1036 *J. Org. Chem.* **2002,** *67,* 1036−1037

The First Example of a Singlet Oxygen Induced Double Bond Migration during Sulfide Photooxidation. Experimental Evidence for Sulfone Formation via a Hydroperoxy Sulfonium Ylide

Edward L. Clennan* and David Aebisher

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

Clennane@uwyo.edu

Received October 19, 2001

Abstract: The first example of the formation of a sulfone concomitant with double bond migration during photooxidation of a sulfide is reported. Evidence is presented which demonstrates that the double bond migration is not a result of a prior acid-catalyzed rearrangement of an unrearranged sulfone precursor. This unusual observation is used to argue that the sulfone is formed via rearrangement of a hydroperoxy sulfonium ylide intermediate.

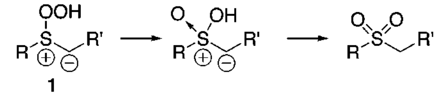
The reactions of singlet oxygen with organic sulfides have been vigorously studied[1−5] since the seminal report of Schenck and Krauch in 1962.[6] The recognition of the ability of sulfides to act as antioxidants and of their pivotal role in biological systems has been the driving force behind the intense interest in these reactions. Despite the flurry of activity in this area, new fascinating aspects of these reactions are still being reported. For example, in 1996 Ishiguro, Hayashi, and Sawaki[7]suggested that the small amount of sulfone formation in these reactions was in part derived from rearrangement of a hydroperoxy sulfonium ylide, **1** (Scheme 1). Their evidence consisted of the observations that the two oxygen atoms were derived from the same oxygen molecule and that isotopic exchange at the α-position accompanied sulfone formation.

We report here the first example of a double bond migration during photooxidation at sulfur.[8] We also argue that this reaction provides independent verification of the role of the hydroperoxy sulfonium ylide, **1**, in sulfone formation.

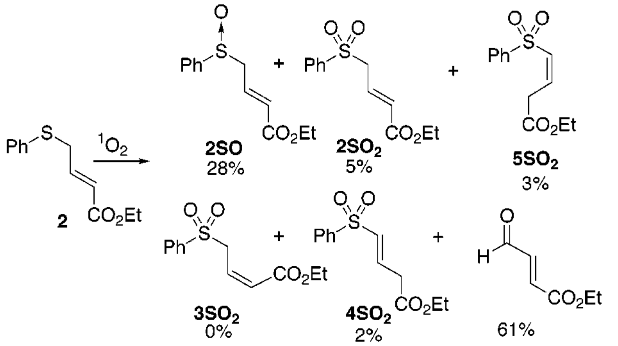
Photooxidation of a 0.05 M C_6D_6 oxygen saturated solution of ethyl γ-phenylthiocrotonate, **2**, containing 2.5×10^{-4} M tetraphenylporphyrin to 80% conversion resulted in formation of the products shown in Scheme 2. Nearly identical results were obtained in $CDCl_3$ with the exception of the formation of a trace amount of **3SO$_2$** and formation of 5% of an unknown.

Sulfoxide **2SO** and sulfone **2SO$_2$** were identical to the products formed when **2** was treated with 1 and 2 equiv of MCPBA, respectively. To provide unambiguous assignments for the remaining sulfones, **2** was treated with Et$_3$N to provide a thermodynamic mixture of sulfides as depicted in Scheme 3. These were then treated with 2 equiv of MCPBA to generate the corresponding sulfones in the same ratio as the sulfide precursors. The structures of the sulfides and sulfones could be unambiguously assigned by examination of the chemical shifts and coupling constants of the diagnostic H_α, H_β, and H_γ protons.[9]

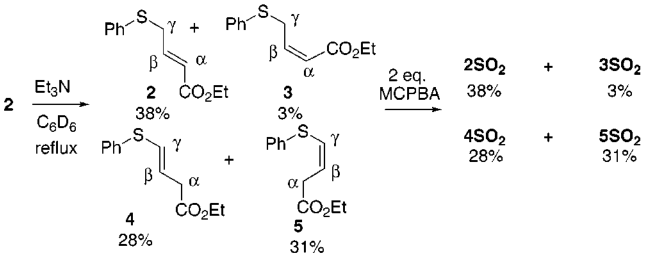
Scheme 1. Sulfone Formation via the Hydroperoxy Sulfonium Ylide



Scheme 2. Products from Photooxidation of 2



Scheme 3



The possibility that sulfone **2SO$_2$** could have served as the precursor of the unanticipated double bond migrated sulfones **4SO$_2$** and **5SO$_2$** was ruled out in two different experiments. (1) Treatment of the **2SO$_2$**:**3SO$_2$**:**4SO$_2$**:**5SO$_2$** mixture shown in Scheme 3 with Et$_3$N in refluxing benzene resulted in the quantitative formation of 89% of **2SO$_2$** and 11% of **3SO$_2$**. The absence of the double bond migrated isomers **4SO$_2$** and **5SO$_2$** demonstrate that they are kinetic and not thermodynamic products in the photooxidation of **2**. (2) Cophotooxidation of methyl allyl sulfide and **2SO$_2$** under the identical conditions utilized for the reaction of **2** resulted in

---

[1] Clennan, E. L. *Tetrahedron* **2000**, *56*, 9151−9179.

[2] Jensen, F.; Greer, A.; Clennan, E. L. *J. Am. Chem. Soc.* **1998**, *120*, 4439−4449.

[3] Bonesi, S. M.; Albini, A. *J. Org. Chem.* **2000**, *65*, 4532−4536.

[4] Bonesi, S. M.; Torriani, R.; Mella, M.; Albini, A. *Eur. J. Org. Chem.* **1999**, 1723−1728.

[5] Bonesi, S. M.; Mella, M.; d'Alessandro, N.; Aloisi, G. G.; Vanossi, M.; Albini, A. *J. Org. Chem.* **1998**, *63*, 9946−9955.

[6] Schenck, G. O.; Krauch, C. H. *Angew. Chem.* **1962**, *74*, 510.

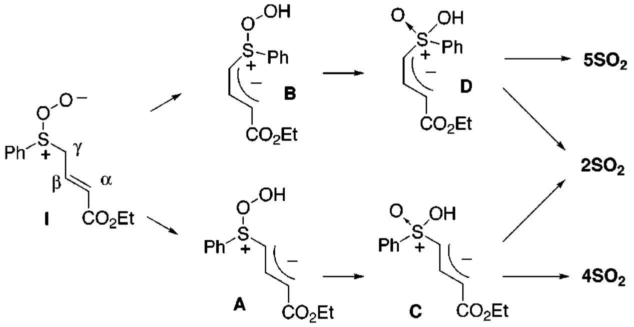
[7] Ishiguro, K.; Hayashi, M.; Sawaki, Y. *J. Am. Chem. Soc.* **1996**, *118*, 7265−7271.

[8] A double bond migration occurs during the singlet oxygen ene reaction but in that case the double bond is the seat of reactivity.

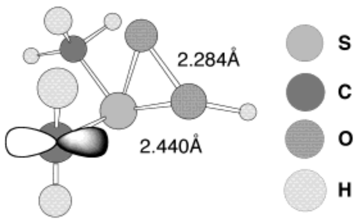
[9] ^{1}H NMR (benzene-d_6) δ Compound **2** δ 5.75(H_α, dt, $J = 16, 1$ Hz), $\approx$ 6.9(H_β, buried in the aromatic region), 3.00(H_γ dd, $J = 7, 1$ Hz); Compound **3** δ 5.60(H_α, dt, $J = 11, 1$ Hz), 5.87(H_β, dt, $J = 11, 8$ Hz), 4.11(H_γ dd, $J = 8, 1$ Hz); Compound **4** δ 2.70(H_α, d, $J = 6.5$ Hz), 5.96(H_β, dt, $J = 16, 7$ Hz), 6.04(H_γ d, $J = 15$ Hz); Compound **5** δ 3.20(H_α, dd, $J = 7, 2$ Hz), 5.95(H_β, dt, $J = 9, 7$ Hz), 6.16(H_γ dt, $J = 9, 2$ Hz); Compound **2SO$_2$** δ 5.54(H_α, bd, $J = 16$ Hz), (H_β, buried in aromatic region), 3.20(H_γ dd, $J = 8, 1$ Hz); Compound **3SO$_2$** δ 5.61(H_α, dt, $J = 11, 1$ Hz), 5.91(H_β, dt, $J = 11, 8$ Hz), 4.43(H_γ dd, $J = 8, 1$ Hz); Compound **4SO$_2$** δ 2.46(H_α, dd, $J = 7, 2$ Hz), (H_β, buried in aromatic region), 6.00(H_γ dt, $J = 15, 2$ Hz); Compound **5SO$_2$** δ 3.67(H_α, dd, $J = 7, 2$ Hz), 6.11(H_β, dt, $J = 11, 7$ Hz), 5.87(H_γ dt, $J = 11, 2$ Hz).)

10.1021/jo016219t CCC: $22.00

Scheme 4



Scheme 5



quantitative recovery of $\mathbf{2SO_2}$ without formation of the double bond migrated isomers.[10]

The formation of the albeit minor but nevertheless mechanistically diagnostic double bond migrated sulfones can most easily be rationalized as shown in Scheme 4. The persulfoxide **I** formed from the addition of singlet oxygen to **2** can form two hydroperoxy sulfonium ylides **A** and **B** by abstraction of diastereomeric protons from the γ-carbon in the persulfoxide. The hydroperoxy sulfonium ylides can subsequently rearrange by a 1,2-hydroxy shift to give sulfone enolates **C** and **D** which can be protonated at the ends of the allyl anion to give $\mathbf{2SO_2}$ and a double bond migrated product. This mechanism also provides a very satisfying rationale for the absence of $\mathbf{3SO_2}$ since its formation would require prohibitively difficult isomerization around either the double bond in the persulfoxide, **I**, or the allyl anion in **A** or **B**.[11]

The transition state for the migration of the hydroxy group from oxygen to sulfur in the hydroperoxy sulfonium ylide derived from dimethyl sulfide has been located and optimized at the MP2/6-31G(d) level[2] (Scheme 5). The ylide carbon is rotated and the p-orbital is directed toward the migrating OH group in order to provide conjugative stabilization to the transition state. An analysis of the rotational profile about the ylide carbon suggested that this overlap provides approximately 10 kcal/mol stabilization of the transition state.[11] Consequently, the delocalized negative charge in the novel hydroperoxy sulfonium ylides **A** and **B** (Scheme 4) might be responsible in part for the very small yields of sulfones produced in the reaction of **2** and other allylic and benzylic sulfides.[12]

These results highlight the multifaceted behavior of the hydroperoxy sulfonium ylide (**1** in Scheme 1 and **A** and **B** in Scheme 4). These versatile intermediates have now been implicated in reductive conversion to sulfides,[13] in rearrangement to sulfones, and in the Pummerer rearrangement to α-hydroperoxy sulfides and ultimately S−C bond cleavage products.[14]

Experimental Section

Proton NMR spectra of $CDCl_3$ or C_6D_6 solutions of substrates and reaction mixtures were recorded at 400.13 MHz. The peaks corresponding to the residual protons of $CDCl_3$ (7.37 ppm) or C_6D_6 (7.16 ppm) were used as the internal reference. An HP-5 (30 m × 0.25 mm × 0.25 μm (length × inside diameter × film thickness)) capillary column and a 5% diphenyl-95% dimethyl polysiloxane (30 m × 0.32 mm × 1.0 μm (length × inside diameter × film thickness)) fused silica column were used to monitor the formation of a key intermediate (ethyl γ-bromo-*trans*-crotonate)[15−17] in the synthesis of **2**. Radial chromatography to purify **2** was carried out using silica gel 60 PF_{254} from EM Science.

Chloroform-*d* (110 g; Cambridge Isotope Laboratories) was extracted with 40 mL of saturated aqueous sodium bicarbonate, dried with magnesium sulfate, and stored over 4A molecular sieves prior to use. Benzene-d_6 was obtained from Cambridge Isotope Laboratories and used without further purification. Triethylamine was obtained from Eastman Chemical and distilled prior to use. Thiophenol was obtained from Acros Chemical and used without further purification. Compounds **2**,[15−17] **2SO**,[18] $\mathbf{2SO_2}$,[19] **3**,[20] **4**,[16,17] $\mathbf{4SO_2}$,[21] **5**,[16,17] and ethyl 4-oxo-2-butenoate[22] are all known compounds and provide spectral data consistent with their structures. Ethyl *trans*-crotonate was obtained from Aldrich Chemical and distilled prior to use.

Photooxidation Procedure. Photooxidation reaction mixtures 0.05 M in **2** and 2.5×10^{-4} M in tetraphenylporphyrin (TPP) were prepared in either $CDCl_3$ or C_6D_6 in 5 mL volumetric flasks. The mixtures in $CDCl_3$ were treated with 0.25 g of Na_2CO_3 and allowed to stir for 10 min in the dark to remove residual acid. The solutions were then filtered and divided into 1 mL portions for irradiation in 100 mL test tubes. The samples were presaturated with oxygen for 2 min and then irradiated under a constant stream of oxygen with a 600 W tungsten lamp at 23 °C through 1 cm of a 12 M $NaNO_2$ filter solution. After the photooxidations, the samples were kept in the dark and analyzed by ^1H NMR as quickly as possible (5−10 min after photooxidation). The product ratios represent the averages of from three to four independently photooxidized samples.

Isomerization of 2. The isomerization procedure used was that of O'Connor and Lyness.[23] A mixture of 0.1 g of **2** and 5 mL of triethylamine was refluxed for 1 to 3 h. Triethylamine was then removed by rotary evaporation to yield a dark liquid consisting of 38% **2**, 3% **3**, 28% **4**, and 31% **5**. This product composition was independent of reflux time between 1 and 3 h.

Acknowledgment. The generous support of the National Science Foundation and the donors of the Petroleum Research Fund, administered by the American Chemical Society, is gratefully acknowledged.

JO016219T

---

[10] The methyl allyl sulfide reacted to produce 85% of the corresponding sulfoxide, 6% of the corresponding sulfone, and 9% of the Pummerer S−C bond cleavage products.

[11] The barrier for rotation around a thiophenyl substituted allyl anion has been reported to be 19 kcal/mol. Biellmann, J. F.; Ducep, J. B. *Tetrahedron* **1971**, *27*, 5861−5872.

[12] Toutchkine, A.; Aebisher, D.; Clennan, E. L. *J. Am. Chem. Soc.* **2001**, *123*, 4966−4973.

[13] Toutchkine, A.; Clennan, E. L. *J. Org. Chem.* **1999**, *64*, 5620−5625.

[14] Toutchkine, A.; Clennan, E. L. *J. Am. Chem. Soc.* **2000**, *122*, 1834−1835.

[15] Fleming, I.; Goldhill, J.; Paterson, I. *Tetrahedron Lett.* **1979**, 3205−3208.

[16] Brownbridge, P.; Hunt, P. G.; Warren, S. *Tetrahedron Lett.* **1983**, *24*, 3391−3394.

[17] Brownbridge, P.; Durman, J.; Hunt, P. G.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1947−1958.

[18] Lansbury, P. T.; Erwin, R. W.; Jeffrey, D. A. *J. Am. Chem. Soc.* **1980**, *102*, 1602−1608.

[19] Annunziata, R.; Barbarella, G. *Org. Magn. Reson.* **1984**, *22*, 250−254.

[20] Rho, Y. S.; Kang, H. S.; Sin, H. S. *Yakhak Hoechi* **1993**, *37*, 555−560.

[21] Davies, H. M. L.; Clark, T. J.; Smith, H. D. *J. Org. Chem.* **1991**, *56*, 3817−3824.

[22] Naef, F.; Decorzant, R.; Thommen, W. *Helv. Chim. Acta* **1982**, *65*, 2212−2223.

[23] O'Connor, D. E.; Lyness, W. I. *J. Am. Chem. Soc.* **1964**, *86*, 3840−3846.