A Water-soluble, Nitroso-aromatic Spin-trap

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Summary The preparation and use in spin-trapping experiments of sodium 3,5-dibromo-4-nitrosobenzenesulphonate and its dideuterio-analogue are described.

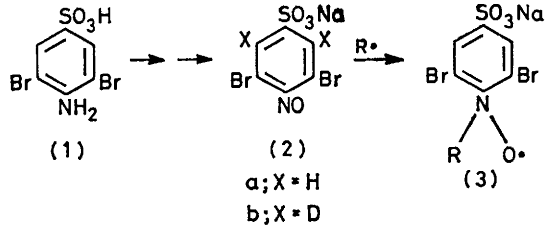
WHILST it is generally acknowledged that the literature of spin-trapping contains many suspect interpretations of the results, the technique has been widely used.[1] In recent years, the technique has been used in biological chemistry[2,3] and a number of nitrone traps have been synthesised with hydrophilic[4] or amphiphilic[5] character for biochemical investigations. The e.s.r. spectra of nitrone spin-adducts are generally less informative than spectra obtained using nitroso-spin-traps.[1] Nevertheless, nitroso-compounds have been little used in aqueous solutions and to our knowledge only one, 2-(hydroxymethyl)-2-nitrosopropane, has been synthesised specifically to use its water solubility.[6] This compound, like 2-methyl-2-nitrosopropane (MNP), which is slightly soluble in water, is very sensitive to visible light and readily yields a di-tertiary-alkyl nitroxide on photolysis.

TABLE. Hyperfine splitting data for selected spin-adducts of (**2b**).

Radical trapped ($R\cdot$)	Method of generation of $R\cdot$[a]	Hyperfine splittings for the spin adduct [(**2b**)$R\cdot$] (gauss)		
		a_N	a_H	a_{other}
$Me\cdot$	$h\nu$–H_2O–DMSO–H_2O	14·5	13·5 (3 H)	
”	DBPO–HOAc	13·7	12·2 (3 H)	
$HOCH_2\cdot$	$h\nu$–H_2O_2–MeOH–H_2O	13·7	9·2 (2 H)	
$HOCH_2CH_2\cdot$	$h\nu$–H_2O_2–EtOH–H_2O	14·1	11·3 (2 H)	
$Me\dot{C}HOH$	” ” ” ”	14·0	9·2 (1 H)	
$Me\dot{C}HOEt$	Et_2O–DBPO–HOAc–H_2O	12·5	7·1 (1 H)	
$Ph\cdot$	$(PhCO_2)_2$–HOAc	9·9	*ca.* 1·0 (2 H; *m*) *ca.* 2·75 (3 H; *o,p*)	
$Me_2CH\cdot$	$(Me_2CHCO_2)_2$–HOAc	14·2	9·3 (1 H)	
$Me_3C\cdot$	$h\nu$–MNP–H_2O	14·5		
$MeCH(OH)CH_2\cdot$	$h\nu$–H_2O_2–Me_2CHOH–H_2O	14·0	9·8 (1 H)[b] 11·25 (1 H)[b]	
$BH_3\cdot^-$[c]	$NaBH_4$–DMF	13·1	13·1 (3 H)	5·9 (1 B)
$HO_2C(NH_2)CHCH_2\cdot$	$h\nu$–H_2O_2–$MeCH(NH_2)CO_2H$–H_2O	14·0	9·9 (1 H)	

[a] DBPO = di-t-butyl peroxyoxalate; MNP = 2-methyl-2-nitrosopropane; DMSO = dimethyl sulphoxide; DMF = dimethylformamide. [b] Diastereotopic. [c] Following the procedure of Crozet and Tordo (M. P. Crozet and P. Tordo, *J. Am. Chem. Soc.*, 1980, **102**, 5696); we have been unable to obtain spectra of the hydro-nitroxides ($ArNHO\cdot$) from (**2**).

Sensitivity to visible light is less of a problem with aromatic *C*-nitroso-compounds and we have now synthesised the sodium salt of 3,5-dibromo-4-nitrosobenzenesulphonic acid (**2a**), as well as its 2,6-dideuterio-analogue (**2b**), and have found them to be efficient radical scavengers in aqueous, or partially aqueous, solutions. The compounds have a solubility of *ca.* 100 g l^{-1} in water at 20 °C, but are substantially dimeric in solution. Thus, the saturated solutions are pale green and a more pronounced blue-green colour develops only on warming. Nevertheless, even in dilute solutions there is sufficient monomer present to give spin-adducts (**3**) (Scheme), *e.g.* by thermal decomposition of di-t-butyl peroxyoxalate in H_2O–HOAc–Et_2O (4:5:1) at 25 °C or by photochemical reactions of aqueous solutions of H_2O_2 and organic substrates at 20 °C.



SCHEME

The new traps do not yield observable spin-adducts with hydroxyl radicals, but the inclusion of dimethyl sulphoxide (DMSO) in the aqueous H_2O_2 system gives intense spectra of the adducts of methyl radicals which arise *via* hydroxyl radical attack on DMSO; this provides an indirect indication of hydroxyl participation.[7] Methyl radical adducts were also obtained from the peroxyoxalate (by fragmentation of $Bu^tO\cdot$) in glacial acetic acid; spectra of the methyl adducts of (**2a**) and (**2b**) produced in this way are compared in the Figure. The absence of *meta*-splittings in the spectra obtained from (**2b**) greatly improves the resolution of more complex spin-adduct spectra such as those from aryl radicals.

Hyperfine splittings for a selection of the spin-adducts of (**2b**) are listed in the Table, together with the methods of generation.

First indications are that in biological systems the traps introduced here may afford information different from that obtained using lipid-soluble traps, such as MNP. An account of these studies will be presented separately.

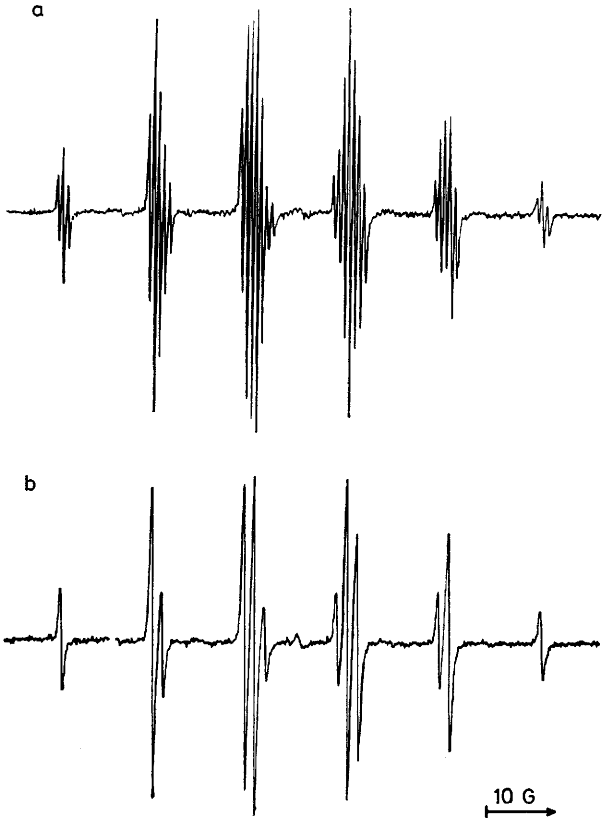


FIGURE. E.s.r. spectra of the methyl spin-adducts (a) of (**2a**) and (b) of (**2b**), obtained as described in the text.

Compound (**2a**) was obtained from 3,5-dibromosulphanilic acid[8] (**1**) by oxidation with H_2O_2 in glacial acetic acid, after first adding 1 equiv. of sodium acetate.† It could also be obtained, but in inferior yield, by carrying out the oxidation with *m*-chloroperoxybenzoic acid in acetic acid.

The deuteriated analogue (**2b**) was prepared similarly, starting from perdeuterioaniline which was sulphonated (D_2SO_4) and brominated to give the di-deuterio-analogue of (**1**).

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† A solution of 3,5-dibromosulphanilic acid (10 mmol) in a mixture of glacial acetic acid (30 ml), 30% aqueous hydrogen peroxide solution (70 mmol), and anhydrous sodium acetate (10 mmol) was warmed gently to bring the solids into solution. The solution was allowed to stand at room temperature for 14 days, when the straw-coloured blades which had formed were separated and washed with acetic acid (5 ml) and three times with dried ether (50 ml). Acetic acid was removed by crystallisation from ethanol to give analytically pure sodium 3,5-dibromo-4-nitrosobenzenesulphonate as a pale yellow powder, m.p. >300 °C. The yield was 34%.

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