical centre and the LUMO of the π-system is achieved in the transition state for 1,5- than 1,6-cyclisation. Ring-closure consequently takes place under kinetic control and provided it occurs irreversibly, preferential formation of the thermodynamically-disfavoured 1,5-cyclised adduct radical is observed.

In contrast, radical cyclisations onto aromatic rings usually take place reversibly[7,14] and unless the spiro radical intermediate is intercepted efficiently, products derived from the *endo*-cyclised radical usually predominate. However, our present and also earlier results[7,10] have shown that the cyclisation reactions of γ-aryl alkanoxyl radicals frequently display pronounced sensitivity to the effect of any substituents present on the ring.

We have therefore endeavoured to gain further insights into these substituent effects by carrying out semiempirical molecular orbital calculations on a series of model compounds **17**–**26**. These model compounds are expected to reflect the substituent effects likely to arise in their bicyclic analogues which result from cyclisation of the 3-arylprop-1-yloxy radicals **5a**–**d**. π-Molecular orbital energies and associated p_z-atomic orbital coefficients, and also net atomic charges for toluene **17a** and its *para*-substituted derivatives **17b**–**d** (Tables 5–8), as well as the heats of formation of all the methyl-, chloro- and methoxy-substituted species **17**–**26** (Table 9) were therefore calculated, at the PM3 level of approximation. The heats of formation obtained for the structures **18**–**26** (Table 9) are in each case given relative to the heats of formation of the corresponding precursor **17**. In addition, the effect of the methyl, chloro and methoxy substituents on the heats of formation of the series **18b**–**26d**, relative to those of their unsubstituted counterparts **18a**–**26a**, are also shown.

It is apparent that satisfactory predictions based on a frontier molecular orbital approach cannot be made regarding the regioselectivity of intramolecular attack on the aryl system by the side-chain alkoxyl radical. Firstly, the geometrical constraints alone imposed on the transition state for cyclisation are likely to override any contrary predictions which might arise from consideration of the relative magnitudes of the coefficients of the interacting orbitals. Furthermore, the characteristics of the aryl molecular orbital which interacts with the SOMO of the radical cannot be determined with any confidence. It is well

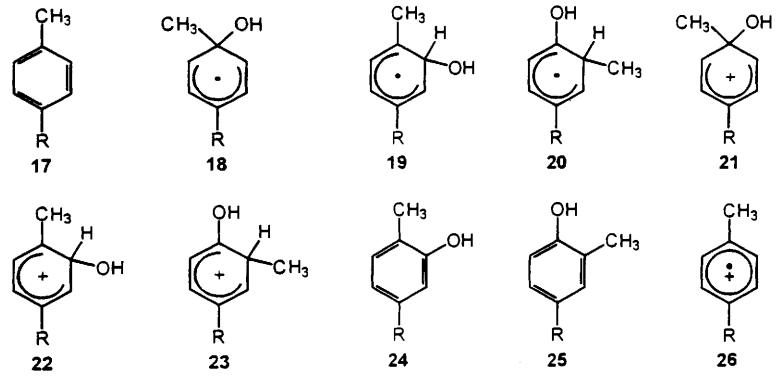


Table 5 Calculated[a] MO energies, atomic coefficients and net atomic charges for toluene **17a**

	π-MO energy and p_z-atomic orbital coefficient[b]				Net atomic charge
	HOMO-1	HOMO	LUMO	LUMO + 1	
MO energy (eV)	−9.72[c]	−9.45	0.38	0.45[d]	
C-1	0.01	0.55	−0.58	0.02	−0.07
C-2	−0.50	0.32	0.31	0.49	−0.10
C-3	−0.50	−0.25	0.26	−0.51	−0.10
C-4	−0.01	−0.55	−0.56	0.02	−0.11
C-5	0.50	−0.26	0.29	0.49	−0.10
C-6	0.51	0.31	0.27	−0.51	−0.10
C-7	0.00	−0.15	−0.02	0.00	−0.06

[a] Calculated using the RHF method with the PM3 Hamiltonian, as implemented in MOPAC (version 6.00).[15] [b] In all cases, no significant contributions from the other orbitals present on the listed atoms are evident. [c] The energy of HOMO-2 is −12.24 eV. [d] The energy of LUMO + 2 is 2.83 eV.

Table 6 Calculated[a] MO energies, atomic coefficients and net atomic charges for *p*-methyltoluene **17b**

	π-MO energy and p_z-atomic orbital coefficient[b]				Net atomic charge
	HOMO-1	HOMO	LUMO	LUMO + 1	
MO energy (eV)	−9.70[c]	−9.18	0.36	0.49[d]	
C-1	0.00	−0.53	−0.56	0.01	−0.08
C-2	0.50	−0.28	0.27	−0.50	−0.10
C-3	0.50	0.28	0.28	0.50	−0.10
C-4	0.00	0.53	−0.56	0.01	−0.08
C-5	−0.50	0.28	0.28	−0.50	−0.10
C-6	−0.50	−0.28	0.29	0.50	−0.10
C-7	0.00	0.14	−0.02	0.00	−0.06
C-8	0.00	−0.14	−0.02	0.00	−0.06

[a] Calculated using the RHF method with the PM3 Hamiltonian, as implemented in MOPAC (version 6.00).[15] [b] In all cases, no significant contributions from the other orbitals present on the listed atoms are evident. [c] The energy of HOMO-2 is −12.15 eV. [d] The energy of LUMO + 2 is 2.78 eV.

known that in reactions between radicals and unsaturated systems, there is usually interaction between the SOMO of the radical and both the HOMO and LUMO of the π-system.[16] In the case of an alkoxyl radical, where the unpaired electron is centred on an electronegative atom, the SOMO will be relatively low in energy‡ which is likely to evoke a considerably stronger interaction with the HOMO than the LUMO of the aromatic π-system. However, our calculations have shown (Tables 5–8) that the HOMOs of the series of toluenes **17a–d** are nearly degenerate since in each case the energy of the HOMO is only marginally higher than that of the immediately underlying occupied molecular orbital, (HOMO-1). A similar situation pertains in each case for the LUMOs which are energetically even more closely spaced to the next highest unoccupied molecular orbitals, (LUMO + 1). Therefore, since interaction of the alkoxyl radical with the ring is highly likely to involve a mix of molecular orbitals with different symmetry characteristics,§ it does not seem possible to predict with any conviction

‡ *e.g.*, the SOMO energies of HO•, MeO• and EtO• are estimated (PM3–UHF method as implemented in MOPAC, version 6.00)[15] to be −12.97, −11.24 and −11.45 eV, respectively.

§ *e.g.*, in each case the *ipso* carbon (C-1) bears a larger coefficient than the *ortho* carbon (C-2) in the HOMO, while the reverse is true for the immediately underlying orbital, HOMO − 1. Similar differences are also evident between the LUMO and LUMO + 1.

Table 7 Calculated[a] MO energies, atomic coefficients and net atomic charges for *p*-chlorotoluene **17c**

	π-MO energy and p_z-atomic orbital coefficient[b]				Net atomic charge
	HOMO-1	HOMO	LUMO	LUMO + 1	
MO energy (eV)	−9.97[c]	−9.19	0.06	0.21[d]	
C-1	0.00	0.46	−0.56	−0.01	−0.07
C-2	−0.50	0.23	0.28	−0.50	−0.09
C-3	−0.51	−0.27	0.28	0.50	−0.10
C-4	0.00	−0.45	−0.57	−0.01	−0.13
C-5	0.50	−0.28	0.31	−0.49	−0.10
C-6	0.50	0.23	0.26	0.51	−0.09
C-7	0.00	−0.12	−0.02	0.00	−0.07
Cl	0.00	0.54	0.13	0.00	0.06

[a] Calculated using the RHF method with the PM3 Hamiltonian, as implemented in MOPAC (version 6.00).[15] [b] In all cases, no significant contributions from the other orbitals present on the listed atoms are evident. [c] The energy of HOMO-2 is −10.51 eV. [d] The energy of LUMO + 2 is 1.52 eV.

Table 8 Calculated[a] MO energies, atomic coefficients and net atomic charges for *p*-methoxytoluene **17d** (planar)

	π-MO energy and p_z-atomic orbital coefficient[b]				Net atomic charge
	HOMO-1	HOMO	LUMO	LUMO + 1	
MO energy (eV)	−9.80[c]	−8.89	0.39	0.42[d]	
C-1	0.04	−0.51	0.16	0.53	−0.11
C-2[e]	0.52	−0.20	−0.57	−0.12	−0.07
C-3[e]	0.50	0.34	0.39	−0.39	−0.14
C-4	−0.03	0.46	0.20	0.55	0.08
C-5	−0.52	0.30	−0.55	−0.09	−0.18
C-6	−0.46	−0.27	0.40	−0.44	−0.07
C-7	−0.01	0.12	0.01	0.02	−0.06
O	0.00	−0.37	−0.06	−0.15	−0.19
C-9	0.02	0.04	0.00	−0.03	0.05

[a] Calculated using the RHF method with the PM3 Hamiltonian, as implemented in MOPAC (version 6.00).[15] [b] In all cases, no significant contributions from the other orbitals present on the listed atoms are evident. [c] The energy of HOMO-2 is −11.55 eV. [d] The energy of LUMO + 2 is 2.51 eV. [e] Carbon atoms 2 and 3 are located *trans* with respect to the methoxy methyl group; carbon atoms 5 and 6 are *cis*.

Table 9 Calculated heats of formation[a] for the structures **17–26**

	$\Delta_f H$/kJ mol^{-1}						
	a	**b**	**(b − a)**	**c**	**(c − a)**	**d**[c]	**(d − a)**
17[d]	[58.47]	[19.06]		[29.67]		[−100.58]	
18	−107.06	−111.09	−4.03	−111.36	−4.30	−112.93	−5.87
19	−120.00	−120.05	−0.05	−120.25	−0.25	−119.21	0.79
20	−139.49	−139.28	0.21	−140.27	−0.78	−137.21	2.28
21	685.08	656.84	−28.24	660.97	−24.11	616.08	−69.00
22	648.76	648.79	0.03	665.72	16.96	655.41	6.65
23	588.67	584.45	−4.22	602.56	13.89	596.45	7.78
24	−182.95	−183.08	−0.13	−183.14	−0.19	−184.55	−1.60
25	−183.19	−182.82	0.37	−182.83	0.36	−180.81	2.38
26	862.93	836.25	−26.68	828.38	−34.55	798.60	−64.33
(19 − 18)	−12.94	−8.96	3.98	−8.89	4.05	−6.28	6.66
(20 − 18)	−32.43	−28.19	4.24	−28.91	3.52	−24.28	8.15
(20 − 19)	−19.49	−19.23	0.26	−20.02	−0.53	−18.00	1.49
(22 − 21)	−36.32	−8.05	28.27	4.75	41.07	39.33	75.65
(23 − 21)	−96.41	−72.39	24.02	−58.41	38.00	−19.63	76.78
(23 − 22)	−60.09	−64.34	−4.25	−63.16	−3.07	−58.96	1.13
(21 − 18)	792.14	767.93	−24.21	772.33	−19.81	729.01	−63.13
(22 − 19)	768.76	768.84	0.08	785.97	17.21	774.62	5.86
(23 − 20)	728.16	723.73	−4.43	742.83	14.67	733.66	5.50

[a] Calculated using the UHF method with the PM3 Hamiltonian, as implemented in MOPAC (version 6.00).[15] [b] Heats of formation of structures **18–26** are in each case given relative to that of the corresponding precursor **17**. [c] In all cases the methoxy group is constrained to remain coplanar with the ring. [d] The absolute heats of formation of the precursors **17** are shown in parentheses.

the regioselectivity of cyclisation on the basis of frontier molecular orbital interactions.

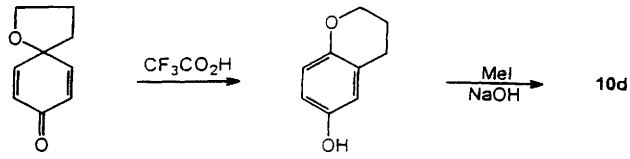
An alternative approach is to consider the net charge distribution in the molecules **17a–d**. The net charge on the *ortho* carbon of toluene is calculated to be slightly more negative than that on the *ipso* position (Table 5) and as a result, the *ortho* carbon is likely (in the absence of any other factors) to show greater susceptibility to attack by an electrophilic alkoxyl

radical. The difference, albeit smaller, is maintained when *para*-methyl or *para*-chloro substituents are introduced. However, this situation is reversed by a *para*-methoxy group which renders the *ipso* position more likely to be attacked. Although the latter effect was clearly manifested in the reaction of 3-(*p*-methoxyphenyl)propan-1-ol **15d** with $HgO–I_2$ which afforded exclusively 1,5-cyclised products,[10] the same regioselectivity was not evident in the redox reaction of the corresponding peroxide **14d**.

Comparison of the heats of formation of the model radical adducts **18** and **19** (Table 9) reveals that the *ortho* adduct **19** is marginally more stable than its *ipso* counterpart **18** in all four cases.¶ The magnitude of the difference varies from 12.94 kJ mol^{-1} between the unsubstituted pair **18a** and **19a** to 8.96, 8.89 and 6.28 kJ mol^{-1}, respectively, for their methyl-, chloro- and methoxy-substituted analogues. These variations are clearly due to the substituents influencing the stabilities of the *ipso* adducts more strongly than those of the *ortho* isomers. It would appear that the methoxy group is slightly more stabilising than methyl and chloro are. The isomer **20** which would result from a radical rearrangement of the *ipso* adduct **18** involving migration of the methyl group, is more stable than **19** by *ca.* 18–20 kJ mol^{-1}, which doubtless reflects the superior radical-stabilising effect of the 1-hydroxy relative to 1-methyl group. Although the differences in stability between the *ipso* isomers **18** on one hand, and their *ortho* counterparts **19** and **20** on the other are significant (ranging from 6.28 to 32.43 kJ mol^{-1}), there is little evidence that radical rearrangements of the type exemplified by the conversion of **18** to **19** or **20** occur readily.[7]

As expected, the substituent effects are more pronounced in the corresponding carbenium ions **21–23**, and particularly so in the case of the *ipso* isomer **21**. In the *ipso* isomer, the 4-chloro group is found to be marginally less stabilising than methyl, while the methoxy group is strongly stabilising as a result of its resonance interaction with the carbenium ion. The chloro- and methoxy-substituted *ortho* isomers **22c** and **22d**, respectively, are both destabilised by their substituents. A combination of these effects results in lower stabilities for the isomers **22c** and **22d** relative to their *ipso* counterparts **21c** and **21d**, respectively. There would clearly be little or no driving force for any rearrangement of the *ipso* carbenium ion **21** to its *ortho* analogue **22** in which migration of the oxygen atom occurred in preference to carbon.

In contrast, the driving force for migration of carbon in **21** to give the rearranged isomer **23** is significant, with the stability differences between the two carbenium ions calculated to be 96.41, 72.39, 58.41 and 19.63 kJ mol^{-1}, respectively, for the unsubstituted and methyl-, chloro- and methoxy-substituted species.‖ Although the stability difference is sharply reduced by the methoxy substituent owing to its stabilisation of the *ipso* isomer, it is nevertheless still large enough for the rearrangement to proceed smoothly. For example, treatment of the spirodienone **27** with trifluoroacetic acid gave a phenolic chroman which upon methylation was shown to be identical to 6-methoxychroman **10d** (Scheme 4).



27

Scheme 4

All three substituents and in particular, the methoxy group, are found to stabilise the aryl radical cation **26**. The magnitudes of these stabilisation effects are comparable to those observed in the carbenium ions **21**. However, it is interesting to note that the chloro group, in contrast to methyl and methoxy, stabilises the radical cation significantly more effectively than the carbenium ion.

Estimates of the reaction enthalpies for the gas phase acid-catalysed conversion of the radical intermediates **18** or **19** to the radical cation **26** [eqn. (2)] show that the reactions are

$$\mathbf{18}\text{ or }\mathbf{19} + H^+ \longrightarrow \mathbf{26} + H_2O \qquad (2)$$

exothermic by *ca.* 800 kJ mol^{-1}.** This supports our contention that the alkoxyl radical **1** could be converted to the aryl radical cation **2** through acid-catalysed ring-opening of the cyclised radical intermediates **3** and **4**. Furthermore, such a process would be expected to display a substituent effect.

In conclusion, similar types of products have been found to result in each case from the iron(II)-catalysed reduction of the series of ring-substituted 3-phenylprop-1-yl hydroperoxides **14b–d**, although variations in their relative yields with both the nature of the ring substituent and the pH of the reaction medium were evident. Of the isomeric chromans obtained, the isomer resulting from 1,6-cyclisation was always found to predominate. This effect is attributed to inefficient interception of the 1,5-cyclised radical intermediate which permits equilibration to the thermodynamically more stable 1,6-cyclised radical isomer to occur. Consideration of the effect of pH on the chroman yields has led to the conclusion that acid-catalysed ring-opening of the cyclised radical intermediates **6** and **11** to form the aryl radical cation could take place. Our failure to observe any products typically formed from aryl radical cation intermediates is attributed to rapid reduction of these intermediates. Semiempirical MO calculations have aided our understanding of the effect the substituents exert upon the stabilities of the various intermediates arising from the cyclisation reactions of 3-phenylpropan-1-oxyl radicals. Furthermore, these calculations support our assumptions regarding the probability and specificity of rearrangements of the spirodienyl intermediates.

Experimental

Melting points were determined on a Reichert hot stage apparatus and are uncorrected. IR spectra were recorded on Perkin-Elmer IR spectrometers (models 297 and 1600 FT-IR) using $CHCl_3$ as solvent, unless otherwise stated. UV–VIS spectra were recorded on a Shimadzu UV–VIS–NIR

¶ This effect is mirrored in the cyclised radical intermediates **3** and **4** whose heats of formation were estimated [HyperChem-RHF (CI with single excitations only, in a manifold of three used and three unused orbitals)] to be 20.9 and 5.1 kJ mol^{-1}, respectively; the 1,6-adduct **4** is therefore more stable than the 1,5-isomer **3** by 15.8 kJ mol^{-1}.

‖ However, the stabilising effect of the oxygen atom in this cationic rearrangement is expected to be attenuated in the bicyclic system **9** as a result of conformational factors. Examination of models shows that in **9** the oxygen-containing ring is likely to assume a relatively unstrained chair conformation, with C-2 located above the plane of the cyclohexadienyl ring. The consequent twisting of the C-9–O bond rotates the oxygen p-orbital containing the lone pair away from the ideal co-linear orientation with respect to the p_z orbital on C-9 and as a result, mesomeric stabilisation of the cyclohexadienyl carbocation by the oxygen atom will be reduced.

** Based on the calculated heats of formation of **18**, **19** and **26** (Table 9) and literature values of 241.9 and 1536.9 kJ mol^{-1}, respectively, for H_2O(g) and H^+(g).[17]

spectrophotometer (model UV-3100). ^1H and ^{13}C NMR spectra were recorded at 200 MHz and 50 MHz, respectively, on a Varian Gemini 200 spectrometer using $CDCl_3$ as solvent, unless otherwise stated. GLC analyses were carried out on a Varian 3300 GC, linked to a Varian 4290 integrator. The capillary column used was an intermediate polarity Supelco SBP™-20 column with dimensions 30 m × 0.25 mm and film-thickness of 0.25 μm. Mass spectra were recorded on a Hewlett Packard HP 1000E mass spectrometer generating a 70 eV electron beam.

General procedure for the preparation of 3-phenylpropan-1-ols 15b–d

The *para*-methyl-, *para*-chloro- and *para*-methoxy-substituted 3-phenylpropan-1-ols were prepared by reduction (LAH followed by catalytic hydrogenation) of the appropriate *para*-substituted ethyl cinnamate which was in turn synthesised *via* base-catalysed condensation of the appropriate *para*-substituted benzaldehyde with diethyl malonate, followed by esterification of the resulting cinnamic acid.

3-(*p*-Methylphenyl)propan-1-ol **15b** was obtained in 85% yield, bp 162–166 °C/0.75 mmHg (Found: C, 79.5; H, 9.15. $C_{10}H_{14}O$ requires C, 79.96; H, 9.39%); δ_H 7.2 (4 H, s, Ph), 3.7 (2 H, t, 1-H), 2.75 (2 H, t, 3-H), 2.4 (3 H, s, Me) and 1.95 (2 H, m, 2-H); δ_C 140.93 and 137.28 (quaternary Ph), 131.16 and 130.41 (*ortho* and *meta* Ph), 64.10 (C-1), 36.40 (C-2), 33.75 (C-3) and 23.07 (Me); $\nu_{max}(CHCl_3)/cm^{-1}$ 3400, 3000, 2850 and 1630; *m/z* 150 (M^+, 46.5%), 133 (3.5), 132 (31.5), 131 (10.3), 119 (7.6), 118 (9.3), 117 (86.1), 106 (36.9), 105 (100), 104 (6.9), 91 (41.3), 79 (12.3), 77 (22.3) and 65 (8.2).

3-(*p*-Chlorophenyl)propan-1-ol **15c** was obtained in 78% yield, bp 176–178 °C/0.65 mmHg (Found: C, 63.55; H, 6.65. $C_9H_{11}ClO$ requires: C, 63.35; H, 6.5%); δ_H 7.27 (2 H, d, Ph), 7.15 (2 H, d, Ph), 3.85 (1 H, br and disappears with D_2O, O–H), 3.67 (2 H, t, 1-H), 2.70 (2 H, t, 3-H) and 1.88 (2 H, m, 2-H); δ_C 142.24 and 133.58 (quaternary Ph), 131.77 and 130.47 (*meta* and *ortho* Ph), 63.92 (C-1), 36.05 (C-3) and 33.39 (C-2); $\nu_{max}(CHCl_3)/cm^{-1}$ 3610, 3500, 3000, 2850 and 1600; *m/z* 172 (M + 2, 9.6%), 170 (M^+, 34.5%), 154 (11.5), 152 (36.5), 127 (25.6), 126 (10.5), 125 (88.0), 118 (13.3), 117 (100), 116 (7.3), 115 (25.2), 105 (3.0), 103 (25.2), 102 (6.1), 99 (6.7), 91 (30.2), 89 (22.3), 77 (21.7), 75 (11.8), 63 (10.5), 51 (6.7) and 50 (5.4).

3-(*p*-Methoxyphenyl)propan-1-ol **15d** was obtained in 19% yield, bp 188–190 °C/0.8 mmHg; δ_H 7.12 (2 H, d, Ph), 6.85 (2 H, d, Ph), 4.30 (1 H, s, br, O–H), 3.60 (3 H, s, CH_3O), 3.48 (2 H, t, 1-H), 2.52 (2 H, t, 3-H) and 1.70 (2 H, m, 2-H); δ_C 159.79 and 135.91 (quaternary Ph), 131.99 and 115.84 (*ortho* and *meta* Ph), 64.16 (C-1), 57.27 (C-3), 36.44 (CH_3O) and 33.16 (C-2); $\nu_{max}(CHCl_3)/cm^{-1}$ 3610, 3425 and 1610; *m/z* 167 (M + 2, 2.7%), 166 (M^+, 26.5), 148 (7), 147 (8), 135 (3), 122 (16), 121 (100), 119 (3), 105 (5), 103 (5), 92 (6), 91 (24), 89 (5), 79 (8), 78 (19), 77 (23), 65 (8), 63 (6), 52 (4), 51 (7), 39 (3) and 31 (8).

General procedure for the preparation of 3-phenylprop-1-yl hydroperoxides 14b–d ††

(*i*) Dry pyridine (39.6 g, 0.5 mol) was added dropwise over a period of 2h to a stirred solution of a mixture of the appropriate *para*-substituted 3-phenylpropan-1-ol (0.25 mol) and methanesulfonyl chloride (34.4 g, 0.3 mol) in dichloromethane (150 cm^3), which was maintained at 0 °C for 1 h while stirring was continued. Thereafter, the solution was allowed to warm to room temperature. The progress of the reaction was monitored by GLC and when complete, the mixture was washed successively with water (2 × 100 cm^3), dil. hydrochloric acid (2 × 100 cm^3), water (2 × 100 cm^3), saturated sodium hydrogen carbonate solution (2 × 100 cm^3) and water (2 × 100 cm^3), before being dried (anhydrous Na_2SO_4) and concentrated under vacuum. The resulting crude product was purified by recrystallisation or distillation.

3-(*p*-Methylphenyl)prop-1-yl methanesulfonate was obtained as a pale brown oil in 57% yield, bp 166–168 °C/0.3 mmHg; δ_H 7.11 (4 H, s, Ph), 4.23 (2 H, t, 1-H), 3.00 (3 H, s, CH_3S), 2.73 (2 H, t, 3-H), 2.34 (3 H, s CH_3) and 2.07 (2 H, m, 2-H); δ_C 139.15 and 137.80 (quaternary Ph), 132.26 and 131.31 (Ph), 71.15 (C-1), 39.36 (CH_3S), 33.08 (C-3), 32.73 (C-2) and 22.98 (CH_3); $\nu_{max}(CHCl_3)/cm^{-1}$ 1349 and 1173.

3-(*p*-Chlorophenyl)prop-1-yl methanesulfonate was obtained as a white solid in 90% yield, mp 33.5–34.5 °C (from benzene–light petroleum, bp 60–80 °C); δ_H 7.11 (4 H, m, Ph), 4.10 (2 H, t, 1-H), 2.90 (3 H, s, CH_3S), 2.65 (2 H, t, 3-H) and 1.90 (2 H, m, 2-H); δ_C 140.7 and 130.5 (quaternary Ph), 131.8 and 130.7 (Ph), 70.8 (C-1), 39.4 (CH_3), 32.9 (C-3) and 32.6 (C-2); $\nu_{max}(CHCl_3)/cm^{-1}$ 1350 and 1170.

3-(*p*-Methoxyphenyl)prop-1-yl methanesulfonate was obtained as a white solid in 59% yield, bp 194–195 °C/0.5 mmHg, mp 37–38 °C; δ_H 7.10 (2 H, d, *ortho* Ph), 6.84 (2 H, d, *meta* Ph), 4.21 (2 H, t, 1-H), 3.79 (3 H, s, CH_3S), 2.98 (3 H, s, CH_3O), 2.69 (2 H, t, 3-H) and 2.04 (2 H, m, 2-H); δ_C 160.13 and 134.29 (quaternary Ph), 131.38 and 116.01 (Ph), 71.21 (C-1), 57.23 (CH_3S), 39.25 (CH_3), 32.87 (C-3) and 32.60 (C-2); $\nu_{max}(CHCl_3)/cm^{-1}$ 1357 and 1177.

(*ii*) A solution of the appropriate *para*-substituted 3-phenylprop-1-yl methanesulfonate (10 mmol) in methanol (50 cm^3) was cooled to 0 °C and H_2O_2 (100 vol, 10 cm^3) was added in one batch, with stirring. A 50% aq. potassium hydroxide solution (1 cm^3) was then added dropwise while maintaining the temperature at 0 °C. Stirring was then continued in the dark at room temperature for three days after which the reaction mixture was carefully acidified to pH *ca.* 3.5 before being extracted with dichloromethane (3 × 50 cm^3). The combined extracts were dried and concentrated under vacuum to yield an oil which upon chromatography (prep. TLC; silica gel, dichloromethane) afforded the appropriate 3-phenylprop-1-yl hydroperoxide. NMR analysis revealed that the hydroperoxides were free of significant contaminants and they were furthermore standardised iodometrically (purities given below are as determined iodometrically).

3-(*p*-Methylphenyl)prop-1-yl hydroperoxide **14b** was obtained as a clear oil in 62% yield (97% pure); δ_H 8.05 (1 H, s, OOH), 7.12 (4 H, s, Ph), 4.06 (2 H, t, 1-H), 2.69 (2 H, t, 3-H), 2.34 (3 H, s, CH_3) and 1.97 (2 H, m, 2-H); δ_C 140.39 and 137.42 (quaternary Ph), 131.12 (*ortho* Ph), 130.31 (*meta* Ph), 78.28 (C-1), 33.59 (C-3), 31.27 (C-2) and 23.02 (CH_3); $\nu_{max}(CHCl_3)/cm^{-1}$ 3524, 3384, 3000, 2900 and 1600.

3-(*p*-Chlorophenyl)prop-1-yl hydroperoxide **14c** was obtained as a pale yellow oil in 15% yield (96% pure); δ_H 8.42 (1 H, s, OOH), 7.17 (4 H, q, Ph), 4.02 (2 H, t, 1-H), 2.67 (2 H, t, 3-H) and 1.95 (2 H, m, 2-H); δ_C 141.91 and 130.44 (quaternary Ph), 131.79 and 130.52 (*ortho* and *meta* Ph), 77.93 (C-1), 33.35 (C-3) and 31.09 (C-2); $\nu_{max}(CHCl_3)/cm^{-1}$ 3533, 3420, 2937 and 1602.

3-(*p*-Methoxyphenyl)prop-1-yl hydroperoxide **14d** was obtained as a pale pink oil in 20% yield (97% pure); δ_H 7.95 (1 H, s, OOH), 7.12 (2 H, d, ortho Ph), 6.84 (2 H, d, *meta* Ph), 4.04 (2 H, t, 1-H), 3.80 (3 H, s, CH_3O), 2.66 (2 H, t, 3-H) and 1.95 (2 H, m, 2-H); δ_C 188.23 and 135.53 (quaternary Ph), 131.31 and 115.86 (*ortho* and *meta* Ph), 78.21 (C-1), 57.28 (CH_3O), 33.11 (C-3) and 31.39 (C-2); $\nu_{max}(CHCl_3)/cm^{-1}$ 3533, 3308, 2937 and 1609.

†† Adapted from a method described previously by Mosher and Williams.[18]

General procedure for the preparation of 3-phenylpropanals 16b–d

A solution of pyridine (27.8 g, 30 cm^3, 0.35 mol) in dichloromethane (300 cm^3) was cooled to 5 °C, whereupon chromium trioxide (17.6 g, 0.18 mol) was added and the mixture stirred at 5 °C for an additional 5 min before the temperature was allowed to rise to 20 °C over a period of *ca.* 1 h. A solution of the appropriate 3-phenylpropan-1-ol **15b–d** (0.02 mol) in dichloromethane (50 cm^3) was then added in one portion and stirring continued for 15 min. The solution was then decanted from the black tarry deposit which formed and the latter washed with diethyl ether (3 × 100 cm^3). The ether washings were combined with the decanted solution and washed successively with ice-cold 5% solutions of sodium hydroxide (3 × 100 cm^3), hydrochloric acid (3 × 100 cm^3) and sodium hydrogen carbonate (3 × 100 cm^3). After being dried (Na_2SO_4), the solution was concentrated under vacuum to yield the appropriate aldehyde, which was purified further if required.

3-(*p*-Methylphenyl)propanal **16b** was obtained as a pale yellow oil in 77% yield after chromatography of the crude reaction mixture (prep. TLC; silica gel, dichloromethane); δ_H 9.82 (1 H, s, CHO), 7.10 (4 H, s, Ph), 2.95 (2 H, t, 3-H), 2.79 (2 H, t, 2-H) and 2.35 (3 H, s, CH_3); δ_C 203.80 (C=O), 139.24 and 137.80 (quaternary Ph), 131.29 and 130.16 (*ortho* and *meta* Ph), 47.39 (C-3), 29.75 (C-2) and 23.00 (CH_3); $\nu_{max}(CHCl_3)/cm^{-1}$ 3018, 2927, 2730 and 1717; *m/z* 148 (M^+, 64.0%), 147 (5.7), 133 (17.5), 119 (12.5), 117 (11.3), 115 (12.4), 106 (34.9), 105 (100), 92 (49.7), 91 (41.0), 86 (30.0), 79 (17.4), 77 (24.9), 65 (9.8), 57 (12.0), 51 (7.7), 43 (11.6) and 41 (10.7).

3-(*p*-Chlorophenyl)propanal **16c** was obtained as an oil in 87% yield; δ_H 9.60 (1 H, s, C*H*O), 7.05 (4 H, s, Ph), 2.68 (4 H, m, 2- and 3-H); δ_C 180.27 (C=O), 140.54 and 131.76 (quaternary Ph), 131.65 and 130.68 (*ortho* and *meta* Ph), 37.33 (C-2) and 31.89 (C-3); $\nu_{max}(CHCl_3)/cm^{-1}$ 2950, 2740, 1710, 1600 and 1580; *m/z* 170 (M + 2, 20.8%), 168 (M^+, 55.0), 139 (9.6), 133 (58.3), 127 (34.2), 126 (23.7), 125 (100), 115 (13.0), 114 (13.1), 112 (31.8), 105 (15.9), 103 (36.3), 102 (10.4), 101 (9.3), 91 (35.6), 89 (23.7), 77 (37.2), 75 (17.1), 63 (13.0) and 51 (11.8).

3-(*p*-Methoxyphenyl)propanal **16d** was obtained as an oil in 56% yield after microdistillation of the crude reaction mixture; δ_H 9.83 (1 H, s, CHO), 7.12 (2 H, d, Ph), 6.85 (2 H, d, Ph), 3.80 (3 H, s, CH_3O), 2.92 (2 H, t, 3-H) and 2.76 (2 H, t, 2-H); δ_C 203.72 (C=O), 134.34 and 115.64 (quaternary Ph), 131.24 and 116.20 (*ortho* and *meta* Ph), 57.26 (C-3), 47.57 (C-2) and 29.30 (CH_3O); $\nu_{max}(CHCl_3)/cm^{-1}$ 3013, 2837, 1725 and 1614.

General procedure for the preparation of chromans 10b–d and 13b–d

(*i*) Sodium metal (3.8 g, 0.094 mol) was dissolved in absolute ethanol (380 cm^3), after which the appropriate ring-substituted phenol (0.094 mol) was added to the stirred solution. After 10 min 3-chloropropan-1-ol (8.9 g, 0.094 mol) was added and the mixture refluxed overnight. The reaction mixture was then concentrated, added to water and extracted with dichloromethane. The extracts were combined and washed successively with water (3 × 100 cm^3), concentrated sodium hydroxide (2 × 100 cm^3) and water (3 × 100 cm^3) before being dried (anhydrous Na_2SO_4) and then concentrated under reduced pressure. The resulting oil was distilled under reduced pressure to yield the appropriate ring-substituted 3-phenoxypropan-1-ol.

3-(*p*-Methylphenoxy)propan-1-ol was obtained as a white solid in 23% yield, mp 27–29 °C (from light petroleum, bp 80–100 °C); δ_H 7.10 (1 H, d, Ph), 6.83 (1 H, d, Ph), 4.09 (2 H, t, 3-H), 3.85 (2 H, t, 1-H), 3.18 (1 H, s, OH), 2.32 (3 H, s, CH_3) and 2.04 (2 H, quintet, 2-H); δ_C 158.65 and 132.05 (quaternary Ph), 131.93 and 116.40 (*ortho* and *meta* Ph), 67.76 (C-3), 62.36 (C-1), 34.05 (C-2) and 22.50 (CH_3); $\nu_{max}(CHCl_3)/cm^{-1}$ 3580, 3450, 2950, 2850 and 1600.

3-(*m*-Methylphenoxy)propan-1-ol was obtained as a pale yellow oil in 45% yield, δ_H 7.23 (1 H, t, Ph), 6.80 (3 H, m, Ph), 4.11 (2 H, t, 3-H), 3.89 (3 H, t, 1-H and OH), 2.40 (3 H, s, CH_3) and 2.07 (2 H, quintet, 2-H); δ_C 161.00 and 141.50 (quaternary Ph), 131.22, 123.72, 117.37 and 113.34 (Ph), 67.59 (C-3), 62.47 (C-1), 34.00 (C-2) and 23.53 (CH_3); $\nu_{max}(CHCl_3)/cm^{-1}$ 3550, 3400, 3000, 2800, 1600 and 1580.

3-(*p*-Chlorophenoxy)propan-1-ol was obtained as an oil in 46% yield, bp 194–196 °C/45 mmHg; δ_H 7.23 (2 H, m, Ph), 6.83 (2 H, m, Ph), 4.09 (2 H, t, 3-H), 3.86 (2 H, t, 1-H), 3.55 (1 H, s, OH) and 2.04 (3 H, quintet, 2-H and OH); δ_C 159.38 and 118.68 (quaternary Ph), 131.43, 131.32, 127.67 and 117.74 (*ortho* and *meta* Ph), 67.72 (C-3), 62.01 (C-1) and 33.89 (C-2); $\nu_{max}(CHCl_3)/cm^{-1}$ 3250, 4110, 2900, 3000 and 1600.

3-(*m*-Chlorophenoxy)propan-1-ol was obtained as a pale yellow oil in 71% yield; δ_H 6.8 (4 H, m, Ph), 3.8 (5 H, m, 1-, 3-H and OH) and 1.9 (2 H, q, 2-H); δ_C 161.60 and 122.70 (quaternary Ph), 132.23, 122.97, 116.88 and 115.00 (Ph), 67.56 (C-3), 61.86 (C-1) and 33.87 (C-2); $\nu_{max}(CHCl_3)/cm^{-1}$ 3600, 3400, 3000, 2880 and 1600.

3-(*p*-Methoxyphenoxy)propan-1-ol was obtained as a pale brown low-melting solid in 79% yield; δ_H 6.83 (4 H, s, Ph), 4.07 (2 H, t, 3-H), 3.85 (2 H, t, 1-H), 3.77 (3 H, s, CH_3O), 2.02 (2 H, m, 2-H) and 1.90 (1 H, s, OH); δ_C 155.87 and 154.92 (quaternary Ph), 117.44 and 116.65 (*ortho* and *meta* Ph), 68.33 (C-3), 62.28 (C-1), 57.66 (C-2) and 34.10 (CH_3O); $\nu_{max}(CHCl_3)/cm^{-1}$ 3620, 3442, 3016, 2837 and 1624.

3-(*m*-Methoxyphenoxy)propan-1-ol was obtained as a pale pink oil in 60% yield; δ_H 7.10 (1 H, m, *ortho* Ph), 6.45 (3 H, m, Ph), 3.90 (8 H, m, O*H*, C*H*$_3$O, 1-H and 3-H) and 1.95 (2 H, q, 2-H); $\nu_{max}(CHCl_3)/cm^{-1}$ 3540, 3400, 2900, 2800 and 1595.

(*ii*) The appropriate 3-phenoxypropan-1-ol (0.014 mol) was added in one batch to a cooled, stirred solution of phosphorus pentachloride (42.7 g, 0.30 mol) in 85% polyphosphoric acid (42.3 g, 0.37 mol). After stirring for 30 min, an ice-water slurry was added and the solution extracted with dichloromethane (3 × 100 cm^3). The combined extracts were washed successively with water (2 × 100 cm^3), saturated sodium hydrogen carbonate solution (2 × 100 cm^3) and water (2 × 100 cm^3) before being dried (Na_2SO_4) and then concentrated to an oil which was microdistilled to yield the appropriate chroman.

3-(*p*-Methylphenoxy)propan-1-ol afforded 6-methylchroman **10b** as an oil in 30% yield, bp 106–109 °C/10 mmHg; δ_H 6.99–6.85 (2 H, m, Ph), 6.75 (1 H, d, Ph), 4.20 (1 H, d, 2-H), 4.18 (1 H, d, 2-H), 2.79 (2 H, t, 4-H), 2.29 (3 H, s, Me) and 2.09–1.96 (2 H, m, 3-H); δ_C 154.7, 131.2 and 123.9 (quaternary Ph), 132.2, 129.8 and 118.5 (Ph), 68.4 (C-2), 26.9 (C-4), 24.6 (CH_3) and 22.5 (C-3).

3-(*m*-Methylphenoxy)propan-1-ol afforded an inseparable mixture of 5-methylchroman and 7-methylchroman **13b**, bp 110–111 °C/10 mmHg; δ_H 7.10–6.93 (1 H, m, Ph), 6.82–6.65 (2 H, m, Ph), 4.21 (t, 2-H) and 4.18 (combined 2 H, t, 2-H), 2.79 (t, 4-H) and 2.69 (combined 2 H in ratio 0.56 : 0.44, t, 4-H), 2.32 (s, Me) and 2.26 (combined 3 H, s, Me) and 2.15–1.96 (2 H, m, 3-H); δ_C 157.1, 156.7, 139.6, 139.1 and 121.1 (quaternary Ph), 131.6, 128.6, 123.7, 123.1, 119.1 and 116.6 (Ph), 68.4 and 67.9 (C-2), 26.6 (C-4), 24.6 (C-3, C-3 and C-4), and 23.1 and 21.1 (Me).

3-(*p*-Chlorophenoxy)propan-1-ol afforded 6-chlorochroman **10c** as an oil in 46% yield, bp 105–110 °C/45 mmHg; δ_H 6.75 (3 H, t, Ph), 4.10 (2 H, t, 2-H), 2.70 (2 H, t, 4-H) and 1.95 (2 H, q, 3-H); δ_C 155.0, 126.7 and 125.7 (quaternary Ph), 131.3, 129.1 and 120.0 (Ph), 68.5 (C-2), 26.8 (C-4) and 24.0 (C-3); $\nu_{max}(CHCl_3)/cm^{-1}$ 2870, 2960, 1595 and 1260; *m/z* 170 (M + 2; 22.4%), 168 (M^+, 65.5%), 153 (6.6), 141 (6.3), 140 (14.0), 134 (8.3), 133 (100), 125 (10.0), 115 (9.7), 114 (11.7), 112 (29.8), 105 (31.6), 103 (14.4), 89 (8.4), 77 (35.5) and 51 (9.7).

3-(*m*-Chlorophenoxy)propan-1-ol afforded an inseparable

mixture of 5-chlorochroman and 7-chlorochroman **13c** as a pale yellow oil in 17% yield from centrifugal chromatography (silica gel PF_{254}; light petroleum, bp 40–60 °C); δ_H 7.10–6.69 (8 H, m, Ph), 4.15 (4 H, t, 2-H), 2.82–2.69 (4 H, m, 4-H) and 2.11–1.90 (4 H, m, 3-H); $\nu_{max}(CHCl_3)/cm^{-1}$ 2850, 3000, 1600 and 1080.

3-(*p*-Methoxyphenoxy)propan-1-ol afforded, after chromatography (silica gel; chloroform), 6-methoxychroman **10d** as a pale pink oil with a distinctive odour in 13% yield (Found: C, 73.1; H, 7.5. $C_{10}H_{12}O_2$ requires C, 73.15; H, 7.37%); δ_H 6.66 (3 H, m, Ph), 4.15 (2 H, t, 2-H), 3.76 (3 H, s, CH_3O), 2.79 (2 H, t, 4-H), 2.00 (2 H, m, 2-H); δ_C 155.00, 151.00 and 124.70 (quaternary Ph), 119.20, 116.34 and 115.30 (Ph), 68.31 (C-2), 57.67 (C-4), 27.19 (C-3) and 24.49 (CH_3O); $\nu_{max}(CHCl_3)/cm^{-1}$ 3000, 2800 and 1605; *m/z* 165 (M + 1; 9.8%), 164 (M^+, 100), 150 (8.6), 149 (82.1), 137 (5.1), 136 (53.1), 135 (3.5), 134 (4), 133 (4.1), 121 (13.7), 109 (4.5), 108 (42.5), 107 (15.7), 105 (7.1), 103 (15.0), 93 (15.5), 91 (36.2), 89 (6.7), 79 (24.2), 78 (30.8), 77 (47.2), 74 (6.6), 55 (9.8), 54 (7.8), 53 (11.3), 52 (6.4), 51 (20.9), 50 (9.8), 43 (6.0) and 39 (20.6).

3-(*m*-Methoxyphenoxy)propan-1-ol afforded from chromatography (silica gel; chloroform) an inseparable mixture of 5-methoxychroman and 7-methoxychroman **13d** as a pale yellow oil in 24% yield; δ_H 7.29–6.90 (1 H, m, Ph), 6.59–6.35 (2 H, m, Ph), 4.17 (2 H, m, 2-H), 3.82 (3 H, s, CH_3O), 3.78 (3 H, s, CH_3O), 2.72 (2 H, m, 4-H) and 2.00 (2 H, m, 3-H); $\nu_{max}(CHCl_3)/cm^{-1}$ 2940, 2850 and 1615.

Redox decomposition of 3-arylprop-1-yl hydroperoxides

A solution of the appropriate *para*-substituted 3-phenylprop-1-yl hydroperoxide **14b–d** (1 mmol) and $Cu(OAc)_2 \cdot H_2O$ (0.6 g, 3 mmol) in 20% aq. acetonitrile (15 cm^3) was stirred magnetically while aq. $FeSO_4$ (0.83 g, 3 mmol; 5 cm^3) was added dropwise over a period of *ca.* 30 min. After completion of the addition, the reaction mixture was stirred at room temperature for a further 2 h. The pH values of both the initial solution and final reaction mixture were determined. The final reaction mixture was then extracted with dichloromethane (3 × 25 cm^3) and the combined extracts dried (Na_2SO_4). Thereafter a known quantity of ethyl benzoate was added as an internal standard and the reaction mixture analysed by capillary GLC. The pH values of the initial hydroperoxide solutions were adjusted by addition of concentrated hydrochloric acid or sodium acetate. The effect of variations in the pH on the reaction products and their yields are given in Tables 1–3.

Thermal reaction of 3-(*p*-methylphenyl)prop-1-yl hydroperoxide 14b

A solution of 3-(*p*-methylphenyl)prop-1-yl hydroperoxide **14b** (1 mmol) in 20% aq. acetonitrile (18 cm^3) was refluxed with stirring for 2 h. The reaction mixture was then cooled before being worked up and analysed as described above. The reaction was then repeated in the presence of $Cu(OAc)_2$ (3 mmol). The reaction products and their yields are given in Table 4.

Acid-catalysed rearrangement and subsequent methylation of 1-oxaspiro[4.5]deca-6,9-dien-8-one 27

The spirodienone **27** was prepared [10] and subjected to acid-catalysed rearrangement [7] as described previously. The phenolic chroman which resulted was taken up in aq. sodium hydroxide and then treated with methyl iodide. Thereupon the solution was extracted with diethyl ether after which the combined extracts were dried and concentrated. Capillary GC analysis of the resulting oil revealed the presence of 6-methoxychroman **10d**, by comparison with an authentic specimen.

Acknowledgements

Financial support from the Foundation for Research Development and Karbochem (F. C. R.) is acknowledged.

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Paper 4/07605B
Received 13*th December* 1994
Accepted 15*th March* 1995