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# Photooxidations of Sulfenic Acid Derivatives 2. A Remarkable Solvent Effect on the Reactions of Singlet Oxygen with Disulfides.

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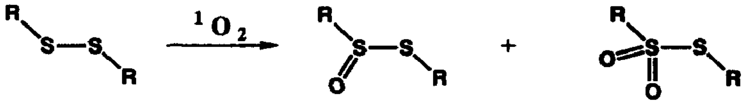
**Abstract:** Photooxidations of a series of 9 disulfides reveal that the thiosulfinate/thiosulfonate product ratios can be dramatically influenced by the nature of the solvent. The unique ability of methanol to influence this ratio is attributed to nucleophilic addition to a thiopersulfoxide intermediate.

The unquestionable biochemical importance of disulfides is reflected in the large number of experimental and theoretical investigations of this fascinating functional group.[1-8] We report here a study of the photooxidations of several disulfides which reveal that the sulfinate/sulfonate, **1/2**, ratios are much more dependent on the identity of the solvent than previously recognized.[9] We also speculate on the origin of this dramatic and potentially useful solvent effect.

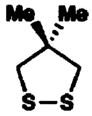
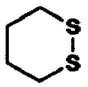
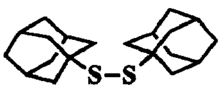


**Sulfinate**
**1**

**Sulfonate**
**2**

Photooxidations of solutions 2-4 x $10^{-5}$M in sensitizer and 0.04-0.15M in disulfides **3-11** (Table 1) were conducted at room temperature in a variety of oxygen saturated solvents by irradiation with a 650W tungsten bulb through a 1cm 0.5% $K_2Cr_2O_7$ filter solution. In several of the reactions 3-4% by weight pyridine was used to retard the bleaching of the dye with no effect on product distributions. All of the disulfides except di-t-butyldisulfide, **6**, and 1,1'-diadamantyldisulfide, **11**, reacted to give both **1** and **2**. Disulfides **6** and **11** were not oxidized even after several hours of irradiation. The progress of the reactions were monitored by $^1$H NMR and the product ratios were determined using a gas chromatograph calibrated with authentic samples of the sulfinates and sulfonates. The identities of the sulfinate and sulfonate products formed in the photooxidations of **8** and **9** were also verified using a GC/MS.

Table 1. **Thiosulfinate and Thiosulfonate Ratios During Photooxidations of Disulfides.**[a]

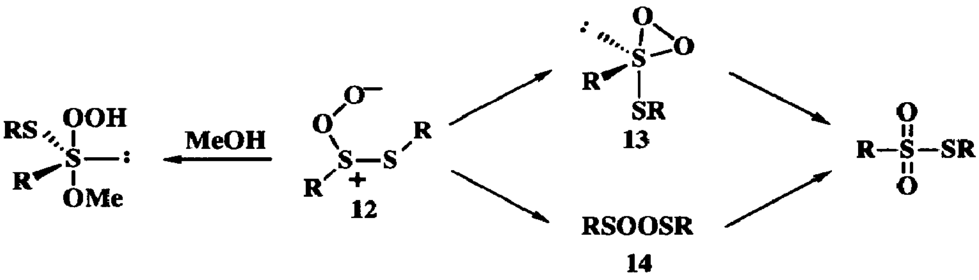
| **Compound** | **hν (min)** | **solvent** | **T°C** | **% conversion** | **% RS(O)SR** | **% $RS(O)_2SR$** |
|---|---|---|---|---|---|---|
| MeSSMe<br>**3** | 30 | acetone-$d_6$ | 20 | 63 | 40 | 60 |
| EtSSEt<br>**4** | 10 | acetone-$d_6$ | 20 | 3 | 14 | 86 |
| | 30 | acetone-$d_6$ | -78 | 2 | 55 | 45 |
| | 5 | $CD_3OD$ | 20 | 22 | 85 | 15 |
| | 5 | $CD_3OD$ | -78 | 6 | 59 | 41 |
| iPrSSiPr<br>**5** | 30 | acetone-$d_6$ | 20 | <2 | trace | trace |
| tBuSStBu<br>**6** | 30 | acetone-$d_6$ | 20 | 0 | --- | --- |
| <br>7 | 30 | acetone-$d_6$ | 20 | 20 | 32 | 68 |
| | 30 | $CD_3OD$ | 20 | 38 | 79 | 21 |
| <br>**8** | $360^{b}$ | $CDCl_3$ | 20 | 100 | 30 | 70 |
| | $180^{b}$ | $CH_3CN$ | 20 | 100 | 23 | 77 |
| | $120^{b,c}$ | benzene-$d_6$ | 20 | 100 | 38 | 62 |
| | $60^{b}$ | acetone-$d_6$ | 20 | 100 | 16 | 84 |
| | $180^{b}$ | $CD_3OD$ | 20 | 100 | 86 | 14 |
| <br>**9** | $30^{b}$ | acetone-$d_6$ | 20 | 32 | 20 | 80 |
| | $10^{b}$ | $CD_3OD$ | 20 | 47 | 80 | 20 |
| <br>**10** | $120^{b}$ | acetone-$d_6$ | 20 | 100 | 32 | 68 |
| | $50^{b}$ | $CD_3OD$ | 20 | 100 | 66 | 34 |
| <br>**11** | $180^{c}$ | $CDCl_3$ | -44.5 | | no reaction | |

a. Solutions 0.04 to 0.15M in disulfide and 2-4 x $10^{-5}$M in Rose Bengal except where indicated. b. 3-4% pyridine by weight. c. tetraphenylporphyrin used as sensitizer.

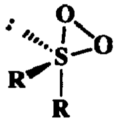
In stark contrast to the photooxidations of dialkylsulfides which give predominantly sulfoxides,[10] the major products (60-88%) formed in the reactions of $^1O_2$ with disulfides in aprotic solvents are the thiosulfonates, **2**. (Table 1) The yields of thiosulfinates, **1**, however, do increase at the expense of **2** at either low temperature or in the protic solvent methanol. In the case of 4,4-diethyl-1,2-dithiolane, **9**, a complete reversal from 20/80 to 80/20 thiosulfinate/thiosulfonate occurred upon changing the solvent from acetone-$d_6$ to $CD_3OD$. The singlet oxygen origins of both **1** and **2** were confirmed by quenching experiments with DABCO and by demonstrating that the product ratios were independent of sensitizer. Control reactions also indicate that under the reaction conditions the thiosulfinates are inert to singlet oxygen and do not serve as precursors to the thiosulfonates.

Monitoring of the photooxidation reaction mixtures over a period of several hours revealed the occurrence of a slow disproportionation[11,12] of **1** to **2**. The disproportionation was most rapid for dimethyldisulfide, **3**, as previously observed by Murray and Jindal,[13] and did not occur at all for the dithiolanes, **8** and **9**, or for the dithiane, **10**. The similarity in the product distributions for the photooxidations of these cyclic disulfides and the product ratios for the acyclic disulfides **3-7** where disproportionation occurs slowly, demonstrates that rapid monitoring produces product ratios that are not significantly altered by this dynamic process.

It is tempting to speculate that methanol traps the thiopersulfinate intermediate **12** to give a hydroperoxy sulfurane competitively inhibiting formation of intermediates **13** and/or **14** which could potentially serve as precursors to the thiosulfonate. Intramolecular nucleophilic additions of hydroxy groups to persulfoxide intermediates formed in the photooxidations of aryl alkyl sulfides have previously been invoke to explain the migration of the hydroxy oxygen to sulfur in the sulfone products.[14-16] Murray and coworkers[9] previously suggested that the small effect of methanol observed during the photooxidation of methyl-α-lipoate was a result of hydrogen bonding to **12** which would also be expected to inhibit sulfonate formation. Inconsistent with the hydrogen bonding argument, however, is the observation that photooxidations of **8** in 7/3 v/v mixtures of tBuOH/benzene and MeOH/benzene resulted in dramatically different sulfinate/sulfonate ratios of 23/77 and 90/10, respectively. The inability of tBuOH in comparison to MeOH to inhibit sulfonate formation is most consistent with a steric effect on the formation of the hydroperoxy sulfurane.



The much larger yields of sulfonates observed during the photooxidations of disulfides in comparison to sulfides can be explain by either invoking intermediate **13** or **14**. Intermediate **14** provides a mechanistic channel to the sulfonate unavailable in the photooxidations of sulfides. Thiadioxirane **13**, on the other hand, is undoubtedly more stable than **15** and consequently more likely to be populated as a result of the increased ability of sulfur in comparison to carbon to accommodate the localization of negative charge on the apical ligand of a trigonal bipyramidal sulfurane.



**15**

Additional studies designed to explore the photooxidations of these disulfides are currently in progress and will be reported in the near future.

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