Hammett Correlations in the Photosensitized Oxidation of 4-Substituted Thioanisoles

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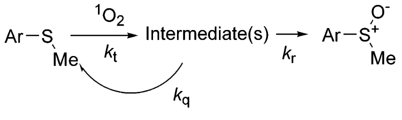
Singlet oxygen is quenched by a series of 4-substituted thioanisoles (methoxy to nitro), with rate constant $k_t = 7 \times 10^4$ to 7×10^6 M^{-1} s^{-1}, close to the value observed for the myoglobin-catalyzed sulfoxidation of the same sulfides. Correlations with σ ($\rho = -1.97$) and with E_{ox} (slope -3.9 V^{-1}) are evidence for an electrophilic mechanism. In methanol sulfoxides are formed (85%) via an intermediate quenched by diphenyl sulfoxide; competing minor paths lead to arylthiols, arylsulfenic acid, and aryl sulfoxides. In aprotic solvents, the sulfoxidation is quite sluggish, but carboxylic acids (mostly $\leq$0.1 M) enhance the rate by a factor of >100. The protonated persulfoxide is formed in this case and acts as an electrophile with sulfides, again with a rate constant correlating with σ ($\rho = -1.78$).

The oxidation of sulfides to sulfoxides is an important process from both the synthetic and mechanistic points of view, and many reagents are available for the conversion.[1,2] The reaction with singlet oxygen is an appealing procedure, in view of the mild conditions, but the outcome is highly dependent on the reagent structure and on the conditions, and the reaction has proved to be mechanistically intricate. In fact, according to the solvent chosen, formation of the sulfoxide involves different intermediates, the structure of which has been clarified through trapping studies[3] and computations.[4] The Hammett criterion was used early to establish the electrophilic character of initial attack of singlet oxygen onto thioanisoles (rate constant k_t, Scheme 1),[5] though the span of σ explored has been relatively small. The Hammet criterion, however, has not been used to determine the electronic character of the second step (k_r).

SCHEME 1



In general, aryl alkyl (as well as diaryl) sulfides appear to be less reactive and have received less attention than dialkyl derivatives, though some thioanisoles have been considered in important mechanistic papers.[6] On the other hand, the (enantioselective) oxidation of thioanisoles is quite important for several applications[2] and has been performed by using a variety of inorganic reagents,[7] enzymes,[8] and photochemical methods not involving singlet oxygen.[9] This prompted us to investigate the reaction of singlet oxygen with a series of thioanisoles, taking advantage of the fact that direct measurement of the quenching of $^1O_2$ allows the determination of a larger span of k_t than previous less sensitive methods. In addition, recent evidence suggest that protic additives,[10] zeolites,[11] and clays[12] can make reluctant photooxidations of sulfides more efficient, thus broadening the scope of the reaction as a preparative method.

Results

Quenching of Singlet Oxygen. Thioanisole (**1a**) and a series of ring-substituted derivatives (**1b**−**f**) were

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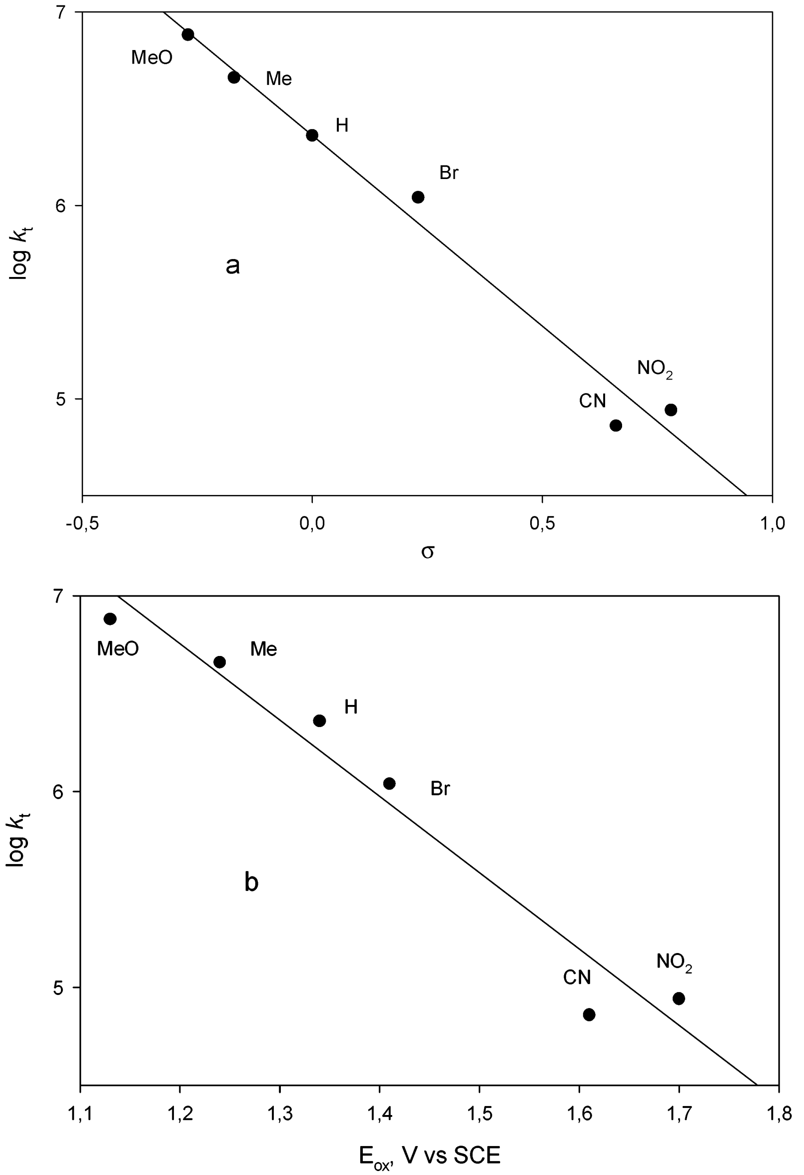


FIGURE 1. Correlation of the rate constants for singlet oxygen quenching by thioanisoles **1** with (a) σ coefficients and (b) oxidation potentials.

examined. The quenching rates of singlet oxygen were determined by laser flash photolysis by measuring the $^1O_2$ emission lifetime at 1270 nm after oxygen sensitization. This allowed the acquisition of precise measurements even for poor quenchers. Thus, compounds bearing a strong electron-withdrawing group such as 4-cyano (**1e**) and 4-nitro (**1f**) were examined. Table 1 and Figure 1 demonstrate that the rate constants span a 2 orders of magnitude range and are linearly correlated with both σ and E_{ox}.

Photooxygenation in Methanol. Rose Bengal (RB)-sensitized oxygenation of **1a** in methanol gave the sulfoxide as the main product (**2a**, 85%) with minor amounts of the sulfone (**3a**, 5%), diphenyl disulfide (**4a**, 1%), and methyl benzenesulfenate (**5a**, 4%) and benzenesulfinate (**6a**, 3%, Scheme 2). The product distribution did not change during the reaction, up to >80% conversion, except for **6a**, which increased with increasing conversion (see Figure 2). The same results were obtained in ethanol, with the only difference that products **5a** and **6a** were replaced by the corresponding ethyl esters.

TABLE 1. Quenching Constants (k_t) of Singlet Oxygen by Sulfides 1a–f and Amount of Thioanisole Reacted ($[S]_r$) in Methanol and in Acetonitrile as Compared to That of Diethyl Sulfide under the Same Conditions

	X	E_{ox},[a] V vs SCE	IP[b]	k_t,[c] M^{-1} s^{-1}	$[S]_r$,[d] MeOH	$[SO]_r$, MeCN
1b	OMe	1.13	7.8	7.6×10^6	0.22	0.0014
1c	Me	1.24	7.87	4.6×10^6	0.25	0.00034
1a	H	1.34	8.07	2.3×10^6	0.046	0.00014
1d	Br	1.41	7.8, 8.4[e]	1.1×10^6	0.011	0.00014
1e	CN	1.61		7.3×10^4	0.004[f]	0.0004[f]
1f	NO$_2$	1.70	8.5[g]	8.7×10^4	0.002[f]	0.0002[f]
Et_2S		1.65[h]	8.44[i]	2×10^7[j]	1	0.05

[a] Reference 13. [b] Reference 14. [c] In $CDCl_3$. [d] Amount of thioanisole reacted relative to that of diethyl sulfide reacted in MeOH in the same time; starting concentration 0.01 M. [e] Reference 15. [f] Starting concentration 0.1 M. [g] Reference 16. [h] Reference 5a. [i] Reference 17. [j] Reference 18.

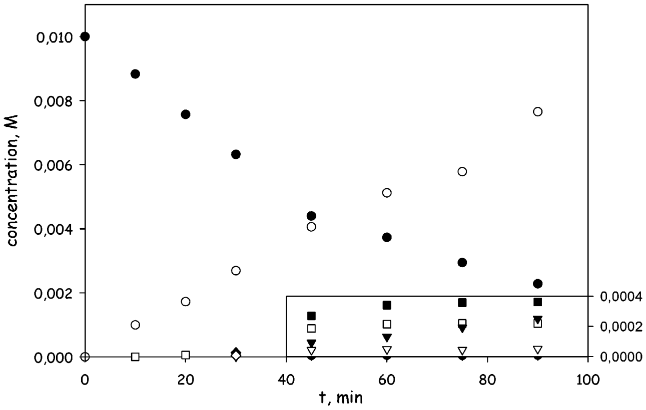
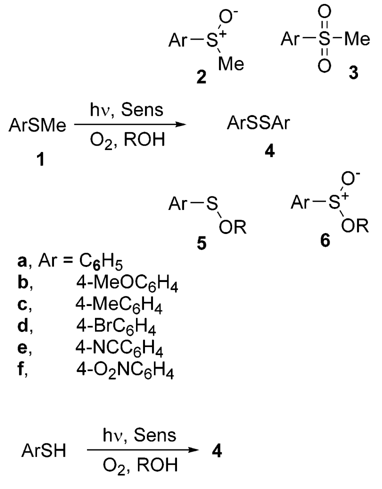


FIGURE 2. Reaction of thioanisole (**1a**, ●) and formation of sulfoxide (**2a**, ○), sulfone (**3a**, ■), diphenyl disulfide (**4a**, ▽), and methyl benzensulfenate (**5a**, □) and sulfinate (**6a**, ▼) upon RB-sensitized photooxygenation in methanol. Inset: the four last compounds on an expanded scale (right-hand side).

SCHEME 2



Control experiments showed that sulfoxide **2a** was not significantly oxidized on this time scale, while thiophenol reacted at a rate comparable to that of **1a**, giving disulfide **4a** as virtually the only product.

RB-sensitized oxygenation of both 4-methoxythioanisole (**1b**) and 4-cyanothioanisole (**1e**) proceeded analogously to that of the parent compound, giving the sulfoxide ($\cong$85%) accompanied by small amounts of the sulfoxide and the sulfinate (**1b** also gave the sulfenate and traces of the sulfonate). The sulfoxide was also formed in about 85% yield with the other substituted thioanisoles examined (4-methyl, **1c**; 4-bromo, **1d**; 4-nitro, **1f**). The amount of sulfide reacted was compared to that measured for diethyl sulfide under the same conditions. The relative amounts of thioanisole reacted ($[S]_r$) are reported in Table 1. No reaction occurred in the absence of oxygen.

The role of oxygenated intermediates has been often investigated through their oxygen-transfer properties to appropriate acceptors. As done with other sulfur derivatives,[3,18] we used diphenyl sulfoxide, which per se is not significantly photoreactive, and found that it was cooxidized in the presence of thioanisoles. The arylmethyl sulfoxide/diphenyl sulfone ratio ($[ArMeSO]/[Ph_2SO_2]$) showed a reverse correlation with $[Ph_2SO]$ under these conditions, and the slope (see Table 2) depended on the starting thioanisole concentration (see the case of **1a** in Figure 3).

TABLE 2. Ratios k_{SO}/k_{PhO} and Respectively k'_{SO}/k'_{PhO} Obtained from the $[ArMeO]/[Ph_2SO_2]$ vs $1/[Ph_2SO]$ Plots in the Cooxidation of Diphenyl Sulfoxide and Thioanisoles 1a–f in Methanol (Figure 3) and Acetonitrile, Respectively, Containing 0.5 M Acetic Acid (Figure 6)

	X	k_{SO}/k_{PhO}, M, MeOH	k'_{SO}/k'_{PhO},M, AcOH (0.5 M in MeCN)
1b	OMe	1.5	14
1c	Me	3.2	11
1a	H	4.2	7.3
1d	Br	1.5	4.2
1e	CN	0.5	0.5
1f	NO_2	0.4	0.5

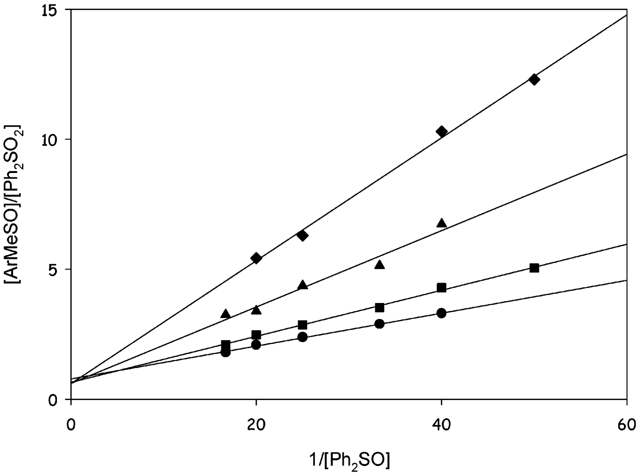


FIGURE 3. Ratio of sulfoxide **2a** vs diphenyl sulfone formed upon photooxygenation of thioanisoles in methanol in the presence of diphenyl sulfoxide **1a**: 0.1 (◆), 0.071 (▲), 0.05 (■), 0.03 (●) M.

Photooxygenation in Aprotic Media. Oxygenation of **1a** in other solvents was also attempted, but both the RB-sensitized irradiation in acetonitrile (Table 1) and tetraphenylporphine-sensitized irradiation in benzene were exceedingly sluggish (rate <1/100 that in methanol) when the solvents were freshly dried. The only product at moderate conversion was the sulfoxide. Previous researchers likewise found the sulfoxide with a yield of sulfone ranging from <1% to 32% in these solvents.[6,11] The RB-sensitized oxygenation in acetonitrile was extended to the above substituted thioanisoles, and all of them were converted to the sulfoxide, although the reaction was quite slow particularly with those bearing

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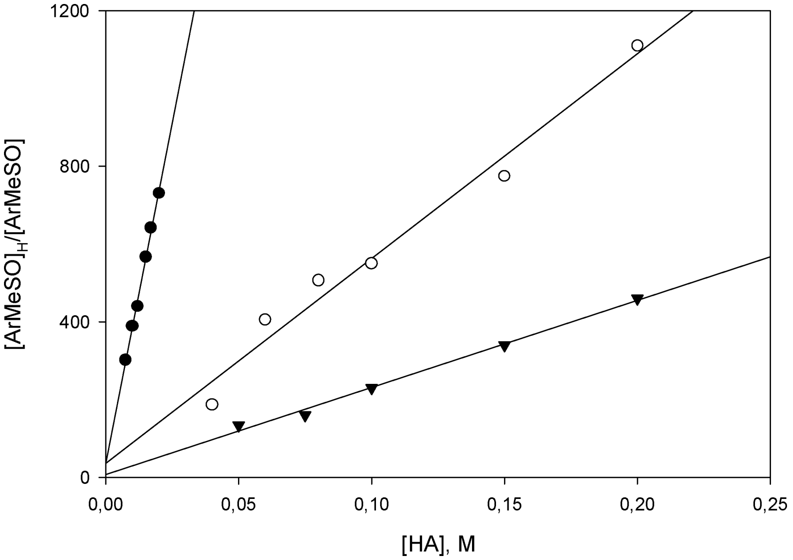


FIGURE 4. Ratio of the yield of sulfoxide in the presence vs in the absence of acids in the RB-photosensitized oxidation of thioanisole **1c**: Diphenylacetic (●), acetic (○), and pivalic (▼) acid added.

TABLE 3. Ratio of Reacted Moles of the Sulfide in the Presence vs in the Absence of Carboxylic Acids: Slopes of Such Ratios vs the Acid Concentration (k_H/k_x; See Figure 4) in Acetonitrile

		k_H/k_x, M^{-1}		
	X	t-BuCO$_2$H	AcOH	Ph$_2$CHCO$_2$H
1b	OMe	1.8×10^3	3.7×10^3	22.8×10^3
1c	Me	2.8	4.7	34.9
1a	H	8.3	9.3	33.7
1d	Br	8.0	10.1	10.4
1e	CN	0.8	1.1	1.1
1f	NO$_2$	0.6	0.7	0.7[a]

[a] PhCH$_2$CO$_2$H.

an electron-withdrawing group, e.g., 20 h for a 0.2% conversion with **1f** (0.1 M).

Previous experiments with aliphatic sulfides had shown that protic additives such as alcohols[10a] and, much more efficiently, carboxylic acids[10b] considerably speeded up the photooxygenation in aprotic solvents. Some effect of the alcohols was obtained also with thioanisoles; e.g., 2 M methanol in MeCN increased the oxygenation of **1a** by a factor of 10, and 2 M trifluoroethanol led to an oxygenation as fast as in neat methanol. These effects were lower than those found with aliphatic sulfides. The effect with carboxylic acids was more marked, but the acidity window available for the exploration was limited, since the oxygenation still required a rather long irradiation time, and under these conditions the sensitizer was unstable to acids as strong as chloroacetic acid. Pivalic, acetic, and diphenylacetic acid could be used with no inconvenience and were chosen for examination of the series **1a**–**f**. With these additives, the rates of oxygenation were increased by a factor of >100 already at a 0.1 M concentration or below. The ratio of the moles of sulfoxide formed in the presence vs in the absence of the acid linearly correlated with the acid concentration, as shown for a representative sulfide (**1c**) in Figure 4.

The slopes are reported as k_H/k_x (see the Discussion) in Table 3, where it appears that the effect varied with the acid and the sulfide. This is illustrated in Figure 5 by plotting the slopes of the linear plots obtained as above vs the pK_a of the acids used for sulfides **1a**–**f**. The same acids also increased the rate of the TPP-sensitized photooxygenation of **1a** in benzene, with an effect qualitatively similar to that in MeCN, though much less marked.

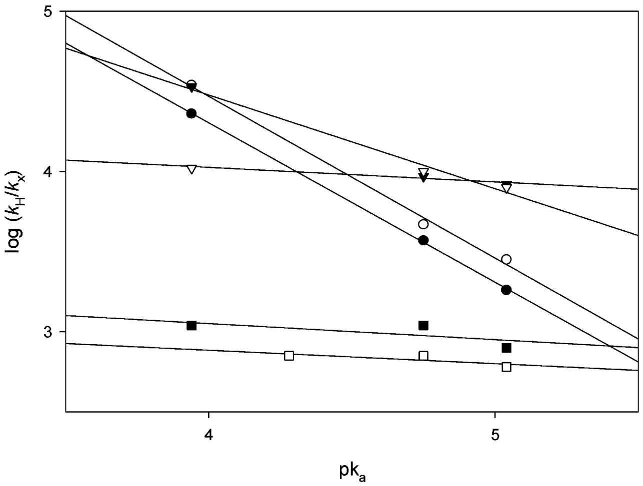


FIGURE 5. Dependence of the slopes in Figure 4 on the pK_a of the acid added: **1a** (▼), **1b** (●), **1c** (○), **1d** (▽), **1e** (■), **1f** (□).

The reasonably rapid photooxidation in acid-containing acetonitrile suggested the exploration of trapping by diphenyl sulfoxide under these conditions. Indeed, cooxygenation of Ph$_2$SO was obtained, and the ratio [**2**]/[Ph$_2$SO$_2$] showed a reciprocal dependence on the concentration of the acids, as shown for thioanisole **1a** in MeCN containing 0.05 M acetic acid in Figure 6. The slope of the plots depended on the concentration of both thioanisole and the sulfoxide. The investigation was extended to the other sulfides, as shown in Table 2.

Discussion

Quenching of Singlet Oxygen. The data above afford information concerning three aspects of the reac-

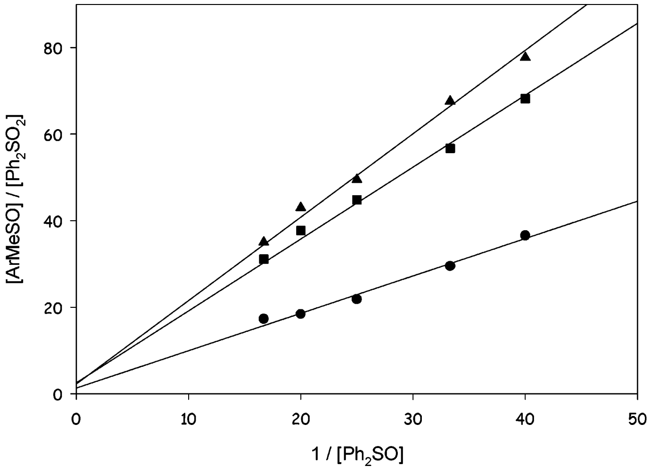
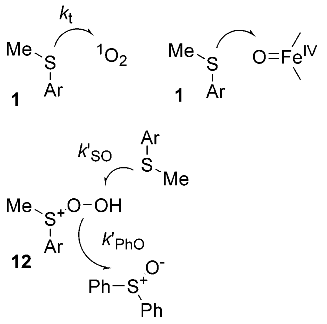


FIGURE 6. Ratio of sulfoxide **2a** vs diphenyl sulfone formed upon photooxygenation of thioanisole in methanol in the presence of diphenyl sulfoxide **1a**: 0.075 (▲), 0.05 (■), 0.03 (●) M.

tion as summarized in Scheme 1, viz., (1) interaction with singlet oxygen generating the first intermediate, (2) formation of the sulfoxide from it, and (3) competing chemical paths. The rate constants for singlet oxyen quenching by the *para*-substituted thioanisoles (k_t; see Table 1) show that these compounds, as in general aryl alkyl (and diaryl) sulfides, are poor oxygen quenchers compared to dialkyl derivatives (e.g., the rate constant for **1a** is lower by a factor of 10 than that measured for diethyl sulfide), despite the fact that they have a lower IP, as was earlier noted.[5a] The features of the thioanisole PE spectrum suggest that there is an equilibrium between a (largely predominant) planar rotamer and a perpendicular rotamer.[19] The first one has maximum n(p_y)−π(b_1) conjugation, and it is the only one that can participate in the complexation with tetracyanoethylene (TCNE).[20] The stability constant of the complex between **1a** and TCNE is 2 orders of magnitude lower than with diethyl sulfide.[21,22] Complexation with this π acceptor can be taken as a reasonable model for the formation of a weakly bound adduct with singlet oxygen (see below), in view of the similar redox characteristics; E_{red}(TCNE) = +0.23 and $E_{\text{red}}(^1O_2) = +0.16$ V vs SCE.[23] This supports that the reaction with electrophilic $^1O_2$ is slower than with dialkyl sulfides because the HOMO in thioanisole is only partially localized on the sulfur atom, making this a poor nucleophile. This also leads to the expectation that ring substituents will affect the rate of reaction with $^1O_2$.

SCHEME 3



Indeed, the values obtained (varying over 2 orders of magnitude) correlate satisfactorily ($r = 0.99$) with σ, giving $\rho = -1.97$ (Figure 1a; the correlation with σ^+, on the other hand, is poor, $r = 0.96$). This is somewhat higher than previously found with a series of thioanisoles not containing strong electron-withdrawing substituents ($\rho = -1.6, -1.67$).[5]

The k_t values for the series **1a**−**f** also correlate, though less satisfactorily, with E_{ox} (slope -3.9 V^{-1}, $r = 0.977$, Figure 1b). This is again a higher value than found in a more limited series,[5] but confirms the notion that the process does not involve full electron transfer (which would require a slope of -16.4 V^{-1}).[24] In fact, $\Delta G°$ for electron transfer from **1a** to $^1O_2$ is markedly endothermic (26.4 kcal/mol).[25]

These results have a bearing on the current debate on the mechanism of cytochrome P450 catalyzed sulfoxidation,[26] viz., either electron transfer/oxygen coupling (overall two electrons oxo transfer) or sequential electron transfer. Interestingly, the present absolute rates closely match those measured for the oxidation of the same sulfides by the His64Ser myoglobin mutant, which are also in the range 10^4−10^6 M^{-1} s^{-1}, though showing a less steep dependence on E_{ox} (slope -2.2 V^{-1}).[13]

Synthetic models, such as oxoferryl tetramesithylporphyrin dianion show a dependence on E_{ox} similar to that of myoglobin, but rates are slower by a factor of 100. On the other hand, when *S*-oxidation proceeds via an electron-transfer mechanism, as with the horseradish peroxidase compound I system, rates are much lower (e.g., $k_{\text{obs}} = 1$ M^{-1} s^{-1} for **1a**), though the dependence of E_{ox} is much steeper (-10 V^{-1}).[13] Thus, singlet oxygen is a simple and appropriate model for the oxygen-transfer mechanism in cytochrome P450 oxygenation of thioanisoles (see the parallel reactions of **1** in Scheme 3), and the easy determination of k_t ($^1O_2$) may be used to test the reactivity of a sulfurated biomolecule.

Sulfoxidation. While the overall rate of reaction with singlet oxygen (k_t) closely matches that of the enzymatic oxidation process, the fundamental difference remains

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[22] (a) Similar results have been obtained for the iodine complexes: Tsobumura, H.; Lang, R. P. *J. Am. Chem. Soc.* **1961**, *83*, 4329. Kroll, M. *J. Am. Chem. Soc.* **1968**, *90*, 1097. (b) Satisfactory correlations with σ have been found for the complexes of thioanisoles and diaryl sulfides, e.g., with iodine: Santini, S.; Reichenbach, G.; Mazzuccato, U. *J. Chem. Soc., Perkin Trans. 2* **1974**, 494. See also ref 16.

[23] (a) The reduction potential of singlet oxygen is taken as that of triplet oxgyen (ref 23b) plus the electronic excitation energy; E_{red}-($^1O_2$) = $E_{\text{red}}(^1O_2) + \Delta E°° = -0.84 + (22.5/23.04) = 0.15$ V vs SCE. (b) Clennan, E. L.; Noe, L. J.; Szneler, E.; Wen, T. *J. Am. Chem. Soc.* **1990**, *112*, 5080.

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[25] $\Delta G°$ for electron transfer from **1a** to $^1O_2$ is obtained through the Rehm−Weller equation, ref 24: $\Delta G° = 23.04[E_{\text{ox}}(\mathbf{1a}) - E_{\text{red}}(O_2) - 0.04] - \Delta E°°$. The values required are in Table 1 and ref 23.

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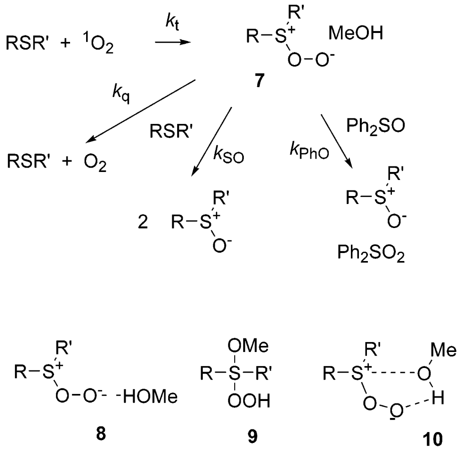
SCHEME 4



that interaction with singlet oxygen does not lead necessarily to sulfoxidation, since physical quenching (k_q) competes with chemical reaction (k_r, Scheme 1). Table 1 provides evidence that sulfoxidation is much less efficient than with Et_2S. The amounts of sulfide transformed ($[S]_r$, Table 1) are not proportional to the rate constants for chemical reaction, k_r, since, in contrast to the case of Et_2S, singlet oxygen is not completely quenched by thioanisoles, particularly by the electron-withdrawing-substituted derivatives even at a 0.1 M starting concentration. However, k_r appears to be in most cases lower than k_d.

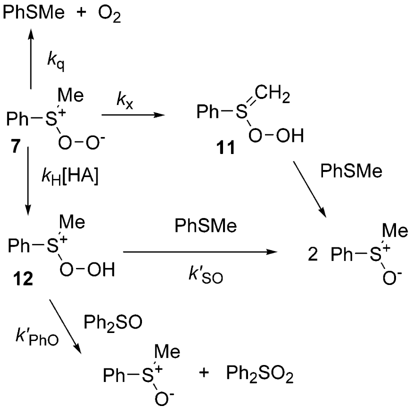
This is not surprising, since with dimethyl sulfides it has been demonstrated that the first intermediate, persulfoxide **7** (Scheme 4), is formed as the first stationary point on a very flat surface[4] and rapidly decays to the sulfide and oxygen (k_q), so that the predominant process (≥95%) is physical quenching, not sulfoxidation. The same reasons that make thioanisole a poorer nucleophile than dialkyl sulfide suggest that the S–O bond in persulfoxide is if anything weaker with these substrates, and suggest that k_q dominates over k_r, as indeed observed in aprotic solvents. However, the reaction becomes significant in methanol, where it is 10 to >100 times faster than in MeCN with both Et_2S and ArSMe. Detailed work on dialkyl sulfides by Foote and by Clennan[3] has long demonstrated that reaction in alcohols involve an intermediate, arising from persulfoxide **7** by hydrogen bonding (structure **8**, Scheme 4), nucleophile addition (alkoxyperoxysulfurane **9**), or both hydrogen bonding and nucleophile stabilization (**10**). This reacts both as an electrophile, forming 2 mol of sulfoxide by reaction with a sulfide, and as a nucleophile, forming sulfones from sulfoxides.

This model perfectly fits the case of thioanisole in methanol (R = Ar, R′ = Me, Scheme 4). Diphenyl sulfoxide is indeed cophotooxidized under these conditions, similarly to the Et_2S case. As Foote has shown,[3a] eq 1 is valid.

$$\frac{[\mathrm{RR'SO}]}{[\mathrm{Ph_2SO_2}]} = 1 + \frac{2k_{\mathrm{SO}}[\mathrm{RR'S}]}{k_{\mathrm{PhO}}[\mathrm{Ph_2SO}]} \tag{1}$$

The slope of the $[ArMeSO]/[Ph_2SO_2]$ vs $[Ph_2SO]$ plots (e.g., Figure 3) allows evaluation of the ratio k_{SO}/k_{PhO}. The values obtained (Table 2) for thioanisoles **1a**–**d** oscillate around the value observed with diethyl sulfide (k_{SO}/k_{PhO} = 2.77), and only with strongly-electron-withdrawing-substituted derivatives such as **1e** and **1f** the ratio drops to 0.4–0.5, since these sulfides are poorer nucleophiles.

SCHEME 5



On the other hand, the nonstabilized persulfoxide is not sufficiently long-lived to react directly, and the only path operating in aprotic solvents involves (inefficient) rearrangement to a second intermediate, for which both computational and experimental evidence suggest the structure of *S*-hydroxypersulfonium ylide.[3,4,6] A drastic drop in efficiency occurs also with thioanisoles in MeCN or benzene (Table 1), supporting that ylide **11** is inefficiently formed ($k_x \ll k_q$, Scheme 5). With Et_2S, diphenyl sulfoxide has been used as a probe for the second (nucleophilic) intermediate, but with the present derivatives oxygenation is too slow to adopt this course.

However, the effect of acids is informative. As mentioned in the Introduction, the addition of small amounts of carboxylic acids to aprotic solvents strongly enhances the sulfoxidation of diethyl sulfide, and the observed rate is proportional to the acid strength, supporting that general-acid catalysis is operating via protonation of the weakly basic persulfoxide.[10b] Indeed also with thioanisoles sulfoxidation is strongly enhanced by acids. Although for the reasons mentioned above only a limited pK_a range could be explored, the data in Table 3 and Figure 3 show that there is a marked dependence on the acid strength. This supports that protonated persulfoxide **12** (Schemes 3 and 5) is the intermediate.

The amount of sulfoxide formed in a given time is determined by competition between protonation and decay (eq 2), and the ratio of sulfoxide formed in the presence ($[ArMeSO]_H$) vs in the absence of the acid is proportional to the acid concentration (eq 3, valid in the simplified form because the large increase in the oxidation rate in the presence of acids supports that $k_H[HA] \gg k_x$).

$$[\mathrm{ArMeSO}] = K\frac{2k_{\mathrm{H}}[\mathrm{HA}] + 2k_{\mathrm{x}}}{k_{\mathrm{q}} + k_{\mathrm{x}} + k_{\mathrm{H}}[\mathrm{HA}]} \tag{2}$$

$$\frac{[\mathrm{ArMeSO}]_{\mathrm{H}}}{[\mathrm{ArMeSO}]} = \frac{k_{\mathrm{H}}[\mathrm{HA}] + k_{\mathrm{x}}}{k_{\mathrm{x}}} \cong \frac{k_{\mathrm{H}}[\mathrm{HA}]}{k_{\mathrm{x}}} \tag{3}$$

In fact, linear plots according to eq 3 are obtained (Figure 4), and the ratios k_H/k_x are measured. These ratios are on the order of 10^3, consistently with the fact

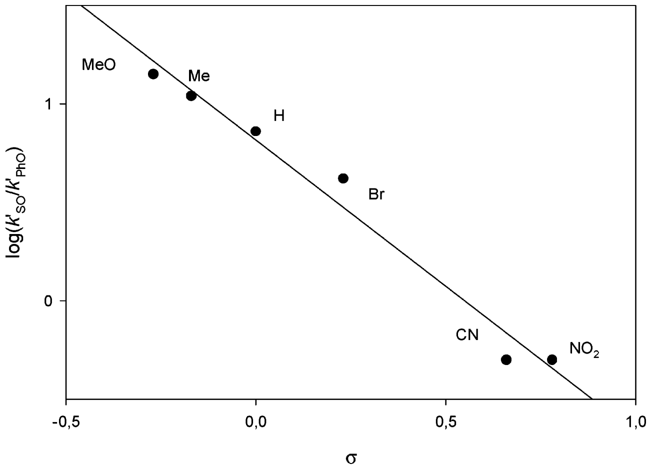


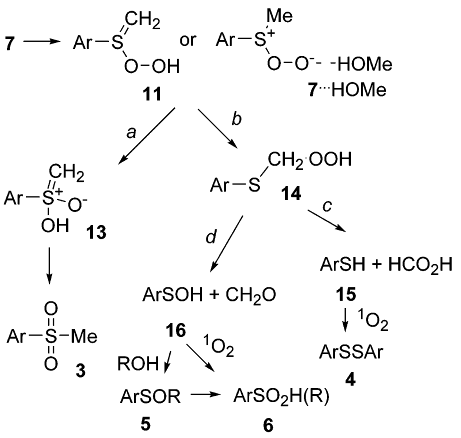
FIGURE 7. Correlation of the $\log(k'_{SO}/k'_{PhO})$ values with σ coefficients.

that rearrangement **7** → **11** (k_x) is slow. Furthermore, with non-electron-withdrawing-substituted anisoles (**1a**–**c**) there is a clear increase of the ratio with the pK_a of the acid, supporting that acid catalysis is operating via **12** (k_H in Scheme 5; see Figure 5). With electron-withdrawing substituents the ratio k_H/k_x is lower and does not depends on pK_a, reasonably because the less basic persulfoxides make a weaker hydrogen bond with the acids and the relation with pK_a cannot be appreciated in the small span explored.

Support of this mechanism comes from the cooxidation studies. Thus, experiments with diphenyl sulfoxide in 0.05 M acetic acid in acetonitrile (Figure 6) show that, just as it occurs in alcohols, the [ArMeSO]/[Ph_2O_2] ratio depends on the concentration of *both* thioanisole and Ph_2SO, and thus both reagents compete for a *single* intermediate. This is clearly protonated sulfoxide **12**. The k'_{SO}/k'_{PhO} ratio shows a regular trend, decreasing by a factor of 30 from electron-donating-substituted **1b** to nitro-substituted **1f**. The values $\log(k'_{SO}) - \log(k'_{PhO})$ linearly correlate with σ (Figure 7, slope −1.78, $r = 0.989$, no correlation with σ^+).

The similarity with Figure 1a suggests that k'_{PhO} does not change appreciably while k'_{SO} decreases regularly in electrophilic OH transfer to the less-electron-rich sulfides; thus, there is a close parallelism between the electrophilic attack of sulfides **1** by $^1O_2$ and by **12** (see Scheme 3). A trend in the same direction, but not a clear dependence, is noticed in alcohols, since here hydrogen bonding is weaker and possibly the balance between k_{SO} and k_{PhO} is more complex. Previous measurements of the oxidation of substituted diphenyl sulfides by the oxidized intermediates from diethyl sulfide and cyclohexene sulfide in methanol had indeed given lower ρ values (−0.61 and −0.74, respectively).[27] The value obtained with protonated persulfoxide **12** is quite close to that observed with flavin 4a-hydroperoxide ($\rho = -1.68$)[28a] and approaches that obtained with a classical electrophilic oxidant such as perbenzoic acid ($\rho = -2.50$),[28b] though low values have been obtained with some metal-catalyzed hydrogen peroxide oxidations.[28c]

SCHEME 6



Competing Chemical Paths. The third point involves different paths from the persulfoxide. As mentioned above, with dialkyl sulfides there is evidence that an *S*-hydroxypersulfonium ylide is the key intermediate in aprotic solvents. Sawaki found support for the ylide involvement in the formation of the sulfone (not the sulfoxide) from thioanisole in benzene containing trace water.[6] We did not further investigate the very slow oxidation in aprotic media. In the reaction in methanol, however, about 15% of the thioanisole is converted to products different from the sulfoxide, viz., the sulfone (**3a**), diphenyl disulfide (**4a**), and methyl benzenesulfenate (**5a**). These appear to result from parallel paths via a common intermediate, since the yields change little during the progress of the reaction (Figure 2). The paths are gathered in Scheme 6, following predictions based on calculation with dimethyl sulfide,[4] which consider ylide **11** the key intermediate, although this may be envisaged also as the hydrogen-bonded persulfoxide under these conditions. The sulfone, expected to arise via OH group migration to the sulfur atom (path a, intermediate **13**), is the most abundant of the products. An alternative path involves migration of the OOH group to the α carbon (path b, Pummerer-type rearrangement to hydroperoxythioacetal **14**), as calculated for Me_2S[4] and evidenced through the isolation of products resulting from α-hydroxylation[29] or C–S bond fragmentation[30] in other cases. Hydrolysis of **14** forma thiophenol **15**, which under the conditions is converted to the disulfide as shown by independent experiments, and is well established by analogy to benzyl sulfides.

Formation of phenylsulfenic acid **16** is revealed through the identification of the corresponding esters in MeOH and EtOH and has been previously suggested on the basis of the isolation of thiosulfinates from some sulfides,[31] and on the results of calculations in the case of Me_2S.[4b] The conversion of sulfenic (**5**) to sulfinic (**6**) (and

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ultimately sulfonic) derivatives has been previously well characterized.[32] Neither the proportion with respect to sulfoxide formation nor that of each of the individual cleavage processes is dramatically affected by ring substitution in the photoreactions in methanol, as shown by the fact that both cyano- and methoxythioanisole give a product distribution similar to that obtained with the parent compound **1a**. This suggests that no strongly basic or polar intermediate is involved on the various paths, as indeed suggested by calculation.[4]

Conclusion

The nonlocalized nature of the HOMO makes thioanisoles react less efficiently than dialkyl sulfides with a moderate electrophile such as singlet oxygen. The effect of substituents in a series of 4-substituted thioanisoles allows a better characterization of the initial reaction with $^1O_2$, of the basicity of the resulting persulfoxide, and of electrophilic OH transfer from protonated persulfoxide to sulfides. Minor paths have been characterized in methanol, including the cleavage to arylsulfenates, but account for $\leq$15%. The Hammet criterion allows a better framing of sulfoxidation via singlet oxygen among other chemical and biochemical oxidations. The availability of a general mechanistic frame and the fact that small amounts of acids (or, as shown by Clennan, of zeolites)[11] make the reaction reasonably fast give more interest to the hitherto scarcely utilized singlet oxygen path for the sulfoxidation of these derivatives, which is useful for the preparative point of view and for comparison with biological oxidations.

Experimental Section

Materials. Thioanisoles and diphenyl sulfone were commercial products or were synthesized via published procedures.[33] Sulfoxides and sulfones used as reference compounds were prepared via published procedures.[34]

Photoreactions. The photooxidations were carried out by using 0.01−0.1 M solutions of the sulfides in the presence of tetraphenylporphine (in benzene) or of Rose Bengal (in acetone or acetonitrile). The solutions were contained in rubber-stoppered, 1 cm diameter Pyrex tubes. These were exposed to four phosphor-coated 15 W lamps emitting from 350 to 700 nm while a steam of dry oxygen saturated with the appropriate solvent was passed into the solution through a needle.

The products were determined by GC on the basis of calibration curves in the presence of dodecane as the internal standard and by HPLC with biphenyl as internal standard. The identification of the minor products (disulfides,[35] benzensulfenates,[36] and benzensulfinates)[37] was based on the comparison of the GC/MS characteristics to those of samples prepared through published procedures. The photooxidation of diethyl sulfide was carried out in parallel experiments in the same (mixed) solvents and likewise monitored by both by GC and by HPLC.

Quenching Measurements. Rate constants for the quenching of singlet oxygen were obtained from the shorthening of the $(O_2)^1\Delta_g$ emission lifetime at 1.27 μm in the presence of known amounts of sulfides in aerated $CDCl_3$. Singlet oxygen was generated by energy transfer to O_2 from the triplet state of TPP, populated by laser excitation (Nd:YAG laser, 532 nm). The near-IR luminescence of molecular oxygen was observed at 90° geometry through a 5 mm thick AR-coated silicon metal filter with wavelength pass $>$1.1 μm and an interference filter at 1.27 μm by means of a preamplified (low-impedance) Ge photodiode cooled at 77 K (time resolution 300 ns). Single-exponential analysis of the emission decay was performed with the exclusion of the initial part of the signal, affected by scattered light, sensitizer fluorescence, and the formation profile of the emission signal itself.

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