

Long-range Couplings in 2-Alkoxy-carbonylphenyl Nitroxide Radicals

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Solutions of 2-alkoxy-carbonylphenylhydroxylamines in carbon tetrachloride contain long-lived 2-alkoxy-carbonylphenyl nitroxide radicals which show long-range hyperfine splitting constants due to coupling with protons in the alkyl residue of the ester group, in their e.s.r. spectra. Selective line broadening in the ^1H n.m.r. spectra of the hydroxylamines due to exchange with the radical is observed.

DURING a kinetic investigation¹ on the solvolysis of *o*-hydroxyamino-benzoate esters (1) we observed that the ^1H n.m.r. spectra of solutions of these esters were devoid of signals due to the aromatic protons, and that significant line broadening of the ester $\text{O}\cdot\text{CH}_2\text{R}$ signal was in evidence. Thus the spectrum of the ethyl ester (1; $\text{R} = \text{Et}$) in CDCl_3 showed a characteristic triplet at τ 8.7 [Figure 1(a)] as the only distinguishing feature. Attempts to exclude atmospheric oxygen resulted in no

2-benzyloxycarbonylphenyl nitroxide (2; $\text{R} = \text{CH}_2\text{Ph}$); the computer-simulated spectrum [Figure 2(b)] was in close agreement with that observed.

In all the ester solutions examined, the concentration of the nitroxide radical was small but significant (Table 1), and the hyperfine splitting constants (Table 2) are in close agreement with those of related radical species.³ In the e.s.r. spectra of the methyl, ethyl, and benzyl esters, there was evidence of a further hyperfine splitting

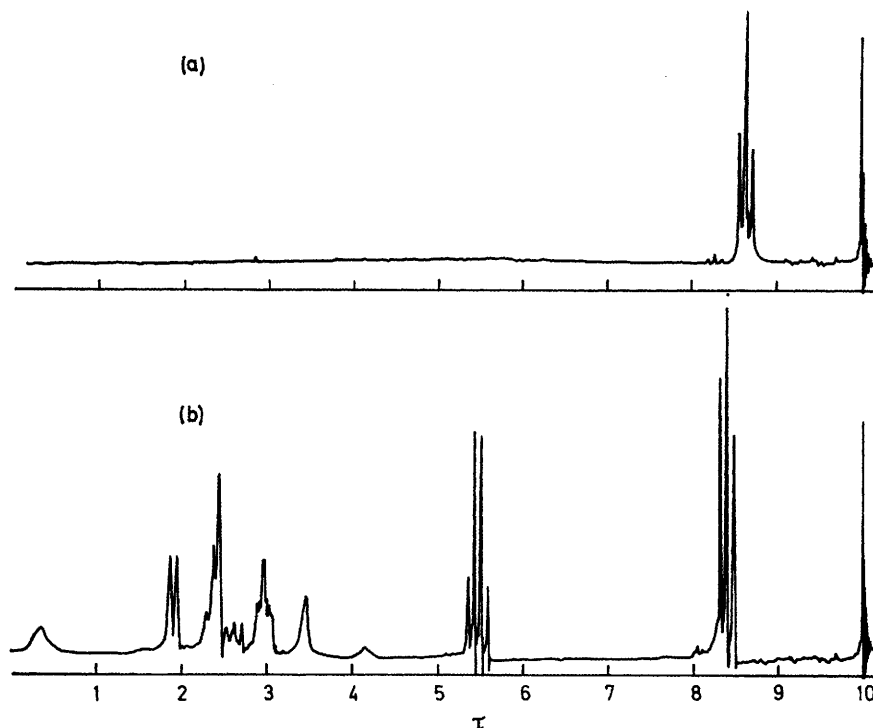


FIGURE 1 (a) ^1H n.m.r. spectrum of ethyl *o*-hydroxyaminobenzoate (10% w/v) and (b) with added hydrazobenzene

significant alteration of this phenomenon, but the addition of hydrazobenzene resulted in the expected spectrum [Figure 1(b)].

Other esters in this series showed similar selective line broadening² of some of their ^1H n.m.r. signals.

The existence of a paramagnetic species in the ester solutions was indicated and an e.s.r. study on the benzyl ester in CCl_4 [Figure 2(a)] demonstrated that this was

¹ B. G. Cox, D. McL. A. Grievie, and A. E. A. Porter, *J.C.S. Perkin II*, 1975, 1512.

² I. Baxter and J. K. M. Sanders, *J.C.S. Chem. Comm.*, 1974, 255.

due to interaction with protons not associated with the π -system, but the relatively large line-widths and low radical concentrations precluded an accurate determination of the magnitude of this splitting.

The broadening of the methylene signals in the ^1H n.m.r. spectra of the ethyl and benzyl esters indicated that the further hyperfine splitting could be attributed to an interaction with these protons.

On addition of 1 equiv. of 2-methyl-2-nitrosopropane

³ G. A. Russell, C. L. Meyers, P. Bruni, F. A. Neugebauer, and R. Blankespoor, *J. Amer. Chem. Soc.*, 1970, **92**, 276.

to a solution of the benzyl ester a significant increase in radical concentration was observed and the resultant improvement in resolution of the e.s.r. spectrum permitted the evaluation of the triplet-splitting due to the benzylic methylene protons as 0.16×10^{-4} T; a similar value was obtained for the quartet splitting of the methyl ester. In the high resolution e.s.r. spectrum of the t-butyl ester this splitting was absent, confirming its association with the methylene protons. This is relatively unusual as the unpaired electron would appear to interact with these protons by a 'through-space' or 'through σ -bond' mechanism.⁴

Reports on the generation of phenyl nitroxide radicals by reduction of nitrobenzene,⁵ oxidation of aniline,⁶ and

degassed. Kazakova and his co-workers⁹ have claimed that solutions of phenylhydroxylamine in benzene show e.s.r. spectra characteristic of the phenyl nitroxide

TABLE 1
Concentrations of nitroxide radicals

Ester	[Ester]/mol ⁻¹	10 ⁴ [Radical]/mol ⁻¹
Methyl	1.25×10^{-2}	1.99
Ethyl	1.07×10^{-2}	0.43
Benzyl	1.15×10^{-2}	0.23
Benzyl ^a	5.00×10^{-3}	2.02
t-Butyl	1.00×10^{-2}	1.77

^a 2-Methyl-2-nitrosopropane (1 equiv.) added to increase radical concentration.

radical even when precautions to exclude air were not taken, and stated that the concentration of the radical changed little with time. Our results with the 2-alkoxy-carbonylphenyl nitroxide radicals are consistent with

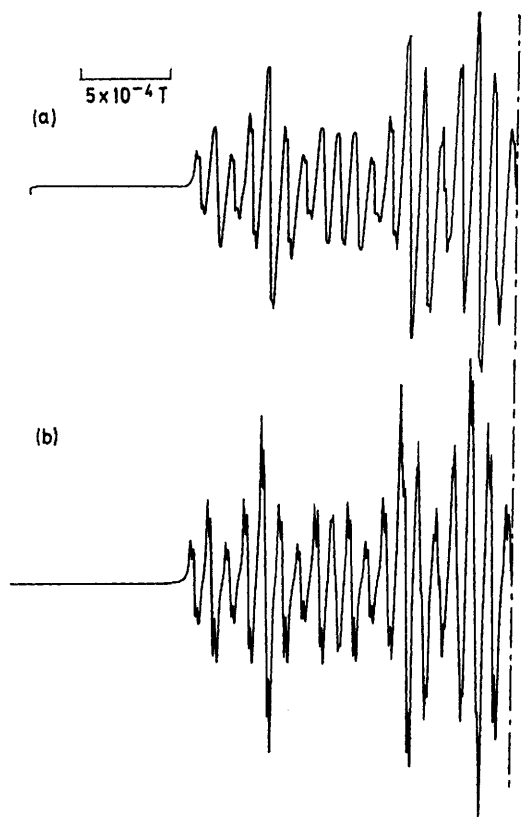


FIGURE 2 (a) Half e.s.r. spectrum of 2-benzyloxycarbonylphenyl nitroxide; (b) calculated e.s.r. spectrum of 2-benzyloxycarbonylphenyl nitroxide using values from Table 2

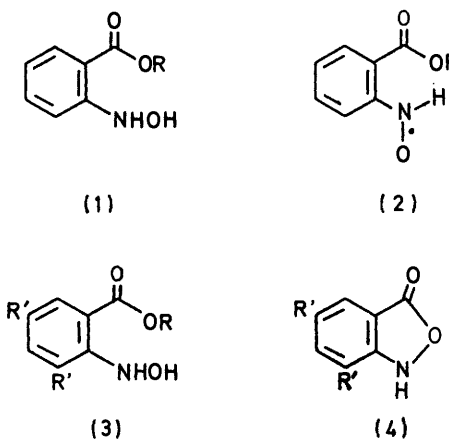
the oxidation of phenylhydroxylamine⁷ have appeared, and characterisation of these species by e.s.r. methods⁸ is well established. Conflicting reports on their lifetimes exist: thus Kikuchi and Someno observed that phenyl nitroxide generated by the oxidation of phenylhydroxylamine with dibenzoyl peroxide rapidly decomposed, having a lifetime of *ca.* 10 h when thoroughly

⁴ C. M. Camaggi, R. J. Holman, and M. J. Perkins, *J.C.S. Perkin II*, 1972, 501.

⁵ G. Chapelet-Letourneaux, H. Lemaire, A. Rassat, and J. P. Ravet, *Bull. Soc. chim. France*, 1965, 1975.

⁶ T. Nishikawa and K. Someno, *Bull. Chem. Soc. Japan*, 1971, 44, 851.

⁷ H. Lemaire, A. Rassat, and J. P. Ravet, *Tetrahedron Letters*, 1964, 3507.



this latter observation, with solutions showing little sign of deterioration after several weeks.

The oxidation of phenylhydroxylamine with molecular oxygen has been shown to be kinetically of the second order and is apparently a slow process with a half-life of

TABLE 2
Hyperfine splitting constants^a

R	a_H	a_N	a_H (4,6)	a_H (3,5)	$a_H(\text{OCH}_2\text{R})$
Me	11.39	7.64	2.91	0.96	0.16 ^b
Et					^c
PhCH ₂	11.39	7.64	2.91	0.96	^c
Bu ^t	11.54	7.78	2.92	0.97	0.16

^a All hyperfine splitting constants and line-widths in 10^{-4} T.

^b Radical concentration increased by the addition of 2-methyl-2-nitrosopropane (1 equiv.). ^c Estimated line-width of 0.44 (± 0.02) precluded accurate determination of these values.

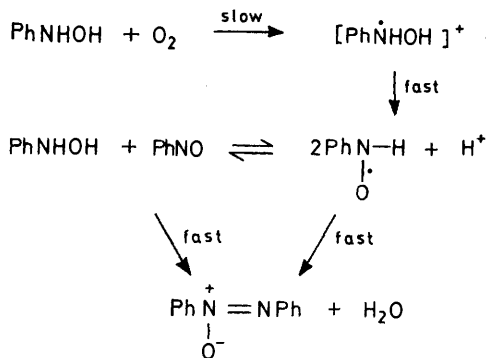
ca. 10² h at 308 K¹⁰ under 1 atm of oxygen. The rate-determining step has been postulated to involve a one-electron transfer from the hydroxylamine to oxygen, yielding a protonated nitroxide which subsequently

⁸ O. Kikuchi and K. Someno, *Bull. Chem. Soc. Japan*, 1967, 40, 2549.

⁹ V. M. Kazakova, I. G. Makarov, L. A. Nieman, and M. M. Shemayakin, *Zhur. obshchei Khim.*, 1968, 38, 941.

¹⁰ Y. Ogata, Y. Sawaki, J. Mibae, and T. Morimoto, *J. Amer. Chem. Soc.*, 1964, 86, 3854.

undergoes rapid proton loss (Scheme). The intermediate nitroxide radical is thought to be in rapid equilibrium with nitrosobenzene and phenylhydroxylamine (by H \cdot transfer), and two alternative pathways may then lead to the observed product, azoxybenzene.

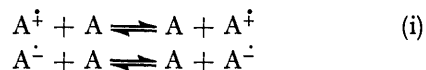


SCHEME

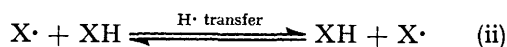
Groups located at the *meta*- and *para*-positions with large $-I$ effects retard the oxidation, and although rate constants for *ortho*-substituted derivatives are not available, it seems reasonable that *ortho*-substituents with large $-I$ and $-M$ effects would retard the overall reaction, in particular the dimerisation step leading to azoxybenzene. Thus, if the initial electron-transfer step becomes fast relative to dimerisation and the equilibrium involving phenyl nitroxide, nitrosobenzene, and phenylhydroxylamine exists, then the only factor which controls the concentration of the phenyl nitroxide in solution will be the position of the equilibrium.

Thus, the addition of nitrosobenzene or some other suitable nitroso-compound would be expected to displace the equilibrium and should result in an increased radical concentration, in accord with the observed effect after the addition of 2-methyl-2-nitrosopropane.

The known propensity of radical cations and anions to undergo rapid electron exchange with their neutral species [equation (i)] has been shown to result in selective



line broadening in the ^1H n.m.r. spectra of semiquinone radical anions² and metalloporphyrin radical cations.¹¹ In view of the observed selectivity of the line broadening \ast in the ^1H n.m.r. spectra of the solutions containing the nitroxide radicals, it appears that a similar equilibrium process must be occurring; three processes are possible: (a) a simple H \cdot transfer [equation (ii)];



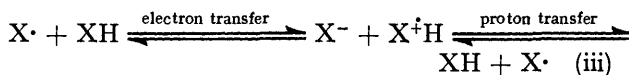
(b) electron transfer followed by proton transfer [equation (iii)]; and (c) proton transfer followed by electron transfer [equation (iv)]. However, because of

\ast There is some evidence of line broadening in the ethyl triplet, thus in Figure 1(a) ω_4 is 2.2 Hz whereas a value of 1.5 Hz was observed in the quenched spectrum [1(b)].

¹¹ J. K. M. Sanders and I. Baxter, *Tetrahedron Letters*, 1974, 4543.

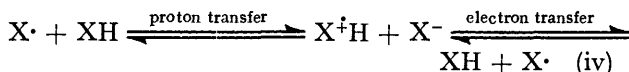
the necessary reversibility, equations (iii) and (iv) are effectively equivalent.

The broad signal due to the aromatic protons of the ethyl ester becomes broader on increasing the temperature over the range 233–343 K, indicating that the



exchange process is slow on the n.m.r. time-scale,¹² with all the aromatic proton signals being broadened to the same extent. Attempts to resolve the broadened aromatic signal by cooling the solution below 233 K failed, owing to the low solubility of the hydroxyamino-benzoate in any suitable solvent below that temperature.

Although these results do not distinguish between the processes outlined in equations (ii) and (iii)/(iv), some



X is the nitroxide (2)

comments can be made. Thus, a rapid electron transfer followed by a slower proton transfer [equation (iii)] might be expected to give rise to detectable concentrations of the cation radical (protonated nitroxide) and a further splitting due to hyperfine coupling with the O–H proton would be expected.¹³ Since no such coupling is in evidence in the e.s.r. spectrum, no significant concentration of the protonated nitroxide can be present. This condition also applies to the ‘rapid proton transfer/slow electron transfer’ of equation (iv).

Over the temperature range 233–343 K no $\text{O}\cdot\text{CH}_2$ signal was present, and thus no information on the exchange limits for these protons could be determined.

The stability of the 2-alkoxycarbonylphenyl nitroxides led us to believe that by preparing suitably substituted derivatives such as (3) we might stabilise the system sufficiently to permit the isolation of a pure monoaryl nitroxide radical. However, reduction of 2-nitro-3,5-di-*t*-butylbenzoate esters with zinc-ammonium acetate did not produce the expected hydroxyamino-compound (3; R' = Bu^t) but yielded instead the di-*t*-butyl-2,1-benzisoxazol-3(1*H*)-one (4; R' = Bu^t); similar results were obtained in the dimethyl series (3; R' = Me). The intramolecular displacement of alcohols from *o*-hydroxyamino-benzoates has been shown to be rapid, and it appears that the buttressing effect¹⁴ of the alkyl groups adjacent to the hydroxyamino-group enhances the rate of this reaction.

EXPERIMENTAL

The hydroxyamino-esters were prepared as previously described and were crystallised from carbon tetrachloride. All solutions of the esters were made up in CCl_4 , degassed, and sealed under vacuum (10^{-3} – 10^{-4} Torr). Solutions containing the radical species were stable for several weeks.

¹² E. De Boer and C. MacLean, *J. Chem. Phys.*, 1965, **44**, 1334.

¹³ V. Molatista and K. U. Ingold, *J. Amer. Chem. Soc.*, 1972, **95**, 6404.

¹⁴ E. L. Eliel in 'Stereochemistry of Carbon Compounds,' McGraw-Hill, New York, 1962.

E.s.r. spectra were recorded with a JEOL JES-PE-IX spectrometer and n.m.r. spectra with a Perkin-Elmer R32 instrument. The concentrations of the radical species were determined by comparison of the doubly integrated e.s.r. spectra with that of a standard solution of 2,2-diphenyl-1-picrylhydrazyl run under similar conditions. The double integration was computed by using a modified program,¹⁵ and spectral simulation was carried out by a modification of a program provided by Professor M. J. Perkins.

We are indebted to Professor R. W. Franck for a sample of 2-nitro-3,5-di-*t*-butylbenzoic acid, Professor M. J. Perkins for details of his spectral simulation program, and Dr. J. K. M. Sanders for comments. One of us (R. S. H.) thanks the S.R.C. for financial support.

[6/1753 Received, 16th September, 1976]

¹⁵ M. J. S. Bowden, Ph.D. Thesis, University of Queensland, 1969.