

pressure are effectively identical with measurements at constant volume is, therefore, unjustified.

### EPR Measurements of Vibrational Frequencies.

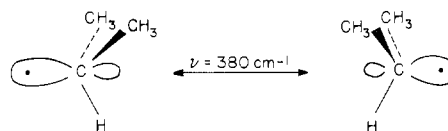
As a final example of the versatility of EPR we describe its use to measure the out-of-plane vibrational frequencies of alkyl radicals. An EPR spectrum provides an average picture of all the radicals in a sample. Most of the radicals will be in the zero-point vibrational level, but as the temperature is raised higher levels will become increasingly populated. When the out-of-plane vibration can be described by the simple harmonic oscillator approximation the average amplitude<sup>74</sup> of vibration will increase with temperature. This will lead to an increase in the degree of s character of the semioccupied orbital and hence to an increase in the  $^{13}\text{C}_\alpha$  hfs,  $a^{13}\text{C}_\alpha$ . The out-of-plane vibrational frequency,  $\nu$ , can be obtained together with the theoretical hfs,  $a_0$ , for the radical rigidly held in its theoretical planar configuration, and also the constant  $a_2/2F$ , by measuring  $a^{13}\text{C}_\alpha$  over a range of temperature and using

$$a^{13}\text{C}_\alpha(T) = a_0 + \frac{a_2 h \nu}{2F} \coth \frac{h \nu}{2kT}$$

When applied to the isopropyl radical<sup>75</sup> this procedure yielded  $\nu = 380 \text{ cm}^{-1}$ , in excellent agreement with a value of  $375 \text{ cm}^{-1}$  obtained by an infrared spectroscopic study of matrix isolated isopropyl radicals.<sup>76</sup> If

(74) More specifically, in the EPR experiment we are dealing with the mean-square amplitude of vibration.

(75) Griller, D.; Preston, K. F. *J. Am. Chem. Soc.* 1979, 101, 1975.



reasonable assumptions are made about geometry of isopropyl, the force constant,  $F$ , for the out-of-plane vibration can be obtained, and this in turn can be used to calculate  $\nu$  for other simple alkyls.<sup>72</sup> There is excellent agreement between the calculated frequencies and the frequencies measured by infrared, e.g.,  $\text{CH}_3$ , 596 vs, 617  $\text{cm}^{-1}$ ;  $\text{CD}_3$ , 462 vs, 463  $\text{cm}^{-1}$ ;  $\text{CH}_3\text{CH}_2$ , 499 vs, 541  $\text{cm}^{-1}$ .

A similar study of  $a^{13}\text{C}_\alpha$  for  $\text{Me}_3\text{C}\cdot$  has shown that this radical has a minimum energy of configuration which is nonplanar.<sup>77</sup> Its out-of-plane vibration is best described by a double-minimum potential function.

### Concluding Remarks

In this Account we have tried to show that very simple EPR experiments can provide interesting and important data. The majority of techniques described are very easy to apply and, with a few exceptions, do not require any special equipment. The versatility of EPR encourages the design of elegant and simple experiments to further the art of physical-organic chemistry.

(76) Pacansky, J.; Horne, D. E.; Gardini, G. P.; Bargon, J. *J. Phys. Chem.* 1977, 81, 2149.

(77) Griller, D.; Ingold, K. U.; Krusic, P. J.; Fischer, H. *J. Am. Chem. Soc.* 1978, 100, 6750.

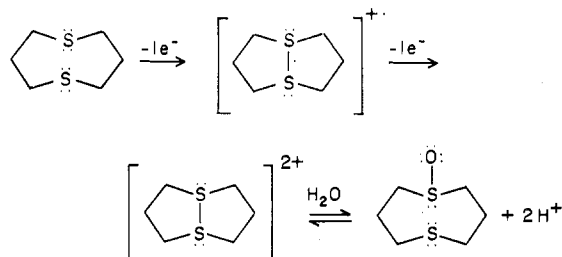
## Chemistry of Aliphatic Thioether Cation Radicals and Dications

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This Account is concerned with the preparation and properties of aliphatic thioether cation radicals and dications of the type shown below. These cations can



be obtained either by a stepwise one-electron oxidation of 1,5-dithiacyclooctane (1,5-DTCO) or by an acidifi-

cation of 1,5-dithiacyclooctane 1-oxide.<sup>1,2</sup> As shown, cation formation occurs with concomitant coupling of the two sulfur atoms. Most of the compounds studied have been mesocyclic (7- to 10-membered rings) dithioethers, but it appears that any appropriately substituted aliphatic thioether may be used and any group (amine, alcohol, etc.) which can function as a lone-pair donor can participate in the oxidative coupling reaction. The reason for initially choosing mesocyclic dithioethers was based on studies of transannular reactions by N. J. Leonard. In a recent Account he has described the consequences of using the trimethylene bridge as a synthetic spacer of functional groups.<sup>3</sup>

The intramolecular coupling of heteroatoms on oxidation of aliphatic dithioethers is in marked contrast to the species formed on oxidation of aromatic thio-

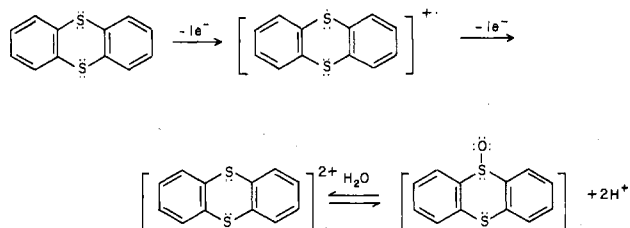
W. Kenneth Musker was born in Oak Park, IL, in 1934. He obtained his B.S. at Bradley University and the Ph.D. at the University of Illinois. After 2 years in the Air Force and 1 year as a postdoctoral student at the University of Michigan, he joined the faculty at the University of California, Davis. His research interests concern intramolecular effects on electron-transfer processes and the structure and reactivity of copper-thioether complexes.

(1) Musker, W. K.; Wolford, T. L.; Roush, P. B. *J. Am. Chem. Soc.* 1978, 100, 6416.

(2) Musker, W. K.; Hirschon, A. S.; Doi, J. T. *J. Am. Chem. Soc.* 1978, 100, 7754.

(3) Leonard, N. J. *Acc. Chem. Res.* 1979, 12, 423.

ethers related to thianthrene. These aromatic cations,



which have been extensively studied by Shine and co-workers, do not contain an intramolecular sulfur-sulfur bond.<sup>4</sup> They are more stable than the aliphatic thioether cations because the charge may be delocalized by the ring system; however, there is evidence that the thianthrene cation radical can dimerize to give a species with an intermolecular sulfur-sulfur bond.<sup>5</sup>

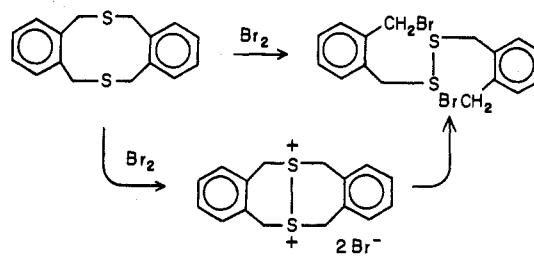
Because an intramolecular interaction is important in stabilizing aliphatic thioether cations, the redox properties of an aliphatic thioether group are appreciably altered in the presence of proximate lone-pair donors.<sup>6</sup> For example, the peak potential for the first oxidation peak of 1-thiacyclooctane and 1,5-dithiacyclooctane differs by almost 1 V.<sup>6</sup> In biochemical systems this property may be utilized to mediate electron-transfer processes.

Our interest in aliphatic thioether cation chemistry began quite by accident when we discovered a long-lived thioether cation radical. During a study of complexes of mesocyclic dithioethers with metal ions, we found that 1,5-dithiacyclooctane (1,5-DTCO) was easily oxidized by  $\text{Cu}(\text{ClO}_4)_2$ .<sup>1</sup> Later, on treatment of 1,5-DTCO with 1 equiv of  $\text{NOBF}_4$  in  $\text{CH}_3\text{CN}$  or  $\text{CH}_3\text{NO}_2$ , an ESR spectrum of a thioether cation radical was observed in solution. The ESR signal persisted for several days at room temperature. With excess  $\text{NOBF}_4$ , 1,5-DTCO was oxidized to a dication which was isolable as a stable tetrafluoroborate salt.<sup>1</sup> Dications of this nature had not been reported before. They are essentially dialkylated disulfides, and prior to this work only monoalkylated disulfides had been prepared.<sup>7</sup>

Aliphatic thioether cation radicals, but not dications, have been prepared in water and hydrocarbon solvents using pulse radiolysis. This technique and the possible structures of the cation radicals have recently been reviewed by K.-D. Asmus.<sup>8</sup>

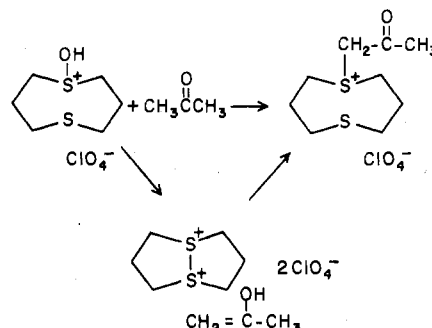
### Historical Dications and Cation Radicals

In 1903, the first suggestion of a dithioether dication was offered by Autenrieth and Bruning who treated 2,5,7,10-tetrahydrodibenzo[*c,h*]-1,6-dithiecin with bromine in  $\text{CHCl}_3$ .<sup>9</sup> Subsequently, Breslow and Skolnick proposed that the product was the disulfide and not the dication.<sup>10</sup> We confirmed that the product was the disulfide but, in light of our current knowledge, we suggest that the originally proposed dication is an in-



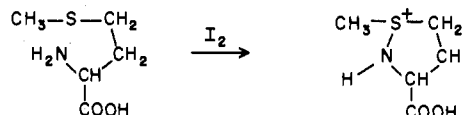
termediate in the reaction.

In Leonard's laboratory, Yethon observed that 1,5-DTCO 1-oxide reacted with acetone in the presence of perchloric acid to give an acetonysulfonium salt.<sup>11</sup>



This behavior was not exhibited by related monosulfides which did not have three methylene groups separating the two sulfur atoms. In this reaction a dicationic intermediate would also account for the product obtained. A thioether dication was recently proposed by Ruffato and Miotti as a possible intermediate in the oxygen-exchange reaction between dialkyl sulfoxides and aryl methyl sulfides.<sup>12</sup>

In 1942 Lavine reported that the reaction of methionine with  $\text{I}_2$  gave dehydromethionine, a cyclic molecule

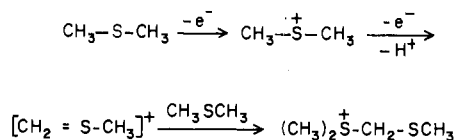


which was believed to contain an  $\text{N}^+-\text{S}$  bond.<sup>13</sup> The structure was later confirmed by Glass and Duchek by an X-ray crystal structure analysis.<sup>14</sup> Recent studies of the mechanism of the oxidation of methionine with  $\text{I}_2$ <sup>15</sup> and of the reduction of dehydromethionine by thiols<sup>16</sup> have shown that a cation with an  $\text{N}-\text{S}$  bond is a possible intermediate in these reactions. Whether this intermediate is a dication or a monocation depends on the timing of proton loss from the amine.

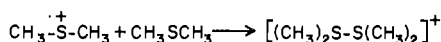
Although aliphatic thioether dication formation had been described, the first report of cation radical formation was in 1967 when Cottrell and Mann published an electrochemical study of thioether oxidation in  $\text{CH}_3\text{CN}$ .<sup>17</sup> They suggested that a cation radical was initially formed upon oxidation of dimethyl sulfide at an electrode surface. However, the cation radical was unstable because of proton loss from the  $\alpha$  carbon, and further oxidation gave an alkylidinesulfonium salt. This salt then reacted with dimethyl sulfide to give a sulfonium salt,  $[\text{CH}_3\text{SCH}_2\text{S}(\text{CH}_3)_2]^+$ .

(4) Bard, A. J.; Shine, H. J. *Adv. Phys. Org. Chem.* 1976, 13.  
 (5) DeSongo, M.; Wasserman, B.; Szwarc, M. *J. Phys. Chem.* 1972, 76, 3468.  
 (6) Wilson, G.; Swanson, D.; Klug, J.; Glass, R.; Ryan, M.; Musker, W. K. *J. Am. Chem. Soc.*, 1979, 101, 1040.  
 (7) Meerwein, H.; Zenner, K. F.; Gipp, R. *Justus Liebigs Ann. Chem.* 1965, 688, 67.  
 (8) Asmus, K.-D. *Acc. Chem. Res.* 1979, 12, 436.  
 (9) Autenrieth, W.; Bruning, A. *Chem. Ber.* 1903, 36, 183.  
 (10) Breslow, D. S.; Skolnick, H. "The Chemistry of Heterocyclic Compounds"; Interscience: New York, 1966; Vol. 21.

(11) Yethon, A., Ph.D. Thesis, University of Illinois, 1963.  
 (12) Ruffato, V.; Miotti, U. *J. Gazz. Chim. Ital.* 1978, 108, 91.  
 (13) Lavine, T. *J. Biol. Chem.* 1943, 151, 281.  
 (14) Glass, R.; Duchek, J. *J. Am. Chem. Soc.* 1976, 98, 965.  
 (15) Young, P. R.; Hsieh, L.-S. *J. Am. Chem. Soc.* 1978, 100, 7121.  
 (16) Lambeth, D. *J. Am. Chem. Soc.* 1978, 100, 4808.  
 (17) Cottrell, P. T.; Mann, C. K. *J. Electrochem. Soc.* 1969, 116, 1499.



In 1967, Meissner and co-workers<sup>18</sup> and Yang and co-workers<sup>19</sup> independently proposed the formation of thioether cation radicals. Meissner, using pulse radiolysis techniques, showed that the reaction of hydroxyl radicals with dimethyl sulfide in water gives a dimeric cation radical  $(\text{CH}_3\text{SCH}_3)_2^+$ .<sup>18</sup> Under these conditions, no dications were observed.



To account for the production of ethylene from methionine and related compounds in the presence of flavin mononucleotide and light, Yang, Ku, and Pratt proposed an initial oxidation of the thioether group to a cation radical.<sup>19</sup> In a series of subsequent papers<sup>20</sup> on ethylene production, sulfoxide formation, and deamination of various sulfur-containing amino acids under a variety of oxidizing conditions, Yang and co-workers offered convincing evidence that the thioether group played an important role in the oxidation reaction. A thioether cation radical was also invoked by Beauchamp and Fridovich to account for the formation of ethylene when methional was oxidized by hydroxyl radicals.<sup>21</sup>

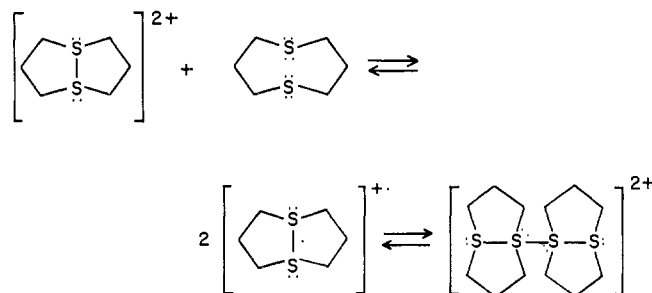
The first ESR spectra of thioether cation radicals were reported by Norman and co-workers in 1973.<sup>22</sup> Their observation of a 13-line spectrum on oxidation of dimethyl sulfide with hydroxyl radicals was consistent with the previous observation by Meissner and co-workers<sup>18</sup> that monomeric thioether cation radicals are extremely reactive and interact immediately with an unoxidized thioether to give a dimeric cation radical. This reaction of the cationic sulfur with a nucleophile seems to be an important way of stabilizing a thioether cation radical.<sup>8,18</sup>

### Oxidation of 1,5-Dithiacyclooctane (1,5-DTCO)

We were originally interested in examining an eight-membered ring dithioether simply as a chelating agent since we had carried out extensive studies of the coordination chemistry of the eight-membered ring diamine, 1,5-diazacyclooctane.<sup>23</sup> In the course of this investigation we observed rapid reduction of Cu(II) to Cu(I) when  $\text{Cu}(\text{ClO}_4)_2$  was mixed with 1,5-DTCO in  $\text{CH}_3\text{OH}$ . This behavior was in marked contrast to simple monothioethers such as tetrahydrothiophene and dithioethers such as 1,4-dithiane (1,4-DT) where no reduction was observed under similar conditions.<sup>1,24</sup>

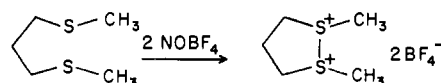
Subsequent experiments using  $\text{NOBF}_4$  as the oxidizing agent in  $\text{CH}_3\text{CN}$  led to the characterization of the yellow 1,5-DTCO cation radical and colorless dication.<sup>1</sup> Since that time we have found that most thioethers can be oxidized by  $\text{NOBF}_4$ , but only the eight- and nine-membered ring dithioethers give long-lived

cation radicals. However, the cation radical undergoes facile oxidation by  $\text{NOBF}_4$  to give a dication having an  $\text{S}^+-\text{S}^+$  bond.<sup>25</sup> It was therefore thought that 1,5-DTCO, its cation radical, and its dication were all in equilibrium in acetonitrile. This suggestion was confirmed by treatment of the 1,5-DTCO dication with 1,5-DTCO itself to give the 1,5-DTCO cation radical which was observed by ESR. However, at least one additional species is present in solution. When 1,5-DTCO was treated with 1 equiv of  $\text{NOPF}_6$  in  $\text{CH}_3\text{CH}_2\text{CN}$ , a red precipitate formed. The precipitate had the correct elemental analysis for the cation radical, (1,5-DTCO)- $\text{PF}_6$ , but it was diamagnetic, suggesting that the cation radical had dimerized to give a compound with an S-S bond, i.e., (1,5-DTCO)<sub>2</sub>( $\text{PF}_6$ )<sub>2</sub>. Indeed, dissolution of



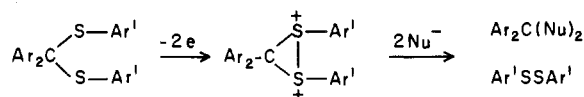
the red precipitate in  $\text{CH}_3\text{CN}$  gave a yellow solution which exhibited an ESR signal identical with that of the cation radical.<sup>1</sup> This dimer of the cation radical was also observed during an electrochemical study of the oxidation of 1,5-DTCO in  $\text{CH}_3\text{CN}$ .<sup>6</sup>

Although no radicals were observed when other dithioethers were treated with 1 equiv of  $\text{NOBF}_4$  or  $\text{NOPF}_6$ , treatment with 2 equiv of  $\text{NOBF}_4$  resulted in the formation of dications of cyclic dithioethers having 6- to 10-membered rings and acyclic dithioethers in which the two sulfur atoms were separated by two, three, or four methylene groups.<sup>1</sup> In 2,6-dithiaheptane and 2,7-dithiaoctane stable solid dications were isolated.



These solid dications readily react with water to give monosulfoxides.<sup>26</sup> This reaction to give monosulfoxides was then used as a confirmatory test for the presence of dications in solution when solid dications could not be isolated and purified.

Although we have not studied the oxidation of dithioethers where the two sulfur atoms are separated by only one methylene group (thioacetals and thioketals), Simonet and co-workers proposed an  $\text{S}^+-\text{S}^+$  bonded dicationic intermediate on anodic oxidation of aromatic thioketals to give disulfides.<sup>27</sup> When no methylene



groups separate the two sulfur atoms (a disulfide), cation radicals can also be observed by pulse radiolysis techniques.<sup>28</sup>

(18) G. Meissner, G.; Henglein, A.; Beck, G. *Z. Naturforsch.* **1967**, *22b*, 13.

(19) Yang, S. F.; Ku, H. S.; Pratt, H. K. *J. Biol. Chem.* **1967**, *242*, 5274.

(20) Bowen, J. R.; Yang, S. F. *Photochem. Photobiol.* **1975**, *21*, 201.

(21) Beauchamp, C.; Fridovich, I. *J. Biol. Chem.* **1970**, *245*, 4611.

(22) Gilbert, B. C.; Hodgeman, D. K. C.; Norman, R. O. C. *J. Chem. Soc., Perkin Trans. 2* **1973**, 1748.

(23) Musker, W. K.; Hussain, M. S. *Inorg. Chem.* **1969**, *8*, 528.

(24) Siemak, J.; Murphey, M., unpublished work.

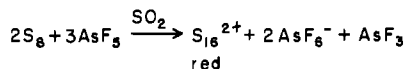
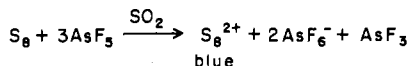
(25) Musker, W. K.; Roush, P. B. *J. Am. Chem. Soc.*, **1976**, *98*, 6745.

(26) Roush, P. B.; Musker, W. K. *J. Org. Chem.* **1978**, *43*, 4295.

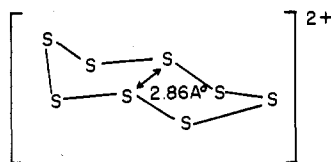
(27) Gourcy, J. G.; Jeminet, G. J.; Simonet, J. *J. Chem. Soc., Chem. Commun.* **1974**, 634.

(28) Bonifacic, M.; Schafer, K.; Mockel, H.; Asmus, K.-D. *J. Phys. Chem.*, **1975**, *79*, 1496.

To be complete, the parent compound of this series should be included—elemental sulfur,  $S_8$ . Gillespie and co-workers oxidized  $S_8$  to  $S_8^{2+}$  and  $S_{16}^{2+}$  with  $AsF_5$  in liquid  $SO_2$ .<sup>29</sup> Later they showed that the structure of

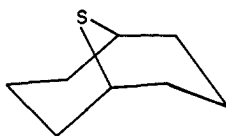


$S_8^{2+}$  consisted of a cis-fused bicyclic [3.3.0] ring system.<sup>30</sup> The  $S_{16}^{2+}$  ion, the dimer of the  $S_8^+$  cation radical, may be analogous to the dimer of the 1,5-DTCO cation radical.



### Monothioethers

Norman had previously studied the oxidation of tetrahydrothiophene (THT) by hydroxyl radicals and observed an ESR spectrum of  $(THT)_2^+$ .<sup>22</sup> However, compounds of this nature would be expected to decompose rapidly by losing a proton from the  $\alpha$  carbon as proposed by Cottrell and Mann. Therefore, when tetrahydrothiophene was treated with  $NOBF_4$ , NO gas was evolved but no pure organic products could be isolated. A monothioether in which this tendency was reduced was examined to minimize facile decomposition by proton loss. Nelsen previously showed that the hydrazine cation radical from 9,9'-bis(9-azabicyclo[3.3.1]nonane) was stable.<sup>31</sup> The reason for the stability of this molecule is due to the fact that proton loss from the bridgehead position would lead to an unstable intermediate. Following this example, we prepared the corresponding thioether, 9-thiabicyclo[3.3.1]nonane.

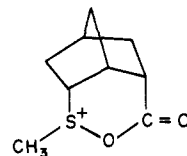


Oxidation with 1 equiv of  $NOBF_4$  produced the correct amount of NO, but a satisfactory analysis of the dimer of the cation radical could not be obtained.<sup>32</sup> Apparently alternative decomposition modes still prevent the isolation of simple oxidation products of monothioethers under these conditions.

### Oxidative Coupling to Proximate Electron Pair Donors

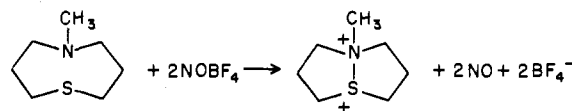
Although Yang and co-workers postulated that a thioether cation radical formed upon one-electron oxidation of methionine, they did not propose an intermediate containing an  $S^+-O^-$  bond.<sup>19</sup> Later, Glass and co-workers reported that an intermediate with an  $S^+-O^-$  bond was probably formed in the two-electron

oxidation of 2,6-di-endo-norbornyl derivatives where thiomethyl and carboxylate moieties are in proximity.<sup>33</sup>

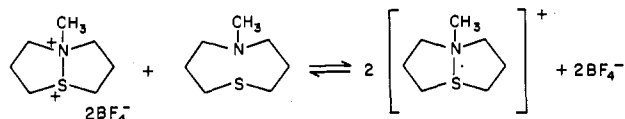


Likewise Allenmark proposed an  $S^+-O^-$  intermediate in the reduction of a sulfoxide with HI in the presence of a neighboring carboxylate.<sup>34</sup>

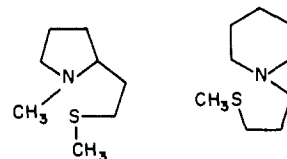
Since we had established that a proximate thioether group interacts strongly with an oxidized thioether group in mesocyclic compounds, we felt that mesocycles having a thioether group transannular to other groups with lone-pair electrons might undergo an oxidative coupling reaction to give stable cations. The eight-membered ring amino thioether, 5-methyl-1-thia-5-azacyclooctane (TACO), was prepared<sup>2</sup> to test this possibility. No radical was observed on oxidation with 1 equiv of  $NOPF_6$ , but a solid dication having an  $N^+-S^+$  bond was isolated when 2 equiv of  $NOBF_4$  was used.



Then, by analogy to 1,5-DTCO, equimolar amounts of the dication were combined with the starting amino thioether to dry acetonitrile.<sup>2</sup> The resulting solution exhibited an ESR signal due to a cation radical having the spin localized on sulfur. However, the signal per-



sisted for only a short time, indicating that the  $S-N$  cation radical is much less stable than the  $S-S$  cation radical. Additional evidence of  $N-S$  bond formation was obtained in a few acyclic amino thioethers where the two heteroatoms were separated by three methylene groups.<sup>32</sup>



### S-S Dication Formation during Sulfoxide Reduction

Because of the facile oxidation of 1,5-DTCO to the dication and hydrolysis to the sulfoxide, we thought that the reverse process—reduction of the sulfoxide to the thioether by aqueous HI—might proceed via the dication.

Indeed, when 1,5-DTCO monosulfoxide was treated with HI, the rate of reduction was  $10^6$  times faster than that of  $Me_2SO$  under similar conditions and the rate law was second order in acid, but independent of iodide.<sup>35</sup> The rate of reduction of a related but acyclic dithio-

(29) Gillespie, R. J.; Passmore, J.; Ummat, P. K.; Vaidya, O. C. *Inorg. Chem.*, 1971, 10, 1327.

(30) Davies, C. G.; Gillespie, R. J.; Park, J. J.; Passmore, J. *Inorg. Chem.*, 1971, 10, 2781.

(31) Nelsen, S. F.; Kelles, C. R. *J. Am. Chem. Soc.*, 1977, 99, 2392.

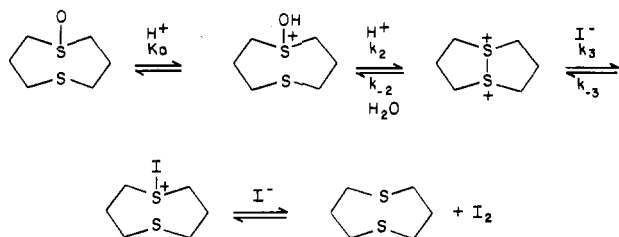
(32) Hirschon, A. S.; Ph.D. Thesis, University of California, Davis, 1979.

(33) Glass, R.; Duchek, J.; Klug, J.; Wilson, G. *J. Am. Chem. Soc.*, 1977, 99, 7349.

(34) Allenmark, S. *Acta Chem. Scand.* 1961, 15, 928; 1965, 19, 1.

(35) Doi, J. T.; Musker, W. K. *J. Am. Chem. Soc.* 1978, 100, 3533.

ether, 2,6-dithiaheptane 2-oxide (2,6-DTHP monosulfoxide), was also independent of iodide, but the rate was also only about 200 times that of  $\text{Me}_2\text{SO}$ . The lower rate for the acyclic compound probably reflects the flexibility of the chain which prevents rapid formation of an S-S bond. Nevertheless, the rate law suggests that an S-S bonded cationic intermediate is formed in both cases. In a molecule where a four-



membered ring intermediate containing an S-S bond would be required (2,5-dithiahexane 2-oxide), the rate is no longer accelerated and the rate law is no longer iodide independent—the reduction is similar to that of a simple sulfoxide.<sup>35</sup>

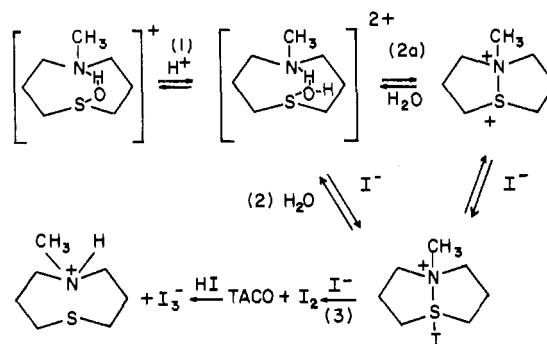
The mechanism of a related reaction involving the acid-catalyzed cleavage of the monosulfoxides of thioacetals and thioketals has not been reported.<sup>36</sup> However, since the products of this reaction are the carbonyl compound and a disulfide, it appears that a dicationic intermediate could form during the reaction.

### S-N Bond Formation during Sulfoxide Reductions

The observation that heteroatoms other than sulfur participate in the oxidation of thioethers prompted an investigation of the mechanism of the iodide reduction of 5-methyl-1-thia-5-azacyclooctane 1-oxide.<sup>2</sup> The structure of the perchlorate salt of this sulfoxide had been determined and showed that a hydrogen bond bridged the amine nitrogen and the sulfoxide oxygen.<sup>37,38</sup> The rates of reduction of 1,5-DTCO monosulfoxide and 5-methyl-1-thia-5-azacyclooctane 1-oxide are similar at 0.1 M  $\text{H}^+$  and 0.3 M  $\text{I}^-$ , but the rate laws are different. The rate of reduction of the amine sulfoxide is first order in acid and second order in iodide—a most unusual situation. That the reaction is first order in acid can be explained by recalling that the starting material is already hydrogen bonded.<sup>38</sup>

The second-order dependence on iodide is more difficult to explain. In a study of the mechanism of the oxidation of methionine by  $\text{I}_2$ , Young and Hsieh proposed that a sulfurane intermediate with an S-N bond was required to account for the kinetic behavior.<sup>15</sup> We also considered invoking a sulfurane intermediate in the reduction of 5-methyl-1-thia-5-azacyclooctane 1-oxide with HI although it was not demanded by the kinetics. However, we believe that the difference in the stability of  $\text{N}^+-\text{S}-\text{I}$  and  $\text{S}^+-\text{S}-\text{I}$  sulfuranes could be the reason why the rate laws for the reduction of 5-methyl-1-thia-5-azacyclooctane 1-oxide and 1,5-dithiacyclooctane 1-oxide have different dependence on iodide.

Although definitive proof of a dicationic intermediate cannot be obtained from the kinetic data, dication formation would provide an extremely facile path to an



iodosulfonium salt. In contrast, the acyclic analogue and the six- and seven-membered ring homologues have rates and rate laws similar to simple sulfoxides.<sup>39</sup>

### Electrochemical Studies of Thioether Oxidations

In cooperation with George Wilson at the University of Arizona, a cyclic voltammetric study of the oxidation of a series of thioethers was undertaken.<sup>6</sup> Simple thioethers normally exhibit a peak potential of about 1.2 to 1.3 V (Ag/0.1 M  $\text{AgNO}_3$  in  $\text{CH}_3\text{CN}$ ) but Glass, Duchek, Klug, and Wilson reported that the peak potential is lowered appreciably when neighboring groups containing lone pairs can interact with the thioether sulfur.<sup>33</sup> For example, a series of 6-exo and 6-endo isomers of *endo*-2-(thiomethyl)norbornanes were examined, and the two isomers differed significantly in their ease of oxidation. In the hydroxymethyl derivatives, the 6-endo isomer exhibited a peak potential of 0.56 V whereas the 6-exo isomer was 1.20 V. This was a general phenomenon since the corresponding isomeric thioether carboxylates discussed earlier exhibited similar electrochemical behavior.<sup>33</sup>

Unfortunately none of the substituted norbornanes exhibited reversible redox behavior, so thermodynamic data could not be obtained. However, when the mesocyclic dithioethers (1,5-DTCO, 1,5-dithiocyclononane, 1,6-dithiocyclodecane, and 7,8-dibenzo-1,5-dithiocyclononane) were examined, they all showed extremely low peak potentials (1,5-DTCO = 0.34 V) and, remarkably, all were reversible. Because of this reversibility, 1,5-DTCO was examined in detail.<sup>6</sup> Electrochemically, 1,5-DTCO behaves like 2,6-di-*tert*-butyl-4-ethylphenoxide.<sup>40</sup> At fast scan rates dimer formation is noted, but as the scan rate decreases, the dimer dissociates and a reduction peak due to the monomeric cation radical is observed. Thus, the electrochemical study is consistent with the chemical data obtained by  $\text{NOPF}_6$  oxidation in  $\text{CH}_3\text{CH}_2\text{CN}$  where a diamagnetic dimer was obtained. The data unexpectedly show that oxidation of the cation radicals to the dications proceeds more easily than that of the parent dithioethers.

Acyclic dithioethers with from two to four methylene groups between the two sulfur atoms are also oxidized at lower peak potential than simple thioethers, but they exhibit irreversible behavior. The amino thioether, 5-methyl-1-aza-5-thiacyclooctane, exhibits a peak potential for oxidation which is lower (0.23 V) than any thioether or tertiary amine, but again the process is irreversible. Since tertiary amines are normally oxidized at lower peak potentials ( $\sim 0.7$  V) than monothio-

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ethers,<sup>41</sup> it may be argued that the transannular thioether group facilitates amine oxidation. A number of other derivatives have also been examined, but the trend is the same—neighboring groups facilitate the oxidation of heteroatoms, and of these the transannular thioether group appears to be the most efficient.

### Some Physical Properties of Dithioethers and Their Ions

The photoelectron spectra (PES) of several dithioethers have been reported. Two maxima at rather low energy are observed in the spectrum of 1,3-dithiane,<sup>42,43</sup> 1,4-dithiane,<sup>42,43</sup> and 1,5-DTCO.<sup>44</sup> This result suggests that the lone pairs on the two thioether groups in all these molecules interact in the ground state.<sup>42,43,45</sup> In 1,3-dithiane both through-bond and through-space interactions can occur, although the through-space interaction probably predominates.<sup>43</sup> In 1,4-dithiane, through-bond coupling predominates in the chair form whereas through-space coupling dominates in the boat form.<sup>43</sup> In 1,5-DTCO no through-bond interaction can occur, and therefore a through-space transannular interaction must be responsible for the two peaks in the spectrum.<sup>44</sup> Because of this ground-state interaction, it may be incorrect to state that, upon oxidation, a neighboring thioether group interacts with the oxidized thioether group in these cases. A better explanation may be to assume that the oxidizing agent simply removes an electron from the HOMO of the dithioether and the electronic absorption spectra of the cation radical arises from electron transfer from the bonding to the antibonding combination of the interacted lone-pair orbitals. An interpretation of the spectrum of DABCO (triethylenediamine) in these terms has been reported.<sup>46</sup> Subsequent removal of the remaining electron in the antibonding orbital of the cation radical (in which the separation between the  $\sigma$  and  $\sigma^*$  orbitals is greater) gives the dication. This interpretation is consistent with the electrochemical study of the oxidation of mesocyclic dithioethers which showed that the second oxidation occurs more readily than the first.<sup>6</sup>

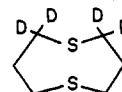
When dithioethers which have three or four methylene groups separating the two sulfur atoms are analyzed by mass spectroscopy, an intense signal due to a fragment with an S-S bond is observed.<sup>47</sup> For example, 1,5-dithiacyclononane gives rather intense peaks at  $m/e$  120 and 106 due to 1,2-dithiane and 1,2-dithiolane cation radicals, respectively. 1,2-Dithiolane cation radical formation is so favored in the fragmentation of 1,5-DTCO that it is the base peak. In acyclic dithioethers a terminal methyl group is often lost when S-S bond formation leads to five- and six-membered rings.

The ESR spectrum of the 1,5-DTCO cation radical in  $\text{CH}_3\text{CN}$  exhibited a triplet of triplets with coupling constants of 10.4 and 15.2 G. We initially suggested that the electron was located in an orbital on only one sulfur and was split by the two sets of two nonequivalent hydrogens on the  $\alpha$  carbons.<sup>48</sup> However, an al-

ternative interpretation of the data would be consistent with the free electron occupying a  $\sigma^*$  orbital located on both sulfurs if the coupling to four of the eight  $\alpha$  hydrogens was extremely small.<sup>1</sup>

The ESR spectrum of 1,5-DTCO dissolved in concentrated sulfuric acid is different. It is a symmetrical spectrum consisting of five lines with a coupling constant of 10 G. Thus, in this solvent, four of the eight hydrogens appear equivalent.<sup>32</sup>

Recently we prepared 2,2,8,8-tetradeuterio-1,5-dithiacyclooctane by hydrogen-deuterium exchange of 1,5-DTCO monosulfoxide and subsequent reduction to the dithioether. When the tetradeuterated compound

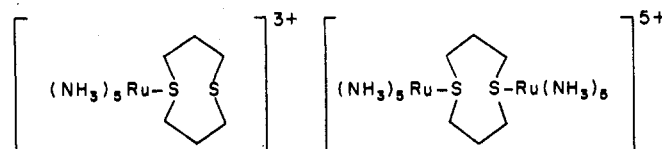


was dissolved in sulfuric acid, only a symmetrical triplet was observed, suggesting that the free electron must be interacting with only one of the two hydrogen atoms on each of the carbons adjacent to sulfur.<sup>32</sup> The spectrum obtained by oxidation of the tetradeuterated compound with  $\text{NOBF}_4$  is also a triplet, but it does not correspond to a simple triplet.

It is not clear why different spectra are observed under different conditions, but a possible explanation may involve the presence of the dimer of the cation radical and the counterion in  $\text{CH}_3\text{CN}$ . In the dimer the two sulfur atoms in each 1,5-DTCO molecule are nonequivalent. If the sulfur atoms remain nonequivalent during the homolytic cleavage of the S-S bond due to asymmetric solvation or ion pairing, the electron would couple to the  $\alpha$  hydrogens differently. If dimers are not formed in sulfuric acid and the cation radical is symmetric, a symmetric spectrum would be observed.

### Metal Ion Induced Sulfur-Sulfur Interaction

In 1978, Stein and Taube showed that a monodentate 1,5-DTCO complex of pentaammineruthenium(III) exhibited two absorption maxima in the visible spectrum and that a bridging 1,5-DTCO molecule permitted extremely facile electron transfer between two ruthenium atoms of different oxidation states.<sup>49</sup> The mononuclear ruthenium(II) complex  $[(\text{NH}_3)_5\text{Ru}(1,5\text{-DTCO})]^{2+}$  can be oxidized successively to  $[(\text{NH}_3)_5\text{Ru}(1,5\text{-DTCO})]^{3+}$  and  $[(\text{NH}_3)_5\text{Ru}(1,5\text{-DTCO})]^{4+}$ . The ruthenium(II) complex exhibits two (LMCT) absorption bands in the visible spectrum which can be attributed to a splitting of the sulfur lone pairs in the ligand and subsequent transfer of  $\sigma$  and  $\sigma^*$  electrons to the metal.<sup>44</sup> The ruthenium(IV) complex actually corresponds to a complex between ruthenium(III) and the 1,5-DTCO cation radical rather than to a complex between ruthenium(II) and the dication.<sup>44</sup>



Of the binuclear bridged dications  $[(\text{NH}_3)_5\text{Ru}(1,5\text{-DTCO})\text{Ru}(\text{NH}_3)_5]^{n+}$  ( $n = 4-6$ ), the +5 mixed-valence complex exhibits an intervalence transition (IT band) at 1210 nm ( $\epsilon = 75 \pm 5$ ). The intensity of this absorp-

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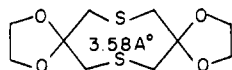
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tion suggests that electron transfer between ruthenium atoms occurs essentially adiabatically. The monomeric 1,4-dithiane complexes of ruthenium(III) show only one band in the visible absorption spectrum rather than two bands, and in the bridged dimer the intensity of the IT band at 962 is only 6.<sup>44</sup>

The binuclear ruthenium complex of the bis(ethylene ketal) of 1,5-dithiacyclooctane-3,7-dione also exhibits a low-energy IT band (1168 nm), but it is not as intense as it is in the 1,5-DTCO complex ( $\epsilon$  46).<sup>44</sup> It appears that 1,5-DTCO is the most effective of all the dithioethers in facilitating electron-transfer processes.

A crystal structure of the uncomplexed diketal was recently completed. The molecule is the chair-boat form with a cross-ring sulfur-sulfur distance of 3.58 Å.<sup>50</sup>



Although the crystal structure of the binuclear ruthenium complex has not been determined, the structure of a nickel complex of 1,5-DTCO, where 1,5-DTCO bridges two nickel atoms, was determined by Hill and Hope.<sup>51</sup> In this case the cross-ring sulfur-sulfur distance is 3.33 Å. We also determined the structure of 1,5-DTCO·2I<sub>2</sub> and found an S-S distance of 3.44 Å.<sup>52</sup> From this crystallographic evidence, the electron transfer in the binuclear mixed-valence ruthenium complex may take place through space over a distance of 3.3 to 3.6 Å. This is at the frontier of the van der Waals radii of the sulfur (~3.7 Å).

## Conclusion

From the data that have now been accumulated it is clear that the chemistry of the thioether group is strongly influenced by neighboring atoms. This influence is seen by the facilitation of its oxidation and its involvement in the formation of long-lived cation radical

and dications. In biochemical systems this property of a thioether group may be utilized to provide (1) a low-energy path for electron transfer between oxidant and reductant, (2) a place within a molecule where oxidizing power can be stored and recovered, (3) a place for oxidative coupling in aprotic regions, (4) a source of highly polarizable electrons which can mediate electronic environments over long distances. Likewise, the presence of a sulfoxide group can lead to dication formation in the presence of suitable lone-pair donors.

This discussion has been limited to compounds having no more than two thioether sulfurs. However, preliminary evidence suggests that multisulfur systems give cation radicals which have even longer lifetimes than the compounds described here. For example, the bis(trimethylene dithioether) of 2,4-pentanedione gives a radical that is stable indefinitely.<sup>53</sup>

**Note Added in Proof.** Since the time that this manuscript was submitted for publication we found additional evidence of thioether cation formation by neighboring group participation in thioether oxidations. Hydroxyl group participation has been confirmed with the isolation and crystal structure determination of 9-oxa-1-thioniabicyclo[3.3.1]nonane triiodide. This sulfoxonium salt forms on oxidation of 5-hydroxy-1-thiacyclooctane with aqueous I<sub>2</sub>. We have also completed a study of the kinetics of the oxidation of both 1,5-DTCO and TACO with aqueous I<sub>2</sub> and found that rapid and reversible thioether-sulfoxide interconversions can be accomplished by a slight variation in pH.

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