Reactions of Bis(*p*-methoxyphenyl)trisulfane and Its Oxides with Dimethyldioxirane and (Trifluoromethyl)methyldioxirane

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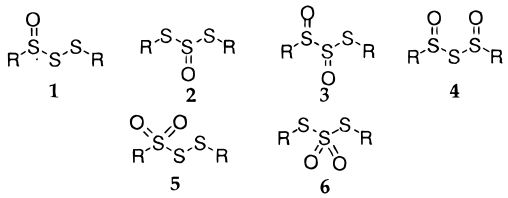
The reactions of dimethyldioxirane and (trifluoromethyl)methyldioxirane with bis(*p*-methoxyphenyl)-trisulfane, its 1-oxide, its 2-oxide, and its 1,1-dioxide derivatives have been investigated. The reactions were followed by careful monitoring of the methoxy region of the ^{1}H NMR spectra and where possible by doping with authentic samples of the products. The decomposition of labile intermediates and products was investigated. A new mechanism for the rearrangement of a trisulfane 1,3-dioxide to a trisulfane 1,1-dioxide is proposed.

Interest in the trisulfane linkage has increased rapidly in the past few years in part as a result of the isolation and structural assignment[1,2] of calicheamicin γ_1 and the Esperamicins.[3,4] The trisulfane linkage in these antitumor antibiotics acts as the trigger for a Bergman cyclization[5] of the enediyne unit to give a 1,4-diyl that when bound in the minor groove of DNA abstracts hydrogen atoms, resulting in single- and double-stranded scissions.[6−9] Despite the occurrence of the trisulfane linkage in a variety of natural products,[10] including these antitumor antibiotics, its chemistry has not been examined as extensively as its disulfane homologue. The most prominent reactions of trisulfanes include nucleophilic attack,[11] which leads to desulfurization in the cases of phosphines,[12] phosphites, or chalcogenides,[13] and oxidations.[14,15]

The oxidation chemistry is complicated by the possible formations of both regio- and stereoisomeric products and by the well-established lability of many of these compounds. The mono- and bis-oxidations of symmetrical trisulfanes could presumably lead to a trisulfane 1-oxide **1**, a trisulfane 2-oxide **2**, diastereomeric trisulfane 1,2-dioxides **3**, diastereomeric trisulfane 1,3-dioxides, **4**, a trisulfane 1, 1-dioxide **5**, or a trisulfane 2,2-dioxide, **6**.[16]

Despite the difficulties associated with the studies of these oxidations, elegant and detailed reports of the oxidations of di-*tert*-butyltrisulfane and its oxidized derivatives have started to appear. Di-*tert*-butyltrisulfane was chosen for examination because of the well-known increase in stability of its oxidized derivatives, **1**−**6**, in comparison to analogues with a lower degree of substitution (stability sequence; tertiary > secondary > primary).[17,18] These reports provide the impetus for the disclosure of our analogous study of the oxidations of bis-(*p*-methoxyphenyl)trisulfane and its oxidized derivatives. These latter compounds were chosen for our studies because the methoxy groups provide a convenient NMR handle that can be used to identify the products of the oxidations (vide infra). The results reported here are different in some respects from those reported for di-*tert*-butyltrisulfane and its derivatives. These results also point out a potential mechanistic dichotomy for which we propose a possible solution.



Results

The oxidations of bis(4-methoxyphenyl)trisulfane and its derivatives were monitored by ^{1}H NMR using the methoxy protons as diagnostic signals. The methoxy group on the *p*-methoxyphenyl ring appeared between 3.804 and 3.872 ppm when attached to a sulfenyl sulfur (−S−), between 3.899 and 3.912 when attached to a sulfinyl sulfur (−SO−), and between 3.913 and 3.960 when attached to a sulfonyl sulfur (−SO_2−), all relative to TMS at room temperature (Table 1). The only exception to these generalizations occurred in the bis(4-methoxyphenyl)trisulfane 1,1,3-trioxide, which exhibited somewhat unanticipated downfield (3.924 and 3.990 ppm) chemical shifts. Complicating the analysis, however, was the tendency of the chemical shifts of the methoxy groups

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(1) Lee, M. D.; Dunne, T. S.; Siegel, M. M.; Chang, C. C.; Morton, G. O.; Borders, D. B. *J. Am. Chem. Soc.* **1987**, *109*, 3464−3466.
(2) Lee, M. D.; Dunne, T. S.; Chang, C. C.; Ellestad, G. A.; Siegel, M. M.; Morton, G. O.; McGahren, W. J.; Borders, D. B. *J. Am. Chem. Soc.* **1987**, *109*, 3466−3468.
(3) Golik, J.; Clardy, J.; Dubay, G.; Groenewold, G.; Kawaguchi, H.; Konishi, M.; Krishnan, B.; Ohkuma, H.; Saitoh, K.; Doyle, T. W. *J. Am. Chem. Soc.* **1987**, *109*, 3461−3462.
(4) Golik, J.; Dubay, G.; Groenewold, G.; Kawaguchi, H.; Konishi, M.; Krishnan, B.; Ohkuma, H.; Saitoh, K.; Doyle, T. W. *J. Am. Chem. Soc.* **1987**, *109*, 3462−3464.
(5) Bergman, R. G. *Acc. Chem. Res.* **1973**, *6*, 25−31.
(6) Nicolaou, K. C.; Dai, W.-M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1387−1416.
(7) Nicolaou, K. C.; Smith, A. L. *Acc. Chem. Res.* **1992**, *25*, 497−503.
(8) Magnus, P.; Carter, P.; Elliott, J.; Lewis, R.; Harling, J.; Pitterna, T.; Bauta, W. E.; Fortt, S. *J. Am. Chem. Soc.* **1992**, *114*, 2544−2559.
(9) Magnus, P.; Lewis, R.; Bennett, F. *J. Am. Chem. Soc.* **1992**, *114*, 2560−2567.
(10) Yomoji, N.; Satoh, S.; Ogawa, S.; Sato, R. *Tetrahedron Lett.* **1993**, *34*, 673−676.
(11) Sato, R.; Sato, T.; Takikawa, Y.; Takizawa, S. *Tech. Rep. Iwate Univ.* **1979**, *13*, 37−41.
(12) Harpp, D. N.; Ash, D. K.; Smith, R. A. *J. Org. Chem.* **1980**, *45*, 5155−5160.
(13) Li, C. J.; Harpp, D. N. *Tetrahedron Lett.* **1993**, *34*, 903−906.
(14) Steudel, R.; Latte, J. *Chem. Ber.* **1977**, *110*, 423−429.
(15) Steudel, R. *Phosphorus Sulfur* **1985**, *23*, 33−64.

(16) We have decided to use the sulfane nomenclature because we will only discuss a symmetrical trisulfide and its derivatives where it is less cumbersome than perhaps other alternatives. In addition, it has been pointed out that the "sulfane" nomenclature can be extended conveniently to polyoxides and to sulfanes with more than two contiguous sulfur atoms.[15]

(17) Derbesy, G.; Harpp, D. N. *J. Org. Chem.* **1995**, *60*, 4468−4474.
(18) Derbesy, G.; Harpp, D. N. *J. Org. Chem.* **1996**, *61*, 991−997.

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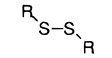
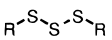
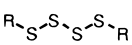
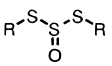
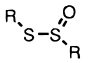
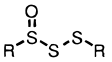
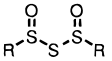
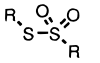
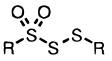
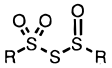
Table 1. Proton Chemical Shifts of *p*-Methoxy Groups Bound to Sulfenyl, Sulfinyl, and Sulfonyl Groups

Compound[a]	δ_{OMe}^{S} [b]	δ_{OMe}^{SO} [c]	$\delta_{OMe}^{SO_2}$ [d]
	3.804		
	3.811		
	3.839		
	3.872		
	3.865	3.900	
	3.838, 3.848[e]	3.899, 3.910[e]	
		3.912[e]	
	3.853		3.913
	3.840[e], 3.830		3.960[e], 3.946
		3.924[e]	3.990[e]

[a] R = *p*-MeOPh. [b] Proton chemical shifts of methoxy group on the phenyl ring bound to sulfenyl sulfur. [c] Same as *b* but bound to sulfinyl sulfur. [d] Same as b but bound to sulfonyl sulfur. [e] At −20 °C.

to fluctuate by ±0.03 ppm as a function of several experimental variables including temperature. As a result, definitive identification of the products was obtained in several cases by doping the NMR reaction mixtures with authentic samples of the potential products.

Dimethyldioxirane (DMD) and (trifluoromethyl)methyldioxirane (TMD) were used as the oxidants. *m*-CPBA gave less satisfactory results presumably as a result of the formation of the very acidic *p*-methoxybenzoic acid byproduct. The formation of products that incorporated the benzoate byproduct has previously been noted during oxidations of disulfanes.[19]

Oxidation of Bis(*p*-methoxyphenyl)trisulfane. One equiv of DMD was added to an acetone-d_6 NMR sample of the trisulfane at −20 °C, and the 400 MHz proton NMR spectrum was immediately recorded. Two new singlets at 3.910 and 3.848 ppm (peaks a in Figure 1a) were observed consistent with formation of the trisulfane 1-oxide. In addition, a small amount of the trisulfane 1,1-dioxide (peaks b in Figure 1a), residual trisulfane (peak c), and two peaks at 3.92 and 3.99 ppm (peaks d), which we assign to the trisulfane 1,1,3-trioxide (vide infra), were also detected in the reaction mixture. This regiochemistry is consistent with that observed in the *m*-CPBA oxidations of dimethyl,[20] diethyl,[20] dipropyl,[20] di-*tert*-butyl,[14,20,21] dibenzyl,[20] and diallyl trisulfanes.[22]

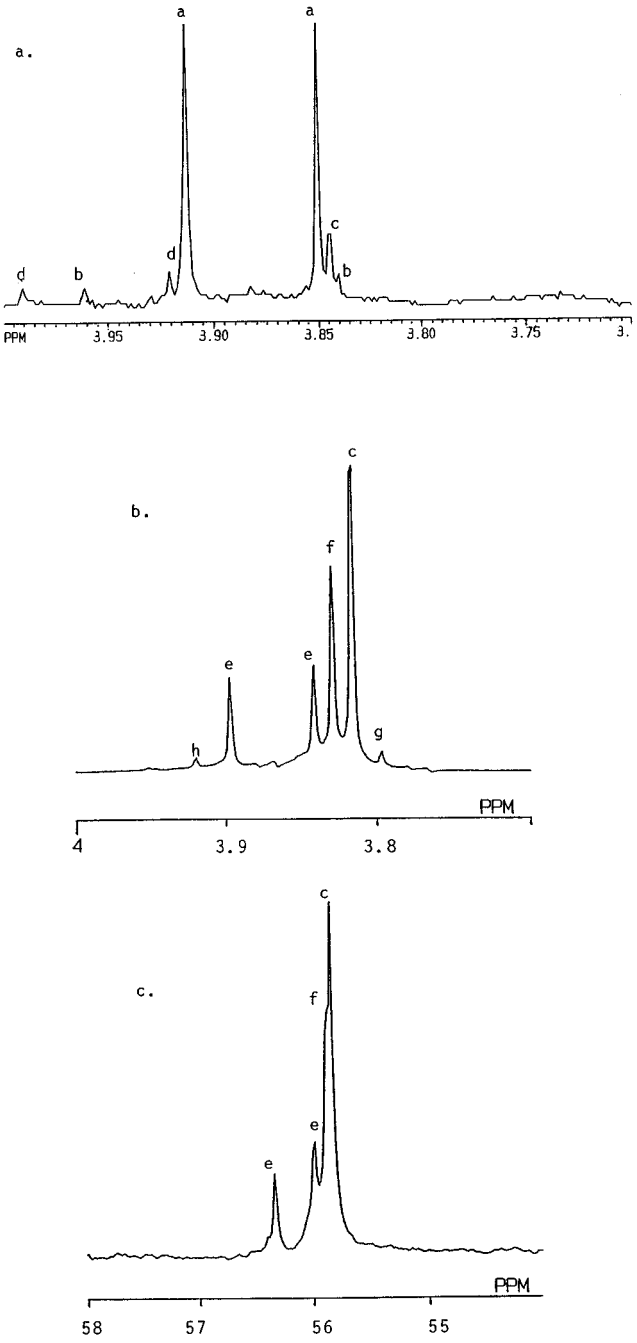


Figure 1. (a) ^{1}H NMR at −20 °C of the methoxy region immediately after addition of 1 equiv of DMD to the trisulfane. Key: (a) trisulfane 1-oxide; (b) trisulfane 1,1-dioxide; (c) trisulfane; (d) trisulfane 1,1,3-trioxide. (b) ^{1}H NMR at room temperature of the methoxy region 2−3 h after addition of 0.6 equiv of DMD to the trisulfane. Key: (c) trisulfane; (e) disulfane-1,1-dioxide; (f) tetrasulfane; (g) disulfane; (h) unknown. (c) ^{13}C NMR of methoxy region at room temperature of the sample corresponding to the ^{1}H NMR in Figure 2b. Key: (c) trisulfane; (e) disulfane 1,1-dioxide; (f) tetrasulfane.

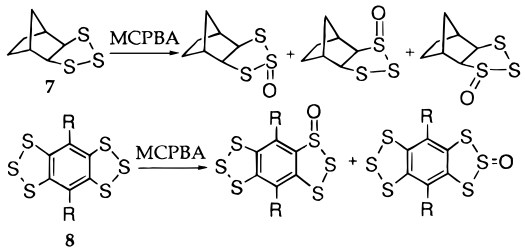
Only in the case of some cyclic trisulfanes such as **7**[23] and **8**[24] have nonregiospecific reactions been observed.

The thermal lability of sulfane 1-oxides has been noted in the literature, and it has been pointed out that the stability increases with the degree of substitution (tertiary > secondary > primary).[17] Indeed, warming the

(19) Freeman, F.; Angeletakis, C. N. *J. Am. Chem. Soc.* **1982**, *104*, 5766−5774.

(20) Auger, J.; Koussourakos, Y.; Thibout, E. *Chim. Chron., New Ser.* **1985**, *14*, 263−264.

(21) Derbesy, G.; Harpp, D. N. *Sulfur Lett.* **1995**, *18*, 167−172.



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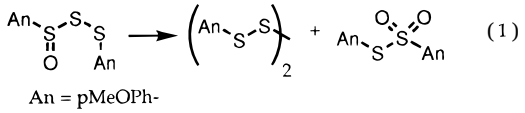
NMR reaction mixture containing bis(*p*-methoxyphenyl)-trisulfane 1-oxide to room temperature resulted in its decomposition. Kinetic experiments at room temperature conducted by following the disappearance of the trisulfane 1-oxide resulted in a clean first-order decay with a rate constant of $(1.67 \pm 0.22) \times 10^{-4}$ s^{-1} corresponding to a half-life of 69 min at room temperature. Greater than 95% of the trisulfane 1-oxide had decomposed within 5 h at 25 °C. For comparison, Derbesy and Harpp[17] reported that di-*tert*-butyltrisulfane 1-oxide required 12 h at 45 °C to completely decompose.

NMR examination of a reaction mixture (Figure 1b) containing the trisulfane and 0.6 equiv of DMD after 2−3 h revealed formation of a 1:1 mixture of the bis(*p*-methoxyphenyl)disulfane 1,1-dioxide (peaks e) and bis-(*p*-methoxyphenyl) tetrasulfane (peak f) as a result of the decomposition of the transient trisulfane 1-oxide (eq 1).

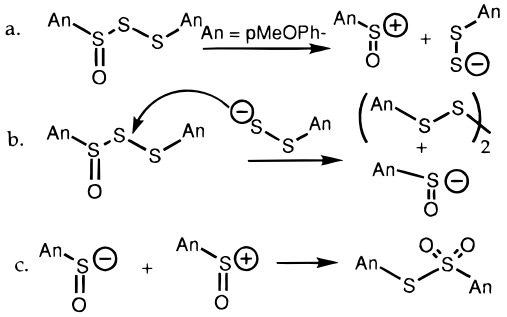


An = pMeOPh- (1)

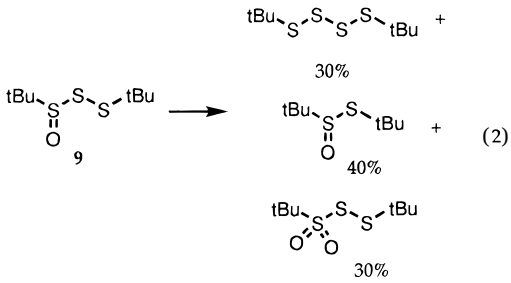
Small amounts of the disulfane (peak g) and an unknown reaction component (peak h) were also observed in addition to unreacted trisulfane (peak c). This assignment was corroborated by the methoxy region of the ^{13}C NMR (Figure 1c), which showed formation of the same major products in approximately the same ratio as in the ^{1}H NMR.

A mechanism consistent with formation of a 1:1 mixture of the tetrasulfane and disulfane 1,1-dioxide is shown in Scheme 1. The first step involves a heterolytic cleavage of the 1-oxide to give the (*p*-methoxyphenyl)-sulfinyl cation and a disulfide anion. A heterolytic cleavage of di-*tert*-butyltrisulfane 1-oxide was suggested by Derbesy and Harpp[17] on the basis of the inability of radical inhibitors to affect the rate of decomposition and crystallographic data, which shows that S(O)−S bonds are longer than either S−S or $S(O)_2$−S bonds. Step b in Scheme 1 is supported by the observation that thiolates are known to attack at the sulfenyl sulfur in phenyl benzenethiolsulfinate (PhS(O)SPh) rather than at the harder sulfinyl sulfur.[25] In step c of the mechanism, annihilation of the sulfinyl cation and anion would ultimately result in formation of the 1,1-dioxide via a mechanism similar to that suggested for the rearrangements of α-disulfoxides.[26]

Scheme 1



The reaction of the sulfinyl anion and cation (c in Scheme 1) is somewhat unusual since it has been pointed out that this dimerization is very sensitive to steric effects and does not occur at all during the decomposition of di-*tert*-butyltrisulfane 1-oxide, **9**.[17] Consequently, **9**, decomposed to give a more complex reaction mixture (eq 2) than observed in our system via a more complicated mechanism.[17]



(2)

Oxidation of Bis(*p*-methoxyphenyl)trisulfane 1-Oxide. This oxidation was the most complex of those that we have examined, and its analysis was exacerbated by our inability to completely oxidize the starting material without concomitant overoxidation. As a result, the products from decompositions of the trisulfane 1-oxide and trisulfane 1,1,3-trioxide (vide infra) were unavoidably formed in every reaction mixture complicating the analysis. Nevertheless, useful conclusions could be drawn by careful examinations of the reactions under a variety of conditions.

One equiv of DMD was added to the preformed trisulfane 1-oxide at −20 °C followed by immediate analysis of the reaction mixture by low-temperature NMR. (Figure 2a). A major new peak was observed at 3.912 (peak i) and a minor new peak at 3.899 (peak j), and the peaks at 3.838, 3.920, 3.960, and 3.990 ppm (peaks b and d), which were present to a minor extent in the preformed trisulfane 1-oxide (Figure 1a) increased in intensity. Peaks d were also formed as the overwhelming product during the oxidation of the trisulfane 1,1-dioxide with DMD at −20 °C and are consequently assigned to the overoxidation product, the trisulfane 1,1,3-trioxide. Warming the reaction mixture to room temperature (Figure 2b) resulted in the increase of peaks b and the formation of new peaks, e, f, g, and u, at the expense of the major peak at 3.912 (peak i), the residual trisulfane 1-oxide (peaks a), and the trisulfane 1,1,3-trioxide (peaks d), which completely disappeared. Derbesy and Harpp have pointed out that the diastereomeric di-*tert*-butyltrisulfane 1,3-dioxides are barely stable at

(22) Freeman, F.; Ma, X.-B.; Lin, R. I.-S. *Sulfur Lett.* **1993**, *15*, 253−262.
(23) Ghosh, T.; Bartlett, P. D. *J. Am. Chem. Soc.* **1988**, *110*, 7499−7506.
(24) Yomojii, N.; Takahashi, S.; Chida, S.; Ogawa, S.; Sato, R. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1995−2000.
(25) Kice, J. L. In *Advances in Physical Organic Chemistry*; Gold, V., Bethell, D., Ed.; Academic Press: London, 1980; Vol. 17; pp 65−181.
(26) Folkins, P. L.; Harpp, D. N. *J. Am. Chem. Soc.* **1993**, *115*, 3066−3070.

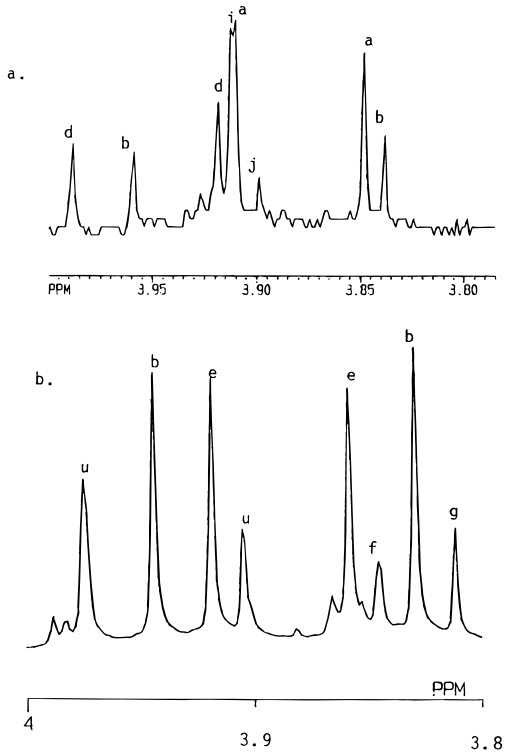


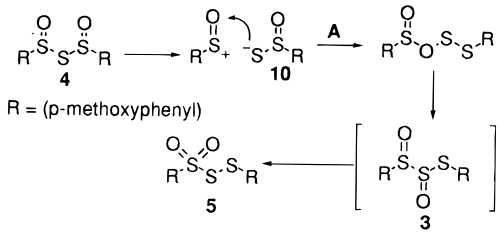
Figure 2. (a) ^{1}H NMR of methoxy region at −20 °C immediately after addition of 1 equiv of DMD to preformed trisulfane 1-oxide. Key: (a) trisulfane 1-oxide; (b) trisulfane 1,1-dioxide; (d) trisulfane 1,1,3-trioxide; (i) trisulfane 1,3-dioxide; (j) unknown. (b) ^{1}H NMR of methoxy region of a sample similar to that shown in panel a after several hours at room temperature. Key: (b) trisulfane 1,1-dioxide; (e) disulfane 1,1-dioxide; (f) tetrasulfane; (g) disulfane; (u) unknown.

room temperature, and consequently, we assign the intense peak at 3.912 ppm to bis(*p*-methoxyphenyl)-trisulfane 1,3-dioxide. This new trisulfane 1,3-dioxide is likely to exist as a pair of diastereomers,[21] which unfortunately, cannot be verified since only one methoxy peak is resolvable.

The intensity ratios of the NMR peaks at room temperature (Figure 2b) were a sensitive function of the sample treatment and fluctuated as a function of whether the 2 equiv of DMD were both administered at room temperature or stepwise at low temperature. In addition, the relative intensities of the peaks changed as a function of the time between addition of the dioxirane and the time of analysis. In particular, peaks e, the disulfane-1,1-dioxide, increase dramatically with increasing time. However, under all the conditions examined the initial major product of the reaction with peaks at 3.838 and 3.960 ppm (peaks b) is the trisulfane 1,1-dioxide. The remaining peaks belong to the disulfane 1,1-dioxide (peaks e) and tetrasulfane (peak f), which are the decomposition products of the residual trisulfane 1-oxide,[27] the disulfane (peak g), and unknowns (peaks u), which appear to be products of the decomposition of the very labile trisulfane 1,1,3-trioxide. The disulfane 1-oxide (thiolsulfinate) that formed as a major product in the

(27) The disulfane 1,1-dioxide/tetrasulfane ratio was not 1/1 as anticipated from decomposition of the trisulfane 1-oxide; however, Harpp has pointed out that trisulfane 1,1-dioxides spontaneously extrude sulfur to form disulfane 1,1-dioxides: Harpp, D. N.; Ash, D. K.; Smith, R. A. *J. Org. Chem.* **1979**, *44*, 4135−4140.

Scheme 2



decomposition of di-*tert*-butyltrisulfane 1,3-dioxide[18] was not observed to any extent under any of our experimental conditions.

The mechanism in Scheme 2 was suggested by Harpp[18] to explain the formation of di-*tert*-butyltrisulfane 1,1-dioxide from decomposition of the 1,3-dioxide precursor and could also be invoked in this case to provide an explanation for formation of the 1,1-dioxide as the major product from decomposition of (*p*-methoxyphenyl)trisulfane 1,3-dioxide. (See, however, oxidation of the trisulfane 2-oxide; *vide infra*.) Similar rearrangements have been convincingly demonstrated to occur during decompositions of disulfane 1,2-dioxides.[26]

Oxidation of Bis(*p*-methoxyphenyl)trisulfane 2-Oxide. Oxidations of the trisulfane 2-oxide with DMD in acetone or in acetone/CH_2Cl_2 and with TFD in acetone/trifluoroacetone or in CH_2Cl_2/trifluoroacetone solvent mixtures at room temperature resulted in formation of the bis(*p*-methoxyphenyl)disulfane (peak g) and trisulfane (peak c) as the overwhelming products (Figure 3a). A small amount of bis(*p*-methoxyphenyl)disulfane 1,1-dioxide (peaks e), the tetrasulfane (peak f), and decomposition products of trisulfane 1,1,3-trioxide (peaks u), along with residual trisulfane 2-oxide (peak k), were also detected in the reaction mixtures in acetone, benzene, CH_2Cl_2, and anhydrous diethylether. In all these solvents the disulfane appeared to form in slight excess of the trisulfane. A complete and clean conversion of the trisulfane 2-oxide to the di- and trisulfanes was never achieved since these products are more easily oxidized than the starting material. However, in several solvents, 1 equiv of dioxirane resulted in both complete decomposition of the trisulfane 2-oxide and formation of overoxidation products. (Figure 3b).

Initial attempts to identify reactive intermediates responsible for the formation of the di- and trisulfanes using DMD as the oxidant at low temperatures failed as a result of its low reactivity. Fortunately, the more potent oxidant TFD reacted with the trisulfane 2-oxide even at −80 °C (Figure 3c). To our surprise, however, the disulfane (peak g) was the only product observed at these low temperatures.

Discussion

The oxidized derivatives of bis(*p*-methoxyphenyl)trisulfane appear to be considerably less stable than the oxidized derivatives of di-*tert*-butyltrisulfane. Nevertheless, several primary oxidation products are still observable. Bis(*p*-methoxyphenyl)trisulfane 1-oxide is stable for nearly 5 h at room temperature, and the trisulfane 1,3-dioxide (**4**, R = *p*-MeOPh−) can be seen at −20 °C but decomposes as the sample is warmed to room temperature. Only in the case of bis(*p*-methoxyphenyl)trisulfane 2-oxide were we unable to detect a primary oxidation product.

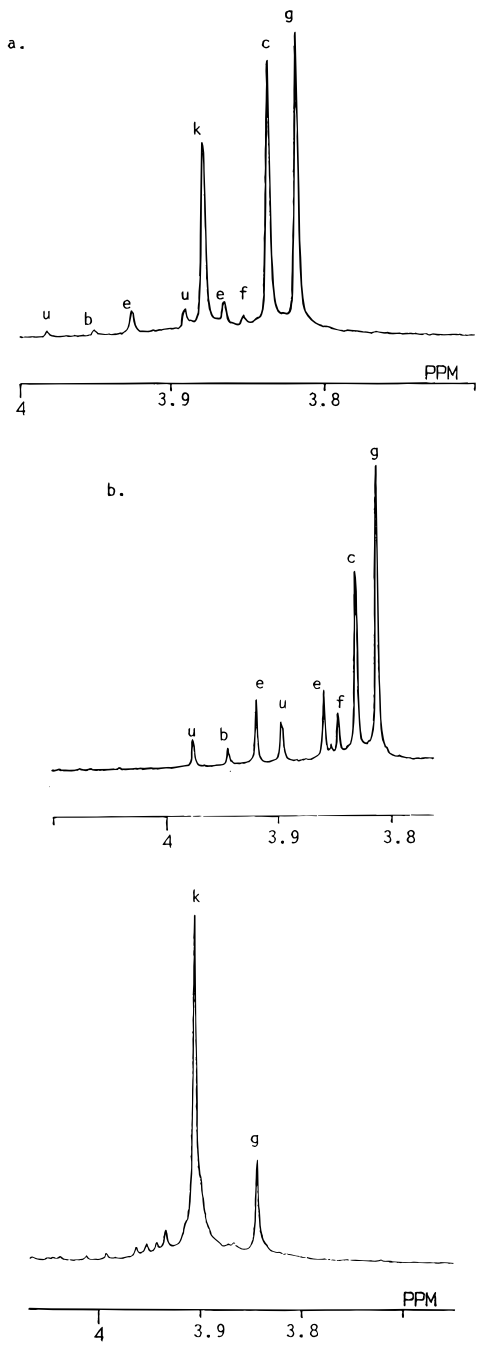
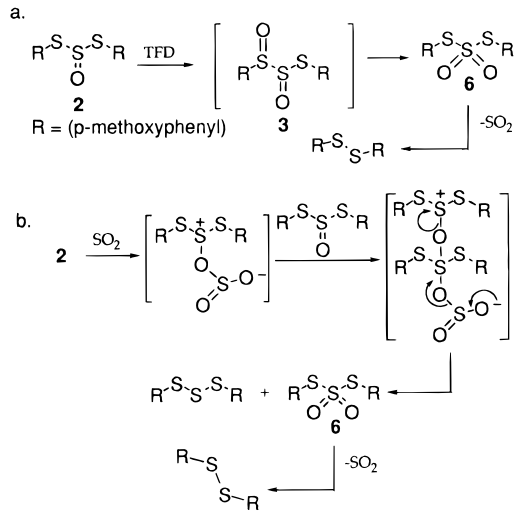


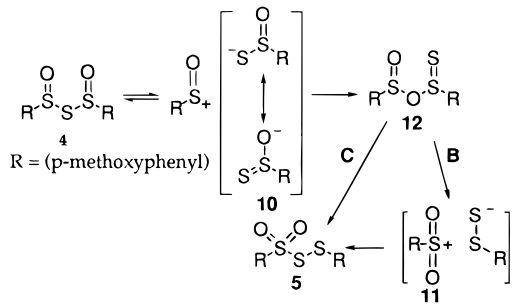
Figure 3. (a) ^{1}H NMR of the methoxy region at room temperature of a sample of the trisulfane 2-oxide that had been treated with 1.0−1.5 equiv of TFD in methylene chloride. Key: (b) trisulfane 1,1-dioxide; (c) trisulfane; (e) disulfane-1,1-dioxide; (f) tetrasulfane; (k) trisulfane 2-oxide; (g) disulfane; (u) unknown. (b) ^{1}H NMR of the methoxy region at room temperature of a sample of the trisulfane 2-oxide that had been treated with 1 equiv of DMD in benzene. Key: (b) trisulfane 1,1-dioxide; (c) trisulfane; (e) disulfane-1,1-dioxide; (f) tetrasulfane; (g) disulfane; (u) unknown. (c) ^{1}H NMR of the reaction of TFD with the trisulfane 2-oxide at −80 °C. Key: (g) disulfane; (k) trisulfane 2-oxide.

Reaction of the trisulfane 2-oxide (**2**, R = *p*-MeOPh−) at low temperature with TFD to form the disulfane is consistent with oxidation to give the trisulfane 1,2-dioxide (**3**, R = *p*-MeOPh−) followed by rearrangement to the trisulfane 2,2-dioxide (**6**, R = *p*-MeOPh−) and loss of SO_2 (Scheme 3a). At room temperature, however, we suggest that the results can be rationalized by the SO_2-catalyzed decomposition of the trisulfane 2-oxide by the route

Scheme 3



Scheme 4



similar to that proposed by Field and Lacefield[28] (Scheme 3b). We have independently demonstrated that this catalysis with the *p*-methoxyphenyl derivative is effective at room temperature but does not occur at an appreciable rate at −40 °C. These results preclude low-temperature formation of the catalyzed products as experimentally observed. In addition, the operation of the catalyzed route also provides an explanation why 1 equiv of dioxirane at room temperature is capable of completely decomposing the trisulfane 2-oxide and producing over-oxidation products.

The proposed key intermediate in the formation of both the trisulfane 1,1-dioxide (Scheme 2) and the trisulfane 2,2-dioxide (Scheme 3a) at low temperatures is the trisulfane 1,2-dioxide. Either these key intermediates are diastereomers, which we feel is unlikely, or one of the two mechanisms (Scheme 2 or 3) is wrong.[29] The key intermediate, **10**, in Scheme 2 is an ambident nucleophile that is unlikely to attack with either the nucleophilic sulfur or oxygen at the electron-rich oxygen atom of the sulfinyl cation as shown in step **A**. An alternative mechanism to explain the formation of the trisulfane 1,1-dioxide from the trisulfane 1,3-dioxide is shown in Scheme 4. This mechanism invokes a more palatable attack of nucleophile **10** at the more electron-deficient

(28) Field, L.; Lacefield, W. B. *J. Org. Chem.* **1966**, *31*, 3555−3561.
(29) (Trifluoromethyl)methyldioxirane (TFD) has a tendency to give more sulfone than observed in reactions of dimethyldioxirane (DMD). A mechanism to explain the excess sulfone formation that invokes a sulfurane intermediate has been suggested. Asensio, G.; Mello, R.; González-Núñez, M. E. *Tetrahedron Lett.* **1996**, *37*, 2299−2302. Consequently, it is conceivable that TFD reacts via a different mechanism than DMD. However, we consider this unlikely because at room temperature where the two reagents can be compared directly the oxidations of the trisulfane 2-oxide gave identical product mixtures.

center in the sulfinyl cation to either return to starting material or to give intermediate **12**. A potential drawback to the mechanistic scenario depicted in Scheme 4 is the formation of the electronically destabilized sulfonyl cation **11** in step **B**. The formation of this energetically costly intermediate, however, could be circumvented by a four-centered direct conversion of **12** to the trisulfane 1,1-dioxide (step **C**). On the other hand, the possibility that oxidation occurs at the oxidized sulfur in **2** completely bypassing formation of the trisulfane 1,2-dioxide to give directly the trisulfane 2,2-dioxide, **6** (Scheme 3a) cannot be unambiguously eliminated from consideration.

Experimental Section

General Aspects. Proton and carbon NMR were obtained either on a 270 or 400 MHz NMR and are referenced internally to TMS. Melting points were taken in open capillaries on a Thomas-Hoover melting point apparatus and are uncorrected. Silica gel chromatography was carried out on silica gel 60 PF_{254} purchased from EM Science. Combustion analysis was obtained from Atlantic Microlabs, Inc., in Norcross, GA. IR analysis was obtained on a Perkin-Elmer 1600 Series FTIR.

Oxone ($2KHSO_5$, $KHSO_4$, K_2SO_4), sulfur dioxide (lecture bottle), thioanisole (99%), 4-methoxybenzenethiol (97%), *m*-chloroperoxybenzoic acid (80−90%), sodium sulfide nonahydrate (98%), 4-methoxybenzenesulfonyl chloride (99%), ethylenediaminetetraacetic acid disodium salt dihydrate (99%), and sulfuryl chloride (97%), SO_2Cl_2, were obtained from Aldrich and used without further purification. Anhydrous potassium carbonate and sodium bicarbonate were purchased from J. T. Baker and used as received. Anhydrous diethyl ether (Mallinkrodt), anhydrous magnesium sulfate (Spectrum), and absolute ethanol (McCormick distilling Co., Inc.) were used as received. Sulfur dichloride, SCl_2, (Aldrich, 80% technical) was twice distilled under N_2 into a flask containing phosphorus pentachloride. Thionyl chloride, $SOCl_2$ (Aldrich, 97%), was refluxed over S_8, distilled, and redistilled over boiled linseed oil. Sulfur monochloride, S_2Cl_2 (Aldrich, 98%), was distilled at reduced pressure prior to use. Pyridine was purchased from Fisher and stored over potassium hydroxide. Dimethyl sulfoxide (Fisher Biotech.) was stirred over calcium hydride, distilled under reduced pressure, and stored under nitrogen over 4A sieves. Acetone (Spectrum) was refluxed over potassium permanganate, distilled, dried over potassium carbonate, filtered, and redistilled. (Storing purified acetone over molecular sieves is not recommended.) A mixture of hexanes (*n*-hexane, 2-methylpentane, 3-methylpentane, 2,3-dimethylbutane, methylcyclopentane, and 2,2-dimethylpentane (Fisher)) was dried over anhydrous calcium chloride, distilled, and stored over 4A sieves. Methylene chloride (J. T. Baker) was also dried over calcium chloride and distilled prior to use. Benzene (Spectrum) was refluxed over phosphorus pentoxide and distilled prior to use. 1,1,1-Trifluoroacetone (Acros, 98+%) was distilled at low temperature before use. Acetone-d_6, 99.9%, was purchased from Cambridge Isotope Laboratories.

Preparation of Dioxiranes. Dimethyldioxirane (DMD) and (trifluoromethyl)methyldioxirane (TFD) were prepared according to literature procedures.[30−32] These dioxiranes were stored at −20 °C and protected from light. The concentrations of the pale yellow solutions were determined by titration with thioanisole to its sulfoxide/sulfone and quantifying by ^{1}H NMR. The very reactive TFD was used immediately after preparation.

Preparation of Bis(*p*-methoxyphenyl)disulfane and Its Oxidized Derivatives. Bis(*p*-methoxyphenyl)disulfane was synthesized by a dimethyl sulfoxide oxidation[33] of *p*-methoxythiophenol in a 76% yield. Mp: 42.5−43.5 °C (lit.[34] mp 44−45 °C). ^{1}H NMR (acetone-d_6): δ 3.80 (s, 6H), 6.93 (m, 4H), 7.42 (m, 4H). ^{13}C NMR (acetone-d_6): δ 55.84, 115.74, 128.75, 133.39, 161.28.

Bis(*p*-methoxyphenyl)disulfane 1-oxide was prepared by oxidation of the disulfane with dimethyldioxirane. Purification (lit.[35] mp 96 °C) was achieved using a 2 mm silica gel plate on the chromatotron eluting with 3:2 hexanes/ethyl acetate. ^{1}H NMR (acetone-d_6): δ 3.87 (s, 3H), 3.90 (s, 3H), 7.01 (m, 2H), 7.13 (m, 2H), 7.44 (m, 2H), 7.63 (m, 2H). ^{13}C NMR (acetone-d_6): δ 55.97, 56.16, 115.44, 115.81, 121.32, 126.97, 136.62, 138.22, 162.84, 163.47.

Bis(*p*-methoxyphenyl)disulfane 1,1 dioxide was synthesized from the disulfane using 2 equiv of *m*-CPBA. Purification by chromatotron using a 2 mm silica gel plate (4:1 hexanes/ethyl acetate) produced white crystals. Mp: 89−89.5 °C (lit.[36] mp 92−94 °C). ^{1}H NMR (acetone-d_6): δ 3.85 (s, 3H), 3.91 (s, 3H), 6.96 (m, 2H), 7.06 (m, 2H), 7.26 (m, 2H), 7.50 (m, 2H). ^{13}C NMR (acetone-d_6): δ 56.05, 56.40, 115.08, 115.97, 119.72, 130.76, 135.77, 139.16, 163.49, 164.88.

Preparation of Bis(*p*-methoxyphenyl)trisulfane. Bis(*p*-methoxyphenyl) trisulfane was prepared according to Harpp's procedure.[37] The product was purified by recrystallization with hexanes and obtained in a 68% yield. Mp: 73−74 °C (lit.[5] mp 73−74 °C). ^{1}H NMR (acetone-d_6): δ 3.81 (s, 6H), 6.90 (m, 4H), 7.50 (m, 4H). ^{13}C NMR (acetone-d_6): δ 55.87, 115.79, 127.65, 134.82, 161.77.

Preparation of Bis(*p*-methoxyphenyl)tetrasulfane. A literature procedure[38] was followed producing a 98% yield of crystals with mp 54−56.5 °C (lit.[39] mp 56.5−58.5 °C). ^{1}H NMR (acetone-d_6): δ 3.84 (s, 6H), 6.98 (m, 4H), 7.53 (m, 4H). ^{13}C NMR (acetone-d_6): δ 55.93, 115.95, 127.31, 135.09, 162.11.

Preparation of Bis(*p*-methoxyphenyl)trisulfane 2-Oxide. The Field method[28] was followed, and the product was obtained in a 75% yield after recrystallization from 1:1 hexanes/methylene chloride. Mp: 94−97 °C (lit.[28] mp 101−101.5 °C). When further purification was necessary, the chromatotron was used with a 2 mm silica gel plate and 4:1 hexanes/ethyl acetate as eluant. ^{1}H NMR (acetone-d_6): δ 3.87 (s, 6H), 7.06 (m, 4H), 7.57 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 55.43, 115.03, 120.16, 138.08, 161.96.

Preparation of Bis(*p*-methoxyphenyl)trisulfane 1,1-Dioxide. A literature method[40] was used to prepare the *sodium thiosulfonate salt* (*p*-$MeOPhSO_2S^-Na^+$). After recrystallization with absolute ethanol, a 19% yield (not optimized) was obtained. Both IR and NMR data were consistent with formation of this salt. An *Organic Synthesis*[41] procedure was used to make *p*-methoxyphenylsulfenyl chloride. This dark, orange-red compound distilled at 2 mmHg (99−103 °C) in a 71% yield. Following a 1927 procedure,[42] the sodium thiosulfonate salt was first ground into a powder and then added to the *p*-methoxyphenylsulfenyl chloride, which was dissolved in anhydrous diethyl ether under a nitrogen atmosphere. After workup and recrystallization with hexanes, a 50.4% yield of clear crystals was collected. Mp: 59−61.5 °C. ^{1}H NMR (acetone-d_6): δ 3.83 (s, 3H), 3.95 (s, 3H), 6.89 (m, 2H), 7.12 (m, 2H), 7.46 (m, 2H), 7.87(m, 2H). ^{13}C NMR (acetone-d_6): δ 55.95, 56.48, 115.55, 115.84, 125.34, 131.36, 134.77, 135.30, 162.18, 165.47. IR: (KBr) 1138, 1324 cm^{-1} (SO_2 stretching).

(30) Adam, W.; Bialas, J.; Hadjiarapoglou, L. *Chem. Ber.* **1991**, *124*, 2377.
(31) Mello, R.; Fiorentino, M.; Sciacovelli, O.; Curci, R. *J. Org. Chem.* **1988**, *53*, 3890−3891.
(32) Mello, R.; Fiorentino, M.; Fusco, C.; Curci, R. *J. Am. Chem. Soc.* **1989**, *111*, 6749−6757.
(33) Yiannios, C. N.; Karabinos, J. V. *J. Org. Chem.* **1963**, *28*, 3246−3248.
(34) Fehér, F.; Kurz, D. *Z. Naturforsch.* **1968**, *23b*, 1030−1033.
(35) Vinkler, E.; Klivenyi, F. *Acta Chim. Acad. Sci.* **1957**, *11*, 15−22.
(36) Palumbo, G.; Caputo, R. *Synthesis* **1981**, *11*, 888−890.
(37) Harpp, D. N.; Smith, R. A. *J. Org. Chem.* **1979**, *44*, 4140−4144.
(38) Derbesy, G.; Harpp, D. N. *Tetrahedron Lett.* **1994**, *35*, 5381−5384.
(39) Kawamura, S.; Horii, T.; Tsurugi, J. *J. Org. Chem.* **1971**, *36*, 3677−3680.
(40) Mintel, R.; Westley, J. *J. Biol. Chem.* **1966**, *241*, 3381−3385.
(41) Barrett, A. G. M.; Dhanak, D.; Graboski, G. G.; Taylor, S. J. In *Organic Synthesis*; White, D., Ed.; John Wiley & Sons: New York, 1989; Vol. 68; pp 8−13.
(42) Brooker, L. G. S.; Child, R.; Smiles, S. *J. Chem. Soc.* **1927**, 1384−1388.

Anal. Calcd for $C_{14}H_{14}O_4S_3$: C, 49.10; H, 4.12; S, 28.09. Found: C, 49.17; H, 4.20; S, 27.99.

General Trisulfane Dioxirane Oxidation Procedures. Room-temperature reactions were carried out by adding 0.2−3.0 equiv amounts of dioxirane to 0.10 mmol of the trisulfane dissolved in 2 mL of acetone (0.05 M). The mixture was stirred from 2 to 24 h in the dark. The solvent was removed under reduced pressure followed by dissolution into an NMR tube. Acetone-d_6 was employed as the NMR solvent as it afforded the best separation of peaks in the spectra.

Low-temperature reactions were carried out by dissolving 0.02 mmol (0.037 M) of trisulfane in a 4 mm NMR tube containing acetone-d_6, cooling the NMR to −30 °C in 20 °C intervals while tuning the probe on the sample, ejecting the sample, quickly adding the dioxirane (within 15 s), followed by immediate acquisition (16 transients). The temperature was then raised at 10 °C intervals, and the spectra were observed.

NMR Rate Measurements. Rates were calculated by measuring the disappearance of the 1-oxide as a function of time at room temperature using ^{1}H NMR. The spectra were cut and weighed to determine the decrease in the amount of the 1-oxide.

General Trisulfane 2-Oxide Dioxirane Oxidation Procedures. Room-temperature DMD reactions were carried out by adding 0.2−1.0 equiv amounts of dioxirane to 0.05 M of the trisulfane 2-oxide dissolved in various solvents (benzene, ether, acetone, methylene chloride). The mixture was stirred from 2−24 h in the dark. The solvent was removed under reduced pressure followed by dissolution into an NMR tube.

Room-temperature TFD reactions were carried out by adding 0.2−1.0 equiv of dioxirane to 0.003 M of the trisulfane 2-oxide dissolved in acetone or methylene chloride. The mixture was stirred from 2 to 24 h in the dark. The solvent was removed under reduced pressure followed by dissolution into an NMR tube.

Low-temperature TFD reactions were carried out by dissolving 0.05 M trisulfane 2-oxide in a 4 mm NMR tube containing acetone-d_6. Both the TFD and 2-oxide were maintained at −78 °C in a Dewar. TFD (0.5 equiv) was added to the tube and immediately placed in the NMR at −80 °C. The solution turned a deep yellow color upon TFD addition. The temperature was then raised at 20 °C intervals, and the spectra observed.

Low-temperature DMD reactions were attempted by adding 1 equiv of DMD to the trisulfane 2-oxide at −78, −43, and −29 °C for at least 24 h. In each case, the reaction was very sluggish with mainly starting material appearing in the NMR spectrum.

Sulfur Dioxide Catalysis of Bis(*p*-methoxyphenyl)-trisulfane 2-Oxide. Approximately 1 equiv of SO_2 (bp −10 °C) was condensed into a mixture of 0.03 mmol of 2-oxide and 2 mL of acetone. This was stirred for 24 h with a −42 °C (CH_3-CN/dry ice) condensor attached. Only minimal decomposition was observed. The sample was then allowed to stand at room temperature for 24 h. Total decomposition did not occur, but a 65% conversion to disulfane and trisulfane in a 1:1 ratio was observed. A purified 2-oxide sample was stored in the freezer (−20 °C) for 2 months with no added SO_2, and only 50% of the starting material had decomposed to disulfane and trisulfane.

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