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SPIN TRAPPING BY USE OF A WATER-SOLUBLE NITROSO COMPOUND[1)]

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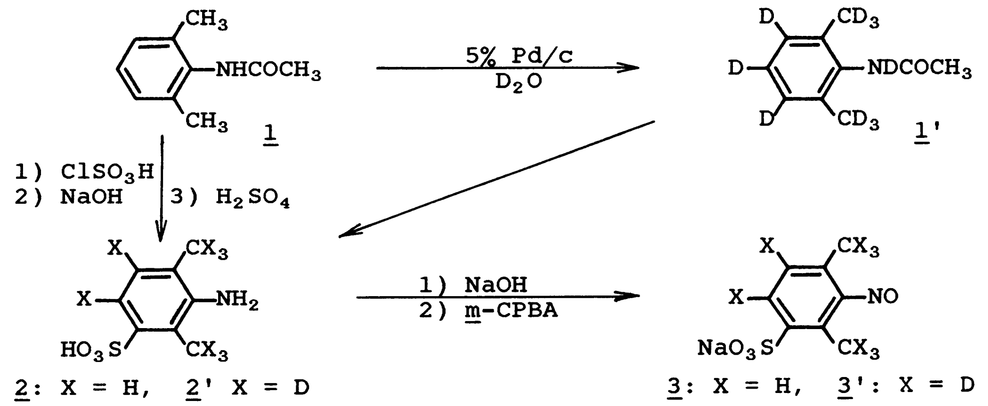
The preparation of sodium 2,4-dimethyl-3-nitrosobenzenesulfonate and its perdeuterio-analogue and their use in spin trapping in aqueous solutions are described.

Since 1968, much literature concerning the spin trapping technique has been published.[2-6)] Although in these reports spin trapping in organic solvents is well-documented, the recent trend has been to apply this technique to the field of free radical biochemistry, and a number of nitrone traps with hydrophilic or amphiphilic character have been synthesized for this purpose.[7,8)] Recently, Kirino and co-workers reported that 5,5-dimethylpyrroline-N-oxide (DMPO) is more suitable for use in aqueous solutions than phenyl N-tert-butyl nitrone (PBN), 2,5,5-trimethylpyrroline-N-oxide (TMPO) and 2-methyl-2-nitrosopropane (MNP).[9)] On the other hand, in 1981 Perkins and co-workers reported the preparation of sodium 3,5-dibromo-4-nitrosobenzenesulfonate and its dideuterio-analogue as a water-soluble nitroso spin trap which generally yields more information than spectra obtained using nitrone spin traps.[10)]

We previously reported that nitrosodurene (ND) is an excellent spin trap because of the following advantageous points: 1) the simplicity of ESR spectra of nitroxide radicals formed, 2) the stability to photolysis, 3) the wide scattering of β-hydrogen splitting constants, and 4) the high efficiency of trapping.[11)] However, ND is not usable for aqueous systems due to its insolubility in water.

Various attempts were made to synthesize nitrosodurenesulfonic acid to obtain a water-soluble ND-type compound, but they were unsuccessful because durene is subject to the Jacobsen reaction. Thus we synthesized sodium 2,4-dimethyl-3-nitrosobenzenesulfonate (DMNS) as well as its perdeuterio compound (DMNS-d_8)[12)]



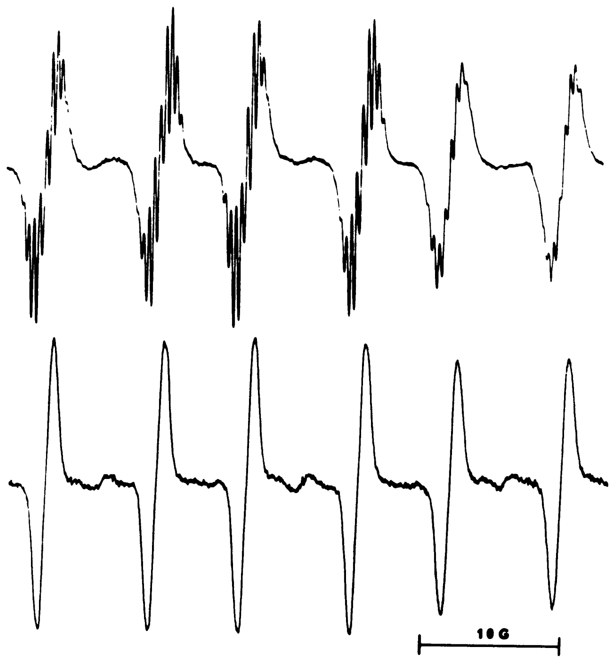


Fig. 1. (a) ESR spectrum of the α-hydroxyethyl spin adduct of DMNS obtained from ethanol by photolysis of an aqueous H_2O_2 solution at room temperature. (b) ESR spectrum of the α-hydroxyethyl spin adduct of DMNS-d_8 obtained under the same conditions as (a).

and found DMNS-d_8 to be an efficient spin trap in aqueous, or partially aqueous solutions. The structure of compound 2 was confirmed by means of NMR and X-ray diffraction. DMNS and DMNS-d_8 are colorless dimers in the crystalline state and are almost colorless even in solutions at room temperature. This indicates that DMNS and DMNS-d_8 are strongly dimerized in solution. Nevertheless, even in dilute solutions a sufficient amount of monomer is present to give spin adducts, nitroxide radicals.

A solution of DMNS or DMNS-d_8 irradiated with light from a 500 W high-pressure mercury lamp produces no detectable paramagnetic species, while DMPO is sensitive to light, generating some paramagnetic species, which give signals that interfer with the spectral analysis of spin adducts. Accordingly, DMNS or DMNS-d_8 may be preferably used as a spin trap in photochemistry. ESR spectra of the α-hydroxyethyl radical spin adducts of DMNS and DMNS-d_8 generated from ethanol in an aqueous hydrogen peroxide solution by photolysis are shown in Figure 1. These spectra revealed that the nine fine splittings of (a) arise from hydrogens of two methyl groups and the phenyl ring. The spectrum (b) is very similar to that of the α-hydroxyethyl radical spin adduct of ND.[11)] It is noteworthy that DMNS-d_8 yields a spectrum which seems to be the spin adduct with the hydroxyl radical generated photochemically from a dilute hydrogen peroxide solution itself.

ESR parameters of some spin adducts of DMNS-d_8 in aqueous solutions are listed in Table 1. The nitrogen splittings of the alkyl radical spin adducts are slightly larger than those of ND in organic solvents and similar to those of sodium 3,5-dibromo-4-nitrosobenzenesulfonate in aqueous solutions.[10)]

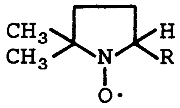
Comparisons of trapping efficiencies and half-lives of spin adducts of DMNS-d_8 and DMPO are shown in Table 2. Although DMNS-d_8 is inferior to DMPO for spin trapping of the hydroxyl radical, the former is clearly superior to the latter for trapping of the alkyl radicals.

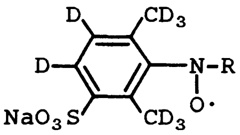
Table 1. ESR parameters for spin adducts of DMNS-d_8 on spin trapping in aqueous solutions[a)]

Trapped radical	Source	g-Value	a_N(Gauss)	a_H^β(Gauss)
$\cdot OH$	3% H_2O_2-hv	2.0054	14.02	
$\cdot CH_3$	CH_3I-CH_3OH-hv	2.0057	14.76	13.84
$\cdot CH_2OH$	CH_3OH-H_2O_2-hv or CH_3OH-$Na_2S_2O_8$-hv	2.0057	14.10	8.76
$\cdot CH_2CH_2OH$	EtOH-H_2O_2-hv [b)]	2.0056	14.32	8.67
$\cdot CH(OH)CH_3$	EtOH-H_2O_2-hv or EtOH-$Na_2S_2O_8$-hv	2.0057	14.39	8.02
$\cdot C(OH)Me_2$	i-PrOH-H_2O_2-hv	2.0058	14.61	
$\cdot SPh$	Ph_2S-CH_3CN-hv	2.0066	16.16	

a) Irradiation with a high-pressure mercury lamp. b) 310 nm.

Table 2. Efficiency of trapping and half-lives of spin adducts of DMPO and DMNS-d_8





R	Efficiency[a)]	Half-life[b)] (min)	Efficiency[a)]	Half-life[b)] (min)
OH	very high	11.5	very low	--
CH_2OH	1	7.5	5	12.0
$CH(OH)CH_3$	1	7.0	10	9.1

a) Based on the relative signal height of adducts under the same conconcentration of DMPO and DMNS-d_8. b) From the decay curves after the light was switched off.

Generally, in the spin trapping experiments, it is important to use more than one spin trap to probe each reaction system. The new compound DMNS-d_8 is recommended as a water-soluble nitroso spin trap owing to its excellent features described above.

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12) Three repeated treatments of 5 g of 1 with 5 g of 5% palladium carbon in 20 ml of D_2O at 120°C for 20 days produce 1'. Alkaline hydrolysis of the sulfonated product prepared from 1 or 1' by chlorosulfonic acid affords the sulfonate of 2 or 2', which when treated with dilute sulfuric acid gives 2 or 2'. Compound 2 or 2', purified by recrystallization with H_2O, is converted again to its sodium sulfonate which is oxidized to 3 or 3' with *m*-chloroperbenzoic acid (*m*-CPBA) in methanol. Addition of ether to the methanol solution of crude 3 or 3' precipitates pure 3 or 3'. mp >300°C; UV (H_2O) λ_{max} 305 nm, ε 3218; IR (KBr) 1193 cm^{-1} (SO_3), 1252 cm^{-1} (N=O, trans dimer); Raman (solid) 1449 cm^{-1} (N=N, dimer); NMR (D_2O) δ 2.47 (3H, s), 2.71 (3H, s), 7.49 (1H, d, J = 8 Hz), 8.14 (1H, d, J = 8 Hz). The deuteration ratio of 3' was determined by NMR using dimethylsulfone as an internal standard and showed that six hydrogens of two methyl groups and one hydrogen of the 6-position were deuterated completely, and about 40% of the hydrogen of the 5-position was unchanged, which has little effect on the spectra because of the small couplings of ring hydrogens.

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