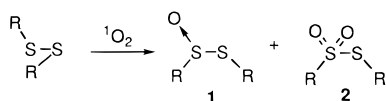*J. Am. Chem. Soc.* **1997**, *119*, 9081−9082

9081

Geometry-Dependent Quenching of Singlet Oxygen by Dialkyl Disulfides

E. L. Clennan,* Dongyi Wang, C. Clifton, and M.-F. Chen

*Department of Chemistry, University of Wyoming
Laramie, Wyoming 82071*

Studies of the reactions of singlet oxygen with disulfides have shown that the primary products of these reactions are thiol sulfinates, (**1**) and thiol sulfonates (**2**).[1−5] We report here a detailed kinetic study of these photooxidations which demonstrate that in addition to this chemical reaction, disulfides also have the unique capability of deactivating singlet oxygen by two different physical quenching mechanisms. Furthermore, we show that the predominant mechanism of physical quenching is dictated by the >RSSR dihedral angle and by the steric requirements of the substituent R.


The total rate constants, k_T, for quenching of $^1O_2$ by the disulfides **3**−**10** are given in Table 1 along with previously determined values for representative dialkyl sulfides and for a trisulfide (**17**). All of the k_T values were determined by monitoring the ability of the substrate to quench the time-resolved emission of $^1O_2$ at 1270 nm as described previously.[6] These total rate constants, k_T, represent a composite of all chemical, k_r, and physical, k_q, channels of $^1O_2$ deactivation induced by the disulfide (i.e., $k_T = k_r + k_q$).

Several important trends are apparent from examination of the data in Table 1, including the following: (1) Disulfides are in general less-efficient quenchers of $^1O_2$ than sulfides but are more-efficient quenchers than trisulfides. (2) The size (steric bulk) of the substituents do not appear to control reactivity. The rate constant for total quenching, k_T, is actually larger for *tert*-butyl disulfide (**6**) than for either ethyl- (**4**) or isopropyl- (**5**) disulfide. This is in dramatic contrast to monosulfides[7,8] and hydrazines[9] where steric interactions play dominant roles. The rate constant k_T decreases by over 2 orders of magnitude along the series Et₂S > iPr₂S ≫ tBu₂S (Table 1) and by over a factor of 30 as the 1,2-substituents on the hydrazines are changed from methyl to neopentyl (Table 2). The steric origin of the kinetic effect in the hydrazine series is supported by the observation of a reasonable correlation with the Taft steric parameter (Figure 1).

We have previously suggested that hydrazines[9] quench $^1O_2$ by a contact charge-transfer mechanism similar to that first suggested by Wilson[10] and Ogryzlo[11] for quenching by amines.
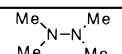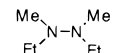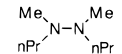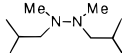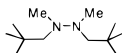
(1) Barltrop, J. A.; Hayes, P. M.; Calvin, M. *J. Am. Chem. Soc.* **1954**, *76*, 4348−4367.
(2) Murray, R. W.; Smetana, R. D.; Block, E. *Tetrahedron Lett.* **1971**, 299−302.
(3) Murray, R. W.; Jindal, S. L. *J. Org. Chem.* **1972**, *37*, 3516−3520.
(4) Murray, R. W.; Jindal, S. L. *Photochem. Photobiol.* **1972**, *16*, 147−151.
(5) Clennan, E. L.; Wang, D.; Zhang, H.; Clifton, C. H. *Tetrahedron Lett.* **1994**, *35*, 4723−4726.
(6) Clennan, E. L.; Noe, L. J.; Wen, T.; Szneler, E. *J. Org. Chem.* **1989**, *54*, 3581−3584.
(7) Kacher, M. L.; Foote, C. S. *Photochem. Photobiol.* **1979**, *29*, 765−769.
(8) Monroe, B. M. *Photochem. Photobiol.* **1979**, *29*, 761−764.
(9) Clennan, E. L.; Noe, L. J.; Szneler, E.; Wen, T. *J. Am. Chem. Soc.* **1990**, *112*, 5080−5085.
(10) Ouannes, C.; Wilson, T. *J. Am. Chem. Soc.* **1968**, *90*, 6527−6528.
(11) Ogryzlo, E. A.; Tang, C. W. *J. Am. Chem. Soc.* **1970**, *92*, 5034−5036.

Table 1. Kinetic Data for the Photooxidations of Sulfur-Containing Substrates

Compound	$k_T \times 10^{-5}$ $(M^{-1}s^{-1})^a$	E_g (V vs SCE)	IP_1 (eV)	Θ in degrees
MeSSMe, **3**	4.26±0.25		8.97[c]	84.7,[d] 85.3[e]
EtSSEt, **4**	0.73±0.09		8.70[c]	
iPrSSiPr, **5**	0.65±0.05		8.54[c]	
tBuSStBu, **6**	3.34±0.23		8.17[c]	110[h]
7	1.4 ±0.08		8.36[c]	62[j]
8	3.6		7.86[g]	110.5[f]
9	1440±80 1430[b]		8.02[i]	30[i]
10	1360±40		8.02[i]	30[i]
Et₂S[k], **11**	171±6	1.65	8.42	
iPr₂S[k], **12**	25.1±0.3	1.63		
tBu₂S[k], **13**	1.5	1.65		
Et₂S[l], **11**	4.1±0.4		8.42	
Me₂S[l] **14**	1.6±0.2		8.69	
MeSSMe[l], **3**	1.0±0.02		9.05	
MeSH[l], **15**	0.023±0.002		9.44	
thiophene[l], **16**	0.036±0.04		8.86	
(pMeOC₆H₄S)₂S[m], **17**	<0.09	1.43[n]		

[a] In acetone with 4.0×10^{-5} M Rose Bengal. *[b]* In benzene with 5×10^{-5} M tetraphenylporphyrin. *[c]* Reference 18. *[d]* Microwave; ref 19. *[e]* Gas-phase electron diffraction; ref 20. *[f]* X-ray data; ref 21. *[g]* Reference 22. *[h]* Reference 23. *[i]* Estimated using published values for lipoic acid; see ref 23. *[j]* PC Model, Serena Software, Bloomington, IN. *[k]* Reference 7. *[l]* In the gas phase; ref 13. *[m]* Unpublished results, K. Stensaas. *[n]* Irreversible peak potential versus SCE at 200 mV/s.

Table 2. Kinetic Data for the Quenching of Singlet Oxygen by Hydrazines

Compound	$k_T \times 10^{-7}$ $(M^{-1}s^{-1})$	$E^{°'}$(V vs SCE)	$E_s{}^a$
	18.6	0.33	0
	6.76	0.31	-0.07
	4.4	0.31	-0.36
	1.29	0.33	-0.93
	0.525	0.32	-1.74

[a] Taft steric parameters.

This mechanism involves formation of a singlet charge transfer (CT) complex, intersystem crossing to a triplet CT complex, and exothermic dissociation to $^3O_2$ and substrate (Scheme 1a). The pivotally important CT complexes are represented by the wave functions $^1\Delta_g{}^1S_O$ and $^3\Sigma_g{}^1S_O$, which are further stabilized by some amount, δ or λ, of CT character. On the other hand, Kacher and Foote[7] have pointed out that the rate constants for quenching of $^1O_2$ by monosulfides show a better correlation with rate constants of nucleophilic reactions than with electrochemical peak potentials for ionization of the sulfides. Consequently, these workers suggested that quenching occurred in competition with chemical reaction via decomposition of a persulfoxide intermediate (**A**) (Scheme 1b).

A plot of $\log(k_T)$ versus IP_{eV} for the disulfides is linear, with only dimethyl disulfide (**3**) and the 1,2-dithiolanes (**9** and **10**)
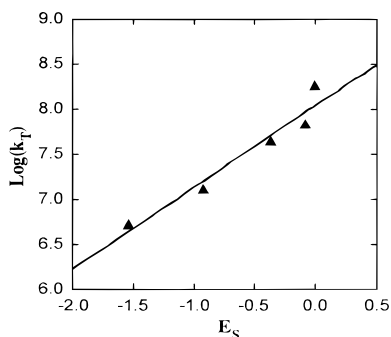
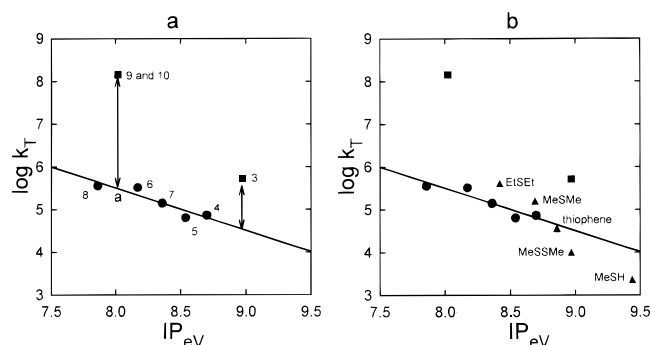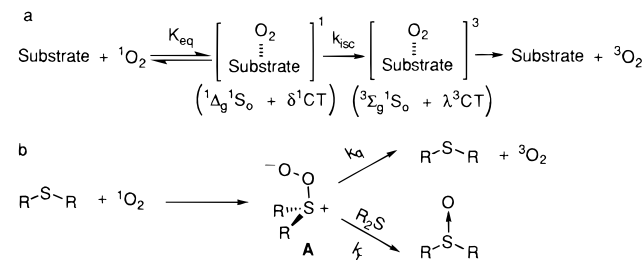**Figure 1.** Log(k_T) versus the taft steric parameter, E_S, for the quenching of singlet oxygen by hydrazines.

Figure 2. Log(k_T) versus photoelectron spectroscopy ionization potentials of the disulfides **3**−**10**. Point a is the extrapolation of the points **9** and **10** to the linear regression line and represents the CT quenching by these substrates. (b) Log(k_T) versus IP_{eV} for several substrates in the gas phase superimposed on the data from Figure 2a.

Scheme 1

deviating significantly from the linear regression line (Figure 2a). This linear relationship is consistent with a charge-transfer mechanism, since, to the extent the charge transfer states are mixed with the ground states of the complex, log(k_T) should be directly related to the ionization potential of the donor.[11,12] Consistent with this suggestion is the fact that k_T values measured in the gas phase[13] for methanethiol, dimethyl disulfide, dialkyl sulfides, and thiophene also fall remarkably close to the correlation line (Figure 2b). Charge-transfer quenching is likely to be the dominant mechanism for quenching by these substrates, since the buildup of charge necessary to form a persulfoxide (**A**) is unlikely to be tolerated in the gas phase.

We suggest that the enhanced reactivities of **3** and the two 1,2-dithiolanes **9** and **10** reflect their ability to form the corresponding persulfoxides. Cophotooxidations of **9** with Ph$_2$-SO, which under the reaction conditions is inert to $^1O_2$, resulted in formation of Ph$_2$SO$_2$ and is consistent with trapping of the persulfoxide intermediate. The small steric demands of the methyl groups in **3**, and the constrained >CSSC dihedral angle

of only 30° in **9** and **10** (Table 1), allow access to the disulfide linkage and are responsible for the ability to form the persulfoxide. In addition, formation of the persulfoxides from **9** and **10** relieves a significant amount of destabilizing lone-pair−lone-pair interaction. Disulfides **6** and **8** are chemically inert to $^1O_2$ under our reaction conditions, consistent with their inability to form the persulfoxide. Disulfides **4** and **7** on the other hand give oxidation products, but only under forcing conditions. For example, after 30 min of irradiation under identical conditions, 63% of **3** but only 2% of **4** is converted to product.[5]

We have determined the chemical rate constant, k_r, for the reaction of **9** with $^1O_2$ by competition with 2-methyl-2-pentene ($k_T = 7.2 \times 10^5$ M^{-1} s^{-1}) using the method of Higgins, Foote, and Cheng.[14] The rate constant, $k_r = (5.87 \pm 0.75) \times 10^6$ M^{-1} s^{-1}, is considerably smaller than k_T. The difference, 1.38×10^8 M^{-1} s^{-1}, represents the rate constant for physical quenching of singlet oxygen by **9**. This value is much larger than the rate constant for charge transfer quenching, 3.05×10^5 M^{-1} s^{-1}, as predicted by the linear regression line (point a in Figure 2a). Consequently, the predominate mechanism for physical quenching by **9** is via decomposition of the persulfoxide (Scheme 1b).

Spin−orbit coupling (k_{isc} in Scheme 1a) does not control the charge-transfer quenching efficiencies of the disulfides which fall on the linear regression line (Figure 2a), since this is expected to increase as Z^4, contrary to to the experimental results[15] (compare the disulfides and hydrazines). We suggest instead that it is the magnitude of K_{eq} (Scheme 1a), which is in turn dictated by the magnitude of δ^1CT, which controls the quenching efficiencies. Furthermore, the lack of a steric effect on the charge-transfer quenching of the disulfides is consistent with a weakly bound charge-transfer complex (small K_{eq}) with a large intracomplex distance between the disulfide and singlet oxygen.

The results presented here demonstrate that disulfides in extended conformations (>RSSR $\approx$ 85°) are ineffective at providing protection from $^1O_2$ damage in biological systems. Exposed disulfides (>RSSR $\approx$ 30° or smaller), however, physically deactivate $^1O_2$ with rate constants comparable to that reported for several important biological molecules,[16] and much more rapidly than others, such as nucleosides.[17]

(12) Tsubomura, H.; Mulliken, R. S. *J. Am. Chem. Soc.* **1960**, *82*, 5966−5974.

(13) Ackerman, R. A.; Rosenthal, I.; Pitts, J. N., Jr. *J. Chem. Phys.* **1971**, *54*, 4960−4961.

(14) Higgins, R.; Foote, C. S.; Cheng, H. In *Advances in Chemistry Series*; Gould, R. F., Ed.; American Chemical Society: Washington, DC, 1968; Vol. 77, pp 102−117. The measured k_r value is a composite of all of the rate constants which contributed to the formation of the oxidized products **1** and **2**. Consequently, if a nonsinglet oxygen process is contributing to the magnitude of k_r, the physical quenching rate constant ($k_q = k_T − k_r$) in Table 1 represents lower limits to its true value.

(15) Corey, E. J.; Khan, A. U.; Ha, D.-C. *Tetrahedron Lett.* **1990**, *31*, 1389−1392.

(16) Wilkinson, F.; Helman, W. P.; Ross, A. B. *J. Phys. Chem. Ref. Data* **1995**, *24*, 663−1021.

(17) Prat, F.; Hou, C.-C.; Foote, C. S. *J. Am. Chem. Soc.* **1997**, *119*, 5051−5052.

(18) Bock, H.; Wagner, G. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 150−151.

(19) Sutter, D.; Dreizler, H.; Rudolph, H. D. *Z. Naturforsch.* **1965**, *20a*, 1676−1681.

(20) Yokozeki, A.; Bauer, S. H. *J. Chem. Phys.* **1976**, *80*, 618−625.

(21) Rindorf, G.; Jørgensen, F. S.; Snyder, J. P. *J. Org. Chem.* **1980**, *45*, 5343−5347.

(22) Jørgensen, F. S.; Snyder, J. P. *J. Org. Chem.* **1980**, *45*, 1015−1020.

(23) Guimon, M.-F.; Guimon, C.; Pfister-Guillouzo, G. *Tetrahedron Lett.* **1975**, 441−444.