

PHOTOSENSITIZED OXYGENATION OF CYCLIC SULFIDES.

SELECTIVE C-S BOND CLEAVAGE

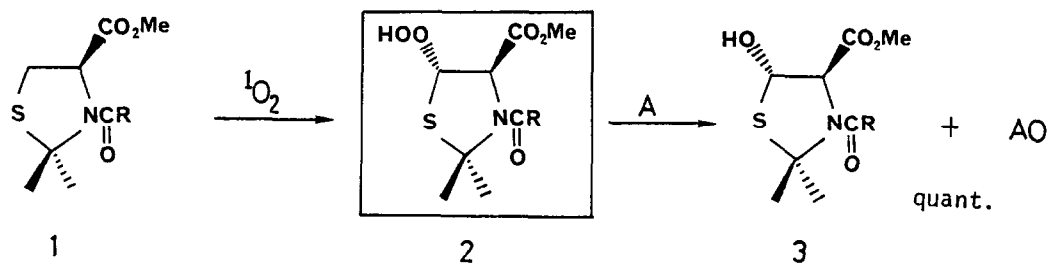
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Summary: TPP-Sensitized photooxidation of five-membered ring sulfides in aprotic solvent afforded C-S bond cleavage products, unlike six- and seven-membered ring sulfides which gave only S-oxidation products. The products as well as substitution and concentration effects suggest that C-S bond cleavage depends upon acidity of  $\alpha$ -proton of persulfoxide intermediate.

Singlet oxygenation of sulfides<sup>1</sup> proceeds along either of two reaction courses involving a common intermediate persulfoxide formed initially: one is S-oxidation in which sulfoxides and/or sulfones are the products, and the other is fragmentation forming C-S bond cleavage products. Although the former has been studied extensively by Foote<sup>2</sup> in terms of kinetics, the latter is not. Corey<sup>3</sup> and Ando<sup>4</sup> originally reported the photooxidation of benzylic sulfides resulted in the fragmentation products by C-S bond cleavage. Corey proposed  $\alpha$ -hydroxy sulfide as a key intermediate, while Ando<sup>4,5</sup> predicted the intermediate  $\alpha$ -hydroperoxy sulfide. Recently, Ando<sup>6</sup> has been succeeded in isolating  $\alpha$ -hydroperoxy sulfide 2 in photooxidation of thiazolidine derivative 1 (Scheme 1). However, all the photooxidation on five- to seven-membered ring

Scheme 1



sulfides reported so far, gave only corresponding sulfoxides and/or sulfones.<sup>1,7</sup> So, it has become interesting how the hydroperoxide was formed. In connection with elucidation of the fragmentation of benzylic sulfide photooxidation we have continued the investigation on the mechanistic aspects of the formation of 2, and found that the fragmentation depends on acidity of  $\alpha$ -proton of persulfoxide intermediate, from results of photooxidation of cyclic sulfides.

A dry THF solution of one of the sulfides listed in Table 1 ( $[C] = 0.05 - 0.15$  M) and TPP (meso-tetraphenylporphyrin, 15 mg/mmol of substrate) in Pyrex tube, was irradiated under bubbling oxygen with 500W halogen lamp at  $-39^\circ\text{C}$ . After the irradiation excess dimethyl sulfide (DMS) was added and the mixture was allowed to stand at room temperature in the dark. The reaction products were analyzed by GLC or isolated by chromatography, and determined by spectroscopies. Results are summarized in Table 1.

Interestingly, inspection of data of Table 1 reveals five-membered ring sulfides afforded C-S bond cleavage products. Six- and Seven-membered ring sulfides as well as diethyl sulfide gave corresponding sulfoxides and sulfones without any fragmentation product. Under the same conditions, cysteinyl sulfide having similar composition to 1 (Run 9) similarly gave corresponding sulfoxide and sulfone. These results clearly indicate oxidative C-S bond cleavage is characteristic of five-membered ring sulfides, being consistent with Scheme 1.

A common property between five-membered ring and benzylic sulfides can be understood by Fava's report on kinetic acidity of  $\alpha$ -ring proton of methyl sulfonium ions of cyclic sulfides,<sup>8</sup> where five-membered ring has particularly high acidity. Therefore, C-S bond cleavage undoubtedly depends on acidity of  $\alpha$ -proton of the persulfoxide intermediate formed initially in the reaction with singlet oxygen. This is in accordance with our experiment in which benzoyl formaldehyde was formed in the photooxidation of methyl phenacylmethyl sulfide under the same conditions.

Thus, the reaction mechanism might be explained by Scheme 2. Namely, Pummerer type rearrangement of initially formed persulfoxide 4 gave rise to

Scheme 2

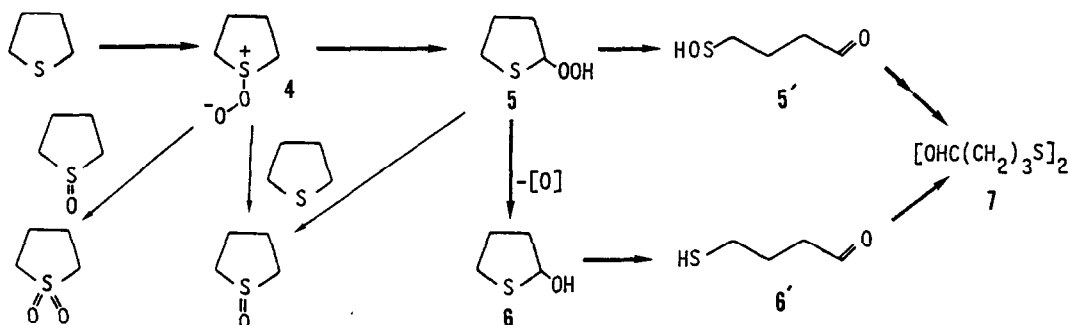


Table 1 TPP-Sensitized Photooxidation of Sulfides in THF at -30°C.<sup>a)</sup>

Run	Substrate	Time/min(conv/%)	S-Oxidation Product/% <sup>b)</sup>		Product by C-S <sup>b)</sup> Bond Cleavage	Note
			Sulfoxide	Sulfone		
1	<chem>C2H5SC2H5</chem>	65(100)	67	33	0	
2		60(100)	71	19	0	c)
3		R=H 100(100)	80	19	0	
4		R=p-ClC <sub>6</sub> H <sub>4</sub> 50(100)	84	ND	0	d)
5		60(100)	65	trace	(OHC(CH <sub>2</sub> ) <sub>4</sub> S) <sub>2</sub> / 34	d)
6		5(33)	16	0	+ (OHC(CH <sub>2</sub> ) <sub>4</sub> S) <sub>2</sub> / 80 + (CH <sub>3</sub> CO(CH <sub>2</sub> ) <sub>4</sub> S) <sub>2</sub>	
7		130(100)	50	trace	(CH <sub>3</sub> CO(CH <sub>2</sub> ) <sub>4</sub> S) <sub>2</sub> / 40	d)
8		6(30)	0	0	(CH <sub>3</sub> CO(CH <sub>2</sub> ) <sub>4</sub> S) <sub>2</sub> / 100	
9		60(100)	56	7	0	d)
10	<chem>PhCH2SCH2Ph</chem>	120(100)	36	19	PhCHO / 45	d),e)

a) Substrate: 1 mmole. b) GLC yield. c) Small amount of unidentified product was obtained.

d) Isolated yield. e) Reaction at 5°C(see ref. 3).

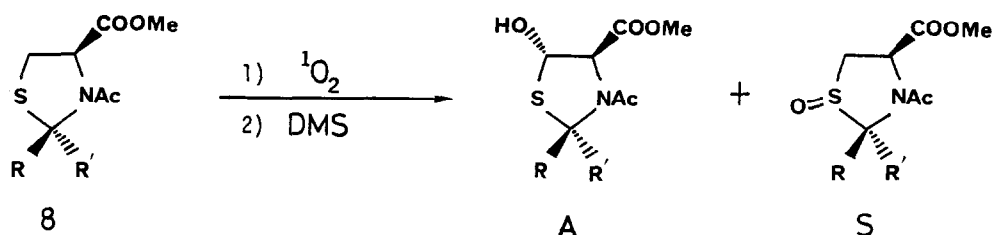
hydroperoxide 5 via intramolecular  $\alpha$ -proton abstraction.<sup>9,10</sup> Then, both 5 and alcohol 6 reduced might be unstable, unlike 2 and 3, to collapse to eventually give disulfide 7.

Scheme 2 reveals that intermolecular(S-oxidation) and intramolecular (hydroperoxylation) reactions are competitive. Therefore the change of substrate concentration dramatically affected product ratio(C-S bond cleavage product/sulfoxide) in the reaction of 2-methylthiolane(substrate of Run 6). The ratio was increased as the concentration fell down(0.45 at [C]=0.2 M and 2.35 at [C]=0.05 M). In the case of 8b(Scheme 3) similar change of ratio(A/S) was observed.

Steric effect of the photooxidation of 8(Scheme 3) led to result in which higher extent of methyl substitution at 2-position made suppressing the sulfoxide formation to raise the ratio(A/S 0.05(8a), 0.67(8b) and 99(8c)), as expected from data of Table 1(Runs 5-8).

Thus, the C-S bond cleavage in sulfide photooxidation was shown to proceed via  $\alpha$ -hydroperoxy sulfide in competition with the S-oxidation, depending upon  $\alpha$ -proton acidity of persulfoxide intermediate formed initially.

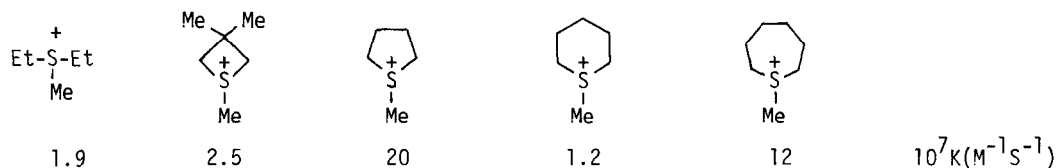
Scheme 3



a: R=R'=H; b: R=H, R'=Me; c: R=R'=Me

#### REFERENCE AND FOOTNOTES

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- 9) In MeOH, by suppressing proton abstraction no C-S cleavage product was observed in the case of substrate of Run 7 in Table 1, but sulfoxide(96%) and sulfone(3%) were obtained.
- 10) Acidic proton abstraction by persulfoxide shown in this work is the first example, and in turn this result seems to support its zwitterionic structure.

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