

Solvent Effects on the Spin-trapping of Primary Alkyl Radicals

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Summary Rate constants for spin-trapping of primary alkyl radicals by nitroso compounds and nitrones are greater in polar than in non-polar solvents.

THERE is a growing recognition that free-radicals often play a significant role in biological processes.¹ The spin-trapping technique^{2,3} is sufficiently versatile that it can be applied to some biochemical systems.⁴ Some preliminary rate constants, k^T , for the spin-trapping of primary alkyl

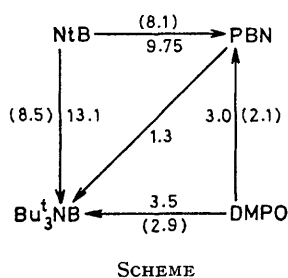
radicals by some common traps in benzene at 40 °C have been reported⁵ [equation (1)]. The question was immedi-



ately raised as to whether these data could be applied to alkyl radicals in solvents of greater biochemical interest.

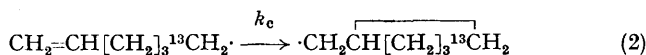
Competitive experiments between pairs of spin-traps were carried out using the n-hexyl radical generated by the

thermal decomposition of n-heptanoyl peroxide (5×10^{-3} M) at 40 °C in C_6H_6 ,⁵ MeOH, and MeCN.† Four of the most commonly used traps were studied: Bu^tNO (NtB), phenyl-t-butyl nitron (PBN), 2,4,6-tri-t-butyl nitrosobenzene (Bu₃^tNB), and 5,5-dimethylpyrroline N-oxide (DMPO). The relative concentrations of the two spin-traps were adjusted so as to give approximately equal yields of the two spin adducts. The results of these experiments are summarized in the Scheme. Arrows connect pairs of traps used in



competition and point from the more reactive to the less reactive trap. The numbers on each arrow represent the ratio of k^T values for the two traps, with bracketed numbers referring to experiments in MeCN and the other numbers to experiments in MeOH.

Spin-trapping rate constants for NtB and Bu₃^tNB were put on an 'absolute' scale by measuring the rate constant ratio, k^T/k_c , where k_c is the rate constant for cyclization of the [1-¹³C]hex-5-enyl radical⁵ [equation (2)]. Our attempts



to measure k_c for unlabelled hex-5-enyl radical by e.s.r. spectroscopy^{6,7} in MeCN and MeOH were frustrated by the freezing point of MeCN (−46 °C) and by the low solubility of the peroxide in MeOH at the temperatures required to make this measurement (ca. −70 °C). An attempt to

† Solubility problems prevented the use of H₂O as a solvent.

‡ At 20 °C, $\epsilon = 2.3, 33.4,$ and 37.4 , for $C_6H_6, MeOH,$ and $MeCN$, respectively.

¹ 'Free Radicals in Biology,' Vols. 1 and 2, ed. W. A. Pryor, Academic Press, New York, 1976.

² M. J. Perkins in 'Essays in Free Radical Chemistry,' Chemical Society Special Publication, No. 24, London, 1970.

³ E. G. Janzen, *Accounts Chem. Res.*, 1971, **4**, 31.

⁴ A. Saprin and L. H. Piette, *Arch. Biochem. Biophys.*, 1977, **180**, 480; C. Lai and L. H. Piette, *Biochem. Biophys. Res. Comm.*, 1977, **78**, 51.

⁵ P. Schmid and K. U. Ingold, *J. Amer. Chem. Soc.*, 1977, **99**, 6434.

⁶ D. Lal, D. Griller, S. Husband, and K. U. Ingold, *J. Amer. Chem. Soc.*, 1974, **96**, 6355.

⁷ P. Schmid, D. Griller, and K. U. Ingold, *Internat. J. Chem. Kinetics*, submitted for publication.

⁸ E. G. Rozantsev and E. N. Gur'yanova, *Izv. Akad. Nauk S.S.S.R., Ser. khim.*, 1966, 979; see also G. D. Mendenhall and K. U. Ingold, *J. Amer. Chem. Soc.*, 1973, **95**, 6390.

measure k_c in propionitrile was also frustrated by solubility problems. However, in the moderately polar solvent, tetrahydrofuran, k_c at −70 °C was equal, within experimental error, to the value found in hydrocarbon solvents. Since there is no measurable solvent effect on k_c we have calculated k^T in MeOH and MeCN using k_c as measured in hydrocarbon solvents.^{6,7} Our most recent data⁷ yield an extrapolated value for $k_c = 1.7_3 \times 10^5$ s^{−1} at 40 °C. This value has been combined with the n-hexyl competitions and with the [1-¹³C]hex-5-enyl data to yield the k^T values listed in the Table.

TABLE. Rate constants for spin-trapping of primary alkyl radicals at 40 °C.^a

Trap	$k^T \times 10^{-5}/l \text{ mol}^{-1} \text{ s}^{-1}$		
	C_6H_6 ^b	MeOH	MeCN
NtB	88	116	131
Bu ₃ ^t NB	4.5	9.0	15
PBN	1.3	12	16
DMPO	25	36	43

^a Based on $k_c = 1.7_3 \times 10^5$ l mol^{−1}. ^b Remeasured for this work.

For each trap, k^T increases with increasing solvent dielectric constant.† This can be attributed to improved solvation of the transition state, since the nitroxide product is known to have a strong N→O dipole.⁸ There do not appear to be any effects in MeOH that should be attributed to specific hydrogen bonding. It therefore seems likely that primary alkyls will be trapped even more readily in water ($\epsilon = 80$ at 20 °C) than in MeOH or MeCN.

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