Cyclisation of 3-Phenylpropan-1-ol *via* Alkoxyl Radical and Aryl Radical-cation Intermediates. A Product and E.S.R. Study

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A comparison is made of the cyclisation reaction of the 3-phenyl-1-propoxyl radical (**2**) generated by metal-catalysed reduction of 3-phenylpropyl hydroperoxide, with that of the aryl radical cation $[Ph(CH_2)_3OH]^{+\bullet}$ (**3**) obtained by oxidising 3-phenylpropan-1-ol (**1**) with $SO_4^{-\bullet}$ [from Fe^{II}–$S_2O_8^{2-}$ and thermolysis of $S_2O_8^{2-}$]. Significant yields of the cyclised product 3,4-dihydro-2*H*-1-benzopyran (**7**) were obtained from the radical (**2**) and radical cation (**3**) only in the presence of Cu^{II} ions which are proposed to oxidise the intermediate cyclised radicals. Reaction of the alcohol (**1**) with Ag^{I}–$S_2O_8^{2-}$ and $HO^{\bullet}$ [from Ti^{III}–H_2O_2] was also investigated, as were e.s.r. spectra of intermediates which formed from its reaction with $SO_4^{-\bullet}$ and $HO^{\bullet}$.

The results are interpreted in terms of the reaction of the 3-phenyl-1-propoxyl radical (**2**) *via* competing 1,2-hydrogen shift and cyclisation [to give, ultimately, the six-membered ring product (**7**)]; generation of the radical cation $[Ph(CH_2)_3OH]^{+\bullet}$ (**3**) (from either $SO_4^{-\bullet}$ or $HO^{\bullet}/H^+$) is followed by cyclisation *via* nucleophilic attack to give a cyclic radical intermediate which can undergo one-electron oxidation to give (**7**), ring-open to give the alkoxyl radical (**2**), or at low pH revert to the radical cation (**3**) to give the benzylic radical $Ph\dot{C}HCH_2CH_2OH$ (**15**).

Considerable interest in the synthetic utility and mechanistic aspects of intramolecular additions of free radicals to unsaturated linkages has been engendered in recent years as a consequence of the high regio- and stereo-selectivity which is frequently displayed.[1] For example, the pent-4-en-1-oxyl radical undergoes exclusively 1,5-ring closure to the 2-tetrahydrofuranylmethyl radical[2] as a result of the stringent stereoelectronic constraints to which such radical cyclisations are subject.

The observation[3,4] of some 1,6-ring closure when pent-4-en-1-ol is treated with peroxydisulphate ($S_2O_8^{2-}$) in the presence of Ag^{I} has been ascribed to the possible intermediacy of a radical cation which undergoes internal nucleophilic attack by the hydroxy group; it has been suggested that the regioselectivity of this process could be lower than that of the corresponding alkoxyl radical cyclisation. A recent e.s.r. study[5] has shown that the reaction of pent-4-en-1-ol and some derivatives with $Cl_2^{-\bullet}$ and $SO_4^{-\bullet}$, as well as $HO^{\bullet}$ (at low pH), gives rise to largely the 2-tetrahydrofuranylalkyl radical, although the formation of smaller amounts of the isomeric tetrahydropyran-3-yl radical could not be ruled out. The intermediacy of radical cations is also proposed for these cyclisations, although the possibility that internal attack by the hydroxy group is synchronous with departure of the appropriate leaving group (i.e. the incipient radical cation may not form a discrete species) could not be excluded.

Determination of the regioselectivity of alkoxyl radical cyclisation onto aromatic rings is complicated by its reversibility[6c] which usually leads to the isolation of exclusively the thermodynamically favoured ring. For example, only 1,6-cyclised products are obtained when 3-phenylpropan-1-ol (**1**) is allowed to react with Pb^{IV}[7] and Ce^{IV}[8] reagents. In contrast, however, both 1,5- and 1,6-cyclised products are formed when this alcohol is photolysed in the presence of HgO and I_2.[6] While the alkoxyl radical (**2**) has been proposed as an intermediate in these reactions, it is well known that higher valence metal ions such as Pb^{IV} and Ce^{IV} are also capable of oxidising aromatic systems to aryl radical cations.[9] It is therefore possible that the aryl radical cation (**3**) could be generated in competition with the alkoxyl radical (**2**), with the cyclised products arising from (**3**) as a result of its intramolecular reaction with the hydroxy group (Scheme 1). Furthermore, interconversion of the radical (**2**) and radical cation (**3**), either by direct electron transfer or *via* cyclised intermediates, is also conceivable.

Examples of cyclisations of aryl alkanols *via* aryl radical-cation intermediates are sparse. Anodic oxidation of γ-aryl alkanols to aryl radical cations has been reported to give almost exclusively 1,5-cyclised products, but the mechanism is proposed to involve an EEC_rC_p process[10] rather than simple internal attack by the hydroxy group on the radical cation. In contrast, only *ortho*-cyclised products were reported from the intramolecular reactions of the aryl radical cations generated from 3,4-dimethoxyphenyl- and naphthalenyl-alkanols in the presence of thallium(III) trifluoroacetate.[11] A similar result was obtained from the reaction of 3-phenylpropan-1-ol (**1**) with $S_2O_8^{2-}$–Cu^{II},[12] although the cyclisation was proposed to involve a carbenium ion derived from the aryl radical cation. This mechanism is described more fully in the Discussion.

In view of the disparate results and mechanisms described above, we initiated a product and e.s.r. study to compare the cyclisations of 3-phenylpropan-1-ol *via* both alkoxyl radical and aryl radical-cation intermediates.

Results

Product Studies.—Our approach entailed generating the alkoxyl radical (**2**) by metal-catalysed reduction of 3-phenylpropyl hydroperoxide [equation (1)].[13] The aryl radical cation (**3**) was produced by oxidation of 3-phenylpropan-1-ol (**1**) with sulphate radical anion ($SO_4^{-\bullet}$) [equation (4)][14–18] [generated from $S_2O_8^{2-}$ either thermally, equation (2), or by metal-catalysed reduction, equation (3)] and also by a free-radical hydroxylation [$HO^{\bullet}$ generated by the Ti^{III}–H_2O_2 redox couple, equation (5)] and subsequent acid-catalysed dehydroxylation process involving the aryl ring [equations (6) and (7)].[16–19]

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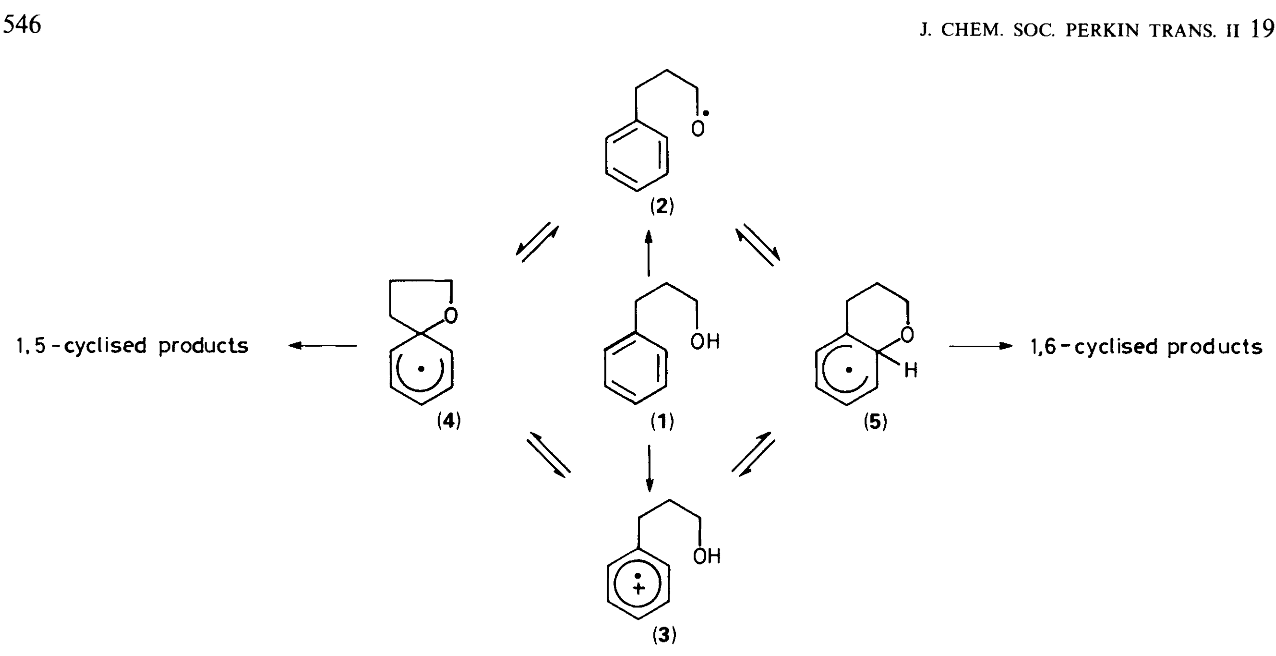

Scheme 1.

$$Ph(CH_2)_3O_2H + M^{n+} \longrightarrow \mathbf{(2)} + HO^- + M^{(n+1)+} \quad (1)$$

$$S_2O_8^{2-} \xrightarrow{\text{heat}} 2SO_4^{-\bullet} \quad (2)$$

$$S_2O_8^{2-} + M^{n+} \longrightarrow SO_4^{-\bullet} + SO_4^{2-} + M^{(n+1)+} \quad (3)$$

$$\mathbf{(1)} + SO_4^{-\bullet} \longrightarrow \mathbf{(3)} + SO_4^{2-} \quad (4)$$

$$H_2O_2 + Ti^{3+} \longrightarrow HO^\bullet + HO^- + Ti^{4+} \quad (5)$$

$$\mathbf{(1)} + HO^\bullet \longrightarrow \mathbf{(20)} \quad (6)$$

$$\mathbf{(20)} + H^+ \longrightarrow \mathbf{(3)} + H_2O \quad (7)$$

(a) *Reduction of* 3-*phenylpropyl hydroperoxide.* Very little 3,4-dihydro-2*H*-1-benzopyran (**7**) and mainly 3-phenylpropan-1-ol (**1**) and 3-phenylpropanal (**12**) resulted from the reduction of 3-phenylpropyl hydroperoxide with Ti$^{\mathrm{III}}$ (Table 1). Use of Fe$^{\mathrm{II}}$ produced a similar result except that the yield of aldehyde far exceeded that of alcohol. However, the addition of Cu$^{\mathrm{II}}$ to both reaction systems markedly improved the yield of (**7**).

(b) *Reactions of* 3-*phenylpropan*-1-*ol* (**1**). (*i*) With $SO_4^{-\bullet}$. The thermal reaction of 3-phenylpropan-1-ol (**1**) with $S_2O_8^{2-}$ afforded mainly the aldehyde (**12**), some ethylbenzene (**13**) and only a trace of the cyclic product (**7**) (Table 2). Addition of Cu$^{\mathrm{II}}$ or $Fe(CN)_6^{3-}$ markedly improved the yield of (**7**). However, optimum yields of (**7**) were obtained when $S_2O_8^{2-}$ was reduced with Fe$^{\mathrm{II}}$ at room temperature in the presence of Cu$^{\mathrm{II}}$.

As in the case of 3-phenylpropyl hydroperoxide, no cyclised products which could be unambiguously assigned to the 1,5-cyclisation route were identified. 3,4-Dihydro-2*H*-1-benzopyran-4-ol (**8**) and 2,3-dihydro-1-benzopyran-4-one (**9**) arise from further oxidation of (**7**) under the reaction conditions; thermolysis of a mixture of equivalent quantities of (**7**) and $S_2O_8^{2-}$ and a tenfold excess of Cu$^{\mathrm{II}}$ afforded unchanged starting material (28%), alcohol (**8**) (55%) and ketone (**9**) (13%). However, experiment showed that excessive over-oxidation did not occur under the conditions listed in Table 2 and the use of a three and a half-fold excess of $S_2O_8^{2-}$ over alcohol (**1**) resulted in synthetically useful yields of (**7**) (entries 7 and 8).

(*ii*) With Ag$^{\mathrm{II}}$. While $S_2O_8^{2-}$ oxidises aliphatic alcohols to α-hydroxyalkyl radicals as a result of hydrogen abstraction by $SO_4^{-\bullet}$[21,22] [equation (8)], addition of Ag$^{\mathrm{I}}$ is proposed to alter the course of the reaction and produce alkoxyl radicals *via* Ag$^{\mathrm{II}}$ species [equations (9) and (10)].[3,21,23] Since Ag$^{\mathrm{II}}$ also oxidises aromatic systems to radical cations,[16,23] we investigated the reaction of the arylalkanol (**1**) with the $S_2O_8^{2-}$–Ag$^{\mathrm{I}}$ reagent in order to ascertain the preferred site of attack in this substrate which contains both a hydroxy group and an aromatic ring (Table 3). The effect of added Cu$^{\mathrm{II}}$ on the reactions was also determined.

$$RCH_2OH + SO_4^{-\bullet} \longrightarrow R\dot{C}HOH + H^+ + SO_4^{2-} \quad (8)$$

$$S_2O_8^{2-} + Ag^+ \longrightarrow SO_4^{-\bullet} + SO_4^{2-} + Ag^{2+} \quad (9)$$

$$RCH_2OH + Ag^{2+} \longrightarrow RCH_2\dot{O} + H^+ + Ag^+ \quad (10)$$

The total yield of cyclised products (**7**)–(**9**) obtained was much lower than that arising from the metal ion-catalysed reduction of 3-phenylpropyl hydroperoxide, and comparable to those obtained from the alcohol (**1**) in both its thermal and Fe$^{\mathrm{II}}$-catalysed reactions with $S_2O_8^{2-}$ [Table 2, experiments 2 (where allowance should be made for $S_2O_8^{2-}$ producing two equivalents of $SO_4^{-\bullet}$) and 4].

(*iii*) With $HO^\bullet/H^+$. Treatment of alcohol (**1**) with H_2O_2–Ti$^{\mathrm{III}}$ under acidic conditions (pH *ca.* 1) resulted in a low yield (5%) of (**7**) along with some aldehyde (**12**) (2%). These yields were decreased upon addition of Cu$^{\mathrm{II}}$ to the reaction mixtures.

E.S.R. Studies.—Previous e.s.r. experiments in these laboratories[2c] in which 3-phenylpropyl hydroperoxide was reduced with Ti$^{\mathrm{III}}$, led to the observation of the radical (**10**) which was proposed to arise from the alkoxyl radical (**2**) as a result of a 1,2-hydrogen shift.[2c,24] In a subsequent e.s.r. study[25] we endeavoured to generate the aryl radical cation (**3**) and some derivatives in order to compare their reactions with those of the alkoxyl radical (**2**).

Three approaches for generating these species in the cavity of the e.s.r. spectrometer were employed. In the first, the substrate was oxidised with $SO_4^{-\bullet}$ which was generated by u.v. irradiation of an aqueous solution of the alcohol and $S_2O_8^{2-}$ to which propanone had been added as a photosensitiser.[5a] The second procedure[5a] entailed mixing two aqueous solutions *ca.* 50 ms before passage of the combined solution through the cavity.

Table 1. Reduction of 3-phenylpropyl hydroperoxide[a].

Expt.[b]	Metal ions	Molar ratio[c]	$[H^+]$	Products (%)[d]		
				(**7**)	(**12**)[f]	(**1**)[f]
1	Ti^{3+}	1:1.8	1.6	2	12	23
2	Ti^{3+}	1:2	*e*	2	60	13
3	Ti^{3+}, Cu^{2+}	1:1.8:18.4	1.9	41	20	7
4	Ti^{3+}, Cu^{2+}	1:2:20	1.6×10^{-2}	70	53	4
5	Fe^{2+}	1:2.4	0.16	3	92	13
6	Fe^{2+}	1:2	7.2×10^{-4}	1	98	5
7	Fe^{2+}, Cu^{2+}	1:3:28	0.10	72	43	29
8	Fe^{2+}, Cu^{2+}	1:2:20	2.7×10^{-4}	79	47	4
9	$Fe(CN)_6^{4-}$, $Fe(CN)_6^{3-}$	1:0.5:5.6	*e*	6	52	11

[a] The following groups of experiments were carried out on common batches of the substrate: 1 and 3; 2, 4, 6, and 8; 5, and 7. [b] Experiments 1, 3, 5, and 7 were conducted in 50% aqueous acetonitrile, and the rest in water. [c] Alkyl hydroperoxide: metal ions (in the order given). [d] Yields based on alkyl hydroperoxide. [e] Not determined. [f] In all the experiments listed, the starting hydroperoxide was invariably contaminated with the alcohol (**1**) and aldehyde (**12**), presumably formed as a result of decomposition[20] during its preparation. Although the yields of (**1**) and (**12**) reported in Table 1 are therefore not absolute values reflecting their formation in the presence of the appropriate metal ions, valid trends can nevertheless still be discerned since reactions were conducted in batches using common hydroperoxide solutions in which the background amounts of (**1**) and (**12**) would have been the same.

Table 2. Oxidation of 3-phenylpropan-1-ol (**1**) with $SO_4^{-\bullet}$.

Expt.[a]	Metal ions	Molar ratio[b]	Products (%)[c]					
			(**1**)	(**7**)	(**8**)	(**9**)	(**12**)	(**13**)
1	—	10:1	*e*	trace	0	0	29	2.5
2	Cu^{2+}	10:10:1	*e*	30	trace	trace	27	0.4
3	$Fe(CN)_6^{3-}$	10:10:1	*e*	30	trace	trace	13	0
4[d]	Fe^{2+}, Cu^{2+}	10:5:10:1	*e*	12	trace	0.6	4	0
5	Fe^{2+}, Cu^{2+}	10:5:25:1	*e*	47	trace	trace	9	0
6	Cu^{2+}	10:24:12	39	3	0	0	0	0
7	Fe^{2+}, Cu^{2+}	10:15:25:35	17	58	5	0.2	3	trace
8	Fe^{2+}, Cu^{2+}	10:35:25:35	1	62	6	1	trace	trace

[a] Experiments 1–3 were conducted under reflux and 4–8 at room temperature. [b] (**1**): metal ions (in the order given): $S_2O_8^{2-}$. [c] Yields in experiments 1–5 are based on $S_2O_8^{2-}$ and those in experiments 6–8 on starting alcohol (**1**). When comparing yields it should be noted that the uncatalysed thermal reaction of $S_2O_8^{2-}$ gives rise to two equivalents of $SO_4^{-\bullet}$. [d] Inverse addition. [e] Not determined.

Table 3. Reaction of 3-phenylpropan-1-ol (**1**) with $S_2O_8^{2-}$–Ag^{I}.

Expt.[a]	Metal ions	Molar ratio[b]	Products (%)[c]				
			(**7**)	(**8**)	(**9**)	(**12**)	(**13**)
1	Ag^+	10:25:1	trace	trace	trace	49	6
2	Ag^+, Cu^{2+}	10:25:10:1	3	8	10	21	0.4
3	Ag^+, Cu^{2+}	10:25:10:1	0	3	14	12	0

[a] Experiments 1 and 2 were carried out under reflux, and 3 at room temperature. [b] (**1**): metal ions (in the order given): $S_2O_8^{2-}$. [c] Yields based on $S_2O_8^{2-}$.

The first stream contained a mixture of the substrate and Ti^{III} (together with disodium ethylenediaminetetra-acetate as sequestering agent and sufficient ammonia or sulphuric acid to achieve the required pH after mixing), and the second stream a mixture of the substrate and $K_2S_2O_8$; $SO_4^{-\bullet}$ is formed according to equation (3), where $M^{n+} = Ti^{III}$.

The third approach was identical with the second, except that the $S_2O_8^{2-}$ stream was replaced by an H_2O_2 solution which also contained substrate. This redox couple leads to the formation of $HO^\bullet$ according to equation (5). E.s.r. parameters of the radicals detected are collected in Table 4.

(a) *Reactions of 3-phenylpropan-1-ol* (**1**) *with* $SO_4^{-\bullet}$ *and* $HO^\bullet$. An extremely weak spectrum which could not be satisfactorily analysed was obtained when the alcohol (**1**) was irradiated in the presence of $S_2O_8^{2-}$. However, when (**1**) was allowed to react with $SO_4^{-\bullet}$ generated by the Ti^{III}–$S_2O_8^{2-}$ couple at pH 1.6, a spectrum of the benzylic radical (**15**) was obtained. Attempts to determine the effect of raising the pH were complicated by the formation of a deposit in the e.s.r. mixing cell which adversely affected the signal-to-noise ratio and also gave rise to an intense broad background absorption. Nevertheless, in the pH range *ca.* 3–7.5 weak signals which were common to those observed with Ti^{III}–H_2O_2 over a similar pH range and attributed to a mixture of the hydroxycyclohexadienyl species (**20**) were evident.

When alcohol (**1**) was allowed to react with $HO^\bullet$ generated by the Ti^{III}–H_2O_2 couple in the pH range 3.5–7, a complex spectrum ranging over *ca.* 7 mT resulted. We attribute this spectrum, which could not be satisfactorily analysed, to a mixture of the adducts (**20**) resulting from attack by $HO^\bullet$ on the aryl ring.[19b,26] These signals weakened when the pH was lowered and at *ca.* 2 were succeeded by a spectrum of the α-hydroxyalkyl radical (**10**). Further lowering of the pH led to

Table 4. E.s.r. parameters of radicals detected in the reactions of 3-phenylpropan-1-ol (**1**) and derivatives with $HO^{\bullet}$ and $SO_4^{-\bullet}$.

			Hyperfine splittings/mT[a]			
Substrate	Radical	Method (A, $HO^{\bullet}$; B, $SO_4^{-\bullet}$)	a(α-H)	a(β-H)	a(other)	g[b]
$Ph(CH_2)_3OH$	(**15**)	A, B	1.60(1)	1.60(2)	0.60(1, p-H) 0.50(2, o-H) 0.17(2, m-H)	2.0025
	(**10**)	A	1.535(1)	1.955(2)	0.075(2, γ-H)	2.0030
$Ph(CH_2)_3OMe$	(**16**)	A	1.60(1)	1.60(2)	0.60(1, p-H) 0.50(2, o-H) 0.17(2, m-H)	c
$Ph(CH_2)_4OH$	(**18**)	A	1.60(1)	1.60(2)	0.60(1, p-H) 0.50(2, o-H) 0.17(2, m-H)	2.0025

[a] Typically ±0.005 mT. [b] ±0.0001. [c] Not determined.

weakening of this spectrum and its replacement by new signals which were attributed to the benzylic radical (**15**).

(b) *Reaction of methyl* 3-*phenylpropyl ether with* $HO^{\bullet}$. At pH *ca.* 7 a complex wide-ranging spectrum the general features of which were similar to those obtained from the alcohol (**1**) under similar conditions, was observed. It can be ascribed to a mixture of isomeric hydroxycyclohexadienyl species. At pH *ca.* 2 a strong spectrum of the benzylic radical (**16**) became apparent and weakened as the pH was lowered to 1. However, there was little evidence for the formation of significant amounts of the α-methoxyalkyl radical (**17**).

(c) *Reaction of* 4-*phenylbutan*-1-*ol with* $HO^{\bullet}$. In the intermediate pH range there was evidence for the formation of $HO^{\bullet}$-adducts which were replaced at pH *ca.* 2 by a spectrum attributed to the benzylic radical (**18**). There was no evidence for the α-hydroxyalkyl radical (**19**).

Discussion

(a) *Reduction of* 3-*phenylpropyl hydroperoxide.* The results obtained with this substrate clearly establish that the intermediate alkoxyl radical readily cyclises. Optimum yields of (**7**) were obtained when the reaction was carried out in the presence of Cu^{II}; since it has been shown that the 2-phenoxyethoxyl radical [and probably also (**2**)] cyclises reversibly,[6c] significant amounts of cyclic products will result only if the intermediate cyclised radicals (**4**) and/or (**5**) are oxidised[14,27] to carbenium ions (**14**) and/or (**6**), respectively (Scheme 2).* Cu^{II} is clearly more effective than Ti^{IV}, Fe^{III}, or $Fe(CN_6)^{3-}$ in this regard. In the absence of Cu^{II}, reversion of the cyclised radical intermediates to the alkoxyl radical evidently results in its decay along alternative pathways.

For example, rearrangement of the alkoxyl radical (**2**) to the α-hydroxyalkyl radical (**10**) *via* a 1,2-hydrogen shift[2c,24] could occur, further oxidation of which would account for the formation of the aldehyde (**12**). In addition, reduction of the alkoxyl radical or the cyclic radical intermediates would lead to the formation of alcohol (**1**).

The reduced yield of (**7**) at lower pH reflects either an enhanced rate of acid-catalysed conversion of the cyclic radical intermediates (**4**) and/or (**5**) into the radical cation (**3**), or a reduction in the oxidation potential of the oxidising species.

(b) *Reactions of* 3-*phenylpropan*-1-*ol* (**1**). (*i*) With $SO_4^{-\bullet}$. Our results with this substrate suggest that the aryl radical cation (**3**), generated from alcohol (**1**) upon oxidation by $SO_4^{-\bullet}$,[14,18] also cyclises to the intermediates (**4**) and/or (**5**) which are oxidised when Cu^{II} is present, ultimately affording (**7**) * (Scheme 2).

Cyclisation may involve direct nucleophilic attack by the hydroxy group on the radical cation, or an electron transfer from the hydroxy group to the ring[28] to give an alkoxyl radical which cyclises as above;† the intermediacy of the 3-phenylpropoxyl radical (**2**) would account for the formation of ethyl benzene (**13**) and 3-phenylpropanal (**12**) as a result of fragmentation to the 2-phenylethyl radical, or rearrangement‡ to (**10**), respectively. However, the alkoxyl radical could also result if direct nucleophilic attack by the hydroxy group on the radical cation is followed by homolytic ring-opening of the intermediates (**4**) and/or (**5**); an analogous dissociation of hydroxycyclohexadienyl radicals to benzene and $HO^{\bullet}$ has been reported.[32]

Although e.s.r. studies of its reactions with $SO_4^{-\bullet}$ were limited as a result of fouling of the e.s.r. cell by an unidentified deposit, alcohol (**1**) nevertheless afforded at low pH a spectrum of the benzylic radical (**15**) which results from deprotonation of the radical cation (**3**). Failure to observe the α-hydroxyalkyl radical (**10**) is probably due to its rapid oxidation[33] by $S_2O_8^{2-}$. This is supported by the effect of adding $S_2O_8^{2-}$ to the H_2O_2 stream of an alcohol (**1**)–Ti^{III}–H_2O_2 e.s.r. flow experiment in which the concentration of the radical (**10**) was found to decrease markedly when the $S_2O_8^{2-}$ was added.

(*ii*) With Ag^{II}. Although it has been proposed[4,23] that the major intermediates produced in the reaction of arylalkanols with Ag^{II} are alkoxyl radicals, in our case the Ag^{II} reaction more closely resembles that of $SO_4^{-\bullet}$ (where the aryl radical cation is implicated) than the hydroperoxide reduction. Nevertheless, the formation of both aldehyde (**12**) and ethyl benzene (**13**) shows that the alkoxyl radical (**2**) is also involved, although it could form *via* the radical cation (as proposed for $SO_4^{-\bullet}$) rather than

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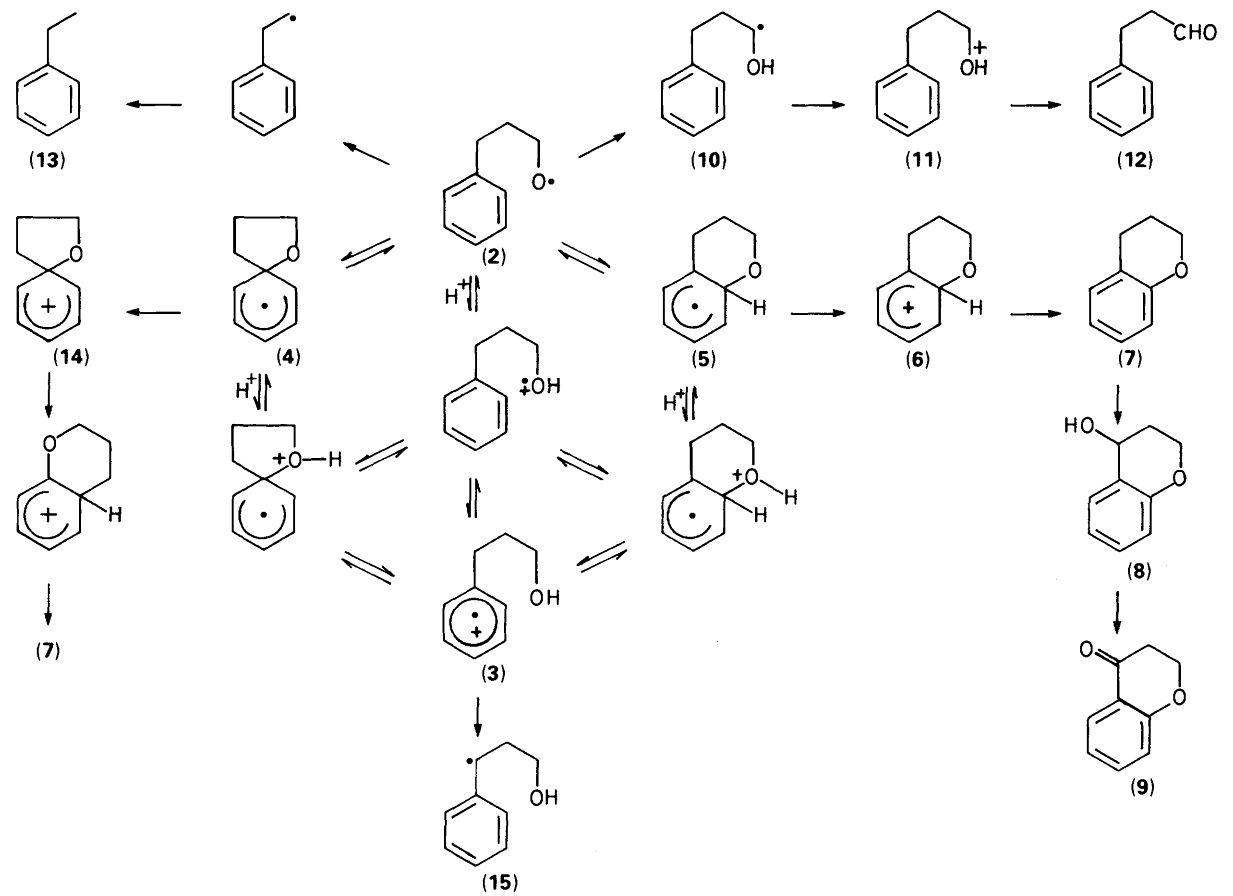
* Although no products unique to the 1,5-cyclisation route could be identified, it cannot be excluded since the intermediate carbenium ion (**14**) would be expected to rearrange to (**7**).[6c]

† Walling and his co-workers[12] have suggested an alternative mechanism for the cyclisation of the radical cation (**3**) in which it first undergoes deprotonation giving the benzylic radical (**15**). This radical is in turn oxidised to a benzylic carbenium ion which, by virtue of delocalisation of charge onto the *ortho*-carbon, is attacked intramolecularly at this position by the hydroxy group. However, our proposed mechanism is preferred because aryl radical cations in which deprotonation is impossible are known to be readily trapped by nucleophiles such as water,[29] and also a recent kinetic isotope study[30] has shown that the p-methoxytoluene radical cation undergoes nuclear substitution through direct attack on the radical cation and not *via* the benzyl cation.

‡ It is unlikely that (**10**) is formed *via* hydrogen abstraction from the alcohol (**1**) by $SO_4^{-\bullet}$.[21,22] since a comparison of typical rate constants for hydrogen abstraction by $SO_4^{-\bullet}$ (*e.g.* 1.6×10^7 dm^3 mol^{-1} s^{-1} for ethanol[22a]) with electron transfer from an aryl ring (*e.g.* 3×10^9 dm^3 mol^{-1} s^{-1} for benzene[31]) indicates that ring oxidation should dominate hydrogen abstraction in the aryl alkanol (**1**).



Scheme 2.

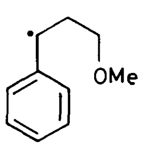
directly from the alcohol with Ag^{II}. While the rates of reaction of $SO_4^{-\bullet}$ with the aromatic substrate (**1**) and Ag^{I} are probably similar (*ca.* 3×10^9 dm^3 mol^{-1} s^{-1}),[23,31] the use of a 2.5-fold excess of Ag^{I} over substrate (**1**) should ensure that the major oxidant is Ag^{II} rather than $SO_4^{-\bullet}$. The marked difference between the product ratios (**7**):(**8**):(**9**) in the $SO_4^{-\bullet}$ and Ag^{II} reactions confirms that the oxidant differs in the two cases.

(*iii*) With HO•. The hydroxycyclohexadienyl intermediates (**20**) obtained when HO• adds to the benzenoid ring of alcohol (**1**), would be expected to undergo readily acid-catalysed dehydroxylation to form the radical cation (**3**). The low yield of cyclic product (**7**) obtained from alcohol (**1**) is not surprising, however, since the acidic conditions necessary for dehydroxylation of the hydroxycyclohexadienyl adducts would also inhibit cyclisation and promote the reverse ring-opening reaction.

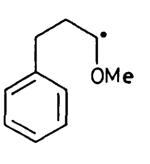
The e.s.r. study of the reactions of alcohol (**1**) with HO• may be rationalised in terms of Scheme 3. HO• adds rapidly to the substrate affording a mixture of the isomeric adducts (**20**). As the pH is lowered, signals arising from (**20**) are steadily replaced by those of the α-hydroxyalkyl radical (**10**) which is in turn succeeded by the benzylic radical (**15**).

These observations are consistent with the acid-catalysed conversion of the HO•-adduct (**20**) to the cyclic intermediates (**4**) and/or (**5**) in a process where internal nucleophilic attack by the side-chain hydroxy group occurs either synchronously with acid-catalysed dehydroxylation of (**20**), or *via* an intermediate radical-cation (**3**). The intermediates (**4**) and/or (**5**) subsequently undergo ring-opening to the alkoxyl radical (**2**) which rapidly rearranges[2c,24] to the α-hydroxyalkyl radical (**10**). The intermediacy of cyclic structures such as (**4**) and/or (**5**) is supported by the observation that the onset of formation of the benzylic radical (**15**) from the alcohol (**1**) as the pH is lowered, is clearly retarded relative to those of both methyl 3-phenylpropyl ether and 4-phenylbutan-1-ol. This indicates that the (incipient) radical cation (**3**) is rapidly scavenged by the side-chain hydroxy group.

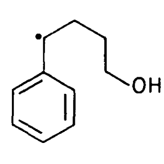
Our observation that neither methyl 3-phenylpropyl ether nor 4-phenylbutan-1-ol afford significant concentrations of the analogous side-chain radicals (**17**) and (**19**), confirms that (**10**) is not formed as a result of direct hydrogen abstraction from the side-chain by HO•. Further, direct electron-transfer from the side-chain oxygen atom to the ring seems unlikely since such a process should occur less readily for the alcohol than its methyl ether and would be unfavourable in both cases (*cf.* ionisation potentials[34] for toluene, diethyl ether and ethanol of 8.82, 9.53, and 10.48 eV, respectively). The failure of 4-phenylbutan-1-ol to afford the radical (**19**) also shows that the rate of ring-closure is retarded by increasing the length of the side-chain.



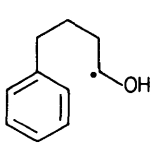
(**16**)



(**17**)

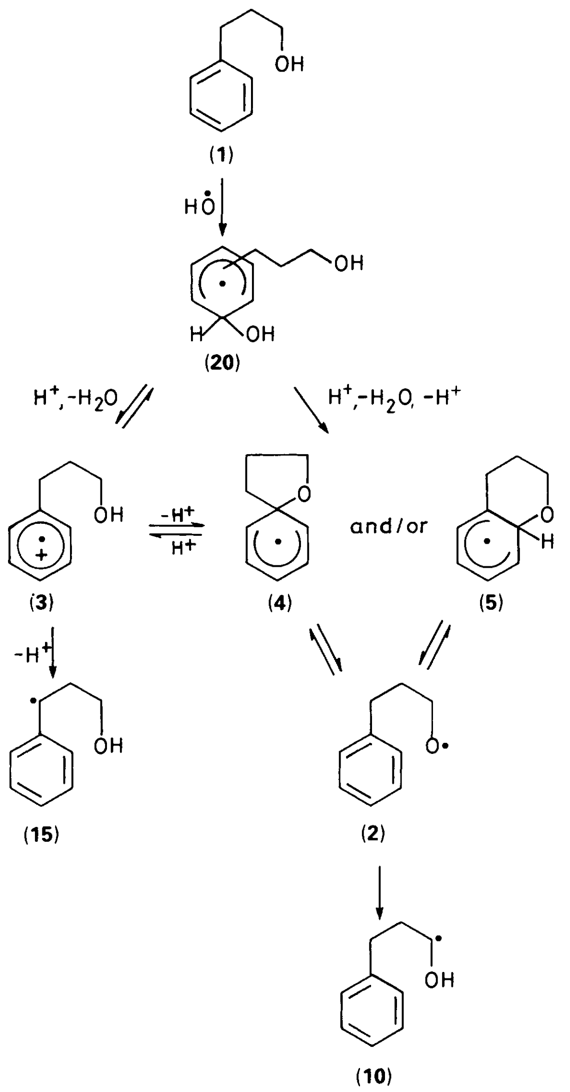


(**18**)



(**19**)

The replacement of the radical (**10**) with that of the benzylic radical (**15**) at lower pH may reflect a reduction in the nucleophilicity of the side-chain hydroxy group as a result of



Scheme 3.

protonation, permitting the competing benzylic deprotonation process to dominate cyclisation of the radical cation (**3**). However, it seems more likely that this pH effect reflects the onset of acid-catalysed ring-opening of (**4**) and/or (**5**) to the radical cation (**3**) which affords radical (**15**).

Experimental

Reagents and solvents were commercially available. 3-Phenylpropyl hydroperoxide was synthesized according to the method of Mosher and Williams[35] and its aqueous solution standardised iodometrically. Authentic materials used in g.l.c. analyses were synthesized by standard procedures and were satisfactorily characterised.

Product Studies.—Reactions were conducted according to the general procedures outlined below. G.l.c. analyses were carried out on a Pye GCD gas chromatograph equipped with 2 m × 4 mm columns containing either 10% Carbowax 20M on Celite or 3% OV-225 on Gaschrom Q. G.c./m.s. analyses were performed on an AEI MS 30 mass spectrometer equipped with a DS-55 data system and a Pye Unicam 104 gas chromatograph.

(a) *Reaction of* 3-*phenylpropyl hydroperoxide.* An aqueous solution of titanium(III) chloride or iron(II) sulphate (typically 0.008 mol dm^{-3}) was added dropwise to a stirred aqueous or 50% aqueous acetonitrile solution of 3-phenylpropyl hydroperoxide (typically 0.006 mol dm^{-3}, 25 cm^3) under a nitrogen atmosphere. Where appropriate, copper(II) sulphate, disodium ethylenediaminetetra-acetate and ammonia were added to the peroxide solution immediately before addition of the titanium(III) or iron(II) solutions. After 3 h of stirring at room temperature, water was added and the solution extracted with dichloromethane. The combined extracts were dried (anhydrous sodium sulphate) before being carefully concentrated in a rotary evaporator. The products were identified by g.l.c. and g.c./m.s. by comparison with authentic materials and reference spectra where available, and quantified by g.l.c. using an internal standard (methyl benzoate). Molar ratios of reactants used and results obtained are summarised in Table 1.

(b) *Reaction of* 3-*phenylpropan*-1-*ol* (**1**). (*i*) With $SO_4^{-\bullet}$. An aqueous solution of potassium peroxydisulphate (0.05 mol dm^{-3}) was added dropwise to a stirred, refluxing aqueous or 30% aqueous acetonitrile solution of 3-phenylpropan-1-ol (**1**) (typically 0.2 mol dm^{-3}; 50 cm^3) containing copper(II) sulphate or potassium ferricyanide where appropriate. Alternatively, an aqueous solution of iron(II) sulphate (typically 0.25 mol dm^{-3}) was added dropwise to a stirred aqueous or 30% aqueous acetonitrile solution of alcohol (**1**) (typically 0.17 mol dm^{-3}, 60 cm^3) containing potassium peroxydisulphate and copper(II) sulphate at room temperature. In the case of inverse additions, a potassium peroxydisulphate solution was added dropwise to a mixture of the other reactants at room temperature. After 3 h the solutions were cooled if necessary, worked up and analysed as described above. Molar ratios of reactants used and results obtained are listed in Table 2. Selected reactions were repeated under a nitrogen atmosphere, but no significant differences in the products or their yields were observed.

(*ii*) With Ag^{II}. An aqueous solution of potassium peroxydisulphate (0.05 mol dm^{-3}) was added dropwise under a nitrogen atmosphere to a stirred 30% aqueous acetonitrile solution of 3-phenylpropan-1-ol (**1**) (0.17 mol dm^{-3}, 60 cm^3) containing silver(I) nitrate and where appropriate, copper(II) sulphate. After 3 h the reaction mixture was worked up and analysed as described above. Molar ratios of reactants used and the results obtained are summarised in Table 3.

(*iii*) With $HO^\bullet$. An aqueous solution of titanium(III) chloride (0.05 mol dm^{-3}; 45 cm^3) was added dropwise to a stirred aqueous solution (50 cm^3) of 3-phenylpropan-1-ol (**1**) (0.04 mol dm^{-3}) containing hydrogen peroxide (0.44 mol dm^{-3}). After 3 h the reaction was worked up and analysed as described above to give unchanged starting alcohol (67%), 3,4-dihydro-2*H*-1-benzopyran (**7**) (5%) and 3-phenylpropanal (**12**) (2%).

When the reaction was repeated in the presence of copper(II) sulphate (0.0021 mol) in the alcohol solution, the yields determined for the above compounds were 85, 1, and 1%, respectively (all yields were based on the starting alcohol).

E.S.R. Studies.—E.s.r. spectra were recorded with a Varian E-104 spectrometer equipped with 100 kHz modulation and an X-band klystron. Splitting constants were measured to within ±0.005 mT and *g*-factors to within ±0.0001 by comparison with an aqueous solution of Fremy's salt [*a*(N) 1.3091 mT,[36] *g* 2.0055 [37]] and are recorded in Table 4. Spectrum analysis was verified by computer simulation on a DEC system KL-10 computer using a program supplied by Dr. M. F. Chiu and also on an Olivetti M24 micro-computer using a modified version of the above program.

(i) *The* $S_2O_8^{2-}$-*photolysis system.* The flow-photolysis experiments were carried out using a typical flattened aqueous solution sample cell with a built-in two-way mixer through which the solutions were forced using a Watson–Marlow

MHRE flow inducer (effluent flow rate *ca.* 4 cm^3 min^{-1}). The cell was irradiated in the cavity of the spectrometer using the unfiltered output of an Hanovia 977B-1 1 kW mercury–xenon compact arc. The two streams typically contained sodium peroxydisulphate (0.2 mol dm^{-3} with variable quantities of propanone added) and the substrate (0.05 mol dm^{-3}), respectively. pH adjustment was made by adding concentrated sulphuric acid to the peroxydisulphate stream.

The rapid-flow experiments with redox couples were conducted using a Watson–Marlow 5025 flow inducer positioned on the inlet tubing of a mixing chamber which allowed the simultaneous mixing of two aqueous reactant streams *ca.* 50 ms before passage through the cavity of the spectrometer. Solutions mixed were as follows:

(ii) *The* Ti^{III}–H_2O_2 *system* ($\text{HO}^\bullet$). The first stream contained the substrate (0.05 mol dm^{-3} or saturated), titanium(III) chloride (0.008 mol dm^{-3}), disodium ethylenediaminetetra-acetate (6 g dm^{-3}), and sufficient concentrated sulphuric acid or ammonia solution (*d* 0.880) to achieve the required pH after mixing and the second stream a mixture of the substrate (0.05 mol dm^{-3} or saturated) and hydrogen peroxide (0.035 mol dm^{-3}). No advantage was gained from using a three-stream system in which the substrate was introduced into the mixing chamber separate from the titanium(III) and hydrogen peroxide.

(iii) *The* Ti^{III}–$\text{S}_2\text{O}_8^{2-}$ *system* ($\text{SO}_4^{-\bullet}$). The first stream contained a mixture of the substrate (0.05 mol dm^{-3}), titanium(III) chloride (0.01 mol dm^{-3}), disodium ethylenediaminetetra-acetate (6 g dm^{-3}) and sufficient sulphuric acid or ammonia solution (*d* 0.880) to achieve the required pH after mixing and the second stream a mixture of the substrate (0.05 mol dm^{-3}) and potassium peroxydisulphate (0.025 mol dm^{-3}).

The disodium ethylenediaminetetra-acetate was omitted from most experiments conducted at pH <2. pH measurements in both the flow and photolysis experiments were made using a Pye–Unicam PW 9410 pH meter with the electrode inserted into the effluent stream. All solutions were degassed before use by being purged with oxygen-free nitrogen.

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