Photooxidation of Sulfenic Acid Derivatives. 1. Sulfenamides. The Surprising Behavior of a New Class of Photooxidation Substrates

Edward L. Clennan* and Houwen Zhang

Department of Chemistry
University of Wyoming
Laramie, Wyoming 82071

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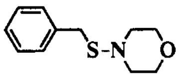
Sulfenamides, (e.g., **1**), have attracted a considerable amount of attention as a result of their use in a myriad of practical applications[1] and because of their unique stereochemical properties.[2] Oxidations of sulfenamides to sulfonamides can be carried out using typical oxidizing agents such as $KMnO_4$[3] and MCPBA.[4] A sulfenamide analogue of ebselen (2-phenyl-1,2-benzisoselenazol-3(2*H*)-one) is also known to quench singlet oxygen, but the identities of the products or whether products are even formed has not been determined.[5] We report here the first detailed study of the photooxidations of sulfenamides which reveals experimental characteristics which differ from those observed in the photooxidations of sulfides or disulfides.[6]

Photooxidations of solutions (2–4) $\times 10^{-5}$ M in the sensitizer TPP and 0.05–0.1 M in sulfenamides **1–5** were conducted in $CDCl_3$ at room temperature by irradiation with a 650-W tungsten–halogen lamp through a 1-cm $NaNO_2$ filter solution.[7] All of the reactions resulted in the exclusive formation of sulfinamides ($RS(O)NR_2$). The absence of sulfonamide ($RS(O)_2NR_2$) formation (<2%) was also observed at room and at low temperatures (−76 °C) in the photooxidations of **1** at either high or low starting material conversions in acetone, benzene, methanol, and chloroform.



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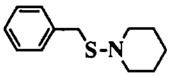

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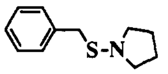

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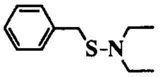

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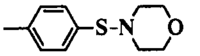

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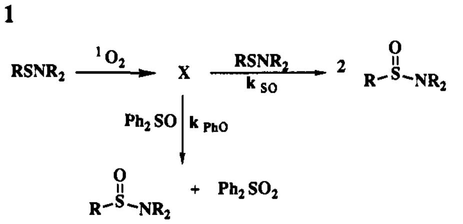
The total rate constants, k_T, which represent a composite of all chemical, k_r, and physical, k_q, channels of singlet oxygen deactivation by sulfenamides **1**, **2**, and **4** were measured in benzene by monitoring their ability to quench singlet oxygen emission at 1270 nm.[8,9] The k_T values for **1** (1.28×10^6 M^{-1} s^{-1}), **2** (3.55×10^6 M^{-1} s^{-1}), and **4** (1.96×10^6 M^{-1} s^{-1}) are approximately 10 times smaller than the k_T value for diethyl sulfide (1.71×10^7 M^{-1} s^{-1})[10,11] and 2–10, times larger than the k_T value for dimethyl disulfide (4.26×10^5 M^{-1} s^{-1} in acetone and 5.18×10^5 M^{-1} s^{-1} in benzene).[6]

Scheme 1



$$RSNR_2 \xrightarrow{^1O_2} X \xrightarrow[k_{SO}]{RSNR_2} 2\ R\text{-}S(=O)\text{-}NR_2$$

$$X \xrightarrow[k_{PhO}]{Ph_2SO} R\text{-}S(=O)\text{-}NR_2 + Ph_2SO_2$$

The chemical rate constant, k_r, for the reaction of **1** (2.94×10^6 M^{-1} s^{-1}) was also measured in benzene in competition with adamantaneadamantylidene ($k_T = 3.49 \times 10^5$ M^{-1} s^{-1}) and octalin ($k_T = 1.84 \times 10^6$ M^{-1} s^{-1}) by the method of Higgins and Foote.[12] This k_r value is approximately twice as large as the k_T value measured for **1** ($k_r = 2k_T$), exactly as one would anticipate if physical quenching were not occurring (i.e., two molecules of sulfinamide form for every singlet oxygen molecule that disappears). In comparison, k_r for diethyl sulfide is less than 5%[13] and k_r for dimethyl disulfide is less than 7% of their respective k_T values. *It is remarkable that molecules which are part amine and part sulfide, both notorious physical quenchers of singlet oxygen, have no physical quenching component.*[14,15]

Cophotooxidation of sulfenamide **1** with diphenyl sulfoxide (Ph_2SO) in benzene resulted in addition to the expected sulfinamide, formation of diphenyl sulfone (Ph_2SO_2). At the concentrations of Ph_2SO used in these experiments, trapping of an intermediate formed between $^1O_2$ and **1** rather than direct photooxidation is responsible for the formation of the sulfone. When **1** and Ph_2SO compete for a common intermediate as shown in Scheme 1, steady-state treatment of intermediate **X** gives eq 1, which predicts that a plot of $[1SO]/[Ph_2SO_2]$ versus $1/[Ph_2SO]$ should be linear with a slope *dependent* upon the concentration of **1**.

$$[1SO]/[Ph_2SO_2] = 1 + 2k_{SO}[1]/k_{PhO}[Ph_2SO] \quad (1)$$

Examination of the experimental data presented in Figure 1, however, demonstrates that the slope is independent of the concentration of **1**. This *insensitivity* of the slope to changing concentrations of **1** is not consistent with a direct competition between **1** and Ph_2SO for a common intermediate and is reminiscent of the behavior reported for diethyl sulfide.[13] The experimental data, however, can be accommodated within a mechanism in which **1** and Ph_2SO do not compete for a common intermediate, as depicted in Scheme 2. Steady-state treatment of this alternative mechanism, which invokes two intermediates, gives eq 2. The value of k_Y/k_{PhO} derived from eq 2 and the data

$$[1SO]/[Ph_2SO_2] = 1 + 2k_Y/k_{PhO}[Ph_2SO] \quad (2)$$

presented in Figure 1 (0.068) is 3 times larger than the same value derived in the photooxidation of Et_2S.[13] Since k_{PhO} is likely to be the same in the two reactions, the larger value reflects the more rapid interconversion to intermediate Y of the persulfinamide in comparison to the persulfoxide. It is tempting to suggest that this provides evidence that Y is the three-membered ring

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[14] Épshtein and co-workers have noted a similar phenomenon during a study of the hydrogen-bonding ability of sulfenamides and pointed out, "the adjacency of two identical or different heteroatoms results in complicated electronic interactions which appreciably changes the donor properties of a bidentate base relative to a monodentate one". Épshtein, L. M.; Zhdanova, A. N.; Khazanova, Y. A.; Fel'dshtein, M. S.; Kazitsyna, L. A. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1974**, 87–89.

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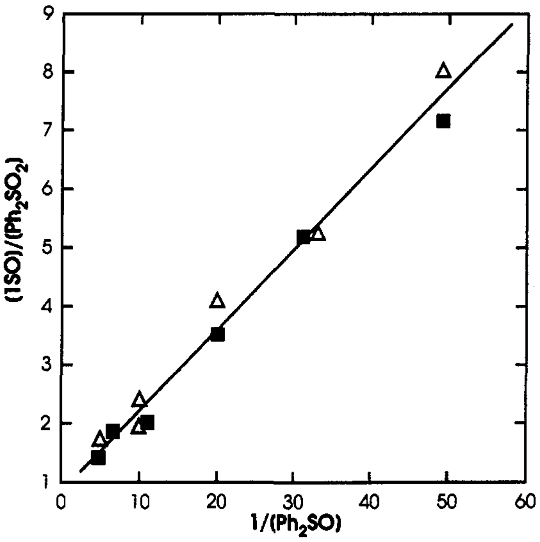
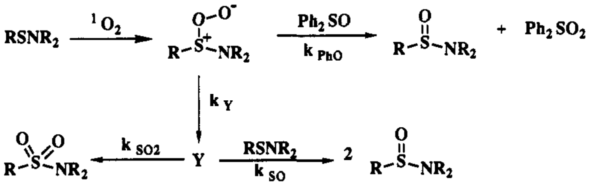


Figure 1. Diphenyl sulfoxide (Ph_2SO) trapping in benzene as a function of the concentrations of **1** and Ph_2SO. ■, [**1**] = 0.1 M; △, [**1**] = 0.2 M. Slope = 0.136.

Scheme 2



thiadioxirane since the larger value reflects the greater stability of **Y** formed in the reaction of **1**, a result which is expected given the greater electronegativity of nitrogen in comparison to carbon.[16] Consistent with this suggestion is the observation that the addition of a 40-fold excess of norbornene resulted in formation of a small amount of norbornene oxide.[17-19]

In contrast to the results in benzene, the slope of a similar plot in methanol (Figure 2) is a function of [**1**] as predicted by eq 1. The *sensitivity* of the slope to the concentrations of **1** is consistent with direct competition between **1** and Ph_2SO for a common intermediate, as depicted in Scheme 1. The value of k_{SO}/k_{PhO} (1.03 ± 0.16) is considerably smaller than the value derived in the photooxidation of Et_2S (2.77 ± 0.5), which we suggest reflects the greater nucleophilicity of Et_2S in comparison to **1**.[20] The difference in nucelophilicity is undoubtably also responsible for the smaller k_T value for the photooxidation of **1** in comparison to the value reported for Et_2S (vide supra).

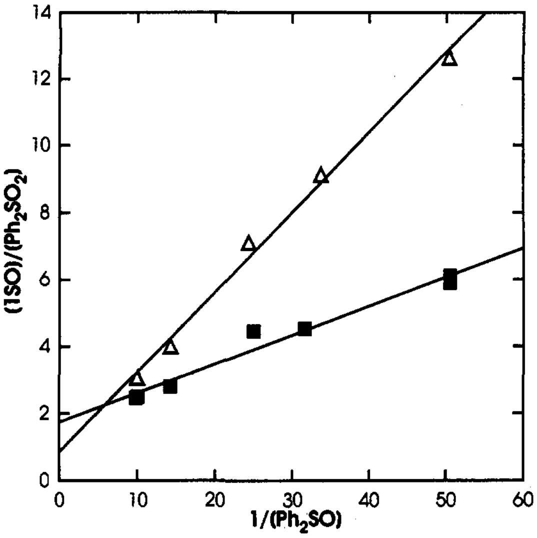
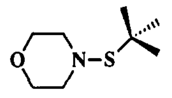


Figure 2. Diphenyl sulfoxide (Ph_2SO) trapping in methanol as a function of the concentrations of **1** and Ph_2SO. ■, [**1**] = 0.05 M, slope = 0.087; △ [**1**] = 0.1 M, slope = 0.238.

The nucleophilicities of the sulfenamides can be sterically modified. For example photooxidation of the sterically encumbered sulfenamide, 4-morpholinyl *tert*-butyl sulfide (**6**),[21] resulted in formation of approximately 10% of the unexpected sulfonamide. Apparently, the steric depression of the magnitude of k_{SO} (Scheme 2) allows the unimolecular decomposition of **Y**, k_{SO_2}, to effectively compete.



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In conclusion, sulfenamides are the first examples of sulfur-containing photooxidation substrates which do not physically quench singlet oxygen. The lack of physical quenching can in part be explained by the rapid competing conversion, k_Y, of the persulfinamide to an azathiadioxirane. Additional studies to examine the scope of this reaction are in progress and will be reported in the near future.

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