Reactivity and Selectivity in the Oxidation of Aryl Methyl Sulfides and Sulfoxides by Hydrogen Peroxide Mediated by Acetonitrile

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In homogeneous methanol solution containing potassium carbonate, hydrogen peroxide and acetonitrile, the active oxidant in the conversion of *p*-substituted-phenyl methyl sulfides into the sulfoxides is selective ($\rho = -1.0$ at 0 °C) but the oxidation of the related sulfoxides at 0 and 24 °C shows low selectivity, which, taken in conjunction with direct kinetic data, throws new light on the active oxidizing species in these nitrile-mediated reactions.

Nitriles promote oxidations by hydrogen peroxide in slightly basic solution (Payne oxidation) of, for example, sulfides to sulfoxides, sulfoxides to sulfones and alkenes to epoxides.[1] Peroxyimidic acids, $RC(O_2H)=NH$, are believed to be active intermediates in such reactions, but there is no direct evidence to confirm this.[2] While *O*-transfer mechanisms can be written by analogy with the isoelectronic peroxycarboxylic acid oxidations, Payne oxidation to form epoxides, for example, often occurs with different stereochemistry.[3] This suggests that the analogy is imperfect and that more than one mechanism or active oxidising species might possibly be involved.

As a part of studies aimed at devising procedures for asymmetric oxidation, particularly of sulfides to sulfoxides,[4] we report on a preliminary examination of structural effects in the substrate on acetonitrile-mediated oxidations by hydrogen peroxide in methanol containing potassium carbonate, using both direct kinetic measurements and competition experiments. The substrates chosen were *p*-substituted phenyl methyl sulfides, but, in the course of the work, it became apparent that the investigation should be extended to the further oxidation of the sulfoxides to sulfones.

Experimental

Aryl methyl sulfides were commercial samples. Sulfoxides were prepared by oxidation using urea–hydrogen peroxide in conjunction with phthalic anhydride.[5]

Reactions were carried out in all cases by mixing a methanol solution of the substrate and an excess of acetonitrile with slightly aqueous methanolic hydrogen peroxide of the appropriate concentration obtained by dilution of 30% aqueous peroxide with methanol. It was established that there was no significant oxidation if the nitrile was omitted. For the quantitative studies (both competitive experiments and direct kinetics), ^1H NMR spectroscopy (200 MHz) was used for the analysis, making use of the *S*-methyl signals of the aryl methyl sulfides, sulfoxides and sulfones which were cleanly resolved in all cases except for the phenyl and *p*-tolyl methyl sulfides (where the aromatic methyl signals of the latter could be used to assist in completing the analysis). In the competitive sulfide oxidations involving *p*-nitrophenyl methyl sulfide, small amounts of the corresponding sulfone accompanied the sulfoxide; in these cases the integrated signal for the sulfone was added to that of the sulfoxide before evaluation.

Results and Discussion

The results of the competitive experiments (Table 1) show that relative reactivities (k_{rel}) for sulfide oxidations at 0 °C vary substantially as the *p*-substituent changes, decreasing with increasing electron withdrawal. The results fit the Hammett equation with $\rho = -1.0$ ($n = 10$; $r = 0.98$), implying an active oxidant somewhat more selective than dimethyldioxirane ($\rho = -0.77$ in acetone at room temperature).[6] For sulfoxide oxidations at 0 and 24 °C, values of k_{rel} showed much less variation; both electron-releasing and electron-withdrawing substituents appear to cause small enhancements of sulfoxide reactivity (a feature sometimes associated with reactions involving biphilic reagents,[7,†] but also consistent with a transition from one mechanism to another[8]). Correlation of the results with Hammett's σ-values gives a reaction constant close to zero, contrasting with the behaviour of dimethyldioxirane for which $\rho = -0.76$ for conversion of aryl methyl sulfoxides into the sulfones in acetone.[6]

Table 1 Relative reactivities in the Payne oxidation of *p*-X-substituted phenyl methyl sulfides and sulfoxides

	k_{rel}[a]			
	$XC_6H_4SCH_3$		$XC_6H_4SOCH_3$	
X	0 °C	0 °C	0 °C	24 °C
CH_3O	1.4_0	2.1_0	1.3_4	1.0_3
CH_3	1.3_7[b]	2.4_3	—	1.0_0
H	(1.00)	2.1_5	(1.00)	(1.00)
Br	0.46	(1.00)	—	1.0_7
NO_2	0.15	0.25	1.1_5	1.3_6

[a] Using substrate pairs (0.1 mol dm^{-3} each), H_2O_2 (0.1 mol dm^{-3}), CH_3CN (0.3 mol dm^{-3}), K_2CO_3 (0.1 mol dm^{-3}). [b] Conversions after 15 min; otherwise after 120 min (0 °C) or 60 min (24 °C).

In the direct studies of phenyl methyl sulfoxide oxidation, initial rate measurements demonstrated that the reaction rate is first order in peroxide and acetonitrile but independent of the substrate concentration. This was confirmed by the good linearity of plots according to a simple second order kinetic law over some 80–90% conversion at 24 °C. Values of the derived second-order rate coefficients (k_{obs}/dm^3 mol^{-1} s^{-1}; Table 2) confirm that, within the experimental uncertainty, all the sulfoxides react equally rapidly.

Analogous treatment of the oxidations at 0 °C showed lower reproducibility, but the initial reaction for the oxidation of sulfides was again proportional to the concentrations of hydrogen peroxide and acetonitrile. The reactions adhered less well to a simple second-order kinetic law, even over the first

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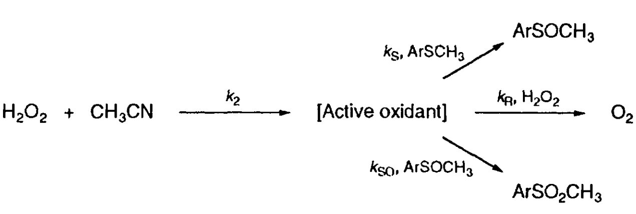
[†] The term 'biphilic reagent' designates a reagent capable of behaving simultaneously in both an electrophilic and nucleophilic capacity.

Table 2 Apparent second order rate coefficients for Payne oxidation of *p*-X-substituted phenyl methyl sulfoxides and sulfides

X	$k_{obs}/10^{-5}$ dm^3 mol^{-1} s^{-1}	
	$XC_6H_4SOCH_3$ (24 °C)	$XC_6H_4SCH_3$ (0 °C)
CH_3O	137 ± 10	11 ± 1
CH_3	136 ± 17	8 ± 1
H	131 ± 7 (8 ± 2[a,b])	13 ± 4[a]
Br	—	16 ± 3
NO_2	123 ± 6	5 ± 1

[a] Mean of several values obtained up to *ca.* 20% conversion using varying reagent concentrations. [b] At 0 °C.

20% conversion [approximate k_{obs} values (Table 2) are roughly the same for sulfides and sulfoxide]. The reactions at 0 °C slowed down more rapidly than expected as the reaction proceeded, consistent with competition for the active oxidant from another reaction, arguably Radziszewski oxidation of hydrogen peroxide.[9] Direct comparison of the rate of oxidation of phenyl methyl sulfide and sulfoxide at 0 °C in an equimolar mixture revealed that the rate of disappearance of the sulfide by oxidation to the sulfoxide was substantially greater than the rate of appearance of the sulfone by oxidation of the sulfoxide, indicative of partitioning of a reactive intermediate. By kinetic simulation, it was found that the time variation of the concentrations of the sulfide, sulfoxide and sulfone could be adequately reproduced using the simple set of reactions shown in Scheme 1 with $0.015\ k_S = 0.1\ k_{SO} = k_R \gg k_2 = 2 \times 10^{-4}$ dm^3 mol^{-1} s^{-1}. More complex schemes involving different oxidising species for the sulfide and sulfoxide reactions could be made to fit the data, however. For a single active oxidant, the differing reactivity and selectivity towards the sulfides and sulfoxides can be understood in general terms by regarding the reactions as biphilic and using frontier orbital considerations.[7]



Scheme 1

It is evident that the rate of oxidation both of the sulfides and sulfoxides under these conditions is controlled by the rate of production of a single intermediate oxidant, derived from one molecule of acetonitrile and one of hydrogen peroxide, and consistent with peroxyimidic acid. On the basis of the present evidence, there is no necessity to invoke additional mechanisms (as suggested for peroxycarboxylic acid oxidation of sulfoxides)[10] or additional intermediate oxidants in oxidation at sulfur; Payne epoxidation of alkenes may, however, be different, and is under current investigation.

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