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Kinetic and equilibrium studies of σ-adduct formation and substitution in the reactions of sulphite ions with some alkyl and aryl ethers and thioethers

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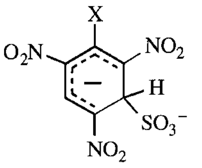
ABSTRACT: Kinetic and equilibrium results are reported for the reactions of sulphite with the ethyl and phenyl ethers of 2,4,6-trinitrophenol and 2,4,6-trinitrothiophenol in 80/20 (v/v) water/DMSO. In each case 1:1 and 1:2 adducts are observed by reaction of sulphite at one or two unsubstituted ring positions respectively. In the case of the ethyl derivatives these adducts are long-lived; however, the phenyl derivatives rapidly yield 2,4,6-trinitrobenzenesulphonate, the substitution product. This difference is attributed to a change in the nature of the rate-determining step, from nucleophilic attack with the phenyl derivatives to leaving group departure with the alkyl derivatives. © 1998 John Wiley & Sons, Ltd.

KEYWORDS: nucleophilic aromatic substitution; Meisenheimer complexes; nucleophilic reactivity; trinitroaromatics

INTRODUCTION

It is known that sulphite readily forms σ-adducts by reaction with electron-deficient aromatic substrates.[1,2] Thus reaction at unsubstituted ring positions of 1-X-2,4,6-trinitrobenzenes, **1**, has been found to yield adducts **2** with 1:1 stoichiometry or **3** with 1:2 stoichiometry.[3–8] Reports of attack at substituted ring positions leading to nucleophilic displacement are relatively scarce, although it is known that substitution of halide ions leads to the formation of derivatives of benzene sulphonic acid,[9,10] and there is one early report of the formation of an adduct by attack at the 1-position of 2,4,6-trinitrobenzaldehyde.[11]



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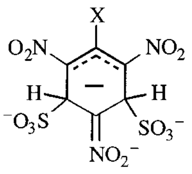

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Here we compare the reactions with sulphite of the ethyl and phenyl ethers of 2,4,6-trinitrophenol and 2,4,6-trinitrothiophenol. It is known[12,13] that phenoxide and thiophenoxide are considerably better leaving groups than their aliphatic analogues, ethoxide and thioethoxide respectively. Hence we were interested in the possibility of observing nucleophilic substitution in these systems.

RESULTS AND DISCUSSION

Kinetic and equilibrium measurements were made with four substrates, **1a–1d**. The phenyl ether and thioether were relatively insoluble in water, so all measurements were made in water/dimethyl sulphoxide (80/20, v/v). The ionic strength was maintained at $I = 0.3$ mol dm^{-3} using sodium sulphate as compensating electrolyte.

The results of UV/visible and ^{1}H NMR spectroscopy provide evidence that reaction with sulphite involves the processes shown in Scheme 1. The UV/visible spectra of the ethyl ether **1a** and ethyl thioether **1b** in the presence of low (*ca* 10^{-3} mol dm^{-3}) concentrations of sulphite are typical of 1:1 adducts[1,3] with λ_{max} 450 and 550 nm (shoulder). At higher sulphite concentrations the spectra show single absorption maxima, at 430 nm in the case of **1a** and 450 nm for **1b**. The latter spectra are consistent with formation of adducts with 1:2 stoichiometry. Confirmation that sulphite addition is occurring at unsubstituted ring positions comes from ^{1}H NMR measurements in deuterium oxide/dimethyl sulphoxide [$^2H_6$] 80/20 (v/v). Thus the spectrum of **1b** in the presence of a fourfold excess of sulphite shows a singlet at δ 6.01 representing the two ring hydrogens of **3b**. The side chain ethyl group gives a triplet (J 7.4 Hz) at δ 1.06 for the methyl hydrogens and two multiplets at δ 3.00 and 3.13 for the methylene hydrogens. The non-equivalence

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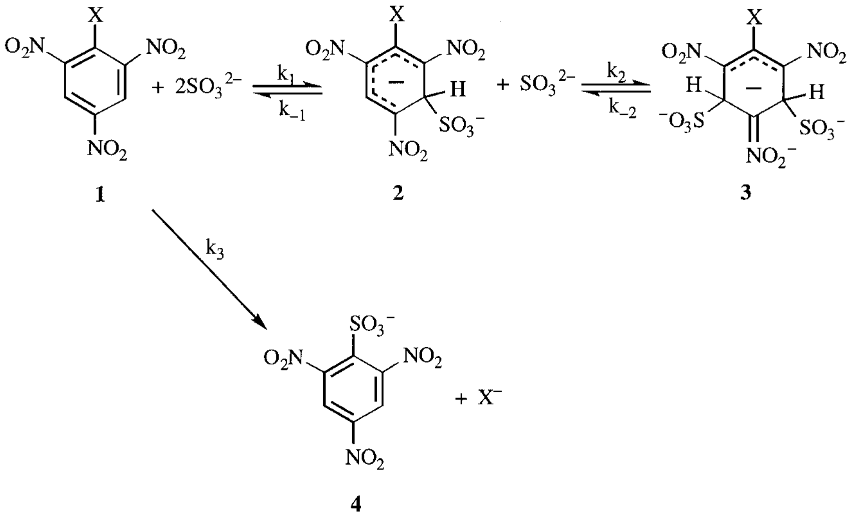


a, X = OEt
b, X = SEt
c, X = OPh
d, X = SPh

Scheme 1

of these hydrogens indicates restricted rotation about the S-CH_2 bond in the adduct. There was no evidence for *cis–trans* isomerism in **3b** as has been observed in the 2:1 adduct from 1,3,5-trinitrobenzene.[4,14,15] The NMR spectrum was unchanged after 1 h, indicating that nucleophilic displacement of the ethylthio group was a very slow process. NMR evidence has been presented previously[3] showing that the 1:2 adduct from methyl 2,4,6-trinitrophenyl ether results from sulphite attack at two unsubstituted ring positions; the ethyl ether is expected to behave analogously to give **3a**.

The UV/visible spectra of the phenyl derivatives **1c** and **1d** produced on initial mixing with sulphite indicate formation of the adducts **2c** (λ_{max} 450 and 530 nm (shoulder)) and **2d** (λ_{max} 450 and 550 nm (shoulder)) at low sulphite concentrations, and adducts **3c** (λ_{max} 490 nm) and **3d** (475 nm) at higher sulphite concentrations. However, in contrast with the behaviour of the ethyl derivatives, the visible absorption faded rapidly and the final spectra were identical to those of the substitution product **4** in the reaction medium. Confirmation that substitution occurs rapidly in these systems comes from NMR measurements. The spectrum of **1c** (0.05 mol dm^{-3}) in the presence of sulphite (0.15 mol dm^{-3}) gave a band at δ 8.73, the position expected for the substitution product **4**, together with multiplets at δ 6.50 and 7.00 due to the displaced phenoxy group. In addition, small bands

Table 1. Kinetic data for reaction of **1a** with sulphite in 80/20 (v/v) water/DMSO at 25 °C

$[Na_2SO_3]/(mol\ dm^{-3})^a$	$k_{fast}/(s^{-1})^b$	$k_{calc}/(s^{-1})^c$	$k_{slow}/(s^{-1})^d$	$k_{calc}/(s^{-1})^e$
0.001	16	16	0.23	0.22
0.002	21	22	0.27	0.26
0.004	30	34	0.29	0.35
0.007	52	52	0.51	0.51
0.010	70	70	0.65	0.67
0.020	130	130	1.20	1.2
0.040	–	–	2.35	2.3
0.060	–	–	3.4	3.4
0.100	–	–	6.2	5.6

[a] Constant ionic strength, $[Na_2SO_3] + [Na_2SO_4] = 0.1$ mol dm^{-3}.
[b] Colour-forming reaction at 550 nm.
[c] Calculated from eqn (1) with $k_1 = 6000$ dm^3 mol^{-1} s^{-1} and $k_{-1} = 10$ s^{-1}.
[d] Fading reaction at 550 nm.
[e] Calculated from eqn (2) with $k_2 = 55$ dm^3 mol^{-1} s^{-1}, $k_{-2} = 0.20$ s^{-1} and $K_1 = 600$ dm^3 mol^{-1}.

Table 2. Kinetic data for reaction of **1b** with sulphite in 80/20 (v/v) water/DMSO at 25 °C

$[Na_2SO_3]/(mol\ dm^{-3})^a$	$k_{fast}/(s^{-1})^b$	$k_{calc}/(s^{-1})^c$	$k_{slow}/(s^{-1})^d$	$k_{calc}/(s^{-1})^e$
0.001	4.7	4.9	0.106	0.098
0.002	7.7	7.5	0.145	0.153
0.003	10	10	0.19	0.21
0.004	12	13	0.23	0.26
0.007	20	20	0.44	0.44
0.010	28	28	0.60	0.62
0.020	54	54	1.20	1.2
0.040	105	105	2.5	2.4
0.060	155	157	3.6	3.6
0.100	260	260	6.1	6.0

[a] Constant ionic strength, $[Na_2SO_3] + [Na_2SO_4] = 0.1$ mol dm^{-3}.
[b] Colour-forming reaction at 550 nm.
[c] Calculated from eqn (1) with $k_1 = 2600$ dm^3 mol^{-1} s^{-1} and $k_{-1} = 2.3$ s^{-1}.
[d] Fading reaction at 550 nm.
[e] Calculated from eqn (2) with $k_2 = 60$ dm^3 mol^{-1} s^{-1}, $k_2 = 0.07$ s^{-1} and $K_1 = 1120$ dm^3 mol^{-1}.

Table 3. Kinetic data for reaction of **1c** with sulphite in 80/20 (v/v) water/DMSO at 25 °C

[Na$_2$SO$_3$]/(mol dm^{-3})[a]	k_{fast}/(s^{-1})[b]	k_{calc}/(s^{-1})[c]	k_{slow}/(s^{-1})[d]	k_{calc}/(s^{-1})[e]	k_{sub}/(s^{-1})[f]	k_{calc}/(s^{-1})[g]
0.001	22	24	–	–	0.0147	0.0152
0.002	46	43	–	–	0.0168	0.0168
0.004	78	81	–	–	0.0180	0.0173
0.007	135	138	–	–	0.0168	0.0171
0.010	196	195	2.1	2.2	0.0160	0.0170
0.020	–	–	2.4	2.5	0.0148	0.0149
0.040	–	–	3.1	3.0	0.0121	0.0122
0.060	–	–	3.6	3.6	0.0109	0.0103
0.100	–	–	4.6	4.7	–	–

[a] Constant ionic strength, [Na$_2$SO$_3$]+[Na$_2$SO$_4$] = 0.10 mol dm^{-3}.
[b] Colour-forming reaction at 550 nm.
[c] Calculated from eqn (1) with k_1 = 19 000 dm^3 mol^{-1} s^{-1} and k_{-1} = 5 s^{-1}.
[d] Fading reaction at 550 nm.
[e] Calculated from eqn (2) with k_2 = 28 dm^3 mol^{-1} s^{-1}, k_{-2} = 1.9 s^{-1} and K_1[SO$_3^{2-}$]1.
[f] Fading reaction at 550 nm.
[g] Calculated from eqn (3) with k_3 = 74 dm^3 mol^{-1} s^{-1}, K_1 = 3800 dm^3 mol^{-1} and K_2 = 14.7 dm^3 mol^{-1}.

Table 4. Kinetic data for reaction of **1d** with sulphite in 80/20 (v/v) water/DMSO at 25 °C

[Na$_2$SO$_3$]/(mol dm^{-3})[a]	k_{fast}/(s^{-1})[b]	k_{calc}/(s^{-1})[c]	k_{slow}/(s^{-1})[d]	k_{calc}/(s^{-1})[e]	k_{sub}/(s^{-1})[f]	k_{calc}/(s^{-1})[g]
0.001	6.7	6.7	–	–	0.050	0.049
0.002	9.6	10.4	–	–	0.070	0.064
0.004	16	18	–	–	–	–
0.007	25	28	0.41	0.41	0.082	0.076
0.010	42	40	0.40	0.42	0.078	0.076
0.020	78	77	0.48	0.46	0.075	0.070
0.040	150	150	0.55	0.55	0.053	0.059
0.060	225	225	0.67	0.64	0.044	0.051
0.080	–	–	0.73	0.74	0.041	0.045
0.100	–	–	0.91	0.83	–	–

[a] Constant ionic strength, [Na$_2$SO$_3$]+[Na$_2$SO$_4$] = 0.10 mol dm^{-3}.
[b] Colour-forming reaction at 550 nm.
[c] Calculated from eqn (1) with k_1 = 3700 dm^3 mol^{-1} s^{-1} and k_{-1} = 3 s^{-1}.
[d] Fading reaction at 550 nm.
[e] Calculated from eqn (2) with k_2 = 4.5 dm^3 mol^{-1}, k_{-2} = 0.38 s^{-1} and K_1 = 1230 dm^3 mol^{-1}.
[f] Fading reaction measured at 550 and/or 480 nm.
[g] Calculated from eqn (3) with k_3 = 110 dm^3 mol^{-1} s^{-1}, K_1 = 1230 dm^3 mol^{-1} and K_2 = 12 dm^3 mol^{-1}.

were observed at δ 5.88 and 8.34 attributable[7] to the adduct formed by attack of sulphite at the 3-position of the substitution product **4**.

Kinetic measurements were made by stopped-flow spectrophotometry with sulphite concentrations in large excess of the substrate concentrations (2×10^{-5} mol dm^{-3}). With the ethyl derivatives **1a** and **1b**, two rate processes, well separated in time, were observed. These are attributed to equilibration of the substrate with adducts **2** and **3** respectively so that the appropriate rate equations[6] are

$$k_{\text{fast}} = k_{-1} + k_1[\text{SO}_3^{2-}] \tag{1}$$

$$k_{\text{slow}} = k_{-2} + \frac{k_2 K_1[\text{SO}_3^{2-}]^2}{1 + K_1[\text{SO}_3^{2-}]} \tag{2}$$

The experimental data in Tables 1 and 2 give an excellent fit with these equations. Best values of individual rate constants were obtained using an iterative procedure minimizing the sums of the squares of the differences between observed and calculated values.

For the phenyl derivatives **1c** and **1d**, three rate processes were observable. The first two correspond to equilibration of the substrate with adducts **2** and **3** respectively. The slowest process leads to the substitution product **4**, and measured rate constants for this process are designated k_{sub}. The assumption that substitution involves attack by sulphite on the substrate itself and not on the adducts **2** or **3** leads to

$$k_{\text{sub}} = \frac{k_3[\text{SO}_3^{2-}]}{1 + K_1[\text{SO}_3^{2-}] + K_1K_2[\text{SO}_3^{2-}]^2} \tag{3}$$

Data are in Table 3 and Table 4 and give excellent fits with eqns (1)–(3). It is interesting that, as predicted by eqn (3), values of k_{sub} increase with increasing sulphite

Table 5. Summary of rate and equilibrium data[a] in 80/20 (v/v) water/DMSO at 25 °C

	1a	**1b**	**1c**	**1d**
$k_1/(\mathrm{dm^3\ mol^{-1}\ s^{-1}})$	6000 ± 100	2600 ± 100	19000 ± 1000	3700 ± 100
$k_{-1}/(\mathrm{s^{-1}})$	10 ± 0.6	2.3 ± 0.2	5 ± 1	3 ± 1
$K_1/(\mathrm{dm^3\ mol^{-1}})^b$	600 ± 30	1100 ± 100	3800 ± 500	1200 ± 400
$k_2/(\mathrm{dm^3\ mol^{-1}\ s^{-1}})$	55 ± 5	60 ± 5	28 ± 2	4.5 ± 0.5
$k_{-2}/(\mathrm{s^{-1}})$	0.20 ± 0.02	0.07 ± 0.01	1.9 ± 0.1	0.38 ± 0.03
$K_2/(\mathrm{dm^3\ mol^{-1}})$	280 ± 40	860 ± 200	15 ± 2	12 ± 2
$k_3/(\mathrm{dm^3\ mol^{-1}\ s^{-1}})$	Not observed	Not observed	74 ± 5	110 ± 10

[a] $I \equiv \frac{1}{2}\sum c_i z_i^2 = 0.3\ \mathrm{mol\ dm^{-3}}$.
[b] $K_1 = k_1/k_{-1}$ and $K_2 = k_2/k_{-2}$.

concentration, reaching a maximum when $[\mathrm{SO_3}^{2-}] \approx 0.005\ \mathrm{mol\ dm^{-3}}$, and then decrease as the sulphite concentration is increased further. It is worth nothing that a plot for **1c** of k_{fast} vs $[\mathrm{SO_3}^{2-}]$ had a small intercept which did not allow an accurate determination of k_{-1}. However, an acceptable fit of the data for eqn (3) could be obtained only with a value for K_1 of $3800 \pm 500\ \mathrm{dm^3\ mol^{-1}}$. This leads to a value for k_{-1} ($\equiv k_1/K_1$) of $5 \pm 1\ \mathrm{s^{-1}}$. For both **1c** and **1d** the amplitude of the process, k_{slow}, leading to adduct **3** was small at low sulphite concentrations, $\leq 0.007\ \mathrm{mol\ dm^{-3}}$, so that values of k_{slow} were unreliable.

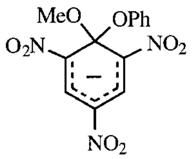
RELATIVE STABILITIES OF σ-ADDUCTS

Rate and equilibrium constants are collected in Table 5. The values of K_1, the equilibrium constant relating to sulphite attack at the unsubstituted 3-position, decrease in the order of 1-substituent OPh > SPh ≈ SEt > OEt. Steric as well as electronic effects are expected to be important.[1,2] It is known that the presence of a bulky substituent at the 1-position may result in rotation from the ring plane of the nitro groups at the 2- and 6-positions, reducing their electron-withdrawing capacity. The inductive effect of the 1-substituents at the 3-position may be judged by σ_{meta} values. The values for OPh and OEt groups are reported as 0.25 and 0.10 respectively.[16,17] Values for SPh and SEt groups are not available, but the value for the SMe group is 0.15. A similar value is expected for the SEt group, with a larger value for SPh. It seems that the K_1 values largely reflect the inductive effects of the 1-substituents. For comparison, values of K_1 for sulphite attack in 100% water are $290\ \mathrm{dm^3\ mol^{-1}}$ for 1,3,5-trinitrobenzene[4] and $140\ \mathrm{dm^3\ mol^{-1}}$ for methyl 2,4,6-trinitrophenyl ether.[6] The presence of 20% DMSO in our systems is expected[1,2] to result in increased stabilities of the 1:1 adducts.

Our results, kinetic and spectroscopic, provide no evidence for *cis–trans* isomerism in the 1:2 adducts. It is likely that, as in related systems,[6] the *trans* isomers are favoured. Here the added sulphite groups are on opposite faces of the ring, minimizing unfavourable interactions. It is interesting that the values of K_2 for formation of adducts **3** are considerably higher for the alkyl derivatives **3a** and **3b** than for the phenyl derivatives **3c** and **3d**. The K_1 values provide no evidence that the phenyl derivatives are sterically disadvantaged relative to the ethyl derivatives. It has been argued that in related systems solvation is of prime importance in determining adduct stability.[5] In the 1:2 adducts **3** which carry four negative charges, solvation by the largely aqueous medium will be very important. The presence of hydrophobic groups will reduce such solvation. Thus it is likely that the lower stabilities of the phenyl derivatives than of their alkyl counterparts may result from greater inhibition of hydration of the ionic groups.

NUCLEOPHILIC SUBSTITUTION

A major difference between the phenyl, **1c** and **1d**, and alkyl, **1a** and **1b**, derivatives is in the rate of displacement of the 1-substituent. With the former, substitution was found to occur relatively rapidly, whereas with the latter there was no observable reaction after 1 h. One factor contributing to this difference will be the higher stabilities of the 1:2 adducts **3** formed from the alkyl derivatives, resulting in lower equilibrium concentrations of the substrates. However, the major factor is the enhanced leaving group ability of phenoxide and phenyl sulphide compared with ethoxide and ethyl sulphide.[12,13]



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Thus it is known[12] that phenoxide departure is 10^6 times faster than methoxide departure from the adduct **5**. The likely effect of this difference is shown in a schematic energy level diagram in Fig. 1. Although substitution will involve the intermediates **6**, there is no evidence, either spectroscopic or kinetic, for the accumulation of such intermediates, and the inference is that they have lower

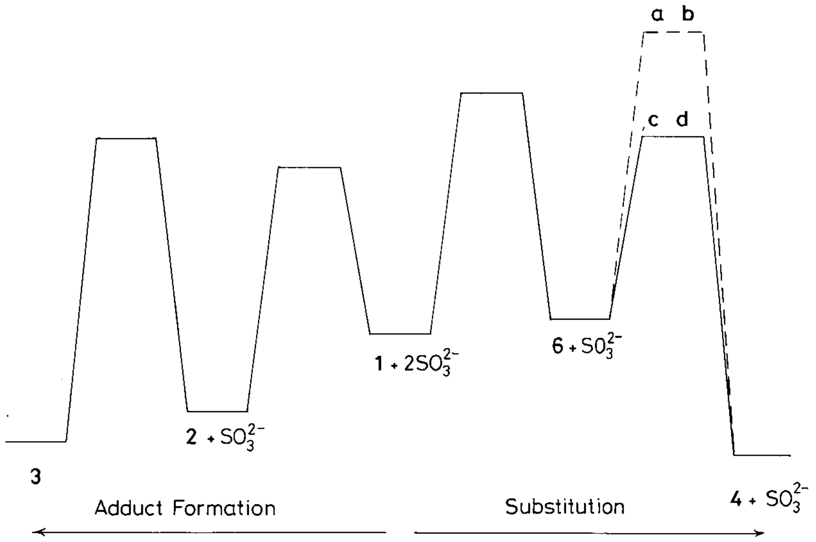
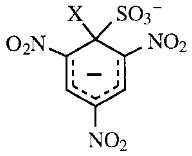


Figure 1. Suggested schematic potential energy profile for reaction of **1** with sulphite

thermodynamic stabilities than their isomers **2** formed by addition at the unsubstituted 3-position. The data in Table 5 allow the comparison of values of rate constants for attack at unsubstituted (k_1) and substituted (k_3) ring positions. The ratios are 250 in the case of **1c** and 34 for **1d**. The slower attack at the substituted positions is likely to derive from F-strain[18] associated with the proximity of two bulky groups. Inhibition of hydration of the adding sulphite ion by the presence of the 1-substituent may also be a factor. The kinetic and thermodynamic preference for attack at the 3-position may be described as K3T3 in Buncel's nomenclature.[19,20]



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In view of the excellent leaving group abilities of phenoxide and phenyl sulphide, it is likely that nucleophilic attack by sulphite will be rate-limiting in the overall substitution process. Hence intermediates **6c** and **6d**, once formed, will rapidly yield the substitution product. The contrastingly slow substitution in the ethyl derivatives is likely to derive from a change in the rate-determining step so that cleavage of the leaving group becomes rate-limiting. It is worth noting that in the substitution reactions of **1a–1d** with hydroxide ions to produce picric acid, where nucelophilic attack is rate-limiting, the alkyl and phenyl derivatives react at very similar rates.[17] Hence it is to be expected that the values of k_3 for attack of sulphite at the 1-position of **1a** and **1b** will be similar to those observed for **1c** and **1d**. The slow substitution in the ethyl derivatives derives from the poor leaving group abilities of ethoxide and ethyl sulphide coupled with the low thermodynamic stabilities of the adducts **6c** and **6d**. The results suggest a leaving group order in these systems of PhO^-, $PhS^- > SO_3^{2-} > EtO^-$, EtS^-.

EXPERIMENTAL

Compounds **1a, 1c** and **1d** were available from previous work.[17] Compound **1b** was prepared by reaction in ethanol of picryl chloride with one equivalent of ethane thiol in the presence of sodium ethanoate. Recrystallization from methanol yielded yellow crystals, m.p. 44 °C (lit. 45 °C[21]). Sodium sulphite, sodium sulphate and DMSO were the purest grades commercially available. Distilled water was boiled to remove carbon dioxide and subsequently protected from the atmosphere. NMR spectra were recorded using a Varian VXR-400 spectrometer with D_2O and [$^2H_6$] DMSO as solvent. UV/vis spectra and kinetic measurements were made with a Perkin-Elmer Lambda 12 spectrometer or with an Applied Photophysics SX-17 MV stopped-flow spectrometer. Reported rate constants are the means of several determinations and are precise to ±5%. To check that no depletion of sulphite concentration occurred by reaction with acidic impurities in the solvent, measurements were made both in the presence and absence of borax buffers (pH 9); no differences in rate constants were observed between buffered and unbuffered solutions.

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