

Electron Spin Resonance Studies. Part L. Reactions of Alkoxy Radicals generated from Alkyl Hydroperoxides and Titanium(III) Ion in Aqueous Solution

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A variety of alkoxy radicals has been generated in aqueous solution by the one-electron reduction of alkyl hydroperoxides by titanium(III) ion, and their behaviour has been studied by e.s.r. spectroscopy in conjunction with a rapid-flow system. Although the alkoxy radicals themselves are not directly detectable by e.s.r., both the adducts which they form with the spin-trap $\text{CH}_2\text{:NO}_2^-$ and the carbon-centred radicals into which they are transformed can be monitored; in this way, a novel 1,2-shift [*e.g.* $\text{PrO}\cdot \rightarrow \cdot\text{CH}(\text{OH})\text{Et}$], as well as intramolecular 1,5-hydrogen transfer, intramolecular addition to an olefinic bond, and fragmentation, have been demonstrated. Estimates have been obtained for the rate constants for some of these processes (*e.g.* that for the 1,2-shift mentioned is *ca.* 10^7 s^{-1}), and the behaviour of alkoxy radicals in aqueous and non-aqueous media has been compared.

In the preceding papers,^{1,2} we reported e.s.r. results which showed that the hydroxyl radical reacts with di-

¹ Part II, A. J. Dobbs, B. C. Gilbert, H. A. H. Laue, and R. O. C. Norman, preceding paper.

alkyl sulphites and some substituted oxirans in aqueous solution to yield 1-hydroxyalkyl and 1-hydroxyallyl

² B. C. Gilbert, H. A. H. Laue, R. O. C. Norman, and R. C. Sealy, *J.C.S. Perkin II*, 1976, 1040.

radicals, respectively. We concluded that the immediate precursors of these species are the isomeric alkoxy and allyloxy radicals, and obtained evidence for the mediation of these oxy radicals from spin-trapping experiments. Berdnikov *et al.* have also obtained evidence that the ethoxy radical, generated from the corresponding hydroperoxide and titanium(III) ion, isomerises to the 1-hydroxyethyl radical.³

1,2-Hydrogen-atom shifts in alkoxy radicals have not been observed in non-aqueous solution, and indeed both experiment and theory are inconsistent with their occurrence.⁴ We therefore chose to probe further the suggested alkoxy-hydroxyalkyl rearrangement, and to study other reactions of alkoxy radicals which might compete with their isomerisation, by studying the reactions of a series of hydroperoxides with Ti^{III} , using e.s.r. spectroscopy.

RESULTS AND DISCUSSION

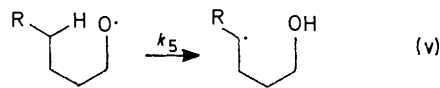
Reactions were carried out at room temperature by mixing aqueous solutions of the hydroperoxide and titanium(III) chloride *ca.* 0.05 s before the combined solution entered the cavity of the e.s.r. spectrometer. Reactions were also carried out in the presence of the *aci*-anion of nitromethane as a spin-trap.^{1,2}

Propyl Hydroperoxide.—When this compound was reduced by Ti^{III} at either low pH (*ca.* 1.5) or high pH (*ca.* 8), only the spectrum of the 1-hydroxypropyl radical⁵ was observed. We first considered the possibility that this was formed by the reaction of either the propoxy radical [from reaction (i; $R = Et$)] or the hydroxyl radical (from Ti^{III} with adventitious hydrogen peroxide) with the propanol that could be formed by reduction of propyl hydroperoxide. However, when the experiment in acid solution was repeated in the presence of ethanol, at the same concentration as propyl hydroperoxide, the signal from $\cdot CH(OH)Et$ remained unaltered and no more than a trace of a signal from the radical $\cdot CH(OH)Me$ could be detected. Since the methylene groups in ethanol and propanol are likely to be of closely similar reactivity towards an oxygen-centred radical, we infer that hydrogen-atom abstraction from any propanol which might be formed is not important under these conditions. Further, when propanol is oxidised with hydroxyl, other carbon-centred radicals in addition to $\cdot CH(OH)Et$ are detected.⁵ We therefore suggest that the 1-hydroxypropyl radical is formed by isomerisation of the propoxy radical [reaction (ii; $R = Et$)], and support for this was obtained by our finding that, when nitromethane was included in the reaction of propyl hydroperoxide with Ti^{III} at high pH, not only was the adduct⁶ of the radical $\cdot CH(OH)Et$ with $CH_2:NO_2^-$ detected but also a spectrum was obtained which is assigned to the adduct $PrOCH_2NO_2^-$ (Table 2; *cf.* refs. 1 and 2); and when $[CH_2:NO_2^-]$ was increased, the observed concentration of $PrOCH_2NO_2^-$ relative to that of

$EtCH(OH)CH_2NO_2^-$ increased. These observations are consistent with the occurrence of reactions (i)—(iv) ($R = Et$).



Butyl Hydroperoxide.—As compared with $PrO\cdot$, the butyloxy radical has a possible additional mode of reaction available to it, namely the 1,5-hydrogen atom transfer shown in reaction (v; $R = H$). Reaction of butyl hydroperoxide with titanium(III) at pH *ca.* 1, 2, or 8 gave both $\cdot CH(OH)Pr$ and $\cdot CH_2(CH_2)_2CH_2OH$ (Table 1); the spectra were assigned on the basis of the similarities of their hyperfine splittings to those of 1-hydroxyalkyl⁵ and alkyl radicals,⁷ respectively, the higher *g*-factor of the former species (Δg 0.000 6), and their likely modes of formation [reactions (ii; $R = Pr$) and (v; $R = H$), respectively]. The radicals were present in approximately equal concentration at each pH. Moreover, the relative concentrations were unaltered when reaction in acid solution was carried out in the presence of the same concentrations of butanol as of butyl hydroperoxide, indicating that the radical $\cdot CH(OH)Pr$ does not originate from the butanol which may be formed from the hydroperoxide.



When reduction was carried out in the presence of $CH_2:NO_2^-$, three radicals originating from the hydroperoxide were trapped (Table 2); assignments to $BuO\cdot$, $\cdot CH(OH)Pr$, and $\cdot CH_2(CH_2)_2CH_2OH$ are based on the splittings of the corresponding spin-adducts compared with those of related species.^{2,6}

Hexyl Hydroperoxide.—Reduction with titanium(III) gave only one radical in detectable concentration; the parameters clearly characterise a secondary alkyl radical, assigned the structure $\cdot CHEt(CH_2)_2CH_2OH$ in view of its likely mode of formation [reaction (v; $R = Et$)].

Reaction in the presence of $CH_2:NO_2^-$ gave only one radical from the hydroperoxide, evidently the adduct $HOCH_2(CH_2)_2CHEtCH_2NO_2^-$. It is to be noted that the magnetic inequivalence of the nitro-bonded methylene protons which is to be expected from the presence of the adjacent chiral carbon atom⁶ is insufficient to give detectably different proton splittings.

Pent-4-enyl Hydroperoxide.—Only one radical was detected from the hydroperoxide, in either absence or presence of the trap. That observed under the former

⁵ H. Zeldes and R. Livingston, *J. Chem. Phys.*, 1966, **44**, 1245.

⁶ B. C. Gilbert, J. P. Larkin, and R. O. C. Norman, *J.C.S. Perkin II*, 1972, 1272.

⁷ R. W. Fessenden and R. H. Schuler, *J. Chem. Phys.*, 1963, **39**, 2147.

³ V. M. Berdnikov, N. M. Bazhin, V. K. Fedorov, and O. V. Polyakov, *Kinetika i Kataliz*, 1972, **13**, 1093.

⁴ See, e.g., C. Walling, in 'Molecular Rearrangements,' ed. P. de Mayo, Interscience, vol. 1, 1963, pp. 418, 427.

conditions is assigned the structure (1) on the basis of the similarity of $a(\alpha\text{-H})$ and g to those of other alkyl radicals⁷ and its expected mode of formation [reaction (vi)].* The trapped radical is assigned structure (2); it is notable that there is a small difference in $a(\text{H})$ between the two

species $\cdot\text{CH}(\text{OH})\text{CH}_2\text{CH}_2\text{Ph}$. In the presence of $\text{CH}_2\cdot\text{NO}_2^-$, there was evidence not only for the trapping of this radical but also for the trapping of $\text{Ph}(\text{CH}_2)_3\text{O}\cdot$. Evidently, under our conditions, the cyclisation in reaction (vii) is not fast enough to compete effectively with

TABLE 1
Radicals from alkyl hydroperoxides with titanium(III)
Hyperfine splittings/mT

R in RO_2H	Radical	Hyperfine splittings/mT			g
		$a(\alpha\text{-H})$	$a(\beta\text{-H})$	$a(\text{other})$	
Pr	$\cdot\text{CH}(\text{OH})\text{Et}$	1.47 (1 H)	2.12 (2 H)		2.003 3
Bu	$\cdot\text{CH}(\text{OH})\text{Pr}$	1.50 (1 H)	1.95 (2 H)	0.05 (2 H)	Δg 0.000 6
	$\cdot\text{CH}_2(\text{CH}_2)_2\text{CH}_2\text{OH}$	2.18 (2 H)	2.81 (2 H)		
Hex	$\cdot\text{CHEt}(\text{CH}_2)_2\text{CH}_2\text{OH}$	2.09 (1 H)	2.50 (4 H)		2.002 7
$\text{CH}_2\cdot\text{CH}(\text{CH}_2)_2\text{CH}_2$	(1)	2.19 (2 H)	1.85 (1 H)		2.002 5
$\text{Me}(\text{CH}_2)_3\text{CMe}_2$	$\cdot\text{CHMe}(\text{CH}_2)_2\text{CMe}_2(\text{OH})$	2.10 (1 H)	2.50 (5 H)		
	$\cdot\text{CH}_2(\text{CH}_2)_2\text{Me}$	2.19 (1 H)	2.81 (2 H)		
$\text{Ph}(\text{CH}_2)_2\text{CH}_2$	$\cdot\text{CH}(\text{OH})(\text{CH}_2)_2\text{Ph}$	1.57 (1 H)	1.94 (2 H)		

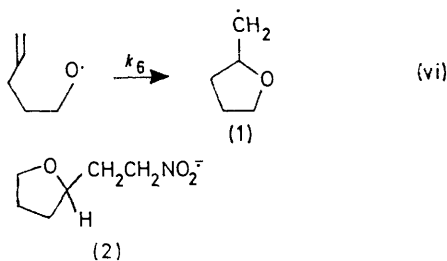
TABLE 2
Radicals a formed in the presence of $\text{CH}_2\cdot\text{NO}_2^-$
Hyperfine splittings/mT

R in RO_2H	R' in $\text{R}'\text{CH}_2\text{NO}_2^-$	Hyperfine splittings/mT		
		$a(1\text{ N})$	$a(2\text{ H})^b$	$a(\text{other})$
Pr	$\{\text{PrO}$	2.38	0.85	
	$\{\text{CH}(\text{OH})\text{Et}$	2.52	1.15, 0.93	0.06 (1 H)
	$\{\text{BuO}$	2.38	0.85	
Bu	$\{\text{CH}(\text{OH})\text{Pr}^d$	2.48	1.22, 0.96	0.05 (1 H)
	$\{\text{CH}_2(\text{CH}_2)_2\text{CH}_2\text{OH}^d$	2.51	1.03	0.05 (2 H)
	$\{\text{CHEt}(\text{CH}_2)_2\text{CH}_2\text{OH}$	2.50	1.06	0.06 (1 H)
Hex	(1)	2.56	1.06, 0.94 ^c	0.06 (2 H)
$\text{CH}_2\cdot\text{CH}(\text{CH}_2)_2\text{CH}_2$	$\{\text{CHMe}(\text{CH}_2)_2\text{CMe}_2(\text{OH})$	2.46	1.01, 0.93	0.06 (1 H)
	$\{\text{CH}_2(\text{CH}_2)_2\text{Me}$	2.46	1.00	0.06 (2 H)
$\text{Me}(\text{CH}_2)_3\text{CMe}_2$	$\{\text{Ph}(\text{CH}_2)_3\text{O}$	2.39	0.84	
	$\{\text{CH}(\text{OH})(\text{CH}_2)_2\text{Ph}$	2.50	1.18, 0.88	0.05 (1 H)

^a g 2.005 0 in each case. ^b Where two values are given, the methylene protons are magnetically inequivalent owing to the chirality of the adjacent (or ^c nearby) carbon atom. ^d The parameters are approximate owing to overlapping spectra.

nitro-bonded methylene protons (β) which is doubtless related to the presence of the next-but-one chiral carbon atom (however, the splitting from the γ -protons is evidently too small for their expected magnetic inequivalence to be resolved).

3-Phenylpropyl Hydroperoxide.—Photolysis of a mixture of 3-phenylpropan-1-ol and lead tetra-acetate in benzene gives, amongst other products, compound (5),

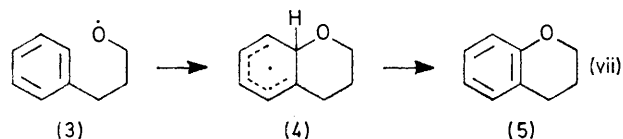


which is presumed to arise by way of reaction (vii).⁹ However, there was no evidence for radical (4) when 3-phenylpropyl hydroperoxide was reduced with titanium(III) ion in aqueous solution. Only a weak spectrum (probably owing to the low solubility of the hydroperoxide) was observed; it is tentatively assigned to the

* In non-aqueous solution, the pent-4-enyloxy radical has been shown to cyclise to give exclusively 5-membered ring products.⁸

⁸ R. D. Rieke and N. A. Moore, *Tetrahedron Letters*, 1969, 2035.

the addition of radical (3) to $\text{CH}_2\cdot\text{NO}_2^-$ or its isomerisation to the 1-hydroxyalkyl radical.



***t*-Butyl Hydroperoxide.**—Reduction with titanium(III) ion under our condition gives the methyl radical as the only detectable species.¹⁰ In the hope of trapping its precursor, $\text{Bu}^t\text{O}\cdot$, we carried out the reaction in the presence of $\text{CH}_2\cdot\text{NO}_2^-$; however, even with 0.2M- MeNO_2 , only the species $\text{MeCH}_2\text{NO}_2^-$ could be detected.

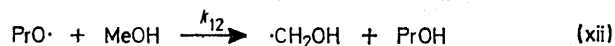
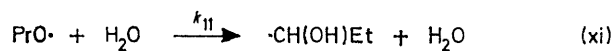
2-Hexyl-2-methyl Hydroperoxide. Reduction with titanium(III) gave the spectra of two radicals which are assigned, following the principles described above, to the radicals (6) and (7), which are expected from the intramolecular hydrogen-atom abstraction (viii) and the fragmentation (ix), respectively. Their observed concentrations were approximately equal, so that the result supports that of an independent study which showed that products presumably derived from radicals (6) and (7) were formed in 44 and 39% yield, respectively.¹¹

⁹ M. Lj. Mihailovic, L. Zivkovic, Z. Maksimovic, D. Jeremic, Z. Cekovic, and R. Matic, *Tetrahedron*, 1967, 23, 3095.

¹⁰ W. T. Dixon and R. O. C. Norman, *J. Chem. Soc.*, 1963, 3119.

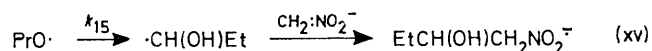
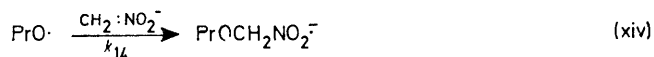
¹¹ B. Acott and A. L. J. Beckwith, *Austral. J. Chem.*, 1964, 17, 1342.

steady-state conditions should apply to the short-lived radicals $\cdot\text{CH}_2\text{OH}$ and $\cdot\text{CH}(\text{OH})\text{Et}$,¹³ and the bimolecular termination rate constants for these two species should be approximately equal,¹⁶ it can be shown that equation (xiii) should hold. In accord with this, we found that $[\cdot\text{CH}_2\text{OH}]/[\cdot\text{CH}(\text{OH})\text{Et}]$ varied with $[\text{MeOH}]/[\text{H}_2\text{O}]$ in a linear manner (Figure 2). Taking k_{12} as $2.6 \times 10^5 \text{ l mol}^{-1} \text{ s}^{-1}$ (the value obtained by pulse radiolysis for $\text{MeO}\cdot + \text{MeOH} \rightarrow \text{MeOH} + \cdot\text{CH}_2\text{OH}$ in methanol¹⁷), then the gradient from Figure 2 gives $k_{11} = 1.4 \times 10^5 \text{ l mol}^{-1} \text{ s}^{-1}$. If the rate constant does not vary significantly with solvent composition (there is no sign that it does so, as judged by the linearity of Figure 2, over the range of methanol-water mixtures examined), then the pseudo-first-order rate constant for the isomerisation, $\text{PrO}\cdot \rightarrow \cdot\text{CH}(\text{OH})\text{Et}$, in pure water should be $k_{11}[55.5\text{M}] = 8 \times 10^6 \text{ s}^{-1}$.



$$[\cdot\text{CH}_2\text{OH}] / [\cdot\text{CH}(\text{OH})\text{Et}] = k_{12}[\text{MeOH}] / k_{11}[\text{H}_2\text{O}] \quad (\text{xiii})$$

It was not possible to evaluate the rate constant for the addition of $\text{PrO}\cdot$ to $\text{CH}_2\cdot\text{NO}_2^-$ accurately owing to the fact that, in addition to the species $\text{PrOCH}_2\text{NO}_2^-$ and $\text{EtCH}(\text{OH})\text{CH}_2\text{NO}_2^-$, MeNO_2^- was also formed; this may be derived at least in part from the one-electron reducing species $\cdot\text{CH}(\text{OH})\text{Et}$. However, the ratio $[\text{PrOCH}_2\text{NO}_2^-]/[\text{EtCH}(\text{OH})\text{CH}_2\text{NO}_2^-]$ was found to vary with $[\text{MeNO}_2^-]$ at a given pH in an approximately linear manner, as expected for competition between reactions (xiv) and (xv) [equation (xvi)]; the termination rate constants for these two radical-anions are likely to be closely similar]. Use of a buffered solution (pH 8.2) so that $[\text{CH}_2\cdot\text{NO}_2^-]$ could be determined (nitromethane has¹⁸ $\text{p}K_a$ 10.2) and measurement of the concentration ratio for these species indicated that $k_{14} > 10^8 \text{ l mol}^{-1} \text{ s}^{-1}$.



$$[\text{PrOCH}_2\text{NO}_2^-] / [\text{EtCH}(\text{OH})\text{CH}_2\text{NO}_2^-] = k_{14}[\text{CH}_2\cdot\text{NO}_2^-] / k_{15} \quad (\text{xvi})$$

We can also compare the rate constants for the isomerisation of $\text{PrO}\cdot$ to $\cdot\text{CH}(\text{OH})\text{Et}$ with those of some other intramolecular reactions. On the assumption that the rate of the isomerisation $\text{BuO}\cdot \rightarrow \cdot\text{CH}(\text{OH})\text{Pr}$ will not be significantly different from that for $\text{PrO}\cdot \rightarrow \cdot\text{CH}(\text{OH})\text{Et}$, and that the radicals $\cdot\text{CH}(\text{OH})\text{Pr}$ and $\cdot\text{CH}_2(\text{CH}_2)_2\text{CH}_2\text{OH}$ undergo bimolecular termination at

¹⁶ M. Simic, P. Neta, and E. Hayon, *J. Phys. Chem.*, 1969, **73**, 3794.

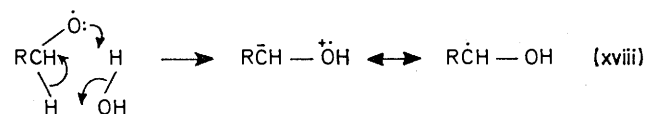
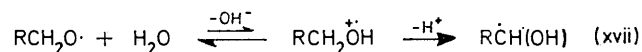
¹⁷ D. H. Ellison, G. A. Salmon, and F. Wilkinson, *Proc. Roy. Soc.*, 1972, **A**, 323, 23.

¹⁸ A. Albert and E. P. Serjeant, 'Ionisation constants of acids and bases,' Methuen, London, 1962.

approximately the same rate,¹⁶ then the observation that butyl hydroperoxide gives about equal concentrations of $\cdot\text{CH}(\text{OH})\text{Pr}$ and $\cdot\text{CH}_2(\text{CH}_2)_2\text{CH}_2\text{OH}$ indicates that k_5 ($\text{R} = \text{H}$) is *ca.* $8 \times 10^6 \text{ s}^{-1}$. In contrast, only the radical $\cdot\text{CH}(\text{OH})(\text{CH}_2)_2\text{CH}_2\text{OH}$ was detected from hexyl hydroperoxide [indicating a concentration at least 20-fold greater than that of the radical, $\cdot\text{CH}(\text{OH})(\text{CH}_2)_3\text{Me}$, which would result from 1,2-isomerisation], and only the former radical was trapped; we infer that $k_5(\text{R} = \text{Et}) > 10^8 \text{ l mol}^{-1} \text{ s}^{-1}$. Likewise, the rate constant for the intramolecular addition (vi) is evidently $> 10^8 \text{ l mol}^{-1} \text{ s}^{-1}$.

The behaviour of alkoxy radicals in aqueous and non-aqueous media can be contrasted in two respects. First, our results show that, in aqueous solution, the t-alkoxy radical, $\text{BuMe}_2\text{CO}\cdot$, fragments approximately as rapidly as it undergoes a 1,5-hydrogen atom shift, whereas in cyclohexane the relative ease of these two reactions (k_9/k_8) is *ca.* 2:81.¹⁹ Huyser has concluded that solvation of an alkoxy radical affects its rate of fragmentation more than that of abstractions.²⁰

Secondly, it is clear that the isomerisation (ii) is facilitated in water. We could find no evidence for acid catalysis; thus, butyl hydroperoxide yielded the radicals which result from the isomerisation (ii; $\text{R} = \text{Pr}$) and the 1,5-hydrogen transfer (v) in approximately equal concentrations at pH 1, 2, and 8, and since it is unlikely that the latter reaction is catalysed by acid (or, if so, would show the same dependence as the former), we infer that acid catalysis of the isomerisation (ii) does not significantly, or at all, enhance its rate. Two possible mechanisms for the isomerisation, which differ essentially only in the timing of events, are in reactions (xvii) and



(xviii). Overall, the reaction is analogous to the transformation of alkylamino into α -aminoalkyl radicals which occurs in aqueous solution.²¹

EXPERIMENTAL

Materials.—The primary hydroperoxides were prepared by the general procedure of Williams and Mosher.²² 1,1-Dimethylpentyl hydroperoxide was prepared from the corresponding alcohol.¹¹ All other materials were obtained commercially and were used without further purification.

Methods.—The e.s.r. spectrometer, flow system,⁸ and method for the determination of spectral parameters² have been described. One reagent stream contained 0.01M-titanium(III) chloride and the other contained the hydroperoxide (*ca.* 0.05M, or a saturated solution if the solubility was

¹⁹ C. Walling and A. Padwa, *J. Amer. Chem. Soc.*, 1963, **85**, 1597.

²⁰ E. S. Huyser, *Adv. Free-Radical Chem.*, 1965, **1**, 77.

²¹ N. H. Anderson and R. O. C. Norman, *J. Chem. Soc. (B)*, 1971, 993.

²² H. R. Williams and H. S. Mosher, *J. Amer. Chem. Soc.*, 1954, **76**, 2984.

lower). For reactions at pH 1—2, each solution was acidified with concentrated sulphuric acid (usually *ca.* 2 ml l⁻¹); for those at pH > 8, EDTA (*ca.* 4 g l⁻¹) and concentrated ammonia (*ca.* 4 ml l⁻¹) were included in the titanium(III) solution and concentrated ammonia (*ca.* 8 ml l⁻¹) was included in the hydroperoxide solution. For the spin-trapping experiments, nitromethane (1—6 ml l⁻¹) was added to the hydroperoxide stream and the pH was adjusted to > 8 as above.

Kinetic studies of the reactions of propyl hydroperoxide in the presence of methanol were carried out at pH > 2. Methanol was contained in equal concentration in each

stream, the reported molarity (see Figure 2) being that after mixing. For the study with the nitromethane *aci*-anion, each solution contained a borate buffer to give pH 8.2 after mixing, and the propyl hydroperoxide stream contained nitromethane (2 ml l⁻¹). Relative concentrations of radicals were obtained by double integration of selected peaks.

All solutions were thoroughly purged with nitrogen before flowing.

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