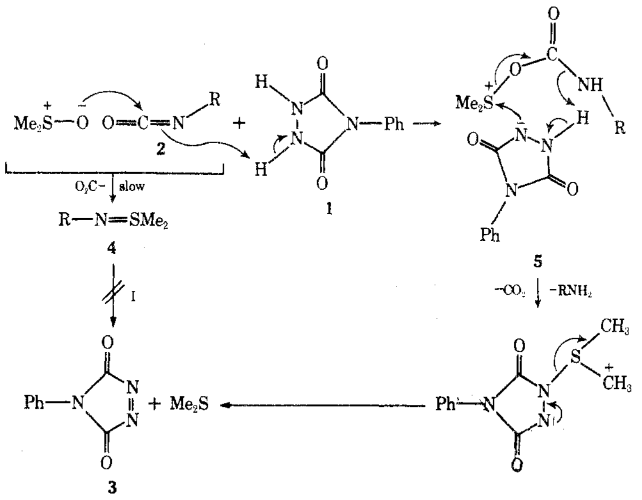
within 15 min. Related heterocumulenes, PhNCS and PhNSO, were completely unreactive in this system. For the purpose of comparison, 1 was oxidized using DMSO–DCC–H_3PO_4 (maximum yield, 33% after 30 min), DMSO–Ac_2O (86% yield after 2 hr), and DMSO–P_2O_5 (yield uncertain because of turbid solutions which could not be clarified; no further increase in absorbance was noted after 5–10 min). The reaction appeared to proceed as well in benzene, toluene, chloroform, carbon tetrachloride, 1,2-dichloroethane, ethyl acetate, acetone, neat DMSO, dioxane, tetrahydrofuran, and 1,2-dimethoxyethane but not in diethyl ether or pyridine. The interference of ether in the course of this reaction remains a puzzle. Considering the similarities between this system and the Pfitzner-Moffatt-type systems, we propose the following mechanistic scheme to rationalize our results.



3 was not formed when 1 was treated with dimethyl sulfilimine **4b**.[13] Furthermore, the reaction between DMSO and isocyanate alone required 3–5 hr for the formation of the sulfilimine to be complete. Thus the initial adduct between DMSO and 2 is effectively trapped before it can eliminate CO_2. This is in keeping with the observed acidity of 1 (soluble in 50% NH_4OH) and with the inhibitory effect of pyridine on the oxidation.

Experimental Section[14]

General Procedure for *in situ* Generation of 4-Phenyl-1,2,4-triazoline-3,5-dione (3). To 1.77 g (0.01 mol) of 4-phenylurazole[10] dissolved in 5 ml of dry DMSO (molecular sieves), cooled to 0° in an ice–water bath, in a magnetically stirred 25-ml round-bottom flask, sealed with a serum cap, was added 1.33 ml (0.01 mol) of *p*-toluenesulfonyl isocyanate (Upjohn Chemical Co.). Care was taken to avoid freezing of the DMSO solution. The isocyanate addition was made slowly to avoid overheating which leads to formation of the corresponding sulfilimine (4). Gas evolution was allowed to subside between additions of drops of isocyanate. After the addition of isocyanate was completed the cooling bath was removed and the mixture was stirred at room temperature until gas was no longer evolved (~15 min). The chosen diene can be injected into the solution of 3 if it is a liquid, or a DMSO solution of the solid diene can be added. Evidence of the completion of the reaction is the discharge of the characteristic color of 3. The reaction mixture is poured into 100 ml of chloroform and the resulting solution is extracted with 5% aqueous sodium hydroxide solution and then distilled water. The chloroform layer is dried over calcium chloride, filtered, and concentrated to an oil on a rotary evaporator. Ethanol is added to the oil and the solution is warmed to dissolve suspended solid, if any is present. The product is precipitated by addition of water to the ethanol solution and may generally be recrystallized from alcohol.

***N*-Phenyl-2,3-diazabicyclo[2.2.1]hept-5-ene-2,3-dicarboximide.** This compound was obtained from 0.82 g (0.01 mol) of freshly prepared[15] cyclopentadiene, according to the general procedure given above, yield 1.42 g (59%), melting point 138–39° (lit.[8] 131–133°, 142–144°,[16] 142–144°). The nmr spectrum of the product was in accord with that reported in the literature.[16] If a 1 equiv excess of isocyanate was added along with 5 ml more of DMSO, the yield rose to 79%.

***N*,1,4-Triphenyl-1,2,3,4-tetrahydro-1,4-epidioxo-2,3-diazanapthalene-2,3-dicarboximide.** This compound was obtained from 2.70 g (0.01 mol) of diphenylisobenzofuran,[17] according to the general procedure given above, yield 2.4 g (54%), mp 144°.

Acknowledgment. We wish to acknowledge the assistance, in the form of advice and encouragement, of Professors K. T. Potts and J. P. Anselme, and a generous gift of *p*-toluenesulfonyl isocyanate from the Upjohn Co., Kalamazoo, Mich.

Registry No.—**1**, 15988-11-1; **2a**, 3019-71-4; **2b**, 4083-64-1; **2c**, 4461-33-0; **3**, 4233-33-4; *N*-phenyl-2,3-diazabicyclo[2.2.1]hept-5-ene-2,3-dicarboximide, 15971-63-8; cyclopentadiene, 542-92-7; *N*,1,4-triphenyl-1,2,3,4-tetrahydro-1,4-epidioxo-2,3-diazanaphthalene-2,3-dicarboximide, 52950-79-5; diphenylisobenzofuran, 5471-63-6.

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Medium Effects on the Electron Spin Resonance Hyperfine Splitting Constants of *tert*-Butyl Nitroxide in Mixed Aqueous Solvents

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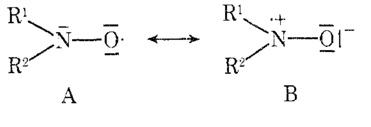
Received August 2, 1974

The substantial variation of the nitrogen hyperfine splitting constants (hfc), A_N, of nitroxide free radicals as a function of substitution pattern or solvent medium has commonly been attributed to a change in spin distribution in the nitroxide π system. In many cases these effects have been rationalized by considering the relative contributions of the two main resonance structures, A and B, to the actual molecular structure.[1,2] In these studies it is assumed that



A B

Table I
Medium Effects on A_N and A_H Values of Nitroxide 1 in Aqueous Solutions (25°)

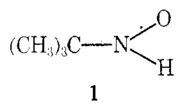
Solvent	Range of ϵ	A_N^S		A_H^S		K
		$a \times 10^3$	b	$c \times 10^3$	d	
H_2O–MeOH	31.5[a]–78.5	17.3	13.24	27.9	11.72	0.84
H_2O–EtOH	26.0–78.5	17.5	13.22	24.4	11.97	0.51
H_2O–*i*-PrOH	20.0–78.5	14.7	13.39	22.6	12.12	0.31
H_2O–*t*-BuOH	15.5–78.5	12.7	13.56	19.3	12.41	0.21
H_2O–*p*-dioxane	17.5–78.5	15.4	13.47	23.2	12.14	0.39

[a] Pure methanol.

A_N is (nearly) isotropic and is determined by the unpaired spin density at the nitrogen nucleus ($|\psi(0)^2|$) by eq 1 in which g and g_N are the electron and nuclear g factors, respectively, β is the electron Bohr magneton, and β_N is the nuclear magneton. Effects that favor structure B relative to A will then be associated with an increase in the magnitude of A_N. For substituent effects on A_N this treatment may be a serious oversimplification since bending from planarity around the nitrogen atom is ignored.[3,4] The above rationale seems to be more justified for a semiquantitative treatment of the environmental perturbations of A_N values. However, now the question arises as to the nature of the solvent effect: *a priori* both solvent polarity as well as hydrogen bonding capability may play an important role. Both effects will exert a similar influence on the relative contributions of A and B because hydrogen bonding is expected to occur predominantly with an oxygen lone pair in structure B.[5] Insight into the solvation process is desirable because nitroxides have been frequently used as spin-label in studies on molecules of biological interest.[6]

$$A_N = \frac{8\pi}{3} g g_N \beta \beta_N |\psi(0)^2| \qquad (1)$$

Previous investigations of the solvent-induced redistribution of spin density in nitroxides have been mainly limited to pure solvents and there exists considerable controversy regarding which solvent parameter is most suitable for correlation with A_N. Thus, A_N has been linearly correlated with bulk dielectric constant,[7] Kosower's Z values,[8] Reichardt's E_T parameters,[9] and dipole moments of the solvents.[10] Correlation coefficients are sometimes poor[7,9b] and there is at least one case in which an excellent correlation with dielectric constant has been overlooked.[11] Only very few studies have been performed on nitroxide radicals in mixed solvents.[11] Since we anticipated that measurements of A_N in binary solvent systems as a function of solvent composition could have a considerable potential in delineating A_N solvent sensitivity, we have measured both A_N as well as A_H values of *tert*-butyl nitroxide (1) in some mixed aqueous solvents and in some aqueous salt solutions.



1

This nitroxide was chosen because of the expected propensity for hydrogen bonding interaction, both at oxygen (as a H-bond acceptor) and at N–H (as a H-bond donor).

We find that in mixtures (S) of water with methanol, ethanol, 2-propanol, *tert*-butyl alcohol, and *p*-dioxane, both A_N and A_H values are linearly correlated with bulk dielectric constant (ϵ) through eq 2 and 3. The correlation has a surprisingly great precision (correlation coefficients >0.98) provided that ϵ is not too low. The magnitudes of $a,b,c,$ and d, which are characteristic for the particular solvent mixture, are given in Table I. A high dielectric constant clearly favors the polar resonance structure B relative to A. The observed linear correlation of A_N and A_H with ϵ is difficult to reconcile with the assumption that solute–solvent hydrogen bonding is the dominating solvation factor in determining how the hfc's vary with solvent composition.[12] Especially in highly aqueous *tert*-butyl alcohol (mole fraction of water between 1.00 and 0.90; ϵ 78.5–52.0; 25°) there exists a definite trend toward a discontinuous variation in solute–solvent H-bond interaction.[13] This is not revealed in our data. In fact the medium dependency of the hfc's may be analyzed in terms of a simple model assuming localized complexes between the N–O π system of 1 and the organic solvent (S_A) or water (S_B). Fraenkel and his associates[14] have proposed that the average observed nitrogen splitting ($\bar{A}_N$) under conditions of fast exchange (on the esr time scale) will be given by

$$A_N^S = a\epsilon + b \qquad (2)$$

$$A_H^S = c\epsilon + d \qquad (3)$$

$$\bar{A}_N = \tfrac{1}{2}(A_{S_A} + A_{S_B}) + \tfrac{1}{2}[(K\alpha - 1)/(K\alpha + 1)]\Delta \qquad (4)$$

where A_{S_A} and A_{S_B} are the A_N values in the pure solvents S_A and S_B, α is the ratio of solvent concentrations ($\alpha = [S_A]/[S_B]$), Δ is ($A_{S_B} - A_{S_A}$), and K is the equilibrium constant for the solvation equilibrium (eq 5). K values obtained by this procedure are also given in Table I. They indicate that there is a clear tendency for preferential solvation by the organic solvent of low charge-solvating ability, resulting in a reduced sensitivity of A_N (and A_H) for bulk dielectric constant.

$$\mathbf{1}(S_A) + S_B \overset{K}{\rightleftharpoons} \mathbf{1}(S_B) + S_A \qquad (5)$$

The hydrophobic nature of 1 is confirmed by the low perturbation of A_N and A_H in aqueous salt solutions at 25°. For example, A_N varies from 14.55 G in pure water (ϵ 78.5) to 14.68 G in 6 N NaBr (ϵ 42.0) or to 14.26 G in 6 N $(CH_3)_4NCl$ (ϵ *ca.* 38). Apparently, incorporation of 1 in the hydration shells of the ions is very unfavorable and consequently A_N scarcely responds to the considerable variation in the macroscopic dielectric constant of the solution.

As noted before, the solvent-induced variation of A_N and A_H in the mixed solvents only fits the linear correlation lines (eq 2 and 3) above a critical value of ϵ (see Table I). For example, in pure dioxane A_N = 12.96 G while eq 2 predicts a value of 13.50 G. Apparently, in the strongly apolar media the local electrostatic fields induced by the solvent in the cybotactic region around the nitroxide function are no longer described by a macroscopic solvent parameter like the dielectric constant of the bulk solvent. Under these conditions, water can hardly compete with organic solvent for solvation of 1 and the spin distribution will now respond to highly specific dipole–dipole and van der Waals interactions.

Finally, we emphasize that A_N or A_H values will be no adequate probes for solvent dielectric constant around bonding sites of nitroxide spin-labels since the constants *a–d* in eq 2 and 3 are dependent on the nature of the particular medium. However, A_N and A_H values may have some potential for comparative studies of effects due to changes in solvent polarity on solvation phenomena in these molecules.

Experimental Section

Esr hfc's (in gauss) were determined on a Varian E-4 apparatus fitted with a Varian A 1268 variable-temperature controller. Using optimal machine operating conditions, A_N and A_H could be measured to within ±0.04 G. Nitroxide 1 was prepared *in situ* by oxidation of *N-tert*-butylhydroxylamine[15] with PbO_2. The small amount of PbO_2 introduced into the solution had a negligible effect on the magnitudes of A_N and A_H. The solutions were deoxygenated with a nitrogen purge. The hfc's of 1 were measured at at least nine solvent compositions in the range of ϵ given in Table I. The correlation lines were obtained by least-squares analysis. The estimated error in the K values is *ca.* 30%. These values have been calculated for the solvent composition range where A is most sensitive for variation of α.

Supplementary Material Available. Esr hfc's of nitroxide 1 as a function of solvent composition will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N. W., Washington, D. C. 20036. Remit check or money order for \$3.00 for photocopy or \$2.00 for microfiche, referring to code number JOC-74-3800.

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(12) (a) Of course, we do not imply that nitroxides are incapable of hydrogen bonding. For example, we find considerable OH stretching frequency shifts ($\Delta\nu_{OH}$) for the hydrogen bonded complexes between di-*tert*-butyl nitroxide and methanol ($\Delta\nu_{OH}$ = 150 cm^{-1}) or *p*-nitrophenol ($\Delta\nu_{OH}$ = 380 cm^{-1}) in carbon tetrachloride at 35° (B. Paping and J. B. F. N. Engberts, unpublished results). Drago, *et al.*,[5a] find $\Delta\nu_{OH}$ = 135 cm^{-1} for the H-bonded complex between 2,2,6,6-tetramethylpiperidine *N*-oxyl and ethanol. (b) It is interesting to note that there is a large difference in the temperature dependence of A_N and A_H. In pure water in the range 5–85° (ϵ 59.0–86.0), $A_H = 0.017\epsilon + 12.50$ and A_N varies only from 14.55 (5°) to 14.51 G (85°).

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