Intramolecular Catalysis. Part 7.[1] The Smiles Rearrangement of Substituted 2-Hydroxy-2'-nitro- and -2',4'-Dinitro-diphenyl Sulphones, as well as 2-Amino-2',4'-dinitrodiphenyl Sulphide, 2-[(2-Aminophenyl)thio]-3-nitropyridine and 2-Hydroxy-2',4'-dinitrodiphenyl Ether

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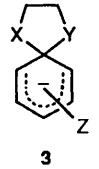
Rate coefficients have been measured for the Smiles rearrangement of a series of 4- and 5-substituted 2-hydroxy-2'-nitrodiphenyl sulphones in 70% (v/v) dioxane–water at 60.0 °C, and for three substrates at several temperatures. The activation parameters for these substrates have been evaluated, as has the dependence on solvent composition [aqueous dioxane and dimethyl sulphoxide (DMSO)] of the rates for these substrates. The effects of substitution have been assessed by means of the Hammett equation using *meta*- and *para*- σ values for the 4- and 5-substituents, respectively, to give ρ *ca.* −2.0. All the evidence indicates reaction *via* a spiro Meisenheimer intermediate with the formation of the intermediate being rate determining. Rate coefficients have been also measured for the Smiles rearrangement of a series of 5-substituted 2-hydroxy-2',4'-dinitrodiphenyl sulphones in 70% (v/v) dioxane–water at 24.8 °C and for three typical substrates at several temperatures. The activation parameters for these substrates have been evaluated, as has the dependence of rate on aqueous dioxane and aqueous DMSO solvent composition. In aqueous DMSO spiro Meisenheimer complexes are observed as the DMSO content increases. Above 50 mol% DMSO these intermediates are very rapidly and completely formed. The effects of substitution in 70% (v/v) dioxane–water have been assessed by means of the Hammett equation using *meta*-σ values to give ρ *ca.* 1.7. The evidence indicates that, in aqueous dioxane, reaction occurs *via* the spiro intermediate, with rate-determining decomposition of the Meisenheimer intermediate, and, in aqueous DMSO, the spiro intermediate becomes effectively the 'initial' state. The rate coefficients for the formation of the symmetrical spiro complex from 2-hydroxy-2',4'-dinitrodiphenyl ether in DMSO–water and DMSO–*tert*-butyl alcohol containing base have been measured. The rate coefficients for the rearrangements of 2-amino-2',4'-dinitrodiphenyl sulphide and 2-[(2-aminophenyl)thio]-3-nitropyridine have been measured in the same systems. Under these conditions, the 'initial' state is the spiro complex and the rate-determining step is the decomposition of the intermediate to form the product.

The Smiles rearrangement[2–4] is an intramolecular rearrangement involving an activated nucleophilic aromatic substitution. This involves inversion of the side chains, as shown in Scheme 1 below. Thus, the group Z in **1** and **2** is an activating substituent

1 **2**

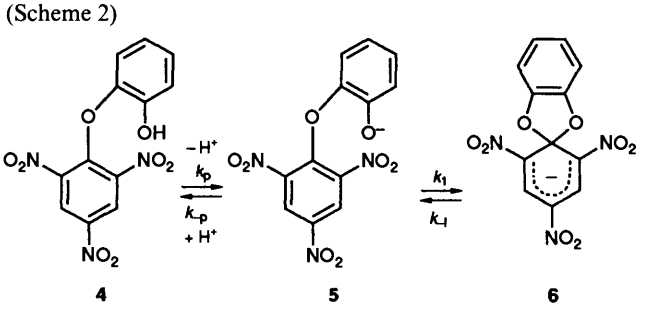
Scheme 1

and the displacement of X is often by Y^-; the reaction being conducted in strong base. The carbon chain joining X and Y may be saturated or part of an aromatic system. The intervention of unsymmetrical spiro Meisenheimer complexes **3**



3

has been demonstrated.[5] Their formation and decay has been studied in detail. Whereas most examples of the Smiles rearrangements from earlier literature involved compounds where the carbon chain is aromatic,[4] more recent detailed studies are where the carbon chain is saturated.[5] However, Bernasconi and Wang[6] have studied the formation of the spiro complex **6** from catechol 2,4,6-trinitrophenyl ether **4**, *via* **5**, in 50% (v/v) aqueous dimethyl sulphoxide (DMSO) which involves a very rapid nucleophilic attack on the aromatic carbon (Scheme 2)



4 **5** **6**

Scheme 2

McClement and Smiles,[6] in 1937, reported some estimated rates for the rearrangement of substituted 2-hydroxy-2'-nitrodiphenyl sulphones, **7**, in base to form the corresponding 2-(*o*-nitrophenoxy)benzenesulphinic acids, **8**, as in Scheme 3 below. Bunnett and Okamoto[7] studied the effects of 3-, 4- and/or 6-substitution on the rates of this reaction for the 5-methyl sulphone. Their main conclusions relate to the steric origin of the acceleration observed for the 6-substituents. However, the effects of substituents at the 4-position showed ambiguity with regard to the substituent polar effects. Bowden *et al.*[8,9] have shown that the effect of increasing the DMSO

Table 1 Rate coefficients (k_1) for the rearrangement of substituted 2-hydroxy-2′-nitrodiphenyl sulphones in 70% (v/v) aqueous dioxane containing base, at 60.0 °C[a]

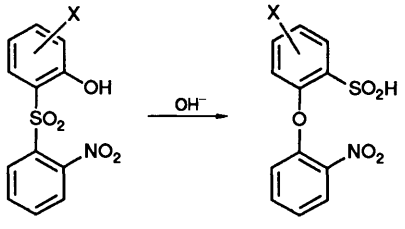
Substituent	$k_1/10^{-4}$ s^{-1}	λnm
H	7.19	350
5-CH_3	27.0	350
4-CH_3	19.5	338
5-$C(CH_3)_3$	26.3	400
5-$COCH_3$	0.305	300
5-CO_2^-	5.03	330
5-OCH_3	44.6	450
5-O^-	166	350
4-O^-	20.5	350
5-NH_2	166	360
5-NO_2	0.0971	402
4-NO_2	1.36	420
5-Cl	3.05	338
5-Br	0.972	345
4-Br	2.08	340

[a] Rate coefficients are reproducible to within ±3%.

Table 2 Activation parameters for the rearrangement of substituted 2-hydroxy-2′-nitrodiphenyl sulphones in 70% (v/v) aqueous dioxane containing base, at 30.0 °C[a]

Substituent	$\Delta H^{\ddagger}$/kcal mol^{-1} [b]	$\Delta S^{\ddagger}$/cal mol^{-1} K^{-1} [b]
H	22.7	−3
5-CH_3	22.0	−5
5-Cl	26.3	−6

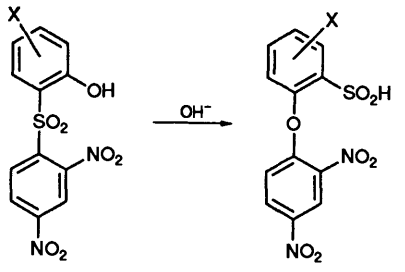
[a] Values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are considered accurate to within ±400 cal mol^{-1} and ±2 cal mol^{-1} K^{-1}, respectively. Temperature range was 20.0 to 70.4 °C and five duplicate rate coefficients were measured. [b] 1 cal = 4.18 J.



7 8

Scheme 3

content of aqueous or methanolic DMSO solutions gives rise to significant effects on the rates of nucleophilic aromatic substitution reactions. The increased activity of the nucleophile and stability of Meisenheimer intermediates as the DMSO content increases allows the detailed mechanisms of these reactions to be elucidated and intermediates can be observed to form and decompose. Smiles *et al.*[10] observed the relatively rapid rates of reaction of 2-hydroxy-5-methyl-2′,4′-dinitrophenyl sulphones, **9**, in base to form 2-(2,4-dinitrophenoxy)-5-methylbenzenesulphinic acids, **10** (Scheme 4). A number of other activating groups are known and various leaving or nucleophilic groups have been studied.[2,4] The only detailed kinetic investigation[11] of aryl migration is that of the formation of the spiro Meisenheimer complex from catechol 2,4,6-trinitrophenyl ether. The formation of the relatively stable spiro complexes as intermediates in Smiles rearrangements has been demonstrated in a number of studies,[5] some of which involve the formation of 2,4-dinitrobenzene spiro complexes. Drozd *et al.*[12] have reported their studies of the reaction of 2-hydroxy-2′,4′-dinitrodiphenyl ether with base in aqueous DMSO in which they detail evidence for an *ortho*-complex.



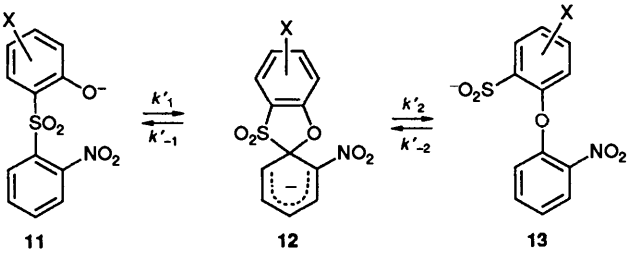
9 10

Scheme 4

In the present study we report the rates of rearrangement of a series of 4- and 5-substituted 2-hydroxy-2′-nitrodiphenyl sulphones, **7**, in aqueous dioxane and DMSO. The activation parameters and the effects of solvent composition on the rates have been evaluated for selected substrates. Furthermore, we report the rates of rearrangement of a series of 5-substituted 2-hydroxy-2′,4′-dinitrodiphenyl sulphones, **9**, in aqueous dioxane and DMSO. The occurrence of intermediates has been demonstrated in aqueous DMSO. Their rates of formation and decomposition have been determined. The activation parameters and the effects of solvent composition on the rates have been evaluated for selected substrates. The results are related to a detailed mechanistic pathway for both these reactions. Furthermore, the rearrangements of 2-amino-2′,4′-dinitrodiphenyl sulphide, 2-[(2-aminophenyl)thio]-3-nitropyridine and 2-hydroxy-2′,4′-dinitrodiphenyl ether have been studied.

Results

The rate coefficients, k_1, for the rearrangement of 4- and 5-substituted 2-hydroxy-2′-nitrodiphenyl sulphones in 70% (v/v) aqueous dioxane containing base at 60.0 °C are shown in Table 1. The reactions were found to be first order in substrate and were unaffected by base greater than 1.5 equivs. The products of the reaction were the salts of the corresponding 2-(*o*-nitrophenoxy)benzenesulphinic acids. The by-products, which are formed (see the Experimental section), are very minor and do not affect the kinetics. The rates have also been studied at several temperatures for the unsubstituted and 5-methyl- and 5-chloro-substituted reagents. The derived activation parameters are shown in Table 2. The effects of solvent composition on the rates in aqueous dioxane and DMSO are shown in Table 3. No intermediates, either transient or long-lived, were observed even at the highest DMSO concentrations. Previous studies by Clement and Smiles[6] were only rough estimates. The study of Bunnett and Okamoto[7] employed both titrimetric and polarographic methods in 50% (w/w) aqueous dioxane and gave parameters comparable activation to those found here for the 5-methyl substrate, the only common substrate studied. A mechanistic pathway is suggested in Scheme 5. The rate



11 12 13

Scheme 5

coefficients, k_1, for the rearrangements of 5-substituted 2-hydroxy-2′,4′-dinitrodiphenyl sulphones in 70% (v/v) aqueous

Table 3 Effect of solvent composition on the rate coefficients (k_1) for the rearrangement of substituted 2-hydroxy-2′-nitrodiphenyl sulphones in aqueous dioxane and DMSO containing base, at 60.0 °C[a]

Mol% non-aqueous solvent	$k_1/10^{-4}$ s^{-1}					
	5-H		5-CH_3		5-Cl	
	dioxane	DMSO	dioxane	DMSO	dioxane	DMSO
10	4.69	9.53	17.3	28.3	2.05	3.31
20	5.78	18.1	—	54.8	2.80	5.74
30	6.31	32.2	25.5	88.7	3.59	8.30
40	7.29	30.6	27.3	—	3.97	14.4
50	6.31	51.1	25.9	207	3.97	23.9
60	6.33	117	22.9	260	3.92	41.5
70	6.32	125	14.2	333	3.52	54.7
80	5.08	223	—	685	3.65	79.0
90	5.89	807	9.00	—	4.44	267

[a] See Table 1.

Table 4 Rate coefficients (k_1) for the rearrangement of 5-substituted 2-hydroxy-2′,4′-dinitrodiphenyl sulphones in 70% (v/v) aqueous dioxane containing base, at 24.8 °C[a]

Substituent	$k_1/10^{-3}$ s^{-1}	λ/nm
H	1.44	422
CH_3	1.01	425
$C(CH_3)_3$	1.35	430
Ph	2.37	422
$COCH_3$	11.4	395
CO_2^-	1.68	422
O^-	0.213	425
OPh	2.92	395
$NHCOCH_3$	6.23	425
NO_2	2.18	425
Cl	3.90	425
Br	5.78	425

[a] See Table 1.

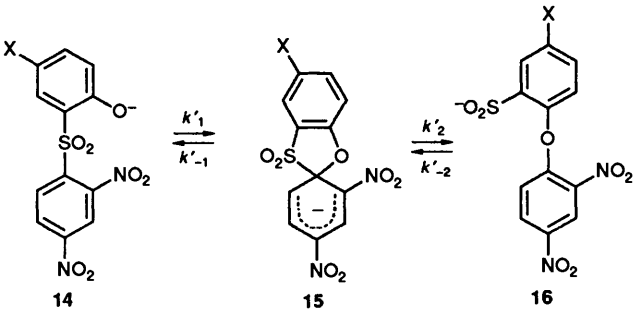
Table 5 Activation parameters for the rearrangement of 5-substituted 2-hydroxy-2′,4′-dinitrodiphenyl sulphones in 70% (v/v) aqueous dioxane containing base, at 30.0 °C[a]

Substituent	$\Delta H^{\ddagger}$/kcal mol^{-1}	$\Delta S^{\ddagger}$/cal mol^{-1} K^{-1}
H	16.0	−1
O^-	18.9	−2
NO_2	15.3	−1

[a] Values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are considered accurate to within ±300 cal mol^{-1} and ±2 cal mol^{-1} K^{-1}, respectively. Temperature range was 18.6 to 55.2 °C and five duplicate rate coefficients were measured.

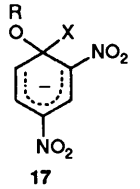
dioxane containing base at 24.8 °C are shown in Table 4. The reactions were found to be first order in substrate and were almost unaffected by base greater than 1.25 equivs. The products of the reactions were the salts of the corresponding 2-(2,4-dinitrophenoxy)benzenesulphinic acids. By-products, which are formed (see the Experimental section), are very minor under these conditions and do not affect the kinetics. The rates have also been studied at several temperatures for the unsubstituted, 5-nitro- and anion of the 5-hydroxy-substrates. The derived activation parameters are shown in Table 5. The effects of solvent composition on the rates in aqueous dioxane are shown in Table 6.

In aqueous DMSO the reaction is more complex. For the 2′,4′-dinitro sulphone substrates, a purple intermediate, with λ_{max} in the range 490–520 nm, was observed. The formation of this intermediate could be followed, as well as its disappearance. Above 50 mol% DMSO the intermediate is effectively the stable 'initial' state in the formation of the product. Scheme 6 is proposed as the pathway for the reaction of the sulphones. The



Scheme 6

intermediate can be confidently identified as **15** in Scheme 6. A number of such Meisenheimer intermediates of the general type **17** have UV–VIS spectra under similar conditions to this



17

study with λ_{max} in the range 487 to 506 nm.[5] The results were confirmed by ^{1}H NMR spectroscopic studies of 90 mol% [H_6]DMSO–D_2O solutions of the three substrates selected above. The spectra shows two absorptions, which differ from both those of the products and reactants, and which are observed at *ca.* 6.1 (singlet) and 8.8 (multiplet) ppm, with approximately equal intensities. These absorptions are typical of hydrogen attached to a cyclohexadienate ring.[5] An expected third absorption appears to be masked by other absorptions of hydrogens of the sulphones. Table 6 shows the rate coefficients for the rearrangement of the three selected substrates in various compositions of aqueous DMSO. The results for 50–90 mol% aqueous DMSO are obtained by monitoring the disappearance of the intermediates. The effect of solvent composition on the rates of formation of the intermediates are shown in Table 7. The activation parameters for the decomposition (rearrangement) and formation of the intermediates of the three 5-substituted 2-hydroxy-2′,4′-dinitrodiphenyl sulphones are shown in Table 8. The Smiles rearrangements of 2-amino-2′,4′-dinitrodiphenyl sulphide (**18**), 2-[(2-aminophenyl)thio]-3-nitropyridine (**19**) and 2-hydroxy-2′,4′-dinitrodiphenyl ether (**20**) have also been studied. Their rate coefficients, k_1, in 70 mol% DMSO–water and DMSO–*tert*-butyl alcohol containing base at 25.5 °C are shown in Table 9. The ether **20** was studied in the presence of 1.5 equivs. of base and the anilines **18** and **19** in the

Table 6 Effect of solvent composition on the rate coefficient (k_1) for the rearrangement of substituted 2-hydroxy-2′,4′-dinitrodiphenyl sulphones in aqueous dioxane and DMSO containing base at 25.4 °C[a,b]

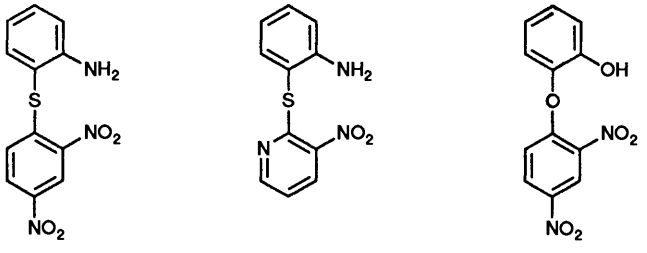
Mol% non-aqueous solvent	$k_1/10^{-3}$ s^{-1}					
	5-H		5-NO_2		5-O^-	
	dioxane	DMSO	dioxane	DMSO	dioxane	DMSO
10	1.79	5.99	1.84	18.9	0.123	7.72
20	1.64	14.4	2.55	11.4	0.162	7.55
30	1.87	18.5	3.78	14.1	0.239	8.27
40	1.45	8.28	3.00	14.4	0.300	—
50	0.719	2.50	2.08	16.5	0.233	0.912
60	0.972	1.28	1.61	3.30	0.267	0.331
70	1.71	0.690	1.73	2.23	0.361	0.234
80	1.58	1.90	2.28	4.35	0.788	0.436
90	3.44	12.8	3.22	5.07	20.7	13.7

[a] See Table 1. [b] λ used in 10–40 mol% DMSO was 422 nm, in 50–90 mol% aqueous DMSO 510 or 516 nm.

Table 7 Effect of solvent composition on the rate coefficient (k_1) for the formation of the intermediate in the rearrangement of substituted 2-hydroxy-2′,4′-dinitrodiphenyl sulphones in aqueous DMSO containing base, at 24.3 °C[a,b]

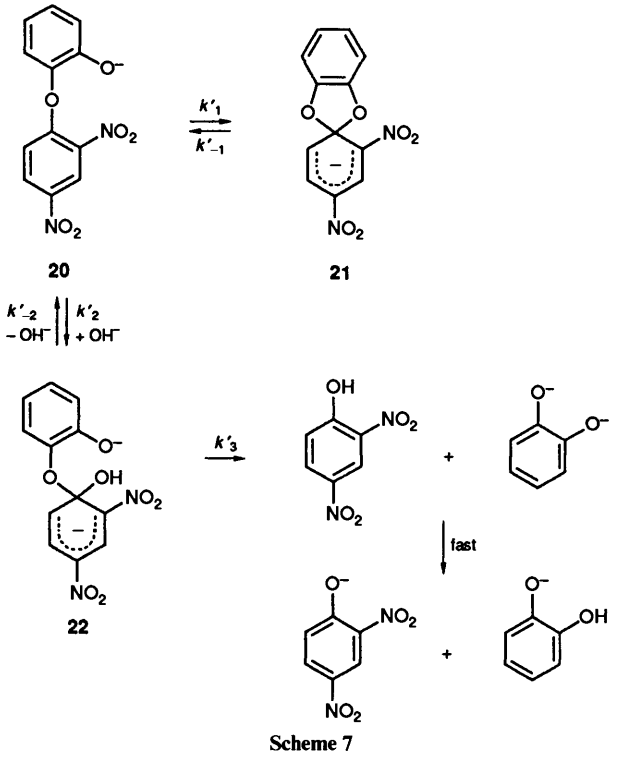
Mol% DMSO	$k_1/10^{-2}$ s^{-1}		
	5-H	5-NO_2	5-O^-
20	27.4	9.07	—
30	—	8.28	—
40	—	12.8	—
50	9.72	16.1	3.72
60	5.23	6.58	0.319
70	2.94	10.4	0.229
80	2.65	11.7	0.343
90	22.8	12.0	0.501

[a] See Table 1. [b] λ used was 510 or 516 nm.



18 **19** **20**

presence of 10 equivs. of base. The ether **20** was reacted to form a bright red species, having λ_{max} = 495 nm. In aqueous DMSO this slowly forms the anion of 2,4-dinitrophenol,[8] *via* a second intermediate, having λ_{max} = 510 nm. Scheme 7 is proposed as the pathway for reaction of this ether **20**. The anilines **18** and **19** react very slowly in aqueous dioxane, but more rapidly in aqueous DMSO. Even at low DMSO concentrations, red intermediates were rapidly produced as soon as base was added. The reaction was followed by monitoring the formation of the diphenylamine products from the intermediates. Table 10 shows the effect of solvent composition on these rates and the activation parameters are given in Table 11. A reaction pathway for **18** is proposed in Scheme 8. The steps shown as k'_1 and k'_2 in Scheme 8 could be concerted to give **25** directly from **18**, *cf.* refs. 5 and 13.



Scheme 7

Discussion

2-Hydroxy-2′-nitrodiphenyl Sulphones.—In Scheme 5 the suggested mechanistic pathway for the intramolecular Smiles rearrangement of substituted 2-hydroxy-2′-nitrodiphenyl sulphones is shown. Under the conditions of basicity (see Experimental) the phenolic starting materials are anionic, *cf.* the pK_a of 2-hydroxydiphenyl sulphone is 9.10 in 48% aqueous ethanol at 25 °C.[14] The reaction is reversible under acid conditions.[4] Under basic conditions, the thermodynamically stable product is the anion of the sulphinic acid.

The effects of 4- and 5-substituents on the rates in 70% (v/v) aqueous dioxane at 60 °C are in the order: 5-O^- ~ 5-NH_2 > 5-OCH_3 > 5-CH_3 > 5-$C(CH_3)_3$ > 4-O^- > 4-CH_3 > H > 5-CO_2^- > 5-Cl > 4-Br > 4-NO_2 > 5-Br > 5-$COCH_3$ > 5-NO_2, as shown in Table 1. It has been suggested that the substituent effects of this type will be complex as they can operate *via* either the SO_2 or O-links or incipient links.[7] In principle such substituent effects can be correlated by the Hammett equation[15] [eqn. (1)]. An adaptation of this relation by Jaffé,[16] [eqn. (2)], allows such effects to be modelled as being

$$\log(k/k_o) = \rho\sigma \quad (1)$$

$$\log(k/k_o) = \rho_1\sigma_1 + \rho_2\sigma_2 \quad (2)$$

transmitted *via* two links. A further method of modelling is by

Table 8 Activation parameters for the decomposition (rearrangement) and formation of the intermediates in the rearrangement of 5-substituted 2-hydroxy-2′,4′-dinitrodiphenyl sulphones in aqueous DMSO containing base at 30.0 °C[a]

5-Substituent	Mol% DMSO	Formation of intermediate		Decomposition of intermediate (rearrangement)	
		$\Delta H^{\ddagger}$/kcal mol^{-1}	$\Delta S^{\ddagger}$/cal mol^{-1} k^{-1}	$\Delta H^{\ddagger}$/kcal mol^{-1}	$\Delta S^{\ddagger}$/cal mol^{-1} K^{-1}
H	20	6.7	−20	18.4	−13
	60	11.5	−13	13.9	−20
	90	16.0	−8	10.5	−20
O^-	60	10.8	−17	14.8	−15
	90	11.7	−13	8.6	−24
NO_2	20	18.2	−2	12.6	−15
	60	22.2	−11	12.4	−12
	90	13.8	0	14.1	−8

[a] See Table 5.

Table 9 Rate coefficients (k_1) for the rearrangement of certain compounds in 70 mol% DMSO–water or DMSO–*tert*-butyl alcohol containing base at 25.5 °C[a]

Compd.	$k_1/10^{-4}$ s^{-1}		λ/nm
	Water	*tert*-butyl alcohol	
2-Amino-2′,4′-dinitrodiphenyl sulphide **18**	8.20	11.6	485
2-[(2-Aminophenyl)thio]-3-nitro pyridine **19**	1.74	2.94	422
2-Hydroxy-2′,4′-dinitrodiphenyl ether **20**	26.1	45.3	495, 510

[a] See Table 1.

Table 10 Effect of solvent composition on the rate coefficient (k_1) for the rearrangement of 2-amino-2′,4′-dinitrodiphenyl sulphide **18** and 2-[(2-aminophenyl)thio]-3-nitropyridine **19** in aqueous DMSO containing base, at 25.4 °C[a]

Mol% DMSO	$k_1/10^{-4}$ s^{-1}	
	18	**19**
30	7.73	2.74
40	12.7	4.37
50	6.14	9.43
60	6.86	2.52
70	7.42	1.74
80	8.23	2.74
90	24.9	12.6

[a] See Table 1.

Table 11 Activation parameters for the rearrangement of certain compounds in 70 mol% DMSO–water containing base at 30.0 °C[a]

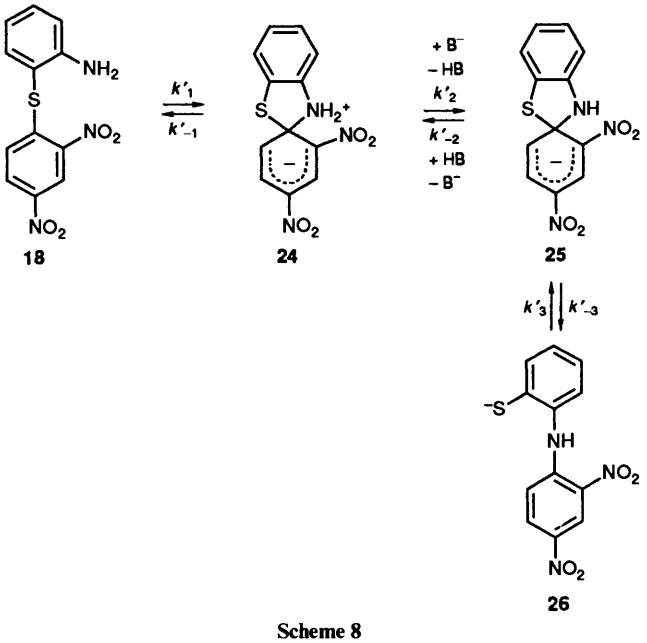
Compound	$\Delta H^{\ddagger}$/kcal mol^{-1}	$\Delta S^{\ddagger}$/cal mol^{-1} K^{-1}
2-Amino-2′,4′-dinitrodiphenyl sulphide (**18**)	24.6	−25
2-[(2-Aminophenyl)thio]-3-nitropyridine (**19**)	30.4	−14

[a] See Table 5.

use of separate field (inductive) and resonance effects, *F* and *R*, respectively,[17] as in eqn. (3) below. It is possible to use the

$$\log(k/k_o) = aF + bR \qquad (3)$$

former eqns. (1) and (2) to correlate 4- and 5-substitution either



Scheme 8

separately or in combination; but eqn. (3) can be used only for 4- or 5-substitution separately. Hammett substituent constants, σ^n, σ^- and σ^+,[18] have been used with eqns. (1) and (2) to attempt correlations of the substituent effects. The only significantly successful correlations are those using *para*-σ values for 5-substituents and *meta*-σ values for 4-substituents, as shown in Table 12. Treatment of the results by the Jaffé equation using the latter substituent constants to give ρ_O and the reverse substituent constants to give ρ_{SO_2} does not give a significant improvement on the simple equation. Use of *para*-σ^- and/or σ^+ values also gives no improvement. The employment of *F* and *R* for the correlation of the effects of the 5-substituents only gives a result close to that for the simple Hammett equation using *para*-σ values. It must be pointed out that the situation for this reaction is complex, having two transmissive links, the possibilities for cross-conjugation between substituents and both linking groups and a five-membered strained ring intermediate **12**. The intermediate **12** will have orthogonal aromatic rings as suggested by Bunnett and Okamoto.[7] However, the ρ value found in Table 12 is between −2.0 and −2.5 with the 4- and 5-substituents acting on the phenolic group.

Model systems for the various states in Scheme 5 can now be considered. The initial state **11** to intermediate **12** can be compared either to the reverse of the ionisation of substituted

Table 12 Hammett equation correlations for the rearrangement of 4- and/or 5-substituted 2-hydroxy-2′-nitro or -2′,4′-dinitrodiphenyl sulphones in 70% (v/v) aqueous dioxane containing base[a]

	ρ	*s*	log k_o	*r*	*n*
2′-Nitro at 60.0 °C					
5-Substituents (using *para*-σ values)	−2.500	0.124	−3.151	0.989	11
4,5-Substituents (using *meta*- and *para*-σ values, respectively)	−2.049	0.210	−3.195	0.938	15
2′,4′-Dinitro at 24.8 °C					
5-Substituents[b] (using *meta*-σ values)	1.654	0.200	−2.785	0.940	11

[a] *s* is the standard deviation, *r* the correlation coefficient and *n* the number of substituents studied. [b] Excluding 5-nitro substrate.

phenols (ρ 2.6 in 50% aqueous ethanol at 25 °C)[19] or, more realistically, the reaction of substituted phenoxides with 1-chloro-2,4-dinitrobenzene (ρ −2.03 in methanol at 50 °C and −1.8 at 65 °C).[20] The intermediate **12** to final state **13** might be similarly compared to the ionisation of substituted benzenesulphinic acids (ρ value can be estimated to be *ca.* 1.0 in water or 1.5 in 70% aqueous dioxane.[21,22] A further model required is that the ρ value for attack of hydroxide anions on 1-(substituted phenoxy)-2,4-dinitrobenzenes in 70% aqueous dioxane at 50 °C is 0.85.[23] Estimates for ρ values for k'_1 in Scheme 5 would thus be *ca.* −1.8 and for $K'_1k'_2$, rather uncertainly, close to zero. Consideration of the two leaving group mobilities in Scheme 5, corresponding to k'_{-1} and k'_2, would indicate that, in general, the phenoxide can be expected to have somewhat poorer leaving group 'mobility' than that of the phenylsulphonyl group in aromatic nucleophilic substitution by addition–elimination reactions, *cf.* ref. 24; but it could be similar. However, this is not the leaving group ability as the data for nucleophilic aromatic substitution[24] often refers to reactions having rate-determining attack of the nucleophile. Thus, the observed ρ value clearly indicates k_1 in Scheme 5 to be the rate-determining step.

The activation parameters shown in Table 2 are very informative. The entropies of activation, $\Delta S^{\ddagger}$, which are −3 to −6 cal mol^{-1} K^{-1}, clearly indicate an intramolecular and unimolecular rate-determining step such as k'_1 in Scheme 5. The enthalpies of activation, which are quite large, represent the difficulty of forming the five-membered strained ring intermediate and also show the facilitation by electron-withdrawing substituents and *vice versa*.

The effect of the solvent composition on the rate coefficients of three substrates, *i.e.* the unsubstituted, 5-methyl- and 5-chloro-, are shown in Table 3. Firstly, the order of reactivity, *i.e.* 5-Me > H > 5-Cl, remains the same in all compositions of both dioxane and DMSO. Secondly, the rate variations for all three substrates are approximately parallel both in aqueous

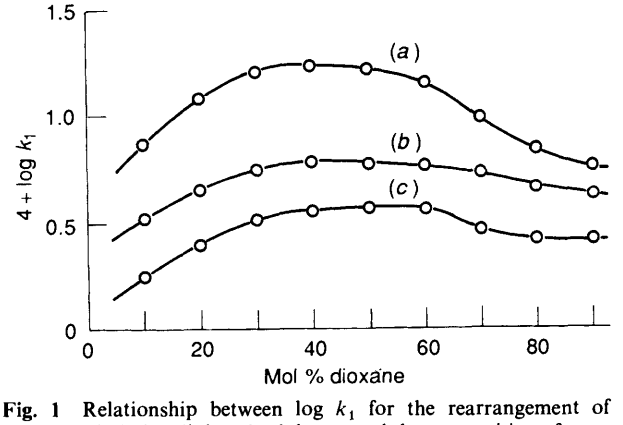


Fig. 1 Relationship between log k_1 for the rearrangement of 5-substituted 2′-nitrodiphenyl sulphones and the composition of aqueous dioxane mixtures; (*a*), 5-CH_3; (*b*), 5-H; (*c*), 5-Cl

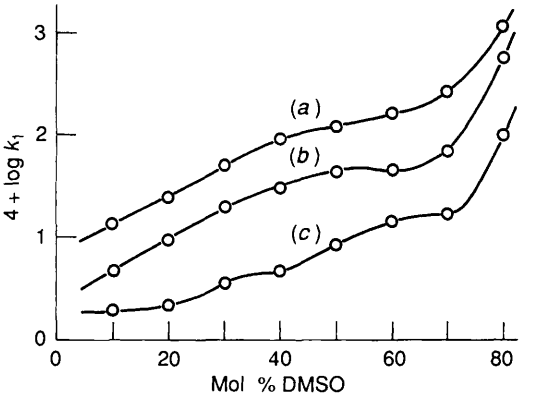
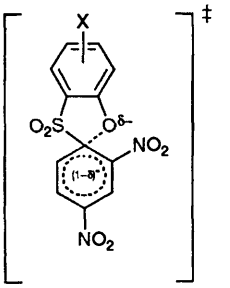


Fig. 2 Relationship between log k_1 for the rearrangement of 5-substituted 2′-nitrodiphenyl sulphones and the composition of aqueous mixtures; (*a*), 5-CH_3; (*b*), 5-H; (*c*), Cl

dioxane and in aqueous DMSO (see Figs. 1 and 2). The rates are about 24 times faster in 80 mol% than in 10 mol% DMSO. This would appear to be the result of increased activity of the phenoxide anion and decreased activity of the water as the DMSO content is increased. Furthermore, the charge-dispersal structure of the spiro Meisenheimer complex will be stabilised better by DMSO than water.[5] The effects observed here for phenoxide anions are not as dramatic as those observed for hydroxide or methoxide anions,[8,9] as would be expected. As the dioxane content increases, the rates first increase slightly and then decrease. Such behaviour is analogous to that of 1-alkoxy-2,4-dinitrobenzenes and 2,4-dinitro-1-phenoxybenzene reacting with hydroxide in aqueous dioxane.[23] The results found in this study appear to arise mainly from the depletion of water by replacement by dioxane and the inability of dioxane effectively to stabilise extended-charge structures.

All the evidence confirms the mechanistic pathway shown in Scheme 5, with k'_1 as the rate-determining step in aqueous dioxane and DMSO. As was noted in our previous study,[9] such molecules are not sufficiently activated for Meisenheimer intermediates to be observed, even in aqueous DMSO rich in DMSO. The transition state will be that shown below as **27**.



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2-Hydroxy-2′,4′-dinitrodiphenyl Sulphones.—The suggested mechanistic pathway for the intramolecular Smiles rearrangement of 5-substituted 2-hydroxy-2′,4′-dinitrodiphenyl sulphones is shown in Scheme 6. The initial state for the reaction is the anion of the phenols under the basic conditions of the reaction (see the Experimental), *cf.* the pK_a of 2-hydroxydiphenyl sulphone is 9.10 in 48% aqueous ethanol at 25 °C.[25] Under basic conditions, the thermodynamically stable product is the anion of the sulphinic acid. However, the reaction is reversible and can be reversed under acid conditions.[4]

Reactions in aqueous dioxane. The rate coefficient for the 2′,4′-dinitro sulphone substrate is about 200 times faster at 40 °C than the 2′-nitro substrate. This effect of a 4-NO_2 group is of the same type, but much smaller than that observed in simple nucleophilic aromatic substitution reactions.[24] However, it is that qualitatively observed for several Smiles rearrangements.[4]

The effect of 5-substituents on the rates in 70% (v/v) aqueous dioxane at 24.8 °C are in the order: $COCH_3$ > $NHCOCH_3$ > Br > Cl > OPh > Ph > NO_2 > CO_2^- > H > $C(CH_3)_3$ > CH_3 > O^-, as shown in Table 4. As before, the possibility of complex substituent effects operating *via* either the SO_2 or O-links or incipient links. The Hammett equation (1) again can be used to correlate the substituent effects,[15] with or without adaptions by Jaffé,[16] separation into field (inductive) and resonance effects,[17] or use of σ^n, σ^- and σ^+.[18] The only significantly successful correlation is that using *meta*-σ values, as shown in Table 12, and excluding the NO_2 group. The substituent effect situation for this and related reactions is complex, as discussed previously. However, the ρ value found here is *ca.* 1.7, which is clearly in great contrast with the value of between −2.0 and −2.5 (using *para*-σ values for comparable substitution) found for the corresponding 2′-nitro substrates. As discussed earlier, estimates for ρ values for k'_1 in Scheme 6 were considered to be *ca.* −1.8 and for $K'_1k'_2$, rather uncertainly, close to zero. Thus, the ρ value of *ca.* 1.7 found in this study can only correspond to k'_2 as the rate-determining step in Scheme 6 and fits with the stabilisation of the incipient sulphinyl anion, even though the ρ value found for the overall process is perhaps surprisingly large. A possible explanation for the inadequacy of the model is that in k'_2 a carbon–sulphur bond is being broken and charge develops on the sulphur in the first case. In the model reactions considered, negative charge resides mainly on the oxygens.

The activation parameters shown in Table 5 clearly demonstrates the nature of the reaction. The entropies of activation, $\Delta S^{\ddagger}$, which are −1 to −2 cal mol^{-1} K^{-1}, indicate an intramolecular and unimolecular reaction. The enthalpies of activation are significantly less than those previously observed for the 2′-nitro substrates and also show the expected effects of electron-withdrawing and -releasing 5-substitution.

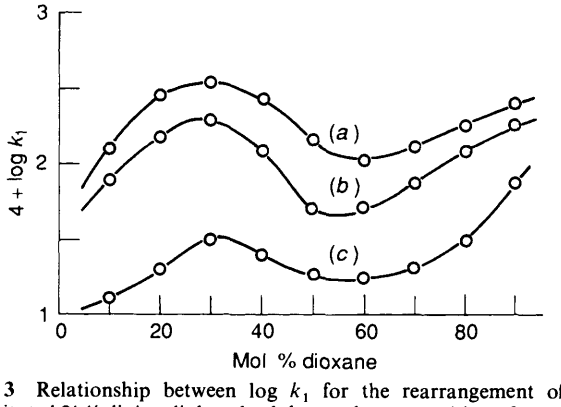
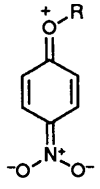


Fig. 3 Relationship between log k_1 for the rearrangement of 5-substituted 2′,4′-dinitrodiphenyl sulphones the composition of aqueous dioxane mixtures; (*a*), 5-NO_2; (*b*), 5-H; (*c*), 5-O^-

The effect of the dioxane–water composition on the rate coefficients of the three selected substrates are shown in Table 6. Firstly, the order of reactivity, *i.e.* 5-NO_2 > 5-H > 5-O^-, remains the same in all solvent compositions. Secondly, the rate variations are approximately parallel (see Fig. 3). As the dioxane content increases, the rates first increase slightly, decrease similarly and then increase again. This behaviour is analogous to that of both the 2′-nitro substrates and the 1-alkoxy- or -phenoxy-2,4-dinitrobenzenes reacting with hydroxide in aqueous dioxane.[23]

Thus, the reaction in aqueous dioxane appears to proceed as Scheme 6, with k'_2 as the rate-determining step. This is in contrast with the 2-nitro substrates, which have k'_1 as the rate-determining step. This switch in mechanism arises from the introduction of the 4′-nitro group. The latter has a powerful resonance interaction with the 2-phenoxy group in the product or incipient products as in **28** below. This appears to result in



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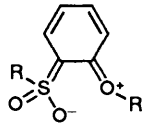
making k'_{-1} in Scheme 6 significantly faster than k'_2. The latter effect in **16** blocks interactions such as **29** below in the product



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or incipient product. Such an effect also appears to result in the reduced rate observed for the 5-nitro group, which causes this group to be excluded from the correlation shown in Table 13.

Reaction in aqueous DMSO. In aqueous DMSO an intermediate which has been identified as **15** in Scheme 4 is observed. Effectively above 50 mol% DMSO, the 'initial' states are the spiro Meisenheimer complexes and the rearrangement is then followed by observing the disappearance of this intermediate. The variation in rates with DMSO–water composition is shown in Table 6 and illustrated in Fig. 4. Except at extreme compositions, the order of reactivity, *i.e.* 5-NO_2 > 5-H > 5-O^-, remains constant and is the same as that observed in aqueous

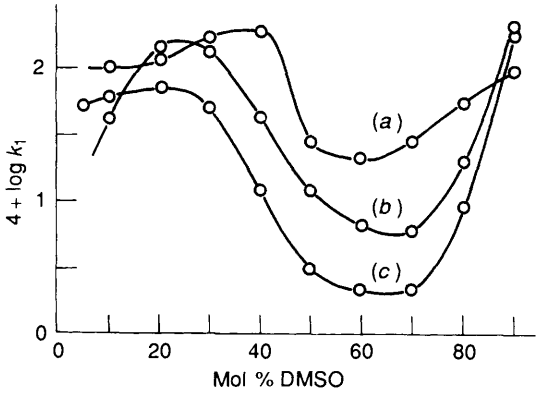


Fig. 4 Relationship between log k_1 for the rearrangement of 5-substituted 2′,4′-dinitrodiphenyl sulphones and the composition of aqueous DMSO mixtures; (*a*), 5-NO_2; (*b*), 5-H; (*c*), 5-O^-

Table 13 The physical constants of previously unreported substituted 2-hydroxy-2′-nitrodiphenyl sulphones

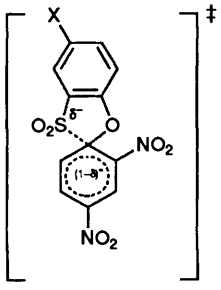
			Found (%)					Required (%)					
Substituent	M.p./°C	Formula	C	H	N	S	Br	C	H	N	S	Br	Recrystall. solvent
4-CH_3	217–219	$C_{13}H_{11}NO_5S$	52.6	3.4	4.8	10.7	—	53.2	3.8	4.8	10.7	—	Acetic acid
5-CO_2H	236–238	$C_{13}H_9NO_7S$	48.3	2.4	4.3	9.9	—	48.5	2.9	4.1	10.3	—	Aqueous acetic acid
5-$C(CH_3)_3$	183–185	$C_{16}H_{17}NO_5S$	57.5	3.7	3.8	9.6	—	57.3	3.4	4.1	10.7	—	Acetic acid
5-Br	174–176	$C_{12}H_8BrNO_5S$	38.7	2.7	3.4	8.6	22.8	40.2	2.3	3.9	8.9	22.3	Acetic acid
5-NO_2	324–326	$C_{12}H_8N_2O_7S$	35.4	2.3	6.1	8.4	—	35.7	2.5	6.6	8.5	—	Acetic acid
5-NH_2	213	$C_{12}H_{10}N_2O_5S$	50.6	3.2	9.6	10.6	—	49.0	3.4	9.5	10.9	—	Light petroleum (b.p. 60–80 °C)
4-Br	175–177	$C_{12}H_8BrNO_5S$	39.6	2.5	4.6	8.7	21.6	40.2	2.3	3.9	8.9	22.3	Acetic acid
H	254–256	$C_{12}H_9NO_5S$	46.2	2.6	8.8	10.1	—	44.9	2.5	8.6	9.9	—	Acetic acid
5-OCH_3	216–218[a]	$C_{13}H_{11}NO_6S$	50.0	3.5	4.9	10.2	—	50.8	3.6	4.6	10.4	—	Acetic acid

[a] Lit.,[31] m.p. 152 °C.

Table 14 The physical constants of previously unreported 5-substituted 2-hydroxy-2′,4′-dinitrodiphenyl sulphones

			Found (%)					Required (%)					
Substituent	M.p./°C	Formula	C	H	N	S	Other	C	H	N	S	Other	Recrystall. solvent
H	322–324	$C_{12}H_8N_2O_7S$	46.2	2.6	8.8	10.1	—	44.9	2.5	8.6	9.9	—	Acetic acid
$C(CH_3)_3$	342–346	$C_{16}H_{16}H_2O_7S$	54.9	4.6	7.0	8.1	—	53.8	4.2	7.4	8.4	—	Acetic acid
C_6H_5	162–164	$C_{18}H_{12}N_2O_7S$	52.6	3.0	7.6	8.3	—	54.0	3.0	7.0	8.0	—	Acetic acid
$COCH_3$	196–198	$C_{14}H_{10}N_2O_8S$	44.5	2.6	8.0	9.2	—	43.8	2.8	7.9	9.0	—	*tert*-Butyl alcohol
CO_2H	256–258	$C_{13}H_7N_2O_9S$	41.6	2.9	7.6	8.6	—	42.4	2.8	7.6	8.7	—	50% Aqueous acetic acid
OPh	166–168	$C_{18}H_{12}N_2O_8S$	51.2	2.7	6.9	7.2	—	51.9	2.9	6.7	7.7	—	Acetic acid
OH	316–318	$C_{12}H_8N_2O_8S$	43.0	2.5	8.4	9.7	—	42.4	2.4	8.2	9.4	—	50% Aqueous acetic acid
NO_2	155–156	$C_{12}H_7N_3O_9S$	39.1	1.8	11.7	8.2	—	39.0	1.9	11.4	8.7	—	Acetic acid
Br	316–318	$C_{12}H_7ClN_2O_7S$	40.4	1.8	7.5	9.6	10.3 (Cl)	40.2	2.0	7.8	9.0	9.9 (Cl)	50% Aqueous acetic acid
Cl	324–326	$C_{12}H_7BrN_2O_7S$	36.2	1.5	7.6	8.1	20.3 (Br)	35.8	1.8	7.0	8.0	19.8 (Br)	50% Aqueous acetic acid

dioxane. Thus, the rate variations are approximately parallel in this composition region of aqueous DMSO. The behaviour observed here is quite unlike, and in great contrast with, that observed for the rearrangement of the 2′-nitro substrates and for the reaction of hydroxide and methoxide anions with several substrates,[8,9,26] in which significant rate accelerations are noted as the DMSO content increases. However, for the reaction with hydroxide anions of 1-substituted 2,4-dinitrobenzenes as substrates, the intervention of Meisenheimer complexes at high DMSO content[8,19] gives rise to behaviour similar to that observed in this study. The major factor responsible for the present behaviour appears to be that the charge-dispersed structure of the spiro Meisenheimer complex will be more stabilised by DMSO than by water, as shown by the results given in Tables 6 and 7. As shown in Table 8, the enthalpies of activation for the formation of the intermediates, in the main, decrease with increasing DMSO content, while the converse occurs for the decomposition of the intermediate. A comparison of the rate coefficients for the three substrates in Tables 6 and 7 show that the rates of formation of all the spiro complexes are significantly greater than their rates of decomposition. The observed ρ value appears to indicate significant C–S bond fission. These results confirm the mechanistic pathway shown in Scheme 6. The transition state will be that shown below as **30**.



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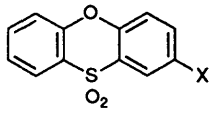
Rearrangement of the 2-Aminophenyl Sulphides.—The rate coefficients for the rearrangement of the 2-aminophenyl sulphides **18** and **19** in excess base are shown in Table 9. The reaction pathway is shown in Scheme 8 and, in DMSO–water and DMSO–*tert*-butyl alcohol, the spiro Meisenheimer intermediate is effectively the 'initial' state. The dependence of the rate of the solvent composition, shown in Table 10, is comparable to those for substituted 2-hydroxy-2′,4′-dinitrodiphenyl sulphones shown in Table 6 and Fig. 4. The excess of base present has two functions; firstly, to ionise the product to drive the reaction to completion and, secondly, to catalyse the formation of the complex by removal of the proton from **23** in Scheme 8. The activation parameters are shown in Table 11 for the rearrangements of **19** and **20**. The values of $\Delta S^{\ddagger}$ are similar to those shown in Table 8 for the sulphones; but the values of $\Delta H^{\ddagger}$ for the 2-aminophenyl sulphides are significantly greater. The reaction pathway appears to have k'_3 in Scheme 8 as the rate-determining step and the intermediate **25** as the 'initial' state.

Rearrangement of 2-Hydroxy-2′,4′-dinitrodiphenyl Ether.—The rate coefficients for the formation of the spiro Meisenheimer complex **22** are shown in Table 9. The rate coefficient in aqueous DMSO can be compared with that for the formation of the intermediate **15** in Scheme 6 for 2-hydroxy-2′,4′-dinitrodiphenyl sulphone, as shown in Table 7. The sulphone is *ca.* 11 times more reactive than the ether, which is the result expected on the basis of their relative field or 'inductive' effects[17] or leaving group 'mobilities'[24] of the phenylsulphonyl or phenoxy groups. The reaction pathway will be that as shown in Scheme 7, with the rate-determining step being k'_1.

Experimental

Materials.—The substituted 2-hydroxy-2′-nitrodiphenyl sulphones were prepared from 2-nitrobenzenesulphinic acid as described below. The latter acid was synthesised by two

methods; the first[27,28] gave the monohydrate and the second[29,30] the anhydrous acid. The sulphones with electron-withdrawing 4- or 5-substituents were prepared by condensation of 2-nitrobenzenesulphinic acid with the appropriate phenol, either as a melt or by concentrated sulphuric acid catalysis,[31,32] to give the substituted 2-hydroxy-2′-nitrodiphenyl sulphide. The sulphides were oxidised to the corresponding sulphones by hydrogen peroxide.[32] The sulphones with electron-releasing 4- or 5-substituents were prepared by condensation of 2-nitrobenzenesulphenyl chloride with the appropriate phenol, either as a melt or in a minimum of anhydrous chloroform,[31] followed by oxidation as described above. The preparation of 2-hydroxy-2′-nitrodiphenyl sulphone was completed by decomposition of the diazonium salt derived from 2-amino-2′-nitrodiphenyl sulphide[33] in boiling 50% aqueous sulphuric acid, using the method of Ravziss *et al.*,[34] followed by oxidation as above. The latter sulphide was acetylated, nitrated and hydrolysed in boiling 50% aqueous sulphuric acid to give the 2-amino-2′,4′-dinitrodiphenyl sulphide, using the method of Ravziss *et al.*[34] The latter sulphide was then converted to 2-hydroxy-2′,4′-dinitrodiphenyl sulphone *via* the diazonium salt and oxidation as above. The bromination of 2-hydroxy-2′-nitrodiphenyl sulphide in acetic acid at 15 °C, followed by oxidation as above, gave the 4-bromo sulphone. 5-Amino-2-hydroxy-2′-nitrodiphenyl sulphone was prepared from the 5-carboxylic acid by the Schmidt reaction.[35] Substituted phenathin dioxides are known to be by-products of the Smiles rearrangement of these substrates,[36] but the 3-substituted dioxides **31** are best prepared by the method of



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Sutter and Green.[37] All the products had IR, ^{1}H and ^{13}C NMR and mass spectra in accord with the stated structures. The m.p.s, recrystallisation solvents and elemental analysis of previously unreported sulphones are shown in Table 13. All other 2′-nitro substrates had m.p.s identical with or close to those reported in the literature,[31,38] with the exception noted in Table 13. The 5-substituted 2-hydroxy-2′,4′-dinitrodiphenyl sulphones were prepared from 2,4-dinitrobenzenesulphinic acid as described below. The latter anhydrous acid was synthesised by the two methods indicated above for 2-nitrobenzenesulphinic acid. The sulphones with electron-withdrawing 5-substituents were prepared by condensation of 2,4-dinitrobenzenesulphinic acid with the appropriate *para*-substituted phenol by concentrated sulphuric acid catalysis.[31,39] The sulphides were oxidised to the corresponding sulphones by hydrogen peroxide.[31,39] The sulphones with electron-releasing 5-substituents were prepared by condensation of 2,4-dinitrobenzenesulphenyl chloride with the appropriate *para*-substituted phenol in a minimum of chloroform,[31] followed by oxidation as described above. The reaction of the sodium salt of 2-aminothiophenol with 2,4-dinitrochlorobenzene gave 2-amino-2′,4′-dinitrodiphenyl sulphide.[40] The latter compound was diazotised and decomposed by addition to boiling 20% aqueous sulphuric acid to give 2-hydroxy-2′,4′-dinitrodiphenyl sulphide, using the method of Ravziss *et al.*[34] The corresponding sulphone was prepared by oxidation of the sulphide using peracetic acid. 2-Hydroxy-2′,4′-dinitrodiphenyl ether was synthesised by the reaction of catechol with 2,4-dinitrochlorobenzene in acetone.[41] The reaction of the triethylamine salt of 2-aminothiophenol with 2-chloro-3-nitropyridine gave 2-[(2-aminophenyl)thio]-3-nitropyridine, which was isolated as the hydrochloride, *cf.* ref. 42. Again, all the products had IR, ^{1}H and ^{13}C NMR and mass spectra in accord with the stated structure. The m.p.s, recrystallisation solvents and elemental analysis of previously unreported sulphones are shown in Table 14. All other substrates had m.p.s identical with or close to those reported in the literature.[31,39–42]

The solvents and bases were prepared as previously described.[26,43]

Kinetic Procedure.—Rate coefficients were obtained spectrophotometrically by use of Unicam SP800 and SP8000 spectrophotometers. The cell temperatures were controlled to ±0.05 °C by means of a Churchill thermoregulator and the reactions were followed at suitable wavelengths as shown in Tables 1, 4, 6, 7 and 9. The substrate concentrations were 2–5 × 10^{-4} mol dm^{-3} and the base (sodium hydroxide or *tert*-butoxide) was studied in 1–10 mol equivs. For the simple phenols the rate coefficients were almost constant between 1.25 and 10 equivs., for the diacidic substrate between 3 and 10 equivs. and for the anilines between 6 and 10 equivs. The base concentrations used in the studies in Tables 1–8 were 1.25 or 2.5 (diacids) equivs. and in Tables 10 and 11 were 1.25 or 10 (anilines) equivs. The reactions were all found to be first-order in the anion of the substrates or intermediates and were measured as k_1 values as previously described.[26] The plots were strictly linear over at least three half-lives and the final absorbance was assumed to be that measure after ten half-lives.

Intermediate Investigations.—The UV–VIS spectroscopic investigations were made as described above. The 2′,4′-dinitro sulphones gave spectra indicating almost complete conversion into the intermediates above 50 mol% DMSO. The ^{1}H NMR spectra were investigated using Anaspect EM360 and Bruker WP80SY spectrometers. The solutions were prepared by dissolving the substrate (*ca.* 0.1 mol dm^{-3}) in $(CD_3)_2SO$–D_2O mixtures at 20 °C and adding NaOD in D_2O. The spectra were then rapidly and repeatedly scanned over periods up to 24 h.

Product Analysis.—The products of the Smiles rearrangement of the substituted 2-hydroxy-2′-nitrodiphenyl sulphones are the anions of the substituted 2-sulphino-2′-nitrodiphenyl ethers.[6,31] However, a substituted phenathin dioxide by-product can occur and results from intramolecular nucleophilic attack in the Smiles rearrangement product by displacement of the 2′-nitro group. The reaction products were isolated by acidification with dilute hydrochloric acid. The product was redissolved in base and extracted with diethyl ether. Evaporation of the ethereal layer, after separation and drying ($MgSO_4$), gave any phenathin dioxide. The aqueous layer was then neutralised by gaseous CO_2 and extracted with diethyl ether. After separation of ethereal layer, drying ($MgSO_4$) and evaporation, any unchanged sulphone was left. Acidification of the aqueous layer gave the substituted diphenyl ether products. The sulphones and the ethers, in base, have λ_{max} in the ranges 330–420 and 295–345 nm, respectively. Under the kinetic conditions, the isolation studies, TLC and UV–VIS spectroscopy all indicated that the substituted diphenyl ethers were the only significant product of the reaction, *i.e.* >98%.

The products of the Smiles rearrangement of 5-substituted 2-hydroxy-2′,4′-dinitrodiphenyl sulphones are the anions of the 4-substituted 2-sulphinoxy-2′,4′-dinitrodiphenyl ethers.[4,20] The products were isolated as described above. Under kinetic conditions, the isolation studies, TLC and UV–VIS spectroscopy all indicated that the substituted diphenyl ethers were the only significant product of the reaction, *i.e.* >98%. For 2-hydroxy-2′,4′-dinitrodiphenyl ether, the substrate was re-isolated. However, in particular for the latter substrate, 2,4-dinitrophenol can be detected in significant yield if the reaction times are significantly longer than ten 'half-lives' of the primary

reaction. The products of the Smiles rearrangement of the two sulphides were identified in the following manner. After the rearrangement reaction in 70% aqueous DMSO was complete, one equiv. of iodomethane was added and the solution was stirred for 2 h. The methylated products were precipitated by addition of ice, while the pH was adjusted to *ca.* 9. The products were recrystallised from acetic acid and identified as the appropriate methylthio amine,[4] *i.e.* 6-nitro-2-pyridyl(2-methylthiophenyl)amine and 2-methylthio-2′,4′-dinitrodiphenylamine. The structure of the latter compounds were confirmed by their ^1H and ^{13}C NMR spectra and elemental analysis, as well as comparison with known m.p.[4,40,44] The sulphides themselves could be isolated, although oxidising easily, and gave, under identical conditions, UV–VIS spectra closely matching the spectra obtained from the kinetic products of the rearrangements of the amino sulphides.

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