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The Relative Reactivity of Thioethers and Sulfoxides toward Oxygen Transfer Reagents: the Case of Dioxiranes.

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Abstract: In the competitive oxidation of thioethers and sulfoxides by electrophilic reagents the reactivity ratio may be small enough to cause the formation of mixtures of products. This has been studied in the reaction of dimethyldioxirane, DMD, and trifluoromethyl-methyldioxirane, TMMD. In particular TMMD oxidizes both thioethers and sulfoxides whereas DMD attacks only thioethers. By applying the logic which has been used to develop mechanistic probes based on such competitive oxidations, the unrealistic conclusion that TMMD is less electrophilic than DMD would be reached. On the contrary we show also by means of Hammett plots on substituted sulfoxides that DMD and TMMD are both electrophilic oxidants toward sulfoxides and that TMMD is less selective than DMD being a stronger oxidant.

Thioethers, which are strong nucleophiles, are oxidized to sulfoxides exclusively by electrophilic oxygen transfer reagents[1]. By contrast sulfoxides, which are biphilic substrates,[2] are oxidized to sulfones by both electrophiles and nucleophiles.[2] In the competitive oxidation of thioethers and sulfoxides by electrophilic reagents the reactivity ratio strongly depends on the nature of the thioether since sulfoxides are less sensitive to the substitution pattern at the sulfur atom.[3] Accordingly, if the thioether is a very nucleophilic one, e.g. dialkyl substituted, such a ratio is large, whereas if it is weakly nucleophilic, e.g. diaryl substituted, the ratio may be small. Finally, for the same couple thioether-sulfoxide, smaller reactivity ratios are expected for stronger and hence less selective electrophilic oxidants. Therefore, mechanistic probes [4-6] which predict the electronic character of an oxidant by measuring its relative reactivity toward thioethers and sulfoxides must be employed with caution. The assumption[4,5] that nucleophilic oxidants will oxidize the sulfoxide whereas the electrophilic ones will attack the thioether is, at least for the latter oxidants, a too simplistic one. A typical example is the thiantrene-5-oxide based probe.[4,5] Although the idea of putting the two functionalities within the same molecule may appear, at first glance, a clever one, the choice of the substrate is unfortunate. In fact, the nucleophilicity of the thioether sulfur is even lower than that of diaryl substituted compounds because of the interaction of the orbitals of the two sulfur atoms present in the molecule.[7] Therefore the probe is expected to give unambiguous results only for nucleophilic oxidants, which are unable to attack the thioether center, and for weakly electrophilic oxidants. In fact, in other cases,[4-6] e.g. percarboxylic acids[4,5], peroxometal complexes[6], bicyclic gem-dialkyl-peroxonium ion[8], dioxirane[4,5], mixtures of thiantrene-5,5-dioxide (attack to the sulfoxide sulfur) and thiantrene-5,10-dioxide (attack to the thioether sulfur) together with products resulting from overoxidation are obtained. This has been taken as evidence that these are all biphilic oxidants with a more or less electrophilic character. On the contrary we favor the alternative via that they are definitely electrophiles and that the mixtures of products are the result of a small reactivity ratio of the two centres in thiantrene-5-oxide. Also on the basis of recently reported results[9], we employed dimethyldioxirane DMD[10] and trifluoromethyl-methyldioxirane TMMD[11] in the competitive oxidation of thioethers and sulfoxides and in the competitive oxidation of sulfoxides[12]. Our results are collected in Table 1 and shown in the Hammett plots of Figure 1.

Table 1: Competitive Oxidations[a] by DMD (dimethyldioxirane) and TMMD (trifluoromethyl-methyldioxirane).

#	Oxidant	Competing Substrates	Products	(%)[b]
1	DMD[c]	$pCl-C_6H_4-S-CH_3$ $C_6H_5-SO-CH_3$	$pCl-C_6H_4-SO-CH_3$	(100)
2	TMMD[c]	$pCl-C_6H_4-S-CH_3$ $C_6H_5-SO-CH_3$	$pCl-C_6H_4-SO-CH_3$ $pCl-C_6H_4-SO_2-CH_3$ $C_6H_5-SO_2-CH_3$	(61) (13) (26)
3	DMD	$pCl-C_6H_4-SO-CH_3$ $C_6H_5-SO-CH_3$	$pCl-C_6H_4-SO_2-CH_3$ $C_6H_5-SO_2-CH_3$	(44) (56)
4	DMD	$pNO_2-C_6H_4-SO-CH_3$ $pCH_3O-C_6H_4-SO-CH_3$	$pNO_2-C_6H_4-SO_2-CH_3$ $pCH_3O-C_6H_4-SO_2-CH_3$	(5) (95)
5	DMD	$pCl-C_6H_4-SO-CH_3$ $pCH_3O-C_6H_4-SO-CH_3$	$pCl-C_6H_4-SO_2-CH_3$ $pCH_3O-C_6H_4-SO_2-CH_3$	(29) (71)
6	TMMD	$pCl-C_6H_4-SO-CH_3$ $C_6H_5-SO-CH_3$	$pCl-C_6H_4-SO_2-CH_3$ $C_6H_5-SO_2-CH_3$	(49) (51)
7	TMMD	$pNO_2-C_6H_4-SO-CH_3$ $pCH_3O-C_6H_4-SO-CH_3$	$pNO_2-C_6H_4-SO_2-CH_3$ $pCH_3O-C_6H_4-SO_2-CH_3$	(27) (73)
8	TMMD	$pCl-C_6H_4-SO-CH_3$ $pCH_3O-C_6H_4-SO-CH_3$	$pCl-C_6H_4-SO_2-CH_3$ $pCH_3O-C_6H_4-SO_2-CH_3$	(44) (56)

a) Reactions performed in the presence of equal amounts of the two substrates, in $CHCl_3$ at 0°C under nitrogen atmosphere; [substrate] = 0.1 mol L^{-1}, [oxidant] = 0.03 mol L^{-1}.

b) % distribution of products determined by g.c. at 90% consumption of the oxidant Based on the oxidant consumed, the yields are in all cases almost quantitative (>95%).

c) [oxidant] = 0.01 mol L^{-1}.

The data of entries 1 and 2 are conveniently analyzed by considering the two alternatives mentioned above. According to the former, one should conclude that TMMD is a biphilic oxidant since it attacks both the thioether and the sulfoxide, whereas DMD is only electrophilic. Such a conclusion is clearly inconsistent with the electronic effect of the trifluoromethyl group compared with the methyl one. By contrast, according to the latter hypothesis, DMD and TMMD are both electrophilic reagents. Indeed, TMMD is so strong that its selectivity is very low leading to a mixture of products.

The other data of Table 1, entries 3-8, which allow to obtain the Hammett plots of Figure 1,[13] support this second alternative. Although the number of substituted sulfoxides examined is rather small, one may calculate a rho value of -1.00 for DMD[14] (r=0.98) and -0.34 for TMMD (r=0.97) from competitive experiments in $CHCl_3$. These data confirm that both DMD and TMMD are electrophiles and that the latter is less selective than the former. A rough estimate of the reactivity ratios: k(pCl-C_6H_4-S-CH_3)/k(C_6H_5-SO-CH_3), assuming a 3% limit of detection of the g.c. technique[12] gives a value ≥ 32 for DMD and a value of ca. 3 for TMMD, again in line with the predictions. The information obtained here for dioxiranes may be of more general significance. In particular, it should apply to all those electrophilic oxidants strong enough to oxidize sulfoxides.

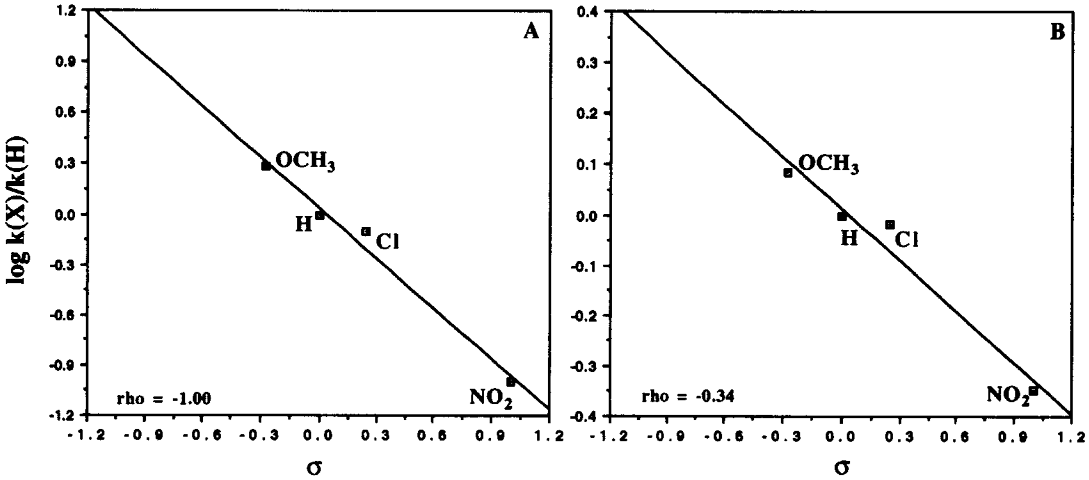

Figure 1. Hammett plots for the oxidation of pX-substituted aryl methyl sulfoxides by DMD (graph A) and TMMD (graph B).

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12. Competitive oxidation experiments were performed under a nitrogen atmosphere by dissolving in 5 ml of $CHCl_3$ at 0 °C equal amounts (0.5 mmol) of the two substrates together with 0.08 mmol of the appropriate internal standard (n-decane, n-tridecane, n-nonadecane) and by adding the solution of the oxidant (0.01-0.03 mmol). Gas chromatographic analyses of the reaction mixtures were carried out on a Perkin Elmer 8420 gas chromatograph equipped with a flame ionization detector and program capability. Oxidation products were identified by comparison of their MS and NMR spectra with those of authentic samples. GC-MS analyses were performed by Hewlett-Parckard Model 5890 gas-chromatograph (using a 25 mt HP-1 dimethyl polysiloxane capillary column), equipped with a Hewlett-Parckard MS computerized system, Model 5971A. ^1H NMR spectra were recorded on a Bruker WP-80 spectrometer with TMS as internal standard. Sulfoxides and sulfones were prepared by a oxidation of the corresponding thioethers, all commercially avaible products (Aldrich), with hydrogen peroxide in the presence of catalytic amounts of $MoO_2(acac)_2$ in ethanol by using 1 or 2 equivalents of H_2O_2 respectively. All the sulfides, sulfoxides and sulfones were purified by column chromatography and identified by their spectroscopic and MS properties.

13. The k(X)/k(H) values were obtained from the ratios of the yields of the products according to the following relationships:
$[pX\text{-}C_6H_4\text{-}SO_2\text{-}CH_3]_\infty/[pX'\text{-}C_6H_4\text{-}SO_2\text{-}CH_3]_\infty = k(X)/k(X')$ and $k(X)/k(H) = k(X)/k(X') \times k(X')/k(H)$
A σ value of 1.00 for $X=NO_2$ has been employed (cfr. Modena, G.; Maioli, L. Gazz. Chim. Ital. **1957**, *87*, 1306 and references therein).

14. A ρ value of -0.76 has been obtained by Murray et al. (cfr. Murray, R. W.; Jeyaraman, R.; Pillay, M. K. *J. Org. Chem.* **1987**, *52*, 746.) for the oxidation of a series of aryl methyl sulfoxides by DMD in acetone solution at room temperature.

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