Kinetic studies on the oxidation of aryl methyl sulfides and sulfoxides by dimethyldioxirane; absolute rate constants and activation parameters for 4-nitrophenyl methyl sulfide and sulfoxide†

Peter Hanson,* Ramon A. A. J. Hendrickx‡ and John R. Lindsay Smith*

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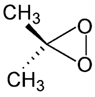
The oxidations of methyl 4-nitrophenyl sulfide and sulfoxide by dimethyldioxirane, in acetone and mixtures of acetone with water, methanol, acetonitrile and hexane, have been followed by UV-Vis spectroscopy to monitor the decay of the substrates. The data show that, under all the conditions studied, both oxidations obey second-order kinetics. Grunwald–Winstein and Kamlet–Taft analyses of the influence of solvents on the second-order rate constants have been used to obtain mechanistic information on the two reactions. Activation parameters for the two oxidations in acetone and aqueous acetone have been calculated from rate constants for reactions in the temperature range 283–313 K and compared with those from sulfide and sulfoxide oxidations with other oxidants. For sulfoxide oxidations in acetone and 1–20% v/v water in acetone, the results support a concerted nucleophilic displacement by sulfur of oxygen from dimethyldioxirane with the rate being dependent on the solvent's polarity. Sulfide oxidations in acetone and 1–5% v/v water in acetone also proceed by a concerted mechanism. However, in the most polar solvent system studied, 20% v/v water in acetone, the mechanism changes in favour of a two-step reaction involving a betaine intermediate. Importantly, the sulfide oxidation shows a different solvent dependence to that of the sulfoxide, with the rate of oxidation being determined by the hydrogen bond donor capacity and electron-pair donicity of the solvent.

Introduction

Dioxiranes can be readily prepared and used *in situ* by oxidation of ketones with Oxone®.[2] The simple, volatile dioxiranes, dimethyldioxirane (**1**) and (trifluoromethyl)methyldioxirane (**2**), have been the most extensively studied since they can also be isolated as dilute solutions (*ca.* 0.1 mol dm^{-3}) in the parent ketone by distillation from their respective oxidation mixtures[3] or be obtained free of ketone by extraction into chloromethane solvents.[4]



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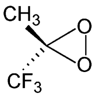

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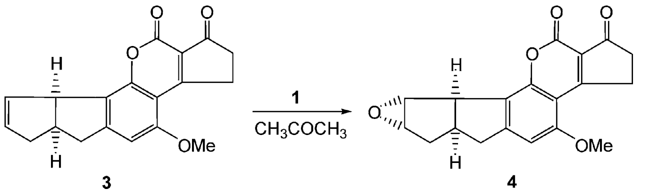
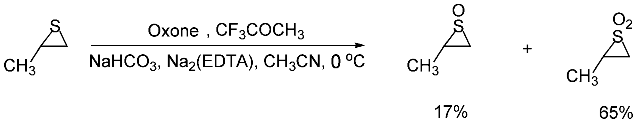
Dioxiranes can transfer an oxygen atom to a variety of substrates under mild conditions, without the requirement for acid or base catalysis, and have found many applications as oxidants.[5] These oxidations include epoxidation of alkenes[2a,b,d,3a,6] and alkynes,[4b,7] oxygen transfer to the heteroatom in amines[8] and sulfides,[9] and insertion into C–H bonds.[3a,10] A clear advantage of using dioxiranes as oxidants in syntheses is with compounds which are sensitive to acid- or base-catalysed solvolysis. This is well illustrated by the successful preparation of aflatoxin B$_1$ *exo*-8,9-epoxide (**4**), the carcinogenic metabolite of the mycotoxin aflatoxin B$_1$ (**3**), using dimethyldioxirane,[11] when all previous attempts to bring about this epoxidation with other reagents had failed (Scheme 1).[12] Another example of the use of dioxiranes in synthesis is in the first successful oxidation of episulfides to episulfones using (trifluoromethyl)methyldioxirane (**2**), when a range of alternative oxidants had been employed without success (Scheme 2).[13]



Scheme 1



Scheme 2

The most extensively investigated of the dioxirane oxidations has been alkene epoxidation, and this has been developed, using chiral ketones and the *in situ* protocol for dioxirane synthesis, into an efficient method for the enantioselective epoxidation of unfunctionalised alkenes (see for example Scheme 3[14]).[15]

Department of Chemistry, University of York, Heslington, York, YO10 5DD, UK. E-mail: ph8@york.ac.uk, jrls1@york.ac.uk

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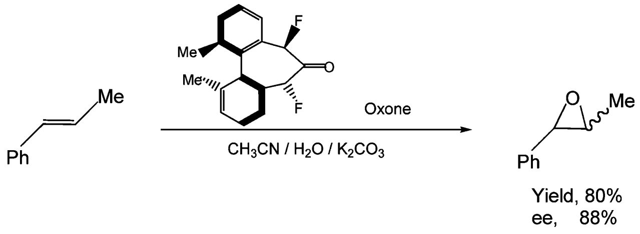
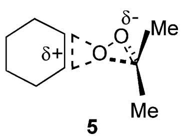
‡ Present address: Department DMPK & Bio-analysis, AstraZeneca, AB 221 87 Lund, Sweden. E-mail: ramon.hendrickx@astrazeneca.com



Scheme 3

Alkene epoxidation obeys the second-order rate law, first-order with respect to both dioxirane and substrate. Hammett plots for epoxidation of styrenes and ethyl cinnamates with dimethyldioxirane in acetone gave ρ values of -0.90[6c] and -1.53,[16] respectively, identifying the electrophilic nature of dioxiranes in these reactions. This information, coupled with the activation parameters reported for the oxidation of cyclohexene with dimethyldioxirane in acetone ($\Delta H^{\ddagger}$ 30.8 kJ mol^{-1} and $\Delta S^{\ddagger}$ -149 J mol^{-1} K^{-1}) suggested a concerted reaction mechanism involving a spiro-shaped transition state (**5**) with partial positive and negative charge on the alkene and the dioxirane, respectively.[6b,17]



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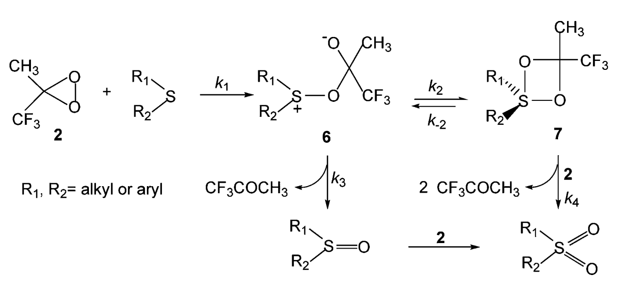
Hammett studies, by Murray and coworkers,[18] on the oxidation of aryl methyl sulfides and sulfoxides with dimethyldioxirane in acetone gave ρ values of -0.77 and -0.76 for the respective oxidations. Here, the signs confirm dioxiranes as electrophilic oxidants and the magnitudes imply that both oxidations occur by a concerted oxygen atom-transfer with only partial charge separation. More recently Asensio *et al.*[19] suggested an alternative mechanism for sulfide oxidation with dioxiranes, involving a betaine intermediate **6** which can either eliminate the ketone to give the sulfoxide or ring-close to the dioxathietane (cyclic sulfurane), **7** (Scheme 4). The key observation was the oxidation of sulfides with (trifluoromethyl)methyldioxirane to the corresponding sulfones, even in the presence of an excess of the sulfide. This was accounted for by the rate of cyclisation of the betaine **6** being greater than that of the elimination of CF_3COCH_3 ($k_2 > k_3$) and the sulfurane intermediate reacting with the oxidant much faster (to give the observed sulfone) than does the parent sulfide ($k_4 > k_1$).



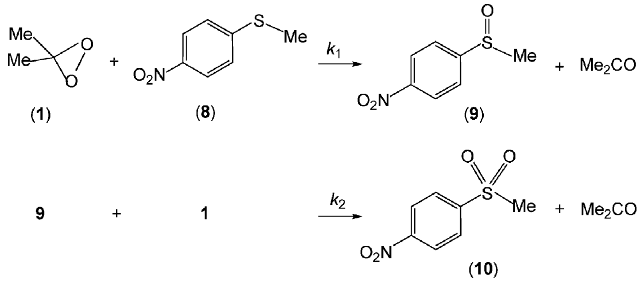
Scheme 4

In our previous paper we carried out a detailed analysis of substituent effects in the oxidation of aryl methyl sulfides and sulfoxides by dimethyldioxirane.[1] Hammett correlations using relative rate data from competitive oxidations, in acetone and mixtures of acetone with aprotic and protic co-solvents, show that in all but the most polar solvent system (20% v/v water in acetone) both oxidations proceed by a concerted mechanism. In this last solvent mixture, however, there is clear evidence for a change from a concerted to a two-step mechanism involving a betaine intermediate. In this paper we explore the mechanisms of the two oxidations further and report the first absolute rate constants and activation parameters for the oxidation of a sulfide and a sulfoxide by dimethyldioxirane in acetone, aqueous acetone and a selection of other acetone–co-solvent mixtures. The data are analysed using the Grunwald–Winstein and Kamlet–Taft equations and the results provide further evidence for the mechanistic conclusions in our first paper.

Results

Kinetics of sulfide and sulfoxide oxidation by dimethyldioxirane

(i) Methodology. Methyl 4-nitrophenyl sulfide and sulfoxide were selected as representative substrates for kinetic studies from the twelve methyl substituted-phenyl sulfides and sulfoxides used in our previous investigation (Scheme 5).[1] These compounds have the lowest rates of oxidation by dimethyldioxirane, which make them the most amenable for conventional kinetic studies. Furthermore, their UV-Vis absorption maxima, unlike the majority of the substrates in our previous study, are clear of interference from the solvent's absorption, allowing the kinetics to be followed by monitoring the decrease in the substrate's absorption with time.



Scheme 5

The oxidation of both substrates was studied in acetone and in a selection of solvents (hexane, acetonitrile, water and methanol) mixed with acetone. Two reaction protocols were employed: (a) all the sulfide and some of the sulfoxide oxidations were carried out with ~2.5-fold excess of substrate (typically 0.1×10^{-4} mol dm^{-3}) over oxidant and analysed as second-order reactions; (b) the remaining sulfoxide oxidations used pseudo-first-order conditions with a large excess of oxidant over substrate (under these conditions, the sulfide oxidations were too fast to be easily studied).

The absorptions of the sulfide, sulfoxide and sulfone overlap and this needs to be taken into account in both the first- and second-order protocols. It was confirmed that each compound obeys the Beer–Lambert law and their molar absorption coefficients, ε, for the solvents and wavelengths used are given in the ESI.† Dimethyldioxirane in acetone is yellow in colour, however, its absorption (λ_{max} 336 nm, 1.58 ± 0.042 m^2 mol^{-1}) is negligible, compared to those of the methyl 4-nitrophenyl sulfide, sulfoxide or sulfone, and it does not interfere with the rate measurements.

Generally, for unit path length the application of the Beer–Lambert law gives $A_0 = [\mathbf{S}]_0\varepsilon_S$ and $A_\infty = [\mathbf{P}]_\infty\varepsilon_P = [\mathbf{S}]_0\varepsilon_P$ (for complete reaction of **S**) where A_0 and A_∞ are the initial and final absorbances, **S** and **P** are the substrate and product and ε_S and ε_P their respective molar absorption coefficients. On account of the overlapping absorptions of substrate and product, the absorbance, A_t, at an intermediate time t is given by eqn (1),

$$\begin{aligned} A_t &= [\mathbf{S}]_t\varepsilon_S + [\mathbf{P}]_t\varepsilon_P \\ &= [\mathbf{S}]_t\varepsilon_S + ([\mathbf{S}]_0 - [\mathbf{S}]_t)\varepsilon_P \\ &= [\mathbf{S}]_0\varepsilon_P + [\mathbf{S}]_t(\varepsilon_S - \varepsilon_P) \end{aligned} \tag{1}$$

From these expressions it follows that

$$[\mathbf{S}]_0 = \frac{A_0 - A_\infty}{\varepsilon_S - \varepsilon_P} \quad \text{and} \quad [\mathbf{S}]_t = \frac{A_t - A_\infty}{\varepsilon_S - \varepsilon_P}$$

For the first-order protocol we have, for a substrate **S** reacting with a large excess of oxidant,

$$\ln\left(\frac{[\mathbf{S}]_0}{[\mathbf{S}]_t}\right) = k_1 t \tag{2}$$

Substitution of $[\mathbf{S}]_0$ and $[\mathbf{S}]_t$ from above gives eqn (3),

$$\ln\left(\frac{A_0 - A_\infty}{A_t - A_\infty}\right) = k_1 t \tag{3}$$

The pseudo-first-order data for sulfoxide oxidations (*i.e.* **S** = **9**) were analysed using eqn (3) for absorbance at 330 nm. The slopes of the linear plots of $\ln[(A_0 - A_\infty)/(A_t - A_\infty)]$ *versus* t gave k_1 from which, knowing $[\mathbf{1}]_0$, the second-order rate constants k_2 were calculated.

For the second-order protocol, we have for a substrate **S** reacting with **1**,

$$\frac{1}{[\mathbf{1}]_0 - [\mathbf{S}]_0}\ln\left(\frac{[\mathbf{S}]_0([\mathbf{1}]_0 - [\mathbf{P}]_t)}{[\mathbf{1}]_0([\mathbf{S}]_0 - [\mathbf{P}]_t)}\right) = k_2 t \tag{4}$$

from which it may be shown (see ESI†) that

$$[\mathbf{P}]_t = [\mathbf{S}]_0[\mathbf{1}]_0\frac{\exp\{([\mathbf{1}]_0 - [\mathbf{S}]_0)k_2 t\} - 1}{[\mathbf{1}]_0\exp\{([\mathbf{1}]_0 - [\mathbf{S}]_0)k_2 t\} - [\mathbf{S}]_0} \tag{5}$$

Since $[\mathbf{P}]_t = [\mathbf{S}]_0 - [\mathbf{S}]_t$, eqn (5) may be rearranged to give eqn (6) (see ESI),

$$[\mathbf{S}]_t = \frac{[\mathbf{1}]_0 - [\mathbf{S}]_0}{\dfrac{[\mathbf{1}]_0}{[\mathbf{S}]_0}\exp\{([\mathbf{1}]_0 - [\mathbf{S}]_0)k_2 t\} - 1} \tag{6}$$

Substitution of $[\mathbf{S}]_t$ from eqn (6) in eqn (1) gives eqn (7),

$$A_t = [\mathbf{S}]_0\varepsilon_P + \frac{([\mathbf{1}]_0 - [\mathbf{S}]_0)(\varepsilon_S - \varepsilon_P)}{\dfrac{[\mathbf{1}]_0}{[\mathbf{S}]_0}\exp\{([\mathbf{1}]_0 - [\mathbf{S}]_0)k_2 t\} - 1} \tag{7}$$

Knowing appropriate parameters $[\mathbf{S}]_0$, $[\mathbf{1}]_0$, ε_S and ε_P, eqn (7) can, in principle, be used to fit the sulfide or sulfoxide decay profiles. However, due to the time required for manipulation of solutions and the reaction cell, there is an uncertain time-lapse, t_0, between the formal onset of reaction and the recording of the first observation. It is therefore convenient to adjust eqn (7) to incorporate this [eqn (8)]. The resulting multiparameter fittings thus lead to evaluation of both k_2 and t_0.

$$A_t = [\mathbf{S}]_0\varepsilon_P + \frac{([\mathbf{1}]_0 - [\mathbf{S}]_0)(\varepsilon_S - \varepsilon_P)}{\dfrac{[\mathbf{1}]_0}{[\mathbf{S}]_0}\exp\{([\mathbf{1}]_0 - [\mathbf{S}]_0)k_2(t - t_0)\} - 1} \tag{8}$$

Using the procedures described above, the oxidations of methyl 4-nitrophenyl sulfide and sulfoxide in all the solvent systems were found to obey good second-order kinetics. The reactions of the sulfoxide under pseudo-first-order conditions showed linear correlations in the plots of $\ln[(A_0 - A_\infty)/(A_t - A_\infty)]$ *vs.* time (in all cases $r^2 > 0.999$). Likewise, all the sulfide and sulfoxide oxidations under second-order conditions gave excellent fittings (R^2 of > 0.999) to eqn (8) (see, for example, ESI Fig. S1†). Where the second-order rate constant for sulfoxide oxidation was obtained by both methods, agreement was also excellent. Each reported rate constant is the average of the values obtained from at least five experiments.

(ii) Oxidations in acetone and mixtures of acetone with hexane, acetonitrile, H_2O, and methanol. The second-order rate constants for the oxidation of methyl 4-nitrophenyl sulfide and sulfoxide in acetone and mixed acetone–co-solvent systems are recorded in Tables 1 and 2. In our previous study, we employed DMF (relative permittivity 38.2[20a]) as the co-solvent to increase the polarity of the solvent, acetone (relative permittivity 20.7[20a]), while maintaining the aprotic environment.[1] However, the slow oxidation of DMF by dimethyldioxirane limited the use of this co-solvent to sulfide oxidations only. To avoid this problem in the present study, the polarity was increased with acetonitrile (relative permittivity 37.5[20b]), which is not oxidised by dimethyldioxirane and, as previously, it was decreased by the addition of hexane (relative permittivity 1.9[20c]). For the sulfide oxidation, increasing the proportion of hexane in the solvent from 0 to 90% v/v led to a 2.5-fold decrease and the use of acetonitrile–acetone

Table 1 The second-order rate constants for the oxidation of methyl 4-nitrophenyl sulfide by dimethyldioxirane in selected solvent systems

Solvent[a]	Co-solvent[a]	Temperature/K	$10^{-2}k_{2(\text{sulfide})}$/dm^3 mol^{-1} s^{-1} [b]
Acetone			
100	0	293	6.05 ± 0.17
Acetone	Acetonitrile		
50	50	293	30.8 ± 1.0
Acetone	Hexane		
100	0	294	6.76 ± 0.24
75	25	294	6.26 ± 0.12
50	50	294	4.35 ± 0.13
10	90	294	2.68 ± 0.11
Acetone	Water		
100	0	294	6.76 ± 0.24
98	2	294	9.79 ± 0.68
95	5	294	12.0 ± 0.6
90	10	294	24.0 ± 1.6
85	15	294	40.3 ± 2.1
80	20	294	47.0 ± 1.9
75	25	294	66.3 ± 2.5
Acetone	Methanol		
100	0	299	7.21 ± 0.17
99	1	299	7.07 ± 0.14
90	10	299	8.73 ± 0.17
80	20	299	13.7 ± 0.8

[a] Solvent composition in % v/v. [b] Uncertainties are 95% confidence intervals.

Table 2 The second-order rate constants for the oxidation of methyl 4-nitrophenyl sulfoxide by dimethyldioxirane in selected solvent systems

Solvent[a]	Co-solvent[a]	Temperature/K	$k_{2(\mathrm{sulfoxide})}$/dm^3 mol^{-1} s^{-1} [b]
Acetone			
100	0	293	7.06 ± 0.41
100	0	293	7.52 ± 0.42[c]
Acetone	Acetonitrile		
50	50	293	9.58 ± 0.18
Acetone	Hexane		
100	0	294	8.31 ± 0.51[c]
50	50	294	9.08 ± 0.47[c]
15	85	294	19.4 ± 0.8[c]
Acetone	Water		
100	0	294	7.33 ± 0.25
98	2	294	7.54 ± 0.21
95	5	294	8.47 ± 0.28
90	10	294	9.74 ± 0.34
85	15	294	10.5 ± 0.3
80	20	294	12.5 ± 0.4
75	25	294	13.2 ± 0.4
Acetone	Methanol		
100	0	295	8.31 ± 0.51[c]
99	1	295	8.38 ± 0.58[c]
80	20	295	8.23 ± 0.58[c]
50	50	295	7.94 ± 0.69[c]

[a] Solvent composition in % v/v. [b] Uncertainties are 95% confidence intervals. [c] Values of k_2 calculated from k_1 from pseudo-first-order conditions.

(1 : 1, v/v) resulted in a 4.5-fold increase in k_2. By contrast, k_2 for the sulfoxide reaction in acetone increased 2.5-fold in 90% v/v hexane in acetone, and showed a small increase (1.1-fold) in a 50% v/v acetonitrile–acetone mixture.

The second-order rate constant for sulfide oxidation was also increased by the addition of the polar protic co-solvents water and methanol (relative permittivity 80.2[20d] and 33.0,[20e] respectively). Thus, changing the water content from 0 to 25% v/v resulted in a 10-fold increase in k_2, and for methanol a somewhat smaller 4.3-fold increase was obtained with a 0 to 50% v/v change in co-solvent concentration. The corresponding changes in the rate constant for the sulfoxide oxidation were significantly smaller, a 1.8-fold increase and ~0, respectively.

The data reveal, in agreement with our previous study on the relative rates of oxidation of aryl methyl sulfides and sulfoxides, that whereas the sulfoxide oxidation is not greatly affected by changes in solvent properties, that of the sulfide is strongly favoured by solvents that are hydrogen-bond and/or electron-pair donors. These observations are investigated in more detail below using Grunwald–Winstein and Kamlet–Taft analyses.

(iii) Activation parameters. The oxidation of methyl 4-nitrophenyl sulfide in acetone and aqueous acetone (5 and 20% v/v) was carried out at five temperatures between 283 and 313 K, and likewise that of the sulfoxide in acetone and aqueous acetone (20% v/v). The second-order rate constants from these studies (Tables 3–5) were used to obtain the activation parameters $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ from their respective Eyring plots (see for example Fig. 1 and 2) (Table 6).

Table 3 The temperature dependence of the second-order rate constants, k_2, for the oxidation of methyl 4-nitrophenyl sulfide and sulfoxide by dimethyldioxirane in acetone

Temperature/K	$10^{-2}k_{2(\mathrm{sulfide})}$/ dm^3 mol^{-1} s^{-1} [a]	Temperature/K	$k_{2(\mathrm{sulfoxide})}$/ dm^3 mol^{-1} s^{-1} [a]
288	4.88 ± 0.16	283	3.86 ± 0.15
293	6.05 ± 0.17	289	5.69 ± 0.25
302	8.11 ± 0.24	293	7.06 ± 0.41
308	9.68 ± 0.30	298	10.3 ± 0.3
313	11.6 ± 3.8	302	12.8 ± 0.4

[a] Uncertainties are 95% confidence intervals.

Table 4 The temperature dependence of the second-order rate constants, k_2, for the oxidation of methyl 4-nitrophenyl sulfide and sulfoxide by dimethyldioxirane in 20% v/v water in acetone

Temperature/K	$10^{-2}k_{2(\mathrm{sulfide})}$/ dm^3 mol^{-1} s^{-1} [a]	Temperature/K	$k_{2(\mathrm{sulfoxide})}$/ dm^3 mol^{-1} s^{-1} [a]
290	35.5 ± 1.5	290	9.25 ± 0.33
295	47.0 ± 1.9	295	12.5 ± 0.4
298	53.2 ± 2.0	298	14.3 ± 0.5
305	71.5 ± 2.5	305	19.5 ± 0.7
309	86.0 ± 2.1	309	25.4 ± 0.6

[a] Uncertainties are 95% confidence intervals.

Table 5 The temperature dependence of the second-order rate constant, k_2, for the oxidation of methyl 4-nitrophenyl sulfide by dimethyldioxirane in 5% v/v water in acetone

Temperature/K	$10^{-2}k_{2(\mathrm{sulfide})}$/dm^3 mol^{-1} s^{-1} [a]
290	10.1 ± 0.3
295	12.0 ± 0.6
298	13.6 ± 0.6
305	16.4 ± 1.1
309	19.7 ± 1.2

[a] Uncertainties are 95% confidence intervals.

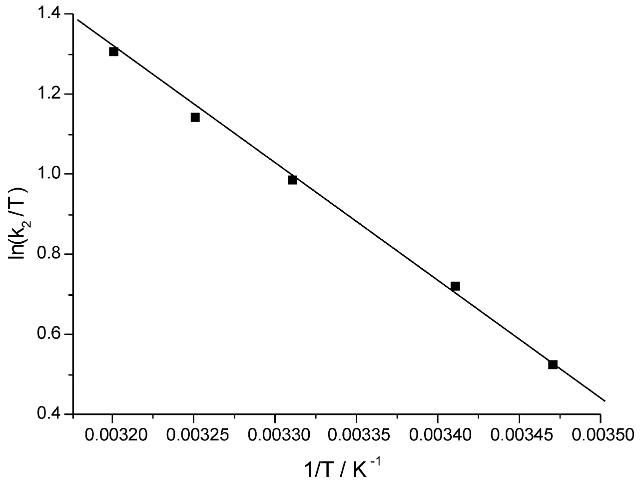


Fig. 1 Eyring plot for the oxidation of methyl 4-nitrophenyl sulfide by dimethyldioxirane in acetone.

Table 6 The activation parameters for the oxidation of methyl 4-nitrophenyl sulfide and sulfoxide by dimethyldioxirane in acetone and aqueous acetone mixtures

Substrate	Solvent	$\Delta H^{\ddagger}$/kJ mol^{-1} [a]	$\Delta S^{\ddagger}$/J K^{-1} mol^{-1} [a]
Sulfide	Acetone	22.6 ± 2.2	−114.7 ± 7.4
Sulfide	Acetone–water (95 : 5 % v/v)	22.7 ± 2.3	−108.9 ± 7.5
Sulfide	Acetone–water (80 : 20 % v/v)	31.1 ± 2.2	−69.1 ± 6.7
Sulfoxide	Acetone	42.4 ± 4.4	−83.6 ± 15.2
Sulfoxide	Acetone–water (80 : 20 % v/v)	35.2 ± 3.6	−104.4 ± 11.9

[a] Uncertainties are 95% confidence intervals.

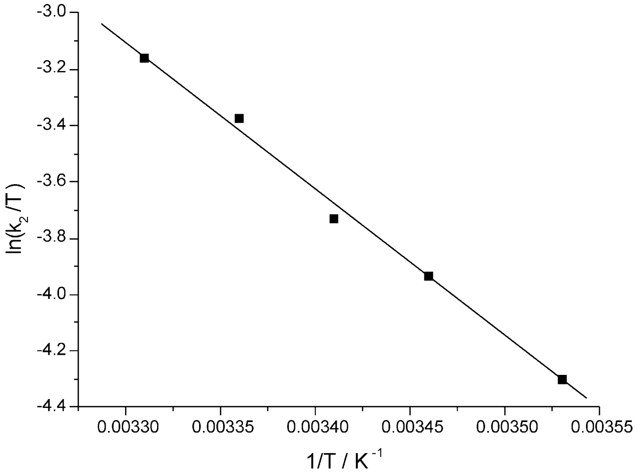


Fig. 2 Eyring plot for the oxidation of methyl 4-nitrophenyl sulfoxide by dimethyldioxirane in acetone.

Table 7 The second-order rate constants, k_2, for the oxidation of aryl methyl sulfides and sulfoxides with dimethyldioxirane in acetone at 293 K

Substituent	$10^{-2}k_{2(\text{sulfide})}$/ dm^3 mol^{-1} s^{-1} [a]	$k_{2(\text{sulfoxide})}$/ dm^3 mol^{-1} s^{-1} [a]	$k_{2(\text{sulfide})}/k_{2(\text{sulfoxide})}$
4-OMe	37.6 ± 4.7	46.3 ± 10.2	81.2
4-Me	31.6 ± 3.7	38.7 ± 7.9	81.6
H	23.5 ± 2.4	28.6 ± 5.1	82.2
3-OMe	19.1 ± 1.7	23.0 ± 3.7	83.0
4-Cl	15.8 ± 1.2	18.9 ± 2.7	83.6
3-Cl	12.3 ± 0.8	14.7 ± 1.8	83.7
3-CF_3	11.1 ± 0.7	13.2 ± 1.5	84.1
4-C(O)Me	9.85 ± 0.53	11.7 ± 1.2	84.2
3-CN	8.87 ± 0.43	10.5 ± 1.0	84.5
4-CN	7.45 ± 0.30	8.75 ± 0.67	85.1
3-NO_2	6.83 ± 0.24	8.00 ± 0.55	85.4
4-NO_2	(6.05 ± 0.17)[b]	(7.06 ± 0.41)[b]	85.7

[a] Calculated from Hammett correlations of relative values (k_X/k_H) except for X = 4-NO_2, which was measured as described above. [b] Average value from at least four experiments.

Discussion

(i) Absolute rate constants for the oxidation of aryl methyl sulfides and sulfoxides by dimethyldioxirane in acetone

The second-order rate constants for the oxidation of methyl 4-nitrophenyl sulfide and sulfoxide were used to calculate absolute k_2 values from the relative rate data presented in our previous paper.[1] Rather than converting the experimental relative values directly, preserving their experimental scatter, we have used relative values given by the Hammett relationship [eqn (9)] and the ρ values −0.76 and −0.78, respectively, for the oxidation of aromatic sulfides and sulfoxides in acetone at 293 K.[1] The derived absolute rate constants are thus optimised within the data set as a whole (Table 7).

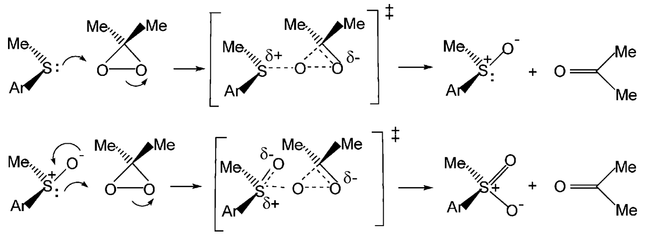
$$\log(k_X/k_H) = \sigma\rho \tag{9}$$

As noted previously, and consistently with the electrophilic character of the oxidant, electron-releasing groups on the substrates lead to an increase in the rate constants. The data in Table 7 also reveal that, for oxidations in acetone, the ratio of rate constants for all the aryl methyl sulfide and sulfoxide pairs are remarkably constant, lying between 81 and 86. Thus the relative reactivities of sulfides to sulfoxides are almost independent of the electronic effect of the substituent. This is a direct result of the very similar negative ρ values for both oxidations in acetone at 293 K.[1]

The absolute rate constants for the aryl methyl sulfides and sulfoxides can also be compared with those for the oxidation of other substrates by dimethyldioxirane (Table 8). This shows that the sulfides are the most reactive of the substrates studied, in the following reactivity order: alkanes, ethers < alcohols < alkenes < amines < sulfoxides < sulfides. For all these substrates, dimethyldioxirane is an electrophilic oxidant and the observed order therefore reflects the ability of the substrate to act as a nucleophile. Table 8 also shows that the addition of water to the dimethyldioxirane oxidations of ethers, alkenes and amines leads to an increased rate of reaction. This and other solvent effects on the oxidation of sulfides and sulfoxides are discussed below.

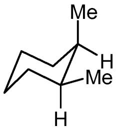
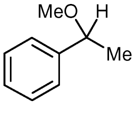
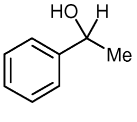
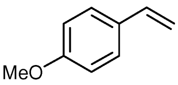
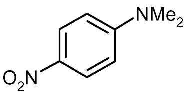
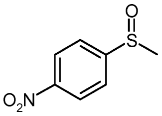
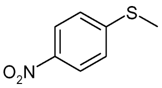
(ii) Solvent effects

In our previous paper we proposed that, in the oxidation of aryl methyl sulfides by dimethyldioxirane, there is a large increase in dipole moment in going from the reactant to the transition state, whereas, by contrast, in the corresponding sulfoxide oxidation there is a decrease (Scheme 6). Using the kinetics protocols developed in this study, it has been possible to test these suggestions by carrying out both reactions in a range of different solvent systems.



Scheme 6

Table 8 Second-order rate constants for the oxidation of selected organic substrates by dimethyldioxirane

Substrate	Product	Temperature/K	Solvent	k_2/dm^3 mol^{-1} s^{-1}	Ref.
	*t*-Alcohol	278	Acetone	1.37×10^{-3}	10*a*
	Ketone	278	Acetone Acetone–water (1 : 0.18 v/v)	1.63×10^{-3} 2.44×10^{-3}	10*d*
	Ketone	278	Acetone	2.24×10^{-2}	10*d*
	Epoxide	276	Acetone Acetone–water (1 : 0.22 v/v)	0.55 7.1	6*c*
	*N*-Oxide	278	Acetone Acetone–water (1 : 1 v/v)	3.84 94.5	21
	Sulfone	293	Acetone	7.06	This study
	Sulfoxide	293	Acetone	605	This study

(a) Dipolar aprotic solvent systems. The results from the sulfide and sulfoxide oxidations in hexane–acetone mixtures support the proposed charge changes, in the rate-determining steps of the two reactions. Thus the former reaction is disfavoured by increasing the proportion of hexane whereas the latter is favoured. However, using the more polar 50% v/v acetonitrile–acetone as the solvent leads to an increase in the k_2 values of both reactions, whereas the simple polarity model predicts an increase in rate for sulfide but not sulfoxide oxidation. A possible explanation for the increase in the rate of the latter reaction relates to the π^*-solvent parameter in the Kamlet–Taft equation,[22] and is discussed in more detail below.

It is interesting to note that although the sulfide/sulfoxide selectivity of dimethyldioxirane in acetone is insensitive to substituent effects, it is strongly dependent on the solvent composition. Thus the relative rate ratio $k_{2(\text{sulfide})}/k_{2(\text{sulfoxide})}$ is ~14 in 85–90% v/v hexane in acetone and >300 in 50% v/v acetonitrile–acetone. This has important implications for the selective synthesis of sulfoxides from sulfides.

(b) Protic solvent systems. The rate constants for both the sulfide and sulfoxide oxidations are increased by the addition of water, however, the magnitude of this effect is much larger for the former reaction. The rate enhancement of the sulfoxide oxidation from adding water to the solvent was not expected and is discussed further below. The effect of using methanol as the protic co-solvent for sulfide oxidation is similar to that of water although less pronounced; however, it has no effect on the rate of sulfoxide oxidation in methanolic acetone (Tables 1 and 2). As a result of the different solvent dependencies of the two oxidations, the selectivity of the oxidant, $k_{2(\text{sulfide})}/k_{2(\text{sulfoxide})}$, increases more than 50-fold on changing the solvent from acetone to 25% v/v aqueous acetone.

(ii) Analysis of solvent effects

The solvent interactions in the oxidations of methyl 4-nitrophenyl sulfide and methyl 4-nitrophenyl sulfoxide in aqueous acetone have been analysed in more detail using the Grunwald–Winstein[23] and Kamlet–Taft[22] equations [eqn (10) and eqn (11), respectively]. In the former, plots of log k_2 *vs.* solvent parameter Y give m, the susceptibility of the rate of reaction to changes in the solvent. These analyses show that the m value for the sulfide oxidation, 0.307 ± 0.026 ($r^2 = 0.991$ and $s = 0.038$), is 3.7 times larger than that for the sulfoxide oxidation of 0.082 ± 0.009 ($r^2 = 0.983$ and $s = 0.014$).

$$\log k_2 = \log k_0 + mY \tag{10}$$

Our previous study, of the relative rates of aryl methyl sulfide oxidation by dimethyldioxirane, shows how the presence of a small concentration of water (1% and 5% v/v) in acetone leads to significant increases in the Hammett reaction constant (57% and 75%, respectively) compared to that from acetone alone. This effect is attributed to the ability of water to favour a larger charge separation during the reaction, through specific solvation rather than changes in solvent polarity. Thus by electron donation to the partial positive charge on sulfur and by hydrogen bonding to the partial negative charge on oxygen, it solvates and stabilises the transition state **11**. In contrast, the Hammett ρ values, from the relative rates of aryl methyl sulfoxide oxidation, show a much smaller solvent dependence (11% decrease in going from acetone to 20% v/v aqueous acetone). This indicates that the substituent effect on the oxidation of sulfoxides is insensitive to specific solvating properties of water, suggesting that there is only a small change in charge distribution in the rate-determining step in this reaction. Analysis of solvent effects on the absolute rate data, for the oxidations in the protic solvent systems from the present study, support our earlier conclusions. Thus the Grunwald–Winstein treatment shows that the oxidation of the sulfide is more sensitive than that of the sulfoxide to solvent changes (m values 0.31 and 0.08, respectively).

Comparison with literature data shows that the m value for the sulfide oxidation is lower than those obtained for the oxidation of methyl phenyl sulfide with $NaIO_4$[24] and peroxomonosulfate[25] (0.72 and 0.84, respectively). However, both these oxidants are ionic and their larger m values may well arise from specific solvation of these charges. A more comparable system to the sulfur oxidations studied here, the one-step epoxidation of 4-methoxystyrene by dimethyldioxirane in aqueous acetone mixtures, has a very similar m value of 0.328 ± 0.022 ($r^2 = 0.994$, $s = 0.037$ and $\psi = 0.092$).[6c]

The Kamlet–Taft analysis [eqn (11)] gives the regression coefficients a, b and s, which measure the susceptibility of the second-order rate constants, k_2, to the solvent parameters, α, β and π^*.[22,26]

$$\log k_2 = \text{constant} + a\alpha + b\beta + s\pi^* \qquad (11)$$

where α is a measure of the solvent's hydrogen bond donor (HBD) capacity, β is a measure of the solvent's electron pair donicity, and π^* is a measure of the solvent's capacity to stabilise a charge or dipole *via* its dielectric effect.

The solvent parameters α, β and π^* used in this study for the water–acetone mixtures were interpolated from data reported by Marcus (α and π^*)[27] and Reichardt and co-workers (β)[27,28] (Table 9).

Table 9 The values for the Kamlet–Taft parameters for aqueous acetone mixtures[27,28]

% v/v of H_2O	Mole fraction	α	β	π^*
0	0	0.081	0.530	0.690
2	0.077	0.275	0.539	0.714
5	0.177	0.457	0.540	0.736
10	0.312	0.610	0.561	0.764
15	0.419	0.682	0.585	0.796
20	0.505	0.726	0.597	0.831
25	0.576	0.759	0.597	0.867

Kamlet–Taft correlation of $\log k_{\text{sulfide}}$ values was achieved using α and β, π^* not being significant at or below the 0.1 level of probability [eqn (12) and Fig. 3]. Standardisation of the $\log k_{2(\text{sulfide})}$ regression gives regression coefficients of 0.341 and 0.672 for α and β, respectively, indicating the lone-pair donicity of water to be about twice as important as its hydrogen bond donating capacity in stabilising the transition state **11** for oxidation of 4-nitrophenyl methyl sulfide, in aqueous acetone. By contrast, $\log k_{2(\text{sulfoxide})}$ was correlated by π^* alone, with neither α nor β being significant at the 0.1 level of probability [eqn (13) and Fig. 4] [the uncertainties in eqn (12) and eqn (13) are standard errors].

$$\log k_{2(\text{sulfide})} = -(1.949 \pm 0.879) + (0.507 \pm 0.193)\alpha + (8.914 \pm 1.717)\beta \qquad (12)$$

$$\log k_{2(\text{sulfoxide})} = -(0.226 \pm 0.076) + (1.572 \pm 0.099)\pi^* \qquad (13)$$

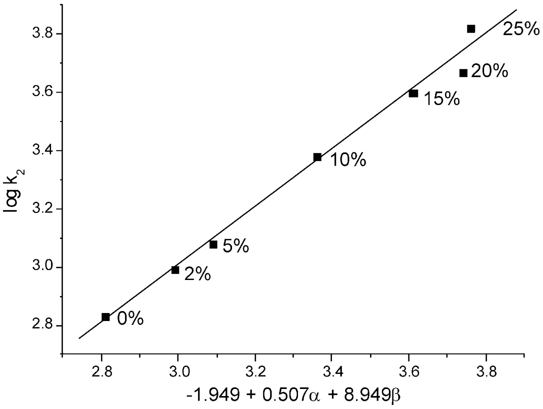


Fig. 3 The Kamlet–Taft treatment of the oxidation of methyl 4-nitrophenyl sulfide with dimethyldioxirane in aqueous acetone at 294.4 K.

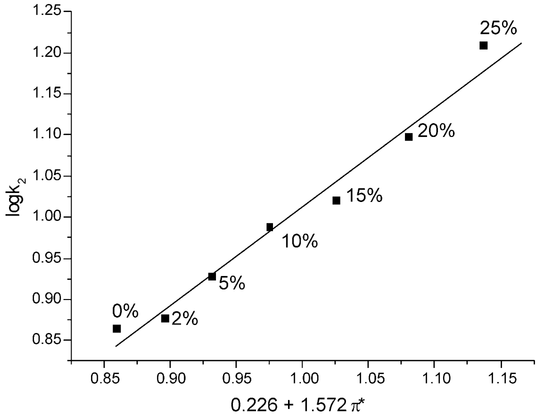
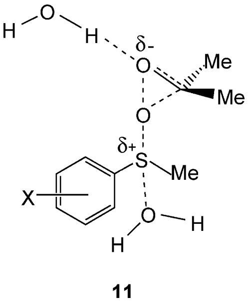


Fig. 4 The Kamlet–Taft treatment of the oxidation of methyl 4-nitrophenyl sulfoxide with dimethyldioxirane in aqueous acetone at 294.4 K.



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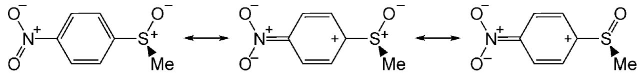
The finding expressed by eqn (12) supports the conclusions drawn in the previous paper,[1] where relative permittivity, a property measured by π^*, proved to be unimportant in the oxidation of different sulfides by the concerted mechanism, whereas the specific solvating property of water was important. (Reactions in neat acetone and 80% v/v DMF in acetone have essentially the same reaction constant whilst the reaction constant is increased in aqueous acetone.)

The lack of significant α and β terms in eqn (13) accords with the earlier observation[1] that the oxidations of sulfoxides are insensitive to the specific solvating properties of water. The positive sign of the coefficient of π^* indicates that the activation energy for the oxidation of 4-nitrophenyl methyl sulfoxide decreases with increasing solvent polarity (relative permittivity). At first sight this is surprising, as we had found that sulfoxides bearing both $+M$ and $-M$ substituents show *increased* relative rate constants as solvent polarity is *reduced.* This was explained in terms of the relative destabilisation of ground-states (which are more polarised the stronger the M effect of whatever sign) and stabilisation of transition-states of reduced polarity relative to the ground-states, as solvent polarity is decreased.

The positive coefficient of π^* in eqn (13) can be explained by consideration of solvent-dependent variation of polarity within the single substrate, **9**, rather than between different substrates.

Since the NO_2 group has more powerful electron-withdrawing effects than S(O)Me, the polarisation of the electrons of the aromatic ring in **9** is such as to deplete electron density at C(1), where S(O)Me is attached (*cf.* canonical structure **9a**). This will affect the relative weighting of the dipolar $S^+–O^-$ and S=O partial structures (*cf.* canonical structure **9b**). If the ring polarisation is subject to variation in degree with the polarity of the solvent, then the weighting of **9b** is expected to increase with increase in solvent polarity (π^*). In the previous paper[1] we suggested a relationship between the polarity of the SO bond and the energy of the lone-pair orbital on S such that the higher is the bond polarity, the lower is the energy of the orbital and *vice versa.* Invoking this again: the more polar a solvent, the greater is the weighting of **9b** and the higher is the energy of the lone-pair orbital; hence the more reactive the substrate in reaction with electrophilic **1**. This explains the positive coefficient of π^* in eqn (13).



9 **9a** **9b**

(iii) Activation parameters

The activation parameters for the oxidation of methyl 4-nitrophenyl sulfide and sulfoxide with dimethyldioxirane in acetone are within the range of published values for the oxidation of aryl sulfides and sulfoxides with other oxidants (Table 10). The large negative entropies of activation support the bimolecular mechanisms of both the dimethyldioxirane oxidations but cannot be used to distinguish between a concerted one-step and a two-step mechanism. Thus despite the similarities in the entropy values in Table 10, the sulfide oxidations in entries 2–9 are reported to proceed by a concerted mechanism whereas those in entries 11–12 are two-step processes. The $\Delta H^‡$ values for the dimethyldioxirane oxidations are amongst the lowest in Table 10, suggesting that it is a powerful oxidant and the reactions involve the simultaneous breaking and formation of bonds in the rate-determining transition state.

Adam[36] and Asensio[19] and their co-workers reported that sulfide oxidation by dimethyldioxirane in acetone takes place by a two-step mechanism. By contrast, the Hammett study in our previous paper shows, with one exception, that this oxidation is a concerted process. Only in the polar 20% v/v water in acetone system was evidence for a two-step mechanism obtained. The sulfoxide oxidation was a concerted one-step process under all the conditions studied.

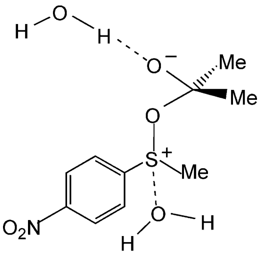
To explore the nature of this solvent-induced change in mechanism further, the activation parameters of both reactions in 20% v/v water in acetone and the sulfide oxidation in 5% v/v water in acetone were measured and compared with the results from the reaction in neat acetone. Adding 5% v/v water to the acetone did not result in a significant change in the value for the entropy of activation (−108.9 ± 7.5 and −114.7 ± 5.5 J K^{-1} mol^{-1}, respectively) for the oxidation of methyl 4-nitrophenyl sulfide. However, with 20% v/v water in acetone there is a large reduction in the negative value for the $\Delta S^‡$ of 40–45 J $K^{-1}mol^{-1}$

Table 10 The activation parameters for a selection of sulfide and sulfoxide oxidations

			Sulfide oxidation		Sulfoxide oxidation		
Entry	Oxidant	Solvent	$\Delta H^‡$/kJ mol^{-1}	$\Delta S^‡$/J K^{-1} mol^{-1}	$\Delta H^‡$/kJ mol^{-1}	$\Delta S^‡$/J K^{-1} mol^{-1}	Ref.
1	Me_2CO_2[a]	Acetone	22.6	−114.7	42.4	−83.6	This study
2	$KHSO_5$[b]	$H_2O–CH_3CN$ (99.5 : 0.5)	17.4	−124.0	—	—	25
3	H_2O_2[c]	Dioxane	65.7	−129.7	—	—	29
4	H_2O_2[c]	H_2O	54.3	−113.0	—	—	29
5	$MeCO_3H$[d]	$MeCO_2H$	43.7	−96.6	59.2	−105.0	30
6	$PhCO_3H$[e]	Benzene	42.7	−100.4	—	—	30
7	$PhCO_3H$[e]	Me_2NCHO	48.5	−133.8	—	—	31
8	$NaIO_4$[b]	EtOH–H_2O (1 : 1)	47.2	−113.3	—	—	24
9	PMPA[b,f]	H_2O–HOAc (1 : 1)	47.3	−123.0	—	—	32
10	PMPA[b,f]	H_2O–MeCN (40 : 60)	—	—	56.3	−89.3	33
11	(salen)Cr^V=O[b]	MeCN	48.6	−132.6	—	—	34
12	$Pb(OAc)_4$[b]	$MeCO_2H$	65.7	−111.0	—	—	35

[a] Substrates: $O_2NC_6H_4SMe$ and $O_2NC_6H_4S(O)Me$. [b] Substrates: methyl phenyl sulfide and sulfoxide. [c] Substrate: thioxane. [d] Substrates: $PhSCH_2CO_2H$ and $PhS(O)CH_2CO_2H$. [e] Substrate: 4-nitrodiphenyl sulfide. [f] Peroxomonophosphoric acid.

and an increase of 8 kJ mol^{-1} in $\Delta H^{\ddagger}$. This reduction in $\Delta S^{\ddagger}$ suggests that the transition state is less constrained and supports the conclusion, in our previous paper, that the mechanism has changed from a concerted one-step process in acetone, with a highly organised transition state, to a less constrained two-step process involving a betaine intermediate in 20% v/v water in acetone. Thus increasing the proportion of water in the solvent leads to an increased stabilisation of the charge separation in the reaction and a weakening of the O–O bond to the point where the fully charged intermediate (**12**) is formed.



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The faster rate of the sulfide oxidation in the 20% v/v water in acetone is due to the change in the entropy of activation, which outweighs the increase in the enthalpy of activation and leads to a decrease in $\Delta G^{\ddagger}$ at 293 K of 4.8 kJ mol^{-1}. For the sulfoxide oxidation there is no evidence for a change in mechanism; the changes in the activation parameters are small and give a value of $\Delta G^{\ddagger}$ at 293 K in 20% v/v water in acetone that is only 1 kJ mol^{-1} less than that observed for the reaction in 100% acetone.

Conclusions

1. The rates of oxidation of methyl 4-nitrophenyl sulfide and sulfoxide by dimethyldioxirane show overall second-order kinetics (first-order in substrate and oxidant).

2. Studies using a selection of acetone–co-solvent systems reveal that the sulfide oxidation is significantly more sensitive to changes in solvent character than the oxidation of the sulfoxide.

3. Grunwald–Winstein and Kamlet–Taft analyses of the rate constants for sulfide oxidation, in aqueous acetone solvent systems, indicate that the reaction is favoured by specific solvation of the transition state by water through hydrogen-bonding to the partial negative charge on oxygen in the dioxirane and electron-pair donation to partial positive charge on sulfur. The dominant solvent effect in the sulfoxide oxidation is solvent polarity.

4. The activation parameters, from reactions in acetone, support the concerted reaction mechanisms proposed previously[1] for both oxidations, on the basis of the small negative Hammett ρ values (−0.76 and −0.78 for the sulfide and sulfoxide oxidation, respectively).

5. Both oxidations are concerted one-step processes under all of the solvent conditions studied, except for the sulfide oxidation in 20% v/v water in acetone. In this solvent system, the specific solvation by water is sufficient to bring about a change in mechanism with the formation of a betaine intermediate in a two-step reaction.

Experimental

Instrumental methods

UV-Vis spectra were recorded on a Hewlett Packard HP8453 diode array spectrophotometer with UV-Vis Chemstation Rev. A.02.05 data processing. Quartz cuvettes (1 cm path length) were used throughout.

Non-linear fittings of absorption decay curves were carried out using SPSS 10.0 for Windows. The multiple linear regression analyses used either SPSS 10.0 for Windows or the Excel add-in Essential Regression 2.219, which was developed by Steppan *et al.*[37] This latter program was also used for standardised multiple linear regressions.

Materials

All the organic solvents employed in these studies were supplied by Fisher and were of analytical or HPLC grade. Deionised water was used throughout. The preparations of methyl 4-nitrophenyl sulfide, sulfoxide and sulfone and dimethyldioxirane in acetone are reported in our previous paper.[1] Two methods were used to measure the concentration of the oxidant. The first involved reacting it with methyl phenyl sulfide and analysing the resulting product mixture by GC. In the second, knowing the molar absorption coefficients at 330 nm of methyl 4-nitrophenyl sulfoxide and methyl 4-nitrophenyl sulfone, UV-Vis spectroscopy was used to analyse the product yield from the reaction of dimethyldioxirane with methyl 4-nitrophenyl sulfoxide. Both methods gave very similar results.

Rate measurements

For both the pseudo-first- and second-order protocols the methyl 4-nitrophenyl sulfide or sulfoxide in the required solvent was added to a cuvette and thermostatted in the spectrometer at the required temperature. After 15 min, a background UV-Vis spectrum (300–500 nm) was recorded before the oxidant was added, the cuvette was then thoroughly shaken and the spectrum of the reaction mixture was recorded (300–500 nm) every 20 s. The decay of absorbance at 350 and 330 nm was used to monitor the oxidations of methyl 4-nitrophenyl sulfide and sulfoxide, respectively. The analysis of the second-order data required measuring the absorption coefficients of substrate and product, at the wavelengths monitored, in each of the different solvent systems (see ESI Tables S1 and S2†). The second-order rate constants were calculated as described above. The pseudo-first-order protocol for sulfoxide oxidations typically used a 12-fold excess of dimethyldioxirane ($3–6 \times 10^{-3}$ mol dm^{-3}) over methyl 4-nitrophenyl sulfoxide ($2.5–5 \times 10^{-4}$ mol dm^{-3}). The second-order studies with methyl 4-nitrophenyl sulfide and sulfoxide employed a 2.5-fold excess of substrate (1.0×10^{-4} mol dm^{-3}) over oxidant (4.0×10^{-5} mol dm^{-3}).

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