Tetrahedron Letters No. 35, pp 3229 - 3232.

0040-4039/79/0822-3229$02.00/0

SPIN TRAPPING CHEMISTRY OF SODIUM 2-SULFONATOPHENYL *t*-BUTYL NITRONE ($Na^{\oplus}$ 2-SPBN$^{\ominus}$). A NEGATIVELY CHARGED WATER-SOLUBLE SPIN TRAP

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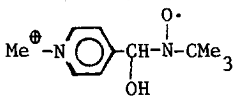
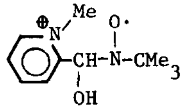
ABSTRACT: A new water-soluble negatively charged spin trap, sodium 2-sulfonatophenyl *t*-butyl nitrone is described.

Recent spin trapping reactions of the positively charged N-alkyl-4-pyridinium *t*-butyl nitrones have been published (1). Typical spectra consisting of PBN-like triplets of doublets (2) are obtained in aqueous solution. The hydroxyl radical adduct gives a unique spectrum containing one γ-H hyperfine splitting (γ-H hfs) due to the proton of the hydroxy group (3). The 2-isomer gives hydroxyl radical spin adduct spectra with relatively large β-H hfs indicating that substantial steric hindrance to free rotation must exist for the substituted benzyl group in this nitroxyl:

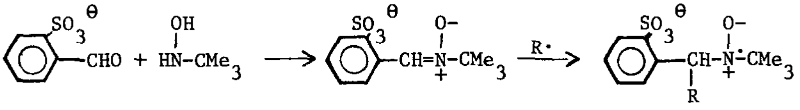


a_N=14.70, a_β^H=1.45, a_γ^{OH}=0.38G



a_N=14.95, a_β^H=3.90 G

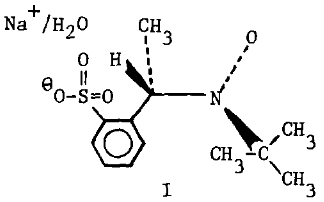
In anticipation of future studies with a series of amphiphilic spin traps the negatively charged 2-sulfonatophenyl *t*-butyl nitrone (2-SPBN) has been synthesized as the sodium salt (4):



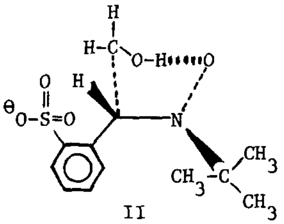
Sodium 2-SPBN is a colorless stable nitrone soluble in water, methanol, ethanol, DMSO and DMF, slightly soluble in CH_3CN and insoluble in benzene or chloroform. The esr spectra of most spin adducts are characterized by a pattern of six relatively sharp lines (~0.6 G linewidth) consisting of triplets of large doublets (see Table 1). All spin adducts seem to be reasonably long-lived.

Under conditions of high resolution (low modulation amplitude and small time constant) additional hyperfine splitting can be observed in the spectra of some adducts, namely in the case of methyl, ethyl and hydroxymethyl adducts. In the spectrum of the methyl adduct 6 (perhaps 8) extra lines are barely resolved which disappear completely upon deuteration of the methyl hydrogens. The hydroxymethyl adduct also gives a spectrum with 6-8 additional lines which are replaced by 3 (perhaps 5) barely resolved lines in the deuterated hydromethyl adduct. The spectrum for the ethyl adduct contains 7 (perhaps 9) unequally spaced lines. Additional splitting has not been observed in the hydroxy, t-butoxy, phenyl, benzoyl, hydrogen and carbon dioxide anion radical adducts although the linewidth is sufficient for extra lines to be present in some cases. Such splitting could perhaps be detected if the right experimental conditions were found.

Assignment of the additional hyperfine splitting is not obvious. In the case of the methyl and hydroxymethyl adducts deuteration shows that the splitting does not come from hydrogens in the t-butyl group or the phenyl ring. For the methyl adduct the possibility of two sets of quartets with slightly different spacing suggests itself, as might be expected from two different conformations of the same spin adduct. However both the N-hfs and the β-H hfs must be exactly the same in the two conformations to give the sharp lines found in the deuterated species. Perhaps a small difference in γ-H hfs exists in different ion pairs or hydrogen bonded complexes involving the sulfonate group(I).



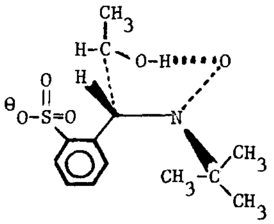
I



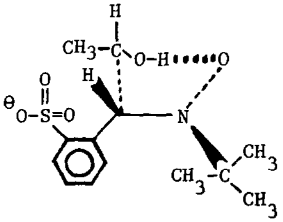
II

In the hydroxymethyl and ethyl adducts the methylene hydrogens are diastereotopic and nonequivalent. Therefore each line should be split into doublets of doublets due to γ-H hfs. Again two different species could give 8 lines. In the case of the hydroxymethyl adduct perhaps an open chain and an intramolecularly H-bonded isomer (II) could be these two species (7) but this possibility does not apply to the ethyl adduct. One γ-D hfs could be large enough for detection in the former adduct.

The spectrum of the hydroxyethyl adduct clearly shows the presence of two nitroxides, undoubtedly diastereomers (8), in about the same concentration. If intramolecular H-bonding exists in these adducts the trans and cis isomers would be expected to have slightly different β-H hfs (III and IV):



III



IV

That the p-orbital on the nitrogen atom approximately bisects the angle between the bond to the β-hydrogen and the group that was the radical is demonstrated by the magnitude of the β-H hfs. If $a_\beta^H = 26 \cos^2\theta$ for nitroxides (9), $a_\beta^H \simeq 6.5G$ for $\theta=60°$.

This value is in good agreement with the β-H hfs found for the methyl adduct. Only a small increase in θ would give the smaller values found for the other adducts.

The value of 9.19G found for β-H hfs for the hydrogen atom adduct indicates that considerable freedom of motion exists in this nitroxide. Two different sets of patterns are not found as in the case of the methyl, ethyl and hydroxymethyl adducts.

In summary it appears that ortho-substituted phenyl *t*-butyl nitrones have special characteristics which may prove to be useful in their use as spin traps.

HYPERFINE SPLITTING CONSTANTS FOR SPIN ADDUCTS
OF SODIUM 2-SULFONATOPHENYL *t*-BUTYL NITRONE[a]

RADICAL	SOURCE/SOLVENT	a_N	a^H_β	$a_{\text{(OTHER)}}$
$Me\cdot$[b]	H_2O_2 + DMSO + hν	16.30	6.45	a^H_γ = 0.21 (6 lines)
$CD_3\cdot$	H_2O_2 + DMSO-d_6 + hν	16.24	6.49	
$CO_2^{\cdot-}/COOH$[c]	HCO_2Na + H_2O + DBPO[d]	15.77	6.16	
$Ph\dot{C}{=}O$[e]	PhCHO + DMSO + DBPO	14.34	5.88	
$Me_2N\dot{C}{=}O$[f]	DMF + DBPO	14.41	5.42	
$CH_3CH_2\cdot$	H_2O_2 + Et_2SO + hν	15.76	5.03	a^H_γ = 0.27 (7 or 9 lines)
$HOCH_2\cdot$[g]	MeOH + Ph_2CO + hν	15.16	5.02	a^H_γ = 0.27 (6 lines)[h]
$DOCD_2\cdot$	CD_3OD + Ph_2CO + hν	15.18	5.09	a^D_γ = 0.19 (3 lines)
$HO\dot{C}HMe$[g]	EtOH + Ph_2CO + hν	15.20	4.34, 3.68	
$Ph\cdot$[e]	PhN_2CPh_3 in DMSO	14.79	3.28	
$Cl_3C\cdot$[i]	$CHCl_3$ + DMSO + DBPO	14.20	1.71	
$Me_3CO\cdot$	DBPO + CH_3CN	14.65	5.69	
$HO\cdot$	H_2O_2 + hν (pH 6 buffer)	15.68	5.20	
$H\cdot$[j]	dioxalane + DBPO	15.09	9.19 (2H)	

(a) Hyperfine splitting constants in gauss at room temperature.

(b) Hydroxyl radicals from photolysis of H_2O_2 produce methyl radicals from addition to DMSO; see C. Lagercrantz and S. Forshult, Acta Chem. Scand., 23, 811 (1969); C. Lagercrantz, J. Phys. Chem., 75, 3466 (1971); S. Rustgi, A. Joshi, H. Moss and P. Riesz, Int. J. Radiat. Biol., 31, 415 (1977).

(c) The reaction between oxy radicals and sodium formate produces carbon dioxide radical anions which can be trapped; see J. R. Harbour and J. R. Bolton, Photochem. Photobiol., 28, 231 (1978).

(d) DBPO=di-*t*-butylperoxalate

(e) Reference 2

(f) *t*-Butoxy radicals produce N,N-dimethylformyl radicals from DMF; see E. G. Janzen, E. R. Davis and D. E. Nutter, Jr., Tetrahedron Letters, 3309 (1978).

(g) E. G. Janzen, D. E. Nutter, Jr. and C. A. Evans, J. Phys. Chem., 79, 1983 (1975).

(h) 8 lines in MeOH/H_2O mixture.

(i) J. L. Poyer, R. A. Floyd, P. B. McCay, E. G. Janzen and E. R. Davis, Biochmica Biophysics Acta, 539, 402 (1978).

(j) Details of this reaction will be submitted separately.

References and Notes

1. E. G. Janzen, R. L. Dudley and R. V. Shetty, J. Am. Chem. Soc., 101, 243 (1979).
2. E. G. Janzen and B. J. Blackburn, J. Am. Chem. Soc., 90, 5909 (1968); 91, 4481 (1969); E. G. Janzen, Acc. Chem. Res., 4, 31 (1971).
3. This kind of spectrum is also found in 3- and 4-pyridyl-N-oxide *t*-butyl nitrone spin adducts of hydroxyl radical; E. G. Janzen, Y. Y. Wang and R. V. Shetty, J. Am. Chem. Soc., 100, 2923 (1978).
4. A solution of 2.1 g (0.01 mole) of o-benzaldehyde sulfonic acid sodium salt (Eastman) and 1.1 g (0.012 mole) of N-*t*-butylhydroxylamine (5) in 40 ml of absolute ethanol was stirred and heated under reflux for 2 days. The solution was concentrated on a rotary evaporator and the residue was recrystallized from absolute ethanol-anhydrous ether (6); mp 253-255° (decompos.); yield 2.2 g (78%). ^{1}H nmr (δ values in D_2O): 1.52 (s, 9H, *t*-butyl), 7.52-7.80 (m, 2H, aromatic), 7.90-8.12 (m, 1H, aromatic), 8.55-8.70 (m, 1H, aromatic), 8.72 (s, 1H, "vinyl"); Anal. calcd for $C_{11}H_{14}NO_4SNa$: C, 47.30; H, 5.06; N, 5.02; Found: C, 47.38; H, 5.03; N, 4.92.
5. N-*t*-butylhydroxylamine was prepared according to A. Caldir, A. R. Forrester and S. P. Hepburn, Org. Syn., 52, 77 (1972).
6. It should be noted that care should be taken to continue recrystallizations until a control experiment shows no hydroxy adduct from solutions of sodium 2-SPBN. Apparently H_2O is incompletely eliminated in the initially formed hydroxylamine.
7. E. G. Janzen and I. G. Lopp, J. Mag. Res., 7, 107 (1972); E. G. Janzen and J. I-P. Liu, J. Mag. Res., 9, 510, 513 (1973).
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9. E. G. Janzen, Topics in Stereochemistry, 6, 177 (1971).

Acknowledgement

This work was supported by grants from the National Research Council of Canada. Grateful acknowledgement is hereby made.

(Received in USA 19 March 1979)