Photooxidation of 1,5-Dithiacyclooctane. A Novel C–S Bond Cleavage

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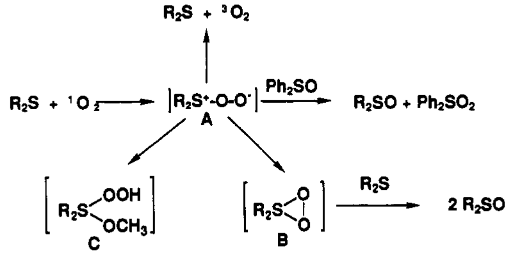
Abstract: Sensitized photooxidation of 1,5-dithiacyclooctane (1,5-DTCO) has been investigated in various solvents. At high conversions, a novel C–S bond cleavage occurs. Significant solvent effects are also observed. At high concentration (0.05–0.1 M) in methanol, more than 90% of the corresponding monosulfoxide and a mixture of *cis*- and *trans*-bissulfoxides are produced. In aprotic solvents (benzene, chloroform, acetone, and acetonitrile), novel cleavage products (1,2-dithiolane 1-oxide, 1,2-dithiolane 1,1-dioxide, and acrolein) were obtained in addition to the monosulfoxide and bissulfoxides. The cleavage products derive mostly from reaction of the primary monosulfoxide (1,5-DTCO 1-oxide) with singlet oxygen. Unstable compounds oxidized α to the sulfur atom were detected by NMR spectroscopy and shown to be intermediate in the formation of the cleavage products.

Introduction

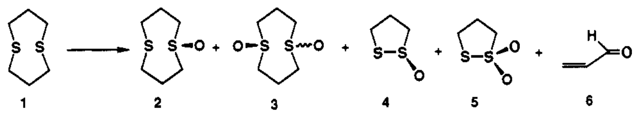
Many sulfur-containing compounds are present in natural biological systems and some play key roles in the activity of some enzymes.[1,2] These enzymes are often deactivated by active oxygen species. For example, the photooxygenation of methionine causes deactivation of several important enzymes.[3,4] The reactions of sulfur with oxygen are very complex because of the number of oxidation states of sulfur, which can lead to a wide variety of intermediates and products. The photooxidation of simple sulfides was first reported by Schenck and Krauch.[5] Since then, reactions of singlet oxygen with a wide variety of sulfur-containing substances have been investigated.[4,6–20]

Several reactive intermediates have been proposed for this reaction. Liang et al. showed kinetically that there are two intermediates in the singlet oxygen reaction of sulfides in aprotic solvents (Scheme I).[8] One of these intermediates has been shown to be nucleophilic[11] and the other to be electrophilic.[17] Although their structures are not certain, these two intermediates have been suggested to be a "persulfoxide", A, and a thiadioxirane, B, respectively. The initially-formed nucleophilic persulfoxide (A) can react with an electrophile, collapse to sulfide and triplet oxygen, or rearrange to form the electrophilic thiadioxirane intermediate (B), which reacts with a nucleophile.

Scheme I



Scheme II



In protic solvents, only one intermediate can be detected, and no loss to ground-state oxygen occurs. Alternative explanations are that the zwitterionic intermediate (A) can be stabilized by the solvent through hydrogen bonding or by the addition of solvent to form a tetravalent sulfurane (C). Intermolecular trapping experiments have provided strong support for the latter suggestion.[14,16] Detailed kinetic studies and trapping experiments[7,8,17] and low-temperature matrix-isolated FT-IR spectroscopy of sulfide–oxygen adducts[21] support the suggestion that the zwitterionic persulfoxide is the primary intermediate in sensitized sulfide photooxidations. Theoretical calculations also support this structure.[9,22]

We chose 1,5-dithiacyclooctane (1,5-DTCO) for study because it has unique and interesting properties, including a remarkably low oxidation potential.[23] We thought that the ability of this sulfide to form a very stable radical cation involving intramolecular transannular interactions might shed light on some of the current mechanistic questions.

Results

Photooxidation of 1,5-Dithiacyclooctane (1). A solution of 1,5-DTCO (1) and tetraphenylporphine (TPP) sensitizer in $CDCl_3$ was irradiated at room temperature. Oxygen was bubbled continuously through the solution during photolysis, and a small amount of pyridine-d_5 was added to prevent dye bleaching. The reaction was monitored by NMR spectroscopy at various times.

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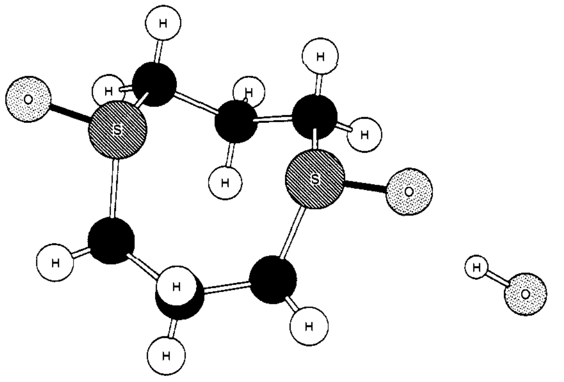


Figure 1. X-ray crystal structure of *cis*-bissulfoxide **3**.

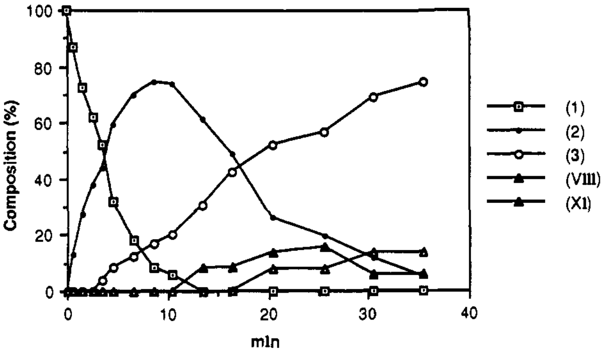


Figure 2. Time course of photooxidation of 1,5-DTCO (0.1 M 1,5-DTCO in $CDCl_3$, 5×10^{-5} M TPP as sensitizer).

Monosulfoxide (1,5-DTCO 1-oxide, **2**) is the primary product, which is converted on further irradiation to a mixture of *cis*- and *trans*-bissulfoxides (1,5-DTCO 1,5-dioxide, **3**) containing approximately 86% of the cis isomer, as determined by the relative peak heights of these isomers in the ^{13}C NMR spectrum. The major isomer was shown to be cis by X-ray crystal structure determination. The structure of this compound is shown in Figure 1.

In addition to these products, 1,2-dithiolane oxide and dioxide (**4** and **5**) were formed at later times, isolated by column chromatography (Scheme II), and identified by their spectral data and by comparison with authentic samples which were independently synthesized. Acrolein (**6**) was identified by comparison of its NMR spectral data and GC retention time with those of an authentic sample.

Control experiments showed that no reaction took place in the absence of light or sensitizer, and the addition of DABCO, a singlet oxygen quencher, inhibited the oxidation of **1** and **2**. These data indicate that the reaction of both compounds is with singlet oxygen.

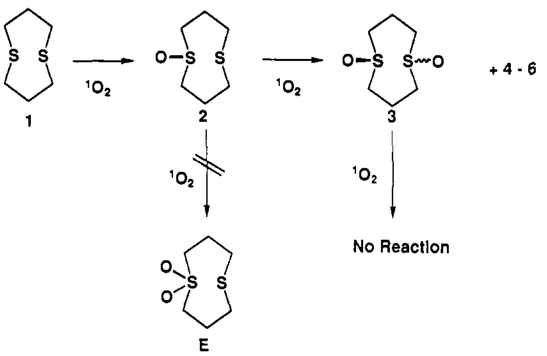
The starting material is consumed very rapidly to form the corresponding monosulfoxide **2** as primary product. This primary product then continues to react with singlet oxygen to form secondary products. The time course of the reaction followed by NMR spectroscopy is shown in Figure 2. The bissulfoxide mixture appears to be formed largely from oxidation of the monosulfoxide, as shown by the delayed appearance of **3** in Figure 2. Smaller amounts of compounds **4** and **5** were formed at the same time (not shown in Figure 2). A GC/MS spectrum of the crude reaction mixture showed that, in addition to compounds **2–6**, another peak with parent mass at 106 appeared right after the solvent. The GC retention time of freshly prepared 1,2-dithiolane matches that of this product.

Table I. Product Formation as a Function of Solvent[a]

solvent	% C–S cleavage[d]
C_6D_6[b]	>45
$CDCl_3$[b]	26
CD_3COCD_3[c]	28
CD_3OD[c]	<5

[a] Photooxidation of 0.1 M DTCO in indicated solvent. [b] Tetraphenylporphine sensitizer (5×10^{-5} M). [c] Rose bengal sensitizer (5×10^{-5} M). [d] **4** + **5** + **6**, total products.

Scheme III



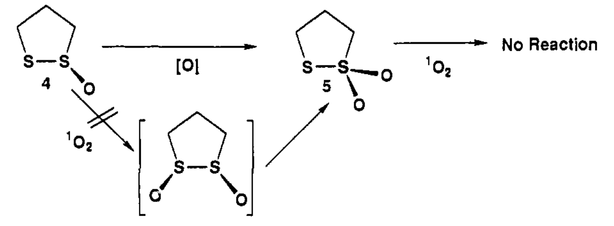
When the starting material had nearly disappeared, a weak peak absorbing at 5.25 ppm (dd, J = 10.7, 4.6 Hz) in the NMR scale started to appear (compound III, not shown in Figure 2). This peak disappeared very quickly and was replaced by a similar peak at 4.95 ppm (dd, J = 10.7, 4.6 Hz) (compound VIII in Figure 2). Attempts to isolate these intermediates failed. However, a ^{13}C NMR spectrum taken at this stage showed that, in addition to the peaks from monosulfoxide and bissulfoxides, six new carbon peaks were present at 88.2, 51.5, 51.2, 25.6, 24.8, and 24.2 ppm. ^1H NMR decoupling experiments show that the peak at 4.95 ppm is coupled to peaks at 2.36–2.45 ppm and the latter group to peaks at 3.25–3.35 ppm. From these spectral data, the intermediate is assigned structure VIII. As photolysis continues, the intermediate peak at 4.95 ppm grows more intense, and a new aldehyde peak starts to appear at 9.8 ppm (compound XI in Figure 2). This compound could also not be isolated.

Photolysis was stopped when the spectrum did not change with further irradiation. The ^{13}C NMR spectrum showed that the monosulfoxide was no longer present and that the bissulfoxide mixture was the major product at this stage, along with smaller peaks for the labile intermediates. The reaction mixtures were left at room temperature for several days and monitored by NMR spectroscopy. During this time, the peak at 9.8 ppm gradually disappeared and a new aldehyde peak at 9.52 ppm (d, J = 7.3 Hz) appeared, accompanied by olefin peaks at 6.43 ppm (dd, J = 9.7, 1.1 Hz), 6.32 ppm (ddd, J = 17.1, 9.7, 7.3 Hz), and 6.24 ppm (dd, J = 17.1, 1.1 Hz). The compound responsible for the latter peaks was shown to be acrolein (**6**) by comparison with NMR spectra and gas chromatographic retention times of an authentic sample. In addition, the intensities of these NMR resonances increased when authentic acrolein was added to the reaction mixture. The formation of acrolein was also accompanied by the formation of a water peak in the NMR spectrum.

Very similar results were obtained by running the reactions in various aprotic solvents (benzene, acetone, and acetonitrile); more cleavage products were formed in the less polar aprotic solvents (Table I). However, no cleavage products were formed in methanol. The ^{13}C NMR spectrum indicated that the monosulfoxide and the bissulfoxide mixture were the two major products in this solvent. The photooxygenation of 1,5-DTCO or 1,5-DTCO 1-oxide in acetone at low temperature (−78 °C) gave only monosulfoxide and bissulfoxide as oxidation products, and no cleavage products were observable.

Photooxidation of Monosulfoxide (2) and Bissulfoxide (3). The following experiments were carried out in order to establish whether the cleavage products were coming from the oxidation of 1,5-DTCO (**1**) at low concentration or from the oxidation products (1,5-DTCO 1-oxide (**2**) or 1,5-DTCO 1,5-dioxide (**3**)). A 0.1 M solution of each component was irradiated separately under similar conditions in various deuterated solvents, and the reactions were monitored by ^1H NMR and ^{13}C NMR spectroscopy. The bissulfoxide mixture (**3**) was not oxidized further under these conditions. However, a product mixture very similar to that

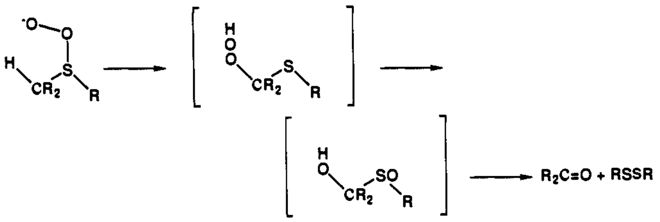
Scheme IV



from 1,5-DTCO was observed when monosulfoxide **2** was photooxidized in various solvents. The 1,5-DTCO 1,5-dioxide mixture (**3**) was the only S-oxidative product from 1,5-DTCO or 1,5-DTCO 1-oxide, and no 1,5-DTCO 1,1-dioxide (sulfone, E) was observed (Scheme III). These results confirm that the bissulfoxide mixture is largely a secondary product and that C–S cleavage results mainly from photooxidation of the monosulfoxide.

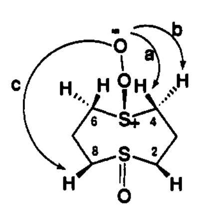
Photooxidation of 1,2-Dithiolane 1-Oxide (4) and 1,2-Dithiolane 1,1-Dioxide (5). Because 1,2-dithiolane 1,1-dioxide (**5**) was obtained when the reaction mixtures were separated by column chromatography, it was necessary to understand the origin of this compound. One possible route to its formation might be via an intermediate 1,2-dioxide[24,25] (Scheme IV). However, when 1,2-dithiolane 1-oxide (**4**) was separately prepared and subjected to irradiation under similar conditions to 1,5-DTCO, no observable dioxide (**5**) was produced; 1,2-dithiolane 1,1-dioxide (**5**) was also inert to singlet oxygenation. These results rule out the possibility that **5** is formed directly from **4** by singlet oxygenation or that the cleavage product acrolein derives from further oxidation of compound **4** or **5** with singlet oxygen, and they suggest that the 1,5-DTCO 1-oxide is the main compound responsible for the formation of the C–S cleavage products. These results suggest that **5** is formed by oxidation of **4** by an intermediate in the oxidation of **1** or **2**, such as a persulfoxide. However since the 1,2-dioxide is known to be unstable and to rearrange to **5**,[24] this compound could also be intermediate in the oxidation.

Photooxidation of 2,2,8,8-Tetradeuterio-1,5-Dithiacyclooctane 1-Oxide. As described above, photooxidation of 1,5-dithiacyclooctane in various aprotic solvents gave two sets of intermediate peaks around 5.2 ppm (dd, J = 10.7, 4.6 Hz) and 5.0 ppm (dd, J = 10.7, 4.6 Hz). These peaks are logically assigned to protons α to sulfur and oxygen in α-hydroperoxy or -hydroxy intermediates formed in a Pummerer-type reaction, which is well known in activated sulfides.[26-28]



Such products could result in principle from abstraction of either of the diastereotopic α-protons of persulfoxide V at the C-4 and C-6 positions (path a or b); alternatively, a product might derive from protons at the C-2 and C-8 positions (path c).

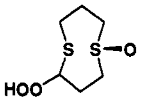
The following experiments were carried out to answer this question. Careful studies of photooxidation of 1,5-DTCO 1-oxide in various aprotic solvents under similar conditions gave only a product with one doublet of doublets around 5.0 ppm. These results suggest that a product with peaks at 5.2 ppm is formed from 1,5-DTCO by α-proton abstraction in persulfoxide I (presumably at low conversions before much sulfoxide is produced) and the product with peaks at 5.0 ppm from the monosulfoxide through persulfoxide V.



(V)

When 2,2,8,8-tetradeuterio-1,5-dithiacyclooctane 1-oxide was oxygenated under similar conditions, the product with peaks around 5.0 ppm was still formed. This result rules out path c, since this would have produced a product with deuterium rather than hydrogen α to the oxygen.

Since only one doublet of doublets at 5.0 ppm is observed, a single diastereomer is produced, which implies that path a (presumably with removal of the cis α-proton) probably predominates. The ^{13}C NMR spectrum and ^1H NMR decoupling experiments described above strongly suggest that this intermediate is a α-hydroperoxy sulfoxide (VIII). We have no information on which to base a stereochemical assignment of this diastereomer, but it is probably cis since the *cis*-bissulfoxide predominates in the mixture of **2**.



(VIII)

Trapping of α-Hydroperoxy Sulfide VIII. Since both α-hydroxy sulfoxides and α-hydroperoxy sulfides have been proposed as key intermediates in sulfide α-oxidation by Corey[26] and Ando et al.,[28,29] further studies were carried out. 1,5-DTCO 1-oxide was photooxygenated in $CDCl_3$ until the peaks at 5.0 ppm were maximal, and then a small amount of Ph_3P was added to the reaction mixture. Once the Ph_3P was added, the peak at 5.0 ppm quickly decreased and a similar peak at 4.9 ppm (dd, J = 10.7, 4.6 Hz) started to appear, which was assigned to the α-hydroxy reduction product of the hydroperoxide. This peak also decreased very quickly, and the aldehyde peak at 9.8 ppm increased proportionately.

This result can be rationalized by formation of the zwitterionic persulfoxide intermediate (V) followed by its subsequent Pummerer-type rearrangement[30,31] via α-proton abstraction to α-hydroperoxy sulfide VIII, which can be reduced by Ph_3P to the corresponding α-hydroxy sulfide IX and Ph_3PO. This reaction is in agreement with the results of Ando et al. on photooxidation of thiazolidine derivatives.[28] This resulting α-hydroxy sulfide (IX) decomposes more easily to aldehyde XI than α-hydroperoxy sulfide VIII.

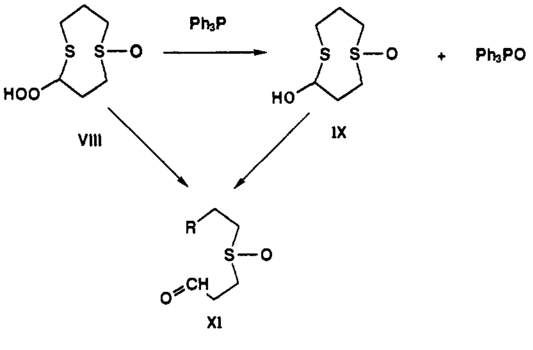


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Table II. Rates of Interaction ($k_r + k_q$) and Reaction (k_r) of Substrates with $^1O_2$ in $CHCl_3$

substrate	$(k_r + k_q)$, $M^{-1}\,s^{-1}$	k_r, $M^{-1}\,s^{-1}$	$k_r/(k_r + k_q)$
1,5-DTCO	$12.4 \times 10^{6\,a}$	$8.2 \times 10^{6\,c}$	0.66
1,5-DTCO 1-oxide	$20.9 \times 10^{4\,a}$	$8.7 \times 10^{4\,d}$	0.42
TME	$27.0 \times 10^{6\,b}$		
2M2P	$75.9 \times 10^{4\,a}$		

[a] This work. [b] Reference 32. [c] Determined by competition with TME at <15% conversion. [d] Determined by competition with 2M2P at <15% conversion.

Direct Determination of Rate Constants of Reaction of 1,5-DTCO and 1,5-DTCO 1-Oxide with $^1O_2$. Measurements of ($k_r + k_q$) (sum of reaction and quenching of $^1O_2$ by substrates) were made by monitoring the effect of added substrates on the observed decay rate of $^1O_2$ as measured by its luminescence at 1270 nm.[32] The measured rate constant of $^1O_2$ decay, k_{obsd}, is described by eq 1, where ($k_r + k_q$) is the total rate constant for $^1O_2$ removal by substrate [S] (the sum of the rate constant for reaction (k_r) and for physical quenching (k_q) by the substrate) and k_d is the rate constant for radiationless decay of $^1O_2$. Plots of k_{obsd} vs [S]

$$k_{obsd} = (k_r + k_q)[S] + k_d \tag{1}$$

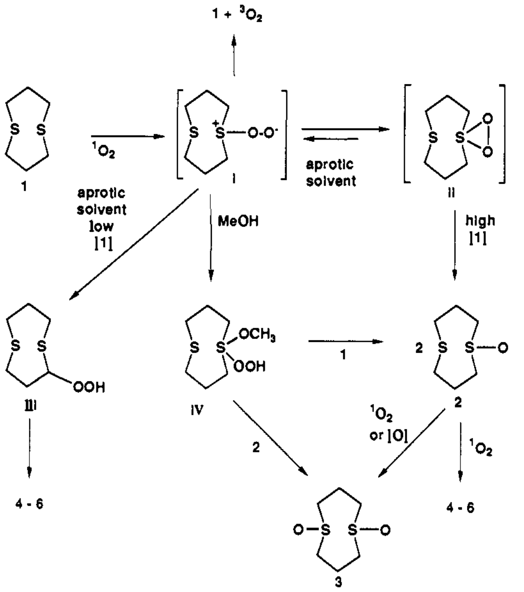
are linear, with slope ($k_r + k_q$) and intercept k_d. The value of k_r for 1,5-DTCO was determined separately by competition with tetramethylethylene (TME) and for 1,5-DTCO 1-oxide (**2**) by competition with 2-methyl-2-pentene (2M2P). These olefins do not quench $^1O_2$, so that $(k_r + k_q) \approx k_r$;[33] ($k_r + k_q$) values for these olefins are determined by direct measurements of $^1O_2$ decay rates. The results are summarized in Table II and are in excellent agreement with values determined by Clennan et al.,[34] except that our values for **2** are 1 order of magnitude lower. However, the solvents used were not the same.

Discussion

The photoelectron spectra (PES) of sulfur heterocycles and DTCO suggest that the lone pairs on the two sulfur atoms of the thioether molecule interact in the ground state.[35-37] Although both through-bond and through-space interactions can occur in principle, there is little possibility for through-bond interactions to occur in 1,5-DTCO. Also, compared to the oxidation potential $E_{1/2} \approx 1.5$ V vs SCE for most sulfides,[38] 1,5-DTCO has an extremely low oxidation potential ($E_{1/2} = 0.68$ V vs SCE in CH_3CN).[39,40] The through-space transannular interactions in the boat-form of 1,5-DTCO must be responsible for its low oxidation potential and high reactivity toward singlet oxygen (Table II). The oxidizing agent (singlet oxygen) could either remove an electron from the HOMO of 1,5-DTCO to form a superoxide radical anion and 1,5-DTCO radical cation ion pair or form a peroxysulfide (I) as an intermediate directly.

The energetics of electron transfer from DTCO to singlet oxygen can be evaluated by using the Weller equation $\Delta G_{et} = 23.1\,[(E_{ox} - E_{red}) - E_{0-0}]$, where E_{ox} and E_{red} are the half-wave potentials for oxidation of DTCO and reduction of the oxygen and E_{0-0} is the excitation energy for singlet oxygen.[41,42] Since the reduction potential of O_2 in CH_3CN is -0.87 V vs SCE and $E_{0-0}(^1O_2) = 1.0$ eV,[43-45] direct electron transfer is endothermic by ~0.5 V. Therefore, the formation of the intermediate peroxysulfide (I) is more likely. Whether or not the resulting peroxysulfide intermediate is also stabilized by a similar transannular interaction is unclear.

Scheme V



Trapping experiments suggest that the dipolar persulfoxide intermediate is a nucleophilic oxidant which will oxidize sulfoxides to sulfones.[6-8,17] Since there is no formation of 1,5-DTCO 1,1-dioxide (E) observed during the photooxidation, it is likely that the persulfoxide intermediate I rearranges rapidly to thiadioxirane II (Scheme V). II would be expected to be electrophilic and react more rapidly with sulfides than with sulfoxides.[8] In aprotic solvent and at high concentrations of **1**, the thiadioxirane reacts with another mole of **1** to form two molecules of monosulfoxide or with another monosulfoxide to form one molecule of bissulfoxide and one molecule of monosulfoxide. At low concentrations of **1**, formation of an α-hydroperoxy sulfide (III) by Pummerer-type rearrangement of the persulfoxide via abstraction of an α-proton occurs, and this is a precursor of the cleavage products. However, this reaction is not very efficient, since the main product is always monosulfoxide **2** and very little of the Pummerer product peak at 5.2 ppm (III) is formed. Methanol probably adds to the persulfoxide to form the tetravalent sulfurane (IV), as it does with other sulfides. These intermediates are powerful oxidants for sulfur and do not lead to side products. This is consistent with the fact that none of the cleavage products are formed in methanol.

That only one diastereoisomer of intermediate VIII is formed via Pummerer-type rearrangement of persulfoxide (V) suggests that only one diastereoisomer of V is formed (presumably with the O–O group cis to the sulfoxide). The fact that *cis*-bissulfoxide was the major S-oxidative product also suggests that only one conformation of the monosulfoxide reacts.

When most of the 1,5-DTCO is consumed, the subsequent reaction of the monosulfoxide (**2**) with singlet oxygen becomes dominant. The reactions at sulfur would be analogous to those shown in Scheme V. In comparison with 1,5-DTCO, **2** has relatively low reactivity toward $^1O_2$ (100 times slower than 1,5-DTCO (Table II) and about 10-fold slower than ordinary sulfides).[38] Therefore, the bissulfoxide (**3**) is formed almost entirely from the monosulfoxide. Some of **3** is probably also formed by oxidation of **2** by persulfoxides, as is well known in other cases. Presumably 1,5-DTCO is also more reactive toward these intermediates as well, but we cannot evaluate the relative contributions of various

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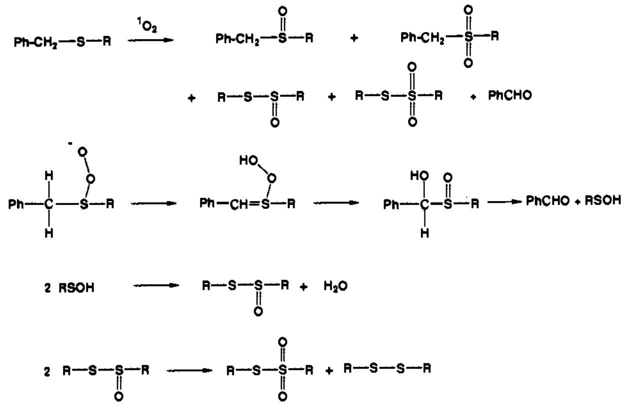
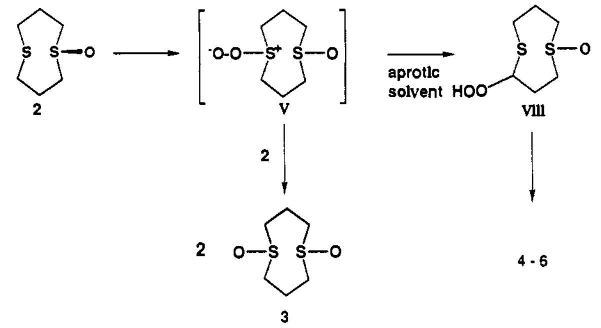
Scheme VI

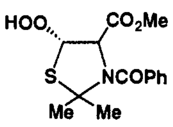


pathways without further experimentation, since the number of possible reactions is very high.

Since sulfoxides are very unreactive toward singlet oxygen, the reactive site in the monosulfoxide is the unreacted sulfide, forming a second persulfoxide (V). In this intermediate, Pummerer-type rearrangement of V to give α-hydroperoxy sulfide VIII competes efficiently with C–S oxidation, since only the relatively unreactive monosulfoxide is present, no intramolecular reaction is possible, and DTCO has been consumed. The observation of C–S bond cleavage in singlet oxygenation of benzylic sulfides was first made by Corey et al. (Scheme VI).[26]



Ando et al. have studied the photooxidation of 9-(ethylthio)-fluorene and suggested the formation of an intermediate α-hydroperoxy sulfide on the basis of the product analysis.[29] Also, singlet oxygenation of a series of thiazolidine derivatives has been reported by Ando et al.[12,28] They found that the α-hydroperoxythiazolidine D is stable at 0 °C and capable of oxidizing sulfides and phosphines to give the corresponding sulfoxides and phosphine oxides.



(D)

Studies by Ando et al. revealed that only five-membered-ring sulfides afforded C–S bond cleavage products.[46] Six- and seven-membered-ring sulfides as well as diethyl sulfide gave only corresponding sulfoxides and sulfones as sensitized photooxidation products, and no fragmentation products were observed.

The α-hydroperoxy sulfide VIII is an oxidizing species which can intermolecularly oxidize another monosulfoxide (**2**) to form **3** and α-hydroxy sulfide IX or undergo intramolecular oxidation to form α-hydroxy sulfoxide X as product. Ring opening of the thiohemiacetal compounds IX and X will form aldehydes XI and XII, respectively, as C–S cleavage products (Scheme VII).

The aldehydes XI and XII then cleave to form sulfenic acids and acrolein. Loss of water from the sulfenic acids produces 1,2-dithiolane (**8**) and 1,2-dithiolane 1-oxide (**4**), respectively. Further oxidation of 1,2-dithiolane will form **4** and 1,2-dithiolane 1,1-dioxide (**5**). The fact that photooxygenation of 1,5-DTCO or 1,5-DTCO 1-oxide in acetone at low temperature (−78 °C) gave no cleavage products was also observed by Clennan et al.[34] and suggests that the Pummerer rearrangement has a larger activation energy than the sulfide oxidation.

Conclusion

Two competing reactions, S-oxidation and C–S bond cleavage, occur in the sensitized photooxygenation of 1,5-DTCO and 1,5-DTCO 1-oxide. The S-oxidation results in the formation of monosulfoxide (**2**) and bissulfoxides (**3**) as products. The C–S bond cleavage forms the fragmentation products acrolein, 1,2-dithiolane 1-oxide, and 1,2-dithiolane 1,1-dioxide. These products derive from α-oxidation products, which are detected as intermediates.

This is the first example of this novel C–S cleavage reaction in photooxidation of cyclic bissulfide compounds. Because 1,5-DTCO does not have acidic hydrogens and photooxidation of 1,4-dithiane or 1,3-dithiane does not give any cleavage products,[19,20] this unique C–S bond cleavage of 1,5-dithiacyclooctane may be caused by a transannular interaction between the two mesocyclic sulfur atoms in the intermediate, although this is highly speculative.

In dithioethers with three or four methylene groups separating the two sulfur atoms, an intense peak corresponding to 1,2-dithiane or 1,2-dithiolane cation radicals is always found as the base peak in the mass spectrum.[47] Also, a terminal methyl group in acyclic dithioethers is often lost when S–S bond formation leads to a five- or six-membered ring.[47] These reactions provide precedence for the formation of acrolein and 1,2-dithiolane and 1,2-dithiolane 1-oxide from intermediates XI and XII.

The results reported here agree well with those of Clennan et al.,[34] who are concerned more with primary steps in the reaction of 1,5-DTCO than with the subsequent steps reported here.

Experimental Section

General. Melting points (uncorrected) were obtained on a Büchi capillary melting point apparatus. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AF-200, AM-360, and AM-500 spectrometers. ^{13}C NMR spectra were taken with the solvent peak as reference. Chemical shift values are in ppm downfield from internal tetramethylsilane in the indicated deuterated solvent. EI mass spectra were recorded on an AEI MS-902 instrument. Ultraviolet-visible spectra were recorded on a Beckman Model 25 spectrophotometer. Infrared spectra were taken on a Perkin-Elmer PE 580 spectrometer and FT-IR on a Perkin-Elmer 1600 instrument. Samples were prepared either neat on NaCl plates or as KBr pellets. Thin-layer chromatograms were obtained using either DC-Fertigplatten Kieselgel 60 F_{254} or DC-Plastikfolien Kieselgel 60 F_{254} from E. Merck. Column chromatography was performed on silica gel 60, 70–230 mesh or 230–400 mesh (flash column), from E. Merck, and on neutral alumina, activity I, from Fisher.

Materials. Commercial solvents were Fisher AR and used without further purification. 3-Chloroperoxybenzoic acid (80–85%), sodium deuterioxide (40 wt %), 1,3-propanedithiol (99%), and 1,3-dibromopropane (98%) were from Aldrich. Deuterated solvents were from Cambridge Isotope Laboratory and were dried over 4-Å molecular sieves before use. Potassium iodide was from Fisher and hydrogen peroxide (30%) was from Mallinckrodt. 5,10,15,20-Tetraphenyl-21*H*,23*H*-porphine (TPP) and rose bengal were also from Aldrich and used as received.

General Photolysis Procedure. Photolyses were carried out in 5-mm NMR tubes with 0.1–0.05 M substrates in 0.5 mL of deuterated solvents. A Cermax 300-W Xenon lamp powered at 14 V, 20 A was the light source. A 1% potassium dichromate filter solution was used to cut off wavelengths below 500 nm. The NMR tubes were immersed in a water bath at room temperature, and a running water filter 18 cm in length was put in front of the sample tube to eliminate the heating of solutions. TPP (5×10^{-5}) was the sensitizer in benzene-d_6 and chloroform-d. Rose bengal (5×10^{-5}) was the sensitizer in methanol-d_4, acetone-d_6, and acetonitrile-d_3. Oxygen was continuously bubbled through the solution during irradiation, and 50 μL of pyridine-d_5 was added to prevent dye bleaching. The reaction progress was monitored by NMR spectroscopy.

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Direct Determination of Singlet Oxygen Quenching Rate ($k_r + k_q$) by Substrates. The rates of interaction ($k_r + k_q$) of 1,5-DTCO and 1,5-DTCO 1-oxide were determined by time-resolved studies of singlet oxygen luminescence at 1270 nm. The basic laser flash system has been described elsewhere.[32] Sensitizing dyes were excited with either the second (532 nm) or third (355 nm) harmonic of a Quanta-Ray (DCR-1) Nd:YAG laser. A Schott KG-3 filter removed any residual fundamental radiation at 1064 nm ($T = 10^{-4}$ at 1064 nm, $T = 0.9$ at 532 nm, $T = 0.8$ at 355 nm). The near-infrared emission from $^1O_2$ was monitored at the right angle to the laser beam and filtered with Schott RG-850 and Silicon 1100 nm (Infrared Optics) cut-off filters. A diode (25 mm^2, Judson Infrared, Inc.) was used with preamplifiers (UCLA Chemistry Department Electronic Shop) whose rise times were sufficient to measure the fastest transients observed. The diode, all amplification stages, and impedance matching stages were powered by two Hewlett-Packard 6215-A power supplies maintained at ±15 V. The signal was averaged (15–20 shots) in a transient digitizer (Analogic Data 6000) and then transferred to a Macintosh IIci computer using Labview software.

Determination of the Reaction Rate (k_r) of the Substrates with Singlet Oxygen. The value of k_r for 1,5-DTCO was determined by competition with tetramethylethylene (TME) and for 1,5-DTCO 1-oxide by competition with 2-methyl-2-pentene (2M2P). In both cases, the relative rates were determined by measuring the relative product formation at low conversion (<15%). The appearance of the products was monitored by NMR spectroscopy.

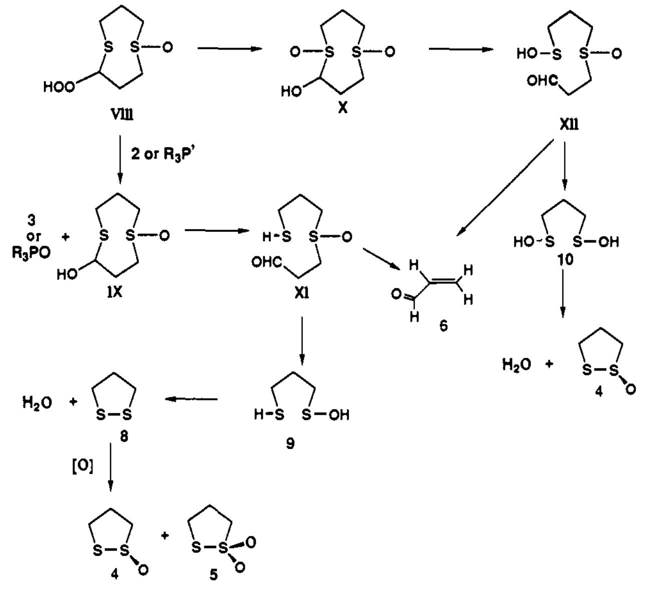
Because olefins do not quench $^1O_2$, both ($k_r + k_q$) and k_r values are often used as measures of relative olefin reactivity.[33] By assuming $k_q \ll k_r$ for TME and 2M2P, $(k_r + k_q) \approx k_r$ values of TME and 2M2P were determined by direct measurements with the laser apparatus. Reaction rates (k_r) of 1,5-DTCO and 1,5-DTCO 1-oxide were determined by competition experiments with the olefin of comparable reactivity.

X-ray Determination of Compound 3. A crystal of approximate dimensions 0.40 × 0.25 × 0.2 mm was glued to the tip of a glass fiber and mounted on a modified Picker four circle diffractometer equipped with a gas-stream low-temperature device and graphite-monochromatized Mo source. Accurate unit cell parameters and orientation matrix are obtained by a least-squares fit to the automatically centered settings of 20 reflections and are given in the supplementary material together with other details. The diffraction data were collected with a $\theta/2-\theta$ scan mode up to a maximum $2-\theta$ of 50° at low temperature (128 K). Three standard reflections were monitored for every 97 reflections collected and showed no significant variations throughout the data collection. Intensities were derived from an analysis of scan profiles.[48] The data were corrected for Lorentz and polarization effects. A psi-scan procedure was used for an empirical absorption correction.

The structures were solved in the orthorhombic space group *Pnab* by direct methods of SHELX86, which revealed the positions of all non-hydrogen atoms. This was followed by several cycles of full-matrix least-squares refinement. Hydrogen atoms were included as fixed contributors to the final refinement cycles. The positions of hydrogen atoms were calculated on the basis of idealized geometry and bond length (C–H = 1.00 Å). In the final cycles of least-squares refinement, all non-hydrogen atoms were refined with anisotropic thermal coefficients. Convergence resulted in final agreement factors of $R = 0.032$ and $R_w = 0.046$.

Preparation of 1,5-Dithiacyclooctane (1,5-DTCO). 1,3-Propanedithiol (27.06 g, 0.25 mol) was added to a sodium *n*-butoxide solution, which was generated and maintained under helium by dissolving 12.65 g of sodium in 0.5 L of butanol. The solution was equilibrated for 1 h and then cooled to 0 °C, and 50.5 g (0.25 mol) of 1,3-dibromopropane was added all at once. The reaction mixture was stirred below 10 °C for 2 h and then at 21 °C for an additional 18 h. The solution was filtered and the filtrate concentrated under vacuum to give an oily residue. Product was concentrated by combining the residues with five 100-mL ether extracts of the filtercake. This solution was washed three times with 150 mL of 10% potassium hydroxide, dried over anhydrous sodium sulfate, and reconcentrated. Fractional distillation under reduced pressure (1 Torr, 87–89 °C) gave 3.26 g of 1,5-DTCO: ^{1}H NMR (δ, ppm, $CDCl_3$) 1.93–2.05 (br, m, 4 H), 2.70–2.80 (br m, 8 H) [lit.[39] δ 2.1 (m, 4, CH_2), 2.8 (m, 8, CH_2S)]; ^{13}C NMR (δ, ppm, $CDCl_3$) 29.99, 30.59; IR (NaCl, cm^{-1}) 2900, 2840, 1430, 1410, 1340, 1270, 1190, 1060, 920.

Scheme VII



Preparation of 1,5-Dithiacyclooctane 1-Oxide and 1,5-Dithiacyclooctane 1,5-Dioxide. Five grams (25 mmol) of 85% *m*-chloroperbenzoic acid in 120 mL of chloroform was added slowly to a rapidly stirring solution of 2.52 g (17.1 mmol) of 1,5-dithiacyclooctane in 120 mL of chloroform maintained in a CCl_4/CO_2 bath (−23 °C) under nitrogen. The solution was stirred for 45 min at −23 °C and then allowed to warm to 20 °C for an additional 60 min. Anhydrous ammonia was bubbled into the reaction mixture. The mixture became cloudy immediately, and ammonium *m*-chlorobenzoate precipitated. The mixture was filtered through a bed of Celite, bubbled once more with ammonia, and filtered. The filtrate was concentrated under reduced pressure to give a yellow oil. The reaction mixture was separated on a silica gel column, changing eluent gradually from 20% MeOH in EtOAc to 50% MeOH in EtOAc, to give 1.16 g of very hygroscopic 1,5-dithiacyclooctane 1-oxide and 0.66 g of 1,5-dithiacyclooctane 1,5-dioxide. 1,5-DTCO 1-oxide: mp 27–29 °C; ^{1}H NMR (δ, ppm, $CDCl_3$) 2.09–2.16 (m, 2 H), 2.47–2.63 (m, 4 H), 2.21–2.29 (m, 2 H), 3.09–3.03 (m, 4 H) [lit.[39] δ 2.25 (m, 4, CH_2), 2.65 (m, 4, CH_2S), 3.15 (m, 4, $CH_2S{=}O$)]; ^{13}C NMR (δ, ppm, $CDCl_3$) 53.1, 30.5, 24.2; IR (NaCl, cm^{-1}) 2920, 1640, 1430, 1260, 1000. 1,5-DTCO 1,1-dioxide: mp 151–152 °C; ^{1}H NMR (δ, ppm, $CDCl_3$) 2.13–2.21 (m, 2 H), 2.41–2.60 (m, 2 H), 2.97–3.04 (m, 4 H), 3.14–3.22 (m, 4 H); [lit.[49] δ 2.60 (m, 4, CH_2), 3.33 (m, 8, $CH_2S{=}O$)]; ^{13}C NMR (δ, ppm, $CDCl_3$) 13.74, 49.59.

Preparation of 1,2-Dithiolane. 1,3-Propanedithiol (5.0 g, 0.046 mol) was added to a stirred solution of 22.1 g (0.05 mol) of lead acetate in 50 mL of water. After 30 min, the yellow precipitate was filtered to give a nearly quantitative yield of lead 1,3-propanedithiolate. To a stirred suspension of 5.0 g (0.02 mol) of the lead salt in 100 mL of benzene was added 0.68 g (0.021 mol) of sulfur. After mixing for a few minutes, the yellow mixture turned black, and after 30 min, lead sulfide was filtered off. When the solvent was removed under reduced pressure, 1,2-dithiolane polymerized readily to form a white solid and could not be isolated as a stable monomer. It was kept in benzene solution and used without further purification.

Preparation of 1,2-Dithiolane 1-Oxide. A solution of 1,3-propanedithiol (5.4 g, 0.05 mol) in 100 mL of acetic acid and a solution of H_2O_2 (5.6 mL, 9.0 M, 0.05 mol) in 100 mL of acetic acid were added to a flask containing 0.2 g of KI (1.25 mmol) in 100 mL of acetic acid. The reaction was maintained at 70 °C and protected from light with aluminum foil. The solution was stirred for 1 h, and H_2O_2 (5.6 mL, 9.0 M, 0.05 mol) in 10 mL of acetic acid was added to the reaction mixture. The reaction was kept at 70 °C for another hour and then at room temperature for 2 days. Removal of solvent gave a yellow oil, which was washed with hexane and then extracted three times with 10 mL of ether. Evaporation left 3.7 g of 1,2-dithiolane-1-oxide as an oil. Low-temperature (−78 °C) recrystallization in ether gave a colorless solid which melted readily at room temperature: ^{1}H NMR (δ, ppm, $CDCl_3$) 2.81–2.89 (br m, 3 H), 3.16–3.25 (br m, 1 H), 3.52–3.56 (br m, 1 H),

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(48) All calculations were performed on a VAX 3100 cluster (Department of Chemistry and Biochemistry, University of California at Los Angeles). The programs used in this work included modified versions of the following programs: REDUCE (Broach, Coppens, Becker, and Blessing), peak profiles analysis, Lorentz and polarization corrections; SHELXS-86 (G. M. Sheldrick), package of programs, including direct methods, Patterson methods, and peak search; ORFLS (Busing, Martin, and Leavy), structure factor calculation and full-matrix least-squares refinement; ORFFE (Busing, Edwards, and Hamilton), distance, angle, and error calculation; HYDROGEN (Trueblood), calculation of hydrogen atomic position; ORTEP (Johnson) figure plotting; PUBLIST (Hoel), structure listing. Scattering factors and corrections for anomalous dispersion components: *International Tables for X-ray Crystallography*; Kynoch Press: Birmingham, England, 1974; Vol. 4.

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3.65–3.69 (br m, 1 H); ^{13}C NMR (δ, ppm, CDCl$_3$) 29.80 ($CH_2CH_2CH_2$), 38.18 (SCH_2), 63.36 ($S(O)CH_2$); IR (NaCl, cm^{-1}) 2950, 1440, 1260, 1070 [lit.[50] ^{13}C NMR δ 29.98, 38.28, 63.65; IR (CCl$_4$) ν (SO) = 1090, 1070 cm^{-1}].

Preparation of 1,2-Dithiolane 1,1-Dioxide. Hydrogen peroxide (0.9 mL, 30%, 8 mmol) in 3 mL of acetic acid was added dropwise to the 1,2-dithiolane 1-oxide (1.0 g, 8 mmol) in 100 mL of acetic acid. After the reaction was stirred at room temperature for 24 h, the solvent was removed under reduced pressure. The residue was first washed with hexane and then extracted with three portions of 5 mL of ether. Evaporation left 0.43 g of 1,2-dithiolane 1,1-dioxide: mp 24–26 °C; ^{1}H NMR (δ, ppm, CDCl$_3$) 2.61 (br m, 2 H), 3.42 (t, J = 7.0 Hz, 2 H), 3.72 (t, J = 6.6 Hz, 2 H) [lit.[51] ^{1}H NMR (CDCl$_3$) δ 2.54 (m, 2 H), 3.47 (t, J = 7.0 Hz, 2 H), 3.75 (t, J = 6.5 Hz, 2 H); ^{13}C NMR (δ, ppm, CDCl$_3$) 23.91 ($CH_2CH_2CH_2$), 35.71 (SCH_2), 57.19 ($S(O_2)CH_2$) [lit.[52] ^{13}C NMR δ 24.87, 36.69, 58.17].

Preparation of 2,2,8,8-Tetradeuterio-1,5-dithiacyclooctane 1-Oxide. A solution of 1,5-dithiacyclooctane (50 mg, 0.3 mmol) in 0.5 mL of deuterium oxide was added to a 40% solution of sodium deuterioxide in 1 mL of deuterium oxide (99.8%). After the solution was stirred under a nitrogen atmosphere at 100 °C for 24 h, the solvent was removed under reduced pressure. The mixture was then extracted three times with 2 mL of chloroform. The combined organic phase was dried over anhydrous MgSO$_4$. After removal of the solvent, the residue was separated by alumina column chromatography using chloroform as eluent, affording 43 mg of 2,2,8,8-tetradeuterio-1,5-dithiacyclooctane 1-oxide. The deuterium content was more than 95 atom % as determined by ^{1}H NMR spectroscopy.

Acknowledgment. The authors thank Dr. S. I. Khan for X-ray structure determination. This work was supported by NSF Grant No. CHE89-11916.

Supplementary Material Available: Tables of crystal data, fractional atomic coordinates, isotropic and anisotropic parameters, and bond distances and angles for **3** (5 pages); listing of observed and calculated structure factors (6 pages). Ordering information is given on any current masthead page.

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Comparison of the Photooxidations of 1,5-Dithiacyclooctane, 1,4-Dithiane, and Pentamethylene Sulfide. Another Example of Remote Participation during Photooxidation at Sulfur?

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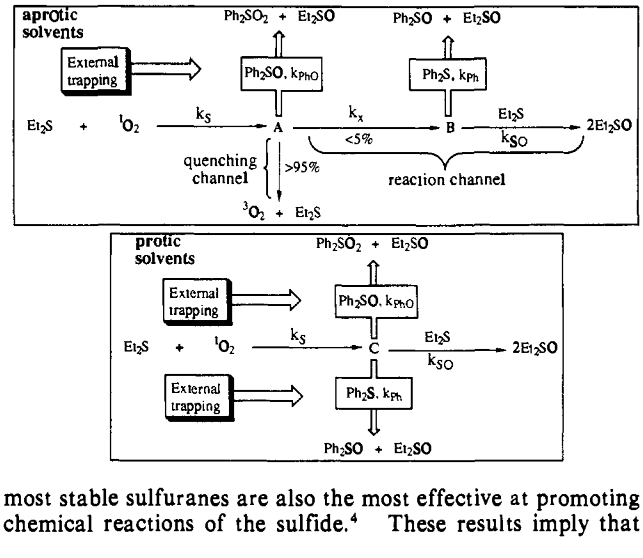
Contribution from the Department of Chemistry, University of Wyoming, Laramie, Wyoming 82071. Received September 11, 1991

Abstract: The photooxidations of 1,5-dithiacyclooctane (1,5-DTCO), 1,4-dithiane, and pentamethylene sulfide have been compared. The photooxidation of 1,5-DTCO differs significantly from the other substrates in several respects: (1) the ratio of chemical quenching to total quenching of singlet oxygen during photooxidation of 1,5-DTCO is 70%, in comparison to 5% for 1,4-dithiane and 2.9% for pentamethylene sulfide; (2) a sulfone is produced in all of the photooxidations except in that of 1,5-DTCO; and (3) the value of k_T is larger for 1,5-DTCO than for any previously reported sulfide. A novel sulfur–sulfur interaction during photooxidation of 1,5-DTCO is utilized in order to explain these results. A *cis*-bissulfoxide was isolated from the photooxidation of 1,5-DTCO. It crystallizes in space group $P\bar{1}$ of the triclinic system with two molecules in a cell of the following dimensions: a = 5.348 (3), b = 6.755 (5), c = 11.677 (7) Å, α = 90.46 (6), β = 97.04 (5), γ = 101.88 (6)°. The structure has been refined to a final value of 0.0477 for the conventional R factor on the basis of 951 independent observed intensities.

The photooxidations of dialkyl sulfides were first reported nearly 30 years ago.[1] In 1983, mechanisms for sulfide photooxidations in protic and aprotic media were suggested that provided explanations for the diverse experimental observations which had been made in this complex system during the previous 21 years.[2] In aprotic solvents, sulfides remove singlet oxygen from solution by both physical and chemical processes (Scheme I). In contrast, in methanol the physical quenching processes are suppressed and the chemical reactions of the sulfides become efficient (Scheme I).

In 1990, Clennan and Yang[3] reported that photooxidations of γ-hydroxy sulfides resulted in the formation of sulfone olefins by migration of the hydroxy group to sulfur. The formations of these unusual oxidative elimination products were rationalized by invoking remote participation of a hydroxy group via a sulfurane intermediate. This suggestion has recently been supported by the observation that hydroxy groups which participate to form the most stable sulfuranes are also the most effective at promoting chemical reactions of the sulfide.[4] These results imply that

Scheme I



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