

Mechanism of Sulfone Formation in the Reaction of Sulfides and Singlet Oxygen: Intermediacy of *S*-Hydroperoxysulfonium Ylide

Katsuya Ishiguro, Masaki Hayashi, and Yasuhiko Sawaki*

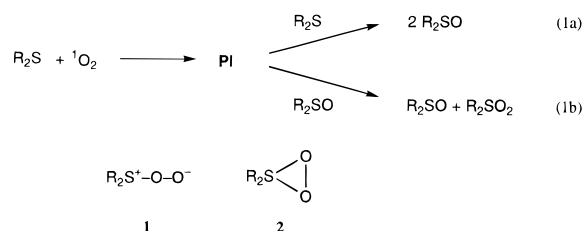
Contribution from the Department of Applied Chemistry, Faculty of Engineering, Nagoya University, Chikusa-ku, Nagoya 464-01, Japan

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Abstract: H–D exchange was observed in the methyl group during the formation of sulfones in the reaction of dimethyl sulfide-*d*₆ or thioanisole- α,α,α -*d*₃ with singlet oxygen in aprotic solvents. No exchange was observed in the sulfoxides obtained. The proton in the sulfones was shown to come from adventitious water, since the oxidation of C₆H₅SCH₃ in the presence of D₂O lead to the formation of sulfones with monodeuteration. The ¹⁶O₂–¹⁸O₂ tracer study demonstrated no oxygen scrambling in the sulfones. All the results indicate that the sulfones are formed intramolecularly via an intermediate possessing one activated proton exchangeable with trace water, a suggested structure for which is *S*-hydroperoxysulfonium ylides (RS⁺(OOH)CH₂[−]). Kinetic isotope effects (*k*_H/*k*_D = 2–4) observed for methyl protons in the sulfone formation suggest that the rate-determining step is the intramolecular proton abstraction in the persulfoxides (RS⁺(OO[−])CH₃) generating *S*-hydroperoxysulfonium ylides. The conversion of the ylide intermediates to sulfones is shown to be facile on the basis of PM3 theoretical calculations.

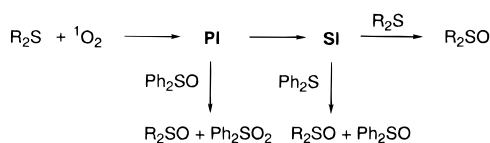
Reactions of singlet oxygen with sulfides affording sulfoxides and sulfones have been extensively studied for over two decades because of mechanistic and biological interest.¹ Three important reactions are the quenching of singlet oxygen and sulfoxide and sulfone formations. The pioneering work was done by Foote et al.,² demonstrating that zwitterionic persulfoxides are an appropriate intermediate on the basis of trapping experiments. The structure of the intermediates and the overall oxygenation mechanism are, however, not yet clarified thoroughly in spite of numerous studies on the ¹O₂ reaction of sulfides.^{1b}

In the reaction of sulfides with singlet oxygen, widely accepted is the intermediacy of zwitterionic persulfoxides (**1**) as the primary intermediate (**PI**). Persulfoxide intermediates

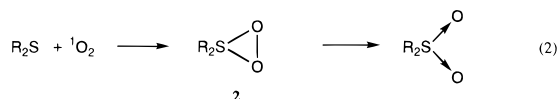


in aprotic solvents oxidize sulfoxides more efficiently than sulfides and behave as nucleophilic oxygen-atom transfer agents.³ From competitive trapping experiments, Foote and co-workers⁴ proposed a reaction mechanism involving the interconversion of **1** into a secondary peroxidic intermediate (**SI**) as shown in Scheme 1. Since the second species oxidizes sulfides electrophilically,⁵ cyclic thiadioxiranes (**2**) were proposed for this intermediate.⁴ On the other hand, ¹⁸O-tracer experiments

Scheme 1



revealed that the photo-oxidation of sulfides with ¹⁸O₂ yielded sulfones with retention of the two oxygen atoms, indicating an unimolecular rearrangement of **2** to sulfones (eq 2).⁶ The yields



of sulfones were not affected by the excess amounts of sulfides or by the addition of diphenyl sulfide and sulfoxide, which suggests that the sulfone-forming intermediate is different from **SI** in Scheme 1. A detailed theoretical study by Jensen⁷ could not give a definitive conclusion for the conversion of **1** to **2** or of **2** to sulfones.

The third important reaction of sulfides and singlet oxygen is C–S cleavage to afford fragmentation products as observed for sulfides bearing active α -C–H bonds, e.g., benzyl,⁸ 9-fluorenylethyl,⁹ and cyclic sulfides.¹⁰ In these reactions a third peroxidic intermediate, *S*-hydroperoxysulfonium ylide (**3**), has been believed to be formed by the intramolecular abstraction of α -proton (Scheme 2). Ylide intermediates from cyclic sulfides¹⁰ were also suggested as active species for epoxidations of olefins.

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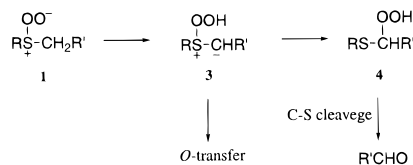
(7) Jensen, F. J. *Org. Chem.* **1992**, *57*, 6478.

(8) Corey, E. J.; Quannès, C. *Tetrahedron Lett.* **1976**, 4263.

(9) Ando, W.; Nagashima, T.; Saito, K.; Kohmoto, S. *J. Chem. Soc., Chem. Commun.* **1979**, 154.

(10) Akasaka, T.; Sakurai, A.; Ando, W. *J. Am. Chem. Soc.* **1991**, *113*, 2696.

Scheme 2

**Table 1.** Products at the Initial Stage of the $^1\text{O}_2$ Oxidation of Sulfide **5a-d₆**^a

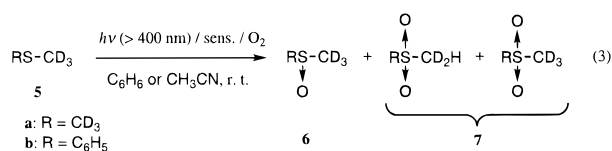
irradiation time, min	yields, %		isotope ratios in 7a ^b	
	6a	7a	7a-d₅	7a-d₆
20	0.3 ^c	0.13	100	11.4 ± 0.3
40	0.9 ^c	0.24	100	19.1 ± 0.3
60	2.5 ^c	0.34	100	35.2 ± 0.2
80	5.2 ^c	0.43	100	52.2 ± 0.2

^a Irradiation (>400 nm) of 0.1 M (CD₃)₂S and 0.1 mM TPP in benzene under O₂. ^b Isotope ratios as determined by GC-MS. Means of three to five determinations. ^c **6a-d₅**:**6a-d₆** = <0.5:>99.5.

We became interested in the intervention of persulfoxides and/or thiodioxiranes for the formation of sulfones and C-S cleavages. Deuterium and ¹⁸O-tracer studies revealed that at low conversions the sulfone formation accompanies, unexpectedly, an exchange of one α-hydrogen atom. Herein we summarize our mechanistic study on the ¹O₂ reaction of sulfides, suggesting that sulfonium ylides (**3**) are intermediates for C-S cleavage and sulfone formation at early stages of the reaction.

Results

Singlet Oxygenation of Deuteriated Sulfides. Irradiation of oxygen-saturated benzene solution of 0.1 M perdeuteriated dimethyl sulfide (**5a-d₆**) and 0.1 mM *meso*-tetraphenylporphyrin (TPP) at wavelengths longer than 400 nm at room temperature yielded dimethyl sulfoxide (**6a**) and dimethyl sulfone (**7a**). The



deuterium contents of the products were determined by GC-MS spectroscopy. As shown in Table 1, a mixture of **7a-d₅** and **7a-d₆** was obtained. The former *d₅* sulfone was the major component at the initial stage of reaction, and no sulfones carrying more than two hydrogens were obtained. It is interesting to note that such an H-D exchange was not observed for sulfoxide **6a** or for the recovered sulfide **5a**. After the irradiation, no deuterium exchange occurred after standing in the dark for 12 h even in the presence of 0.1 M H₂O, suggesting that only one α-deuterium was replaced during the photo-oxidation. The amount of nonexchanged sulfone (**7a-d₆**) was increased linearly with progress of the photo-oxidation and was almost zero at initial time. This fact indicates that only **7a-d₅** was the primary product while **7a-d₆** was formed by the secondary oxidation of sulfoxide **6a-d₆**. This was confirmed by ¹⁶O₂-¹⁸O₂ tracer experiments as described later.

Similarly, the photo-oxidation of 0.05 M thioanisole-*d₃* (**5b-d₃**) in benzene for 20 h yielded the corresponding sulfoxide without H-D exchange (i.e., **6b-d₃**) and predominantly sulfone with H-D exchange (i.e., **7b-d₂**:**7b-d₃** = 100:18). The photo-oxidation of **5a-d₆** in acetonitrile sensitized with 0.1 mM Methylene Blue (MB) gave a similar result.

The Effect of Water. Adventitious H₂O in the solvents is a conceivable source of the hydrogen incorporated in the sulfone.

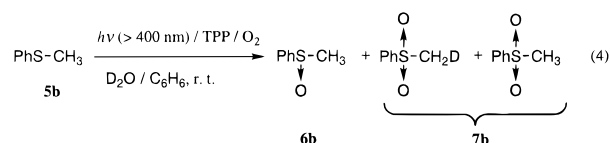
Table 2. Effect of H₂O on the $^1\text{O}_2$ Oxidation of Sulfide **5b-d₃**^a

added [H ₂ O], mM	yields, %		isotope ratios in 7b ^b	
	6b	7b	7b-d₂	7b-d₃
0	1.1 ^c	0.47	100	18.0 ± 0.2
27.8	1.4 ^c	0.41	100	18.5 ± 0.2
55.6	1.7 ^c	0.39	100	16.3 ± 0.2
278	3.3 ^c	0.43	100	31.1 ± 0.2

^a Irradiation of 0.05 M PhSCD₃ (**5b-d₃**) and 0.1 mM TPP in benzene under O₂ atmosphere for 20 h. ^b Isotope ratios as determined by GC-MS. ^c **6b-d₂**:**6b-d₃** = <1:>99.

The effect of the addition of water in the photo-oxidation of **5b-d₃** was examined. As shown in Table 2, the addition of H₂O resulted in the acceleration of sulfoxide formation but did not affect the sulfone formation; sulfone **7b-d₃** without H-D exchange was increased only in the presence of large amount of water. No effect of water on the sulfone yields and on the H-D exchange suggests that the H-D exchange itself is not so kinetically important.

The photo-oxidation of undeuteriated thioanisole (**5b-d₀**) in the presence of 0.05% D₂O (27.6 mM) afforded the monodeuteriated sulfone (eq 4), the ratio of which was **7b-d₀**:**7b-d₁** =



100:48.2 ± 0.1. It is interesting to note that only one proton in **7b** was exchanged with D₂O and no deuterium was incorporated in the sulfoxide (**6b-d₀**, C₆H₅SOCH₃) and the recovered sulfide. These results clearly indicate that the sulfone formation proceeds via an intermediate with only one activated proton exchangeable with water.

¹⁶O₂-¹⁸O₂ Tracer Study. The formations of sulfoxide either by unimolecular reaction or by secondary oxidation of sulfoxide may be distinguished by following the isotope scrambling of oxygen gas.⁶ Consequently, the photo-oxidation of **5a-d₆** with a mixture of ¹⁶O₂ and ¹⁸O₂ (¹⁶O₂:¹⁶O¹⁸O:¹⁸O₂ = 100:0.79:11.9) was examined in the absence or presence of added water. The sulfones with six different isotope contents, **7a-d₅** and **7a-d₆** with ¹⁶O₂, ¹⁶O¹⁸O, and ¹⁸O₂ were analyzed by GC-MS, and the results are summarized in Table 3. The isotope ratios of oxygen atoms in **7a-d₅** were always close to those of the starting oxygen gas, indicating that the *d₅* sulfone with the H-D exchange was formed with incorporation of one oxygen molecule (i.e., retention).

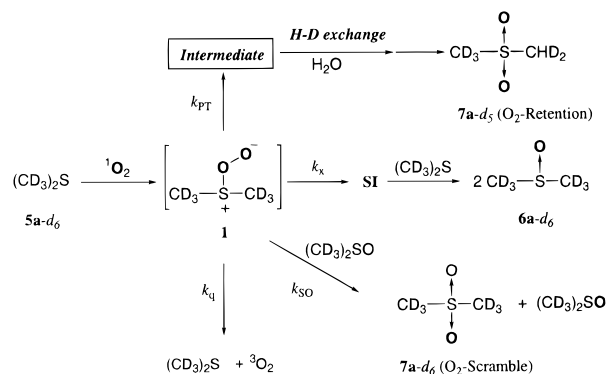
In contrast, the oxygen isotope ratios in **7a-d₆** exhibited the scrambling of oxygen atoms; that is, the doubly labeled ¹⁸O-¹⁸O was incorporated predominantly as scrambled ¹⁶O-¹⁸O. When a small amount of H₂O was added to complete the H-D exchange, the oxygen isotope ratios in **7a-d₆** became close to those calculated for the scrambling mechanism. Thus, in the presence of sufficient water, the two types of sulfones could be characterized clearly as depicted in Scheme 3. That is, all the **7a-d₆** is yielded by the secondary oxidation of sulfoxide **6a-d₆**¹¹ while the sulfone **7a-d₅** is formed intramolecularly with incorporation of the two oxygen atoms of oxygen molecule.

Singlet Oxygenation of Di-*tert*-butyl Sulfide. To see whether or not the H-D exchange is essential for the intramolecular sulfone formation, the ¹O₂ oxidation of sulfides without α-hydrogen has been examined. Although diaryl sulfides and phenyl *tert*-butyl sulfide were unreactive toward singlet oxygen, di-*tert*-butyl sulfide (**8**) was found to be oxidized slowly.⁶

Table 3. ¹⁶O₂-¹⁸O₂ Tracer Study on the Sulfone Formation in the ¹O₂ Oxidation of **5a-d₆**^a

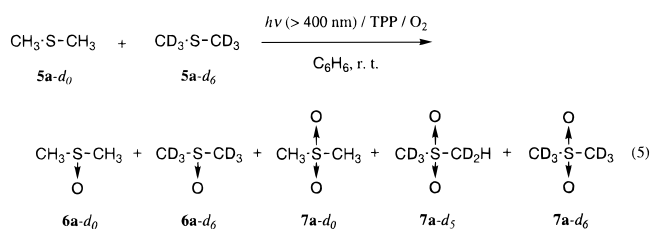
solvent	added [H ₂ O], ^b mM	yields, %		isotope ratios in 7a^c					
		sulfoxide 6a	sulfone 7a	7a-d₅			7a-d₆		
				¹⁶ O- ¹⁶ O	¹⁶ O- ¹⁸ O	¹⁸ O- ¹⁸ O	¹⁶ O- ¹⁶ O	¹⁶ O- ¹⁸ O	¹⁸ O- ¹⁸ O
C ₆ H ₆ ^d	0	2.3	0.13	100	: 0.92 ± 0.11	: 10.82 ± 0.22	: 23.95 ± 0.34	: 2.64 ± 0.04	: 0.97 ± 0.03
	9.3	2.5	0.12	100	: 0.93 ± 0.24	: 10.62 ± 0.21	(100 : 16.58 ± 0.27	: 3.00 ± 0.45	: 4.05 ± 0.14) ^e
	18.5	3.2	0.17	100	: 0.76 ± 0.04	: 10.02 ± 0.08	(100 : 21.32 ± 0.03	: 4.02 ± 0.05	: 0.18 ± 0.01) ^e
CH ₃ CN ^f	0	1.4	0.22	100	: 1.27 ± 0.26	: 11.01 ± 0.24	: 36.17 ± 0.99	: 6.87 ± 0.16	: 0.71 ± 0.06
	9.3	1.7	0.19	100	: 1.07 ± 0.15	: 10.18 ± 0.15	(100 : 40.30 ± 0.25	: 8.83 ± 0.22	: 0.47 ± 0.01) ^e
	18.5	2.3	0.18	100	: 1.29 ± 0.16	: 11.50 ± 0.33	(100 : 31.86 ± 0.48	: 6.93 ± 0.15	: 0.35 ± 0.02) ^e
	calcd for retention calcd for scrambling			100	: 0.79 ± 0.16	: 11.88 ± 0.37	(100 : 21.8 ± 0.6	: 21.8 ± 0.6	: 1.10 ± 0.06) ^e
							100	: 23.8 ± 0.9	: 1.42 ± 0.06

^a Irradiation (>400 nm) of 0.1 M (CD₃)₂S under oxygen gas; ¹⁶O₂:¹⁶O¹⁸O:¹⁸O₂ = 100:0.79 ± 0.16:11.88 ± 0.37. ^b Amounts of added water. ^c Isotope ratios for **7a-d₁** and **-d₆** with ¹⁶O-¹⁶O, ¹⁶O-¹⁸O, and ¹⁸O-¹⁸O as determined by GC-MS. ^d Irradiation in the presence of TPP for 70 min. ^e Normalized ratios in **7a-d₆**. ^f Irradiation in the presence of 0.1 mM MB for 10 min.

Scheme 3

Therefore, the sulfone formation was investigated by tracer experiments. The TPP-sensitized photo-oxidation of 100 mM di-*tert*-butyl sulfide with ¹⁶O₂-¹⁸O₂ (¹⁶O₂:¹⁶O¹⁸O:¹⁸O₂ = 100:0.79:11.9) in benzene for 6 h afforded the corresponding sulfoxide **9** and sulfone **10** in 2.3% and 0.24% yields, respectively. The isotope ratios in the sulfone (**10**-¹⁶O₂:**10**-¹⁶O¹⁸O:**10**-¹⁸O₂ = 100:18.2 ± 0.2:1.2 ± 0.1) showed the complete scrambling of oxygen atoms, indicating that the sulfone was formed via the secondary reaction. Thus, it is apparent that sulfides carrying no α hydrogens are not converted to sulfones directly.

Kinetic Isotope Effect. The kinetic isotope effect of deuterium has been investigated to clarify whether the abstraction of α protons leading to the sulfone formation is the rate-determining step or not. Competitive photo-oxygenation of a 1:1 mixture of (CH₃)₂S and (CD₃)₂S yielded three different sulfones, **7a-d₀**, **-d₅**, and **-d₆**, together with two sulfoxides, **6a-d₀** and **-d₆** (eq 5). While the product ratios of the sulfoxides



were ~1:1, showing no isotope effect, the formation of sulfone **7a-d₀** was clearly faster than that of **7a-d₅**. While **7a-d₅** is formed

unimolecularly as stated above, the estimation of isotope effect is not straightforward since **7a-d₀** can be formed by both intra- and intermolecular pathways. Provided that the secondary oxidation of sulfoxides by peroxidic intermediate **1** has also no isotope effect, the kinetic isotope effect in the unimolecular sulfone formation, k_H/k_D , can be calculated by $[(\mathbf{7a-d}_0) - (\mathbf{7a-d}_6)]/(\mathbf{7a-d}_5)$. As shown in Table 4, however, the values of k_H/k_D for the sulfone formation were increased gradually with the irradiation time, which is probably due to the inclusion of isotope effect on the secondary reactions. Thus, the kinetic isotope effect for the sulfone formation was obtained as 3.0 ± 0.4 by the extrapolation of these values to zero time.

Such a complexity could be eliminated for the ¹O₂ oxidation of PhSCH₃ and PhSCD₃, since the isotope effects obtained were almost constant throughout the reaction as shown in Table 5. The resulting kinetic isotope effects were $k_H/k_D = 2.1 \pm 0.2$, 2.8 ± 0.1 , and 4.1 ± 0.2 in C₆H₆, C₆H₆-Et₂O (1:1), and CH₃CN, respectively.

Thus, all the results indicate that the rate-determining α-proton abstraction is involved in the intramolecular sulfone formation. The apparent constant isotope effects probably reflect the unimportance of the secondary oxidation of sulfoxides for the case of thioanisole.

Discussion

Persulfoxide intermediates (**1**) in the ¹O₂ reaction of sulfides have been characterized by their trapping experiments.²⁻⁵ The intermediacy of thiadioxiranes (**2**) is not clarified adequately although they have been sometimes written as the secondary intermediate as shown in Scheme 1. Previously, we proposed that in the ¹O₂ reaction of sulfides sulfones were formed by an unimolecular rearrangement of **2** (eq 2).⁶ The present results, however, clearly indicate that the sulfone formation necessarily accompanies the exchange of an α proton with adventitious water. This unexpected result denies such a simple mechanism of formation and rearrangement of thiadioxiranes (eq 2).

A direct exchange of protons between water and an α-proton of persulfoxides (**1'**) could be excluded since no proton exchange was observed in resulting sulfoxides and recovered sulfides. The selective one proton exchanged in the sulfone formation suggests an intervention of ylide-type intermediates (**3**) possessing the carbanionic structure of S-CH₂⁻. As stated in the introduction, S-hydroperoxysulfonium ylide (**3**) has been written as an intermediate for C-S cleavage in the ¹O₂ oxidation of sulfides.^{8,9}

Table 4. Kinetic Isotope Effects on the Competitive $^1\text{O}_2$ Oxidation of Sulfides **5a-d₀** and **5a-d₆** in Benzene^a

irradiation time, min	yields, %		isotope ratios ^b						
	sulfoxide 6a	sulfone 7a	sulfoxide			sulfone			
			6a-d₀	6a-d₆	$k_{\text{H}}/k_{\text{D}}^{\text{c}}$	7a-d₀	7a-d₅	7a-d₆	$k_{\text{H}}/k_{\text{D}}^{\text{d}}$
20	0.39	0.18	<i>e</i>	<i>e</i>	<i>e</i>	100	30.5 ± 1.6	1.9 ± 0.1	3.22 ± 0.17
40	0.96	0.34	<i>e</i>	<i>e</i>	<i>e</i>	100	28.0 ± 0.6	3.9 ± 0.1	3.43 ± 0.07
60	2.50	0.48	100	107 ± 3	0.93 ± 0.03	100	25.4 ± 0.1	7.2 ± 0.1	3.65 ± 0.01
80	4.40	0.60	100	104 ± 2	0.96 ± 0.02	100	23.0 ± 0.4	11.5 ± 0.3	3.85 ± 0.07
				average:	0.95 ± 0.04			average:	3.0 ± 0.4 ^f

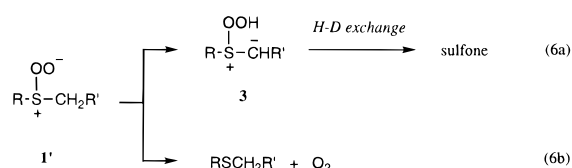
^a Irradiation of $(\text{CH}_3)_2\text{S}$ and $(\text{CD}_3)_2\text{S}$ (50 mM each) and 0.1 mM TPP in benzene under O_2 . ^b Isotope ratios as determined by GC-MS. ^c Kinetic isotope effects defined as $(\mathbf{6a-d}_0)/(\mathbf{6a-d}_6)$. ^d Kinetic isotope effects defined as $[(\mathbf{7a-d}_0) - (\mathbf{7a-d}_6)]/(\mathbf{7a-d}_5)$. ^e Not determined. ^f The kinetic isotope effect obtained by the extrapolation at zero time.

Table 5. Kinetic Isotope Effects on the Competitive $^1\text{O}_2$ Oxidation of Sulfide **5b-d₀** and **5b-d₃**^a

solvent	irradiation time, h	yields, %		isotope ratios ^b						
		sulfoxide 6b	sulfone 7b	sulfoxide			sulfone			
				6b-d₀	6b-d₃	$k_{\text{H}}/k_{\text{D}}^{\text{c}}$	7b-d₀	7b-d₂	7b-d₃	$k_{\text{H}}/k_{\text{D}}^{\text{d}}$
$\text{C}_6\text{H}_6^{\text{e}}$	8	0.28	0.20	100	103 ± 2	0.97 ± 0.02	100	46.7 ± 1.1	2.4 ± 0.1	2.09 ± 0.05
	12	0.62	0.30	100	104 ± 1	0.96 ± 0.01	100	46.1 ± 0.6	2.9 ± 0.2	2.11 ± 0.03
	16	0.77	0.34	100	106 ± 1	0.94 ± 0.01	100	46.5 ± 0.5	3.8 ± 0.1	2.07 ± 0.02
	18	1.20	0.42	100	103 ± 1	0.97 ± 0.01	100	44.7 ± 0.2	6.3 ± 0.2	2.10 ± 0.01
	20	1.40	0.46	100	105 ± 2	0.95 ± 0.02	100	43.1 ± 0.2	7.2 ± 0.1	2.15 ± 0.01
				average:	0.96 ± 0.04			average:	2.1 ± 0.02	
$\text{C}_6\text{H}_6\text{-Et}_2\text{O (1:1)}^{\text{e}}$	8	0.39	0.25	100	104 ± 1	0.96 ± 0.01	100	33.1 ± 0.6	4.0 ± 0.4	2.90 ± 0.05
	12	0.57	0.35	100	105 ± 2	0.95 ± 0.02	100	34.8 ± 1.5	6.0 ± 0.9	2.70 ± 0.12
				average:	0.96 ± 0.02			average:	2.8 ± 0.1	
$\text{CH}_3\text{CN}^{\text{f}}$	2	0.70	0.10	100	103 ± 1	0.97 ± 0.01	100	25.0 ± 0.2	1.4 ± 0.3	3.94 ± 0.03
	4	1.50	0.19	100	98 ± 1	1.02 ± 0.01	100	22.8 ± 0.6	2.7 ± 0.5	4.27 ± 0.11
	8	4.10	0.31	100	106 ± 1	0.94 ± 0.01	100	23.4 ± 0.5	4.2 ± 0.2	4.09 ± 0.09
	12	7.10	0.47	100	105 ± 1	0.95 ± 0.01	100	23.0 ± 0.2	6.8 ± 0.3	4.05 ± 0.04
				average:	0.97 ± 0.03			average:	4.1 ± 0.2	

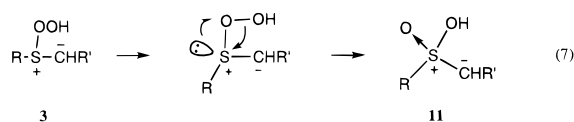
^a Irradiation of PhSCH_3 and PhSCD_3 (50 mM each) under O_2 . ^b Isotope ratios as determined by GC-MS. ^c Kinetic isotope effects defined as $(\mathbf{6b-d}_0)/(\mathbf{6b-d}_3)$. ^d Kinetic isotope effects defined as $[(\mathbf{7b-d}_0) - (\mathbf{7b-d}_3)]/(\mathbf{7b-d}_2)$. ^e Irradiation in the presence of 0.1 mM TPP. ^f Irradiation in the presence of 0.1 mM MB.

The importance of α -proton abstraction for the sulfone formation is reflected in the kinetic isotope effect of $k_{\text{H}}/k_{\text{D}} = 2\text{--}4$ (Tables 4 and 5). The isotope effect is understandable by assuming the competition between the hydrogen abstraction (eq 6a) and the regeneration of sulfides (eq 6b). The latter



dissociation of persulfonates to yield sulfides and oxygen is well-known,¹² and hence, the observation of intermolecular kinetic isotope effect is explicable in terms of competitive reactions of (6a) and (6b). The tracer experiments using doubly labeled oxygen $^{18}\text{O}_2$ in Table 3 demonstrate that the sulfone formation with H-D exchange is produced solely by the retention mechanism of the two ^{18}O atoms. Hence, it is apparent that *S*-hydroperoxysulfonium ylides (**3**) once formed are selectively converted unimolecularly to sulfones according to eq 6a.

PM3 Calculation. Deuterium and ^{18}O -tracer experiments supported the intermediacy of sulfonium ylide **3** for the sulfone formation as stated above. The conversion of ylides **3** to sulfones involves an 1,2-shift of an OH group from the O to S atom (eq 7), affording an *S*-ylide of sulfinic acid (**11**), i.e., a tautomer of sulfone. A similar 1,2-shift of alkyl groups is known in the rearrangement of sulfonates to sulfones.¹³ The observed H-D exchange occurs either in the HOO group in **3** or HO group in **11**.



The detailed mechanism of these transformations may be followed by theoretical calculations. Although ab initio calculations on sulfide- O_2 adducts were shown to be highly sensitive to the level of theory and frequently mislead to erroneous results,^{6,14} a semiempirical RHF-PM3 method¹⁵ was found to give relatively good results for the qualitative purpose. This method affords the thiadioxirane (**2**) as a stable unsymmetrical structure almost isoenergetic to persulfonate **1**, and the geometry and energy of transition states for the inversion of **2** (**TS1**, $\Delta H^\ddagger = 2.7$ kcal/mol) or for the cyclization of **1** (**TS2**, $\Delta H^\ddagger = 17.6$ kcal/mol) are calculated in good agreement with those ($\Delta H^\ddagger = 2.7$ and 19.7 kcal/mol, respectively) by the MP4/6-311G(2d)/MP2/6-31G* calculations reported by Jensen.⁷

The structures and energies (heats of formation, ΔH) calculated by the RHF-PM3 method for the suggested intermediates and transition states are summarized in Figure 1. The *S*-hydroperoxysulfonium ylide (**3**) was calculated slightly lower in energy than dimethyl persulfonate (**1**). The activation energy for the intramolecular proton transfer (**1** to **3**, **TS3**) was 18.9 kcal/mol, which was comparable to that for the isomerization of **1** to **2** (**TS2**). The OH migration from O to S in **3** affording **11** could be traced smoothly and was found to be highly exothermic (-59.7 kcal/mol), the activation energy for **TS4** from **3** being 25.3 kcal/mol. Thus, the present PM3 calculations

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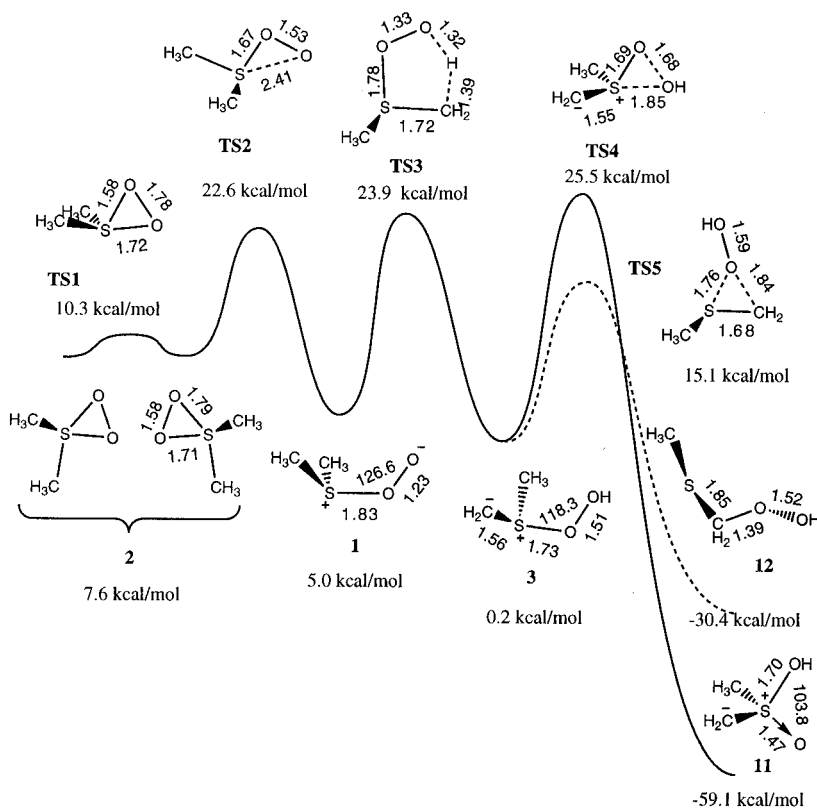


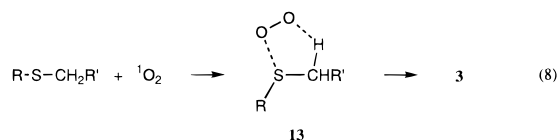
Figure 1. Structures and heats of formation for the intermediates and transition states on the potential energy surface of Me₂S + O₂ as calculated by RHF-PM3.

suggest that the three transition states **TS2–4** are of approximately equal energy and the conversion of **3** to **11** is highly exothermic.

Formation of 3 from 1. We have reported that since the sulfone formation was not affected by an efficient trapping agent for **1**, the possible formation of **2** was not from **1** but via a concerted cycloaddition of ¹O₂ to sulfides.⁶ On the other hand, the present results show the rate-determining generation of *S*-hydroperoxysulfonium ylide (**3**) as the sulfone-forming intermediate, which is explicable by the intramolecular proton transfer in persulfoxide **1**. The present PM3 calculations supported the conversion of **1** to **11** as a reasonable pathway to yield sulfones and the intermediate sulfonium ylide **3** is calculated to be more stable than persulfoxide **1**. It is not surprising that we previously reported that the sulfone-forming pathway was insensitive to trapping agents.⁶ Even in the presence of 0.1 M Ph₂SO, only a 10% change in sulfone yield is anticipated.¹⁶

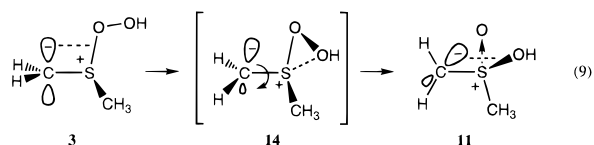
An alternative mechanism is a concerted proton abstraction/addition reaction of ¹O₂ with sulfides, as in the well-known ene reaction with olefins affording allylic hydroperoxides. Such an ene-type transition state (see **13** in eq 8) could not be found on the potential energy surface as calculated by PM3. However, since the reliability of the calculation at this level is not so high, we cannot eliminate such a mechanism. More detailed ab initio calculations with large basis sets including electron correlation are desired.

(16) By the steady-state treatment of Scheme 3 in a manner similar to that by Foote and co-workers,⁴ the ratio of sulfone yields in the presence vs absence of Ph₂SO can be formulated as 1/(1 + α[Ph₂SO]), where α = k_{SO}/(k_x + k_q + k_{PT}). When we apply the relative rate constants for diethyl sulfide, k_q/k_x = 45 (in acetone)¹¹ and k_s/k_{SO} = 0.023 M (in benzene),⁴ and the ratio of sulfone/sulfoxide yields in the present study, [R₂SO₂]/[R₂SO] = k_{PT}/2k_s = 0.4, α = 1.06 is obtained. Thus, the presence of the trapping agent results in only 10% decrease, even in the case of [Ph₂SO] = 0.1 M, in the sulfone yields.



HO vs HOO Migration in 3. The *S*-hydroperoxysulfonium ylides (**3**) have been proposed as the intermediate leading to C–S fission as shown in Scheme 2. In the present cases of dimethyl sulfide and thioanisole, however, the overall yields of sulfoxides and sulfones are always more than 90%, the fragmentation being only a minor side reaction. According to the PM3 calculation, the migration of the OOH group from the S to C atom affording **12** (a dashed curve in Figure 1) was less exothermic (–30.6 kcal/mol) but the transition state (**TS5**) was ~10 kcal/mol lower in energy than that of **TS4**. The TS calculations at this level may have only qualitative meaning, since the prediction of the predominant OOH migration is apparently inconsistent with the experimental results.

The C–S fragmentation is known to become a major pathway in the singlet oxygenation of benzyl or cyclic sulfides.^{8–10} Thus, the reaction pathway for either HO or HOO migration seems to depend on the substituents, which may be explained in terms of the stability and conformation of **3**. The PM3-calculated conformations of **3** and **11** show that the H₂C[–] group is almost orthogonal to S–OOH and S–OH bonds, respectively, indicating that the ylide carbanion interacts with the electron-deficient S–O bonds. The calculation also shows the twisting of the H₂C[–] group during the transformation from **3** to **11** (see **14** in eq 9), which may be the driving force on the HO migration.



For the cases of the ylides from benzyl or 9-fluorenyl sulfides, the π conjugation of the α -carbanion with aryl groups may result in the decreased interaction with S–O bonds, and the twisting of the ylide is evidently restricted in cyclic sulfides. For these cases, the sulfone formation via **3** is practically inhibited.

The kinetic isotope effect observed on the sulfone formation may be compared with that of C–S cleavage since a common intermediate **3** is involved. We have obtained a similar isotope effect (i.e., $k_H/k_D = 4.3$) in the benzaldehyde formation from $^1\text{O}_2$ and PhSCHDPH in acetonitrile,¹⁷ which is comparable to that of the sulfone formation from **5b** in the same solvent, $k_H/k_D = 4.1$. The observation of a similar kinetic isotope effect is quite interesting and supports the intervention of common intermediate **3**.

The Secondary Intermediate (SI) in the Sulfoxide Formation. Thiadioxiranes (**2**) are shown not to be the intermediate leading to sulfones but may participate in the sulfoxide formation as the secondary intermediate (**SI**) as depicted in Scheme 1.⁴ The oxidation via **SI** becomes predominant pathway at low temperature,¹² indicating that the activation energy for the conversion of **1** to **SI** is lower than those of other competing processes, e.g., the intramolecular proton transfer leading to the sulfone formation. However, as already pointed out by Jensen,⁷ the activation energy for the conversion of **1** to **2** may not be so low. Then, the hypothetical intermediacy of **2** as **SI** seems not to be appropriate at present.

The sulfoxide formation in aprotic solvents was found to be significantly affected by a trace amount of adventitious water. Thus, a possible structure for **SI** may be an adduct of water with persulfoxide **1**.^{14,18} A previous trapping study, however, has indicated that the reactivity of the intermediate in protic solvents is different from those of **1** or **SI** in aprotic solvents, and the quite complex solvent effects have been suggested by Clennan.¹⁹ A further detailed study on the effect of protic solvents may clarify the structure of **SI**.

Conclusion

The sulfone formation at earlier stage accompanied an H–D exchange of the α -methyl group in the reaction of sulfides with singlet oxygen in aprotic solvents. In contrast, no exchange was observed in the sulfoxides obtained. The exchanged proton in sulfone was shown to come from adventitious water, and the doubly labeled ^{18}O -tracer study indicated no scrambling of two oxygen atoms. A significant kinetic isotope effect was observed for the α -deuterated sulfides, suggesting the intramolecular proton abstraction in the persulfoxides (e.g., $\text{RS}^+(\text{OO}^-)\text{CH}_3$) being the rate-determining step. These results clearly indicate that the sulfones are formed intramolecularly via *S*-hydroperoxysulfonium ylides ($\text{RS}^+(\text{OOH})\text{CH}_2^-$). The conversion of the sulfonium ylides to sulfones was shown to be facile on the basis of PM3 calculations.

Experimental Section

General Aspects. ^1H NMR spectra were recorded with a Varian GEMINI-200 (200 MHz) NMR spectrometer. GLC analyses were performed with Yanagimoto G180 and Shimadzu GC-14A gas chromatographs, using 2.5 mm \times 1 m column of Carbowax 300 M (2%) on Chromosorb WAW. A Shimadzu Chromatopac C-R3A integrator was used for quantitative analyses. GC–MS analyses were carried out with a JEOL D300 or a Shimadzu QP-5000 mass spectrometer using a 2.5 mm \times 1 m column of Carbowax 300 M (2%) on

Chromosorb WAW or a 0.2 mm \times 25 m capillary column of Silicon OV-1 (J & W Scientific, DB-1).

Materials. Benzene was dried by distillation over sodium benzophenone. Acetonitrile was distilled from phosphorus pentoxide. Dimethyl sulfide (**5a**, Tokyo Kasei) and dimethyl sulfide-*d*₆ (**5a-d**₆, Aldrich, 99.9% atom D) were employed as received. Thioanisole (**5b**, Tokyo Kasei) and di-*tert*-butyl sulfide (**8**, Tokyo Kasei) were distilled before use. Methylene Blue (MB, Tokyo Kasei) and tetraphenylporphyrin (TPP, Tokyo Kasei) were used without further purification. $^{18}\text{O}_2$ (99% pure) gas from CEA was diluted with O_2 gas.

Thioanisole- α,α,α -*d*₃ (5b-d**₃).** To 3.5 g of chlorosulfonic acid (30 mmol), was added 1.0 mL of methanol-*d*₄ (CEA, 99.8 atom % D, 24.6 mmol) dropwise at 0 °C. After 5 min of stirring, a solution of 3.0 mL of thiophenol (29.2 mmol) and 10 g of sodium hydroxide (25 mmol) in 50 mL of water was added at this temperature. The mixture was refluxed for 3 h, and the product was extracted with ether. The extract was washed with brine and dried over anhydrous sodium sulfate. Evaporation of the solvent and chromatographic separation on silica gel (hexane) gave thioanisole- α,α,α -*d*₃ (1.2 g) as a colorless liquid in 38% yield. The purity of deuterium as determined by mass spectroscopy was 99.5 atom % D.

Typical Procedure of the Photo-oxidation. A 10-mL benzene solution of 0.05 M dimethyl sulfide-*d*₆ (**5a-d**₆) and 0.1 mM tetraphenylporphyrin (TPP) in a 25-mL Pyrex test tube with a septum rubber cap was purged with oxygen and was irradiated at 20 ± 2 °C with a 300-W medium-pressure Hg lamp through a 5% NaNO_2 filter solution (i.e., >400 nm). The formation of sulfones and sulfoxides was determined at appropriate intervals of time by GLC.

Determination of Deuterium Contents in the Photoproducts. The resulting solution was concentrated and analyzed by GC–MS. For **6a** and **7a**, the mass spectral data around the parent peak (M) were easily obtained by an EI method with 70 eV ionization voltage. Since their retention times on GC were slightly different depending on the number of deuteriums, the mass intensities should be, for the quantitative analyses, integrated by mass chromatography throughout the GC peaks. A large number of mass data (up to ~ 500 points per peak) were collected by sampling of 0.05 s intervals. The differences in mass intensities of parent peak (M) between perdeuterated and nondeuterated dimethyl sulfoxides or sulfones were not negligible. Then, the relative mass peak intensities were determined from a 1:1 mixture of **6a-d**₀ and **6a-d**₆ and that of **7a-d**₀ and **7a-d**₆, i.e., $(\text{6a-d}_0/\text{6a-d}_6) = 0.883$ and $(\text{7a-d}_0/\text{7a-d}_6) = 0.819$. As the pure sample of **7a-d**₅ was not available, the relative intensity for **7a-d**₅ could not be determined directly but was calculated from that for **7a-d**₆ by assuming that the mass intensity might depend on the number of deuteriums, $[1 - (\text{7a-d}_0/\text{7a-d}_5)] = ^5/6$ of $[1 - (\text{7a-d}_0/\text{7a-d}_6)]$, i.e., $(\text{7a-d}_0/\text{7a-d}_5) = 0.849$.

The mass spectrum of resulting sulfoxide **6a** was identical to that of authentic **6a-d**₆ obtained by the *m*-chloroperbenzoic acid oxidation of **5a-d**₆ within experimental error. The sulfone **7a** was shown to be formed as a mixture of **7a-d**₅ and **7a-d**₆; the integrated peak areas were obtained by mass chromatography monitored at $m/e = 99$ and 100, corresponding to the parent ions of $\text{C}_2\text{D}_5\text{HSO}_2$ and $\text{C}_2\text{D}_6\text{SO}_2$, respectively, the latter data being corrected by abstracting the M + 1 value of natural abundance in C_2SO_2 . After correction of the relative mass intensity, **7a-d**₅ vs **7a-d**₆, the isotope ratios in the sulfone **7a** were obtained. Three to five determinations were averaged, and the results are summarized in Table 1.

The products from the photo-oxidation of **5b-d**₃ in the absence or presence of 0.05–0.5% H_2O were analyzed similarly from integrated mass peak areas at the parent ions (M). Since the mass intensities of parent peaks were almost independent of the number of deuteriums in the sulfoxides **6b** and the sulfones **7b**, no correction was made on the relative mass intensity. The mass data were corrected by abstracting the M + 1 value of natural abundance, and the results averaged on three determinations are listed in Table 2.

Isotope ratios of the products on the photo-oxidation of PhSCH₃ (**5b-d**₀) in the presence of D_2O were analyzed similarly. The irradiation of 0.05 M PhSCH₃ (**5b-d**₀) and 0.1 mM TPP in 0.05% D_2O (27.6 mM)/benzene under O_2 atmosphere for 20 h afforded **6b** and **7b** in 1.5% and 0.58% yields, respectively. The isotope ratio of **7b** as determined by GC–MS was PhSO_2CH_3 (**7b-d**₀): $\text{PhSO}_2\text{CH}_2\text{D}$ (**7b-d**₁) = 100:48.2 \pm 0.1. For **6b**, the ratio of the integrated peak areas monitored at m/e

(17) Sulfone was not obtained: Ishiguro, K.; Hatta, A.; Hayashi, M.; Sawaki, Y. Unpublished result.

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= 140 (M) and 141 (M + 1) of $100:8.57 \pm 0.04$ was almost identical to that of authentic **6b-d₀** ($100:8.43 \pm 0.03$), i.e., **6b-d₀**:**6b-d₁** = >99: <1.

¹⁶O₂-¹⁸O₂ Tracer Experiment. A 1-mL benzene or acetonitrile solution of 0.1 M dimethyl sulfide-*d*₆ (**5a-d₆**) and 0.1 mM TPP or MB, respectively, was placed in a 5-mL test tube with a septum rubber cap. After the solution was purged with argon, oxygen gas (¹⁶O₂:¹⁶O¹⁸O:¹⁸O₂ = 100:0.79:11.9) was introduced into the test tube through a syringe. After irradiation of an appropriate time at >400 nm, the resulting reaction mixture was analyzed by GC-MS. The mass intensities of parent peaks for **7a-d₅** and **7a-d₆** with ¹⁶O₂, ¹⁶O¹⁸O, and ¹⁸O₂, monitored at *m/e* = 99, 100, 101, 102, 103, and 104, were integrated by mass chromatography throughout the GC peaks. After the corrections of the relative intensities for **7a-d₅**/**7a-d₆** and those of the M + 1 and M + 2 values of natural abundance, the isotope ratios were obtained as summarized in Table 3.

The ¹⁶O₂-¹⁸O₂ tracer experiment of di-*tert*-butyl sulfide (**8**) was carried out similarly. The sulfone **10** showed no parent peak (M = 178), but the ratio of oxygen isotopes could be obtained from the major fragment peaks, M - 56 (-CH₂=C(CH₃)₂), since the mass spectrum of authentic **10** showed fragment peaks of *t*-BuS¹⁶O₂H monitored at *m/e* = 121, 122 (M), 123, 124, and 125, in the ratio $3.13 \pm 0.07:100: 5.78 \pm 0.23:5.47 \pm 0.12:0.58 \pm 0.01$, which was close to the theoretical ratio for C₄H₁₀SO₂, M:M + 1:M + 2 = 100:5.34:4.88. The photo-oxidation of 100 mM di-*tert*-butyl sulfide (**8**) and 0.1 mM TPP with ¹⁶O₂-¹⁸O₂ (¹⁶O₂:¹⁶O¹⁸O:¹⁸O₂ = 100:0.79:11.9) in benzene for 6 h afforded the corresponding sulfoxide **9** and sulfone **10** in 2.3% and 0.24% yields, respectively. The sulfone was analyzed by GC-MS, and the integrated peak ratios monitored at *m/e* = 122 (M of *t*-BuS¹⁶O₂H), 123, 124 (M of *t*-BuS¹⁶O¹⁸OH), 125, and 126 (M of *t*-BuS¹⁸O₂H) were corrected with the M - 1, M + 1, and M + 2 values observed at the authentic sample. The isotope ratios in the sulfone **10** obtained by three determinations were **10**-¹⁶O₂:**10**-¹⁶O¹⁸O:**10**-¹⁸O₂ = 100:18.2 ± 0.2:1.2 ± 0.1.

Kinetic Isotope Effect. A benzene solution of 50 mM (CH₃)₂S, 50 mM (CD₃)₂S, and 0.1 mM TPP was irradiated for appropriate time,

and the products, three sulfones, **7a-d₀**, -*d*₅, and -*d*₆, and two sulfoxides, **6a-d₀** and -*d*₆, were analyzed by GC-MS as described above. The kinetic isotope effects, *k_H*/*k_D*, for sulfoxide **6a** at each time were obtained by the product ratios for the sulfoxides **6a-d₀** and -*d*₆, and those in the unimolecular sulfone formation were calculated from [(**7a-d₀**) - (**7a-d₆**)]/(**7a-d₅**), assuming that equal amounts of **7a-d₀** and -*d*₆ were formed by secondary oxidation. The actual kinetic isotope effect for the sulfone formation, 3.0 ± 0.4 , was obtained by the extrapolation of these values to zero time. The results are shown in Table 4.

Kinetic isotope effects on the oxidation of PhSCH₃ and PhSCD₃ in C₆H₆, C₆H₆-Et₂O (1:1), and CH₃CN were obtained similarly, the results being summarized in Table 5.

Theoretical Calculations. Semiempirical RHF/PM3 molecular orbital calculations¹⁵ were carried out on Apple Macintosh computers using the MOPAC version 6.02.²⁰ All of the geometries of intermediates and transition states were optimized with the keyword PRECISE to increase the criteria for the termination of optimization by a factor of 100. Transition states were obtained with the keyword TS and were confirmed by frequency calculation and intrinsic reaction coordination (IRC) procedures. The energies and principal parameters in the optimized structures are shown in Figure 1, and the full geometries in the Z matrix are given in the supporting information.

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Supporting Information Available: Tables of the PM3-calculated geometries and energies for the intermediates and transition states (4 pages). See any current masthead page for ordering and Internet access instructions.

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