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Photooxygenation of 1,5-Thiaselenocane

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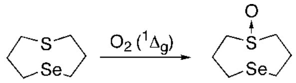
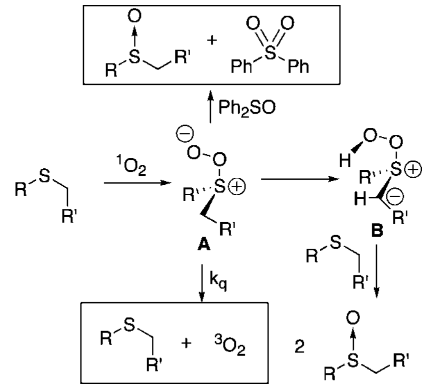


A direct comparison of photooxygenation at sulfur and selenium centers is reported, and the reactivity of 1,5-thiaselenocane is compared to that of 1,5-dithiacyclooctane.

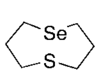
Literature reports on the photooxygenations of organoselenides are both rare and contradictory. In 1976, Hevesi and Krief[1] reported that acyclic selenides such as benzyl phenyl selenide reacted rapidly with singlet oxygen to give selenoxides without overoxidation to form selenones. This reaction coupled with thermal elimination of selenic acid (RSeOH) was later reported as a rapid and quantitative method to convert selenium-containing oxazoles to α,*β*-unsaturated lactones.[2] In 1982, however, Hovey[3] reported that, in micellar medium, benzyl phenyl selenide while rapidly deactivating singlet oxygen did not chemically react to produce any isolable product. In 2002, Krief and Lonez[4] reported that reactions of acyclic selenides were slower than previously reported, but that addition of water and potassium carbonate to methanol solutions of the selenides dramatically enhanced their chemical reactivity with singlet oxygen.

On the other hand, reactions of organic sulfides with singlet oxygen have been extensively investigated since their initial report by Schenck in the early 1960s.[5] These reactions occur with low quantum yields to give sulfoxides along with small amounts of sulfones. Computational[6] and experimental studies[7] support a mechanism that proceeds via both persulfoxide (**A** in Scheme 1) and hydroperoxysulfonium ylide (**B** in Scheme 1) intermediates. The source of the inefficiency in these reactions has been attributed to decomposition of the persulfoxide intermediate in a physical quenching process (k_q).

SCHEME 1



The recent report of the synthesis of 1,5-thiaselenocane, **1**, provides us with the opportunity to compare the reactivity of singlet oxygen with sulfide and selenide functional groups embedded in the same molecule in structurally and electronically similar positions.[8] In contrast, the diarylselenide and dialkylsulfide in the previously reported dibenzo analogue, **2**, do not provide electronically or structurally unbiased comparisons of reactivity at these two centers.[9]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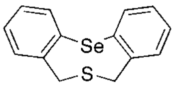
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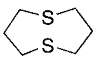
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Evidence that access of singlet oxygen to the chalcogen atoms in **1** and **3** is equally easy was obtained using the MP2/6-31G(d) model that located 11 conformations adopted by **1** that are very similar to those reported for 1,5-dithiacyclooctane, **3**.[10] The global minimum and all conformations within 3 kcal/mol of the global minimum for **1** are shown in Figure 1 (see Supporting Information for more complete structural details).

TSe1 and **TSe3** are both twist-boat-chair conformations with transannular S···Se distances of 3.92 and 3.89 Å, respectively, only slightly longer than the sum of their van der Waals radii of 3.7 Å.[11] **TSe2** is a twist-chair conformation with a transannular S···Se distance of 3.64 Å, slightly smaller than the van der Waals radii of the chalcogens. **TSe4** and **TSe5** are boat-chair conformations that are similar in structure to the global minimum found in cyclooctane.[12] **TSe6** is a C_s symmetric chair-

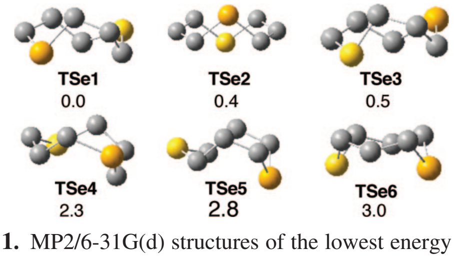

FIGURE 1. MP2/6-31G(d) structures of the lowest energy conformations of **1**, with hydrogens removed for clarity; yellow is S, orange is Se.

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[‡] University of Wyoming.

(1) Hevesi, L; Krief, A. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 381.

(2) Wasserman, H. H.; Lu, T.-J. *Recl. Trav. Chim. Pays-Bas* **1986**, *105*, 345–346.

(3) Hovey, M. C. *J. Am. Chem. Soc.* **1982**, *104*, 4196–4202.

(4) Krief, A.; Lonez, F. *Tetrahedron Lett.* **2002**, 6255–6257.

(5) Schenck, G. O.; Krauch, C. H. *Angew. Chem.* **1962**, *74*, 510.

(6) Jensen, F.; Greer, A.; Clennan, E. L. *J. Am. Chem. Soc.* **1998**, *120*, 4439–4449.

(7) (a) Toutchkine, A.; Clennan, E. L. *J. Org. Chem.* **1999**, *64*, 5620–5625. (b) Toutchkine, A.; Clennan, E. L. *Tetrahedron Lett.* **1999**, *40*, 6519–6522.

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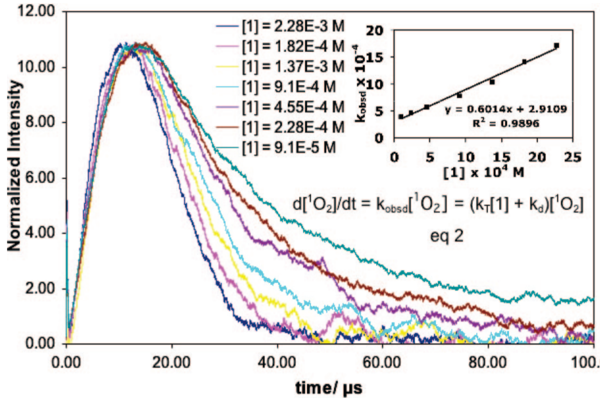
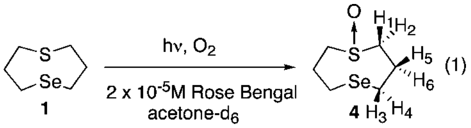


FIGURE 2. Decay of singlet oxygen phosphorescence in the presence of variable concentrations of **1**. Inset; plot of k_{obsd} versus [**1**].

chair conformation with the plane passing through the sulfur and selenium atoms.

An oxygen-saturated 0.02 M acetone-d_6 solution of **1** containing 2×10^{-5} M Rose Bengal was irradiated at room temperature under continuous oxygen agitation through 1 cm of a 0.2% aqueous $K_2Cr_2O_7$ cutoff (510 nm) filter with a 600 W tungsten−halogen lamp. Analysis of the reaction by NMR spectroscopy after 20 min of irradiation demonstrated quantitative conversion to the sulfoxide **4** (eq 1). Protons H_1 and H_2 in the NMR of **4** appeared as two well resolved ddd's. The two chemical shifts and three coupling constants derived from these multiplets provided useful input that allowed successful simulation of the NMR spectrum of **4** as a six-spin system[13] (see Supporting Information for experimental and simulated spectra). No selenoxide or selenone was observed.



In order to demonstrate that singlet oxygen was the reactive species in this reaction, a series of benzene samples containing different concentrations of **1** were irradiated at 532 nm with a Nd:YAG laser, and the singlet oxygen phosphorescence was monitored at 1270 nm in a time-resolved mode (Figure 2). Each of the observed exponential decays is adequately described by a pseudo-first-order rate constant k_{obsd} since [**1**] $\gg$ [$^1O_2$] (eq 2 in Figure 2). The k_T value, which represents the sum of the rate constants for all of the **1**-induced chemical, k_r, and physical, k_q, processes that remove singlet oxygen from solution, is extracted by plotting k_{obsd} versus [**1**] (inset Figure 2). The k_d value, which is available from the intercept, is the electronic to vibronic limited natural lifetime of singlet oxygen in benzene.

TABLE 1. Kinetic Data for Reactions of 1 and 2 with Singlet Oxygen

compound	solvent	$k_T \times 10^{-7}$ M^{-1} s^{-1}	$k_r \times 10^{-6}$ M^{-1} s^{-1}	$k_q \times 10^{-7}$ M^{-1} s^{-1}
1	benzene	5.42 ± 0.60		
	acetone		2.03 ± 0.20	
3[a]	toluene	1.69		
	acetone	5.3	37.3	1.57

[a] Clennan, E. L.; Wang, D.-X.; Yang, K.; Hodgson, D.; Oki, A. R. *J. Am. Chem. Soc.* **1992**, *114*, 3021−3027.

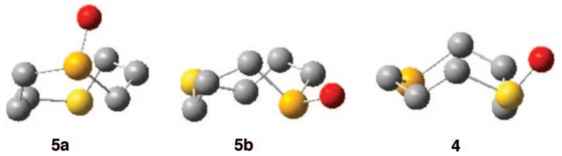


FIGURE 3. B3LYP/6-31G(d) conformations of **1**−selenoxide (**5a** and **5b**) and **1**−sulfoxide (**4**) with the hydrogens removed for clarity.

The chemical rate constant for reaction of **1** with singlet oxygen was determined in acetone-d_6 in competition with the ene reaction of 2,3-dimethyl-2-butene ($k_r = 2.7 \times 10^7$ M^{-1} s^{-1})[14] using the method of Higgins, Foote, and Cheng.[15] The chemical rate constant, k_r, and k_T and k_q, which are determined by the difference $k_q = k_T - k_r$, are collected in Table 1 for both **1** and **3**.

The total rate constant for removal of singlet oxygen from solution, k_T, is more than three times larger for **1** than for **3** in the comparable nonpolar nonprotic solvents benzene and toluene. This ratio is considerably smaller than the 19.7 reported[16] for $k_T(PhSeCH_3)/k_T(PhSCH_3)$ and somewhat smaller than the 7.1 reported for $k_T(PhCH_2SePh)/k_T(PhCH_2SPh)$.[3] The ability of $PhSeCH_3$ to quench singlet oxygen was attributed to a combination of charge transfer and heavy atom quenching mechanisms.[16] This suggestion was supported by observation of an even larger k_T for $PhTeCH_3$ (3.8×10^9 M^{-1} s^{-1}) than for $PhSeCH_3$ (1.4×10^8 M^{-1} s^{-1}) and the fact that charge transfer quenching efficiency should increase with atomic number. In addition, amines with approximately the same ionization potential as $PhTeCH_3$ are considerably less efficient singlet oxygen quenchers. The possibility that chemical reaction might also contribute to the magnitude of the quenching rate constants seems to have been discounted by these authors[16] even though they did not report any attempt to demonstrate the lack of product formation.

The rate constant for chemical reaction, k_r, is 18 times larger for **3** than for **1**. This can be attributed to the more effective physical quenching in **1** by selenium than sulfur that deactivates singlet oxygen as it approaches the molecule and prevents reaction at sulfur. The observed exclusive formation of sulfoxide **4** (eq 1) coupled with our detection threshold also requires an upper limit of k_r for reaction at selenium of approximately 2×10^4 M^{-1} s^{-1}.

The absence of even traces of selenoxide **5** is surprising since it does exist both computationally and experimentally. In Figure 3, two of the three conformations of the selenoxide that were located with the B3LYP/6-31G(d) model are compared to one of

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(8) Block, E.; Dikarev, E. V.; Glass, R. S.; Jin, J.; Li, B.; Li, X.; Zhang, S.-Z. *J. Am. Chem. Soc.* **2006**, *128*, 14949–14961.

(9) (a) Fujihara, H.; Mima, H.; Chiu, J. J.; Furukawa, N. *Tetrahedron Lett.* **1990**, *31*, 2307–2310. (b) Takaguchi, Y.; Fujihara, H.; Furukawa, N. *Organometallics* **1996**, *15*, 1913–1919.

(10) Clennan, E. L.; Hightower, S. E.; Greer, A. *J. Am. Chem. Soc.* **2005**, *127*, 11819–11826.

(11) Bondi, A. *J. Phys. Chem.* **1964**, *68*, 441–451.

(12) Eliel, E. L.; Wilen, S. H. *Stereochemistry of Organic Compounds*; John Wiley & Sons: New York, 1994.

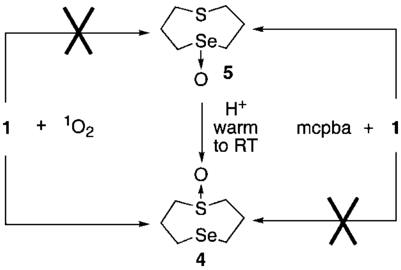
(13) δ 2.33, 2.44, 2.70, 2.72, 3.11, 3.21 (J_{12} = −14.4 Hz; J_{15} = 2.8 Hz; J_{16} = 9.41 Hz; J_{25} = 8.69 Hz; J_{26} = 3.10 Hz; J_{34} = −13.38 Hz; J_{35} = 3.7 Hz; J_{36} = 8.52 Hz; J_{45} = 9.16 Hz; J_{46} = 3.74 Hz; J_{56} = −15.68 Hz); Reich, H. J. *WINDNMR* available at http://www.chem.wisc.edu/areas/reich/chem605/index.htm.

(14) Ogilby, P. R.; Foote, C. S. *J. Am. Chem. Soc.* **1983**, *105*, 3423–3430.

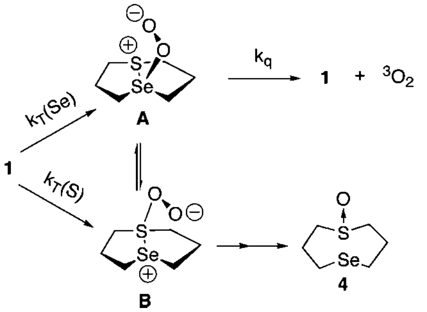
(15) Higgins, R.; Foote, C. S.; Cheng, H. In *Advances in Chemistry Series*; Gould, R. F., Ed.; American Chemical Society: Washington D.C., 1968; Vol. 77, pp 102−117.

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

SCHEME 2



SCHEME 3



the two sulfoxides located at the same level of theory. The conformational surface for both the selenoxide and sulfoxide appears to be similar in complexity to the conformational surface of **1**, and as a consequence, no attempt was made to exhaustively search conformational space. The Se−O bond length in the three computed structures (1.674 ± 0.004 Å) is very similar to that observed in the X-ray structure of dimethyl selenoxide (1.6756(16) Å) and is in the middle of the range (1.621−1.690 Å) for selenoxide Se−O bonds reported in the Cambridge Data Base.[17] On the other hand, the computed Se−C distances in these compounds (2.008 ± 0.013 Å) is slightly longer than the range reported in the Cambridge Data Base for selenoxide Se−C bonds (1.907−1.958 Å).[16] The sum of the angles around the Se in all three compounds is smaller than around the sulfoxide sulfur in the two computationally located sulfoxides (see Supporting Information for more complete structural data on the computed structures). Consequently, the selenoxide is flatter than the sulfoxide functional group, as previously noted by Filatov, Block, and Petrukhina.[17]

The selenoxide, **5**, can also be made and characterized at low temperature using peracid oxidation. It is stable at low temperatures but rearranges within a few hours to the sulfoxide at room temperature (rt), possibly by a mechanism similar to that postulated for intermolecular, acid-catalyzed transfer of oxygen from selenoxides to sulfides.[18] However, photooxygenation of **1** at −78 °C in an NMR tube followed by direct interrogation in a precooled NMR probe resulted in detection of only the sulfoxide, precluding formation of the selenoxide followed by its rearrangement at rt (Scheme 2).

Consequently, the absence of the selenoxide at rt can be attributed to competitive inhibition of perselenoxide, **A**, formation by rapid formation of persulfoxide, **B** (i.e., $k_T(S) \gg k_T(Se)$ in Scheme 3). Alternatively, if perselenoxide **A** does form, its reduction to the selenoxide could be competitively inhibited by physical quenching (k_q in Scheme 3) or by interconversion to the persulfoxide via an intramolecular rearrangement, as shown in Scheme 3.[19] Addition of $P(OCH_3)_3$[20] to a photooxygenation reaction mixture at −78 °C in an attempt to trap the perselenoxide prior to its decomposition produced $OP(OCH_3)_3$ but no selenoxide. Since phosphites are known to reduce selenoxides,[21] we also examined trapping with Ph_2SO[22] but again formation of Ph_2SO_2 but no selenoxide was observed.

A bisected form of dimethyl perselenoxide was located at the MP2/6-31G(d) level of theory with a Se−O bond length of 2.437 Å, within the sum of the van der Waals radii of oxygen (1.5 Å) and selenium (1.9 Å). However, it had one negative frequency. It appears that the negative frequency is associated with twisting about the Se−O bond, and indeed a rotomer was located with an even longer Se−O bond distance of 2.877 Å that is an energy minimum with no imaginary frequencies. This rotomeric perselenoxide appears to be a weakly bound exciplex. Consequently, a single determinant method such as MP2 cannot adequately treat this structure since singlet oxygen is a two-configuration problem in weak complexes. On the other hand, this level of theory has been shown to be adequate to treat persulfoxides, and indeed, 18 persulfoxides of **1** were located that closely correspond to the persulfoxides previously located for **3** (see Supporting Information for more complete structural details).

These studies provide the first direct comparison of the reaction of singlet oxygen with sulfide and selenide functional groups. Selenides are far less chemically reactive than sulfides with singlet oxygen, and an upper limit for k_r of 2×10^4 M^{-1} s^{-1} has been determined. It is likely that the weakly bound character of a perselenoxide intermediate plays a key role in the low chemical reactivity of alkyl selenides with singlet oxygen.

Experimental Section

Photooxygenations. An acetone-d_6 solution containing 0.02 M **1** and 2×10^{-5} M Rose Bengal was irradiated at either room temperature or at −78 °C with a 600 W tungsten−halogen lamp through 1 cm of a 0.2% $K_2Cr_2O_7$ (cutoff 510 nm) filter solution. The solutions were irradiated for 20 min to complete conversion to the sulfoxide. The samples were analyzed by NMR either at room temperature or in a precooled probe.

k_T Determinations. Oxygen-saturated benzene solutions with the concentrations of **1** listed in Figure 2 were irradiated at 355 nm with the output of a 10 Hz Nd:YAG laser. The kinetic apparatus used for these measurements was described previously.[23]

k_r Determinations. The chemical rate constant ratio for reaction of 0.025 M **1** and 0.02 M tetramethylethylene (TME; $k_r = 2.7 \times 10^7$ M^{-1} s^{-1}) with singlet oxygen was measured in an oxygen-saturated acetone-d_6 solution containing 2×10^{-5} M Rose Bengal as a sensitizer and benzyl benzoate as an internal standard. The sample was irradiated by a 600 W tungsten−halogen lamp through 1 cm of a 0.2% $K_2Cr_2O_7$ filter solution (cutoff 510 nm). The concentrations of the products were measured every 3 min by integrating appropriate product peaks in the NMR spectrum. The rate constant ratio, $k_r(\mathbf{1})/k_r(\text{TME})$, was then determined from the slope of a plot of $\log_{10}(1\text{-}[\mathbf{1}\text{-sulfoxide}]/[\mathbf{1}]_o)$ versus $\log_{10}(1\text{-}[\text{TME-OOH}]/[\text{TME}]_o)$. The average slope from two experiments was 0.75 ± 0.08.

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(17) Filatov, A. S.; Block, E.; Petrukhina, M. A. *Acta Crystallogr.* **2005**, *C61*, o596−o598.

(18) (a) Procter, D. J.; Lovell, S. J.; Rayner, C. M. *Synlett* **1994**, 204–206. (b) Procter, D. J.; Thornton-Pett, M.; Rayner, C. M. *Tetrahedron* **1996**, *52*, 1841–1854.

(19) We thank a reviewer for suggesting interconversion of **A** and **B** (Scheme 3).

(20) Nahm, K.; Foote, C. S. *J. Am. Chem. Soc.* **1989**, *111*, 1909–1910.

(21) Sofikiti, N.; Rabalakos, C.; Stratakis, M. *Tetrahedron Lett.* **2004**, *45*, 1335–1337.

(22) Clennan, E. L.; Pace, A. *Tetrahedron* **2005**, *61*, 6665–6691.

(23) Clennan, E. L.; Liao, C. *J. Am. Chem. Soc.* **2008**, *130*, 4057–4068.

Oxidation of 1 with *m*-Chloroperbenzoic Acid.

5-Thiaselenocane 1-oxide (5): To a solution of **1** (50 mg, 0.25 mmol; ^{1}H NMR δ 2.86 (t, J = 5.8 Hz, 4H), 2.77 (t, J = 5.9 Hz, 4H), 2.14 (quintet, J = 5.8 Hz, 4H); ^{13}C NMR δ 31.0, 30.8, 22.1; ^{77}Se NMR δ 164.6 (relative to Me_2Se)) in $CDCl_3$ (0.6 mL) in an NMR tube was added solid *m*-CPBA (75%, 57.5 mg, 0.25 mmol) at −50 °C. The mixture was monitored by NMR at −50 °C: ^{1}H NMR ($CDCl_3$, −50 °C) δ 3.40−3.51 (m, 4H), 2.70−2.85 (m, 4H), 2.30−2.46 (m, 4H); ^{13}C NMR ($CDCl_3$, −50 °C) δ 49.1, 32.5, 26.5; ^{77}Se (relative to Me_2Se) δ 861. The yield of **5** was 90% by NMR.

Rearrangement of 5 to 5-Thiaselenocane 5-oxide (4): To a solution of **1** (390 mg, 2.0 mmol) in $CHCl_3$ (5 mL) was added a solution of *m*-CPBA (75%, 460 mg, 2.0 mmol) in $CHCl_3$ (5 mL) dropwise at −50 °C. The mixture was stirred at −50 °C for 10 min and then warmed to rt and stirred for an additional 1 h. The solution was concentrated in vacuo. The residue was chromatographed (silica gel, 1:8 ethyl acetate/hexanes) to give 5-thiaselenocane 5-oxide (**4**) as a colorless oil (340 mg, 80%): ^{1}H NMR δ 3.28−3.38 (m, 2H), 3.18−3.27 (m, 2H), 2.55−2.70 (m, 4H), 2.28−2.46 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 53.8, 24.3, 22.0; ^{77}Se (relative to Me_2Se) δ 156; IR (KBr) 1003 cm^{-1} (s; S=O).

Computational Studies. All calculations were done using Gaussian 03[24] and the B3LYP/6-31G(d) or MP2/6-31G(d) model. All stationary points were checked with frequency calculations, and the absence of spin contamination was verified by examination of $<S^2>$.

Acknowledgment. We thank the National Science Foundation (EB:CHE-0342660, CHE-0450505, CHE-0744578; ELC: CHE-0805358) for their generous support of this research. We dedicate this paper with our warmest wishes to Professor E.J. Corey on the occasion of his 80th birthday.

Supporting Information Available: B3LYP/6-31G(d) and MP2/6-31G(d) structural parameters, computational details, ^{13}C NMR data for **4** and **5**, ^{1}H NMR of **4**, simulated data for ^{1}H NMR of **4**, and k_r plots. This material is available free of charge via the Internet at http://pubs.acs.org.

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[24] Frisch, M. J. *Gaussian 03*, revision C.02; Gaussian, Inc.: Wallingford, CT, 2004.