Radical–Nucleophilic Substitution ($S_{RN}1$) Reactions: Preparation and Reactions of α-Nitrosulphides

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α-Nitrosulphides were prepared by $S_{RN}1$ reaction of 2-bromo-2-nitropropane with thiolate anions, and by S_N2 attack of sodium 2-nitropropan-2-ide on symmetrical disulphides. The α-nitrosulphides undergo radical–nucleophilic substitution ($S_{RN}1$) by nitronate, sulphinate, and malonate anions, but not by thiolate anions.

THE presence of a nitro-group on a tertiary carbon atom greatly facilitates substitution by some anions at that centre. The reactions proceed by a radical radical-anion chain ($S_{RN}1$) [1] mechanism and not by S_N1 or S_N2 mechanisms. Similar reactions take place when the nitro-group is replaced by a *p*-nitrophenyl group. These substitutions are light-catalysed and proceed under mild conditions to give good yields of product.[2]

The substitution proceeds by one of two pathways depending on the nature of the α-substituent (Scheme 1).

$$Me_2C(X)NO_2 + A^- \longrightarrow Me_2C(A)NO_2 + X^- \quad (E1)$$
$$\longrightarrow Me_2C(X)A + NO_2^- \quad (E2)$$

(E1) for X = I, Br, Cl, SO_2Ph
(E2) for X = NO_2, COR, CO_2R, CN, $C_6H_4NO_2$-*p* and A^- = $R_2CNO_2^-$, RSO_2^-, $RC^-(CO_2Et)_2$, etc.

SCHEME 1

In equation (E1) the nitro-group [3] remains while in equation (E2) it is substituted.[4,5] The $S_{RN}1$ (substitution, radical–nucleophilic, unimolecular) mechanism outlined in Scheme 2 has been proposed and well

$$Me_2C(X)NO_2 + A^- \overset{\text{electron transfer}}{\rightleftharpoons} [Me_2C(X)NO_2]^{-\cdot} + A^\cdot \quad (E3)$$
$$[Me_2C(X)NO_2]^{-\cdot} \longrightarrow Me_2CNO_2^\cdot + X^- \quad (E4)$$
$$Me_2CNO_2^\cdot + A^- \longrightarrow [Me_2C(A)NO_2]^{-\cdot} \quad (E5)$$
$$[Me_2C(A)NO_2]^{-\cdot} + Me_2C(X)NO_2 \xrightarrow{\text{electron transfer}} Me_2C(A)NO_2 + [Me_2C(X)NO_2]^{-\cdot} \quad (E6)$$

SCHEME 2

established.[1,2] An analogous mechanism is proposed for compounds reacting by equation (E2). The initiation step [equation (E3)] is effected by electron-transfer to the α-substituted nitro-compound from a suitable electron-donor; in this case it is the anion. Equations (E4), (E5), and (E6) represent the propagation steps of the chain reaction.

This paper describes the synthesis of α-nitrosulphides by three routes, one of which proceeds by the $S_{RN}1$ mechanism, and discusses the nature of the substitution occurring between these compounds and nucleophiles.

RESULTS AND DISCUSSION

Synthesis of α-Nitrosulphides.—(a) *Reaction of thiolates with 2-bromo-2-nitropropane* (1). 2-Bromo-2-nitropropane (1) reacts with a number of anions,[2] as shown in Schemes 1 and 2, by a radical–nucleophilic substitution ($S_{RN}1$) mechanism, the bromine atom being replaced by the nucleophile. Anions which have been used in this reaction include nitronates, sulphinates, and enolates. Thiolate anions have been shown to take part in substitutions on aromatic halides [1] and α-substituted *p*-nitrocumenes [2] by an $S_{RN}1$ mechanism.

Kornblum [5b] has shown that the phenylsulphinyl group of 2-nitro-2-phenylsulphinylpropane may be replaced by *p*-chlorophenylthiolate and suggested that the reaction proceeds by an $S_{RN}1$ mechanism.

It seemed feasible that thiolates would displace the bromine atom of 2-bromo-2-nitropropane (1) to yield α-nitrosulphides and that the reaction would occur by the $S_{RN}1$ mechanism (Scheme 2 with X = Br and A^- = RS^-).

o-Nitrophenylthiolate (2a), *p*-nitrophenylthiolate (2b), and 1,3-benzothiazol-2-yl thiolate (2c) all reacted with 2-bromo-2-nitropropane at room temperature under an atmosphere of nitrogen with illumination by fluorescent tubes (2 × 15 W) to give good yields (75—90%) of the respective thioethers (3a—c). The reaction of (2a) also produced some of the corresponding disulphide (4a) and 2,3-dimethyl-2,3-dinitrobutane.

Thiolate anions which are more easily oxidised and are stronger nucleophiles, such as *p*-chlorophenylthiolate (2d), *p*-tolylthiolate, benzenethiolate, and various aliphatic thiolates, gave high yields of the corresponding disulphides [6] instead of α-nitrothioethers.

We chose the reaction of *o*-nitrophenylthiolate with 2-bromo-2-nitropropane to investigate the mechanism of α-nitrosulphide formation. The reaction was conducted in the presence of various radical traps and electron-acceptors, and in the absence of light. The results are shown in Table 1. These methods have been established and used by other workers.[1,2]

TABLE 1

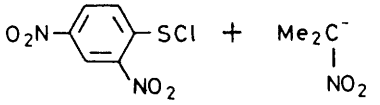
Reaction between 2-nitrophenylthiolate (2a) and the sodium salt of 2-nitropropane

Inhibitor	Yield of sulphide (3a) after 4 h (%)
None	75
Dark	41
Galvinoxyl	37
Oxygen	0
p-Dinitrobenzene (10 mol%)	36
(30 mol%)	0

The reaction is clearly catalysed by light. The yield of α-nitrosulphide in the light-catalysed reaction was

75%, and when the reaction was repeated in the dark the yield dropped to 41%. The exact nature of the light-catalysis is still uncertain, although Bunnett [7] has suggested that a charge-transfer complex of nucleophile and neutral species in the initiation step undergoes electron-transfer from one species to the other upon interaction with a photon.

The reaction is inhibited by catalytic amounts of galvinoxyl and *p*-dinitrobenzene, and the presence of an



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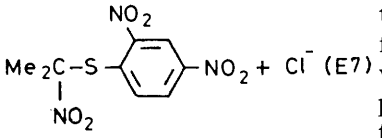
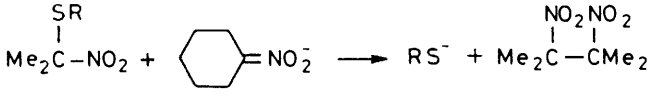
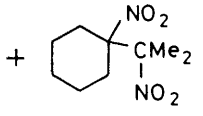


(3e)



(3) (2) (6)



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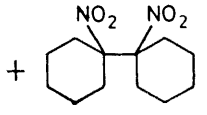
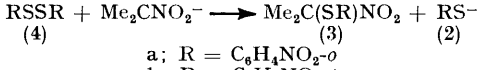


(9)

oxygen atmosphere. *p*-Dinitrobenzene and oxygen have been reported to be efficient electron scavengers [1,2,5c,8] and will inhibit $S_{RN}1$ processes by intercepting the intermediate radical-anions. Oxygen and galvinoxyl [2] have been reported to be efficient free-radical



a; R = $C_6H_4NO_2$-*o*
b; R = $C_6H_4NO_2$-*p*
d; R = C_6H_4Cl-*p*

SCHEME 3

scavengers for the inhibition of $S_{RN}1$ reactions. The profound effect of these substances clearly indicates that the reaction takes place by a radical-chain process.

These experiments provide good evidence that some thiolate anions react with 2-bromo-2-nitropropane to yield α-nitrosulphides by an $S_{RN}1$ mechanism (Scheme 2, X = Br and A^- = RS^-). We are further investigating the mechanism of formation of disulphides from the reaction of thiolates with 2-bromo-2-nitropropane and other α-substituted nitropropanes.

(b) *Reaction of the sodium salt of 2-nitropropane with symmetrical disulphides.* The synthesis of the α-nitrosulphides (3a), (3b), and (3d) has been reported in an earlier paper.[9]

The anion of 2-nitropropane (5) reacts with symmetrical disulphides (4a), (4b), and (4d) to yield the α-nitrosulphides (3a), (3b), and (3d) in good yield *via* an S_N2 mechanism (Scheme 3). The substitution only proceeds if the disulphide has strong electron-withdrawing substituents such as chloro- or nitro-groups.

(c) *Reaction of the sodium salt of 2-nitropropane with sulphenyl chlorides.* Kharasch [10] has reported that the anion reacts with 2,4-dinitrophenylsulphenyl chloride to give the α-nitrosulphide (3e) [equation (E7)]. We found that this route gave a satisfactory yield (34%) and was used in place of method (b) because of difficulty purifying di-(2,4-dinitrophenyl) disulphide, and because the sulphenyl chloride is commercially available.

The method did not prove to be a general one. Benzenesulphenyl chloride did not yield the corresponding α-nitrosulphide but gave a bright blue solution and a mixture of products. Invoking the SHAB principle one can predict that the sulphur centre is considerably harder in the benzene case than in the 2,4-dinitrophenyl case and prefers to react with the harder oxygen in the ambident nitro-anion.[9] Acyl chlorides react in this manner to yield α-acyloxy-nitroso-compounds and we suspect that the bright blue colour indicates reaction *via* oxygen instead of carbon.

The Reaction of α-Nitrosulphides with the Sodium Salt of 2-Nitropropane.—The α-nitrosulphides (3a—d) reacted with the sodium salt of 2-nitropropane in DMF at room temperature under nitrogen to give 2,3-dimethyl-2,3-dinitrobutane (6) in good yield. Thus it is the thiolate moiety which is displaced and not the nitro-group. An indication of the rate of reaction is given in Table 2. The reactions proceed to completion with

TABLE 2

α-Nitrosulphide	% Reaction after 4 h
(3a)	13
(3b)	71
(3c)	25
(3d)	40

longer reaction times; for example, the reaction of (3b) gave a 92% yield after 5 h.

The reactions possess the characteristics of radical-anion chain ($S_{RN}1$) processes as illustrated by the reactions of (3b) (see Table 3). The formation of 2,3-dimethyl-2,3-dinitrobutane (6) is inhibited by catalytic amounts of *p*-dinitrobenzene and galvinoxyl, and by an atmosphere of oxygen. Furthermore, the exclusion of light from the reaction flask slows the reaction, indicating light-catalysis.

A scheme analogous to that proposed by Kornblum [5b] for the reaction of α-nitrosulphones is appropriate (Scheme 2; X = SR, $A^- = Me_2CNO_2^-$). The first or initiation step involves electron-transfer between the anion of 2-nitropropane and the α-nitrosulphide [equation (E3)]. The radical-anion of the α-nitrosulphide formed in the initiation step is unstable and breaks down to the 2-nitropropyl radical and thiolate anion [equation (E4) with X = SR]. An alternative breakdown to the nitro-anion and thiyl radical, suggested by Russell,[2b] does not seem to be operative. The addition of the nitropropyl radical to the anion of 2-nitropropane [equation (E5) with $A^- = Me_2CNO_2^-$] and the transfer of an electron from the radical-anion of (6) to an α-substituted nitro-compound [equation (6)], which complete the sequence, are well known processes.[2]

TABLE 3

Reaction of (3b) with the sodium salt of 2-nitropropane

Inhibitor	% Reaction after 4 h
None	71
p-Dinitrobenzene	9
Oxygen	2
Dark	18
Galvinoxyl	3

The Reaction of α-Nitrosulphides (3b, c) *with the Sodium Salt of Nitrocyclohexane* (7).—The reaction [equation (E8)] leads predominantly to the coupled product (8) with a small amount of 2,3-dimethyl-2,3-dinitrobutane (6) in the case of (3b) and a trace of the bis(dinitrocyclohexane) dimer (9) in the case of (3c).

The results shown in Table 4 indicate that the reaction of (3b) is inhibited by free-radical and electron scavengers (oxygen, galvinoxyl, and *p*-dinitrobenzene) and is accelerated by light. A mechanism similar to Scheme 2 fits these facts. The traces of (6) and (9) are possibly formed by termination reactions involving the coupling of anions and radicals outside the main chain sequence, or by the dimerisation of radicals. Kornblum [5b] has previously noted the formation of traces of (6) in similar reactions. The inhibitory action of *p*-dinitrobenzene is interesting in that it increases the proportion of (6) to (8), suggesting that (6) is formed *via* a non-chain process.

TABLE 4

Reaction between (3b) and the sodium salt of nitrocyclohexane

Inhibitor	Products formed after 4 h (%) (8)	(6)	(9)
None	75	14	0
Oxygen	2	0	0
Galvinoxyl	3	0	0
p-Dinitrobenzene	12	5	Traces
Dark	34	2	0

The Reaction of (3b) *with the Sodium Salt of Ethyl Diethylmalonate* (10).—The reaction [equation (E9)] gave a poor yield (21%) of the expected nitroisopropylmalonate (11), with a substantial amount of (6) being isolated instead. The reaction was completely inhibited for 4 h by molecular oxygen, and starting material was recovered in 90% yield. *p*-Dinitrobenzene completely inhibited the formation of (11), but did not stop the formation of (6). Both inhibition reactions yielded small amounts of disulphide. Repeating the reaction in the dark also completely inhibited the formation of (11).

It seems likely that the product (11) is formed *via* a radical-anion radical chain mechanism, as illustrated in Scheme 2. The malonate anion does not couple with the nitro-radical intermediate as efficiently as the 2-nitropropane anion. These results are similar to those observed for the reaction of the malonate anion (10) with 2-chloro-2-nitropropane,[11] 2-bromo-2-nitropropane or 2,2-dinitropropane.[5c] Authentic material for comparison was prepared by van Tammelin's method.[11]

$$\underset{(3b)}{Me_2C(SR)NO_2} + \underset{(10)}{EtC^-(CO_2Et)_2} \longrightarrow \underset{(11)}{Me_2C(NO_2)\text{-}C(Et)(CO_2Et)_2} + \underset{(2b)}{R\text{-}S^-} \quad (E9)$$

The Reaction of α-Nitrosulphides with Sodium Benzenesulphinate.—The expected α-nitrosulphone (12) was formed in the substitution reactions of the thioethers (3b) and (3e) with sodium benzenesulphinate [equation (E10)]. The respective yields of (12) after 2 h were 32% and 59%, with large amounts of unreacted starting materials.

$$\underset{(3b)\ \&\ (3e)}{Me_2C(SR)NO_2} + PhSO_2^- \longrightarrow \underset{(12)}{Me_2C(NO_2)\cdot SO_2Ph} + RS^- \quad (E10)$$

Complete inhibition of sulphone (12) formation was observed when the reaction of (3e) was repeated under an atmosphere of oxygen. It seems reasonable to presume that these reactions also proceed *via* a radical-anion chain ($S_{RN}1$) mechanism as illustrated in Scheme 2 with X = SR and $A^- = PhSO_2^-$.

The reaction of sulphide (3d) with sodium benzenesulphinate under the same conditions gave quantitative recovery of starting materials after 4 h. Clearly the nature of the thiolate leaving group is important in determining the rate of reaction, since the yields of product are in accord with leaving-group ability. This is a possible indication that the breakdown of the intermediate radical-anion [equation (E4)] is rate-determining.

Kornblum [5b] has carried out the reverse of this reaction for the case when (12) reacts with *p*-chlorophenylthiolate (2d) to yield the α-nitrosulphide (3d). This indicates an interesting possibility that with a balance of leaving-group ability these reactions could be reversible.

Reaction of α-Nitrosulphide with Thiolate Anions.—The reaction of *p*-chlorophenylthiolate (2d) with the corresponding α-nitrosulphide (3d) proceeded very slowly at equimolar ratios, but rapidly when a ten-fold molar excess of the thiolate was used, to give di-(*p*-chlorophenyl) disulphide (84%). The use of *p*-dinitrobenzene and oxygen did not inhibit the reaction, indicating a non-chain non-radical mechanism. Although the inhibitors can themselves oxidise thiolates to disulphides, the rate was shown to be negligible under these conditions.

In order to test whether any $S_{RN}1$ type substitution [equation (E11)] was taking place, *p*-tolylthiolate was

$$Me_2C(SR^1)NO_2 + R^2S^- \rightleftharpoons Me_2C(SR^2)NO_2 + R^1S^- \quad (E11)$$

reacted with (3d). A high yield of disulphides was obtained at a ten-fold molar excess of thiolate. The result was confused by the product being a mixture of di-(*p*-tolyl) disulphide, *p*-chlorophenyl *p*-tolyl disulphide, and the dinitrobutane (6).

This problem was eliminated by reacting *p*-tolylthiolate with the sulphide (3e). An instantaneous reaction took place liberating the red colour of the 2,4-dinitrophenylthiolate anion. Di-(*p*-tolyl) disulphide was isolated pure (94%), with no mixed disulphide or dinitrobutane impurities. In neither reaction [(3d) and (3e) with *p*-tolylthiolate] was there any indication of the expected $S_{RN}1$-type substitution product as represented by equation (E11).

An S_N2 mechanism looks most likely for the reaction [equation (E12)] because of the lack of inhibition, the increased rate at high ratios of thiolate to α-nitrosulphide, and the nature of the products. Furthermore we have shown [6] that the reaction represented by equation (E12) is reversible for the *p*-chlorophenyl case

$$Me_2C(SR^1)NO_2 + R^2S^- \rightleftharpoons Me_2CNO_2^- + R^1SSR^2 \quad (E12)$$

and that the reverse reaction proceeds by an S_N2 mechanism.

In slow reactions of (3d) with *p*-tolylthiolate, small amounts of 2,3-dimethyl-2,3-dinitrobutane (6) were formed, but the formation was completely inhibited when oxygen or *p*-dinitrobenzene were used. This suggests that the dinitrobutane (6) by-product is formed by an $S_{RN}1$ mechanism from the starting α-nitrosulphide and the anion of 2-nitropropane formed in the reaction. The reaction of (3e) with *p*-tolylthiolate is too fast to allow the side reaction to compete effectively. The *p*-tolylthiolate reacts rapidly with (3e) displacing the 2-nitropropyl moiety from the sulphenyl centre. The resulting *p*-nitrophenyl *p*-tolyl disulphide reacts rapidly with a second equivalent of *p*-tolylthiolate to yield di-(*p*-tolyl) disulphide and 2,4-dinitrophenylthiolate.

Stability of α-Nitrothioethers.—Homolytic cleavage of the carbon–sulphur bond, as shown in equation (E13),

$$Me_2C(SR)NO_2 \longrightarrow Me_2CNO_2^{\bullet} + RS^{\bullet}$$
$$\downarrow$$
$$Me_2C(NO_2)\cdot C(NO_2)Me_2 + RSSR \quad (E13)$$

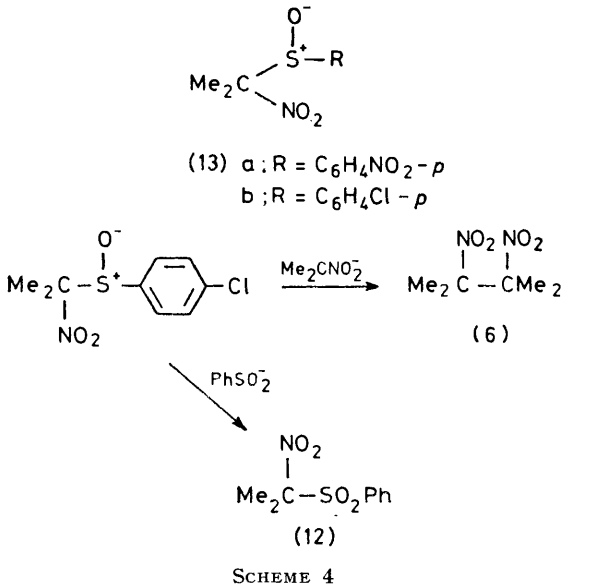
has been suggested [2] as a possible route of reaction in some cases. We therefore investigated the stability of the α-nitrosulphides that we had prepared, and whether the radicals resulting from homolytic cleavage would dimerise to yield disulphides and 2,3-dimethyl-2,3-dinitrobutane [equation (E13)].

Some of the reactions were worked up after acidification with dilute hydrochloric acid. However, all five α-nitrosulphides proved to be unaffected under these conditions even after 24 h.

All the α-nitrosulphides were stable at 0 °C for periods of several months but (3a—d) decomposed slowly at room temperature over several weeks, and (3e) more rapidly. Some of the sulphides were refluxed in toluene under nitrogen in order to speed up possible cleavage; (3c) and (3d) were recovered unchanged after 24 h, whilst (3b) and (3e) decomposed under these conditions to yield intractable tars as products. Analysis by t.l.c. and n.m.r. spectroscopy showed a large number of products, none of which were 2,3-dimethyl-2,3-dinitrobutane (6). The work of Bolsman and de Boer [12] has shown that dimerisation of the 2-nitropropyl radical is not observed during the photolysis of α-iodonitroalkanes even though homolytic cleavage takes place. Our results are further evidence for the non-dimerisation of the 2-nitropropyl radical. Kornblum [13] has also suggested that 2-iodo-2-nitropropane undergoes homolytic cleavage to give the 2-nitropropyl radical.

Preparation and Reactions of α-Nitrosulphoxides.—Two α-nitrosulphides, (3b) and (3d), were oxidised to their respective sulphoxides (13a) and (13b) in high yield with *m*-chloroperbenzoic acid in dichloromethane at −78 °C.

The α-nitrosulphoxide (13b) was reacted with 2-nitropropan-2-ide (see Scheme 4) using the standard



SCHEME 4

reaction procedure to give the dinitrobutane (6) (42%). The use of methanol as a solvent in place of dimethylformamide did not alter the yield significantly. No inhibition studies were carried out to indicate the mechanism but $S_{RN}1$ again seems most likely. No other products were isolated but all the starting material was consumed, presumably by competing reactions.

Likewise the reaction of (13b) with sodium benzenesulphinate (see Scheme 4) only gave a 24% yield of the expected sulphone (12). This α-nitrosulphoxide is clearly reluctant to enter into $S_{RN}1$ reactions of the kind which are so readily undergone by other α-substituted

nitro-compounds. It is interesting to note, however, that the nitro-group is retained in the substitution as is the case for the related sulphides and sulphones.

Our work indicates that α-nitrosulphides react with some anions in a similar manner to α-halogenonitro-compounds and α-nitrosulphones *via* a radical–nucleophilic substitution ($S_{RN}1$) of the thio-group, with retention of the nitro-group.

We are currently investigating the preparation of aliphatic α-nitrosulphides and investigating their reactions.

EXPERIMENTAL

General.—*NN*-Dimethylformamide (DMF) was dried over calcium hydride and stored over molecular sieves. Methanol was dried using magnesium and iodine. Melting points were determined on a Kofler block. I.r. spectra were determined as Nujol mulls in the case of solids or thin films (liquids) on a Perkin-Elmer 177 spectrometer. N.m.r. spectra were determined at 90 MHz with a Perkin-Elmer R32 spectrometer, or at 60 MHz on a Varian EM 360A instrument using $SiMe_4$ as internal standard. Analytical t.l.c. was carried out using Merck silica gel 60 PF_{254}. Analytical gas chromatography was carried out using a Pye 104 series gas chromatograph with a hydrogen flame ionisation detector, on a 5-ft column of 3% SE30 on Gaschrom Q.

Preparation of Sodium p-*Chlorothiophenolate.*—Sodium metal (0.5 g) was added to dry methanol under an atmosphere of nitrogen and the reaction mixture stirred until the sodium dissolved. *p*-Chlorothiophenol (3.1 g) was then added slowly. After a further 30 min the solvent was removed *in vacuo* at low temperature to yield a white powder which was further dried *in vacuo* during 5 h (3.5 g, 98%); δ(D_2O) 7.50 (s).

The other thiolate anions were prepared in a similar manner from the corresponding thiols. The experimental data for these thiolates are: *o*-nitrothiophenolate, m.p. >275 °C; $\lambda_{max.}$ (EtOH) 267 and 433 nm; $\nu_{max.}$ 1 540 and 1 350 cm^{-1}; δ(D_2O) 8.55 (2 H, m) and 8.12 (2 H, m): *p*-nitrothiophenolate, m.p. >275 °C; $\lambda_{max.}$ (EtOH) 424.5 nm; $\nu_{max.}$ 1 535 and 1 350 cm^{-1}; δ(D_2O) 7.67 (AB q): sodium salt of 2-mercaptobenzothiazole, m.p. >275 °C; $\lambda_{max.}$ (EtOH) 239, 255(sh), and 318 nm; δ(D_2O) 7.30 (m).

1-*Methyl*-1-*nitroethyl* p-*Nitrophenyl Sulphide* (3b).—Sodium *p*-nitrothiophenolate (0.54 g, 3.0 mmol) was added to DMF (25 ml) under an atmosphere of nitrogen. When the salt had completely dissolved 2-bromo-2-nitropropane (0.50 g, 3.0 mmol) was added. The reaction mixture was stirred and illuminated with two 15-W fluorescent lamps. The initial deep red colour of the anion faded after *ca.* 20 min. After 1 h the reaction mixture was poured into ice–water (50 ml) and extracted with ether (4 × 30 ml). The combined ether extracts were washed with distilled water (4 × 20 ml), dried ($MgSO_4$), and the solvent removed *in vacuo* to yield a crude product which on recrystallisation (diethyl ether) yielded yellow crystals of the α-*nitrosulphide* (3b) (0.6 g, 83%), m.p. 102—104 °C (Found: C, 44.75; H, 4.2; N, 11.2; S, 13.0. $C_9H_{10}N_2O_4S$ requires C, 44.6; H, 4.1; N, 11.57; S, 13.22%); $\nu_{max.}$ (Nujol) 1 535, 1 345, and 1 600 cm^{-1}; δ($CDCl_3$) 1.90 (6 H, s, 2 Me) and 7.88 (4 H, AB q, aromatic H).

1-*Methyl*-1-*nitroethyl* 1,3-*Benzothiazol*-2-*yl Sulphide* (3c).—This was prepared in a similar manner to above (89%), recrystallised from light petroleum (b.p. 60—80 °C), m.p. 80—81 °C (Found: C, 46.7; H, 3.9; N, 11.0; S, 26.2. $C_{10}H_{10}N_2O_2S$ requires C, 47.2; H, 3.9; N, 11.0; S, 25.2%); $\lambda_{max.}$ (MeOH) 274 nm; $\nu_{max.}$ 1 540 and 1 325 cm^{-1}; δ($CDCl_3$) 2.05 (6 H, s, 2 Me) and 7.62 (4 H, m, aromatic H).

Reaction of Sodium o-*Nitrothiophenolate with* 2-*Bromo*-2-*nitropropane.*—The reaction was carried out by the general method described above for 2 h. N.m.r. analysis of the crude extract indicated the following products: the *o*-nitrophenyl sulphide (3a) (75%), di-(*o*-nitrophenyl) disulphide (14%), and the dinitrobutane (6) (11%). Repeated recrystallisation from cyclohexane gave pure crystals of the sulphide (3a) (32%), m.p. 81—82 °C (lit.,[10] 81—82 °C); $\nu_{max.}$ 1 535, 1 550, and 1 345 cm^{-1}; δ($CDCl_3$) 1.80 (6 H, s, 2 Me) and 7.32 (4 H, m, aromatic H).

The above reaction was used as the 'control' for the inhibition studies. When oxygen was used in place of nitrogen no sulphide was formed. With a nitrogen atmosphere, but with the addition of *p*-dinitrobenzene (10 mol % of the 2-bromo-2-nitropropane) or galvinoxyl (5 mol %) the yields of the sulphide (3a) were 36% and 37% respectively, and the yield of disulphide in the latter case was 27%. When the flask was completely covered by aluminium foil the yield of (3d) was 41%, the yield of disulphide was 57%, and the yield of (6) was 5%.

1-*Methyl*-1-*nitroethyl* p-*Chlorophenyl Sulphide* (3d).—A stream of oxygen was passed through a solution of di-(*p*-chlorophenyl) disulphide (1.11 g, 3.86 mmol) in DMF (150 ml). The sodium salt of 2-nitropropane (4) (1.15 g, 13.5 mmol) was added and the mixture stirred for 2 h. It was poured into ice–water (500 ml), extracted with diethyl ether (4 × 60 ml), and the combined extracts washed with water and dried ($MgSO_4$). The solvent was removed *in vacuo* to yield a yellow-white solid which was recrystallised (hexane) to give the α-nitrosulphide (3d) (0.67 g, 76%) as colourless crystals, m.p. 81—82 °C (lit.,[5b] 82—83 °C).

1-*Methyl*-1-*nitroethyl* o-*Nitrophenyl Sulphide* (3a).—This was prepared, using the same reaction conditions and work-up as above, in 77% yield. The m.p., i.r., and n.m.r. spectra, and t.l.c. properties were identical to those of authentic material.

1-*Methyl*-1-*nitroethyl* p-*Nitrophenyl Sulphide* (3b).—This was prepared, using the same procedure as above, in 66% yield. Recrystallisation from diethyl ether gave pure crystals of (3b) which were identical with authentic material (m.p., i.r. and n.m.r. spectra, and t.l.c.).

1-*Methyl*-1-*nitroethyl* 2,4-*Dinitrophenyl Sulphide* (3e).—The sodium salt of 2-nitropropane (2.77 g, 25 mmol) was added to 2,4-dinitrophenylsulphenyl chloride (5.86 g, 25 mmol) in dry diethyl ether (75 ml) at −5 °C. On completion of the addition the cooling bath was removed, and the mixture was stirred for 30 min at room temperature, and then for 30 min at reflux. The solvent was removed *in vacuo* and the resultant solid washed with water, then recrystallised from MeOH, and again from CCl_4, to yield yellow crystals (2.45 g, 34%), m.p. 102—104 °C (lit.,[10] 101—101.5); $\nu_{max.}$ 1 350, 1 360, and 1 610 cm^{-1}; δ($CDCl_3$) 1.96 (6 H, s, 2 Me), 7.60 (1 H, d), 8.34 (1 H, dd), and 8.64 (1 H, d).

When benzenesulphenyl chloride was used under the same conditions a bright blue solution resulted. Work-up yielded an intractable tar. Analysis by t.l.c. and n.m.r. showed a large number of products. None of the n.m.r. peaks corresponded to values expected for the α-nitrosulphide product.

Sodium Salt of 2-Nitropropane (5).—Sodium (5.8 g, 0.25 g atom) was slowly added as small lumps to dry methanol (100 ml), with stirring, under an atmosphere of nitrogen. When all the sodium had reacted 2-nitropropane (22 g, 0.25 mol) was added and the stirring continued for 30 min. The excess of solvent was removed *in vacuo* and the residual white powder dried at 60 °C and 1 mmHg (27.7 g, 100%); $\delta(D_2O)$ 2.00 (s).

Sodium Salt of Nitrocyclohexane (7).—The above procedure was used except that the resulting powder was triturated with dry ether and filtered off under nitrogen; $\delta(D_2O)$ 1.52 (6 H, br s) and 2.38 (4 H, m).

Reaction of the Sodium Salt of 2-Nitropropane (5) *and 1-Methyl-1-nitroethyl* p-*Chlorophenyl Sulphide* (3d).—The following will serve to illustrate the general procedure for the reaction of the sulphides with the salt of 2-nitropropane and the other anions used.

Dry DMF (25 ml) was pipetted into a three-necked round-bottomed flask fitted with a nitrogen bleed, magnetic stirrer bar, and drying tube. The flask and solvent were purged with oxygen-free dry nitrogen for 30 min, and thereafter a gentle stream of nitrogen was maintained. The sodium salt of 2-nitropropane (106 mg, 0.95 mmol) was added and the reaction stirred until the salt was dissolved. The α-nitrosulphide (3d) (140 mg, 0.6 mmol) was added and the reaction illuminated with two 15-W fluorescent lamps. After 4 h the reaction mixture was poured into ice–water (50 ml), extracted with ether (4 × 20 ml), the combined ether extracts washed with distilled water (4 × 20 ml), and dried ($MgSO_4$). The ether solution was made up to a fixed volume and analysed by g.l.c., which indicated 40% yield of 2,3-dimethyl-2,3-dinitrobutane (6). The solvent was removed *in vacuo* and n.m.r. analysis of the resulting crude mixture showed only one peak [$\delta(CDCl_3)$ 1.74 (s), due to (6)] other than those of starting materials.

Using the same procedure, reaction of the sodium salt of 2-nitropropane with (3a) gave a 13% yield of (6) and 86% recovery of starting material.

Similarly the reaction of the salt of 2-nitropropane with (3c) gave a 25% yield of (6).

Inhibition Studies on the Reaction of the Sodium salt of 2-Nitropropane with 1-Methyl-1-nitroethyl p-*Nitrophenyl Sulphide.*—The control for the reaction of (3b) with the salt of 2-nitropropane was carried out under identical conditions to those of the reaction of (3d), and gave a 71% yield of (6).

When oxygen was used in place of nitrogen, (6) was isolated in 2% yield. With nitrogen atmosphere, but with the addition of *p*-dinitrobenzene [6 mol % of (3b)] or galvinoxyl [10 mol % of (3b)], (6) was isolated in yields of 9% and 3% respectively. When the flask was completely covered by aluminium foil, only an 18% yield of (6) was obtained. In all cases where the yield was low, (3b) was recovered in 80—95% yield.

Reaction of the Sodium Salt of Nitrocyclohexane (7) *with 1-Methyl-1-nitroethyl* p-*Nitrophenyl Sulphide* (3b).—Using the same procedure as in the general experiment, replacing DMF with DMSO to overcome insolubility, the nitro-salt (7) (61 mg, 0.41 mmol) was reacted with the α-nitrosulphide (3b) (100 mg, 0.40 mmol) for 4 h. G.l.c. analysis of the crude product showed that the dinitroisopropylcyclohexane (8) (66 mg, 76%) was the main product, with traces of (6) (10 mg, 14%). None of the nitrocyclohexane dimer (9) was found. Isolation and recrystallisation (cyclohexane) gave pure (8), m.p. 149—150 °C (lit.,[5b] 149—150 °C). Authentic samples of (8) and (9) for analysis and comparison purposes were prepared by the method of Kornblum.[5a]

The above reaction was used as the ' control ' for inhibition studies. When oxygen was used in place of nitrogen the yield of (8) was only 2% with starting material (3b) recovered in nearly quantitative yield, and no (6) was detected. With a nitrogen atmosphere, but with the addition of *p*-dinitrobenzene [6 mol % of (3b)], the yields of (8), (6), and (9) were 12%, 5%, and a minute trace, respectively; starting material (3b) was recovered in 80% yield. When the flask was completely covered by aluminium foil the yield of (8) and (6) were 34% and 2%, respectively.

Reaction of the Sodium Salt of Nitrocyclohexane (7) *with 1-Methyl-1-nitroethyl 1,3-Benzothiazol-2-yl Sulphide* (3c).—Using the previous procedure the dinitroisopropylcyclohexane (8) was obtained (after 4 h) in 20% yield, with traces of the cyclohexane dimer, and a large amount of recovered starting material.

Reaction of the Sodium Salt of Diethyl Ethylmalonate (10) *with 1-Methyl-1-nitroethyl* p-*Nitrophenyl Sulphide* (3b).—Using the general procedure the malonate (10) (100 mg, 0.47 mmol) was reacted with (3b) (115 mg, 0.47 mmol) for 4 h to yield the nitroisopropylmalonate (11) in 21% yield and (6) in 61% yield. T.l.c. separation of (11) gave crystals identical to authentic material.

Authentic (11) was prepared [5c] by the reaction of the salt of (10) with 2-chloro-2-nitropropane in 82% yield, b.p.^{3} 110—120 °C; $\nu_{max.}$ (film) 1 737, 1 558, and 1 285 cm^{-1}; $\delta(CCl_4)$ 1.07 (3 H, t), 1.26 (6 H, t), 1.75 (6 H, s), 1.97 (2 H, q), and 4.26 (4 H, q).

When the reaction of (10) with (3b) was repeated with oxygen in place of nitrogen no (11) was detected and the yield of (6) dropped to 10%, with 90% recovery of (3b). With a nitrogen atmosphere but with the addition of *p*-dinitrobenzene [6 mol % of (3b)] no (11) and only a trace of (6) were detected, with 97% recovery of (3b).

Reaction of Sodium Benzenesulphinate with α-Nitrosulphides.—(a) *1-Methyl-1-nitroethyl* p-*nitrophenyl sulphide* (3b). Using the general procedure sodium benzenesulphinate (72 mg, 0.44 mmol) and (3b) (106 mg, 0.44 mmol) were reacted for 2 h to give, after separation by preparative t.l.c. [silica gel, light petroleum–ether (4 : 1)], 2-nitro-2-phenylsulphonylpropane (12) and (6) in 32% and 6% yields, respectively, with 42% recovery of (3b).

(b) *1-Methyl-1-nitroethyl 2,4-dinitrophenyl sulphide* (3e). Using the above procedure, (3e) and sodium benzenesulphinate gave a 59% yield of (12). When repeated with oxygen in place of nitrogen no (12) was detected, with quantitative recovery of (3e).

(c) *1-Methyl-1-nitroethyl* p-*chlorophenyl sulphide* (3d). The starting materials were recovered unreacted after 4 h.

The reaction of Sodium p-*Toluenethiolate with 1-Methyl-1-nitroethyl 2,4-Dinitrophenyl Sulphide* (3e).—The salt (700 mg, 4.7 mmol) and the sulphide (130 mg, 0.45 mmol) were reacted in dry DMF (25 ml) under an atmosphere of nitrogen for 2 h. The reaction colour immediately turned dark red. Work-up in the normal manner gave a crude product which, on recrystallisation from 50% aqueous EtOH, gave crystals of di-(*p*-tolyl) disulphide (108 mg, 94%), m.p. 47—48 °C (lit.,[14] 47—48 °C), mixed m.p. with an authentic sample not depressed.

The reactions of sodium *p*-chlorothiophenolate and the sulphide (3d) were carried out by the same method to yield di-(*p*-chlorophenyl) disulphide (84%). When *p*-dinitrobenzene [7 mol % of (3c)] was included the yield of disul-

phide was 91%, and under an oxygen atmosphere the yield was 72%.

1-*Methyl*-1-*nitroethyl* p-*Chlorophenyl Sulphoxide* (13b).—A solution of the thioether (3d) (460 mg, 1 mmol) in CH_2Cl_2 (30 ml) was cooled to −78 °C. A solution of *m*-chloroperbenzoic acid (360 mg, 1.97 mmol) in CH_2Cl_2 was added by syringe through a rubber septum. The reaction was stirred overnight and allowed to warm to room temperature. The reaction was poured into ether (100 ml) and saturated brine (20 ml). The organic layer was washed with saturated aqueous $NaHCO_3$ solution, dried ($MgSO_4$), and the solvent removed *in vacuo*. The resulting solid was recrystallised (light petroleum–ether) to yield crystals of the *sulphoxide* (13b), m.p. 101 °C (Found: C, 43.5; H, 4.0; N, 5.5; S, 13.0. $C_9H_{10}NO_3ClS$ requires C, 43.65; H, 4.0; N, 5.65; S, 12.95); $\nu_{max.}$ (Nujol) 1 540, 1 332, (NO_2), and 1 060 cm^{-1} (SO); $\lambda_{max.}$ (EtOH) 225 nm (ε 18 248); δ($CDCl_3$) 1.61 (3 H, s), 1.96 (3 H, s), and 7.46 (4 H, s).

1-*Methyl*-1-*nitroethyl* p-*Nitrophenyl Sulphoxide* (13a).—The above method was used to give the *sulphoxide* (13a) (86%), m.p. 110—111 °C (Found: C, 42.1; H, 3.6; N, 10.6; S, 13.0. $C_9H_{10}N_2O_5S$ requires C, 41.85; H, 3.9; N, 10.85; S, 12.4); $\nu_{max.}$ (Nujol) 1 605, 1 550, 1 350, 1 340, 1 095, and 860 cm^{-1}; δ($CDCl_3$) 1.61 (3 H, s), 2.03 (3 H, s), and 8.05 (4 H, AB q).

Reaction of 1-*Methyl*-1-*nitroethyl* p-*Chlorophenyl Sulphoxide* (13b) *with the Sodium Salt of* 2-*Nitropropane*.—Using the standard procedure the salt (111 mg, 1 mmol) was reacted for 24 h with the sulphoxide (247 mg, 1 mmol) to yield pure 2,3-dimethyl-2,3-dinitrobutane (74 mg, 42%), m.p. 210—211 °C (recrystallised from MeOH), and spectral data identical to those of authentic material; no unreacted sulphoxide was recovered. A similar yield was obtained using MeOH as the reaction solvent.

Reaction of 1-*Methyl*-1-*nitroethyl* p-*Chlorophenyl Sulphoxide* (13b) *with Sodium Benzenesulphinate*.—Using the standard procedure the salt (190 mg, 1.17 mmol) was reacted for 24 h with the sulphoxide (183 mg, 0.72 mmol) to yield pure 1-methyl-1-nitroethyl phenyl sulphone (40 mg, 24%), m.p. 113—114 °C (lit.,[12] 115—116 °C) (recrystallised from EtOH), and spectral data identical to those of authentic material.

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