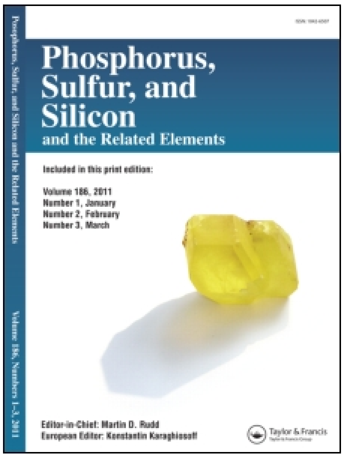

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Electron Transfer from Thioethers

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ELECTRON TRANSFER FROM THIOETHERS

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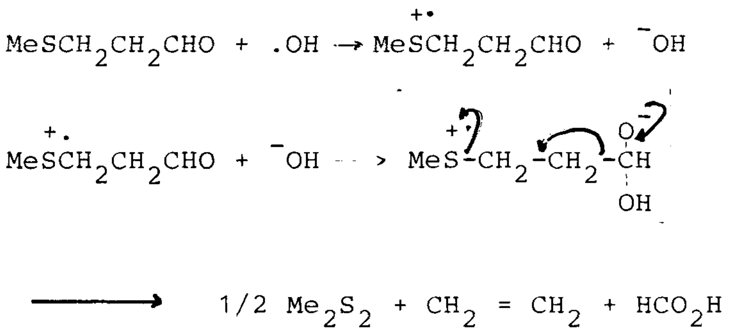
Abstract Oxidation of thioethers is greatly facilitated by neighboring group participation by carboxylate, alcohol, and thioether moieties.

INTRODUCTION

Electron transfer from thioethers to generate sulfur cation radicals as indicated below may be important in biological redox reactions. There are preliminary indi-

$$R_2S \longrightarrow R_2S^{\dot{+}} + e^-$$

cations that this might be the case as illustrated by the following examples. Oxidation of cytochrome c peroxidase with hydrogen peroxide produces enzymatically active compound ES[1] which is two oxidation equivalents above the iron(III)cytochrome. One electron is removed from the iron atom to yield iron(IV) and the other electron comes from the protein portion of the molecule. On the basis of spectroscopic studies (EPR and UV/VIS) it has recently been suggested [2] that an electron is removed from the sulfur atom of a methionine residue to produce a sulfur cation radical which is stabilized by interaction with a neighboring group. Oxidation of p-substituted thioanisole derivatives in a reconstituted enzymic system containing cytochrome P-45o, NADPH, and oxygen afforded the corresponding sulfoxides [3]. Linear correlation between log V_{max} for this enzymic reaction and the anodic peak potential for these compounds and the Hammett substituent constant σ^+ was reported. These results were interpreted in terms of rate-determining one-electron transfer from the substituted thioanisole generating a sulfur cation radical to the so-called oxene intermediate derived from cytochrome P-45o [3,4].



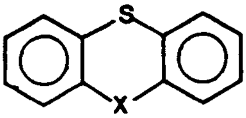
$$\mathrm{MeSCH_2CH_2CHO} + .\mathrm{OH} \rightarrow \mathrm{Me\overset{+\bullet}{S}CH_2CH_2CHO} + {}^{-}\mathrm{OH}$$

$$\mathrm{Me\overset{+\cdot}{S}CH_2CH_2CHO} + {}^{-}\mathrm{OH} \dashrightarrow \mathrm{Me\overset{+\cdot}{S}-CH_2-CH_2-\underset{OH}{\overset{O^{-}}{C}}H}$$

$$\longrightarrow 1/2\ \mathrm{Me_2S_2} + \mathrm{CH_2=CH_2} + \mathrm{HCO_2H}$$

A third example involves methional, 3-methylthiopropanal, which has been widely used in systems of biological interest as a specific probe for hydroxyl radicals[5]. These radicals react with methional to produce ethylene whose evolution is monitored. The mechanism suggested for this reaction is shown below [5a,6]. A key intermediate in this reaction is the sulfur cation radical derived from methional. However, the specificity of this test for hydroxyl radicals and the mechanism by which methional forms ethylene has been questioned [7]. Pulse radiolysis studies [8] showed that hydroxyl radicals rapidly reacted with methional but the reaction is complex. Finally and more speculatively, a structural feature was discerned in proteins in which aromatic amino acid residue and sulfur amino acid residues were in close contact and alternate with one another forming so-called S-π chains [9]. Since many of the proteins which had this structural feature were redox proteins it was suggested that such S-π chains may act as a conduit for electrons.

There have been extensive and elegant studies on electron transfer from heteroaromatic thioethers, such as thianthrene 1, X=S, and on the chemistry of the corresponding cation radicals [10]. Electron-transfer from drugs containing such moieties, e.g. tranquilizers containing the phenothiazine nucleus 1, X = NH, may be important in their biological activities [11]. However, whether electron-transfer from thioethers is of more general biological importance depends in large part on the ease of oxidation of aliphatic thioethers, such as in the side-chain of methionine, because these are the sulfur-containing moieties which are ubiquitous in redox proteins. Dialkyl thioethers, such as dimethyl sulfide, are easy to oxidize to the corresponding sulfoxides by atom transfer. However, literal electron transfer is sufficiently difficult as measured by electrochemical methods [12] to render such reactions unlikely with most biological oxidants. One-electron transfer may occur with or without atom transfer [13]. Alternative pathways for electron transfer may involve only a transition state between redox partners and no intermediate. Long-range electron-transfer is of considerable interest in biological systems and has been studied in rigid chemical systems as well [14]. Therefore, our studies have aimed at discerning those factors, likely or known to be present in biolo-



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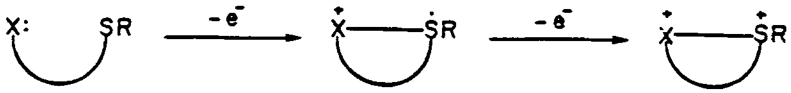
gical systems, which might result in facilitated electron transfer from dialkyl thioethers. One such factor is neighboring group participation by moieties present in proteins. This paper presents evidence for such participation in oxidation of thioethers and some of its consequences.

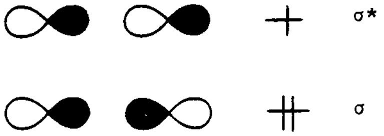
According to Capon and McManus [15],".... when a substituent stabilizes a transition state or intermediate by becoming bonded to the reaction center, this effect is called neighboring group participation". This effect is the same as that described as intramolecular catalysis. The concept of neighboring group participation developed from studies on nucleophilic substitution at carbon [15]. This paper intends to extend this idea to reactions involving electron transfer from dialkyl thioethers. Thus one-electron oxidation of thioether 2 with neighboring group participation by X gives cation radical 3. This reaction is envisioned to occur by removal of a nonbonding electron from sulfur and participation



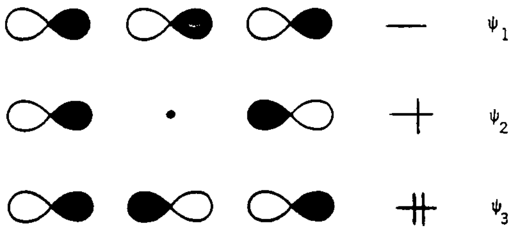
2 3

by two non-bonding electrons on X. This participation may occur concomitantly with electron transfer from the sulfur atom or subsequently.

Three reasonable bonding schemes for cation radical 3, which may be classified as a 9-S-3 species [16],follow. The odd electron may be localized on the sulfur atom. This results in nine electrons in the valence shell of the sulfur atom and requires the use of a d-orbital by the sulfur atom. Another bonding possibility described as a two-center three-electron bond is shown in Scheme 1 [17]. A p-orbital on X and on the sulfur atom are used to form σ and σ^* molecular orbitals. Two spin-paired electrons are accommodated in the σ-molecular orbital and the third electron in the antibonding molecular orbital. An alternative to this two-center three-electron bond is a three-center three-electron bond shown in Scheme 2 [16]. Musher [16] has suggested such bonding for hypervalent molecules. Combination of the S-X and R-S σ bonds with R,S and X colinear gives three molecular orbitals as shown. Two spin-paired electrons are accommodated in Ψ_1 and the third electron is accommodated in the nonbonding Ψ_2 orbital



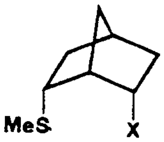
Scheme 1



Scheme 2

RESULTS AND DISCUSSION

To experimentally test whether there would be neighboring group participation on oxidation of aliphatic thioethers, particularly oxidation involving stepwise electron transfer, 2-endo-substituted, 6-endo-methylthiobicyclo[2.2.1]heptyl derivatives 4 were studied [19]. The molecular architecture of these relatively rigid systems enhances the possibility of neighboring group participation by positioning the sulfur atom and potential neighboring groups close to one another. A further advantage to studying such systems is that control compounds are readily at hand. That is, analogs of 4 where either the substituent is exo, i.e., 5, or the methylthio group, i.e., 6 or both, i.e. 7, have geometries which preclude bonding between X and S but inductive effects (albeit not field effects) would be the same throughout the series. A number of derivatives 4-7 have been prepared and studied by cyclic voltammetry [19]. The anodic peak potentials for oxidation of each of the thioethers in anhydrous acetonitrile under constant conditions are recorded in Table 1. Under comparable conditions, simple dialkyl thioethers show peak potentials considerably more positive than 1.oV and usually in the range of



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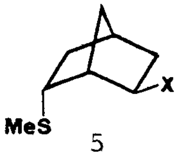

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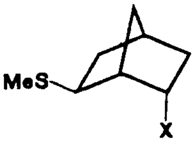

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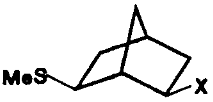

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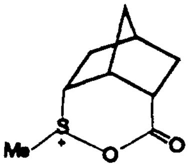
1.4 - 1.7V [12]. All of the oxidations are electrochemically irreversible. Inspection of the Table I reveals that endo-acid salt 4, X = CO_2^- and endo-alcohol 4, X = CH_2OH undergo oxidation at peak potentials over 5oo mV less positive than the corresponding exo compounds, 5, X = CO_2^- and 5, X = CH_2OH. Methods were sought to determine if these greatly facilitated oxidations were accompanied by bond formation between the substituent group and the sulfur atom. Toward this end both acyloxysulfonium salt 8 and alkoxysulfonium salt 9 were prepared by chemical oxidation of 4, X = CO_2^- and 4, X = CH_2OH, to characterize them and elucidate their properties.



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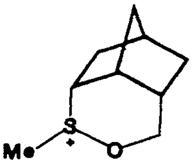

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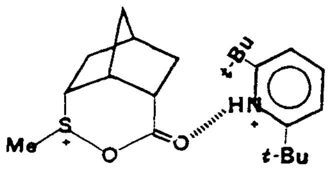
Acyloxysulfonium salt 8 can be prepared by bromine oxidation of the 18-crown-6 complex of the potassium salt of 4, X = CO_2^- at low temperature in acetonitrile solution. This oxidation product undergoes decomposition rapidly when warmed to 0^o or above in solution. Nevertheless, it could be characterized spectroscopically in solution at low temperature. Its carbonyl stretching frequency occurred at 1828 cm^{-1}. The absorption due to methyl protons in 8 overlapped with the large absorption due to the protons in 18-crown-6. To avoid this overlap, the 2,6-di-t-butylpyridinium salt of 4, X = CO_2^- was used in the oxidation. The ^1H NMR spectrum of this product showed absorption due to the methyl protons at δ 3.1 ppm. However, the infrared spectrum of this material showed the carbonyl stretching frequency at 1714 cm^{-1} rather than at 1828 cm^{-1}. This difference is apparently due to hydrogen bonding between the carbonyl oxygen of 8 and the 2,6-di-t-butyl pyridinium ion as shown in 10. The spectroscopic parameters measured for 8 are in agreement with those expected based on literature values for similar species [20]. Furthermore, hydrolysis of acyloxysulfonium salt 8 afforded sulfoxide acid 11, R=H, in good yield.



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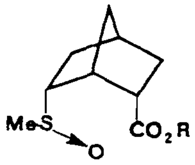

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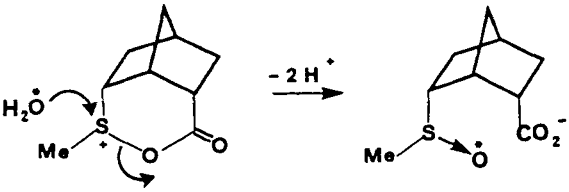
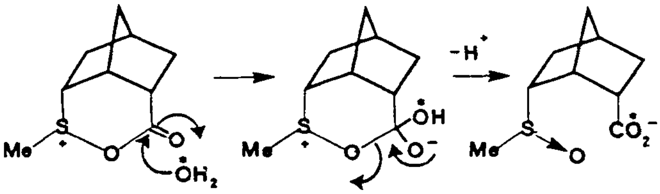
Clearly controlled potential electrolysis of 4, X = CO_2^- at room temperature would not result in a solution of acyloxysulfonium salt 8 because of the instability of the product. Therefore, an indirect method was devised to discern the formation of 8 on electrolyzing 4, X = CO_2^-. Controlled potential electrolysis of a solution of 4, X = CO_2^- containing a trace amount of ^{18}O-labeled water and excess di-t-butyl pyridine resulted in formation of the corresponding sulfoxide. Mass spectroscopic analysis of the sulfoxide ester 11, R = Me revealed ^{18}O incorporation both into the sulfoxide oxygen and carboxylate oxygen atoms. Control experiments revealed no ^{18}O exchange under these conditions. Thus, incorporation of ^{18}O label into both sulfoxide and carboxylate



Scheme 3

moieties strongly support the formation of 8 during the electrolysis. Hydrolysis of acyloxysulfonium salt 8 may occur by either of two mechanisms as shown in Schemes 3 and 4. Nucleophilic attack by water on the sulfur displacing carboxylate results in formation of sulfoxide



Scheme 4

carboxylate with ^{18}O incorporation into the sulfoxide oxygen. However, acyloxysulfonium salt 8 can also act as an acylating agent, that is, nucleophilic attack by water at the acyl carbon to form a tetrahedral intermediate followed by expulsion of the sulfoxide moiety. This sequence results in formation of sulfoxide carboxylate with ^{18}O incorporation in the carboxylate moiety. Using the method developed by Johnson and Jones [21] for the preparation of alkoxysulfonium salts, alcohol 4, X = CH_2OH was converted to 9 in excellent yield.

Thus treatment of 4, X = CH_2OH sequentially with t-butylhypochlorite and mercury(II) chloride gave the trichloromercurate salt of 9 as a crystalline solid [22]. Single crystal X-ray crystallographic analysis yielded the structure shown in Figure I.

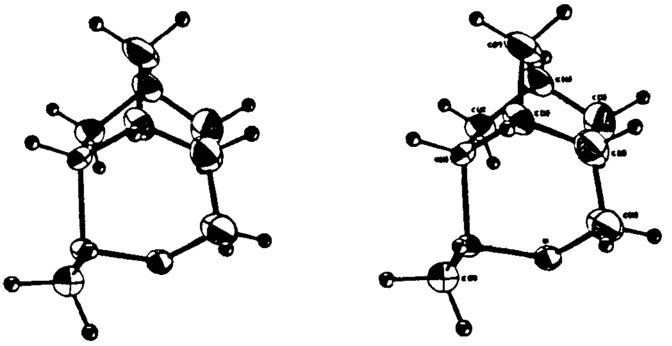
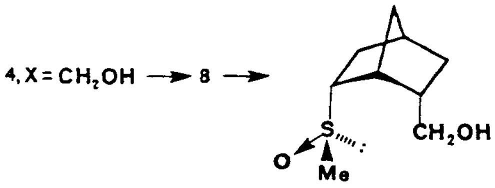


FIGURE 1: ORTEP stereoview of alkoxysulfonium salt 9.

A remarkable feature in this oxidation is that the new chiral center generated at sulfur is formed with complete stereoselectivity so far as we can tell. The stereochemistry at this center relative to the others is derived from the crystal structure study. Hydrolysis of this alkoxysulfonium salt with aqueous base gives only one diastereomeric sulfoxide alcohol. The alternative diastereomeric sulfoxide alcohol is preferentially formed by oxidation of 4, X = CH_2OH with m-chloroperbenzoic acid. The relative configuration of this latter sulfoxide alcohol was unequivocally determined by X-ray studies [22]. Therefore, the relative stereochemistry of the sulfoxide alcohol formed by hydrolysis of alkoxysulfonium salt 9 was deduced to be that shown in structure 12. It is apparent that hydrolysis of 9 occurs with inversion of configuration at sulfur as shown below. Hydrolysis of alkoxysulfonium salts in aqueous base



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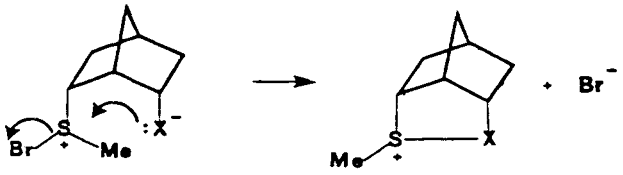
has been reported[23] to occur stereospecifically with inversion of configuration at sulfur. Controlled potential oxidation of 4, X = CH_2OH in presence of 2,6-di-t-butylpyridine resulted in the formation of alkoxysulfonium salt 9 and its diastereomer.

These studies show that the facilitated oxidation of 4, X = CO_2^- and 4, X = CH_2OH occurs with formation of a bond between the sulfur atom and oxygen atom of the substituent. Electrochemical oxidation of these compounds clearly occurs with neighboring group participation. More extensive electrochemical studies of these compounds revealed a peculiarity. Reproducible observation of the oxidation peak at low potentials appeared to depend on the nature of the supporting electrolyte. This dependence was found to be due to contamination of the supporting electrolyte with trace amounts of bromide ion. That is, facilitated oxidation of these compounds required at least trace amounts of bromide ion. Therefore, these oxidations are apparently due to redox catalysis[24]. A reasonable mechanism for this catalysis is shown in Scheme 5. Bromide ion is oxidized

$$2\ Br^- \rightarrow 2e + Br_2$$

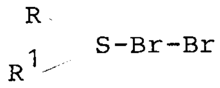
$$R_2S + Br_2 \rightleftharpoons R_2\overset{+}{S}\text{-}Br\ Br^-$$



Scheme 5

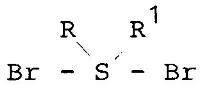
first to bromine. The bromine then reacts with the thioether to form a bromosulfonium bromide in an equilibrium reaction. With most thioethers nothing further happens. Since the bromide is present in such low concentrations the current due to its oxidation in the absence of substrate is essentially not discernible. However, if there is a suitable neighboring group in the substituted thioether, then the bromide is displaced to generate a cyclic sulfonium salt and bromide ion. The bromide ion, so generated, is then electrooxidized to bromine which in turn is reduced by the thioether appended with a neighboring group. Consequently, the trace of bromide ion catalyzes the oxidation of substantial amounts of the thioether and considerable anodic current flows. The result is a large, well-defined peak with a peak potential in the range of o.6 V, close to that for the oxidation of bromide to bromine.

Some alternatives for the last two steps in the mechanism for redox catalysis shown in Scheme 5 should be mentioned. Reaction of thioethers with bromine may give molecular complexes 13 or sulfuranes 14 [25]. Therefore,



$R(R^1)S\text{-}Br\text{-}Br$

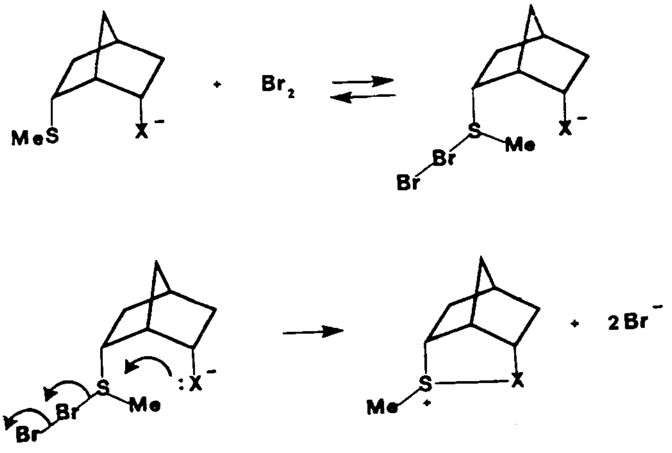
13



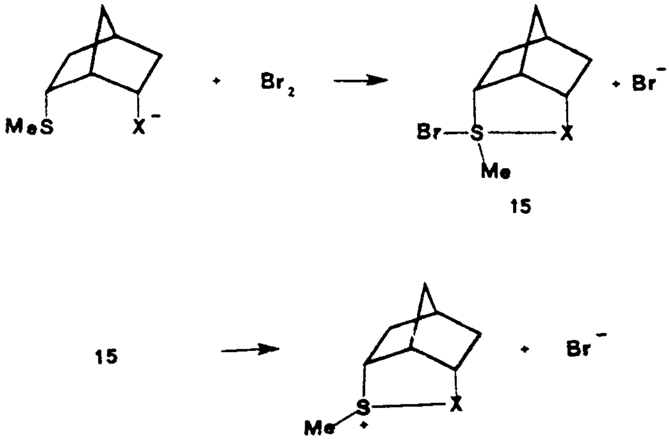
$Br - S(R)(R^1) - Br$

14

reasonable mechanisms can be written involving these intermediates. Scheme 6 illustrates such a mechanism involving a molecular complex. Formation of a dibromosulfurane followed by displacement of bromide by the neighboring group affords sulfurane 15. Alternatively sulfurane 15 can be generated by neighboring group participation concerted with electrophilic attack by bromine on the sulfur atom shown in Scheme 7



Scheme 6



Scheme 7

Neighboring alcohol group participation in the oxidation of thioethers by halogen has been reported before [26]. Neighboring carboxylate group participation has been reported for a number of reactions involving nucleophilic attack at tricoordinate cationic sulfur centers [27]. However, oxidation of o-methylthiobenzoic acid with aqueous iodine, involves general base not nucleophilic catalysis by the carboxylate group [28]. This is interesting because mono- and dicarboxylate ions accelerate the oxidation of thioethers to sulfoxides with aqueous iodine by intermolecular nucleophilic catalysis [29].

The electrochemical oxidations of these thioethers represents further examples of neighboring group participation in formal two-electron atom transfer oxidation. This still leaves open the question of whether neighboring group participation occurs on one-electron oxidation of thioethers. This question has been addressed in two ways. Pulse radiolysis studies on these thioethers and related compounds have shown that sulfur cation radicals are stabilized by neighboring group participation. Electrochemical studies on the oxidation of certain medium sized ring dithioethers revealed remarkable electron transfer behavior owing to neighboring group participation.

In collaboration with Professor K.-D. Asmus of the Hahn-Meitner Institute in Berlin and his group, we have studied the oxidation of 4, X = CO_2^-, CH_2OH and $C(Me)_2OMe$, and 5, X = CO_2^-, CH_2OH, and $C(Me)_2OH$ with hydroxyl radical, using the techniques of pulse radiolysis. A rapidly pulsed high energy electron beam impinges on a dilute aqueous solution of the substrate of interest, saturated with nitrous oxide. The high energy beam ionizes the solvent molecules as shown below. The water cation radicals are rapidly deprotonated to produce

$$H_2O \xrightarrow[\text{beam}]{\text{electron}} H_2O^+ + e^-$$

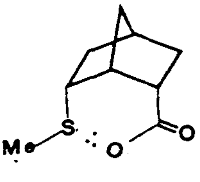
$$H_2O^+ + H_2O \longrightarrow H_3O^+ + .OH$$

$$e^- + H_2O \longrightarrow e_{aq}$$

$$e^- + N_2O \longrightarrow N_2 + O^-$$

$$O^- + H_2O \longrightarrow .OH + OH$$

hydroxyl radicals. The electrons concomitantly produced are solvated, then efficiently trapped by nitrous oxide as shown. The reducing solvated electrons are thereby converted to oxidizing hydroxyl radicals in over 90% yield. The hydroxyl radicals then oxidize the substrate and the reactions are monitored by conductivity measurements and absorption spectroscopy in the microsecond time frame. The value of the method is that the one-electron oxidizing agent hydroxyl radical is very rapidly produced at concentrations sufficiently high that the transient oxidation products of interest can be analyzed by highly time resolved techniques[30]. The technique of pulse radiolysis is especially well-suited for generating highly reactive cation radicals, rapidly measuring their spectroscopic and conductivity properties, and monitoring their decay. Such oxidation of 4, X = CH_2OH and 5, X = CO_2^-, CH_2OH and $C(Me)_2OH$ produced $RR^1\dot{C}SR^2$ radicals characterized by their absorption spectra, λ_{max} = 280 nm and long lifetime. However, oxidation of 4, X=CO_2^-, at pH 3,7, or 10 produced a neutral radical with unique absorption, λ_{max} = 390 nm, and half-lives of 30, 60 and 50 μs at pH 3, 7, and 10 respectively. This radical is assigned structure 16. Similarly, oxi-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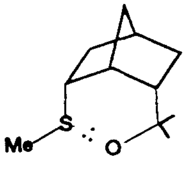
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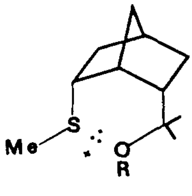
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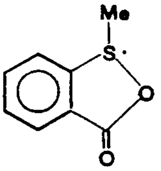
dation of 4, X=C(Me)$_2$OH at pH 8 yielded a neutral radical which absorbed with λ_{max} = 4oo nm and $t_{1/2}$ = 2oo μs and is assigned structure 17. At pH 4 oxidation of this alcohol produced a positively charged radical with λ_{max} = 42o nm and $t_{1/2}$ = 3o μs assigned structure 18, R=H. Similarly 4, X=C(Me)$_2$OMe generated a positively charged radical on oxidation with λ_{max} = 42o and $t_{1/2}$ = 50 μs believed to be 18, R=Me. The structural assignments are based on the unique properties of the radicals produced which formed from the <u>endo</u> substituted compounds for which S, O interaction is possible but not the corresponding <u>exo</u>-substituted compounds for which such interaction is geometrically precluded. Furthermore, the absorption observed for these species is compatible with that observed by Griller and coworkers [31] for radical 19. This radical showed absorption with λ_{max} between 38o and 39o nm in dichloromethane at 238°K. The bonding in 16-18 may be two-center, three-electron or three-center, three-electron as described above. No basis is available for distinguishing these possibilities at this point. However, it may be noted that Perkins et al. [16] assign hypervalent C-S-O three center, three electron bonding to radical 19 produced by irradiation of perester 2o in a frozen matrix and characterized by esr spectroscopy.



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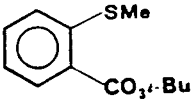
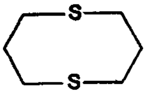


2o

Compelling evidence for neighboring group participation on sequential one electron oxidation of 1,5-dithiacyclooctane (1,5-DTCO), 21, has been obtained.



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Musker and coworkers [32] reported that oxidation of 1,5-DTCO with one equivalent of nitrosonium tetrafluoroborate or copper(II) tetrafluoroborate produced an exceptionally stable cation radical. Further oxidation produced a dication. Our electrochemical studies [33] on 1,5-DTCO support these observations and provide new insight into this remarkable system. The peak potential for oxidation of 1,5-DTCO is o,34 V and does not require the presence of bromide ion. This means that 1,5-DTCO is over 1.oV easier to oxidize than simple dialkyl thioethers. Furthermore, unlike the other thioethers studied 1,5-DTCO undergoes electrochemically reversible oxidation. That is, the oxidized species produced at the electrode as the potential is swept in a positive direction is reduced back to 1,5-DTCO on reversal of the direction of potential sweep on the cyclic voltammetric time scale. The oxidation in dilute solutions of 1,5-DTCO corresponds to an overall two electron oxidation. Theoretical simulation of the cyclic voltammetry experiments provides a very good fit over a range of scan rates assuming the mechanism shown below. An extraordinaty result is that E_2^o is less positive

$$1,5-\mathrm{DTCO}\ \ -e^{-} \rightleftharpoons (1,5-\mathrm{DTCO})^{+\cdot} \qquad E_1^{o}$$

$$(1,5-\mathrm{DTCO})^{+\cdot}\ \ -e^{-} \rightleftharpoons (1,5-\mathrm{DTCO})^{2+} \qquad E_2^{o}$$

than E_1^{o} by approximately 2o mV. That is, it is easier to remove an electron from 1,5-DTCO cation radical than from 1,5-DTCO. This is contrary to expectations based on electrostatics. Removal of a negatively charged electron from uncharged 1,5-DTCO should require less work than removal of a negatively charged electron from positively charged 1,5-DTCO cation radical. The elegant work by Asmus and co-workers[17b] on pulse radiolysis of thioethers in general and 1,5-DTCO in particular provide an attractive electronic basis for our unusual result. These workers cogently account for their experimental reults by assigning two-center, three-electron bonding for the S,S bond in 1,5-DTCO cation radical. Recent ESR studies by Musker et al.[34] also support this bonding assignment. This means that the third electron is in an antibonding σ-molecular orbital. Thus, removal of this electron increases the S-S bond order. This electronic factor more than compensates for the electrostatic interaction. Our electrochemical studies also revealed the dimerization of 1,5-DTCO cation radical[33]. This dimerization is reminiscent of the reported[35] dimerization of $S_8^{\cdot}$ to S_{16}^{2+}.

$$2\ (1,5\text{-}\mathrm{DTCO})^{+\cdot} \rightleftharpoons (\mathrm{DTCO})_2^{2+}$$

To provide additional insight into the extraordinary facile oxidation of 1,5-DTCO its conformation as well as that of related medium-sized ring dithioethers and a trithioether were determined [36]. The photoelectron spectra for these sulfur compounds were measured and in general show splitting of the S-S lone pairs, e.g., o.43 eV splitting for 1,5-DTCO. That is, owing to lone pair-lone pair interaction on the two, or in one case, three, sulfur atoms **two** ionization potentials before and are due to through bond and through space interactions[37]. Assuming Koopman's theorem each ionization potential is the negative of the orbital energy from which the electron is photoejected. By using molecular mechanisms calculations to determine the geometries and energies of the lowest energy conformers and semi-empirical molecular orbital calculations to compute the orbital energies, or by using MINDO/3 the best fit with the experimental photoelectron spectrum provided the basis for assigning the structure of the predominant conformer [36]. For the medium sized ring di- and trithioethers, the splitting is due predominantly to through space interaction, unlike 1,4-dithiane which shows large splitting due to through bond interaction [38]. The extent of through space interaction depends on the S-S distance and the C-S-C dihedral angle. In essence this last parameter measures whether the lone-pair p-orbitals on sulfur are pointed toward each other or somewhat askew. For a given S-S separation, the more the orbitals point toward one another the greater the amount of overlap and hence the larger the splitting. In general the predominant conformers are those in which the sulfur atoms are endodentate and the lone pair orbitals point toward the center of the ring. This is shown schematically for 1,5-DTCO in Figure 2 and for the other dithioethers in

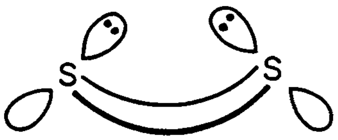

FIGURE 2 Schematic drawing showing the orientation of the sulfur atoms in 1,5-DTCO

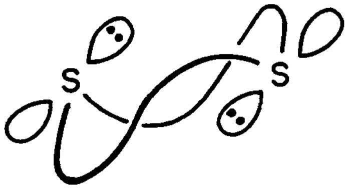

Figure 3 Schematic drawing showing the orientation of the sulfur atoms in 1,4-DTCH, 1,5-DTCN, and 1,6-DTCD.

Figure 3. So there is substantial destabilization of the dithioethers by lone pair-lone pair repulsion.
To understand the basis for the unusually low oxidation potentials for 1,5-DTCO it should be noted that this oxidation is electrochemical reversible. Therefore, the oxidation is independent of the working electrode used and E^{o} depends solely on the difference in free energy between the starting material and products. Factors which destabilize 1,5-DTCO or stabilize its oxidation

products render E^{O} less positive. As already pointed out, 1,5-DTCO is destabilized by lone pair-lone pair repulsion. Furthermore, this repulsion is replaced by a bond in both the cation radical and dication of 1,5-DTCO. That is, the very facile oxidation of 1,5-DTCO is due to destabilization of the uncharged species and transannular bond formation in the oxidation products. However, the relative importance of each of these factors remains to be ascertained.

In summary, several consequences of neighboring group participation in the oxidation of aliphatic thioethers have been demonstrated. Neighboring carboxylate and alcohol groups facilitate bromine oxidation of thioethers. This facilitation results in redox catalysis of the oxidation of sulfides appended with these neighboring groups by trace amounts of bromide ion. Pulse radiolysis studies revealed kinetic stabilization of sulfur cation radicals by neighboring carboxylate and alcohol groups. Finally, one-electron transfer from certain medium-sized ring dithioethers, particularly 1,5-dithiacyclooctane, occur with exceptional ease. Transannular bond formation between sulfur atoms results on electron transfer. The overall energies of this reversible oxidation were determined by electrochemical techniques. Conformational analysis of 1,5-DTCO suggests that electron transfer is favored by lone pair-lone pair destabilization of 1,5-DTCO as well as stabilization of the oxidation products by thioether group participation.

TABLE I Anodic oxidation of norbornyl derivatives using cyclic voltammetry

Compound	Ep[a]	Compound	E_p[a]
4, X = CO_2H	1.2o	5, X = CO_2H	1.28
4, X = CO_2Me	1.21	5, X = CO_2Me	1.29
4, X = CH_2OH	o.56	5, X = CH_2OH	1.2o
4, X = $NHCO_2Et$	o.98	5, X = $NHCO_2Et$	1.2o
4, X = CO_2^-	o.65	5, X = CO_2^-	1.28
4, X = COSMe	1.12	5, X = COSMe	1.42
4, X = $CONH_2$	o.85	5, X = $CONH_2$	1.4o
6, X = CO_2H	1.31	7, X = CO_2H	1.31
6, X = CO_2Me	1.32	7, X = CO_2Me	1.27

[a] Peak potentials of first oxidation peak determined at a Pt electrode (1 cm^2), o.1 - V/s scan rate, and measured in acetonitrile, o.1M $\underline{n}$-Bu_4NClO_4 vs. Ag/o.1M $AgNO_3$ in acetonitrile reference electrode.

REFERENCES

1. T. Yonetani, J.Biol.Chem. 24o, 45o9 (1965).
2. B.M.Hoffman, J.E.Roberts, T.G.Brown, C.H.Kang and E.Margoliash, Proc.Nat.Acad.Sci.(USA) 76, 6132(1979); P.S.Ho, B.M.Hoffman, C.H.Kang, and E.Margoliash, J.Biol.Chem.258, 4356 (1983).
3. Y.Watanabe, T.Iyanagi, and S.Oae, Tetrahedron Lett. 21, 3685(198o); Y.Watanabe, S.Oae, and T.Iyanagi, Bull.Chem.Soc.Jpn. 55, 188 (1982).
4. But see also A.Miller, Tetrahedron Lett. 23, 753 (1982).
5. (a) C.Beauchamp and I.Fridovich, J.Biol.Chem. 245, 4641(197o); (b) A.I.Cederbaum and G.Cohen in Oxygen and Oxy-Radicals in Chemistry and Biology, M.A.J. Rodgers and E.L.Powers, Ed. (Academic, New York, 1981) pp. 612-614
6. S.F.Yang, Arch.Biochem.Biophys. 122,481(1967); S.F. Yang, H.S.Ku, and H.K.Pratt, J.Biol.Chem.242, 5274 (1967); S.F.Yang, Ibid. 244, 436o (1969).
7. W.A.Pryor and R.H.Tang, Biochem.Biophys.Res.Commun. 81, 498 (1978).
8. W.Bors, E.Lenghlder, M.Swan, C.Fuchs, and C.Michel, Biochem.Biophys.Res.Commun. 7o, 81 (1976).
9. R.S.Morgan, C.F.Tatsch, R.H.Gushard, J.M.McAdon, and P.K.Warme, Int.J.Peptide Protein Res. 11, 2o9(1978); R.S.Morgan and J.M.McAdon, Ibid. 15, 177(198o); B.L.Bodner, L.M.Jackman, and R.S.Morgan, Biochem. Biophys.Res.Commun. 94, 8o7 (198o).
1o. H.J.Shine in The Chemistry of the Sulphonium Group, C.J.M.Stirling and S.Patai, Eds. (Wiley, New York, 1981) Chap. 14, pp. 523-57o; L.A.Tinker and A.J. Bard, J.Electroanal.Chem. 133, 275(1982); M.C.Depew, L.Zhongli and J.K.S.Wan, J.Am.Chem.Soc. 1o5, 248o (1983)
11. C.M.Gooley, H.Keyzer, and F.Setchell, Nature, 223, 8o(1969); D.C.Borg in Biological Applications of Electron Spin Resonance, H.M.Swartz, J.R.Bolton, and D.C.Borg, Eds. (Wiley, New York, 1972) pp. 318-321; but see also L.N.Domelsmith, L.L.Munchhausen and K.N.Houk, J.Am.Chem.Soc. 99, 65o6(1977).
12. B.R.Coleman, R.S.Glass, W.N.Setzer, U.D.G.Prabhu, and G.S.Wilson, Adv.Chem.Ser. 2o1, 417(1982)
13. R.D.Cannon in Electron Transfer Reactions (Butterworths, London, 198o).

14. C.A.Stein and H.Taube, J.Am.Chem.Soc. 103, 693(1981); C.A.Stein, N.A.Lewis, and G.Steiz, Ibid.104, 2596 (1982); L.T.Calcaterra, G.L.Closs, and J.R.Miller, Ibid. 105, 670(1983); J.R.Miller, L.T.Calcaterra, and G.L.Closs, Ibid. 106, 3047(1984).
15. B.Capon and S.P.McManus, Neighboring Group Participation (Plenum, New York, 1976).
16. C.W.Perkins, J.C.Martin, A.J.Arduengo, W.Lau, A.Algria, and J.K.Kochi, J.Am.Chem.Soc. 102, 7753(1980).
17. (a) J.C.Martin, ACS Symp. Ser. No. 69, 71(1978); (b) K.-D.Asmus, Acc.Chem.Res.12, 436(1979).
18. J.I.Musher, Angew.Chem.Int.Ed.Engl. 8, 54(1969); J.I.Musher, Adv.Chem.Ser. 110, 44(1972).
19. R.S.Glass, J.R.Duchek, J.T.Klug, and G.S.Wilson, J.Am.Chem.Soc. 99, 7349(1977)
20. P.Livant and J.C.Martin, J.Am.Chem.Soc.99, 5761(1977)
21. C.R.Johnson and M.P.Jones, J.Org.Chem.32, 2014(1967).
22. R.S.Glass, W.N.Setzer, U.D.G.Prabhu, and G.S.Wilson, Tetrahedron Lett. 23, 2335(1982).
23. C.R.Johnson, J.Am.Chem.Soc. 85, 1020(1963); C.R. Johnson and C.McCants,jr. Ibid. 87, 5404(1965); R. Tang and K.Mislow, Ibid. 91, 5644(1969).
24. J.M.Saveant, Acc.Chem.Res. 13, 323(1980).
25. G.E.Wilson, jr., Tetrahedron 38, 2597(1982).
26. J.Kline and H.Stoller, Tetrahedron 30, 2541(1974); A.S.Hirschon, J.D.Beller, M.Olmstead, J.T.Doi and W.K.Musker, Tetrahedron Lett. 22, 1195(1981); A.S. Hirschon, J.T.Doi, and W.K.Musker, J.Am.Chem.Soc. 104, 725(1982).
27. T.Numata, K.Sakai, M.Kise, N.Kuneida, and S.Oae Chem.Ind.576 (1971); T.Numata, K.Sakai, M.Kise, N.Kuneida, and S.Oae, Int.J.Sulfur Chem.A 1, 1 (1971); D.Landini, F.Rolla, G.Torre, Ibid. 2, 43 (1972); D.Landini and F.Rolla, J.Chem.Soc.Perkin Trans.2 1317(1972); S.Allenmark, Int.J.Sulfur Chem. 8, 127(1973); O.Bohman and S.Allenmark, Tetrahedron Lett. 405(1973); O.Bohman and S.Allenmark, Chem.Scr. 4, 202(1973); I.Kapovits, F.Ruff, J.Gulyas, and A. Kucsman, Tetrahedron 32, 1811(1976).
28. W.Tagaki, M.Ochiai, and S.Oae, Tetrahedron Lett. 6131(1968).
29. T.Higuchi and K.-H.Gensch, J.Am.Chem.Soc. 88, 5486 (1966); K.-H.Gensch, I.H.Pitman, and T.Higuchi, Ibid. 90, 2096(1968); P.R.Young and M.Till, J.Org.Chem. 47, 1416(1982)
30. L.M.Dorfman in Investigation of Rates and Mechanisms of Reactions Part II, 3rd Ed, G.G.Hammes, Ed. (Wiley, New York, 1974) Chap. 11, pp 463-519; R.V.Bensasson, E.J.Land, and T.G.Truscott in Flash Photolysis and

Pulse Radiolysis (Pergamon, Oxford, 1983).
31. C.Chatgilialoglu, A.L.Castelhano, and D.Griller, personal communication
32. W.K.Musker, T.L.Wolford, and P.B.Roush, J.Am.Chem. Soc. 1oo, 6416 (1978).
33. G.S.Wilson, D.D.Swanson, J.T.Klug, R.S.Glass, M.D. Ryan, and W.K.Musker, J.Am.Chem.Soc. 1o1, 1o4o(1979); M.D.Ryan, D.D.Swanson, R.S.Glass, and G.S.Wilson, J.Phys.Chem. 85, 1o69(1981).
34. T.G.Brown, A.S.Hirschon, and W.K.Musker, J.Phys. Chem. 85, 3767 (1981).
35. R.J.Gillespie and P.K.Ummat, Inorg.Chem.11, 1674 (1972).
36. W.N.Setzer, G.S.Wilson, and R.S.Glass, Tetrahedron, 37, 2735(1981); W.N.Setzer, B.R.Coleman, G.S.Wilson, and R.S.Glass, Ibid. 37, 2743(1981).
37. R.Gleiter and J.Spanget-Larsen in Topics in Current Chemistry, 86, Spectroscopy (Springer-Verlag,1979) pp. 139-195.
38. D.A.Sweigart and D.W.Turner, J.Am.Chem.Soc. 94, 5599 (1972).

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