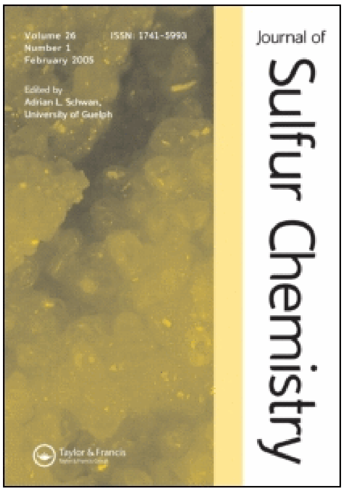

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THE REACTIONS OF SULFIDES AND SULFENIC ACID DERIVATIVES WITH SINGLET OXYGEN

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The reactions of singlet oxygen with sulfides, sulfenamides, disulfides, and sulfenate esters will be critically discussed. The emphasis will be on the mechanistic details of these reactions.

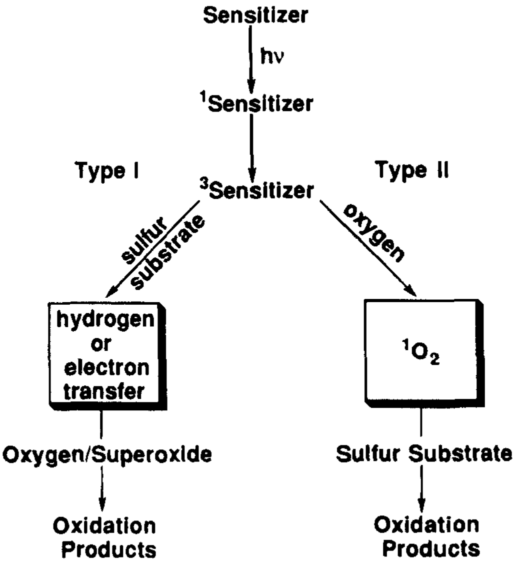
Keywords: Disulfides, persulfoxides, photooxidation, singlet oxygen, sulfenamides, sulfenate esters, sulfides, sulfuranes, thiadioxiranes.

CONTENTS

1. INTRODUCTION

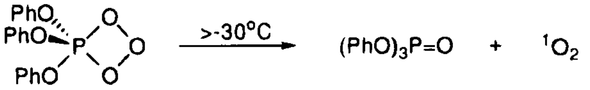
1.1. *Photooxidations*

Photooxidations of organic sulfides can occur either via Type I or Type II mechanisms[1,2] (Scheme 1). The two mechanistic types differ only in the order that the divalent sulfur compound and oxygen appear on the reaction surface. In the Type I mechanism the sulfur compound reacts directly with the sensitizer by either hydrogen or electron transfer followed by reaction with oxygen or superoxide to give the product. In the Type II mechanism singlet oxygen is produced by energy transfer from the sensitizer and then reacts with the sulfur containing substrate to give products which may or may not be the same as those produced via the Type I mechanism.



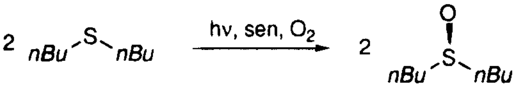
SCHEME 1

Experimental precautions such as high oxygen and low substrate concentrations designed to isolate Type II sulfide photooxidative behavior for detailed study are usually successful despite the low ionization potentials of many organosulfur compounds. In the rare cases where Type I behavior cannot be suppressed the reactions of sulfides towards singlet oxygen can often be studied using chemical rather than photochemical sources of singlet oxygen. From a synthetic viewpoint, however, the large amounts of the chemical precursors (e.g. triphenyl phosphite ozonide; Eqn. 1)[3] of singlet oxygen often required to drive the reactions to completion, result in a very difficult purification procedure.



(1)

The first Type II photooxidations of simple sulfides, although not recognized as such at the time, were reported nearly 35 years ago by Schenck and Krausch[4] (Eqn. 2) Since that time several reviews which have described progress in both the synthetic and mechanistic aspects[5] of these Type II photooxidations have appeared.[6,7] In the following review we will restrict our remarks to a discussion of the latest results which have a bearing on the mechanistic description of the reactions of singlet oxygen with divalent sulfur (RSX; X = C, O, N, and S) compounds. In order to provide a coherent description of these reactions, however, some overlap with earlier reviews will be unavoidable.

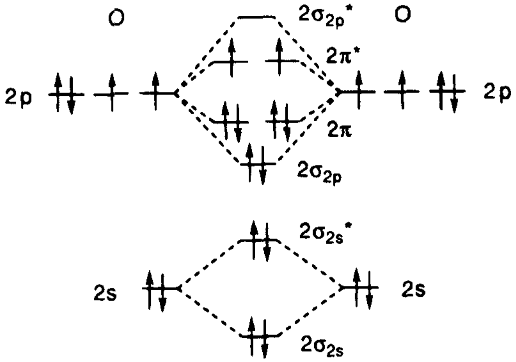


(2)

1.2. *Singlet Oxygen*

The electronic configuration of the oxygen molecule as shown in (Scheme 2) is a triplet ($^3\Sigma_g^-$) as predicted by Hund's rule.[8] The bond energy of the triplet is a result of the presence of a σ-bond and two $\pi^2\pi^{*1}$ three electron bonds. Two singlets, the $^1\Delta_g$ and the $^1\Sigma_g^+$ states, which only differ in the orientation of the electrons in the degenerate $2\pi^*$ orbitals are readily accessible and are found approximately 22.4 and 37.8 kcal/mol above the ground state triplet, respectively. The electronic transitions $^1\Delta_g \rightarrow {}^3\Sigma_g^-$ at 1270 nm,[9] $^1\Sigma_g^+ \rightarrow {}^1\Delta_g$ at 1926 nm,[10] and $^1\Sigma_g^+ \rightarrow {}^3\Sigma_g^-$ at 765 nm[11] have all been observed in solution by their characteristic emissions.[12]

The lifetime of $^1\Sigma_g^+$ oxygen is limited by the very rapid $^1\Sigma_g^+ \rightarrow {}^1\Delta_g$ transition and is only about 130 ns in CCl_4.[11] This very short lifetime precludes any bimolecular reactions with organic substrates with the exception of quenching by the solvent bath.[13] In dramatic contrast, the $^1\Delta_g \rightarrow {}^3\Sigma_g^-$ transition is strictly forbidden resulting in lifetimes for $^1\Delta_g$ oxygen in the microsecond to millisecond time regime in solution. As a consequence, in every case scrutinized in detail $^1\Delta_g$ is the electronic state of oxygen responsible for the oxidations of organic substrates.



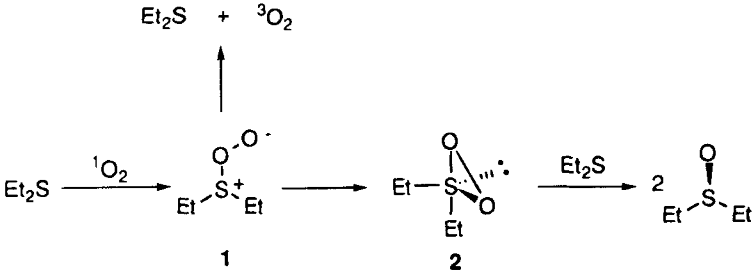
SCHEME 2

2. SULFIDES

2.1. *Photooxidation Mechanism*

The current mechanistic understanding of sulfide photooxidation is in large part a result of seminal work conducted by the Foote research group at UCLA in the 1970's which culminated in 1983 in what is now a classic paper describing the mechanism of diethyl sulfide (Et_2S) photooxidation.[14] The mechanistic proposal put forward by the Foote group is depicted in Scheme 3. The unusual and unanticipated feature of the reaction surface was the presence of two peroxidic intermediates, the persulfoxide, **1**, and the thiadioxirane, **2**.

The evidence supporting two intermediates is compelling and is outlined in Scheme 4. Cophotooxidation of Et_2S and Ph_2SO results in formation of both Et_2SO and Ph_2SO_2. This argues for the presence of at least one trappable intermediate since control reactions demonstrate that Ph_2SO is inert to singlet oxygen under the reaction conditions. A detailed quantitative study of these trapping experiments, however, provides compelling evidence sup-

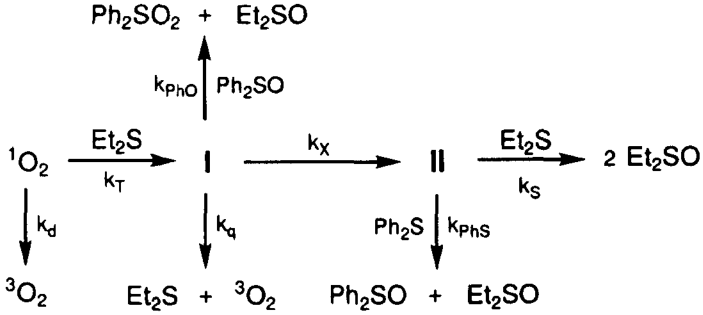


SCHEME 3

porting the existence of two discrete intermediates. The product ratio, $[Et_2SO]/[Ph_2SO_2]$ quantitatively obeys equation (3) which was derived from Scheme 4 by treating intermediates **I** and **II** in terms of the steady state approximation. Most revealing is the observation that the slope of a plot of $[Et_2SO]/[Ph_2SO_2]$ versus $1/[Ph_2SO]$ is *independent* of the concentration of Et_2S which could only occur if Ph_2SO and Et_2S do not compete for a common intermediate.

Trimethyl phosphite, $[(MeO)_3P]$, behaves in a fashion analogous to Ph_2SO, trapping intermediate **I** to give trimethyl phosphate, $[(MeO)_3PO]$.[15] However, the rate constant ratio k_x/k_{PhO} for Ph_2SO (0.082) and $(MeO)_3P$ (0.0029) derived from the plot of equation (3) reveals that the phosphite is 28 times more reactive toward intermediate **I** than the sulfoxide.

On the other hand, cophotooxidations of Et_2S and Ph_2S (Ph_2S does not react directly with $^1O_2$ under the reaction conditions) produce a plot of $[Et_2SO]/[Ph_2SO]$ versus $1/[Ph_2S]$ that exhibits a slope which is *dependent*



SCHEME 4

on the concentration of Et_2S. This is consistent with competitive trapping of intermediate **II** by both Et_2S and Ph_2S. Analysis of the slope of the plot (Eqn. 4) reveals that Et_2S is 36.5 times as reactive a trapping agent as Ph_2S (i.e. k_S/k_{PhS}) in acetonitrile.

$$\frac{[Et_2SO]}{[Ph_2SO_2]} = 1 + \frac{2k_X}{k_{PhO}[PhSO]} \tag{3}$$

$$\frac{[Et_2SO]}{[Ph_2SO]} = 1 + \frac{2k_S[Et_2S]}{k_{PhS}[PhS]} \tag{4}$$

The experimental evidence for physical quenching (k_q) is also compelling. At room temperature Et_2SO is formed much more slowly than $^1O_2$ disappears (less than 5% of the interactions between $^1O_2$ and Et_2S are productive, however, product formation is much more efficient at lower temperatures[16]) revealing an alternative route for singlet oxygen deactivation; presumably physical quenching. This phenomenon is not unique to sulfides; other compounds such as amines,[17,18] carotenoids,[19,20] metal chelates,[21] nitroxides,[21] phenols,[21] inorganic anions,[21] nitroso compounds,[21] and hydrazines[22] also physically deactivate $^1O_2$. The mechanism by which sulfides physically quench $^1O_2$ has not been explicitly investigated. However, the lack of any low lying sulfide excited state argues that the quenching is likely to occur either via a contact charge transfer mechanism or by decomposition of a covalently bound persulfoxide (Scheme 3). The contact charge transfer mechanism involves initial formation of a singlet sulfide/$^1O_2$ exciplex followed by intersystem crossing to a triplet CT complex and subsequent dissociation to sulfide and $^3O_2$. On the other hand, decomposition of a singlet persulfoxide to give triplet oxygen could circumvent the spin inversion barrier as a result of low lying d-orbitals on sulfur. Experimentally it has been observed that Ph_2SO competitively inhibits physical quenching which could occur either by trapping of the persulfoxide as shown in Scheme 3 or by trapping of an exciplex or CT complex formed earlier on the reaction surface. In fact, the experimental evidence supporting the population of transient exciplexes on many $^1O_2$ reaction surfaces is growing.[23,24]

2.2. *The Persulfoxide*

The identification of the persulfoxide, **1**, as the first covalently bound intermediate on the reaction surface appears to be firmly established. An alternative possibility of an electron transfer from diethyl sulfide to singlet oxygen in organic solvents to give the ion pair, **3**, as the first intermediate is unlikely. The oxidation potential of Et_2S is 1.65 V[25] and consequently the free energy of electron transfer as calculated using the Weller equation ($\Delta G^{o} = 23.06[E_{p/2}(Et_2S) - E^{o'}(O_2/O_2^{-}\cdot) - e^2/\varepsilon a] - \Delta E^{oo}$) reveals that formation of **3** is more than 33 kcal/mol endergonic. In addition, a plot of the log of the rate constant for photooxidations of several sulfides versus their oxidation potentials gives a slope of $-1.5\ V^{-1}$ much smaller than that required ($-16.4\ V^{-1}$) for endothermic complete electron transfer.[25] Partial charge transfer, however, certainly does occur as revealed by a linear relationship between the rate constants of photooxidation in the gas phase and the sulfide ionization potentials.[26] In fact, ion pair formation, **3**, can be induced in highly polar media such as water but only with very electron rich sulfides.[27] It is tempting to suggest that a sulfide-singlet oxygen charge transfer complex could react directly with triplet oxygen in a fashion analogous to olefin radical cations;[28,29] however, Asmus and coworkers[30] have demonstrated with pulse radiolysis that sulfur radical cations are reluctant to react with oxygen.

$$Et_2S^{+\cdot}\ O_2^{-\cdot}$$

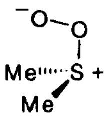
3

Experimental evidence which supports formation of a persulfoxide includes the observation that the rate constants for removal of singlet oxygen from solution by a series of thioanisoles correlate with the Hammett sigma value to give a reaction constant (ρ) of −1.6 as anticipated for build-up of positive charge on sulfur in the transition state.[25,31] Trapping of intermediate **I** with a series of diaryl sulfoxides[32] also gives a Hammett reaction constant indicative of nucleophilic oxygen atom transfer. In addition, the rate constants for reactions of $^1O_2$ with dialkyl sulfides (Table 2-1)[31] are very sensitive to the steric environment surrounding the sulfur atom. As the carbons adjacent to sulfur are changed from 1° to 2° and from 2° to 3° the rate constants for photooxidations decrease by an order of magnitude. Steric effects of this magnitude are not unanticipated when the sulfur acts as a nucleophilic center and are consistent with rate determining formation of a persulfoxide.[25]

TABLE 2.1 Rate Constants for Deactivation of Singlet Oxygen by Dialkyl Sulfides.

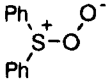
Sulfide	$k \times 10^7\ M^{-1}s^{-1}$
Et_2S	1.7
iPr_2S	0.22
tBu_2S	0.013

The persulfoxide formed in the reaction of dimethyl sulfide and $^1O_2$ is also a viable intermediate at a variety of computational levels.[33,34] In its most stable conformation, **4**, it has C_S symmetry with the outer oxygen bisecting the C-S-C angle. At the MP2/6-31G* level the O-O bond at 1.44 Å is similar to that observed in H_2O_2 (1.47 Å) but the S-O bond at 1.64 Å is slightly longer than in dimethyl sulfoxide (1.51 Å).[35] The Mulliken HF/6-31G* charges are +0.95 for sulfur, and –0.48 and –0.50 for the inner and outer oxygens, respectively, supporting a zwitterionic rather than diradical representation.



4

Ando and coworkers[36] have reported FT-IR evidence for the formation of persulfoxides **5**, **6**, and **7** in solid oxygen matrices upon irradiation of the corresponding sulfide-oxygen CT bands.[37] They based their assignments on the observed splitting of the S-O stretching vibrations (found at 997, 997, and 1034 cm^{-1} for **5**, **6**, and **7**, respectively) into doublets when matrices containing ^{16}O-^{18}O were used. Jensen, however, has questioned this FT-IR evidence for these persulfoxides pointing out that the thiadioxiranes also have non-equivalent oxygens.[35]



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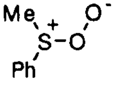

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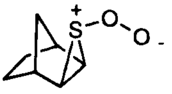
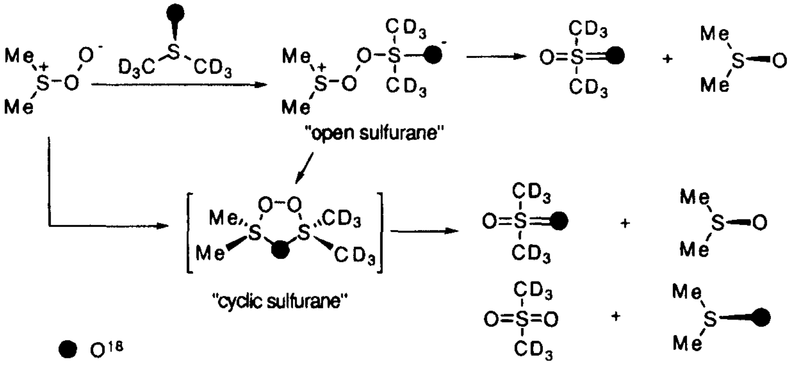


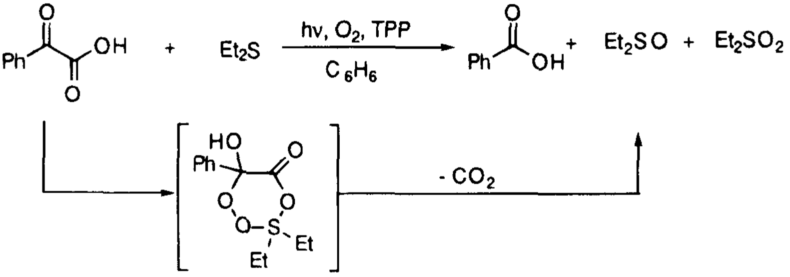
7

Akasaka and Ando[38] examined the reaction of dimethyl persulfoxide in the presence of d_6-dimethyl sulfoxide-^{18}O (Scheme 5) and observed dimethyl sulfoxide formation without incorporation of ^{18}O supporting involvement of an open rather than cyclic sulfurane intermediate. The transfer of an oxygen atom is initiated by nucleophilic attack of the outer oxygen of the persulfoxide at the sulfur of the labeled sulfoxide.



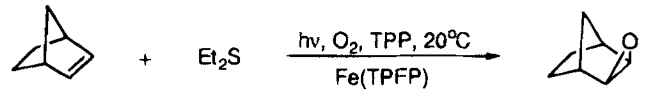
SCHEME 5

Nucleophilic attack of a persulfoxide has also been proposed to explain the decarboxylation of phenylglyoxylic acid during cophotooxidation with diethyl sulfide.[39] (Scheme 6) The authors suggested that this unusual reaction proceeded by 1,3-dipolar cycloaddition of the persulfoxide to the α-keto acid to give a novel cyclic peroxide which decomposed to give the products. It is not entirely clear, however, that a cyclic intermediate is required in order to degrade the α-keto acid.[40]



SCHEME 6

The metalloporphyrin [tetrakis(pentafluorophenyl)porphyrinato]iron(III) chloride [Fe(TPFP)] has been used to catalyze the oxygen transfer from diethyl persulfoxide to olefins to form epoxides[41,42] (Eqn. 5). It was suggested that the outer oxygen of the persulfoxide is transferred to Fe(TPFP) to give the iron oxo species $\mathrm{Fe^{IV}{=}O(TPFP)^{+\cdot}}$. In support of this suggestion was the observation that Fe(TPFP) also catalyzed transfer of the persulfoxide oxygen to anisole-4-d to give *p*-methoxyphenol (Eqn. 6) accompanied by 63% NIH shift of deuterium; a reaction previously observed for authentic iron oxo species.



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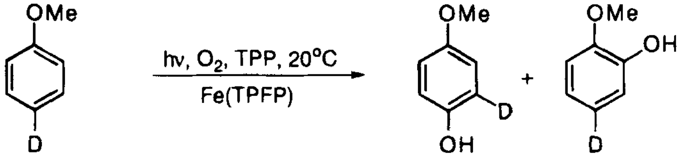
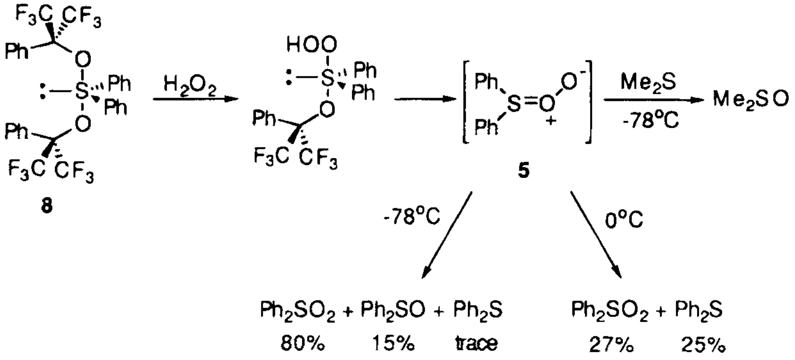


(6)

Persulfoxide **5** has also been suggested as an intermediate in the perhydrolysis of sulfurane **8**[43] (Scheme 7). The formation of the persulfoxide was initiated by ligand exchange to give a hydroperoxy sulfurane which subsequently decomposed by loss of the apical ligand and deprotonation. The putative diphenyl persulfoxide, **5**, could be intercepted at –78 °C with Me$_2$S to give Me$_2$SO. In the absence of Me$_2$S decomposition of **5** gave Ph$_2$SO$_2$, Ph$_2$SO, and a trace of Ph$_2$S. At 0 °C formation of Ph$_2$SO was suppressed and Ph$_2$S became a major product. These results are reminiscent of the behavior of diethyl persulfoxide as reported by Foote and coworkers. On the other hand, it was also reported that an intermediate formed in the perhydrolysis of a bicyclic sulfurane was capable of transferring an oxygen to 1,3-cyclohexadiene and norbornene to give the epoxides.[43] This type of behavior is unprecedented for a persulfoxide intermediate.

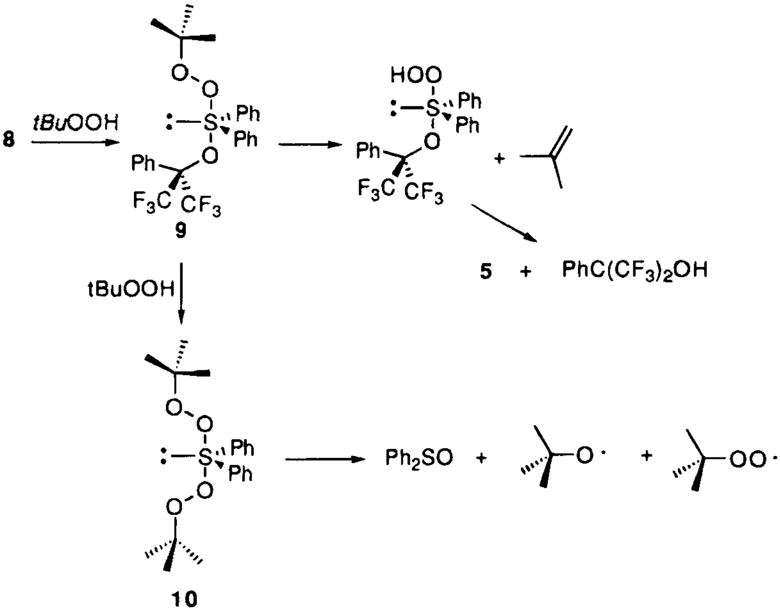
Bartlett and coworkers[44] suggested formation of persulfoxide **5** during the very complicated reaction of **8** with *tert*-butylhydroperoxide. They provided evidence for initial formation of both mono- and diperoxysulfuranes, **9** and **10**, respectively. Luminescence was observed in two stages in the presence of 9,10-dibromoanthracene. The early stage which occurs upon warming to –40 °C coincides with isobutene formation while the latter stage at –20 °C coincides with the appearance of acetone. The mechanism they



SCHEME 7

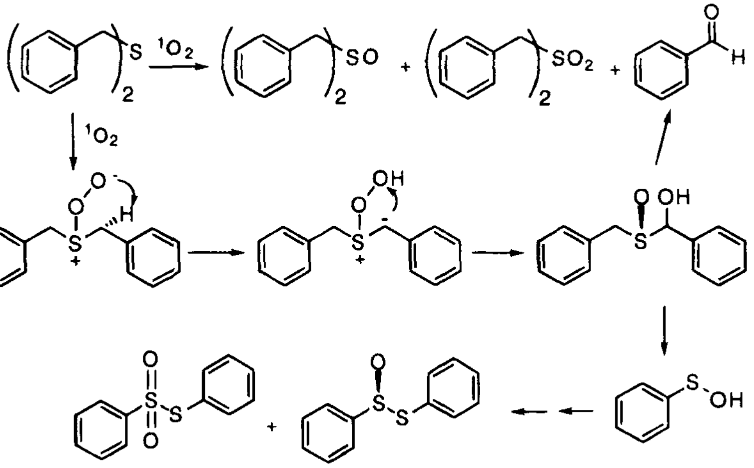
suggested to rationalize these and other experimental observations is depicted in Scheme 8.

Several examples demonstrating the ability of persulfoxides to intramolecularly abstract a proton have appeared.[45] In many of these cases the



SCHEME 8

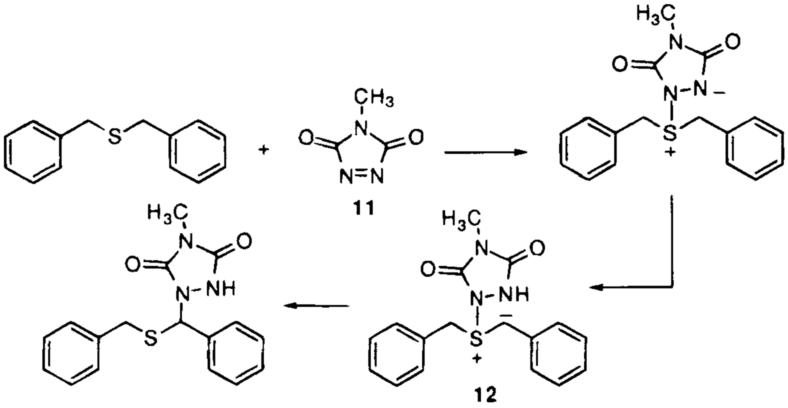
proton abstraction step was postulated based on the observation of a subsequent carbon-sulfur bond cleavage. For example, in 1976 Corey and Ouannes[46] reported that the reaction of dibenzyl sulfide with singlet oxygen produced a substantial amount of benzaldehyde in addition to the anticipated sulfoxide and sulfone (Scheme 9). They suggested that intramolecular hydrogen abstraction occurred to give an ylide which rearranged to generate a hydroxy sulfoxide as the key intermediate that decomposed to give benzaldehyde and benzenesulfenic acid.



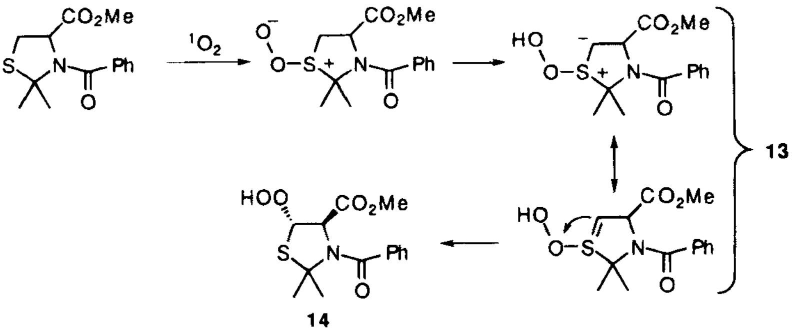
SCHEME 9

Ando and coworkers[47] have criticized the Corey mechanism pointing out that triazolinedione, **11**, reacts with dibenzyl sulfide to give α-oxidation products (Scheme 10). A Pummerer rearrangement of the ylide **12** formed by intramolecular hydrogen abstraction provides a convenient mechanistic explanation for this reaction. Ando[48,49] later showed that thiazolidine derivatives also undergo Pummerer rearrangements rather than the Corey hydroxy transfer reaction to produce α-hydroperoxy sulfides (Scheme 11).

The *S*-hydroperoxysulfonium ylide, **13**, formed in the photooxidations of the thiazolidine depicted in Scheme 11 is capable of donating an oxygen to norbornene and cyclohexene.[50] Control reactions demonstrated that the α-hydroperoxy sulfide product, **14**, was itself incapable of delivering an oxygen atom to several olefinic substrates. Similar intermediates presumably



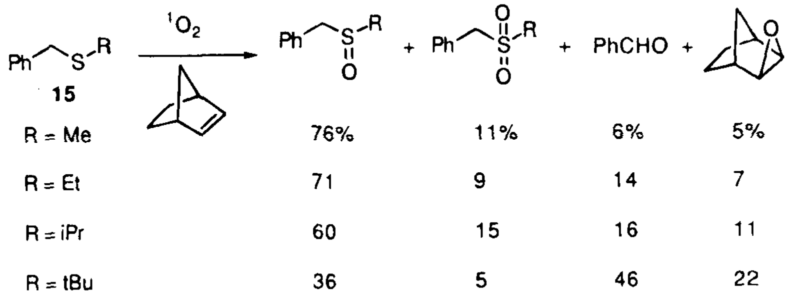
SCHEME 10



SCHEME 11

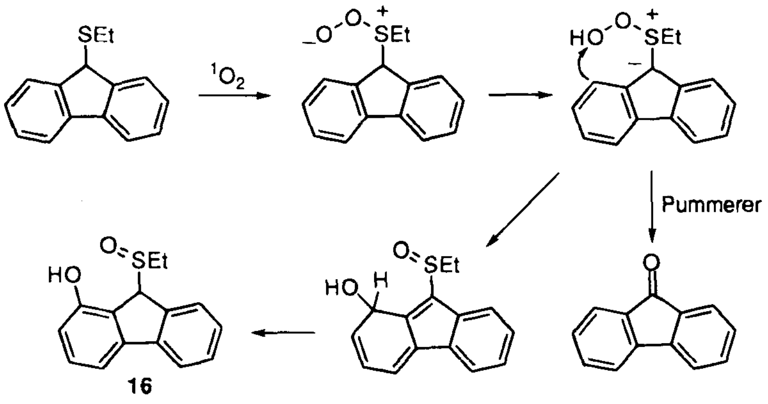
formed in the photooxidations of benzylic sulfides, **15**, also act as epoxidizing agents. (Scheme 12)

The Corey hydroxy transfer reaction, however, does appear to be a key step in a novel hydroxylation of an aromatic ring by a *S*-hydroperoxysulfonium ylide.[51] In this reaction (Scheme 13) the hydroxy transfer occurs by nucleophilic attack of the aromatic ring at the terminal oxygen of the peroxy group. Rearomatization by a subsequent [1.7]-hydrogen shift generates the phenolic product, **16**. The key *S*-hydroperoxysulfonium zwitterion intermediate also undergoes a competitive Pummerer rearrangement.



R = Me	76%	11%	6%	5%
R = Et	71	9	14	7
R = iPr	60	15	16	11
R = tBu	36	5	46	22

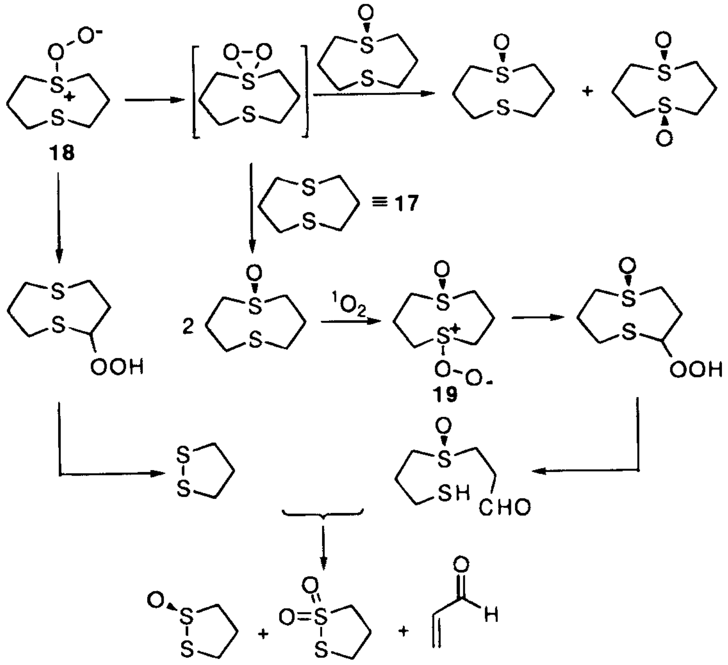
SCHEME 12



SCHEME 13

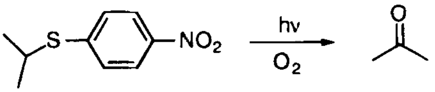
Thiolanes in particular are susceptible to Pummerer rearrangements as a result of the enhanced acidity of the α-hydrogen atom in the 5-membered ring persulfoxide intermediates.[52] For comparison, C-S cleavage products are rarely formed in the photooxidations of unactivated acyclic and 4-, 6-, and 7-membered ring sulfides.

Extended photolysis of 1,5-dithiacyclooctane, **17**, in $CDCl_3$ at room temperature produced a plethora of products via the intermediacy of the spectroscopically detectable α-hydroperoxides which presumably formed by Pummerer rearrangements of persulfoxides **18** and **19**[53] (Scheme 14). However, the Pummerer rearrangements of these persulfoxides were suppressed in methanol or in aprotic solvents at low temperatures and the mono- and bis-sulfoxides were the only isolated products.



SCHEME 14

Pasto and coworkers[54] have suggested an unprecedented reaction of a persulfoxide in order to explain the formations of unusual fragmentation and rearrangement products during the self sensitized photooxidations of *p*-nitrophenyl substituted sulfides, **20**, **21**, and **24** (Eqns. 7, 8, and 9). It was suggested that singlet oxygen was the reactive oxidant in these reactions based upon the observation that the photooxidation of methyl 4-nitrophenyl sulfide was quenched by the addition of a 250% excess of 1,3-cyclohexadiene which was concomitantly consumed to give the endoperoxide. However, the possibility of an electron transfer process, especially for *tert*-alkyl *p*-nitrophenyl sulfides,[55] cannot be rigorously eliminated.



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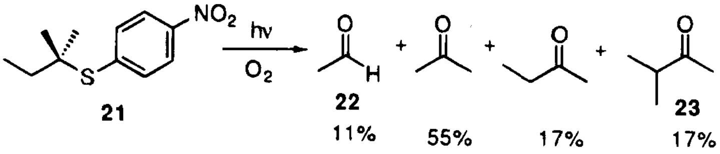

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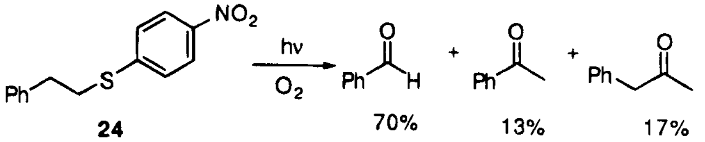
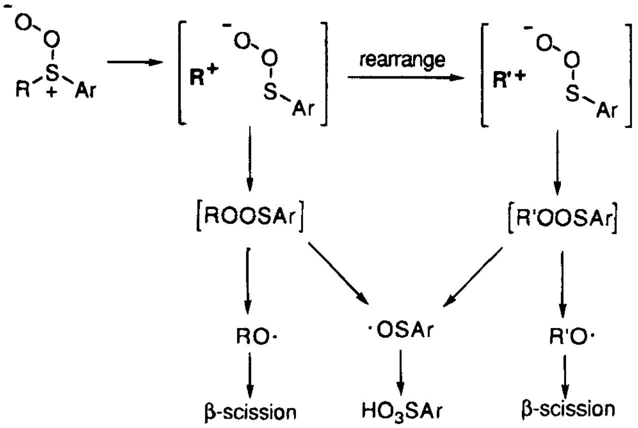


(9)

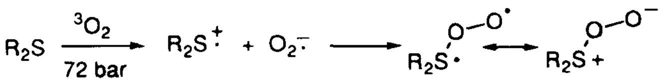
The mechanism shown in Scheme 15 was suggested to account for the formations of the structurally rearranged carbonyl products **22** and **23** from **21**, and benzaldehyde and acetophenone from **24**.[54] This mechanism invokes an unusual cleavage of a persulfoxide intermediate into a persulfenate anion and a carbocation. Meerwein shifts in the carbocation provide a convenient explanation for the skeletal rearrangements observed in these systems. However, cleavage of sulfide radical cation intermediates[55] into thiyl radicals and R^+ followed by reaction of triplet oxygen with the thiyl radicals[56] has literature precedent and is perhaps a more reasonable mechanism for these reactions.

Riley and coworkers have suggested the formation of persulfoxides during both catalyzed and uncatalyzed autooxidations of sulfides with triplet



SCHEME 15

oxygen. The reactions of several dialkyl sulfides in polar protic solvents at 72 bar of O_2 in the absence of any catalyst, initiator, or photosensitizer gave good to excellent yields of sulfoxides with trace amounts of sulfone.[57,58] These reactions are first order in sulfide and oxygen and give enhanced selectivity for sulfoxide formation as the solvent polarity is increased. Activation energies for the oxidations of benzyl methyl sulfide were 22 and 25.8 kcal/mol in 3:2 CH_3CN/H_2O and in CH_3CN, respectively. These results and a ring size effect on the rates of oxidation are consistent with an electron transfer mechanism. Attempts to electrochemically initiate a chain reaction, however, resulted in only stoichiometric quantities of sulfoxide. Consequently, an initial unfavorable rate determining electron transfer followed by direct coupling of the sulfide radical cation and superoxide (Eqn. 10) appears to be the most probable mechanism.



(10)

A catalytic amount of Ce(IV)[59] accelerates these autoxidations by at least a factor of 10^3 allowing reactions to proceed at convenient rates at lower pressures and temperatures than that utilized in the uncatalyzed systems. Mechanistic studies of the catalyzed reactions reveal that they are first order in R_2S, first order in total Ce, zero order in oxygen, and inhibited by Ce(III). *In addition, catalyzed oxidation of decyl methyl sulfide in the presence of* O-18 labeled water resulted in less than 1% ^{18}O incorporation. These results are consistent with the mechanism and the corresponding rate expression depicted in Scheme 16 if $k_2k_3[O_2] >>> (k_{-1}k_{-2} + k_{-1}k_3[Ce^{III}])$.

There is, however, a thermodynamic problem with the mechanism depicted in Scheme 16 which was recognized by the authors.[59] If the equilibria represented by rate constants k_1/k_{-1} and k_3/k_{-3} both lie to the right then $R_2S(+)OO\cdot$ is a stronger oxidant than $R_2S^{+\cdot}$ and the interaction between $R_2S(+)OO\cdot$ and R_2S should give $R_2S(+)OO(-)$ and $R_2S^{+\cdot}$. However, it is precisely this electron transfer or the reaction of $R_2S^{+\cdot}$ with oxygen (process k_2/k_{-2}) which is required to propagate the chain oxidation of sulfides which have been experimentally demonstrated not to occur. In order to get around this problem the authors have suggested with no detail that the reaction represented by rate constants k_3/k_{-3} is an inner sphere process.

Persulfoxides have also been suggested[60] as intermediates in the oxidations of aryl methyl sulfides with dimethylphenylsilyl hydrotrioxide, **25**

$$R_2S + Ce^{IV} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R_2S^{+\cdot} + Ce^{III}$$

$$R_2S^{+\cdot} + {}^3O_2 \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} R_2\overset{+}{S}OO\cdot$$

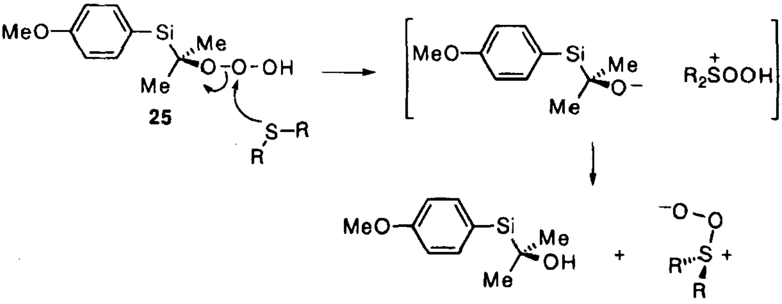
$$R_2\overset{+}{S}OO\cdot + Ce^{III} \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} R_2\overset{+}{S}OO^- + Ce^{IV}$$

$$R_2\overset{+}{S}OO^- + R_2S \underset{k_{-4}}{\overset{k_4}{\rightleftharpoons}} 2R_2SO$$

$$\frac{d[R_2S]}{dt} = \frac{2k_1k_2k_3[R_2S][Ce^{IV}][O_2]}{k_{-1}k_{-2} + k_{-1}k_3[Ce^{III}] + k_2k_3[O_2]}$$

SCHEME 16

(Scheme 17). The reaction was suggested to proceed by nucleophilic attack at the middle oxygen atom to give an ion pair which collapsed to the persulfoxide by hydrogen transfer.



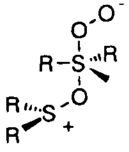
SCHEME 17

2.3. *The Thiadioxirane*

The assignment of intermediate **II** on the Foote reaction surface as the thiadioxirane, **2**, is not as secure as the assignment of the persulfoxide structure to intermediate **I** (Scheme 4). In 1991, Sawaki and coworkers[61] reported an extensive study of the photooxidations of several dialkyl and alkyl aryl sulfides. The salient observations made by these investigators included: (1)

sulfoxide formation is enhanced while sulfone formation is unaffected by protic or coordinating solvents, (2) sulfoxide formation is more sensitive to the electronic character but less sensitive to the steric effects of substitutents than sulfone formation, (3) the sulfone/sulfoxide ratio decreases as a function of irradiation time, and (4) both oxygen atoms in the sulfone product come from the same oxygen molecule. Observation 4 suggests that the sulfone is derived from the thiadioxirane by cleavage of the O-O bond. Observations 1, 2, and 3, on the other hand, appear to decouple formations of the sulfoxide and sulfone and argue that they are formed competitively rather than on the same reaction surface.

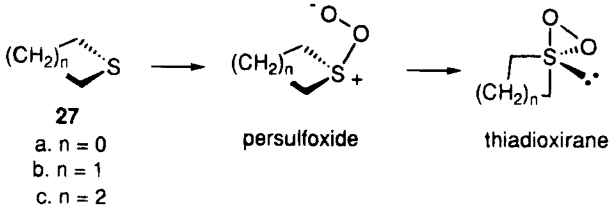
If the Sawaki suggestion is correct[61] it leaves the question of the identity of the second intermediate on the Foote reaction surface open. Sawaki suggested that intermediate **II** in Scheme 4 might best be represented as a persulfoxide coordinated to a sulfoxide, **26**. However, it would be difficult to reconcile the electrophilic reactivity, and the inability of diphenyl sulfoxide to trap intermediate **II**, with structure **26**.[62]



26

Theoretical studies of sulfide photooxidations have done little to resolve the conflict between the Foote and Sawaki mechanisms. In an early theoretical study of the reaction of singlet oxygen with dimethyl sulfide only the persulfoxide was located on the potential energy surface.[33] A thiadioxirane, however, was eventually located on the HF/3–21-G* potential energy surface for the photooxidation of H_2S and was shown to exist in a distorted trigonal bipyramidal geometry characterized by one long (1.894 Å) and one short (1.541 Å) S-O bond.[61] The HF/3–21-G* results have subsequently been refuted and the thiadioxirane minimum assigned to an artifact from the use of a small unbalanced basis set.[34] At the highest computational level yet reported (MP2/6–31G*) both the dimethyl thiadioxirane and persulfoxide are isoenergetic minima separated by a nearly insurmountable barrier of 20 kcal/mol.[34]

Remarkably, the near coincident energies of the persulfoxide and thiadioxirane are insensitive to sulfide structure as shown by recent computational studies using a series of cyclic sulfides, **27a–c**[63] (Scheme 18). Geometry optimizations of the persulfoxides and thiadioxiranes corresponding to **27a–c** at the MP2/6–31G* level show only minor, albeit systematic, changes in geometry as a function of ring size. An examination of the persulfoxides reveal a lengthening of the S-O bond distance, an increase in the S-O-O bond angle, and a reduction in the O-O bond distance as the ring size decreases from 5 to 3. The effect of ring size is in particular very evident in the thiirane persulfoxide, **27a**, where the S-O bond distance (1.67 Å) is significantly longer than that found in the thietane, **27b**, (1.62 Å) or thiolane, **27c**, (1.61 Å) persulfoxides. One may speculate that the inability of the sulfonium-like sulfur in these small ring persulfoxides to attain the geometrically preferred tetrahedral geometry is compensated by a significantly diminished sulfur-oxygen interaction. This suggestion is supported by Mulliken HF/6–31G* analyses that show that the positive charge at the sulfur in the thiirane persulfoxide (+0.80) is smaller than in the thietane (+0.95) or thiolane (+0.99) persulfoxides. The optimized thiadioxiranes are asymmetric with two unequivalent S-O bonds. The geometry is best described as distorted trigonal bipyramidal with long apical and short equatorial bonds.

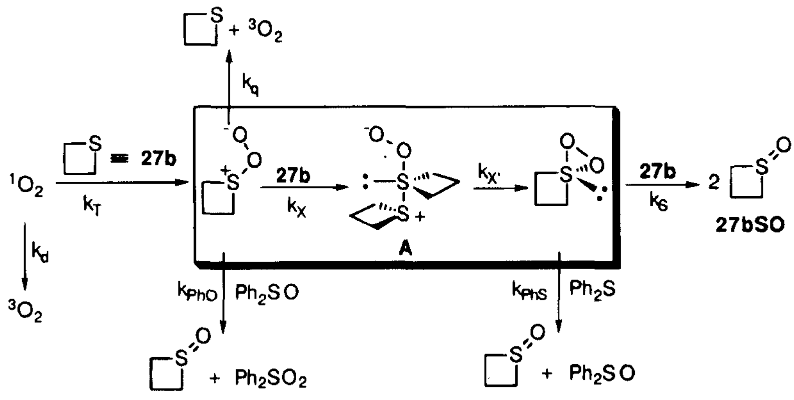


SCHEME 18

A detailed study[64] of the photooxidation of thietane, **27b**, provides compelling circumstantial evidence for a thiadioxirane on the reaction surface for the formation of the sulfoxide, **27bSO**. The mechanism suggested for this reaction is depicted in Scheme 19 and invokes a novel self catalyzed interconversion of the persulfoxide and thiadioxirane.

The evidence supporting the mechanism depicted in Scheme 19 includes:

(1) Cophotooxidations of **27b** with diaryl sulfoxides (Ar_2SO) and diaryl sulfides (Ar_2S) produce diaryl sulfones and sulfoxides with efficiencies characterized by ρ values of +1.05 and −1.26, respectively. The observation of two different Hammett ρ values does not by itself require the presence of two intermediates as shown in Scheme 19 since it is possible for a single intermediate to behave as a nucleophile toward one reagent and as an electrophile toward another. This could be true especially for zwitterionic persulfoxides or persulfoxides with substantial diradical character as has been claimed for some carbonyl oxides.[65] However, the similarity of these Hammett ρ values to those measured for Et_2S photooxidation (+1.41 and −1.25)[66] where the trapping of different intermediates has been kinetically demonstrated argues against this possibility.



SCHEME 19

(2) A plot of [**27bSO**]/[Ph_2SO_2] versus 1/[Ph_2SO] at low conversions (<15%) of **27b** is linear as depicted in Fig. 1 with a slope dependent on the concentration of **27b**. The sensitivity of the slope to the concentration of **27b** (inset of Fig. 1) is consistent with competitive trapping of the persulfoxide by **27b** and Ph_2SO as shown in equation (11) which was derived from Scheme 19 by treating the persulfoxide, **A**, and the thiadioxirane in terms of the steady state approximation. The value for k_X/k_{PhO} is 0.37 which is more than 16 times larger than the same value reported for Et_2S photooxidation (0.023) consistent with the suggestion that **27b** acts as a catalyst for the interconversion of the persulfoxide and thiadioxirane.

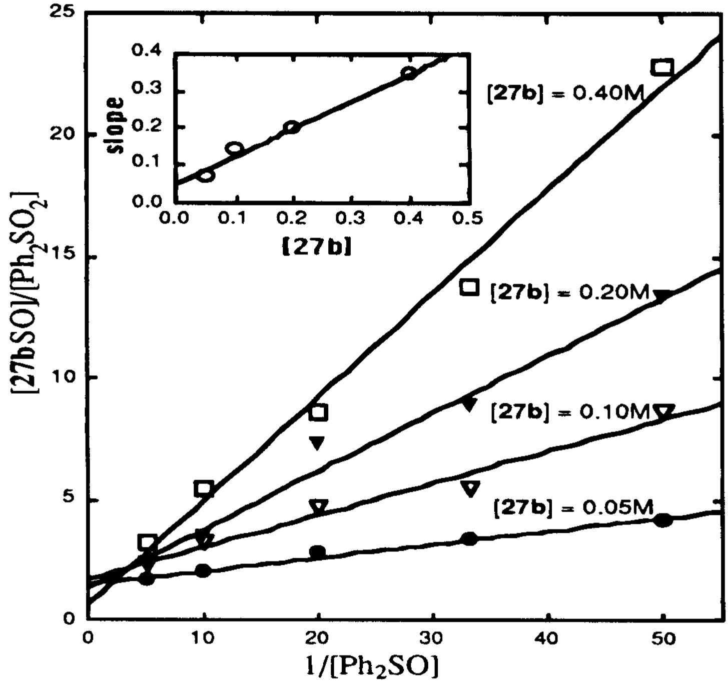


FIGURE 1

$$[\mathbf{27b}]/[Ph_2SO_2] = 1 + 2k_X[\mathbf{27b}]/(k_{PhO}[Ph_2SO]) \qquad (11)$$

(3) The amount of product formed at a given time of irradiation under conditions where $k_d \ll k_T[\mathbf{27b}]$ is a function of the concentration of the trapping agent Ph_2SO consistent with Scheme 19 which shows a direct competition between trapping of the persulfoxide with Ph_2SO and decomposition via physical quenching, k_q.

(4) A plot of [**27b**]/[Ph_2SO] versus 1/[Ph_2S] is linear with a slope *dependent* on the concentration of **27b** consistent with competitive trapping of the thiadioxirane by **27b** and Ph_2S as given by equation (12).

$$[\mathbf{27b}]/[Ph_2SO] = 1 + 2k_S[\mathbf{27b}]/(k_{PhS}[Ph_2S]) \qquad (12)$$

(5) The rate of product formation is a function of the concentration of **27b** as depicted in Fig. 2. This unusual observation is consistent with a direct

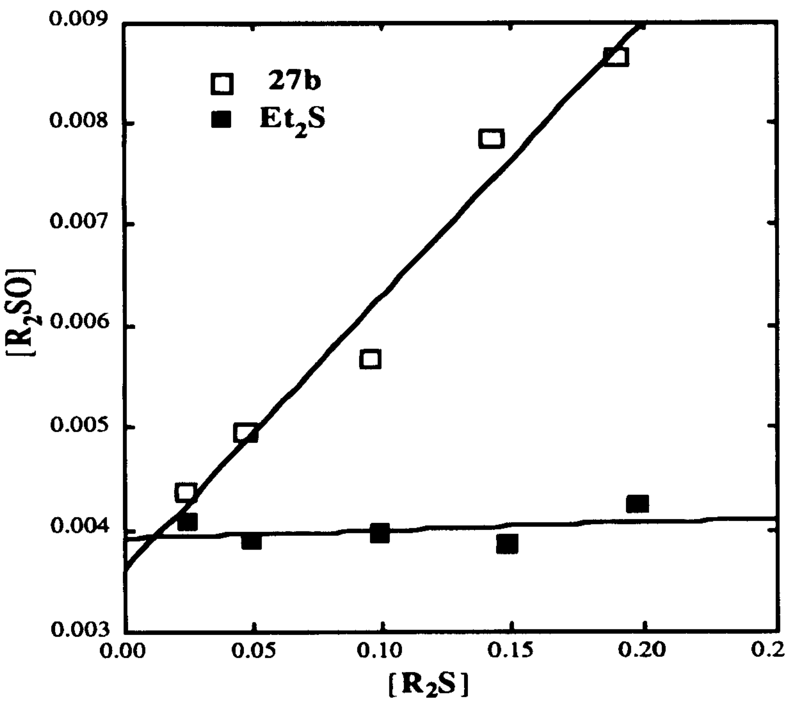


FIGURE 2

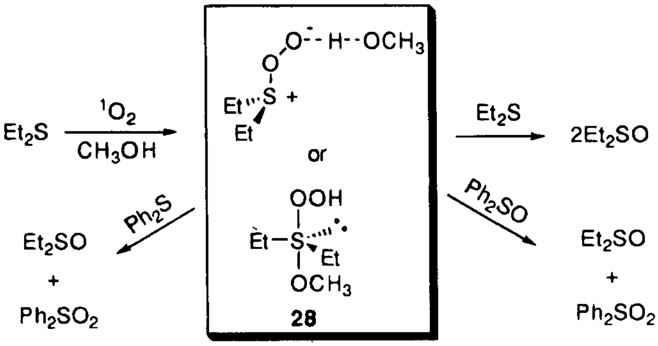
competition between decomposition of the persulfoxide via physical quenching, k_q, and reaction with **27b**. In contrast, the rate of product formation is independent of substrate concentration during Et_2S photooxidation (Fig. 2) consistent with the Foote mechanism (Scheme 4).

The enhanced rate of interconversion of the persulfoxide and thiadioxirane during the photooxidation of **27b** can be understood in terms of a preorganization of the persulfoxide into the 4-coordinate geometry adopted by the thiadioxirane. In the absence of this catalysis internal geometric reorganization and the increase in strain accompanying three-membered ring formation occur in one energetically demanding rather than in two microscopic steps. The authors have suggested that the unique ability of **27b** to catalyze its own oxidation is a result of a small C-S-C angle of 78°[67] which allows an unencumbered approach to the sulfonium sulfur. In contrast, the larger C-S-C angle in Et_2S, (98.9°),[67] sterically precludes the catalysis step and forces a unimolecular collapse of the persulfoxide directly to the thiadioxirane.

2.4. *The Sulfurane*

The photooxidation of Et_2S in methanol differs significantly from photooxidations reported in aprotic solvents.[68,69] Et_2S reacts much faster at room temperature in methanol than in benzene.[70] In addition, the rates of product formations[70] are insensitive to decreasing temperatures in methanol but become significantly faster at lower temperatures in the aprotic solvents, acetone and diethyl ether.[16] In order to provide an explanation for these results it was suggested that physical quenching of $^1O_2$ by Et_2S is suppressed in methanol.

Detailed kinetic studies of Et_2S photooxidation in methanol provided data which could be accommodated by invoking formation of a single intermediate (Scheme 20). The intermediate was suggested to be either the hydrogen bonded persulfoxide or diethyl(hydroperoxy)methoxysulfurane, **28**. The formation of either intermediate is accompanied by a decrease in the negative charge residing on the terminal oxygen of the persulfoxide and would provide an explanation for the enhanced propensity for attack by Et_2S. Rapid formation of either intermediate would also provide an explanation for the observed suppression of physical quenching.



SCHEME 20

The photooxidations of 3-hydroxypropyl *p*-tolyl sulfide, **29**, *n*-butyl *p*-tolyl sulfide, and Et_2S were examined in a variety of solvents and the sulfone/sulfoxide (R_2SO_2/R_2SO) ratios measured as a function of added methanol.[71] The result of this study for the photooxidation of **29** in acetone-d_6/methanol-d_4 mixtures is depicted in Fig. 3. Methanol-d_4 acts to

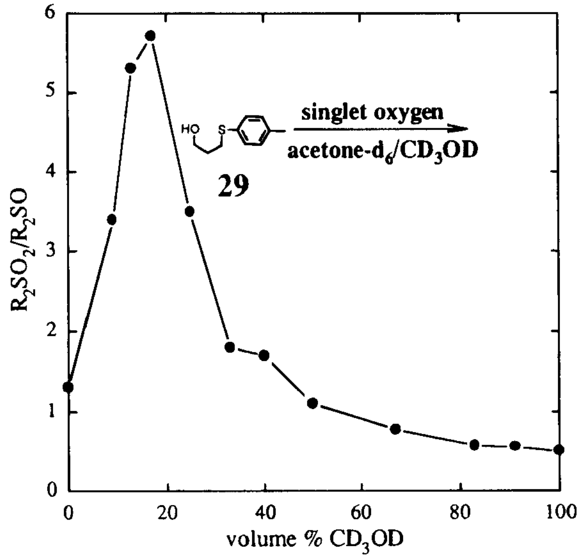
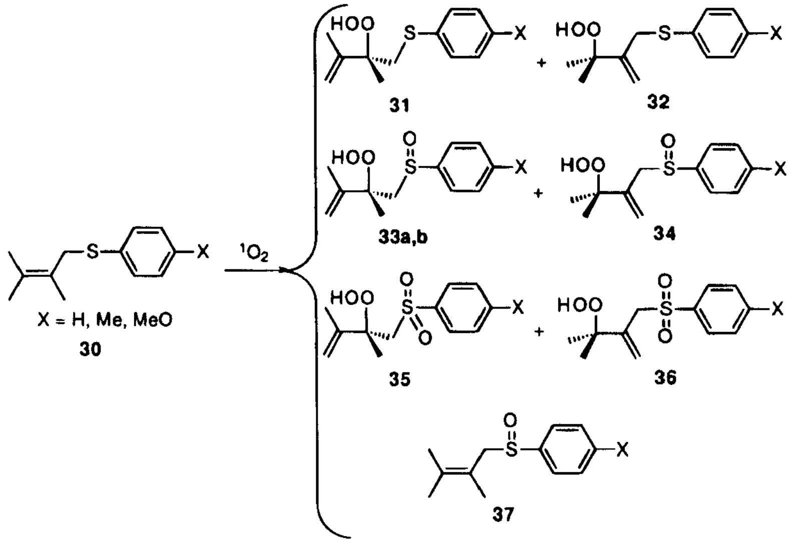


FIGURE 3

increase sulfone formation until its concentration in acetone-d_6 exceeds 17 volume % at which point increasing its concentration leads to a decrease in the sulfone/sulfoxide ratio.

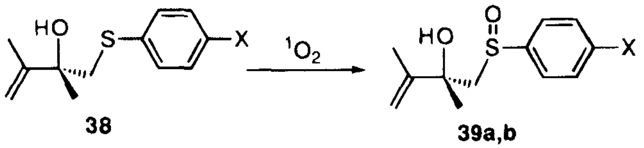
The results depicted in Fig. 3 demand that methanol has at least two discrete functions during the photooxidations of sulfides. At low concentrations it functions to promote and at high concentrations to inhibit sulfone formation. At the present time it is only possible to speculate about the molecular details of this unusual behavior. At low concentrations methanol could hydrogen bond to the sulfoxide product making it more electrophilic and a more potent trapping agent for the persulfoxide. At high concentrations, however, methanol conceivably could act as a catalyst for thiadioxirane formation in a fashion similar to thietane, **27b**. The thiadioxirane is more electrophilic than the persulfoxide and would be anticipated to react preferentially with sulfide to give two sulfoxide products. Alternatively, since CH_3OH is more nucleophilic than H_2O_2, at high concentrations the persulfoxide could be converted into a sulfurane, $Et_2S(OCH_3)_2$ which would be hydrolyzed to the sulfoxide upon work-up.

Additional evidence for the formation of sulfurane intermediates is provided by studies which have examined the reactions of singlet oxygen with sulfides containing a covalently bound oxygen nucleophile as a neighboring group. For example, Clennan and Chen[72–74] have reported the unusual photooxidations of sulfides **31** and **32** which bear neighboring hydroperoxy groups (Scheme 21). These compounds are produced during the photooxidations of a series of allylic sulfides, **30**.



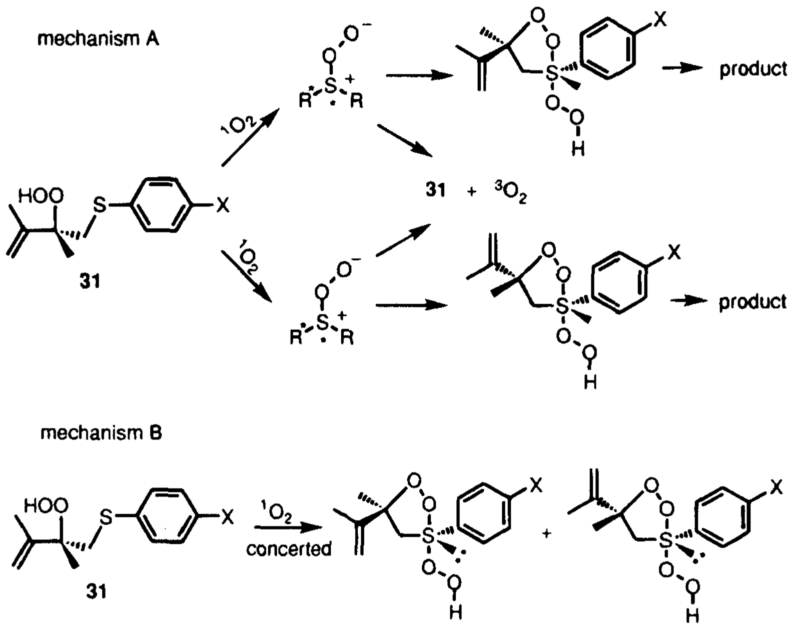
SCHEME 21

Careful analysis of the product ratios during photooxidations of **30** as a function of time demonstrate that the ene products **31** and **32** and the sulfoxide **37** were the only products present at the beginning of the reaction. The diastereomeric sulfoxides, **33a,b**, and sulfoxide **34** were the major over-oxidation products. The sulfones **35** and **36** never exceeded 6% of the reaction mixtures at any time. The diastereomer ratios **33a**/**33b** were greater than 10/1, 13/1, and 20/1 during the early stages of the photooxidation for **30** (X = OMe), **30** (X = Me), and **30** (X = H), respectively. Independent photooxidations of **37** (X = OMe, Me, and H), however, produce **33a,b** in ratios of 1/1.3, 1/1.2, and 1/1.3 providing evidence that **31** and not **37** is the immediate precursor of **33a,b**. Remarkably, independent photooxidation of the alcohol **38** produced the hydroxy sulfoxides, **39a,b**, with a much reduced and reversed diastereoselectivity of 1/2 (Equation 13).



(13)

To explain these unusual results the authors considered the two mechanisms depicted in Scheme 22. In mechanism A photooxidations of hydroperoxides **31** give diastereomeric persulfoxides which partition between sulfurane formation and physical quenching. In this mechanism diastereoselectivity relies on different partitioning ratios for the two persulfoxides since their formations are expected to proceed with little if any diastereoselectivity as supported by the results with alcohol **38** which has a similarly situated chiral center. In mechanism B, however, the sulfuranes are formed concertedly and their rates of formation and not a partitioning ratio must be different. The observation of diastereoselectivity at low temperature where physical quenching is expected to be unimportant argues for this concerted mechanism rather than the stepwise mechanism A.



SCHEME 22

Photooxidations of hydroxy sulfides in which the hydroxy group is tethered to the sulfide by a variable length alkyl chain, **40**, have also been examined[75] (Table 2-2). In contrast to the photooxidation of Et_2S these compounds give substantial amounts of sulfone which appears to be a function of the length of the alkyl chain. The sulfone yield is at a maximum when n = 3 and decreases when the chain is shortened or when it is monotonically increased to n = 6 where the yield of sulfone drops to 0% (Table 2-2). Careful examination of the reaction mixture at less than 2% conversion reveals that the sulfoxide is formed prior to the appearance of the sulfone.[76] In addition, **40SO** is nearly 7 times as potent as Ph_2SO and more than nine times as potent as *n*-butyl *p*-tolyl sulfoxide in its ability to trap diethyl persulfoxide (Scheme 4). These results suggest that intramolecular hydrogen bonding is responsible for the enhanced trapping ability of **40SO**.[77]

A kinetic study of the photooxidations of **40** (n = 2–6) has been carried out in order to provide evidence for sulfurane formation. As part of this study both k_T (the rate constant for substrate induced removal of $^1O_2$) and k_r (the rate constant for product formation) have been experimentally measured, and k_q (the rate constant for physical quenching) determined by difference[78] (Table 2-3). The k_T values are very insensitive to the number of intervening methylenes (n) with a range of less than a factor of two. In contrast, k_r is very sensitive to the number of intervening methylenes between the hydroxy group and the sulfur. The rate constant for product formation from reaction of **40** (n = 3), which can form an energetically favorable 5-membered ring sulfurane,[79] is more than an order of magnitude larger than the rate constant for the reaction of **40** (n = 6), which can only form an 8-membered ring sulfurane. The increase in k_r for the photooxidation of **40** (n = 3) could be accompanied by an increase in k_T (anchimeric assistance) or alternatively by an inhibition of physical quenching, k_q. Unfortunately, the change in k_r for this series of

TABLE 2.2 Product Ratios from the Photooxidations of **40** at –80 °C in Acetone-d_6.

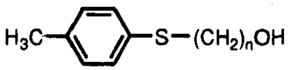
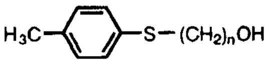
 **40**	*% Sulfoxide*	*% Sulfone*
n = 2	57	43
n = 3	43	56
n = 4	48	52
n = 5	79	21
n = 6	100	0

TABLE 2.3 Kinetic Data for the Photooxidations of **40** in Acetone-d_6

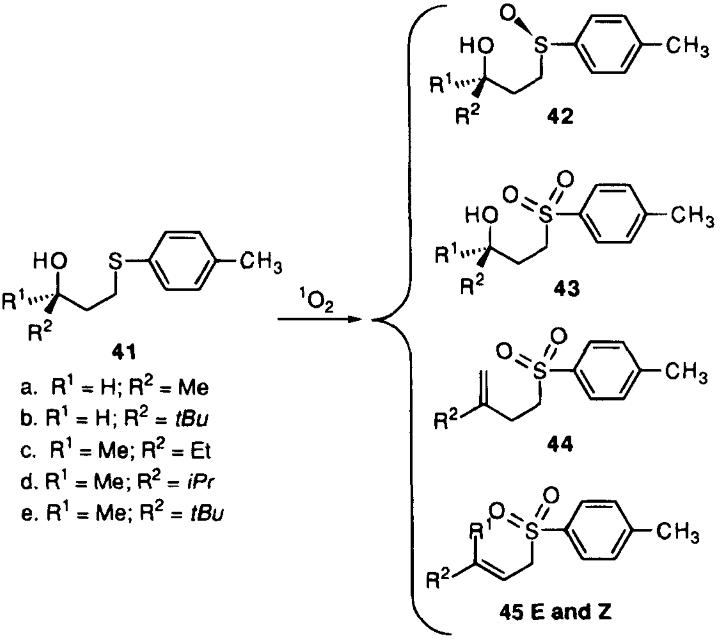
 **40**	$k_T \times 10^{-6}$ $(M^{-1}s^{-1})^a$	$k_r \times 10^{-4}$ $(M^{-1}s^{-1})^a$	$k_q \times 10^{-6}$ $(M^{-1}s^{-1})$	k_q/k_r
n = 2	1.5 – 0.1 (1.0)	4.2 – 0.3 (6.9)	1.46	34.8
n = 3	2.29 – 0.2 (1.5)	7.1 – 0.3 (11.6)	2.22	31.3
n = 4	2.7 – 0.1 (1.8)	4.1 – 0.3 (6.7)	2.66	64.9
n = 5	2.9 – 0.1 (1.9)	1.5 – 0.1 (2.5)	2.88	192
n = 6	2.2 – 0.1 (1.5)	0.61 – 0.02 (1)	2.19	359

a. relative rates in parentheses

compounds (fastest—slowest = 6.49 × 10^4) is small in comparison to the magnitudes of k_T [(1.5–3.7) × 10^6] or k_q [(1.46–3.63) × 10^6] and consequently its effect on these rate constants is experimentally undetectable.

Perhaps the most compelling evidence for a sulfurane intermediate came from a study of the photooxidations of the γ-hydroxy sulfides **40** (n = 3) and **41a–e** (Scheme 23). Photooxidations of **40**, **41a**, and **41c** resulted in formations of the anticipated sulfoxide diastereomers, **42**, and the sulfone, **43**. In contrast, photooxidations of **41b, 41d**, and **41e** produced, in addition to the anticipated sulfoxides and sulfones, the unexpected olefins, **44**, and **45E** and **Z**. The olefin yield increased as a function of the size of the substituents on the carbinol carbon. For example, photooxidations at –80 °C produced 1, 22, and 40% of the olefins in the reactions of hydroxy sulfides **41b, 41d**, and **41e**, respectively. The olefin yield increased to 14% for **41b** if the photooxidation was carried out at –10 °C.

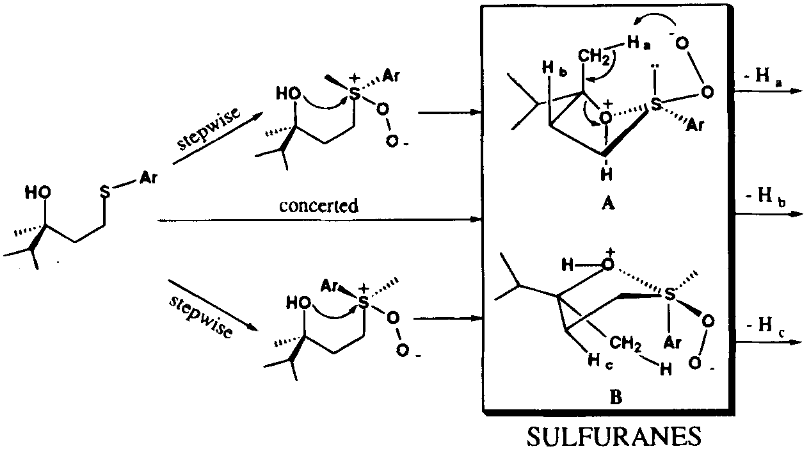
Evidence for the origin of these unusual olefins was obtained by photooxidation of a sample of **41d** which was labeled with ^{17}O (δ^{17}O, 46.5 ppm relative to H_2O). Examination of the reaction mixture after complete disappearance of **41d** revealed both a hydroxyl peak at 46 ppm and a new peak at 141 ppm in the ^{17}O NMR spectrum in an 81/19 ratio. No ^{17}O NMR peaks were observed in the unlabeled reaction mixture under identical acquisition conditions. The ^{17}O chemical shift at 141 ppm is in the range (δ^{17}O, 120–183 ppm) expected for sulfonyl oxygen and substantially downfield of that anticipated for sulfinyl oxygen (δ^{17}O, –20 to +20 ppm). Chromatographic separation of the products followed by ^{17}O NMR revealed that only the hydroxyl oxygens in **42** and **43** and the sulfonyl oxygen in **44**, and **45E** and **Z** were labeled. These results are consistent with intramolecular attack of the hydroxy group at sulfur in either a stepwise or concerted process to give sulfurane



SCHEME 23

intermediates (Scheme 24). Abstraction of hydrogens **a**, **b**, or **c** by the peroxy anion produce novel hydroxy hydroperoxy sulfuranes which decompose by loss of water to give the olefinic sulfones **44** and **45E, Z**.

The participation of a remote sulfur has also been suggested during the photooxidation of 1,5-dithia-cyclooctane, **46**.[80] This suggestion was based upon the kinetic data presented in Table 2-4. The rate constant for the substrate induced removal of singlet oxygen from solution, k_T, for **46** is nearly 11 times larger than for 1,4-dithiacyclohexane, **47**, more than 3 times larger than for pentamethylene sulfide, **48**, and more than 16 times larger than for **46SO**. In addition, k_r for **46** is 155 times larger than for **47** and 79 times larger than for **48**. Physical quenching represents only 30% of the total interactions of singlet oxygen with **46** but 95 and 97% of the total interactions with **47** and **48**, respectively. It was suggested that participation of the remote sulfur in **46** either concertedly or via the persulfoxide competitively inhibits unproductive physical quenching.



SCHEME 24

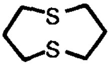
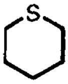
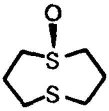
2.5. *Thiiranes*

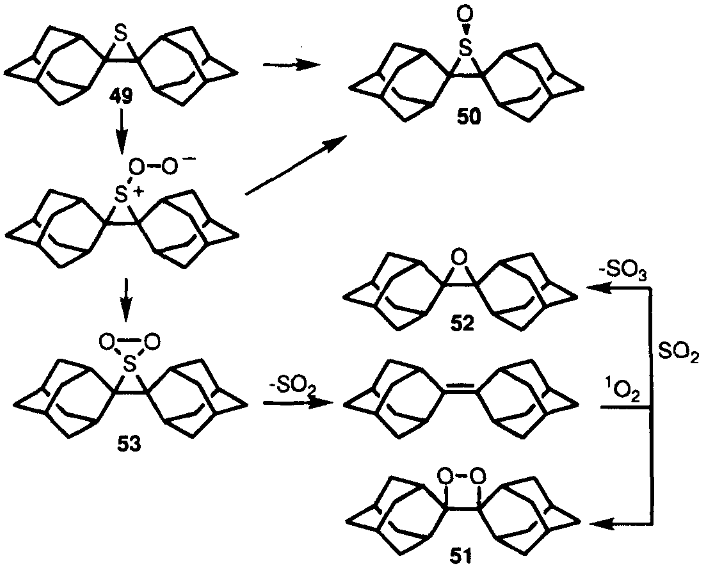
Thiiranes exhibit unique reactivity towards singlet oxygen as revealed by both experimental and theoretical studies. For example Ando and coworkers[81] reported that **49** reacted with singlet oxygen to give the anticipated sulfoxide, **50**, along with dioxetane, **51**, epoxide, **52**, and a trace of adamantylideneadamantane (Scheme 25). The authors suggested that these results implicated a spirodioxathiirane intermediate, **53**, which decomposed to generate the olefin and SO_2. The dioxetane and epoxide are oxidation products of the olefin formed by rearrangement, and SO_2 trapping of the perepoxide intermediate, respectively (Scheme 25).

Jensen and Foote[82] reported that thiirane and simple alkyl substituted thiiranes react readily with singlet oxygen even at low temperatures. The products critically depend upon the nature of the solvent and on the concentrations of the substrates. For example, thiirane itself reacts with singlet oxygen in nonnucleophilic solvents to give exclusively thiirane oxide. However, in methanol at low concentrations ($<10^{-2}$ M) methyl 2-methoxyethanesulfinate, **54**, is the only product observed (Scheme 26). At high concentrations (> 0.5 M) the reaction is dominated by polymer formation.

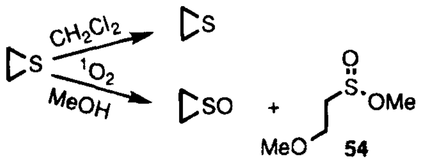
Photooxidations of 2-methylthiirane, **55**, at –20 °C in nonnucleophilic solvents gave both *cis*- and *trans*-2-methylthiirane oxide along with a small amount of polymer (Scheme 27). Identical results were observed in

TABLE 2.4 Kinetic Data for the Reactions of Cyclic Sulfides in Acetone.

compound	$k_T \times 10^{-6}$ ($M^{-1}s^{-1}$)	$k_r \times 10^{-6}$ ($M^{-1}s^{-1}$)	$k_q \times 10^{-6}$ ($M^{-1}s^{-1}$)
 **46**	53	37.3	15.7
 **47**	4.83	0.24	4.59
 **48**	16.1	0.47	15.6
 **46SO**	3.28		

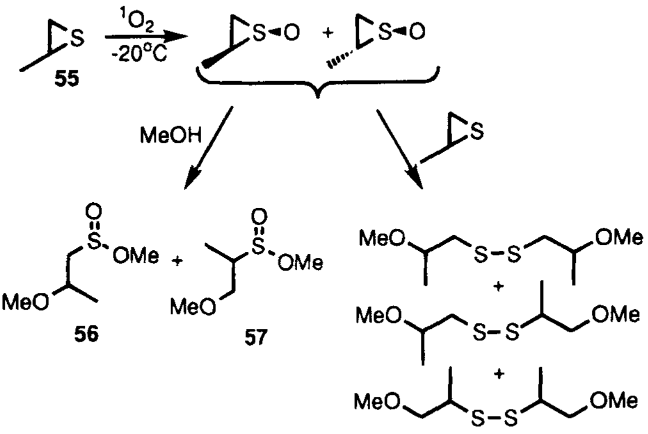


SCHEME 25



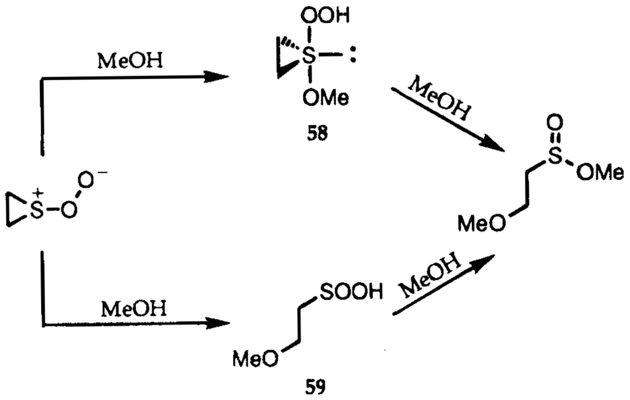
SCHEME 26

methanol at low substrate concentrations and low temperatures. However, at higher temperatures the isomeric thiirane oxides reacted with methanol to generate two sulfinate esters, **56** and **57**. At higher concentrations the thiirane oxides reacted with adventitious thiirane to give a mixture of disulfides. Attempted trapping reactions with Ph_2S, Ph_2SO, and methyl propiolate were unsuccessful.



SCHEME 27

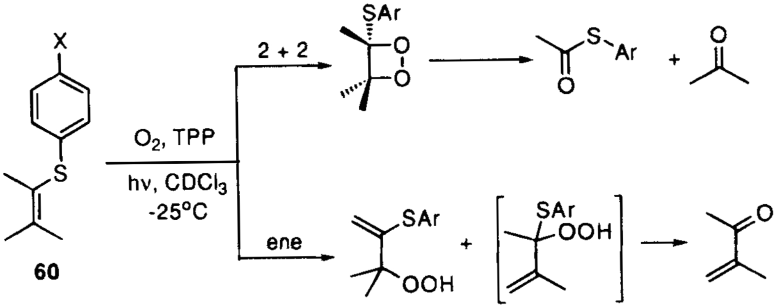
Jensen and Foote[82] pointed out that there are two possible mechanisms for the formations of the sulfinate esters **56** and **57** (Scheme 28). Reaction of methanol could occur at sulfur to generate a hydroperoxysulfurane, **58**, or alternatively it could occur at carbon to generate a persulfenic acid, **59**. Akasaka and coworkers,[83] however, reported that intermediates formed in the photooxidations of thiiranes are capable of epoxidizing olefins and suggested that persulfenic acids such as **59** were the reactive intermediates.



SCHEME 28

2.6. *Vinyl Sulfides*

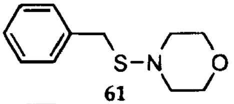
The photooxidation of vinyl sulfides has been discussed in a recent review.[7] Oxidations at sulfur during the photooxidations of these intriguing compounds rarely occur. The small k_r for chemical reaction at sulfur cannot compete effectively with either [2 + 2] or ene reactions at the olefinic linkage.[84] However, Adam and coworkers[85] in a recent report pointed out that despite the lack of reactivity at sulfur its electronic character dramatically influences the partitioning between the [2 + 2] and ene reaction channels. [2 + 2] Cycloaddition to give a dioxetane is exclusively observed when **60** (X = OMe) is photooxidized (Scheme 29). In contrast, when X = NO_2 60% of the reaction goes via the ene reaction channel.



SCHEME 29

3. SULFENAMIDES

Only two studies of the reactions of sulfenamides with singlet oxygen have been reported. A sulfenamide analogue of ebselen (2-phenyl-1,2-benzisoselenazol-3(2*H*)-one) has been reported to quench singlet oxygen,[86] but the identities of the products or whether products are even formed was not noted. In the second study, Clennan and Zhang[87,88] examined the photooxidations of sulfenamides **61**–**69**. Singlet oxygen reacted with **61**–**65** to give exclusively the corresponding sulfinamides while **66**–**69** gave both the sulfinamide and sulfonamide products.



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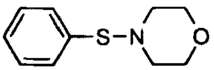

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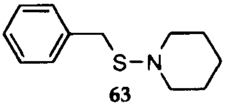
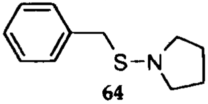
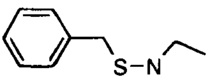


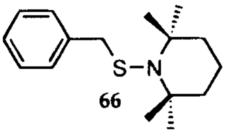
63



64



65



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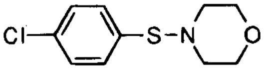

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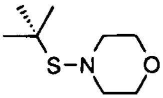

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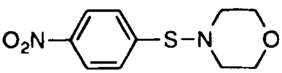
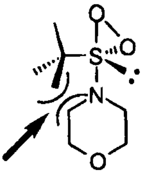


69

Detailed trapping studies with Ph_2S and Ph_2SO during photooxidations of **61** provided evidence for a reaction surface very similar to that reported for Et_2S including the presence of two intermediates. Hammett studies also revealed that aryl sulfoxides trapped a nucleophilic intermediate ($\rho = +1.3$) and aryl sulfides an electrophilic intermediate ($\rho^+ = -0.26$).

As anticipated however, there are differences in the photooxidative behavior of these sulfenamides and Et_2S. For example, **61** gave the sulfinamide product at a rate twice as fast ($k_r = 2.94 \times 10^6 M^{-1}s^{-1}$) as the rate of removal of singlet oxygen from solution, $k_T = 1.28 \times 10^6 M^{-1}s^{-1}$, 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 Et_2S is less than 5% 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.

The k_X/k_{PhO} value (Scheme 4 and Equation 3) for the reaction of **61** is also 3 times larger than the corresponding value obtained for the photooxidation of Et_2S. The authors attributed this to an enhanced stability of the thiadioxirane by the electron withdrawing apical nitrogen atom. The formation of sulfonamides in the reactions of **67** and **69** was attributed to adventitious trapping of the persulfinamide by the electron poor sulfinamide product. On the other hand, the sulfonate formation in the reactions of **66** and **68** was attributed to a decrease in the rate of persulfinamide thiadioxirane interconversion, k_X (Scheme 4) as a result of severe steric interactions in the incipient thiadioxirane, **70**. This decrease in k_X also allows the competitive trapping of the persulfinamide to be observed. Consistent with these suggestions were oxygen isotopic labeling results which demonstrated that the two oxygens in the sulfonamides did not have the same molecular ancestry.



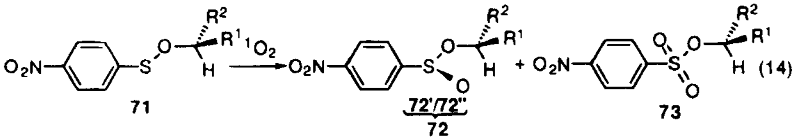
70

The severe steric interactions in **66** and **68** which lead to a decrease in k_x should also allow physical quenching to compete with product formations. Indeed, in contrast to **61** which does not physically quench singlet oxygen, 45 to 55% of the interactions of $^1O_2$ with **68** are unproductive.

4. SULFENATE ESTERS

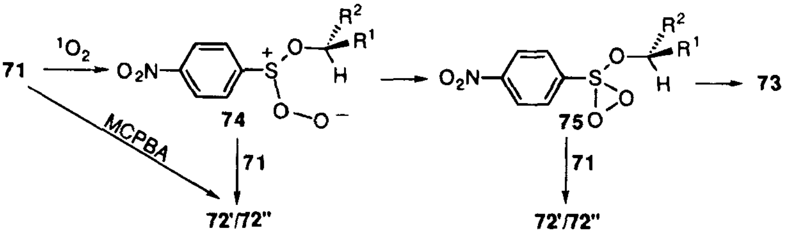
Photolysis of benzenesulfenates and 4-nitrobenzenesulfenates at wavelengths greater than 300 nm results in homolytic cleavages of the O-S bonds to produce alkoxy radicals.[89] In the presence of oxygen, however, the 4-nitrobenzenesulfenate esters competitively undergo oxidations to form the corresponding alkyl sulfinate esters. Addition of 1,3-cyclohexadiene quenches the sulfenate oxidation with concomitant formation of the endoperoxide implicating singlet oxygen as the reactive oxidant.[90] *trans*-Piperylene also quenched the oxidations suggesting that the singlet oxygen is formed via the triplet excited state of the sulfenate ester in a self-sensitization process.

Pasto and Cottard[91] reported a detailed study of the self-sensitized singlet oxygenation of a series of *sec*-alkyl 4-nitrobenzenesulfenates, **71** (Eqn. 14). These esters reacted to form sulfonate esters, **73**, in addition to the anticipated diastereomeric sulfinate esters, **72'** and **72"**, in a ratio dictated by the size of the alkyl group R^2. As the size of R^2 increased the sulfinate/sulfonate ratio, **72/73** decreased concomitantly with a decrease in the overall yield of the sulfinate and sulfonate. The decrease in the total yield of **72** and **73** was attributed to competitive formation of alkyl 4-nitrophenyl sulfides. The formations of these sulfides were initiated by sterically facilitated homolytic cleavages of the sulfur-oxygen bonds to give thiyl and alkoxy radicals. β-Cleavage of the alkoxy radicals followed by bond formation between the resulting carbon centered and thiyl radicals produced the sulfides.



a. $R^1 = CH_3$; $R^2 = CH_2CH_3$
b. $R^1 = CH_3$; $R^2 = CH(CH_3)_2$
c. $R^1 = CH_3$; $R^2 = C(CH_3)_3$
d. $R^1 = Ph$; $R^2 = CH_3$
e. $R^1 = Ph$; $R^2 = CH_2CH_3$
f. $R^1 = Ph$; $R^2 = CH(CH_3)_2$
g. $R^1 = Ph$; $R^2 = C(CH_3)_3$

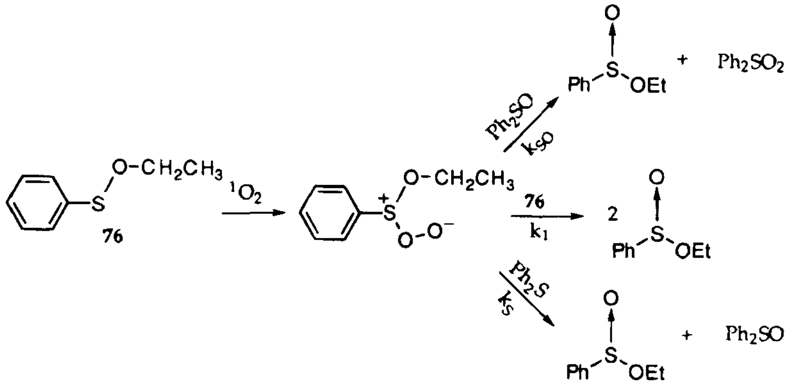
The increase in the sulfonate esters, **73**, relative to sulfinate esters, **72**, with increasing size of R^2 was attributed to increasing lifetimes of the persulfinates, **74**, allowing their unimolecular collapse to the thiadioxiranes, **75**, and subsequent cleavages to the sulfonates (Scheme 30). In the absence of severe steric interactions it was suggested that **74** reacted with the sulfenate esters to give the two sulfinate ester products. In a very complicated stereochemical argument the authors contended that MCPBA and singlet oxygen should attack the same lobe of the sulfur 3p AO ultimately leading to the same diastereomer ratio **72'/72"**. The different diastereoselectivities observed in the MCPBA and singlet oxygen reactions of **71d** and **71e** could therefore only be rationalized by formation of the thiadioxiranes.



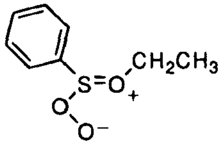
SCHEME 30

Clennan and Chen[92] however failed to generate evidence for a thiadioxirane in a detailed kinetic study of the photooxidation of ethyl benzenesulfenate, **76**. Trapping studies demonstrate that **76**, Ph_2S, and Ph_2SO all compete for the same intermediate as depicted in Scheme 31. Hammett substituent constants, ρ, of 0.34 and 1.41 for trapping with diaryl sulfides and sulfoxides, respectively, are indicative of the nucleophilic character of the trapped intermediate.

All of the singlet oxygen removed from solution by **76** is incorporated into the products, and consequently physical quenching does not occur. The absence of physical quenching and of a second intermediate could potentially be attributed to either (1) enhanced stability of the persulfinate perhaps as a result of the contribution of resonance form **77**, or (2) competitive inhibition of both physical quenching and interconversion to a second intermediate by trapping of **77** with the sulfenate ester starting material.



SCHEME 31

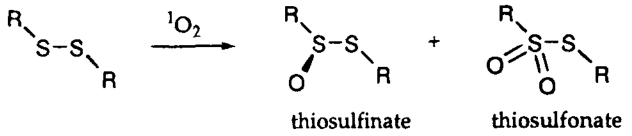


77

The sulfenate ester, **76**, is nearly as good a trapping agent as diphenyl sulfoxide ($k_l/k_{SO} = 0.33$). Corroborating evidence that **76** can remove an oxygen atom from a persulfinate was obtained during an examination of the photooxidations of mixtures of adamantylideneadamantane and **76** which resulted in enhanced formation of the epoxide.

5. DISULFIDES

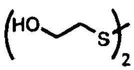
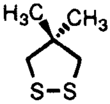
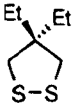
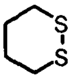
Murray and coworkers[93–95] in the early 1970's reported that disulfides react with singlet oxygen via a Foote-like mechanism (Scheme 3) to give both thiosulfinates and thiosulfonates (Eqn. 15). Recent work, however, has pointed out that the sulfinate/sulfonate ratios are much more dependent on the nature of the solvent than previously reported and has led to the suggestion of a new mechanism for these reactions.[96,97]



(15)

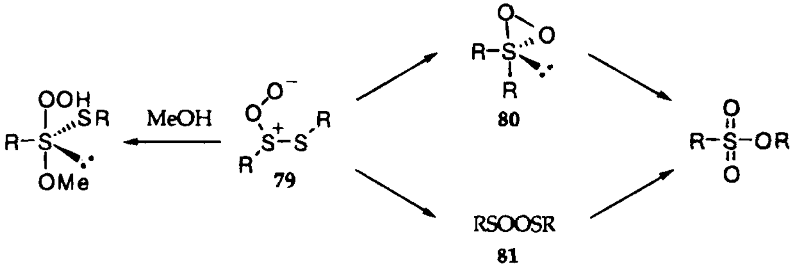
In stark contrast to the photooxidations of dialkyl sulfides which give predominantly sulfoxides the major products formed in the reactions of $^1O_2$ with disulfides in aprotic solvents are the thiosulfonates (Table 5–1). The yields of thiosulfinate, however, do increase at the expense of the sulfonates at either low temperature or in the protic solvent methanol. In the case of 4,4-diethyl-1,2-dithiolane, **78**, a complete reversal from 20/80 to 80/20 thiosulfinate/thiosulfonate occurred upon changing the solvent from acetone-d_6 to CD_3OD. Control reactions indicated that under the reaction conditions the thiosulfinates are inert to singlet oxygen and do not serve as precursors to the thiosulfonates.

TABLE 5.1 Thiosulfinate and Thiosulfonate Ratios During Photooxidations of Disulfides

Compound	solvent	T°C	% RS(O)SR	% $RS(O)_2SR$
MeSSMe	acetone-d_6	20	40	60
EtSSEt	acetone-d_6	20	14	86
	acetone-d_6	−78	55	45
	CD_3OD	20	85	15
	CD_3OD	−78	59	41
iPrSSiPr	acetone-d_6	20	trace	trace
tBuSStBu	acetone-d_6	20	no reaction	no reaction
	acetone-d_6	20	32	68
	CD_3OD	20	79	21
	$CDCl_3$	20	30	70
	CH_3CN	20	23	77
	benzene-d_6	20	38	62
	acetone-d_6	20	16	84
	CD_3OD	20	86	14
 **78**	acetone-d_6	20	20	80
	CD_3OD	20	80	20
	acetone-d_6	20	32	68
	CD_3OD	20	66	34

It is tempting to speculate that methanol traps the thiopersulfinate intermediate, **79**, to give a hydroperoxysulfurane thereby competitively inhibiting formation of the thiadioxirane, **80**, or the bissulfenyl peroxide, **81**, which could potentially serve as precursors to the thiosulfonate (Scheme 32). Murray and coworkers[98] previously suggested that the small effect of methanol observed during the photooxidation of methyl α-lipoate was a result of hydrogen bonding to the persulfinate intermediate which would be expected to inhibit thiosulfonate formation. Inconsistent with the hydrogen bonding argument, however, is the observation that photooxidations of 4,4-dimethyl-1,2-dithiolane in 7/3 v/v mixtures of tBuOH/benzene and MeOH/benzene resulted in dramatically different thiosulfinate/thiosulfonate ratios of 23/77 and 90/10, respectively. The inability of tBuOH in comparison to MeOH to inhibit thiosulfonate formation is most consistent with a steric effect on the formation of the hydroperoxysulfurane.

Isotopic labeling studies with $^{16}O_2/^{18}O_2$ mixtures during photooxidations of sulfides, sulfenamides, and sulfenate esters reveal that the two oxygen



SCHEME 32

atoms in the sulfonate products are from different oxygen molecules.[97] This result is consistent with formation of the sulfonates via adventitious trapping of a persulfinate intermediate. In dramatic contrast to these results the labeling studies during photooxidations of disulfides demand that the oxygen atoms in the thiosulfonates have the same molecular ancestry. Rather than invoke a unique ability of **80** to unimolecularly cleave to give the thiosulfonate product it is most reasonable to postulate the intermediacy of **81**. Consistent with this suggestion is the report of Ando that triazolinediones insert into the S-S bond of disulfides to give the nitrogen analogue of **81**.[99]

Acknowledgments

I am grateful to my able coworkers whose names appear in the references for their many contributions and I thank the National Science Foundation and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for their generous support of this research.

References

[1] Foote, C. S. (1976) In *Free Radicals in Biology*, W. A. Pryor, Ed., Academic Press: New York, NY, Vol. 2; pp. 85–133.
[2] Foote, C. S. (1991) *Photochem. Photobiol.* **54**, 659.
[3] Murray, R. W., Kaplan, H. L. (1969) *J. Am. Chem. Soc.* **91**, 5358–5364.
[4] Schenck, G. O., Krausch, C. H. (1962) *Angew. Chem.* **74**, 510.
[5] Clennan, E. L. In *Advances in Oxygenated Processes*, A. L. Baumstark, Ed. JAI Press: Greenwich, CT., 1995, Vol. IV; pp 49–80.
[6] Ando, W. (1981) *Sulfur Rep.* **1**, 147–213.
[7] Ando, W., Takata, T. (1985) In *Singlet HO_2. Reaction Modes and Products. Part 2;* A. A. Frimer, Ed.; CRC Press, Inc.: Boca Raton, Fl., Vol. III; pp 1–117.
[8] Kasha, M., Brabham, D. E. (1979) In *Singlet Oxygen*; H. H. Wasserman and R. W. Murray, Ed.; Academic Press: New York, N. Y., Vol. 40; pp 1–33.

[9] Krasnovski, A. A. (1979) *Photochem. Photobiol.* **29**, 29.
[10] Chou, P., Frei, H. (1985) *Chem. Phys. Lett.* **29**, 87–92.
[11] Schmidt, R., Bodesheim, M. (1994) *J. Phys. Chem.* **98**, 2874–2876.
[12] Wang, B., Ogilby, P. R. (1995) *J. Photochem. Photobiol.* **90**, 85–89.
[13] Wang, B., Ogilby, P. R. (1993) *J. Phys. Chem.* **97**, 193–195.
[14] Liang, J.-J., Gu, C.-L., Kacher, M. L., Foote, C. S. (1983) *J. Am. Chem. Soc.* **105**, 4717–4721.
[15] Nahm, K., Foote, C. S. (1989) *J. Am. Chem. Soc.* **111**, 1909–1910.
[16] Gu, C.-L., Foote, C. S. (1982) *J. Am. Chem. Soc.* **104**, 6060–6063.
[17] Ouannes, C., Wilson, T. (1968) *J. Am. Chem. Soc.* **90**, 6527–6528.
[18] Ogryzlo, E. A., Tang, C. W. (1970) *J. Am. Chem. Soc.* **92**, 5034–5036.
[19] Foote, C. S., Denny, R. W. (1968) *J. Am. Chem. Soc.* **90**, 6233–6235.
[20] Foote, C. S., Chang, Y. C., Denny, R. W. (1970) *J. Am. Chem. Soc.* **92**, 5216–5218.
[21] Bellus, D. (1979) In *Advances in Photochemistry*; J. N. Pitts, G. S. Hammond and K. Gollnick, Ed.; John Wiley & Sons: New York, Vol. 11; pp 105.
[22] Clennan, E. L., Noe, L. J., Szneler, E., Wen, T. (1990) *J. Am. Chem. Soc.* **112**, 5080–5085.
[23] Gorman, A. A., Hamblett, I., Lambert, C., Spencer, B., Standen, M. C. (1988) *J. Am. Chem. Soc.* **110**, 8053–8059.
[24] Clennan, E. L., Oolman, K. A., Yang, K., Wang, D.-X. (1991) *J. Org. Chem.* **56**, 4286–4289.
[25] Kacher, M. L., Foote, C. S. (1979) *Photochem. Photobiol.* **29**, 765–769.
[26] Ackerman, R. A., Rosenthal, I., Pitts, Jr., J. N. (1971) *J. Chem. Phys.* **54**, 4960–4961.
[27] Inoue, K., Matsuura, T., Saito, I. (1985) *Tetrahedron* **41**, 2177–2181.
[28] Nelsen, S. F., Teasley, M. F., Kapp, D. L. (1986) *J. Am. Chem. Soc.* **108**, 5503–5509.
[29] Clennan, E. L., Simmons, W., Almgren, C. W. (1981) *J. Am. Chem. Soc.* **103**, 2098–2099.
[30] Schäfer, K., Bonifacic, M., Bahnemann, D., Asmus, K.-D. (1978) *J. Phys. Chem.* **82**, 2777–2780.
[31] Monroe, B. M. (1979) *Photochem. Photobiol.* **29**, 761–764.
[32] Sawaki, Y., Ogata, Y. (1981) *J. Am. Chem. Soc.* **103**, 5947–5948.
[33] Jensen, F., Foote, C. S. (1988) *J. Am. Chem. Soc.* **110**, 2368–2375.
[34] Jensen, F. (1992) *J. Org. Chem.* **57**, 6478–6487.
[35] Jensen, F. (1995) In *Advances in Oxygenated Processes*; A. L. Baumstark, Ed.; JAI Press: Greenwich, CT., Vol. IV; pp 1–48.
[36] Akasaka, T., Yabe, A., Ando, W. (1987) *J. Am. Chem. Soc.* **109**, 8085–8087.
[37] Ando, W., Akasaka, T. (1987) In *The Role of Oxygen in Chemistry and Biochemistry. Proceedings of an International Symposium on Activation of Dioxygen and Homogeneous Catalytic Oxidations*; Elsevier Science Publishers: Tsukuba, Japan, pp 99–108.
[38] Akasaka, T., Ando, W. (1983) *J. Chem. Soc. Chem. Commun.* 1203–1204.
[39] Ando, W., Miyazaki, H., Akasaka, T. (1982) *Tetrahedron Lett.* **23**, 2655–2656.
[40] Frimer, A. A., Marks, V., Gilinsky-Sharon, P., Aljadeff, G., Gottlieb, H. E. (1995) *J. Org. Chem.* **60**, 4510–4520.
[41] Akasaka, T., Haranaka, M., Ando, W. (1991) *J. Am. Chem. Soc.* **113**, 9898–9900.
[42] Akasaka, T., Ando, W. (1994) *Phosphorus, Sulfur, Silicon* **95–96**, 437–438.
[43] Martin, L. D., Martin, J. C. (1977) *J. Am. Chem. Soc.* **99**, 3511–3513.
[44] Bartlett, P. D., Aida, T., Chu, H.-K., Fang, T.-S. (1980) *J. Am. Chem. Soc.* **102**, 3515–3524.
[45] Laver, H. S., MacCallum, J. R. (1978) *Photochem. Photobiol.* **28**, 91–93.
[46] Corey, E. J., Ouannes, C. (1976) *Tetrahedron Lett.* 4263–4266.
[47] Ando, W., Ito, K., Takata, T. (1982) *Tetrahedron Lett.* **23**, 3909–3912.
[48] Takata, T., Hoshino, K., Takeuchi, E., Tamura, Y., Ando, W. (1984) *Tetrahedron Lett.* **25**, 4767–4770.
[49] Takata, T., Tamura, Y., Ando, W. (1985) *Tetrahedron* **41**, 2133–2137.

[50] Akasaka, T., Sakurai, A., Ando, W. (1991) *J. Am. Chem. Soc.* **113**, 2696–2701.
[51] Ando, W., Nagashima, T., Saito, K., Kohmoto, S. (1979) *J. Chem. Soc. Chem. Commun.* 154–156.
[52] Takata, T., Ishibashi, K., Ando, W. (1985) *Tetrahedron Lett.* **26**, 4609–4612.
[53] Sheu, C., Foote, C. S., Gu, C.-L. (1992) *J. Am. Chem. Soc.* **114**, 3015–3021.
[54] Pasto, D. J., Cottard, F., Jumelle, L. (1994) *J. Am. Chem. Soc.* **116**, 8978–8984.
[55] Bartlett, P. D. (1978) In *Organic Free Radicals*; W. A. Pryor, Ed.; American Chemical Society: Washington, DC, Vol. 69; pp 15–32.
[56] Banchereau, E., Lacombe, S., Ollivier, J. (1995) *Tetrahedron Lett.* **36**, 8197–8200.
[57] Correa, P. E., Riley, D. P. (1985) *J. Org. Chem.* **50**, 1787–1788.
[58] Correa, P. E., Hardy, G., Riley, D. P. (1988) *J. Org. Chem.* **53**, 1695–1702.
[59] Riley, D. P., Correa, P. E. (1986) *J. Chem. Soc. Chem. Commun.* 1097–1098.
[60] Plesnicar, B., Cerkovnik, J., Koller, J., Kovac, F. (1991) *J. Am. Chem. Soc.* **113**, 4946–4953.
[61] Watanabe, Y., Kuriki, N., Ishiguro, K., Sawaki, Y. (1991) *J. Am. Chem. Soc.* **113**, 2677–2682.
[62] Ando, W., Kabe, Y., Miyazaki, H. (1980) *Photochem. Photobiol.* **31**, 191–194.
[63] Greer, A., Jensen, F., Clennan, E. unpublished results.
[64] Clennan, E. L., Dobrowolski, P., Greer, A. (1995) *J. Am. Chem. Soc.* **117**, 9800–9803.
[65] Yamaguchi, K., Takada, K., Otsuji, Y., Mizuno, K. (1992) In *Organic Peroxides*; W. Ando, Ed.; John Wiley & Sons: New York, pp 1–100.
[66] Clennan, E. L., Greer, A., unpublished results.
[67] Oae, S., Doi, J. T. (1991) *Organic Sulfur Chemistry: Structure and Mechanism*; CRC Press: Boca Raton, FL, pp 433.
[68] Foote, C. S., Denny, R. W., Weaver, L., Chang, Y. (1970) *Ann. N.Y. Acad. Sci.* **171**, 139–148.
[69] Lissi, E. A., Encinas, M. V., Lemp, E., Rubio, M. A. (1993) *Chem. Rev.* **93**, 699–723.
[70] Foote, C. S., Peters, J. W. (1971) *J. Am. Chem. Soc.* **93**, 3795–3796.
[71] Clennan, E. L., Yang, K. (1993) *Tetrahedron Lett.* **34**, 1697–1700.
[72] Clennan, E. L., Chen, X. (1988) *J. Org. Chem.* **53**, 3124–3125.
[73] Clennan, E. L., Chen, X. (1989) *J. Am. Chem. Soc.* **111**, 8212–8218.
[74] Clennan, E. L., Chen, X. (1989) *J. Am. Chem. Soc.* **111**, 5787–5792.
[75] Clennan, E. L., Yang, K. (1992) *J. Org. Chem.* **57**, 4477–4487.
[76] Clennan, E. L., Yang, K. (1993) *Heteroatom Chem.* **4**, 197–201.
[77] Kingsbury, C. A., Auerbach, R. A. (1971) *J. Org. Chem.* **36**, 1737–1742.
[78] Clennan, E. L., Yang, K., Chen, X. (1991) *J. Org. Chem.* **56**, 5251–5252.
[79] Hayes, R. A., Martin, J. C. (1985) In *Organic Sulfur Chemistry. Theoretical and Experimental Advances*; F. Bernardi, I. G. Csizmadia and A. Mangini, Ed.; Elsevier: Amsterdam, The Netherlands, Vol. 19; pp 408–483.
[80] Clennan, E. L., Wang, D.-X., Yang, K., Hodgson, D. J., Oki, A. R. (1992) *J. Am. Chem. Soc.* **114**, 3021–3027.
[81] Ando, W., Sonobe, H., Akasaka, T. (1986) *Tetrahedron Lett.* **27**, 4473–4476.
[82] Jensen, F., Foote, C. S. (1987) *J. Am. Chem. Soc.* **109**, 1478–1485.
[83] Akasaka, T., Kako, M., Sonobe, H., Ando, W. (1988) *J. Am. Chem. Soc.* **110**, 494–496.
[84] Wilkinson, F., Helman, W. P., Ross, A. B. (1995) *J. Phys. Chem. Ref. Data* **24**, 663–1021.
[85] Adam, W., Kumar, A. S., Saha-Möller, C. R. (1995) *Tetrahedron Lett.* **36**, 7853–7854.
[86] Scurlock, R., Rougee, M., Bensasson, R. V., Evers, M., Dereu, N. (1991) *Photochem. Photobiol.* **54**, 733–736.
[87] Clennan, E. L., Zhang, H. (1994) *J. Am. Chem. Soc.* **116**, 809–810.
[88] Clennan, E. L., Zhang, H. (1995) *J. Am. Chem. Soc.* **117**, 4218–4227.
[89] Pasto, D. J., L'Hermine, G. (1990) *J. Org. Chem.* **55**, 5815–5816.
[90] Pasto, D. J., Cottard, F., Horgan, S. (1993) *J. Org. Chem.* **58**, 4110–4112.
[91] Pasto, D. J., Cottard, F. (1994) *J. Am. Chem. Soc.* **116**, 8973–8977.
[92] Clennan, E. L., Chen, M.-F., (1995) *J. Org. Chem.* **60**, 6444–6447.

[93] Murray, R. W., Smetana, R. D., Block, E. (1971) *Tetrahedron Lett.* 299–302.
[94] Murray, R. W., Jindal, S. L. (1972) *Photochem. Photobiol.* **16**, 147–151.
[95] Murray, R. W., Jindal, S. L. (1972) *J. Org. Chem.* **37**, 3516–3520.
[96] Clennan, E. L., Wang, D., Zhang, H., Clifton, C. H. (1994) *Tetrahedron Lett.* **35**, 4723–4726.
[97] Clennan, E. L., Zhang, H. (1994) *J. Org. Chem.* **59**, 7952–7954.
[98] Stary, F. E., Jindal, S. L., Murray, R. W. (1975) *J. Org. Chem.* **40**, 58–62.
[99] Akasaka, T., Ando, W. (1992) In *Organic Peroxides*; W. Ando, Ed.; John Wiley & Sons: Chichester West Sussex England, pp 599–659.