The Ambident Nucleophilicity of Sulphenate Anions [1]

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2-Nitro-4-trifluoromethylbenzene- and 2-nitrobenzene-sulphenate anions, generated by the base-catalysed hydrolysis of the corresponding disulphide or sulphenate ester, undergo *S*-methylation with methyl iodide but predominantly *O*-methylation with the 'harder' methylating agents, methyl fluorosulphonate and dimethyl sulphate. Sulphinate ions react similarly with methyl fluorosulphonate.

THE ambident nucleophilicity of the anions of sulphinic acids, $R{\cdot}SO{\cdot}O^-$, is well established.[2] In contrast sulphenic acids R·S·OH, and their anions have not been studied extensively until comparatively recently, as they are usually too reactive to be isolable. The existence of such species has been inferred from spectral data [3] and from trapping experiments.[4] Before the commencement of this study all the reported nucleophilic reactions of sulphenate anions (II) occurred at the sulphur atom [4] to give the sulphoxide (I; R^2 = alkyl) or a sulphinyl derivative. The corresponding reaction at the oxygen atom would have given a sulphenate ester (III; R^2 = alkyl) or a similar derivative, the isolation of which would have been complicated by its hydrolysis to reform the sulphenate anion (II).

$$\underset{\text{(I)}}{R^1\text{-}\overset{\overset{O}{\|}}{S}\text{-}R^2} \xleftarrow{R^2X} \underset{\text{(II)}}{R^1\text{-}S\text{-}O^-} \underset{OH^-}{\overset{R^2X}{\rightleftharpoons}} \underset{\text{(III)}}{R^1\text{-}S\text{-}O\text{-}R^2} \quad (1)$$

Establishment of the ambident nature of the sulphenate anion therefore required in the first instance a sulphenate anion and ester, or other derivative, having an adequate lifetime in the medium and a convenient method of identification. These requirements were fulfilled by the anion and methyl ester of 2-nitro-4-trifluoromethylbenzenesulphenic acid where the substituents stabilise the derivatives [5] and ^{19}F n.m.r. provides [3b] a convenient method of identification.

Hydrolysis of Bis-(2-nitro-4-trifluoromethylphenyl) Disulphide.—Reaction of bis-(2-nitro-4-trifluoromethylphenyl) disulphide with sodium hydroxide in 30% (v/v) aqueous dioxan gave the intense blue colouration characteristic [6] of 4-substituted 2-nitrobenzenesulphenate anions. The ^{19}F n.m.r. spectrum of the reacting solution consisted initially of two singlets having approximately equal intensities at 1 289 and 1 263 Hz measured downfield from trifluoroacetate ion, the internal reference. These signals were previously assigned [3b] to the thiolate ion and the sulphenate anion respectively. The small change in chemical shift (*ca.* 5 Hz) compared with previous work is considered to arise from a decrease in the ionic strength of the solution. These results are

$$ArSSAr + 2\,OH^- \longrightarrow ArS^- + ArSO^- + H_2O \quad (2)$$

in agreement with equation (2) being the initial step in the hydrolysis.

As the reaction progressed the relative intensity of the sulphenate anion signal decreased, due to its further reaction, until after 30 min the initial signals had relative intensities of 2 : 1. Other minor signals were also apparent by this time in agreement with previous work.[3b]

Addition of a nine-fold excess of methyl iodide to this solution resulted in the immediate disappearance of the signal attributed to the thiolate ion and its replacement by a singlet at 1 208 Hz assigned to methyl 2-nitro-4-trifluoromethylphenyl sulphide formed by methylation of the thiolate ion. The sulphenate anion signal and the relative intensities were initially unaffected. After a further 30 min the solution had become acidic and the sulphenate anion signal had disappeared to be replaced with a signal of slightly lower intensity at 1 177 Hz assigned to methyl 2-nitro-4-trifluoromethylphenyl sulphoxide (I; R^1 = 4-CF_3-2-$NO_2C_6H_3$, R^2 = Me) formed by methylation of the sulphenate ion at sulphur. With a two-fold excess of methyl iodide the methyl sulphide signal at 1 208 Hz was formed immediately, as before, but the signal attributed to the methyl sulphoxide was not observed. The sulphenate anion signal disappeared more slowly in this case (55 min) and was replaced by a signal at 1 363 Hz attributed to the 2-nitro-4-trifluoromethylphenoxide anion. After 24 h the relative intensity of these signals (1 208 Hz : 1 363 Hz) was 3 : 1. With this concentration of methyl iodide the reaction mixture remained alkaline throughout and methyl 2-nitro-4-trifluoromethylphenyl sulphoxide was shown independently to react with hydroxide ion to give the corresponding phenoxide, presumably by a nucleophilic displacement of the methanesulphenate anion from the aryl group [equation (3)].

$$Ar\text{-}\overset{\overset{O}{\|}}{S}Me + 2\,OH^- \longrightarrow ArO^- + MeSO^- + H_2O \quad (3)$$

Addition of a nine-fold excess of methyl fluorosulphonate after 30 min to an identical alkaline disulphide solution acidified the solution virtually instantaneously. The original n.m.r. signals were immediately replaced by two singlets, having relative intensities of 2 : 1, at 1 208 Hz (ArSMe) and 1 215 Hz, assigned to methyl 2-nitro-4-trifluoromethylbenzenesulphenate (III; R^1 = 4-CF_3-2-$NO_2C_6H_3$, R^2 = Me), the product formed by methylation of the sulphenate anion at oxygen. Use of a two-fold excess of methyl fluorosulphonate led to the immediate and quantitative

formation of the methyl sulphide, but no indication of the formation of the methyl sulphenate was observed and the signal attributed to the sulphenate anion was not materially affected.

When a two-fold excess of methyl fluorosulphonate was added to the disulphide in dioxan immediately before addition of the aqueous sodium hydroxide, methylation did not occur. The course of the hydrolysis was unaffected, although the rate was decreased. Presumably the methyl fluorosulphonate hydrolysed to methanol much faster than the disulphide hydrolysed to give the thiolate and sulphenate anions. It is noteworthy that under these conditions the methyl sulphenate is not formed from methanol and either disulphide or sulphenate anion in alkaline solution.

Similar results to those obtained with methyl fluorosulphonate were obtained when dimethyl sulphate was used as the methylating agent, although in this case the relative intensity of the methyl sulphenate signal was lower, due presumably to the less efficient trapping of the sulphenate anion. No clear spectral evidence for the presence of the methyl sulphoxide or the phenoxide ion could be obtained when the last two methylating agents were used.

The difficulties associated with the identification of signals from small amounts of minor products in the presence of background noise were, to some extent, circumvented by product isolation. Yields were calculated from the stoicheiometry of equation (2) and details are in the Table. The low yield of methyl

Methylation products obtained from the alkaline hydrolysate of bis-(2-nitro-4-trifluoromethylphenyl) disulphide

	Percentage yield			
Reagent	ArSMe	ArS·OMe	ArSO·Me	ArSSAr
MeI	117		40	
Me_2SO_4	66	4	8	5
$MeSO_3F$	98	30	1	

sulphoxide and the high yield of methyl sulphide formed with methyl iodide may be due to its comparative inefficiency as a trapping agent. This allows loss of sulphenate anion by reactions [5] (4) and (5) to form thiolate ion and hence, after methylation, give a yield of the methyl sulphide which is greater than theoretical based on equation (2).

$$2ArSO^- + H_2O \longrightarrow ArSO{\cdot}SAr + 2OH^- \quad (4)$$

$$ArSO{\cdot}SAr + 2\,OH^- \longrightarrow ArSO_2^- + ArS^- + H_2O \quad (5)$$

Methyl sulphenate was not detected in the products of this reaction, but small amounts could easily have been formed and hydrolysed back to the sulphenate anion. This is presumably the reason for the low yield of methyl sulphenate obtained with the other reagents, especially with dimethyl sulphate, which has the lower reactivity. Methyl sulphoxide was obtained in all cases; in isolable amounts with dimethyl sulphate and in detectable amounts (^{1}H n.m.r.) with methyl fluorosulphonate. The lower total yields of methylated products obtained from the sulphenate anion with the last two reagents is not accompanied by an enhanced yield of the methyl sulphide. This is attributed to the much faster rate of hydrolysis of these reagents which essentially removes them from solution before an appreciable amount of thiolate ion has been formed by reactions (4) and (5). The disulphide isolated in the dimethyl sulphate reaction might arise from untrapped thiolate ion by equation (6).

$$ArS^- + ArS{-}OMe \longrightarrow ArSSAr + MeO^- \quad (6)$$

Hydrolysis of Bis-(2-nitrophenyl) Disulphide.—Bis-(2-nitrophenyl) disulphide was similarly hydrolysed, the resulting anions methylated, and the products identified using ^{1}H n.m.r. spectroscopy. A similar pattern of reactivity was observed. Methyl iodide gave a mixture of the methyl sulphide and the methyl sulphoxide in the ratio 2.5 : 1. This ratio reflects the lower stability of the 2-nitrobenzenesulphenate anion compared [5] with the 4-trifluoromethyl analogue. Methyl fluorosulphonate gave the methyl sulphide, methyl sulphenate, and a trace of the sulphoxide, but dimethyl sulphate gave only the methyl sulphide.

Hydrolysis of Methyl 2-Nitro-4-trifluoromethylbenzenesulphenate.—Generation of the sulphenate anion by hydrolysis of methyl 2-nitro-4-trifluoromethylbenzenesulphenate (III; R^1 = 4-CF_3-2-$NO_2C_6H_3$, R^2 = Me) and methylation of the half hydrolysed solution should give a mixture of starting material and the methyl sulphoxide (I; R^1 = 4-CF_3-2-$NO_2C_6H_3$, R^2 = Me) as in equation (1). Addition of a seven-fold excess of methyl fluorosulphonate and analysis by ^{19}F n.m.r. indicated a ratio of methylation at oxygen to that at sulphur of 6 : 1 respectively. Dimethyl sulphate gave a ratio of 3 : 2, although a considerable amount of the anion escaped methylation. Methyl iodide gave only methylation at sulphur.

Methyl 2-nitro-4-trifluoromethylbenzenesulphenate was not converted into the corresponding sulphoxide by sodium iodide under the conditions used for methylation. The isolation of the methyl sulphoxide is not therefore due to thermodynamic control of the products when methyl iodide is the reagent.

Methylation of 2-Nitro-4-trifluoromethylbenzenesulphinate Anion.—Sulphinate anion is one of the final products from the hydrolysis of sulphenyl derivatives [6] and 2-nitro-4-trifluoromethylbenzenesulphinate anion was frequently detected in the previous reaction by its signal at 1 199 Hz,[3b] although methylation was not observed under the conditions previously described. Despite a ten-fold increase in concentration, compared with the other substrates, this anion was not methylated by ten equivalents of methyl iodide at 50 °C. When a similar excess of methyl fluorosulphonate was added at room temperature the solution was rapidly acidified and the signal at 1 19g Hz was replaced by signals attributed to the sulphinic acid (1 191 Hz, 50%), the methyl sulphinate (1 159 Hz, 25%), the methyl sulphone (1 126 Hz, 10%), and the sulphonic acid (1 166 Hz, 15%).

Compared with the previous substrates this sulphinate

anion is a poor nucleophile, only 35% being methylated even at these higher concentrations. As expected [2]

$$ArSO_2^- \xrightarrow[H_2O]{MeOSO_2F} ArSO_2{\cdot}Me + ArSO{\cdot}OMe + ArSO_2H \quad (7)$$

ambident nucleophilicity is observed, and methyl fluorosulphonate reacts preferentially at the oxygen atom rather than at sulphur. Formation of sulphonic acid, which also occurred during attempted methylation with methyl iodide, may be due to either aerial oxidation of the sulphinate [3b] or auto-oxidation of sulphinic acid.[6] The latter appears unlikely as no evidence for thiosulphonate formation was observed.

$$3ArSO_2H \longrightarrow ArSO_3H + ArSO_2SAr + H_2O \quad (8)$$

DISCUSSION

These results clearly establish the ambident nature of the sulphenate ion to simple alkylating agents. Methyl iodide gives exclusively the methyl sulphoxide, whereas methyl fluorosulphonate gives predominantly the methyl sulphenate. Dimethyl sulphate is intermediate in behaviour but has a greater resemblance to methyl fluorosulphonate.

The HSAB principle [7] readily rationalizes these observations. In the 'tight' [8] S_N2-type transition state predicted for the reaction involving methyl iodide, the carbon atom should have little cationic character and should therefore bond preferentially with the 'soft' nucleophilic centre, the sulphur atom, to give the sulphoxide. With methyl fluorosulphonate the transition state should be much 'looser' and have considerable S_N1 character. The carbon atom should thus be relatively positive and react more readily with the 'harder' oxygen atom yielding the methyl sulphenate. Although dimethyl sulphate is essentially similar to methyl fluorosulphonate, it has a poorer leaving-group and thus the carbon atom should have a slightly lower cationic character and should show a reduced preference for reaction with the 'harder' atom. The steric effect of the *o*-nitro-group does not appear to influence the site of reaction in this system.

The thiolate anion was always completely methylated before the ^{19}F n.m.r. spectrum could be recorded (*ca.* 2 min) and was a much better *S*-atom nucleophile than sulphenate ion, which required 30 min to complete 90% reaction. No reaction was observed with the sulphinate ion under these conditions. The observed order of reactivity at sulphur, $ArS^- > ArSO^- > ArSO_2^-$, decreases with increasing oxidation and hence with the decreasing polarisability of the sulphur atom. This is in accord with previous observations [9] that, on average, thiolate ions are 5×10^5 times more reactive in S_N2 reactions than sulphinate ions. In this study thiolate ions are at least 15 times more reactive than sulphenate ions in bimolecular methylation.

Methyl fluorosulphonate rapidly methylated all the ions in solution. *S*-Methylation of the thiolate ion was however still faster than *O*-methylation of sulphenate ion, which was only observed when sufficient reagent was used to react with all the sodium hydroxide present in the reaction mixture. Sulphinate ion appeared to be even less competitive.

In agreement with these results, reaction of the anions of oxoazetidinesulphenic acids with methyl fluorosulphonate has been shown [10] to give exclusive *O*-methylation.

EXPERIMENTAL

I.r. spectra were measured for KBr discs of Nujol mulls and n.m.r. spectra for solutions in $CDCl_3$.

Materials.—Dioxan was purified as previously described [5] and used within 2—3 days.

Methyl 2-nitro-4-trifluoromethylbenzenesulphenate was prepared (80%) from the sulphenyl chloride and triethylamine in dry methanol as yellow needles, m.p. 61—64 °C [light petroleum (b.p. 60—80 °C)]; τ 1.44br (1 H, d, *J* 1 Hz), 2.09 (2 H, d, *J* 1 Hz), and 6.15 (3 H, s) (Found: C, 37.9; H, 2.5; N, 5.7; S, 12.6. $C_8H_6F_3NO_3S$ requires C, 37.9; H, 2.4; N, 5.5; S, 12.6%).

2-Nitro-4-trifluoromethylbenzenethiol was prepared (50%), from equimolar quantities of sodium sulphide nonahydrate and 4-chloro-ααα-trifluoro-3-nitrotoluene in ethanol, as a low melting solid, or red oil, b.p. 105—108 °C at 0.06 mmHg, τ 1.40br (1 H, s), 2.37 (2 H, d, *J* 2 Hz), and 5.73 (1 H, s) (Found: C, 37.5; H, 1.6; N, 6.4; S, 14.3. $C_7H_4F_3NO_2S$ requires C, 37.7; H, 1.8; N, 6.3; S, 14.3%). Methylation of the thiol with methyl iodide in aqueous methanolic sodium hydroxide solution gave *methyl 2-nitro-4-trifluoromethylphenyl sulphide* (88%) as yellow plates, m.p. 94—96 °C [light petroleum (b.p. 60—80 °C]; τ 1.46br (1 H, d, *J* 3 Hz), 2.15 (1 H, dd, *J* 9 Hz, 3 Hz), 2.48 (1 H, d, *J* 9 Hz), and 7.43 (3 H, s) (Found: C, 40.4; H, 2.6; N, 5.5; S, 13.6. $C_8H_6F_3NO_2S$ requires C, 40.5; H, 2.5; N, 5.9; S, 13.5%). Oxidation of the sulphide with an equimolar quantity of sodium metaperiodate in 70% aqueous acetic acid under reflux gave *methyl 2-nitro-4-trifluoromethylphenyl sulphoxide* (65%) as pale yellow needles, m.p. 113—116 °C [light petroleum (b.p. 60—80 °C); ν 1 060 cm^{-1} (SO); τ 1.44—1.50 (2 H, m), 1.80 (1 H, d, *J* 4 Hz), and 7.05 (3 H, s) (Found: C, 38.0; H, 2.3; N, 6.3; S, 12.7. $C_8H_6F_3NO_3S$ requires C, 37.9; H, 2.4; N, 5.5; S, 12.6%). An excess of sodium metaperiodate similarly gave *methyl 2-nitro-4-trifluoromethylphenyl sulphone* (66%) as needles, m.p. 141—143 °C (chloroform), ν 1 320 and 1 150 cm^{-1} (SO_2); τ 1.58 (1 H, d, *J* 8 Hz), 1.88 (1 H, s), 1.93 (1 H, d, *J* 8 Hz), and 6.54 (3 H, s) (Found: C, 35.8; H, 2.0; N, 4.9; S, 11.9. $C_8H_6F_3NO_4S$ requires C, 35.7; H, 2.2; N, 5.2; S, 11.9%).

Methyl 2-nitro-4-trifluoromethylbenzenesulphinate was prepared (32%) by sodium metaperiodate oxidation of the sulphenate as yellow needles, m.p. 32.5—34 °C [light petroleum (b.p. 40—60 °C)], ν 1 085 cm^{-1} (OSO); τ 1.48 (1 H, s), 1.56 (1 H, d, *J* 8 Hz), 1.85 (1 H, d, *J* 8 Hz), and 6.24 (3 H, s) (Found: C, 35.3; H, 2.0; N, 5.5; S, 12.1. $C_8H_6F_3NO_4S$ requires C, 35.7; H, 2.2; N, 5.2; S, 11.9%). All other materials were as described.[3b]

^{19}F *N.m.r. Spectra of Reaction Mixtures.*—All spectra were recorded at 30 °C in 30% (v/v) aqueous dioxan using a Varian A100 n.m.r. spectrometer operating at 94.1 MHz. All signals are expressed in Hz downfield from the internal reference; the trifluoroacetate ion (*ca.* 10% in aqueous dioxan) and signals were assigned by comparison with the spectrum obtained after the addition of an authentic

specimen. Hydrolysis reactions were initially 0.02M in disulphide or 0.05M in methyl sulphenate, and 0.25M in sodium hydroxide. The appropriate excess of methylating agent was added after 30 min reaction or as otherwise described. Signals attributed to other intermediates in the hydrolyses were observed as before [3b] but were not obviously affected by methylation.

Methylation of sodium 2-nitro-4-trifluoromethylbenzenesulphinate (0.1M) was studied in 30% (v/v) aqueous dioxan containing sodium hydroxide (0.3M) and methylating agent (1.0M).

Product Isolation.—(a) *Methyl Fluorosulphonate.* 1% Aqueous sodium hydroxide solution (100 ml, 0.025 mol) was added rapidly to a stirred solution of bis-(2-nitro-4-trifluoromethylphenyl) disulphide (0.55 g, 0.001 25 mol) in dioxan (100 ml). Methyl fluorosulphonate (2.85 g, 0.025 mol) in dioxan (10 ml) was added, the solution diluted with water (500 ml), and immediately extracted with dichloromethane. The solvent was removed and the residue chromatographed (t.l.c.) on a 1 m silica gel (HF 254) plate using 4 : 1 light petroleum (b.p. 40—60 °C)–diethyl ether as eluant, to give methyl 2-nitro-4-trifluoromethylbenzenesulphenate (0.077 g, 24.5%), m.p. 55—58 °C, and methyl 2-nitro-4-trifluoromethylphenyl sulphide (0.285 g, 96.5%) which was shown by n.m.r. spectroscopy to contain a trace (*ca.* 2%) of methyl 2-nitro-4-trifluoromethylphenyl sulphoxide.

(b) *Dimethyl sulphate* (1.6 g, 0.012 5 mol) was added, as the methylating agent, to a similar reaction mixture. The blue solution was set aside for 5 min, neutralised with dilute hydrochloric acid, and worked up as before to give the disulphide (28 mg, 5%), methyl sulphenate (16 mg, 5.3%), m.p. 61—64 °C, methyl sulphide (193 mg, 65%), m.p. 93—95 °C, and methyl sulphoxide (24 mg, 8%, m.p. 114—116 °C.

(c) *Methyl iodide* (14.2 g, 0.1 mol) and bis-(2-nitro-4-trifluoromethylphenyl) disulphide (4.44 g, 0.01 mol) were dissolved in dioxan (750 ml), stirred, and a solution of sodium hydroxide (6 g, 0.15 mol) in water (750 ml) was added. The solution was set aside for 30 min, neutralised with dilute hydrochloric acid, and extracted with carbon tetrachloride. The solvent was removed and the residue chromatographed on an alumina column using 2 : 1 chloroform–light petroleum (b.p. 40—60 °C) to give methyl sulphide (2.77 g, 117%), m.p. 94—96 °C, and methyl sulphoxide (1.03 g, 41%), m.p. 109—111 °C.

Methylation of the 2-Nitrobenzenesulphenate Anion.—Bis-(2-nitrophenyl) disulphide (0.154 g, 0.000 5 mol) and methyl iodide (0.71 g, 0.005 mol) were dissolved in dioxan (75 ml), stirred, and a solution of sodium hydroxide (0.3 g, 0.007 5 mol) in water (25 ml) was added. Aliquots were taken at various times, neutralised with dilute hydrochloric acid, poured into water (50 ml), and extracted with chloroform. The solvent was removed and the residue dissolved in deuteriochloroform and analysed using ^{1}H n.m.r. spectroscopy. The relevant methyl signals are τ 6.18 (sulphenate), 7.05 (sulphoxide), and 7.50 (sulphide).

The procedure was repeated using dimethyl sulphate as the methylating agent and without a methylating agent. In the last case the aliquots were neutralised by addition of methyl fluorosulphonate.

Hydrolysis of Methyl 2-Nitro-4-trifluoromethylphenyl Sulphoxide.—Sodium hydroxide (1 g) in water (22.5 ml) was added to a solution of the sulphoxide (1 g, 0.004 mol) in dioxan (52.5 ml). The solution slowly turned a deep red. After 24 h the solution was acidified and extracted with chloroform to give 2-nitro-4-trifluoromethylphenol (0.68 g, 83%) as an orange oil identical with an authentic specimen. The hydrolysing solution did not give an e.s.r. signal and there was no evidence for C.I.D.N.P. in the n.m.r. Examination of the solution at 403 nm ($\lambda_{max.}$, ε = 4 950) indicated that reaction was virtually quantitiative.

One of us (A. R.) thanks the S.R.C. for a research studentship.

[8/803 *Received*, 2nd *May*, 1978]

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