

Formation and Fragmentation of Alkoxy Radicals by Oxidation of Alcohols with Peroxydisulphate Ion

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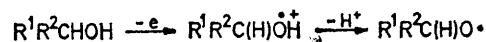
E.s.r. and product studies show that alkoxy radicals are produced by the thermal, photochemical, and silver(I) catalysed oxidation of alcohols by peroxydisulphate ion. With 2-phenylethanol and related alcohols the corresponding alkoxy radicals undergo fragmentation to benzyl radicals and the appropriate carbonyl compound. The results indicate new synthetic utility for the peroxydisulphate ion.

IN previous^{1,2} publications we have shown the importance of alkoxy radicals during the oxidation of simple aliphatic alcohols by various reagents including photoactivated paraquat ion and peroxydisulphate ion $S_2O_8^{2-}$. The alkoxy radicals result from electron-transfer mechanisms and in the paraquat experiments confirm other experimental findings.³ However, the recognition that peroxydisulphate ion oxidises alcohols by an electron-transfer route suggests new utility of this reagent, which is exemplified here by a study of the peroxydisulphate oxidation of 2-phenylethanol and related alcohols.

RESULTS AND DISCUSSION

Oxidation of an alcohol R^1R^2CHOH by an electron transfer mechanism leads to formation of the corresponding alkoxy radical (Scheme 1). With simple primary and secondary alcohols the initially-formed alkoxy

radical rapidly interconverts to its thermodynamically more stable isomer $R^1R^2\dot{C}OH$, thus explaining the difficulty in establishing alkoxy radicals as intermediates in alcohol oxidation processes.²



SCHEME 1

However, the 2-phenylethoxy radical is known to fragment into formaldehyde and a benzyl radical,^{4,5} $PhCH_2CH_2O\cdot \rightarrow PhCH_2\cdot + CH_2O$; thus oxidation of 2-phenylethanol by peroxydisulphate might well be expected to produce benzyl radicals which can subsequently dimerise or be further oxidised to benzyl alcohol and benzaldehyde (Scheme 2).

Indeed Norman and collaborators have shown⁶ (using a $Ti^{III}-S_2O_8^{2-}$ couple at pH 1) that the sulphate radical anion does produce benzyl radicals from 2-phenyl-

¹ A. Ledwith, P. J. Russell, and L. H. Sutcliffe, *Chem. Comm.*, 1971, 964.

² A. Ledwith, P. J. Russell, and L. H. Sutcliffe, *Proc. Roy. Soc.*, in the press.

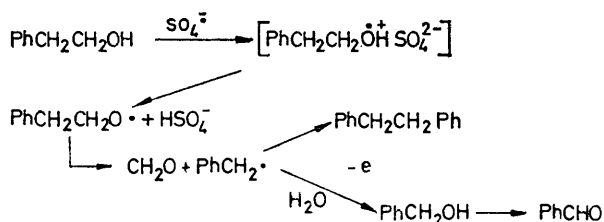
³ A. S. Hopkins, A. Ledwith, and M. F. Stam, *Chem. Comm.*, 1970, 494; A. Ledwith, *Accounts Chem. Res.*, 1972, **5**, 133.

⁴ P. Kabasakalian, E. R. Townley, and M. D. Yudis, *J. Amer. Chem. Soc.*, 1962, **84**, 2716.

⁵ J. K. Kochi, *J. Amer. Chem. Soc.*, 1962, **84**, 1193; C. Walling and A. Padwa, *J. Amer. Chem. Soc.*, 1963, **85**, 1593.

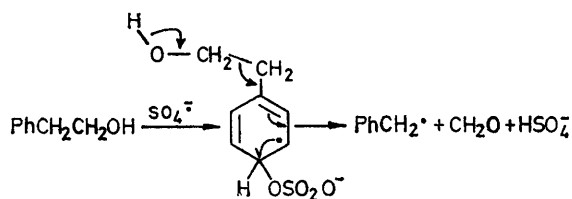
⁶ (a) R. O. C. Norman, P. M. Storey, and P. R. West, *J. Chem. Soc. (B)*, 1970, 1087; (b) R. O. C. Norman and P. M. Storey, *ibid.*, p. 1099.

ethanol and bibenzyl is obtained in 18% yield, together with formaldehyde and traces of benzyl alcohol and benzaldehyde. However, in contrast to our anticipated



SCHEME 2

mechanism (Scheme 2) these workers suggested the addition-elimination sequence (Scheme 3) based largely on the analogy with the reaction of SO_4^{2-} with phenylacetic acid.

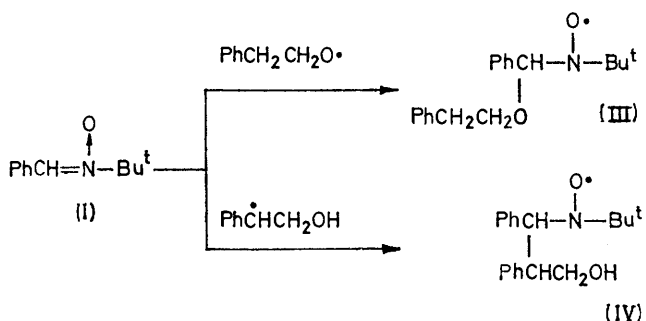


SCHEME 3

The present results, while not excluding Scheme 3, do give positive support for the mechanism depicted in Scheme 2. They also illustrate the use of a radical-trapping technique during oxidative cleavage reactions.

A. Radical-trapping Studies.—Using a radical-scavenging (spin-trapping) technique⁷ previously described,² we have identified the radicals formed by oxidation of 2-phenylethanol and related alcohols under a variety of reaction conditions. The spin traps employed in this work were benzylidene-*t*-butylamine *N*-oxide (I) and 2-methyl-2-nitrosopropane (II).

(i) *Oxidation of 2-phenylethanol.* Table 1 summarises the principal results obtained with the *N*-oxide (I), which is a powerful scavenger of both oxygen- and



SCHEME 4

carbon-centred radicals, producing in this case the stable nitroxide radicals (III) or (IV) (Scheme 4).

⁷ For reviews see M. J. Perkins in 'Essays on Free-radical Chemistry,' Chem. Soc. Special Publ., No. 24, 1970, ch. 5; E. G. Janzen, *Accounts Chem. Res.*, 1971, **4**, 31; C. Lagercrantz, *J. Phys. Chem.*, 1971, **75**, 3466.

It is particularly significant that the *N*-oxide (I) traps 2-phenylethoxy radicals formed by oxidation of the alcohol with peroxydisulphate, activated by thermal, by photochemical, and by metal ion, particularly silver(I) catalysis. As with the simple aliphatic alcohols,² an

TABLE 1

Oxidation of 2-phenylethanol in the presence of *N*-oxide (I)^a

Oxidant; concentration; and conditions ^b	Nitroxide radical splittings		Radical trapped
	a_N/mT	$a_{\beta-H}/mT$	
$\text{K}_2\text{S}_2\text{O}_8$; 0.008M; Heat or u.v.	1.449	0.253	$\text{PhCH}_2\text{CH}_2\text{O}\cdot$
$\text{K}_2\text{S}_2\text{O}_8$; 0.006M; 0.002M- AgNO_3 , room temp.	1.448	0.256	$\text{PhCH}_2\text{CH}_2\text{O}\cdot$
Paraquat dichloride; 0.1M; U.v.	1.446	0.255	$\text{PhCH}_2\text{CH}_2\text{O}\cdot$
$\text{PhCH}_2\text{CH}_2\text{ONO}$; 0.5M; U.v.	1.448	0.248	$\text{PhCH}_2\text{CH}_2\text{O}\cdot$
Bu^tOOBu^t ; 0.5M; U.v.	1.536	0.356	$\text{Ph}\dot{\text{C}}\text{HCH}_2\text{OH}$
$\text{Bu}^t\text{ON}=\text{NOBu}^t$; 0.01M; Heat	1.532	0.354	$\text{Ph}\dot{\text{C}}\text{HCH}_2\text{OH}$
$\text{Ph}_2\text{C}=\text{O}$; 0.05M; U.v.	1.533	0.351	$\text{Ph}\dot{\text{C}}\text{HCH}_2\text{OH}$

^a Concentration of (I) 0.1–0.3M. ^b Experiments in 9:1 (v/v) alcohol-water mixtures. Similar results are obtained in lower ratios using acetonitrile as co-solvent. ^c In neat 2-phenylethanol.

intense signal of the alkoxy adduct [in this case (III)] was observed during the silver(I)-catalysed reaction at room temperature.

In a similar way the alkoxy radical was, as expected,³ shown to be an intermediate in the photochemical oxidation of 2-phenylethanol by paraquat dichloride (PQ^{2+} , 2Cl^-). But oxidation by *t*-butoxy radicals (generated by thermal and photochemical means) and by photoexcited benzophenone gave adducts of the carbon radical $\text{Ph}\dot{\text{C}}\text{HCH}_2\text{OH}$. Confirmation of the structure of nitroxide (III) was obtained by generating the latter by photolysis of 2-phenylethyl nitrite⁴ ($\text{PhCH}_2\text{CH}_2\text{ONO}$) in the presence of the *N*-oxide scavenger (see Table 1).

TABLE 2

Oxidation of 2-phenylethanol in the presence of 2-methyl-2-nitrosopropane^a

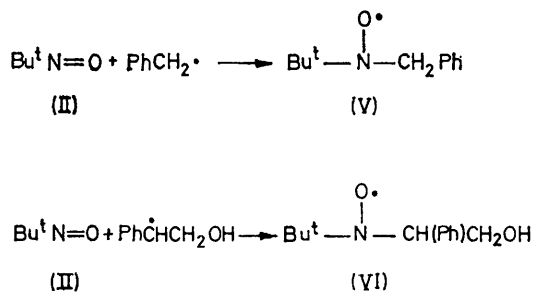
Oxidant; concentration; and conditions ^b	Nitroxide radical splittings		Radical trapped
	a_N/mT	$a_{\beta-H}/mT$	
$\text{K}_2\text{S}_2\text{O}_8$; 0.02M; Activated by either heat or metal-ion catalysis [$\text{Ag}(\text{I})$ or $\text{Fe}(\text{II})$ at room temp.]	(i) ^c 1.62	0.95(t)	$\text{PhCH}_2\cdot$
	(ii) 1.55	0.39(d)	$\text{Ph}\dot{\text{C}}\text{HCH}_2\text{OH}$
$\text{Bu}^t\text{ON}=\text{NOBu}^t$; 0.01M; Heat	(i) ^c 1.54	0.39(d)	$\text{Ph}\dot{\text{C}}\text{HCH}_2\text{OH}$
	(ii) 1.44	0.13(d)	$\text{PhCH}_2\dot{\text{C}}\text{HOH}$

^a Concentration ca. 0.01M. ^b Reactions in 1:1 (v/v) water-acetonitrile. ^c Predominant signal. d = Doublet, t = triplet.

The principal results obtained with 2-methyl-2-nitrosopropane (II) are summarised in Table 2. This nitroso-compound, whilst a very efficient scavenger of carbon-centred radicals, does not trap alkoxy radicals at ambient temperatures because the resulting nitroxides spontaneously dissociate. Hence, in effect, the nitroso-compound allows study of any subsequent reactions of

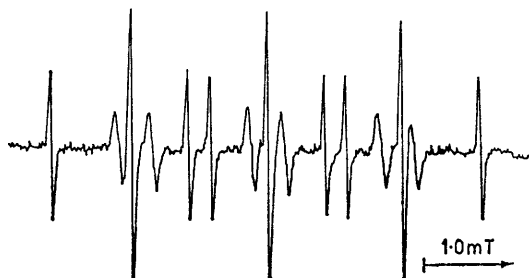
alkoxyl radicals. Recently Surzur and his co-workers⁸ have employed this method in studies of the intramolecular cyclisation of such radicals.

Having demonstrated the existence of 2-phenylethoxy radicals with *N*-oxide (I), the existence of benzyl radicals was now sought using the nitroso-scavenger. Addition of benzyl radicals to (II) forms the nitroxide adduct (V) (Scheme 5) which is readily recognised by the dis-



SCHEME 5

tinctive (1:1:1 triplet of 1:2:1 triplets) hyperfine splitting pattern (see Figure).



E.s.r. spectra of nitroxide (V) (triplet of 1:2:1 triplets) and nitroxide (VI) (triplet of 1:1 doublets) obtained during the peroxydisulphate oxidation of 2-phenylethanol in water-acetonitrile containing $\text{Bu}^t\text{N}=\text{O}$ at ca. 70°. Nitroxide (VI) is more stable than (V) at this temperature and hence its relative concentration increases with time

Both the thermal and metal-ion catalysed [silver(I) or iron(II)] decomposition of peroxydisulphate gave strong signals of (V) when 2-phenylethanol was oxidised in water-acetonitrile mixtures. Much weaker signals of nitroxide (VI) were also obtained in these experiments (see Figure), the identity of this nitroxide being established by hydrogen abstraction experiments with *t*-butoxyl radicals (see Table 2). Weak signals of both nitroxides were again produced when paraquat dichloride was photolysed in 2-phenylethanol solutions containing the nitroso-scavenger.

(ii) *Oxidation of related alcohols.* To support the results with 2-phenylethanol further, the peroxydisulphate ion oxidation of related alcohols 1-phenylpropan-2-ol, 1,2-diphenylethanol, and 2-methyl-1-phenylpropan-2-ol was studied. In each case fragmentation to benzyl radicals (trapped by 2-methyl-2-nitrosopropane) was observed during the uncatalysed and metal-ion catalysed peroxydisulphate oxidation of the alcohols in water-acetonitrile solution (Table 2).

⁸ P. Tordo, M. P. Bertrand, and J.-M. Surzur, *Tetrahedron Letters*, 1970, 3399.

With $\text{PhCH}_2\text{CH}(\text{OH})\text{Ph}$ and $\text{PhCH}_2\text{C}(\text{OH})\text{Me}_2$ only the benzyl adduct (V) was observed, whereas $\text{PhCH}_2\text{CH}(\text{OH})\text{Me}$ gave an additional weak signal very similar to (VI). This was established (by experiments with *t*-butoxyl radicals) to be the nitroxide $\text{Bu}^t\text{N}(\text{-O}\cdot)\text{CH}(\text{Ph})\text{CH}(\text{OH})\text{Me}$. Formation of the latter and nitroxide (VI) probably results from isomerisation processes of the initially formed alkoxy radicals. The absence of such nitroxides in the other two alcohol oxidations is consistent with the faster rate of β -cleavage of the corresponding alkoxy radicals [$\text{PhCH}_2\text{CH}(\text{O}\cdot)\text{Ph}$ and $\text{PhCH}_2\text{C}(\text{O}\cdot)\text{Me}_2$] owing to the greater stability of the carbonyl compound (PhCHO and Me_2CO) produced.

Benzyl radicals were also trapped during the paraquat dichloride photo-oxidation of the two secondary alcohols, but not with the tertiary alcohol, consistent with other experimental findings.⁹

B. Product Studies.—Product studies confirm the radical-trapping results and a selection of the experiments is summarised in Table 3. Bibenzyl is the major

TABLE 3

Yields of bibenzyl from reaction of potassium peroxydisulphate with 2-phenylethanol and related alcohols^a

[Alcohol]/M ^b	[Additive]/M ^c	Bibenzyl (%) ^d
$\text{PhCH}_2\text{CH}_2\text{OH}$	0.40	39
$\text{PhCH}_2\text{CH}_2\text{OH}$	0.40	17
$\text{PhCH}_2\text{CH}_2\text{OH}$	0.10	29
$\text{PhCH}_2\text{CH}(\text{OH})\text{Me}$	0.40	48
$\text{PhCH}_2\text{CH}(\text{OH})\text{Me}$	0.10	42
$\text{PhCH}_2\text{C}(\text{OH})\text{Me}_2$	0.40	47
$\text{PhCH}_2\text{C}(\text{OH})\text{Me}_2$	0.10	68
$\text{PhCH}_2\text{C}(\text{OH})\text{Me}_2$	0.10	35
$\text{PhCH}_2\text{CH}(\text{OH})\text{Ph}$	0.10	30

^a Initial concentration of potassium peroxydisulphate $1.0 \times 10^{-2}\text{M}$; reactions in (1:1) (v/v) water-acetonitrile at 70.0° for 3.0 h. ^b Initial concentration of alcohol. ^c Initial concentration of additive. ^d Based on $\text{K}_2\text{S}_2\text{O}_8 + 2$ alcohol $\longrightarrow \text{PhCH}_2\text{CH}_2\text{Ph}$.

product and the yields for each substrate are shown, with small amounts of benzyl alcohol and benzaldehyde also being found in most cases. Of course, with 1,2-diphenylethanol, benzaldehyde was a major product. Useful yields of bibenzyl are produced in all the uncatalysed peroxydisulphate ion oxidations, with the amounts increasing from the primary $\text{PhCH}_2\text{CH}_2\text{OH}$ to the secondary $\text{PhCH}_2\text{CH}(\text{OH})\text{Me}$ to the tertiary $\text{PhCH}_2\text{C}(\text{OH})\text{Me}_2$ alcohol. This observation again reflects the faster rate of cleavage of the corresponding alkoxy radical due to the increased stability of the eliminated carbonyl compound. The results also show that peroxydisulphate ion can oxidise tertiary alcohols without the aid of silver(I) ion as is needed for example, in the oxidation of *t*-butanol.¹⁰

Silver(I) catalysis (Table 3) increases the rate of peroxydisulphate consumption but decreases the yield of bibenzyl, presumably due to competitive oxidation of the benzyl radical. The 17% yield of bibenzyl for the silver nitrate catalysed peroxydisulphate oxidation of 2-phenyl-

⁹ A. S. Hopkins and A. Ledwith, *Chem. Comm.*, 1971, 830.

¹⁰ L. R. Subbaraman and M. Santappa, *Z. Physik. Chem.*, 1966, 48, 163.

ethanol compares with the 18% found by Norman and Storey^{6b} using the $Ti^{III} + S_2O_8^{2-}$ system at pH 1. However, the latter yield was obtained using very low substrate concentrations, and from Table 3 it may be seen that the yield of bibenzyl does seem to depend somewhat on the initial concentration of alcohol taken.

The results of this study thus confirm our previous conclusions concerning the mechanism of the peroxydisulphate ion oxidation of alcohols.^{1,2} Alkoxy radicals are formed as intermediates and are now shown to be detectable by analysis of their well-known fragmentation reactions.^{4,5} Peroxydisulphate oxidation of the appropriate alcohol may thus provide a convenient source of alkoxy radicals and possible synthetic applications, including cyclisations, are under investigation.

Finally it must be mentioned that oxidative cleavage of 2-phenylethanol and related alcohols has also been observed with other one-equivalent oxidants such as V^V ,¹¹ Ce^{IV} ,¹² Co^{III} ,¹³ and Cr^{IV} ,¹⁴ in fact, oxidative cleavage has been established as a criterion for one-electron oxidation reactions.¹⁵ Whilst mechanisms vary in detail for each individual process, intermediate radicals are invariably postulated to occur at some stage of the reaction. The radical-scavenging technique, exemplified in this study, is a convenient way of identifying such intermediates with certainty.

¹¹ J. R. Jones and W. A. Waters, *J. Chem. Soc.*, 1960, 2772.

¹² P. M. Nave and W. S. Trahanovsky, *J. Amer. Chem. Soc.*, 1971, **93**, 4536.

¹³ D. G. Hoare and W. A. Waters, *J. Chem. Soc.*, 1962, 965.

¹⁴ P. M. Nave and W. S. Trahanovsky, *J. Amer. Chem. Soc.*, 1970, **92**, 1120.

¹⁵ K. Meyer and J. Roček, *J. Amer. Chem. Soc.*, 1972, **94**, 1209.

EXPERIMENTAL

E.s.r. spectra were recorded on a Varian V4500 spectrometer with 100 kHz modulation and an X band klystron. The field sweep was calibrated with alkaline aqueous solutions of potassium nitrosodisulphonate (Fremy's salt) having a_N 1.309 mT. The synthesis of the diamagnetic radical scavengers and the general techniques employed in the trapping experiments have been described.^{2,16} Products were identified by g.l.c. (Pye instrument; series 104, model 24). A 5% silicon oil column (6 ft \times $\frac{1}{4}$ in) was employed.

Potassium peroxydisulphate, silver nitrate, and hydrated ferrous sulphate were AnalaR reagents. Paraquat dichloride was supplied by I.C.I. Mond Division. The alcohols were commercial samples, each found to be pure by g.l.c. analysis. 2-Phenylethyl nitrite was prepared by reaction of the alcohol with nitrous acid¹⁷ at 0° and was distilled immediately before use. Solvents were distilled de-ionised water and acetonitrile twice distilled from P_2O_5 .

All solutions were purged with nitrogen for 1 h before use. In experiments using 2-methyl-2-nitrosopropane only very small amounts can be used as it is also oxidised by peroxydisulphate.¹⁸ In the product studies disappearance of the peroxydisulphate salt was followed iodometrically using Allen's procedure.¹⁹

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¹⁶ A. Ledwith, P. J. Russell, and L. H. Sutcliffe, *J.C.S. Perkin II*, 1972, 1925.

¹⁷ C. S. Coe and T. F. Doumani, *J. Amer. Chem. Soc.*, 1948, **70**, 1516; L. Hunter and J. A. Marriott, *J. Chem. Soc.*, 1936, 285.

¹⁸ I. Kraljić, *Internat. J. Radiation Phys. Chem.*, 1970, **2**, 59.

¹⁹ T. L. Allen, *J. Amer. Chem. Soc.*, 1951, **73**, 3589.