

Sulfide Oxidation and Oxidative Hydrolysis of Thioesters by Peroxymonosulfate Ion

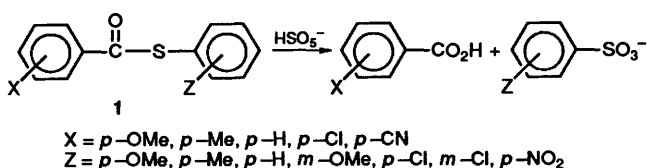
Clifford A. Bunton,* Houshang J. Foroudian and Anurag Kumar

Department of Chemistry, University of California, Santa Barbara, CA 93106, USA

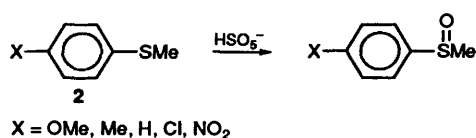
Peroxymonosulfate ion, HSO_5^- , as OXONE, in aqueous MeCN readily converts aryl thiobenzoates, $\text{XC}_6\text{H}_4\text{CO}\cdot\text{SC}_6\text{H}_4\text{Z}$ ($\text{X} = p\text{-OMe}, p\text{-Me}, \text{H}, p\text{-Cl}, p\text{-CN}$; $\text{Z} = p\text{-OMe}, p\text{-Me}, \text{H}, m\text{-OMe}, p\text{-Cl}, m\text{-Cl}, p\text{-NO}_2$) into carboxylic and sulfonic acids. Reactions are second order and have small substituent effects, with $\rho \approx -0.6$ based on σ_m and σ_p substituent parameters, but rates increase markedly with increasing water content in aqueous MeCN and entropies of activation are negative. The initial step is very similar to the oxidation of methyl aryl sulfides by HSO_5^- which has similar solvent and substituent effects. Enthalpies of activation are much lower for oxidation of the sulfides than of the corresponding esters but entropies of activation are similar.

Peroxymonosulfate ion, HSO_5^- , is a versatile anionic oxidant which is usually used as OXONE, 2KHSO_5 , KHSO_4 , K_2SO_4 .¹ Its aqueous solutions are reasonably stable and, as the tetrabutylammonium salt, it can also be used in some aprotic organic solvents.^{1b} Sulfides are rapidly oxidized to sulfoxides by OXONE and subsequent slower oxidation gives sulfones. Reactions are fastest in solvents of high water content,² and the kinetic forms are similar to those for sulfide oxidation by periodate ion (IO_4^-).³ Electron-donating groups and polar solvents increase rates of oxidation by IO_4^- , so the reactions probably have similar mechanisms, as do oxidations by peroxydicarboxylic acids.⁴

OXONE readily decomposes thioalkyl- and thioaryl phosphorus(v) esters to generate phosphorus(v) and sulfonic acids⁵ and is a useful decontaminant for the chemical agent, *O*-ethyl *S*-[2-(diisopropylamino)ethyl] methylphosphonothiolate(v), which is not completely decontaminated by conventional reagents, e.g., aqueous alkali. This reaction appears to involve oxidation at sulfur, followed by breaking of the P-S bond by attack of water or with formation of a labile mixed anhydride and subsequent rapid oxidation of the thiol residue to the sulfonic acid.⁶ This general path should also be available to other thioesters, 1, and we examined the kinetics of reactions



of a series of thiophenyl benzoates where the final products are the benzoic and sulfonic acids. These reactions are formally analogous to hydrolysis catalysed by electrophiles, e.g., Brønsted or Lewis acids, where an electrophile converts a substrate into a species susceptible to nucleophilic attack, except that attack of HSO_5^- is irreversible. The solvent was aqueous MeCN,² because this medium does not react with HSO_5^- and we studied kinetic solvent and substituent effects. Oxidation of sulfides, 2, to sulfoxides was examined for purposes of comparison.



Experimental

Materials.—The sulfides were commercial materials, or were prepared from the thiols by standard methods.⁷ Liquids were distilled *in vacuo* and solids were recrystallized. The m.p. and b.p. agreed with literature values,⁷ and TLC gave a single spot.

The esters were prepared from the substituted benzoyl chloride (Aldrich) 6 mmol,^{8a} which was added dropwise to a stirred solution of the appropriate equimolar thiophenol (Aldrich) and pyridine (Mallinckrodt) 6 mmol in diethyl ether (30 cm³) under N₂. The reaction mixture was stirred for 6 h at room temperature, the pyridinium chloride salt was filtered off, the solution was washed with dilute HCl, with cold NaHCO₃ solution, and then with water. The ether layer was dried (Na₂SO₄), and the filtered solution was evaporated. The solid so obtained was recrystallised twice (EtOH) to give the ester. The melting points of the thioesters agreed with the literature values.⁸ Purity of the thioesters was further checked by TLC silica gel (5% EtOAc–95% hexane) and by ¹H NMR spectrometry.

Kinetics.—Oxidation of the sulfides decreases absorbance at $\lambda \approx 260$ nm for most substrates and was followed spectrophotometrically as described.² Substrates were added in MeCN so that the final reaction solutions contained 0.5 vol% MeCN. With $[\text{HSO}_5^-] < 10^{-3}$ mol dm⁻³ we could follow initial oxidation to sulfoxide. In the earlier work, which involved reactions in micellized surfactants, H₂SO₄ was added to convert SO_4^{2-} into HSO_4^- and we followed that practice here.² We saw an isosbestic point at 253 nm for reaction of 2, $\text{X} = \text{OMe}$ and in the course of the reaction absorbance increased at ca. 240 nm, although signals are noisy at this wavelength.

Reactions of the esters were followed spectrophotometrically with Hewlett-Packard 8450 or 8451 diode-array spectrometers, with HSO_5^- , as OXONE, in large excess over the thioesters, the concentration of which was typically ca. 10^{-5} mol dm⁻³. Variations of concentration by a factor of ca. 12 did not affect the first-order rate constants. Solutions of OXONE were made up frequently and were regularly standardized iodometrically. We generally followed the decreasing absorbance of the thioesters in the wavelength range 260–300 nm, but we could also follow the increasing absorbance due to formation of the carboxylic acid and we observed clean isosbestic points at 235 nm for reactions of $\text{C}_6\text{H}_5\text{CO}\cdot\text{SC}_6\text{H}_4\text{Z}$, $\text{Z} = p\text{-OMe}, p\text{-Cl}$; and at 265 nm for reactions of $\text{XC}_6\text{H}_4\text{CO}\cdot\text{SC}_6\text{H}_5$, $\text{X} = p\text{-OMe}$. Solutions of OXONE have the tail of an absorbance up to ca. 250 nm, depending upon concentration, so we always used these

Table 1 Temperature effects on oxidation of sulfides in aqueous HSO_5^-

	$T/^\circ\text{C}$ ($k_2/\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$)					ΔH^\ddagger ^a	ΔS^\ddagger ^b
<i>p</i> -MeOC ₆ H ₄ SMe	11.1 (815)	21.2 (1060)	25.0 (1180)	29.8 (1308)	34.2 (1494)	16.4	-121
<i>p</i> -MeC ₆ H ₄ SMe	10.0 (612)		25.0 (890)	30.0 (971)	34.6 (1110)	14.8	-130
C ₆ H ₅ SMe	11.8 (444)		25.0 (632)	30.0 (733)	34.6 (828)	17.4	-124
<i>p</i> -ClC ₆ H ₄ SMe	14.7 (385)		25.0 (534)	30.0 (639)	34.6 (708)	20.4	-116
<i>p</i> -O ₂ NC ₆ H ₄ SMe	16.7 (79.6)		25.0 (102)	29.9 (106)	34.5 (125)	15.7	-145
Ph ₂ S	12.2 (54.2)	16.9 (63.5)	25.0 (72.4)	30.0 (83.3)	34.6 (103)	17.0	-145

^a /kJ mol⁻¹, ^b /J K⁻¹ mol⁻¹.

solutions as references. Absorbance of OXONE increased the noise at low wavelengths and we could not observe the increasing absorbance of the benzoic acid or the isosbestic point with $[\text{HSO}_5^-] > 0.03 \text{ mol dm}^{-3}$ in a 10 mm cell or $> 0.11 \text{ mol dm}^{-3}$ in a 2 mm cell.

Reactions were followed in H₂O or aq. MeCN and with the more soluble esters we could follow reactions in up to nominally 100% H₂O. Both esters and ethers were added as concentrated solutions in MeCN. Control tests were made without OXONE to test the solubility of the esters and the absence of spontaneous hydrolysis. The pH of the reaction mixture did not change significantly during reaction and was that of OXONE in water, *i.e.*, *ca.* 2.3. We varied the pH between 1.6 and 4.4 by adding small amounts of KOH or H₂SO₄ without affecting the first-order rate constants, k_ψ (< 5%), but there was a small effect of equimolar H₂SO₄. Addition of K₂SO₄-KHSO₄ at a fixed pH did not significantly affect k_ψ (< 5%). First-order rate plots were linear under all conditions.

Micellar experiments with **1**, Z = *p*-OMe were carried out with equivalent H₂SO₄.² Without surfactant the second-order rate constants were slightly larger than those obtained without added H₂SO₄. Values at 35.0 °C were 11.9×10^{-2} and $10.8 \times 10^{-2} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ with and without H₂SO₄, respectively, and corresponding values at 25.0 °C were 7.65×10^{-2} and $6.86 \times 10^{-2} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$. Ratios of rate constants at 35.0 °C and 25.0 °C were unaffected by H₂SO₄.

The sensitivity and dynamic range of diode array spectrophotometers makes them the instruments of choice for following these reactions of HSO_5^- where absorbance changes are small. However, in these instruments the sample is irradiated over the whole spectrum, which creates problems if samples are sensitive to light. We obtained better data by taking *ca.* 30 data points over 2.5–3 half-lives and resisting the temptation to take the maximum number of data points provided by the instrument.

The very low sensitivity of these reactions of sulfides and esters to temperature limits the accuracy of estimation of the activation parameters, which were calculated by the Arrhenius equation with linear regression.

Products.—The reaction products of the esters were identified as equimolar substituted benzoic and benzenesulfonic acids by examination of the ¹H NMR spectra after complete reaction in D₂O-CD₃CN on a Varian 200 MHz NMR spectrometer. Oxidation of the sulfides initially gives sulfoxides

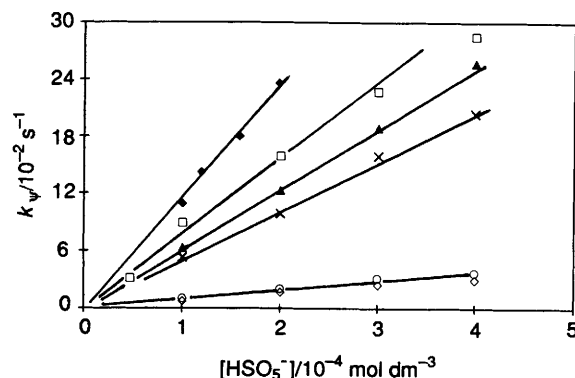


Fig. 1 Oxidation of XC₆H₄SMe and Ph₂S by aqueous HSO_5^- : X = \blacklozenge , *p*-OMe; \square , *p*-Me; \blacktriangle , H; \times , *p*-Cl; \circ , *p*-NO₂; \diamond , Ph₂S

which are further oxidized to sulfones, and oxidations in D₂O with excess HSO_5^- gave spectra with ¹H signals of both sulfoxide and sulfone. Oxidation of sulfide with equimolar HSO_5^- gave spectra with ¹H signals of only sulfoxide. These experiments were made with X = *p*-OMe and *p*-Me, in D₂O-CD₃CN, with $[\text{sulfide}] = [\text{HSO}_5^-] = 2 \times 10^{-3} \text{ mol dm}^{-3}$.

Results

Sulfide Oxidations.—We had to use dilute HSO_5^- ($< 10^{-3} \text{ mol dm}^{-3}$) to examine conversion of sulfide into sulfoxide in solvents of high water content (Fig. 1 and Table 1) and reaction is much faster than that with periodate ion.^{2,3} The difference is due to the very low activation enthalpies of oxidation by HSO_5^- , which are lower than those for periodate oxidation by *ca.* 21 kJ mol⁻¹ for reactions of PhSMe. Activation entropies are similar and negative for oxidations by both HSO_5^- and IO_4^- (Table 1 and ref. 3). The values of ΔH^\ddagger and ΔS^\ddagger were calculated by linear regression which gave the following respective errors (%), *p*-MeO, 10 (6); *p*-Me, 4 (2); H, 2 (1); *p*-Cl, 3 (2); *p*-NO₂, 13 (8); Ph₂S, 11 (7).

Substituent effects are also similar for oxidations by HSO_5^- and IO_4^- , and the Hammett equation is followed with $\rho \approx -1$ for reaction with HSO_5^- , based on σ_p substituent parameters.⁹ The rate constant for reaction of **2**, X = *p*-Cl, is higher than predicted. Although activation enthalpies are very low substituent effects follow the Hammett equation. This

Table 2 Solvent effects on the oxidation of sulfides^a

Sulfide	$k_2/\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$						m
	H ₂ O vol%	100	95	90	85	80	
<i>p</i> -MeOC ₆ H ₄ SMe		1180	833	594	414	284	0.93
<i>p</i> -MeC ₆ H ₄ SMe		890	494	405	326	225	0.91
C ₆ H ₅ SMe		632	464	371	258	175	0.84
<i>p</i> -ClC ₆ H ₄ SMe		534	402	289	194	135	1.00
<i>p</i> -O ₂ NC ₆ H ₄ SMe		102	77	55	34	23	0.96
Ph ₂ S		72	57	38	27	17	0.98

^a At 25.0 °C, in aqueous MeCN.

behaviour is not unusual, for example, substituent effects on rate constants of the very rapid addition of arylchlorocarbene to alkenes follow the Hammett equation.¹⁰

Oxidation is speeded by an increase in the water content of the solvent and rate constants fit the Grunwald–Winstein equation¹¹ [eqn. (1)] with values of Y for aqueous MeCN.¹²

$$\log(k/k_0) = mY \quad (1)$$

The values of $m \approx 0.9$ (Table 2) are similar to those for oxidation by periodate ion³ and are in the range typical of reactions with strongly solvated transition states.¹¹

Reactions of Thioesters.—Reactions of all the esters could be followed in 80% aq. MeCN (v/v) where the esters and OXONE are soluble. We could follow reactions of some substrates in 99% aq. MeCN (v/v), but with 1, Z = *p*-NO₂, we could not use a wetter solvent than 85% aq. MeCN (v/v). Plots of first-order rate constants, with respect to substrate, k_ψ , against [HSO₅⁻] are linear (Figs. 2 and 3), and extrapolate to the origin showing that spontaneous hydrolysis can be neglected. Second-order rate constants, k_2 , calculated from slopes of the rate plots (Figs. 2 and 3) increase modestly with increasing electron donation (Table 3). Plots of $\log k_2$ against σ_p or σ_m substituent parameters⁹ are linear and in 80% aq. MeCN $\rho = -0.63$ and -0.62 for substituents in the thiophenyl and benzoyl groups respectively. Plots of $\log k_2$ against σ^+ are curved.^{3,9}

Although electronic substituent effects are small, solvent effects are large and rate constants increase sharply with increasing water content of the solvent (Table 4). The rate effects follow the Grunwald–Winstein equation¹¹ and plots of $\log k_2$ against Y are linear with slopes, m , of 1.3–1.4 for a range of substituents (Table 4). Values of m are not obviously related to substituent effects, but they indicate a very strong dependence of rate on ionizing power of the solvent, which, for these reactions, is characteristic of a polar, hydrophilic, transition state.

These reactions have relatively low activation enthalpies in the approximate range of 40 to 60 kJ mol⁻¹, and negative activation entropies in the approximate range of -71 to $-130 \text{ J K}^{-1} \text{ mol}^{-1}$, depending slightly upon substituent and more upon solvent (Table 3). Values of ΔH^\ddagger tend to decrease, and those of ΔS^\ddagger become more negative, as the water content of the solvent is increased, but changes are not large. It appears that transition-state hydration decreases ΔH^\ddagger and correspondingly makes ΔS^\ddagger more negative.

Oxidations by peroxy acids involve proton transfers. For reactions in aprotic solvents it is reasonable to postulate intramolecular proton transfer,^{4,13} but in aqueous solution it is more likely that the proton is lost to water.¹⁴ Reactions of thioesters with DSO₅⁻ in D₂O have small kinetic hydrogen isotope effects, $k_H/k_D = 1.2$ and 1.3 for reactions of 1, X = *p*-OMe, Z = H and X = H, Z = H, respectively, which excludes

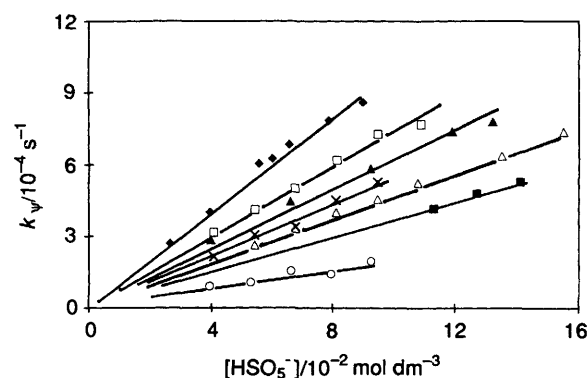


Fig. 2 Reaction of PhCO-SC₆H₄Z with HSO₅⁻ in H₂O–MeCN 4:1 v/v: Z = \blacklozenge , *p*-OMe; \square , *p*-Me; \blacktriangle , H; \times , *p*-Cl; \triangle , *m*-OMe; \blacksquare , *m*-Cl; \circ , *p*-NO₂

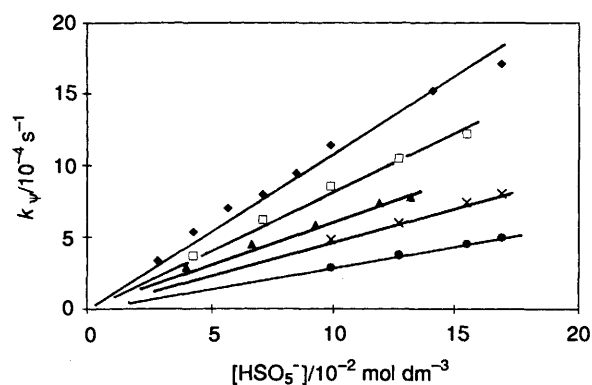


Fig. 3 Reaction of XC₆H₄CO-SPh with HSO₅⁻ in H₂O–MeCN 4:1 v/v: X = \blacklozenge , *p*-OMe; \square , *p*-Me; \blacktriangle , H; \times , *p*-Cl; \circ , *p*-CN

kinetically significant proton transfers in the transition state. The isotope effects are similar to those seen in other oxidations by peroxy acids.¹⁴

Micellar Effects.—Cationic micelles slightly increase rates of oxidation of an aryl sulfide by HSO₅⁻ to a maximum with an approximately 1.5-fold increase in k_ψ and rate constants decrease at higher [surfactant] owing to increasing competition between HSO₅⁻ and the surfactant counterion and to dilution of reactants as the volume of the micellar pseudophase is increased.^{2,15,16} The rate–surfactant profile can be fitted quantitatively in terms of a pseudophase model in which reactant concentrations in the aqueous and the micellar pseudophases are estimated, which also allows calculation of the second-order rate constant in the micellar pseudophase.²

We examined oxidation of 1, Z = *p*-OMe by HSO₅⁻ in micelles of CTAHSO₄ (CTA = C₁₆H₃₃NMe₃, Table 5). Reaction is slow in CTAHSO₄ and we had to use relatively high [surfactant] to solubilise KHSO₄ and KHSO₅, even though

Table 3 Second-order rate constants and activation parameters for reactions of $\text{XC}_6\text{H}_4\text{CO}\cdot\text{SC}_6\text{C}_4\text{Z}^a$

Substituents		%H ₂ O (v/v)	$k_2/10^{-3} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$				ΔH^\ddagger^b	ΔS^\ddagger^c
X	Z		25 °C	35 °C	45 °C	50 °C		
H	<i>p</i> -OMe	80	10.5	20.0	42.3	64.3	55.3	-88
H	<i>p</i> -Me	80	7.59					
H	H	80	6.77	11.2	25.7	36.0	54.0	-96
H	<i>m</i> -OMe	80	4.81	8.15	15.2	22.6	46.4	-126
H	<i>p</i> -Cl	80	5.53					
H	<i>m</i> -Cl	80	3.76					
H	<i>p</i> -NO ₂	80	2.08	4.73	8.88	12.6	57.0	-96
<i>p</i> -OMe	H	80	11.6	22.4	51.2	75.6	59.9	-71
<i>p</i> -Me	H	80	8.65					
<i>p</i> -Cl	H	80	4.80					
<i>p</i> -CN	H	80	2.89	7.56	12.7	19.9	57.7	-92
H	<i>p</i> -NO ₂	85	3.71	8.20	15.9	17.8	50.2	-113
H	<i>p</i> -OMe	99	68.6	108	181	270	42.3	-117
H	H	99	51.6	80.8	150	190	41.0	-121
H	<i>m</i> -OMe	99	36.9	64.3	105	141	40.2	-130
<i>p</i> -OMe	H	99	86.5	149	271	366	44.8	-105
<i>p</i> -CN	H	99	21.8	40.6	88.4	105	50.2	-100

^a At 25.0 °C in H₂O-MeCN. ^b /kJ mol⁻¹. ^c /J mol⁻¹ K⁻¹.

Table 4 Solvent effects on reactions of $\text{XC}_6\text{H}_4\text{CO}\cdot\text{SC}_6\text{C}_4\text{Z}$ with HSO_5^- ^a

H ₂ O wt%	Substituent						
	X: Z: m: ^b	H <i>p</i> -OMe	H <i>m</i> -OMe	H H	H <i>p</i> -NO ₂	<i>p</i> -OMe H	<i>p</i> -CN H
		1.29	1.47	1.39	1.34	1.43	1.36
80.1					1.39		
83.0		10.5		6.77	2.08		
83.4			4.81			11.6	2.80
87.3		20.0	8.70	11.3	3.71		5.10
90.3			13.8			36.3	9.48
91.6		30.2		21.0			
96.8			30.9			61.8	15.2
99.2		68.6	36.9	51.2		85.0	21.1

^a Values of $k_2/10^{-3} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ at 25.0 °C in aq. MeCN. ^b Based on interpolated *Y* values.¹²

Table 5 Micellar effects on the reaction of $\text{C}_6\text{H}_5\text{CO}\cdot\text{SC}_6\text{H}_4\text{OMe}(p)$ with HSO_5^- ^a

[CTAHSO ₄]/ 10 ⁻² mol dm ⁻³	$k_w/10^{-4} \text{ s}^{-1}$	[CTAHSO ₄]/ 10 ⁻² mol dm ⁻³	$k_w/10^{-4} \text{ s}^{-1}$
0.00	31.0	3.02	2.70
1.29	3.41	5.17	2.49
2.16	3.22	7.76	2.24

^a At 35.0 °C and $2.61 \times 10^{-2} \text{ mol dm}^{-3}$ aqueous HSO_5^- .

experiments were at 35.0 °C, and we therefore could not observe a rate maximum, *cf.*, ref. 15. As a result we could not analyse the rate-surfactant profile quantitatively and calculate a second-order rate constant in the micellar pseudophase. The marked decrease of k_w in micellized surfactant, despite the concentration of reagents in the small volume of the micellar pseudophase, is characteristic of a counterion reaction in which second-order rate constants are much higher in the aqueous than in the micellar pseudophase. This behaviour is seen with reactions of other anionic electrophiles in solutions of cationic micelles, *e.g.*, sulfide oxidations by IO_4^- and HSO_5^- and reactions of Br_3^- with alkenes,^{2,15,17} and seems to be due to unfavourable interactions between the cationic micellar head groups and the forming positive charge in the transition state and the lower polarity of the micellar surface relative to water.¹⁸

Discussion

Reactions of the esters with HSO_5^- are first order in each reagent (Figs. 2 and 3) and, based on the observation of isobestic points it appears that an intermediate does not build up in concentration during the reaction or return to starting material (see Experimental section). The rate-limiting step in these conditions is oxidation and the first-formed intermediate then decomposes rapidly with eventual formation of a sulfonic acid. The initial oxidation step should be assisted by electron-donating substituents in both the thiophenyl and benzoyl groups but electronic effects of substituents are small, $\rho \approx -0.6$ (Table 3) and are based on σ_m and σ_p substituent parameters, so resonance effects are relatively unimportant.^{3,9} Electronic effects are largely inductive probably because of poor orbital overlap between sulfur and the phenyl group and the acyl residue blocks conjugation between sulfur and substituents in the benzoyl group. This behaviour contrasts significantly with that for reactions in which there is marked cationic character at the reaction centre in the transition state, as in $\text{S}_{\text{N}}1$ reactions where $\rho \approx -3$ and follows σ^+ parameters.⁹ Electronic effects in oxidations of thioesters by HSO_5^- are similar to those in periodate ion oxidations of sulfides (Table 3 and ref. 3).

Substituent electronic effects are larger in oxidations of sulfides than in reactions of the corresponding esters, even though the ethers are more reactive than the esters by factors of *ca.* 10^4 , depending upon the substituents and reaction

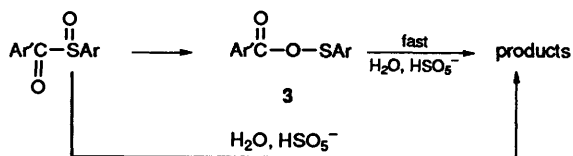
conditions (Tables 1 and 3). The differences in reactivities are due almost completely to large differences of *ca.* 26 kJ mol⁻¹ in ΔH^\ddagger , because values of ΔS^\ddagger are similar.

Substituent effects indicate that there is no extensive build up of positive charge at the reaction centre in the transition state for these oxidations, but reaction rates are nonetheless very sensitive to the water content of the solvent (Tables 2 and 4), as for sulfide oxidations by periodate ion.^{2,3} The transition states must therefore have polar or ionic centres that interact strongly with water. The negative values of ΔS^\ddagger are consistent with several water molecules being involved in transition-state formation, especially considering that HSO₅⁻ is itself hydrophilic and should be strongly hydrated. Hydration of the transition state should decrease ΔH^\ddagger , and make the reaction rate less sensitive to electronic substituent effects.⁹

In many respects, *e.g.*, effects of solvent and substituents on the phenyl group, and values of ΔS^\ddagger , reactions of the thioesters and ethers are kinetically similar and electron withdrawing substituents on sulfur (Ph and CH₂CH₂Cl) are not strong inhibitors of the ether oxidations, but acyl residues are very strongly inhibitory, much more so than predicted from inductive effects of acyl groups. For example, replacement of a methyl group of **2**, X = H, by phenyl decreases the rate by approximately one order of magnitude (Table 1) and the CH₂CH₂Cl group decreases the rate by only a factor of *ca.* 3.2. Based on σ_1 values of 0.10 for Ph, 0.30 for CO₂Et and 0.55 for COCN⁹ we cannot explain the low reactivities of the esters towards HSO₅⁻ in terms of inductive effects of acyl groups.

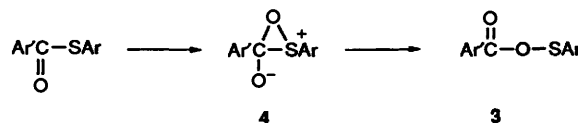
Nature of the Reaction Path.—The products of reaction of the esters could be formed by initial hydrolysis followed by rapid oxidation of the thiol, but this reaction sequence is excluded because plots of k_w against [HSO₅⁻] are linear and generally have zero intercepts (Figs. 2 and 3). In addition k_w is not pH-dependent, at least in the range 1.6–4.4. We can also exclude nucleophilic attack by HSO₅⁻ because, although many peroxyanions are effective nucleophiles, peroxymonosulfate monoanion is a very weak nucleophile and the dianion, which is not an especially effective nucleophile, is present only at a pH well above those of our experiments.¹⁹ We therefore conclude that oxidation of a thioester generates an intermediate which is more electrophilic than its precursor and reacts rapidly with nucleophiles, *e.g.*, water. This reaction sequence is essentially that proposed to account for the HSO₅⁻ induced decomposition of phosphonothiolates,^{5,6} and the effect of other oxidants.²⁰

Sulfide oxidations and reactions of the esters therefore seem to have the same initial step, *i.e.*, transfer of oxygen to sulfur, and 'early' transition states, consistent with low values of ΔH^\ddagger . On this hypothesis a first-formed acyl sulfoxide could undergo further oxidation or suffer C–S bond breakage. The second route is the more probable because although HSO₅⁻ oxidizes sulfoxides to sulfones¹ this reaction is much slower than the initial oxidation of sulfides. We therefore assume that an acyl sulfoxide or other intermediate, *e.g.*, anhydride, **3**, breaks down to give the carboxylic acid and probably a sulfenic acid which will be oxidized rapidly to a sulfonic acid.



A similar reaction has been identified in the HSO₅⁻ induced decomposition of phosphorus(v) thiolates, in solvents of very low water content, where in the absence of nucleophiles further oxidation gives a phosphinyloxysulfonate^{6b} and initial form-

ation of an acyl sulfoxide is analogous to oxidation of sulfides to sulfoxides. We cannot exclude an alternative initial reaction which does not involve formation of a sulfoxide, for example oxygen could add across the C–S bond and directly give **4** which



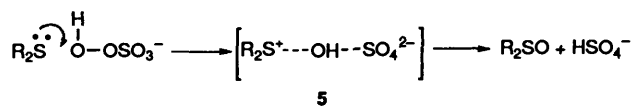
opens to form **3**. Such a reaction is consistent with substituent effects being similar in the benzoyl and thiophenyl groups. Anhydride **3** could be generated by nucleophilic addition to the acyl group and a Baeyer–Villiger rearrangement. This reaction path has been considered for reactions of HO₂⁻ with phosphorus(v) thiol esters,²¹ but we exclude it here in view of the low nucleophilicity¹⁹ of HSO₅⁻ and the electronic effects on rates.

The Transition State for Oxygen Transfer.—We write the rate-limiting step of reaction as an oxygen transfer to sulfur and its mechanism should be similar to those of oxidations of sulfides or I⁻ by anionic oxidants such as HSO₅⁻ or IO₄⁻. Ruff and Kucsman have discussed possible mechanisms of sulfide oxidation by IO₄⁻ which can be regarded as nucleophilic attack^{2,3} by sulfur upon oxygen with displacement of IO₃⁻. A



similar mechanism can be written for oxidation by HSO₅⁻ and other peroxy acids, except that proton transfer has to be included, with, or subsequent to, oxygen transfer.^{13,14,22,23}

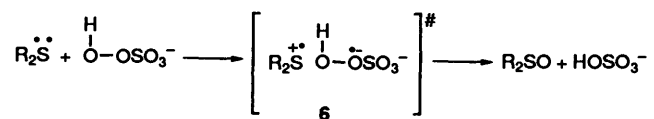
If the transition state is similar to **5** with its positive charge on



sulfur we would expect large kinetic electronic substituent effects, inconsistent with $\rho \approx -0.6$ and -1 for the ester and sulfide reactions, respectively. However, such transition states would be strongly hydrated, as would those in which oxygen and proton transfer are concerted.

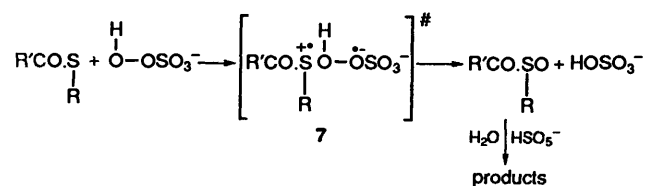
In the reaction schemes shown above electronic motions are written as in classical descriptions of S_N2 reactions with both electrons of the new S–O bond derived from sulfur. This conclusion cannot be justified, as demonstrated in analyses of S_N2 and related reactions,²⁴ and an alternative description involves transfer of an electron into an antibonding orbital of oxygen with rehybridization, proton transfer, and formation of a new S–O bond.

A transition state with a structure similar to **6**, but with less



than unit positive charge on sulfur, should have a relatively small dependence on electron-donating substituents, consistent with $\rho \approx -0.6$ and -1 for reactions of thioesters and ethers, respectively. It should be strongly hydrated by both acceptance and donation of hydrogen bonds, in agreement with the high values of m and negative values of ΔS^\ddagger (Tables 1–4 and ref. 3).

As applied to reactions of thioesters the mechanism can be written as:



Representation of transition states as involving transfer of a single electron from sulfur to oxygen does not imply that the reaction involves free radical intermediates, but it indicates that an overall substitution formally involves transfer of one electron from reductant (nucleophile) to oxidant (electrophile).²⁴

It has been pointed out that oxidations by peroxy acids can be written as if they involve HO^+ as an electrophilic intermediate,²² although there is strong evidence that such an intermediate is never a free species, and we can write the transition states **6** or **7** for sulfide oxidation as resonance hybrids, as shown for the ethers (**8a, b**).



Contribution of the classical structure **8a** is probably not very large, based on the relatively low negative values of ρ , but values of m and ΔS^\ddagger (Tables 1–4) are consistent with transition states that have strong hydrogen-bond acceptor and donor sites. The low values of ΔH^\ddagger in the reactions of HSO_5^- and oxidations by periodate ion³ show that hydration markedly decreases the enthalpic barrier to reaction. Oxidations of the esters are less sensitive than those of the ethers to electronic effects, based on ρ values of ≈ -0.6 and ≈ -1.0 , respectively, but there is more dependence on solvent, based on the higher m values (≈ 1.4 and ≈ 0.9 for esters and ethers respectively). These differences indicate that in the transition states for reactions of the esters the contribution of **8b**, with greater peroxy bond scission and more charge on the sulfate moiety and less on sulfur, is greater than in reactions of the ethers.

Our observation of small substituent effects in the phenyl group and of replacement of Me by Ph or $\text{CH}_2\text{CH}_2\text{Cl}$ at sulfur agrees with other evidence (Table 1 and ref. 2). Johnson and Nickerson have examined oxidations by HSO_5^- of a series of thiols coordinated to ruthenium(III) and cobalt(III)^{1c} and for the first step of oxidation of aryl thiols $\rho \approx -0.66$ which is similar to values that we observe. In addition, second-order rate constants for oxidations of a variety of complexes range from 40–4000 $\text{dm}^3 \text{mol}^{-1} \text{s}^{-1}$, and are similar in magnitude to our values for second-order rate constants of oxidations of the sulfides under similar conditions (Table 1). Therefore ligation to a metal centre does not inhibit oxidation, although acylation slows the reaction very strongly, much more than expected based on inductive effects of acyl groups.⁹

These results are not those predicted for a classical $\text{S}_\text{N}2$ -like attack on oxygen. Nucleophilicities have been related to ionisation potentials,²⁵ and a description of the transition state as a resonance hybrid fits this hypothesis. Ionisation potentials of thiol derivatives increase as one CH_3 group in CH_3SH is replaced by an acetyl group in $\text{CH}_3\text{CO-SH}$ or CH_3 in CH_3SCH_3 is replaced by CH_3CO in $\text{CH}_3\text{CO-SCH}_3$ or CN in CH_3SCN , although replacement of CH_3 by C_6H_5 decreases the ionisation potential.²⁶ Therefore, if single electron transfer is involved in the reaction, one would expect properties such as ionisation potential to be good indicators of nucleophilicity.

However, Hammett parameters, σ_m and σ_p , which are derived from acid–base equilibria could fit substituent effects upon ionisation potentials, provided that substituents only weakly perturb electronic distributions.

The kinetic evidence on the ester reactions indicates that the C–S bond is not breaking in the transition state. It is difficult therefore to explain the low reactivity of the thioesters, relative to the ethers, in terms of widely used explanations of reactivity based on treatments of electronic effects as described by the Hammett, or similar linear free energy, equations including application of the Brønsted equation to nucleophilicity. Although the Brønsted equation is often used to relate nucleophilicity to basicity²⁷ there is evidence that properties such as ionisation potential correlate better, especially for different types of nucleophile.²⁵ Insofar as the transition state for oxidation is represented as **8a, b**, the low nucleophilicity of the thioesters relative to the ethers is understandable in terms of the lower ionisation potentials of thiols and their ethers relative to the esters. Aue has pointed out to us that free energies of alkene epoxidisation by peroxy acids correlate very well with ionisation potentials of the alkenes.²⁸ Replacement of methyl in Me_2S by acetyl increases the vertical ionisation potential by ca. 1.2 eV,^{26a} and if this difference is also present in the aromatic compounds that we study, the sulfides should be much more reactive than the corresponding esters. Our description of the transition state as **8a, b** implies that there is breaking of the peroxy bond in the transition state, consistent with the large m -values and the much higher electrophilicity of peroxy acids relative to H_2O_2 . Dioxiranes are like peroxy acids in their ability to transfer oxygen to nitrogen and sulfur centres^{2,29} and electron transfer is postulated in these reactions.

Acknowledgements

Support of this work by the US Army Research Office and the National Science Foundation (Organic Chemical Dynamics) is gratefully acknowledged. We are grateful to Dr. D. H. Aue for helpful information regarding ionisation potentials.

References

- (a) R. J. Kennedy and A. M. Stock, *J. Org. Chem.*, 1960, **25**, 1901; (b) B. M. Trost and R. J. Braslau, *J. Org. Chem.*, 1988, **53**, 532; (c) M. D. Johnson and D. Nickerson, *Inorg. Chem.*, 1992, **31**, 3971; (d) W. Zhu and W. T. Ford, *J. Org. Chem.*, 1991, **56**, 7022; (e) K. S. Webb, *Tetrahedron Lett.*, 1994, **35**, 3457.
- R. Bacaloglu, A. Blasko, C. A. Bunton and H. Foroudian, *J. Phys. Org. Chem.*, 1992, **5**, 171.
- F. Ruff and A. Kucsmann, *J. Chem. Soc., Perkin Trans. 2*, 1985, 683.
- B. Plesnicar, *The Chemistry of Functional Groups, The Chemistry of Peroxides*, ed. S. Patai, Wiley, New York, 1983, ch. 17.
- Y.-C. Yang, J. A. Baker and J. R. Ward, *Chem. Rev.*, 1992, **92**, 1729.
- (a) Y.-C. Yang, L. L. Szafraniec, W. T. Beaudry and D. K. Rohrbaugh, *J. Am. Chem. Soc.*, 1990, **112**, 6621; (b) D. R. Leslie, W. T. Beaudry, L. L. Szafraniec and D. K. Rohrbaugh, *J. Org. Chem.*, 1991, **56**, 3459.
- (a) M. P. Balfé, R. E. Dabby and J. Kenyon, *J. Chem. Soc.*, 1951, 382; (b) H. Meerwein, G. Dittmar, R. Gollner, K. Hafner, F. Mensch and O. Steinfort, *Chem. Ber.*, 1957, **90**, 841; (c) C. C. Price and G. W. Stacy, *J. Am. Chem. Soc.*, 1946, **68**, 499.
- (a) G. Cilento, *J. Am. Chem. Soc.*, 1953, **75**, 3748; (b) Y. Kanaoka, K. Tanizawa, E. Sato, O. Yonemitsu and Y. Ban, *Chem. Pharm. Bull.*, 1967, **15**, 593.
- T. H. Lowry and K. S. Richardson, *Mechanism and Theory in Organic Chemistry*, 3rd edn., Harper and Row, New York, 1987, ch. 2.2.
- R. A. Moss, L. A. Peres, N. J. Turro, I. R. Gould and N. P. Hacker, *Tetrahedron Lett.*, 1983, **24**, 685.
- A. H. Fainberg and S. Winstein, *J. Am. Chem. Soc.*, 1956, **78**, 2770.
- C. A. Bunton, M. M. Mhala and J. R. Moffatt, *J. Org. Chem.*, 1984, **49**, 3637.
- P. D. Bartlett, *Rec. Chem. Prog.*, 1957, **18**, 111.

- 14 R. P. Hanzlik and G. O. Shearer, *J. Am. Chem. Soc.*, 1975, **97**, 5231.
- 15 A. Blasko, C. A. Bunton and S. Wright, *J. Phys. Chem.*, 1993, **97**, 5435.
- 16 (a) J. H. Fendler, *Membrane Mimetic Chemistry*, Wiley Interscience, New York, 1982; (b) L. S. Romsted in *Surfactants in Solution*, eds. K. L. Mittal and B. Lindman, Plenum, New York, 1984, **2**, 1015; (c) L. S. Romsted, *J. Phys. Chem.*, 1985, **89**, 5107, 5113; (d) C. A. Bunton and G. Savelli, *Adv. Phys. Org. Chem.*, 1986, **22**, 213; (e) F. H. Quina and H. Chaimovich, *J. Phys. Chem.*, 1979, **83**, 1844.
- 17 (a) G. Cerichelli, C. Grande, L. Luchetti, G. Mancini and C. A. Bunton, *J. Org. Chem.*, 1987, **52**, 5167; (b) G. Cerichelli, L. Luchetti and G. Mancini, *J. Org. Chem.*, 1991, **56**, 3025.
- 18 (a) K. A. Zachariase, N. V. Phuc and B. Kozankiewicz, *J. Phys. Chem.*, 1981, **85**, 2672; (b) C. Ramachandran, R. A. Pyter and P. Mukerjee, *J. Phys. Chem.*, 1982, **86**, 3198; (c) A. D. Angeli, A. Cipiciani, R. Germani, G. Savelli, G. Cerichelli and C. A. Bunton, *J. Colloid Interface Sci.*, 1988, **121**, 42.
- 19 D. M. Davis and M. E. Deary, *J. Chem. Soc., Perkin Trans. 2*, 1992, 559.
- 20 Y. Segall and J. E. Casida, *Phosphorus Sulfur*, 1983, **18**, 209.
- 21 Y.-C. Yang, L. L. Szafraniec, W. T. Beaudry and C. A. Bunton, *J. Org. Chem.*, 1993, **58**, 6964.
- 22 J. O. Edwards in *Peroxide Reaction Mechanisms*, ed. J. O. Edwards, Interscience, New York, 1962, p. 67.
- 23 R. D. Bach, A. L. Owensby, C. Gonzalez, H. B. Schlegel and J. J. W. McDouall, *J. Am. Chem. Soc.*, 1991, **113**, 6001.
- 24 (a) A. Pross, *Acc. Chem. Res.*, 1985, **18**, 212; (b) S. S. Shaik, *Acta Chem. Scand.*, 1990, **44**, 205.
- 25 (a) C. D. Ritchie, *J. Am. Chem. Soc.*, 1983, **105**, 7313; (b) E. Buncel, S. S. Shaik, I.-H. Um and S. Wolfe, *J. Am. Chem. Soc.*, 1988, **110**, 1275.
- 26 (a) W. Hanebeck and J. Gasteiger, *J. Comput. Chem.*, 1993, **14**, 138; (b) *Handbook of Chemistry and Physics*, 53rd edn., CRC Press, 1972–1973.
- 27 (a) W. P. Jencks, *Catalysis in Chemistry and Enzymology*, McGraw-Hill, New York, 1969, ch. 2; (b) F. G. Bordwell and X.-M. Zhang, *Acc. Chem. Res.*, 1993, **26**, 510.
- 28 K. W. Hill, Thesis, University of California, Santa Barbara, 1986.
- 29 (a) R. W. Murray, *Chem. Rev.*, 1989, **89**, 1187; (b) W. Adam, R. Curci and J. O. Edwards, *Acc. Chem. Res.*, 1989, **22**, 205.

Paper 4/03660C

Received 16th June 1994

Accepted 18th August 1994