The Origin of the Sulfone in Photooxidations Involving Sulfurane Intermediates

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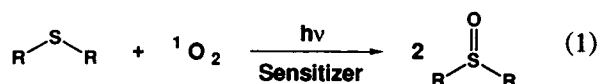
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ABSTRACT

The photooxidations of γ-hydroxysulfides which give abnormally high yields of sulfones have been investigated. This unusual result is attributed to the potent trapping ability of a hydrogen bonded sulfoxide intermediate. This suggestion is supported by measuring the ability of a γ-hydroxysulfoxide to trap the persulfoxide formed in the photooxidation of diethyl sulfide and by careful analysis of the reaction composition as a function of time.

INTRODUCTION

The introduction of oxygen into theoretically interesting and biologically important molecules occurs by a fascinating array of mechanisms and intermediates. Reactions with triplet oxygen ($^3\Sigma_g$) are the most efficient when the substrates are activated by converting them into radicals or anions by hydrogen (autooxidation) or proton abstraction, or into radical cations or anions by electron transfer [1]. Singlet oxygen ($^1\Delta_g$), on the other hand, is more reactive than triplet oxygen and will react with closed shell molecules which have loosely bound electrons in either π- or nonbonding orbitals [2].

$$R{\diagup}^S{\diagdown}R \;+\; {}^1O_2 \;\;\xrightarrow[\text{Sensitizer}]{hv}\;\; 2\;\; R{\diagup}^{\overset{\displaystyle O}{\underset{\displaystyle \parallel}{S}}}{\diagdown}R \qquad (1)$$

Sulfides, which have two sets of loosely bound nonbonding electrons, react as anticipated with singlet oxygen to give sulfoxides (equation 1). The quantum yield for sulfoxide formation is very low in aprotic solvents (benzene or acetonitrile) but approaches the theoretical maximum of two in protic media (CH_3OH). The low quantum yield in aprotic solvents has been attributed to a physical quenching process which competes with product formation [3,4]. A detailed kinetic examination of the photooxidation of diethyl sulfide also reveals divergent behavior in benzene in comparison to methanol; two intermediates are kinetically required in benzene but only one in methanol [5–9].

Photooxidations of several γ-hydroxy sulfides produce novel oxidative elimination products whose formations were recently rationalized by invoking trigonal bipyramidal sulfurane intermediates [10] (Figure 1). A kinetic study of a series of sulfides, in which the position of the tethered hydroxy group is varied by insertion of intervening methylene groups, led to the suggestion that formation of the sulfurane competitively inhibits physical quenching [11]. It was also suggested, by extrapolation, that a similar phenomenon during the photooxidation of diethyl sulfide was responsible for the improved efficiency and the inability to detect a second intermediate in methanol.

However, it is also clear that these γ-hydroxy sulfides are not perfect mimics for the photooxidative behavior of diethyl sulfide in methanol. For example, the sulfone is a major product (>60% in some cases) during the photooxidations of γ-hydroxy sulfides but only a minor product (<5%) during the photooxidation of diethyl sulfide in either methanol or benzene [12].

Two mechanisms for the photooxidative formation of sulfones have been suggested and discussed extensively in the literature. The mechanism depicted in equation 2 was originally proposed
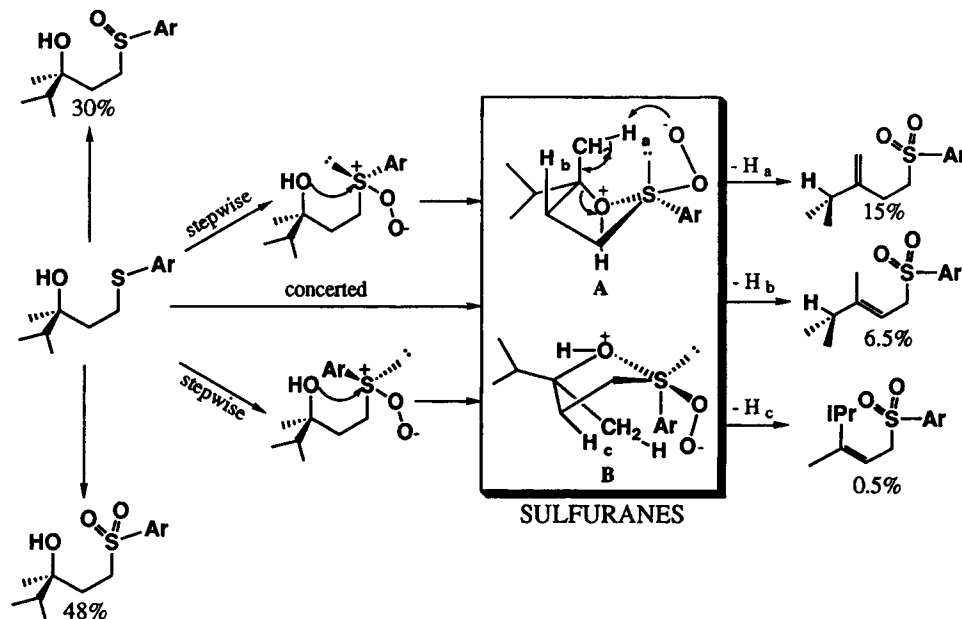

Dedicated to Prof. James Cullen Martin on the occasion of his sixty-fifth birthday.
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1042-7163/93/$5.00 + .25 **197**

FIGURE 1

to rationalize the small amounts of sulfone formed in the reactions of dialkyl sulfides [13] and involves the unimolecular decomposition of a thiadioxirane. Sulfone formation in the alternative mechanistic proposal depicted in equation 3 occurs by oxidation of the sulfoxide product by a persulfoxide intermediate formed in the reaction. In support of this latter mechanism, Foote and coworkers have demonstrated that diphenyl sulfoxide, which is inert in the presence of singlet oxygen, is converted to the sulfone when cophotooxidized with diethyl sulfide.

(2)

(3)
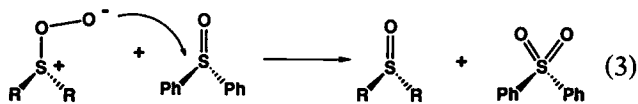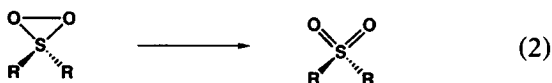
In order to understand the origin of the large amount of sulfone, we have examined the effects of temperature, substituent, and extent of reaction on its formation. The results of these investigations and their mechanistic implications are presented here.

RESULTS AND DISCUSSION

The unique ability of γ-hydroxy sulfides, in comparison to dialkyl sulfides, to react with singlet oxygen to give sulfones as the major products can be accommodated within the framework of either the thiadioxirane (equation 2) or trapping mechanism (equation 3). γ-Hydroxy sulfoxides are known to be intramolecularly hydrogen bonded [14] and should be more electrophilic and consequently better trapping agents than diethyl sulfoxide. On the other hand, the sulfuranes **A** and **B** formed in the photooxidations of γ-hydroxy sulfides (Figure 1) have trigonal bipyramidal geometries [15] and should require little internal reorganization energy to collapse to the trigonal bipyramidal thiadioxirane. In contrast, the persulfoxide (R_2S^+-OO$^-$) intermediates formed in photooxidations of dialkyl sulfides are tetrahedral [16] and would require rehybridization and valence shell expansion at sulfur in order to form the thiadioxirane.

The ability of the sulfoxide **1** to trap a persulfoxide intermediate was measured by cophotooxidation with Et_2S [12]. Sulfoxide **1** is itself inert to singlet oxygen but readily forms the sulfone $1SO_2$ when cophotooxidized with diethyl sulfide. A plot of $[Et_2SO]/[1SO_2]$ vs. $1/[1]$ is linear and independent of sulfide concentration as anticipated from inspection of equation 4 which was derived by Foote

$$\frac{[EtSO]}{[1SO_2]} = 1 + \frac{C}{k_{trap}[1]}$$

(4)

and coworkers [17] to describe diphenyl sulfoxide trapping during photooxidation of diethyl sulfide. The slope of the plot, C/k_{trap}, where C is a constant independent of trapping agent, is 0.024. From this result, the trapping efficiency of **1** relative to diphenyl sulfoxide can be derived [17]. Examination

TABLE 1 Relative Trapping Efficiencies during the Photooxidations of Diethylsulfide[a]

Quencher	k_{trap} (rel)	Quencher	k_{trap} (rel)
Ph_2SO[b]	1	butyl p-tolylsulfoxide	0.74[c]
$P(OMe)_3$[b]	28	1	6.8[c]

[a]Derived from equation 4 by taking ratios of C/k_{trap}. [b]In acetonitrile [20]. [c]In acetone [12].

of this data in Table 1 reveals that **1** is nearly seven times as potent as diphenyl sulfoxide and more than nine times as potent as butyl p-tolyl sulfoxide in its ability to trap a persulfoxide intermediate.
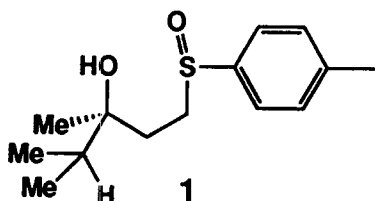
Ostensibly inconsistent with the trapping mechanism, however, are the results of the photooxidations of sulfides **2a–e** which are shown in Table 2. Changing the electrophilicity of the sulfoxide in this series has little or no effect on the yield of the sulfone. A similar observation can be made by examination of substituted 3,4-dimethyl-3-hydroxypentyl aryl sulfides **3a–e**. Very little change is observed in the yields of the sulfones or olefins **4A** and **B** as a function of substituent or temperature (Table 3). However, Sawaki and Ogata reported a very small Hammett ρ value of 0.252 for the trapping of dimethyl persulfoxide with para-substituted diphenyl sulfoxides [18]. This corresponds to less than a factor of two change in the rate as the substituent is changed from chloro to methoxy. It is likely that the substituent effect on the trapping ability of these more reactive γ-hydroxy sulfoxides is even less, and, as a result, the lack of a substituent effect on the sulfone yields cannot be used to rule out the trapping mechanism.

**TABLE 2** Photooxidations of 3-Hydroxypropyl Aryl Sulfides **2a–e**[a,b,c]

Compound	% Yield	
	Sulfoxide	Sulfone
2a	41	59
2b	43	57
2c	45	55
2d	42	58
2e	45	55

[a]In acetone-d_6 at −80°C. [b][**2a–e**] = 1.5 − 1.9 × 10^{-2}M; [Rose Bengal] = 2 × 10^{-5}M. [c]At 100% conversion.

TABLE 3 Photooxidations of 3,4-Dimethyl-3-Hydroxypentyl Aryl Sulfides **3a–e**[a,b]

Compound	T (°C)	% Yield		4A	4B
		Sulfoxide	Sulfone		
3a	−80	32	56	10	2
3b	−80	30	48	15	7
	−56	29	52	14	5
	−45	30	50	15	5
	−35	26	52	15	7
	−30	34	45	15	6
	−10	31	47	14	8
3c	−80	28	59	10	3
3d	−80	28	64	6	2
3e	−80	28	67	4	1

[a]In acetone-d_6; [**3a–e**] = 1.4 − 2.5 × 10^{-2}M; [Rose Bengal] = 1.4 − 2 × 10^{-5}M. [b]All reactions carried to 100% conversion.

a. X = OMe d. X = F
b. X = Me   e. X = Cl
c. X = H
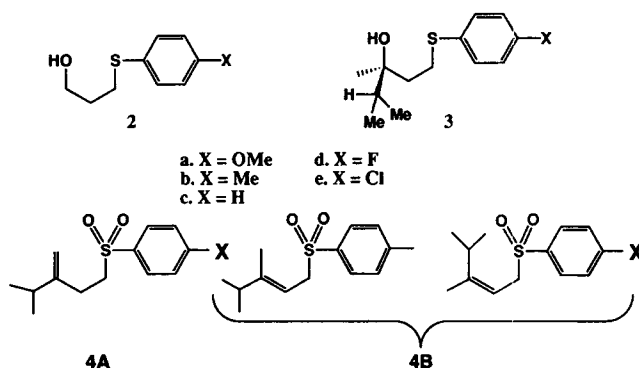
If the trapping mechanism functions alone, it requires that sulfone formation lag behind sulfoxide formation. The reaction profile as a function of percent conversion of 3-hydroxy-3-methylpentyl-4-methylphenyl sulfide **5** (Figure 2) demonstrates that the sulfone forms very early in the reaction. However, careful examination of the reaction mixture at less than 2% conversion also reveals that the sulfoxide appears first in the reaction mixture. In addition, the amount of sulfoxide formed does not appear to systematically increase with extent of reaction but levels off at approximately 50% conversion while the sulfone production continues to increase. These results argue in favor of the trapping mechanism, especially after 50% consumption of the sulfide, but do not rule out possible contributions to sulfone formation from other pathways.

CONCLUSION

We have presented data which suggest that the unexpected high yields of sulfones from photooxidations of γ-hydroxy sulfides are a result of the potent trapping ability of hydrogen bonded sulfoxide intermediates. This is a unique situation in com-
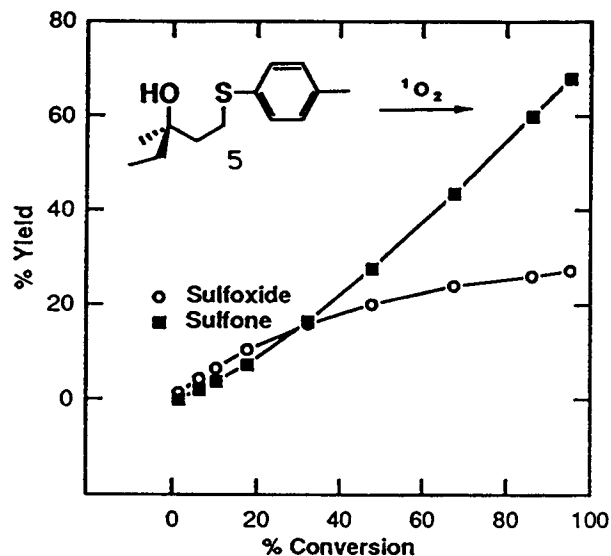
FIGURE 2   Reaction profile for the photooxidation of 5 as a function of percent conversion.

parison to photooxidations in methanol where both the sulfoxide and persulfoxide (peroxysulfurane) intermediates are hydrogen bonded. Hydrogen bonding between the persulfoxide and methanol opposes the effect of hydrogen bonding to the sulfoxide by enhancing the rate of sulfide attack on the persulfoxide intermediate. This hydrogen bonding induced decrease in the nucleophilicity of the persulfoxide is more important than the increase in electrophilicity of the sulfoxide, and sulfone formation is consequently suppressed in methanol. A minor contribution to the yield of sulfone from a thiadioxirane pathway cannot be completely eliminated.

EXPERIMENTAL

Analytical gas chromatographic measurements were carried out on a Perkin-Elmer 8500 gas chromatograph equipped with a flame ionization detector and a 10 m × 0.53 mm cross-linked HP-1 capillary column. Preparative chromatographic separations were carried out on a Harrison Research Model 7624T Chromatotron using plates coated with EM Science 7749 silica gel 60PF254. Proton and carbon NMR spectra were obtained on either a JEOL GX270 at 269.7 and 67.8 MHz or on a GX400 at 399.78 and 100.53 MHz, respectively. All spectra are referenced to internal TMS.

Sulfides 1a–e and 2a–e, sulfoxides 3aSO-eSO, and sulfones 3aSO$_2$-eSO$_2$ were synthesized as previously reported [12]. The photooxidations were conducted as previously described [19].

3-Hydroxypropyl p-Methoxyphenyl Sulfoxide **2aSO.** ^{1}H NMR (CDCl$_3$) δ 1.86–2.00 (m, 2H), 2.85–

3.05 (m, 3H), 3.15–3.25 (m, 2H), 3.86 (s, 3H), 7.03 (d, J = 8.6 Hz, 2H), 7.55 (d, J = 8.6 Hz, 2H).

3-Hydroxypropyl p-Methoxyphenyl Sulfone **2aSO$_2$.** ^{1}H NMR (CDCl$_3$) δ 1.74 (bs, 1H), 1.91–2.20 (m, 2H), 3.19–3.25 (m, 2H), 3.73 (bt, J = 6.0 Hz, 2H), 3.89 (s, 3H), 7.01 (d, J = 8.6 Hz, 2H), 7.82 (d, J = 8.6 Hz, 2H).

3-Hydroxypropyl p-Methylphenyl Sulfoxide **2bSO.** ^{1}H NMR (CDCl$_3$) δ 1.8 (s, 1H), 1.84–2.0 (m, 2H), 2.41 (s, 3H), 2.85–2.95 (m, 1H), 2.95–3.05 (m, 1H), 3.7 (bs, 2H), 7.32 (d, J = 8.1 Hz, 2H), 7.50 (d, J = 8.1 Hz, 2H).

3-Hydroxypropyl p-Methylphenyl Sulfone **2bSO$_2$.** ^{1}H NMR (CDCl$_3$) δ 1.9–2.0 (m, 2H), 2.23 (bs, 1H), 2.45 (s, 3H), 3.20–3.28 (m, 2H), 3.70 (t, J = 6.1 Hz, 2H), 7.37 (d, J = 8.1 Hz, 2H), 7.79 (d, J = 8.1 Hz, 2H). ^{1}H NMR (acetone-d_6) δ 1.75–1.85 (m, 2H), 2.44 (s, 3H), 3.19–3.25 (m, 2H), 3.58 (dt, J = 5.3, 5.9 Hz, 2H), 3.73 (t, J = 5.3 Hz, 1H).

3-Hydroxypropyl Phenyl Sulfoxide **2cSO.** ^{1}H NMR (CDCl$_3$) 1.85–2.05 (m, 2H), 2.86 (bs, 1H), 2.86–2.96 (m, 1H), 3.02–3.12 (m, 1H), 3.65–3.80 (m, 2H), 7.51–7.64 (m, 5H).

3-Hydroxypropyl Phenyl Sulfone **2cSO$_2$.** ^{1}H NMR (CDCl$_3$) 1.69 (bs, 1H), 1.94–2.04 (m, 2H), 3.22–3.28 (m, 2H), 3.75 (bt, J = 5.9 Hz, 2H), 7.55–7.70 (m, 3H), 7.91–7.95 (m, 2H).

3-Hydroxypropyl p-Fluorophenyl Sulfoxide **2dSO.** ^{1}H NMR (CDCl$_3$) 1.85–2.05 (m, 2H), 2.75 (bs, 1H), 2.84–2.94 (m, 1H), 2.99–3.09 (m, 1H), 3.70–3.80 (m, 2H), 7.21–7.27 (m, 2H), 7.60–7.66 (m, 2H).

3-Hydroxypropyl p-Fluorophenyl Sulfone **2dSO$_2$.** ^{1}H NMR (CDCl$_3$) 1.71 (bs, 1H), 1.94–2.04 (m, 2H), 3.22–3.28 (m, 2H), 3.76 (t, J = 5.6 Hz, 2H), 7.26 (m, 2H), 7.95 (m, 2H).

3-Hydroxypropyl p-Chlorophenyl Sulfoxide **2eSO.** ^{1}H NMR (CDCl$_3$) 1.85–2.05 (m, 2H), 2.64 (bs, 1H), 2.83–2.93 (m, 1H), 3.01–3.08 (m, 1H), 3.65–3.80 (m, 2H), 7.50–7.59 (m, 4H).

3-Hydroxypropyl p-Chlorophenyl Sulfone **2eSO$_2$.** ^{1}H NMR (CDCl$_3$) 1.63 (bs, 1H), 1.94–2.04 (m, 2H), 3.22–3.28 (m, 2H), 3.75 (bs, 2H), 7.56 (d, J = 8.6 Hz, 2H), 7.86 (d, J = 8.6 Hz, 2H).

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