# Regiochemical and Stereochemical Studies on Halogen-Induced Ring Expansions of Unsaturated Episulfides

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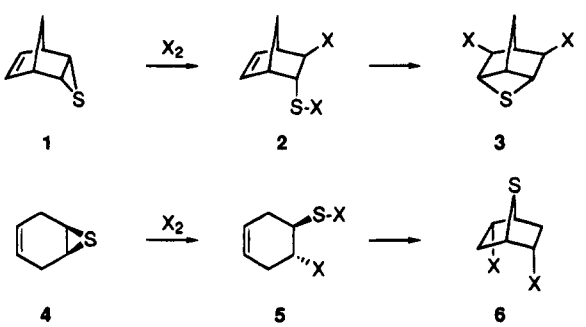
The reactions of unsaturated episulfides with bromine and iodine have been studied. Initially produced in the reaction is a ring-opened sulfenyl halide intermediate, which in the presence of the carbon–carbon double bond or triple bond cyclizes to β,β′-dihalo sulfide cycloadducts. The regiochemistry and relative stereochemistry of these cyclizations have been examined as a function of the length of the tether between the episulfide moiety and the unsaturated functionality, the presence of alkyl substituents, and the type of unsaturation. A discussion of the mechanistic and stereochemical features of the ring-expansion process is presented.

## Introduction

Neighboring group participation by a heterosubstituent at a remote reaction center is a well-known phenomenon that generally enhances the reactivity and stereoselectivity of certain classes of reactions. The rate accelerations and stereochemical effects associated with these intramolecular processes are usually most prevalent when the heteroatom is a sulfur or selenium atom.[1] Under appropriate conditions, the heterosubstituent may add intramolecularly to suitably-positioned sites of unsaturation.[2] Recent studies in our laboratories have focused on the regio- and stereochemical aspects of one such class of addition reactions, the halogen-promoted cyclizations of unsaturated sulfides, which produce five- and six-membered β-functionalized sulfur rings by a process involving the addition of a *nucleophilic* sulfur group to an electrophilically-activated olefin (or acetylene) π-complex.[3] During the course of these investigations, we became interested in sulfur cyclizations whose electronic flow is formally in the reverse direction, namely, by the addition of an *electrophilic* sulfur species to a nucleophilic olefin. Most of the sulfur cyclizations reported in the literature involve the initial generation of an unsaturated sulfenyl halide intermediate, upon either addition of $SCl_2$ to a nonconjugated diene, halogenation of an alkenyl disulfide, or halogenative ring-opening[4] of an unsaturated episulfide.[5–14] Lautenschlaeger was the first to demonstrate the utility of this latter method in the chlorine-promoted transannulation of episulfide **1** to adduct **3**.[9] McCabe and colleagues later showed that the halogenation reactions of unsaturated episulfides **1** and **4** to give bridged compounds **3** and **6** take place through the intermediacy of sulfenyl halides **2** and **5** (or their disulfides) and that the bromination of episulfide **7** leads to the isolation of regioadducts **9** and **10** in 94% combined yield.[10] In this example, products **9** and **10** presumably arise from cyclizations of sulfenyl halides **8** and **11** (regioadduct **12** is not observed) (Scheme 1).[10a]

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(2) Bartlett, P. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1984; Volume 3, Chapter 6, pp 342–404.

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(4) The reaction of halogens with epoxides and episulfides typically gives products derived from electrophilic opening of the three-membered ring. For studies on halogenation reactions of epoxides, see: (a) Konaklieva, M. I.; Dahl, M. L.; Turos, E. *Tetrahedron Lett.* **1992**, *33*, 7093. (b) Neill, D.; Thomas, S. E. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2620. (c) Rodriquez, J.; Dulcere, J. P.; Bertrand, M. *Tetrahedron Lett.* **1983**, *24*, 4423. (d) Movsumzade, M. M.; Sidakova, G. A.; Shabanov, A. L.; Kyazimov, A. S. *Izv. Vyssh. Uchebu. Zaved., Khim. Khim. Tekhnol.* **1976**, *19*, 558; *Chem. Abstr.* **1976**, *85*, 62744j. (e) Movsumzade, M. M.; Sergeev, G. B.; Shabanov, A. L.; Smirnov, V. V. *Chem. Abstr.* **1975**, *83*, 27198w. (f) Movsumzade, M. M.; Shabanov, A. L. *Chem. Abstr.* **1975**, *83*, 205287j. (g) Movsumzade, M. M.; Sergeev, G. B.; Shabanov, A. L.; Smirnov, V. V. *Dokl. Akad. Nauk SSSR* **1972**, 206; *Chem. Abstr.* **1973**, *78*, 3464a. (h) Movsumzade, M. M. *Uch. Zap. Azerb. Inst. Nefti. Khim.* **1971**, *9*, 52; *Chem. Abstr.* **1972**, *77*, 101299z. (i) Movsumzade, M. M.; Shabanov, A. L.; Movsumzade, S. M.; Gurbanov, P.A. *Zh. Org. Khim.* **1971**, *7*, 412; *Chem. Abstr.* **1971**, *74*, 111626f. (j) Movsumzade, M. M.; Shabanov, A. L.; Movsumzade, S. M.; Gurbanov, P. A. *Zh. Org. Khim.* **1971**, *7*, 1106; *Chem. Abstr.* **1971**, *75*, 109910w. (k) Movsumzade, M. M.; Shabanov, A. L.; Movsumzade, S. M.; Gurbanov, P.A. *Zh. Org. Khim.* **1971**, *7*, 1109; *Chem. Abstr.* **1971**, *75*, 109911x. (l) Movsumzade, M. M.; Shabanov, A. L.; Gurbanov, P. A.; Movsumzade, S. M. *Zh. Org. Khim.* **1971**, *7*, 1373; *Chem. Abstr.* **1971**, *75*, 129059d. (m) Movsumzade, M. M.; Shabanov, A. L.; Kyazimov, A. S.; Gurbanov, P. A. *Dokl. Akad. Nauk SSSR* **1970**, 26; *Chem. Abstr.* **1971**, *74*, 111624d. (n) Movsumzade, M. M.; Shabanov, A. L.; Gurbanov, P. A. *Tr. Azerb. Inst. Nefti Khim.* **1969**, 11; *Chem. Abstr.* **1971**, *74*, 111816t. (o) Movsumzade, M. M.; Shabanov, A. L.; Gurbanov, P. A. *Tr. Azerb. Inst. Nefti Khim.* **1969**, 7; *Chem. Abstr.* **1971**, *75*, 19463y. (p) Movsumzade, M. M.; Shabanov, A. L.; Petrova, N. V. *Tr. Azerb. Inst. Nefti Khim.* **1969**, 28; *Chem. Abstr.* **1971**, *74*, 41829y. (q) Movsumzade, M. M.; Gurbanov, P. A.; Shabanov, A. L.; Beibutora, S. S. *Azerb. Khim. Zh.* **1969**, 58; *Chem. Abstr.* **1969**, *71*, 80771f. For studies on halogenation reactions of episulfides, refer to: (r) Helmkamp, G. K.; Pettitt, D. J. *J. Org. Chem.* **1962**, *27*, 2942. (s) Stewart, J. M.; Cordts, H. P. *J. Am. Chem. Soc.* **1952**, *74*, 5880. (t) For a comprehensive review on the chemistry of episulfides, see: Livingstone, R. Compounds With Three- and Four-Membered Heterocyclic Rings. In *Heterocyclic Compounds*; Coffey, S., Ed.; Wiley: New York, 1975; Vol. IVA, Chapter 1.

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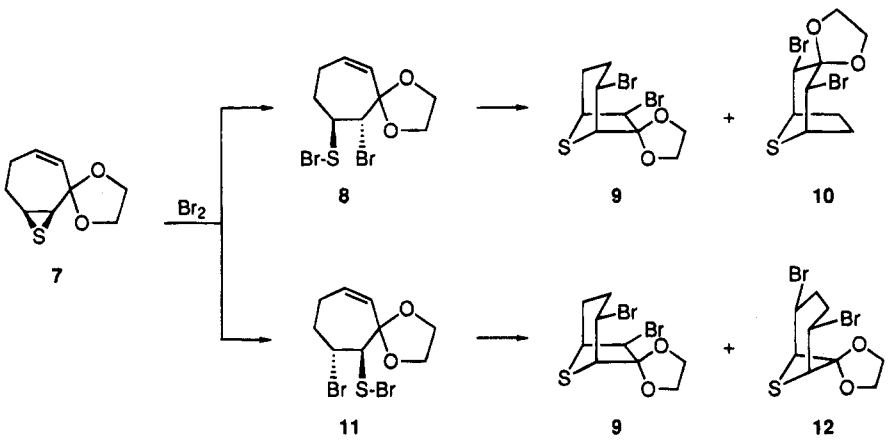
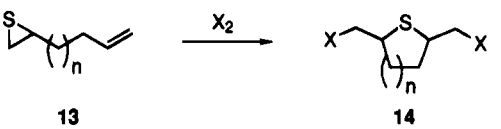
**Scheme 1**




The high yields and stereochemical control associated with these episulfide halocyclizations prompted us to explore the potential utility[15] of this methodology for the synthesis of various-sized sulfur heterocycles having reactive functionality at the $\beta$- and $\beta'$-positions. In this study, we have examined the regiochemical and stereochemical features of these halogen-promoted reactions using *conformationally flexible* unsaturated episulfides **13** as substrates. Our primary concern was to address the factors which control the regiochemistry and relative stereochemistry of the cyclizations and to gain a better mechanistic understanding of the ring expansion process itself.




**General Procedure for the Halogen-Induced Episulfide Ring Expansions.** The episulfides examined in these studies were prepared by stirring the corresponding unsaturated epoxide with thiourea in methanol. The halogenation reactions were carried out by treatment of the unsaturated episulfide with 1 molar equiv of either $Br_2$ or $I_2$ in $CH_2Cl_2$ or $CDCl_3$ solution at room temperature. Due to the lability and difficulty in purifying some of the $\beta,\beta'$-dihalo sulfide adducts produced in the halogenation reactions, the crude product mixtures were treated directly with *m*-chloroperbenzoic acid (*m*-CPBA) to convert the cyclic sulfides to their sulfones. The regiochemistry and stereochemistry of the dihalo sulfide and dihalo sulfone adducts were determined primarily from their $^1H$ and $^{13}C$ NMR spectra. For two of the sulfone adducts (**19a** and **33**) these structural assignments were confirmed by X-ray crystallography.[31] For the *iodination* reactions of the alkenyl episulfide substrates, the diiodo sulfides initially produced in the reaction were quite reactive and, upon *m*-CPBA oxidation, typically yielded mixtures of the dihalo sulfones, monohalo vinyl sulfones, and divinyl sulfones. The rate of HI elimination from these dihalo sulfones depends on the location of the iodide (endocyclic or exocyclic) with respect to the ring, an observation that allowed us to more confidently assign regiochemistry of the cycloadducts.[14] Thus, those sulfones having a $\beta$-iodide exocyclic

(5) Examples of reactions between nonconjugated dienes with $SCl_2$: (a) Lautenschlaeger, F. *J. Org. Chem.* **1969**, *34*, 3998. (b) Lautenschlaeger, F.; Schwartz, N. V. *J. Org. Chem.* **1969**, *34*, 3991. (c) Lautenschlaeger, F. *J. Org. Chem.* **1966**, *31*, 1679. (d) Corey, E. J.; Block, E. *J. Org. Chem.* **1966**, *31*, 1663. (e) Weil, E. D.; Smith, K. J.; Gruber, R. J. *J. Org. Chem.* **1966**, *31*, 1669. (f) Mueller, W. H.; *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 482. (g) Mueller, W. H. *J. Am. Chem. Soc.* **1969**, *91*, 1223.

(6) Generation of unsaturated sulfenyl halide intermediates from disulfides: (a) Ikegami, S.; Asai, T.; Tsuneoka, K.; Matsumura, S.; Akaboshi, S. *Tetrahedron* **1974**, *30*, 2087 and references cited therein. (b) Reike, R. D.; Bales, S. E.; Roberts, L. C. *J. Chem. Soc., Chem. Commun.* **1972**, 974.

(7) (a) Leroy, C.; Martin, M.; Bassery, L. *Bull. Soc. Chim. Fr.* **1974**, 590. (b) Ikegami, S.; Ohishi, J.-i.; Shimizu, Y. *Tetrahedron Lett.* **1975**, *45*, 3923.

(8) Sulfur ring closures in thiaprostacyclin syntheses: (a) Nicolaou; K. C.; Barnette; W. E.; Magolda, R. L. *J. Am. Chem. Soc.* **1981**, *103*, 3472. (b) Nicolaou, K. C.; Barnette, W. E.; Magolda, R. L. *J. Am. Chem. Soc.* **1981**, *103*, 3480. (c) Nicolaou, K. C.; Barnette, W. E.; Magolda, R. L. *J. Am. Chem. Soc.* **1981**, *103*, 3486. (d) Nicolaou, K. C.; Barnette, W. E.; Magolda, R. L. *J. Chem. Soc., Chem. Commun.* **1978**, 375. (e) Nicolaou, K. C.; Barnette, W. E.; Gasic, G. P.; Magolda, R. L. *J. Am. Chem. Soc.* **1977**, *99*, 7736. (f) Shibasaki; M.; Ikegami, S. *Tetrahedron Lett.* **1978**, 559.

(9) Lautenschlager, F. *J. Org. Chem.* **1968**, *33*, 2620.

(10) (a) McCabe, P. H.; Stewart, A. *J. Chem. Soc., Chem. Commun.* **1980**, 100. (b) McCabe, P. H.; Livingston, C. M.; Stewart, A. *J. Chem. Soc., Chem. Commun.* **1977**, 661.

(11) Sulfur cyclizations applied to the construction of the biotin core: (a) Confalone, P. N.; Pizzolato, G.; Baggiolini, E. G.; Lollar, D.; Uskokovic, M. R. *J. Am. Chem. Soc.* **1975**, *97*, 5936. (b) Turos, E.; Parvez, M.; Garigipati, R. S.; Weinreb, S. M. *J. Org. Chem.* **1988**, *53*, 1116. (c) Fujisawa, T.; Nagai, M.; Koike, Y.; Shimizu, M. *J. Org. Chem.* **1994**, *59*, 5865 and references cited.

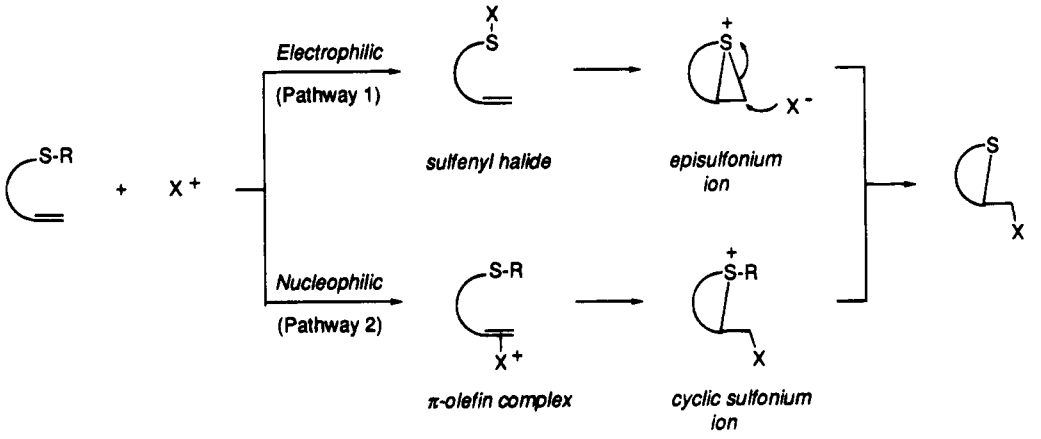
(12) Thioether cyclizations: (a) Bernett, R. G.; Doi, J. T.; Musker, W. K. *J. Am. Chem. Soc.* **1985**, *50*, 2048. (b) Rengevich, E. N.; Staninets, V. I.; Shilov, E. A. *Dokl. Akad. Nauk SSSR* **1962**, *146*, 111; *Dokl. Akad. Nauk SSSR (Engl. Transl.)* **1962**, *146*, 787; *Chem. Abstr.* **1963**, *58*, 3285f.

(13) Cyclizations of unsaturated thioamides and thioureas in which sulfur acts as the nucleophile generally give the 5-*exo-trig* ring closure product. For examples and exceptions, see: (a) Engman, L. *J. Org. Chem.* **1991**, *56*, 3425. (b) Creeke, P. I.; Mellor, J. M. *Tetrahedron Lett.* **1989**, 4435. (c) H. Takahata; T.; Yamazaki *Heterocycles* **1988**, *27*, 1953. (d) Takahata; H.; Suzuki, T.; Maruyama, M.; Moriyama, K.; Mozumi, M.; Takamatsu, T.; Yamasaki, T. *Tetrahedron* **1988**, *44*, 4777. (e) Tamaru, Y.; Mizutani, M.; Furukawa, S.; Kawamura, S.; Yoshida, Z.; Yanagi, K.; Minobe, M. *J. Am. Chem. Soc.* **1984**, *106*, 1079. (f) McManus, S. P.; Ware, D. W.; Hames, R. A. *J. Org. Chem.* **1978**, *43*, 4288. (g) Lown, J. W.; Joshua, A. V. *Can. J. Chem.* **1977**, *55*, 122. (h) Lown, J. W.; Joshua, A. V. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2680. (i) Smith, P. A. S.; Sullivan, J. M. *J. Org. Chem.* **1961**, *26*, 1132.

(14) For examples of related sulfur cyclizations, see: (a) Hutchinson, J. H.; McEachern, E. J.; Scheigetz, J.; Macdonald, D.; Therien, M. *Tetrahedron Lett.* **1992**, *33*, 4713. (b) Eichinger, K.; Mayr, P.; Nussbaumer, P. *Synthesis* **1989**, 210. (c) Kitamura, T.; Takachi, T.; Kawasato, H.; Kobayashi, S.; Taniguchi, H. *Tetrahedron Lett.* **1989**, *30*, 7445. (d) Kitamura, T.; Kawasato, H.; Kobayashi, S.; Taniguchi, H. *Chem. Lett.* **1986**, 399. (e) Wilder, P.; Feliu-Otero, L. A. *J. Org. Chem.* **1966**, *31*, 4264. (f) Wilder, P.; Feliu-Otero, L. A. *J. Org. Chem.* **1965**, *30*, 2560.

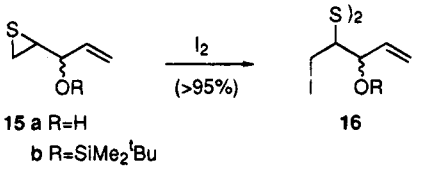
(15) In a formal sense, these ring-expansions are related to those of unsaturated epoxides reported by: (a) Padron; J. I.; Vasquez, J. T.; Morales, E. Q.; Zarraga, M.; Martin, J. D. *Tetrahedron: Asymmetry* **1992**, *3*, 415. (b) Zarraga, M.; Rodriquez, M. L.; Ruiz-Perez, C.; Martin, J. D. *Tetrahedron Lett.* **1989**, *30*, 3725. (c) Alvarez, E.; Manta, E.; Martin, J. D.; Rodriquez, M. L.; Ruiz-Perez, C. *Tetrahedron Lett.* **1988**, *29*, 2093. (d) Alvarez, E.; Manta, E.; Martin, J. D.; Rodriquez, M. L.; Ruiz-Perez, C.; Zurita, D. *Tetrahedron Lett.* **1988**, *29*, 2097. (e) Davies, S. G.; Polywka, M. E. C.; Thomas, S. E. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1277.

**Scheme 2**



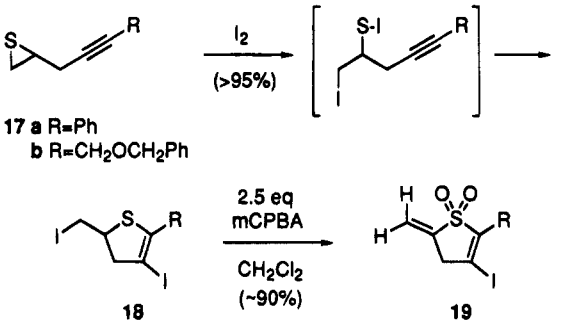

to the ring undergo spontaneous elimination, while those having the iodide directly attached to the ring can be easily isolated after column chromatography.

We began our studies by examining the reaction of $I_2$ with homoallylic episulfides **15**, prepared as diastereomeric mixtures. The only iodination products obtained from the reactions are disulfide adducts **16**, which do not undergo cyclization. McCabe has reported similar findings in attempts to effect the iodocyclizations of a structurally related cyclic analogue of disulfide **16**, which failed to give the product of iodocyclization.[10a]



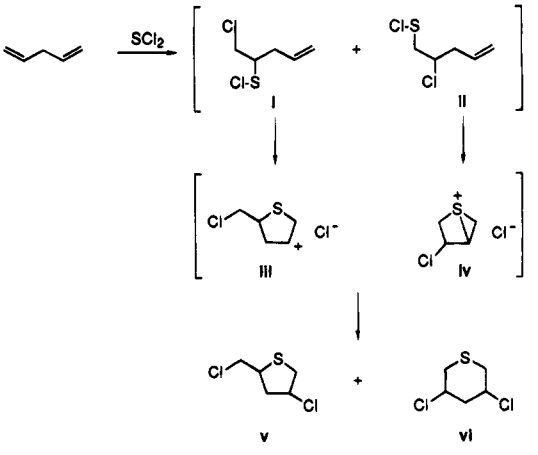

The fact that disulfides **16** are obtained in these reactions rather than the expected[5] cyclization products was somewhat surprising, given the results of our previous studies on the halocyclization reactions of unsaturated benzyl sulfides, in which 3-butenyl sulfides were found to undergo facile *5-endo-trig* cyclization[16] to afford the five-membered ring adducts in high yield.[3a] The resistance of the *sulfenyl halides* generated from episulfides **15** to cyclize in *5-endo* fashion[17] may simply reflect the different conformational requirements for the halocyclizations of the sulfenyl halides versus those of the sulfides. Sulfenyl halide cyclizations are believed to occur by electrophilic addition to the double bond, giving an episulfonium intermediate[18] that ultimately is cleaved to the $\beta$-halo sulfide adduct (pathway 1, Scheme 2). For substrates having short tethers (less than three carbons), the formation of this bicyclic species may be relatively difficult due to the strain of the fused rings. Conversely, the cyclizations of the unsaturated *sulfides* occur by nucleophilic addition to a $\pi$-olefin complex, as shown in pathway 2, yielding a monocyclic sulfonium ion whose formation is less constrained by the short tether.

In contrast, we have found that homo*propargylic* episulfides **17** react cleanly with $I_2$ to afford high yields of the five-membered ring cycloadducts **18**. In an attempt to observe the formation of disulfide intermediates or disulfide products, we followed these reactions by $^1H$ NMR. However, we failed to detect the buildup of these intermediates, even when the halogen is added in small portions over several hours, suggesting that the cyclization of the initially-formed sulfenyl halide intermediate must occur much more rapidly than dimerization.[4r,s] Peracid oxidation of iodoadducts **18** yields the cross-

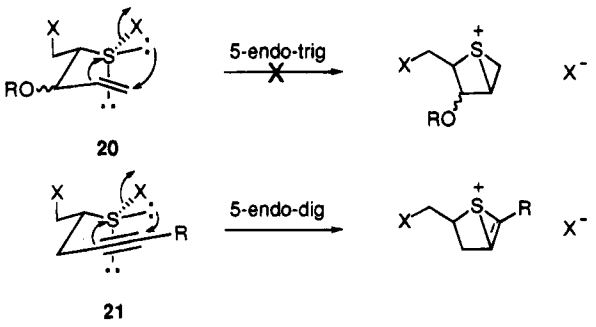



(16) (a) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734. (b) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 736. (c) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 738.

(17) There does appear to be precedent for *5-endo-trig* cyclizations of sulfenyl halides that lack the α-hydroxy substituent. Lautenschlaeger reported that the reaction of 1,4-pentadiene with $SCl_2$ gives a 65:35 mixture of five- and six-membered ring products in 39% yield (ref 9). To account for the formation of the five- membered ring adduct, the author postulates a *5-endo-trig* sulfenyl chloride ring closure from sulfenyl chloride **ii** as a major pathway leading to this product. In his discussion, Lautenschlaeger points out that this route would most likely require the formation of a secondary carbocation **iii** (rather than an episulfonium ion), which to us seems unlikely and unnecessary since the formation of both **v** and **vi** can occur by ring closure of the isomeric sulfenyl halide **ii** through episulfonium intermediate **iv**. Also, Vedejs has executed an acid-promoted *5-endo-trig* ring closure of a sulfenyl acetate onto a conjugated diene, in which the high stereochemical control observed in the reaction is strongly suggestive of an episulfonium intermediate. (a) Vedejs, E.; Buchanan, R. A.; Conrad, P. C.; Meier, G. P.; Mullins, M. J.; Schaffhausen, J. G.; Schwartz, C. E. *J. Am. Chem. Soc.* **1989**, *111*, 8421. (b) Vedejs, E.; Mullins, M. J. *J. Org. Chem.* **1979**, *44*, 2947.



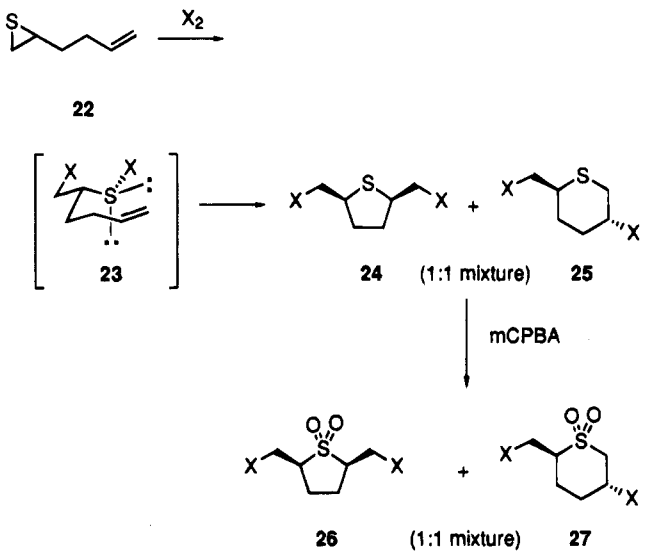
conjugated vinyl sulfones **19** in excellent yield. The exocyclic olefin of **19** is easily recognized in the $^1$H NMR spectrum from the distinctly different chemical shifts and narrow splitting patterns for the two geminal vinyl protons.[19] Furthermore, the structure of **19a** was confirmed by single-crystal X-ray analysis. The remarkable facility in which these ring expansions proceed for the *alkynyl* episulfides **17** compared to the alkenyl substrates is may be due to better stereoelectronic alignment of the sp orbitals with the sulfur lone pair (see **21**) compared to that for the sp$^2$ system (see **20**) perhaps as a result of torsional strain between the $CH_2X$ and OR groups present in intermediate **20**.




**20** **21**

Upon extending the alkyl tether of the alkenyl sulfide by an additional carbon unit, as shown for substrate **22**, we found that the bromocyclization reaction proceeds cleanly to give equimolar amounts of the five-membered and six-membered ring products. The structures and ratios of adducts **24** and **25** were determined from the $^1$H NMR spectrum of the crude reaction mixture. By monitoring the reaction by $^1$H NMR, we confirmed that adducts **24** and **25** appear to be formed at equal rates, perhaps as a result of a rapid equilibrium via a common episulfonium ion. Oxidation of this mixture with *m*-CPBA affords sulfones **26** and **27** as a 1:1 mixture after column chromatography. This result is in accord with the earlier findings of Cerny and Hora who reported that treatment of diol **24** (X = OH) with hydrochloric acid gives a mixture of dichlorides **24** and **25** (X = Cl).[20] Ikegami and colleagues described similar behavior for cyclizations of 4-pentenylsulfenyl chlorides, generated by the *in situ* chlorination of 4-pentenyl disulfide, which give mixtures of the five- and six-membered ring chloro sulfides.[6a] These authors observe that a 4:1 mixture of the five-:six-membered rings is obtained when the reaction is carried out at −30 °C, but upon warming to room temperature, this mixture equilibrates via an episulfonium intermediate to favor the 3-chlorothiopyran ring. On the other hand, Lautenschlaeger reported that the chlorination of **22** gives *exclusively* the five-membered ring sulfide **24** (X = Cl) in 66% yield, but that the oxidation of this compound with $H_2O_2$ gives a rearranged mixture of sulfones **26** and **27**.[9,21]

The relative stereochemistry of adducts **26** and **27** can be rationalized by assuming that the sulfenyl halide intermediate cyclizes through a chairlike transition state **23** in which the olefin $\pi$-bond is *colinear* with the equatorial lone pair of sulfur. The alternative conformation placing the olefin in the axial position (colinear with the axial lone pair of sulfur) would suffer from interactions with the axial ring proton. Consequently, the halomethyl group at the sulfur-bearing center effectively controls the diastereofacial selectivity of the attack on the double bond by maintaining a pseudoequatorial disposition.




**22** **23** **24** (1:1 mixture) **25** **26** (1:1 mixture) **27**

The incorporation of a conformationally constrained ring onto the backbone of the tether of substrate **22** has a noticeable effect on the regiochemical outcome of the cyclization process. To demonstrate this, acetonides **28** and **31** were each prepared as a 2:1 diastereomeric mixture (epimeric at the episulfide center). Treatment of **28** with $I_2$ in $CDCl_3$ gave two bicyclic ring products **29** and **30** whose molecular symmetry is reflected in their $^1$H and $^{13}$C NMR spectra.[22] The fact that only the *5-exo-trig* cyclization products are observed in this reaction illustrates the effect of a rigid five-membered ring on controlling the regiochemistry of this ring closure. Related 5-*exo-trig* ring closures have been reported for the construction of 4.5-cis fused rings of penicillin deriva-

(18) Episulfonium ions have been postulated as intermediates in the reaction of sulfenyl halides with olefins to account for the trans stereochemistry and preference for forming anti-Markovnikoff adducts. For studies and discussions, see: (a) Kartashov, V. R.; Skorobogatova, E. V.; Grudzinskaja, E. Yu.; Akimkina, N. F.; Zefirov, N. S.; Caple, R. *Tetrahedron* **1985**, *41*, 5219. (b) Smit, W. A.; Gybin, A. S.; Bogdanov, V. S.; Krimer, M. Z.; Vorobieva, E.A. *Tetrahedron Lett.* **1978**, *12*, 1085. (c) Mueller, W. H.; Butler, P. E. *J. Am. Chem. Soc.* **1966**, *88*, 2866. (d) Mueller, W. H.; Butler, P. E. *J. Am. Chem. Soc.* **1968**, *90*, 2075. (e) Kharasch, N.; Buess, C. M. *J. Am. Chem. Soc.* **1949**, *71*, 2724.

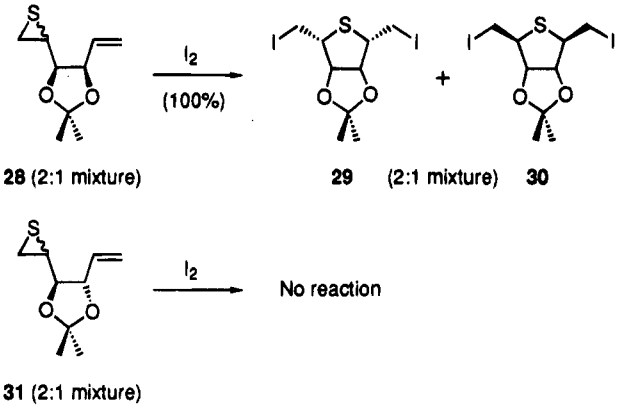
(19) The syn and anti protons of exocyclic vinyl sulfones normally appear as widely-separated geminally-coupled signals in the NMR spectrum due to deshielding of the vinyl proton syn to the sulfone center (Meyers, C. Y.; Sataty, I. *Tetrahedron Lett.* **1972**, 4323). Conversely, the $\alpha$- and $\beta$-vinyl protons of endocyclic vinyl sulfones usually give overlapping signals. For an example, see: Becker, K. B.; Labhart, M. P. *Helv. Chim. Acta* **1983**, *66*, 1090.

(20) Cerny, J.; Hora, J. *Collect. Czech. Chem. Commun.* **1960**, *25*, 711; *Chem. Abstr.* **1960**, *54*, 13113h.

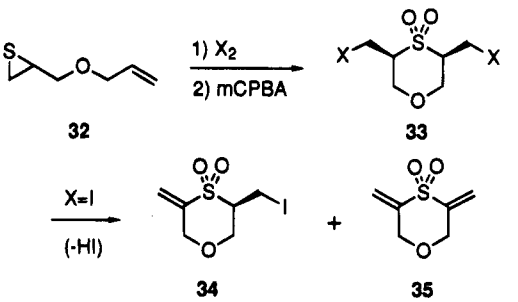
(21) It is not apparent to us why only one regioadduct was observed in this reaction, and why this single compound gives a *mixture* of five- and six-membered ring sulfones upon oxidation. From inspection of the experimental description provided in the paper for this experiment (ref 9), gas chromatography was employed to distinguish adduct **24** from regioisomer **25**. Apparently, only a single peak was observed on the GC trace, suggesting that a single regioisomer was present. While we can only speculate, it is most likely that this single peak may in fact be due to a *mixture* of compounds **24** and **25**, since the thermal conditions within the column should enable rapid equilibration of these rings via the episulfonium ion. Oxidation of this mixture would give sulfones **26** and **27** as indicated. Also see ref 6b.

(22) Unfortunately, we cannot on the basis of these spectra unambiguously distinguish which structure is the major and minor isomer. While the $^1$H NMR spectra of these compounds show differences in the chemical shifts and *J* values for the ring protons, these differences are not sufficient to allow us to firmly establish their relative stereochemistry. For compound **29**, the proton $\alpha$ to sulfur resonates at 3.60 ppm as a multiplet and the proton at the ring fusion appears at 4.80 ppm as a weakly-coupled doublet ($J$ = 2.0 Hz). For isomer **30**, the signals for these nuclei are displayed as a doublet of a doublet ($J$ = 10.8, 5.2 Hz) at 3.75 ppm and a sharp singlet at 4.79 ppm, respectively.

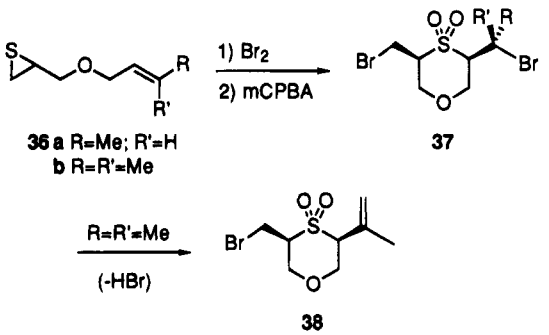
tives[23] and 5.5-cis fused frameworks found in the skeletons of thiaprostacyclins[8] and the cofactor biotin.[11] While the iodocyclizations of **28** proceed in quantitative fashion to the cis-fused products, those of the isomeric compounds **31** fail, demonstrating the inherent difficulty in forming the trans-fused 5.5-ring system.




We next considered the halogenation reactions for the homologous series of substrates using oxygen-tethered episulfides **32**. These episulfides were found to cyclize in high yield in the presence of either $Br_2$ or $I_2$ to afford six-membered ring regioadducts. Unlike the bromination reactions of the 5-hexenyl benzyl sulfides described in our previous paper[3a] where the bromination occurs primarily on the double bond, these episulfide cyclizations proceed efficiently. The bromocyclizations of **32** are completed instantaneously while the iodinations require several hours at room temperature. When X = Br, *m*-CPBA oxidation of the initial sulfide adduct provides dibromo sulfone **33** in high yield as the only product of the reaction. The structure of this adduct was deduced by X-ray single crystal analysis. However, when X = I, a mixture of **33** as well as mono- and divinyl sulfones **34** and **35** are obtained. Oxathiane **33** where X = Cl has been previously synthesized from the reaction of diallyl ether with $SCl_2$, a process which generates the same sulfenyl halide intermediate as in the episulfide reaction.[9] In this case, the authors report that the cis-stereochemistry of this compound was established by oxidation of the sulfide with $H_2O_2$ to afford two diastereoisomeric sulfoxides that upon further oxidation produce **33** as a single sulfone.

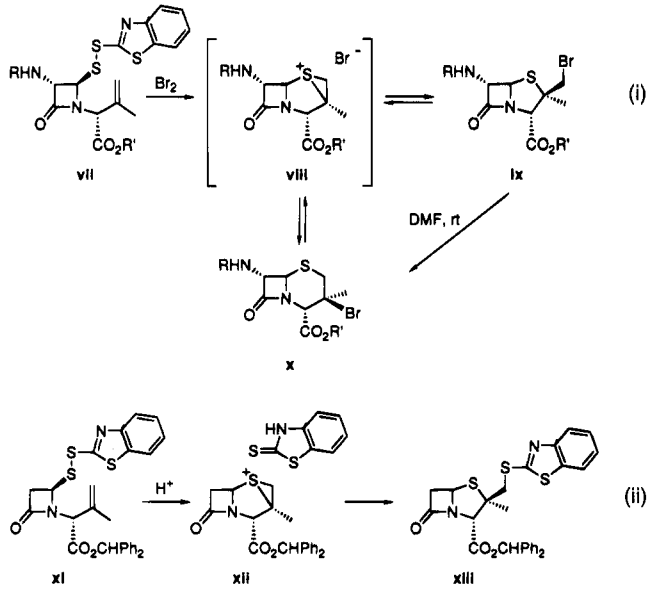



Substitution introduced at the terminus of the alkene chain does not change the regiochemical or stereochemical course of the cyclization, as shown for the bromination reactions of **36a** and **36b**. For episulfide **36b**, elimination product **38** is also isolated with sulfone **37** after flash chromatography.




The complete control of regiochemistry and stereochemistry in these 6-exo ring closures of **32** and **36** merits further discussion. As revealed by the X-ray crystal structure of adduct **33** (X = Br), the six-membered oxathiane ring adopts a chair conformation having both $CH_2Br$ groups in the equatorial position. Lautenschlaeger has rationalized the exclusive formation of the cis cycloadduct as resulting from an equilibrium between the cis and trans adducts via a common episulfonium ion.[9] According to this argument, placing both halomethyl substituents in equatorial positions on the six-membered ring (as for **33**) would greatly favor the cis isomer over the trans isomer having the 1,3-axial–equatorial arrangement. However, we feel this explanation fails on two counts. Firstly, an equilibrium between the 1,3-diequatorial (cis) and 1,3-axial–equatorial (trans) sulfides should not favor the cis isomer by such a large

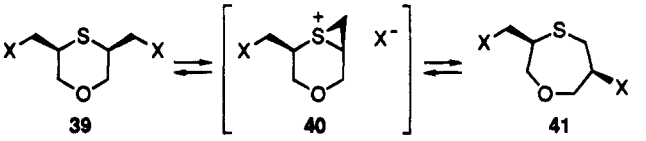
(23) Sulfenyl halide cyclizations have been utilized in the synthesis of bicyclic β-lactams wherein the presence of the four-membered lactam ring promotes the *5-exo-trig* ring closure. Thus, bromination of disulfide **vii** reportedly gives five-membered ring product **ix** in quantitative yield as the kinetic product of the reaction. Upon standing at room temperature in solution, **ix** isomerizes cleanly to the six-membered ring **x** through the episulfonium ion **viii** (eq i) (Kamiya, T.; Teraji, T.; Saito, Y.; Hashimoto, M.; Nakaguchi, O.; Oku, T. *Tetrahedron Lett.* **1973**, *14*, 3001). A closely related procedure was reported for the acid-catalyzed isomerization of azetidinyl disulfides such as **xi**. In this instance, protonation leads to the generation of an episulfonium species **xii** which undergoes nucleophilic ring opening to afford only adduct **xiii**, the product of 5-*exo-trig* cyclization (eq ii) (Alpegiani, M.; Giudici, F.; Perrone, E.; Borghi, D. *Tetrahedron Lett.* **1990**, *31*, 3509). These isomerizations closely resemble the classical Morin rearrangement of penicillin sulfoxides, an isomerization that is mediated by the formation and cyclization of an electrophilic sulfur species onto a double bond. (Morin, R. B.; Jackson, B. G.; Mueller, R. A.; Lavagnino, E. R.; Scanlon, W. B.; Andrews, S. L. *J. Am. Chem. Soc.* **1963**, *85*, 1896.) For discussions and references, see: (a) Cooper, R. D. G.; Hatfield, L. D.; Spry, D. O. *Acc. Chem. Res.* **1973**, *6*, 32. (b) *Chemistry and Biology of β-Lactam Antibiotics*; Morin, R. B., Gorman, M., Eds.; Academic Press: New York, 1982; Vol. 1. For related reactions involving an intramolecular sulfenylation of an allenyl azetidinone system, see: Farina, V.; Kant, J. *Tetrahedron Lett.* **1992**, *33*, 3559.



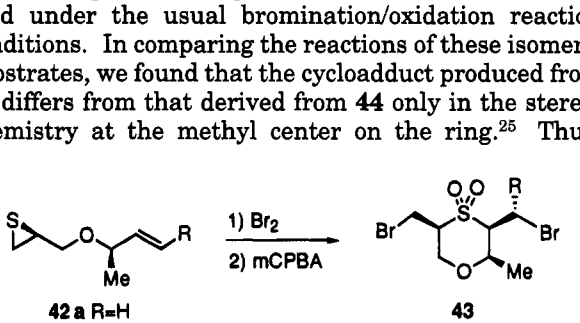
degree so as to completely exclude the formation of the trans compound. Secondly, despite Lautenschlaeger's proposition that the cis and trans stereoisomers can equilibrate via a common episulfonium species, stereochemical considerations would clearly rule this out. In fact, we fail to envision an obvious pathway by which the cis and trans adducts could freely interconvert. Consequently, while thermodynamics can certainly influence the *regiochemistry* of the cyclization by favoring one ring size over another (structures that can equilibrate via a common episulfonium intermediate), the *stereochemistry* of the reaction must originate from the kinetics that control the formation of the episulfonium adducts in the cyclization step.

To account for the 6-exo regiospecificity and 1,3-cis stereochemistry of the cycloadditions of **32** and **36**, we postulate that the intramolecular addition of the sulfenyl halide onto the olefin occurs in a concerted, suprafacial process.[24] Furthermore, we envision that this cyclization proceeds via a chairlike transition state such that the olefinic (or acetylenic) $\pi$-bond is oriented colinearly with the *equatorial* filled orbital of sulfur. In this conformation, the internal p-lobe of the olefin can nucleophilically displace X from the sulfenyl halide in $S_N2$ fashion, while the terminal p-orbital simultaneously accepts the equatorial lone pair of sulfur. Therefore, of the four possible chair conformations (A, B, C, and D) shown in Scheme 3, A and B offer the best opportunity for concerted formation of the episulfonium intermediate by having the olefin group pseudoequatorial. For structures C and D, the cyclization to an episulfonium ion could not occur in a concerted process because the olefin occupies a pseudoaxial position and is therefore not appropriately oriented to receive the lone pair of sulfur. Consequently, C and D can be ruled out on stereoelectronic grounds. The sole difference between the remaining two conformational structures, A and B, is the position of the $CH_2X$ group. In A, this moiety occupies a pseudoequatorial site where it enjoys considerable freedom from intraannular interactions, while in B, this group is pseudoaxial and should experience severe diaxial interactions with the lone pair of the ring oxygen and the vinyl proton. Therefore, from this analysis, the observed cis-disubstituted cycloproduct most likely arises from a transition state emerging from conformer A.

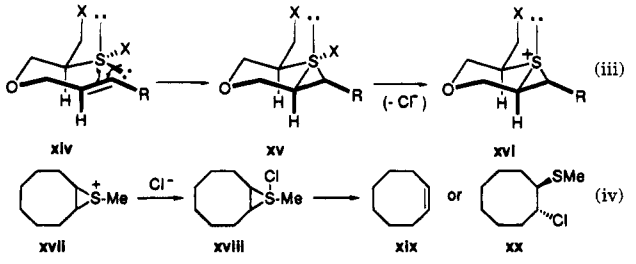
To account for the high levels of *regiochemical* control in these cyclizations, we attribute the exclusive exoselectivity to differences in the thermodynamic stabilities of the six- versus seven-membered ring regioadducts **39** and **41**. It seems reasonable to envision these isomeric $\beta$-halo sulfides to rapidly interconvert via episulfonium species **40** and therefore provide as the final product the energetically favored ring system. Thus, the six-membered ring **39** appears to be highly preferred over its seven-membered ring isomer **41**. An alternative explanation which we cannot discount is that the predominance of the six-membered ring compound may simply be due to a more favorable approach for nucleophilic attack on the episulfonium ion leading to this product. This is illustrated for the episulfonium ion emerging from transition structure A. $S_N2$ attack of the halide on this species can in principle take place at either center of the episulfonium ring, and thereby lead to either the six- or seven-membered ring product. Should the nucleophile approach the *internal* center of the three-membered ring (to produce the seven-membered ring), it would experience rather severe steric interactions with the ring substituents, particularly $R_{eq}$. On the other hand, approach of the nucleophile at the *terminal* center of the ring would be relatively unencumbered.



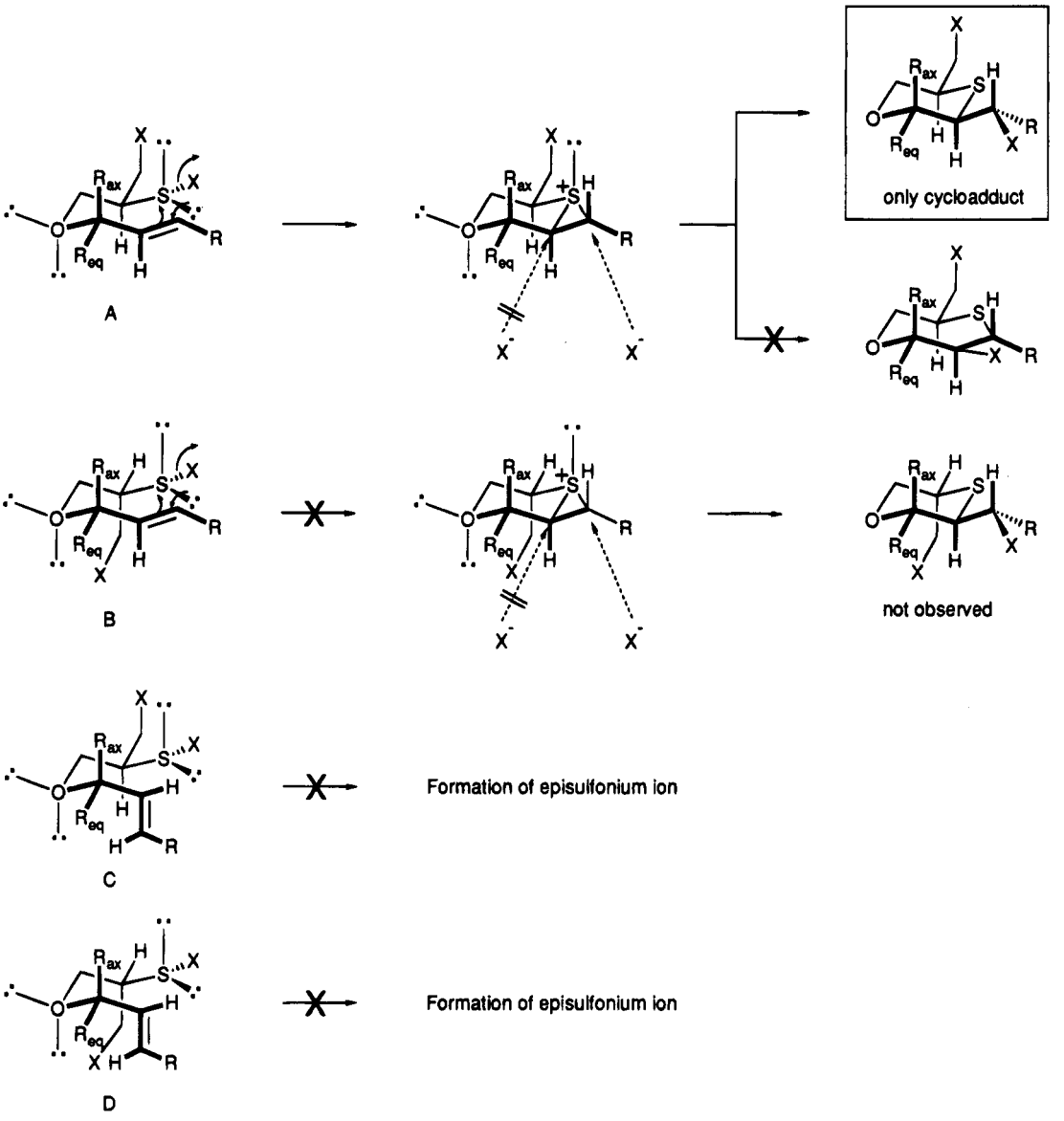

We next set out to establish whether the presence of an allylic methyl group on the tether might influence the regio- or stereochemistry of these 6-exo cyclizations. In particular, one intriguing question we hoped to answer is in regard to which of the stereocenters (if either) in the starting episulfide might play a more dominant role in governing stereochemistry of the cyclization. For these series of experiments, episulfides **42** and **44** were examined under the usual bromination/oxidation reaction conditions. In comparing the reactions of these isomeric substrates, we found that the cycloadduct produced from **42** differs from that derived from **44** only in the stereochemistry at the methyl center on the ring.[25] Thus, episulfide **42** provides adduct **43** while compound **44** gives sulfone **45**. The stereochemical assignments for these bromo adducts are based on analysis of their $^1H$ NMR spectra. While the equatorial proton at the methyl center




(24) An alternative mechanism which can be envisioned for the cyclization of **xiv** is a stepwise addition of sulfenyl halide to the olefin to give a tetravalent sulfur intermediate **xv**, which could provide episulfonium ion **xvi** in a separate mechanistic step (eq iii). Support for this pathway can be found from early NMR studies on the *reverse* process, the halide-promoted desulfurization of methylepisulfonium ion **xvii**, which is thought to occur via nucleophilic attack by chloride on the electropositive sulfur center to give tetravalent sulfur species **xviii** (Owsley, D. C.; Helmkamp, G. K.; Rettig, M. F. *J. Am. Chem. Soc.* **1969**, *91*, 5239). This species is postulated to spontaneously destruct to either olefin **xix** or the trans-$\beta$-chloro sulfenyl chloride adduct **xx** (eq iv). Evidence for the formation of tetravalent sulfur species **xviii** is from the shift in the $^1H$ NMR signal for the episulfonium methyl group at low temperature upon addition of chloride ion. While we agree that species **xviii** could be expected to form rapidly under the reaction conditions, it may not necessarily be responsible for the formation of the observed products. Otherwise, microscopic reversibility would dictate that the *addition* of the sulfenyl chloride *to* the olefin must necessarily proceed through this tetravalent species. We favor the concerted mechanism for formation of the episulfonium intermediate, which would appear to benefit from a lower transition state energy than the valency-expanded sulfur species (which requires energy to rehybridize).

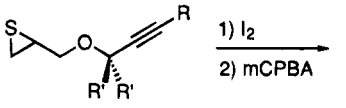


**Scheme 3**

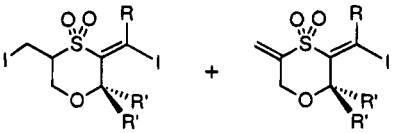



of the ring in **43** appears as a weakly split doublet, all-equatorial adducts **45** show a strongly-coupled doublet for the axial proton. Referring once again to conformer A in Scheme 3, this suggests that the more bulky bromomethyl substituent α to sulfur exercises greater demand for the equatorial position than the allylic alkyl substituent in the transition state for ring closure and therefore is responsible for establishing stereochemistry at the new stereocenters in the cyclization.

Similarly, alkynyl episulfides **46** cyclize exclusively to the six-membered ring product, regardless of whether a substituent is present on the tether *or* on the alkyne moiety. Once again, dehydroiodination of sulfone adduct **47** occurs during workup to give divinyl sulfoxides **48**. In each case, the cycloadduct is obtained as a geometrically pure *E*-isomer arising from trans addition to the triple bond.



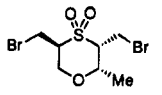

**46** **a** R=R'=H
**b** R=Me; R'=H
**c** R=H; R'=Me



**47** **48**

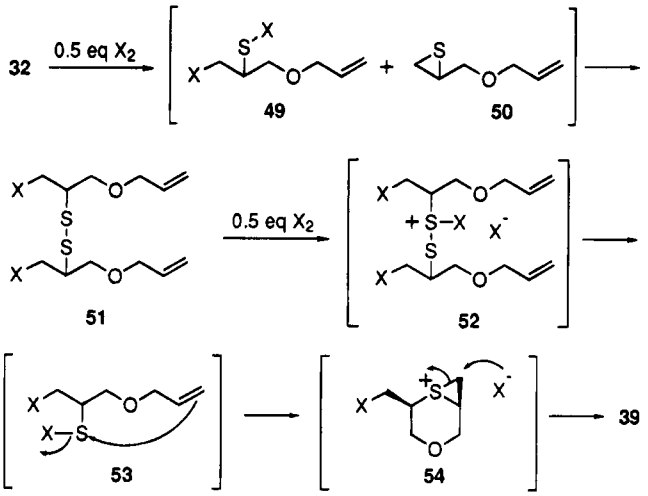
In support of the mechanism first postulated by McCabe for episulfide ring expansions,[10a] we have found that these halocyclization reactions proceed by initial opening of the episulfide ring. As illustrated in Scheme 4 for episulfide **32**, halogenation of the episulfide moiety occurs first, producing β-halo sulfenyl halide intermediate **49**.

(25) A minor amount (<5%) of an isomeric adduct is also obtained from the reaction of **24** that from its NMR data we suspect is sulfone **xxi**: $^1$H NMR (400 MHz, $CDCl_3$) δ 4.46 (m, 1H), 4.38 (app dd, $J$ = 4.9, 12.4 Hz, 1H), 4.16 (m, 1H), 4.07 (dd, $J$ = 2.9, 11.7 Hz, 1H), 3.9 (dd, $J$ = 11.8, 15.6 Hz, 1H), 3.76–3.64 (overlapping m, 2H), 3.50 (dd, $J$ = 2.9, 11.7 Hz, 1H), 3.34 (dd, $J$ = 2.9, 9.7 Hz, 1H), 1.39 (d, $J$ = 6.8 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 79.5, 78.4, 73.2, 61.9, 39.7, 28.9, 21.3; IR (neat film) 1107, 1127, 1310 cm$^{-1}$; HRMS (CI, isobutane) (M + 1) 337.0 (50), 257.1 (66), 255.1 (64), 175.1 (100).



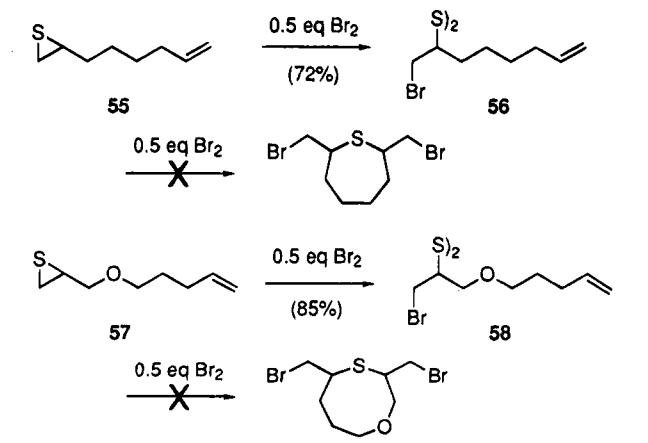
xxi

**Scheme 4**



Under the reaction conditions, **49** adds immediately to unreacted episulfide to give the disulfide adduct **51** which can easily be isolated by evaporation of the solvent. Thus, addition of 0.5 molar equiv of $Br_2$ or $I_2$ to **32** at room temperature gives 1:1 diastereomeric mixtures of disulfides **51**, such that ring-opening of the episulfide[4r,s] occurs exclusively at the less hindered center. Upon reaction with an additional 0.5 equiv of $Br_2$ at room temperature (or $I_2$ in refluxing benzene), **51** reforms the sulfenyl halide before leading to the final cycloadduct **39**. Experiments using substrates that contain a triple bond give similar results when $I_2$ is used, except that the solution must be heated in order to convert the disulfide to the cyclization product.

Finally, thiiranes **55** and **57** were examined to address whether seven- or eight-membered rings could be constructed with this methodology. Not surprisingly, however, the longer chain length within these substrates prevents the formation of ring products. Thus, reaction of **55** or **57** with 0.5 equiv of $Br_2$ produces acyclic disulfides **56** and **58**, respectively. Further attempts to cyclize these disulfides using additional quantities of $Br_2$ or $I_2$ were unsuccessful, demonstrating the resistance of these more highly extended unsaturated systems to undergo annulation.



## Conclusion

The results from this study illustrate that the halocyclizations of episulfides having unsaturated side chains follow predictable regiochemical and stereochemical pathways and provide a straightforward approach to five- and six-membered $\beta,\beta'$-dihalo sulfide rings. The reactions take place under mild conditions using 1 molar equiv of bromine or iodine by initial formation of the $\beta$-halo sulfenyl halide. The cyclization can usually be interrupted by using a limiting amount of $Br_2$ or $I_2$ (0.5 equiv) in the reaction, allowing the sulfenyl halide to react with residual episulfide to form the disulfide. Addition of a second 0.5 equiv of halogen to the disulfide intermediate effects the cyclization process by reformation of the sulfenyl halide. The intramolecular addition of sulfenyl halide to the double or triple bond can be viewed as a concerted, suprafacial process followed by $S_N2$-type opening of the episulfonium ring. The stereochemistry of the cycloaddition products allows us to postulate that this electrophilic sulfenyl halide addition takes place via a highly defined chairlike transition state having the $\pi$-bond of the double bond or triple bond and the filled orbital of sulfur in a colinear arrangement. It is through this conformation that the halomethyl substituent at the sulfur-bearing center governs relative stereochemistry emerging at the new chiral centers. The regiochemistry of these ring enlargements is determined from the thermodynamic preferences of the halo sulfide adducts through an equilibration process involving a common episulfonium species. Current studies in our laboratory are utilizing this ring expansion methodology in selected applications to organic synthesis.

## Experimental Section

**Caution:** $\beta$-Halo sulfides are potent alkylating agents that should be handled with considerable care in well-vented hoods. All air- or moisture-sensitive reactions were performed under an argon atmosphere using glassware and syringes that were predried overnight in an oven at 120 °C and assembled while still hot. Reactions were generally followed by TLC using EM Reagents plates with fluorescence indicator ($SiO_2$-60, F-254). Flash chromatography was performed using J. T. Baker flash chromatography silica gel (40 $\mu$m). $^1H$ NMR spectra were recorded using a Varian 400 NMR instrument at 400 MHz in $CDCl_3$. $^{13}C$ NMR spectra were recorded using a Varian Gemini 300 NMR spectrometer at 75 MHz in $CDCl_3$. IR spectra were obtained as a thin film on NaCl plates on a Perkin-Elmer 1310 spectrophotometer. Mass spectra were run using electron impact or chemical ionization. Combustion analyses were performed by Atlantic Microlabs (Atlanta, GA). THF and $Et_2O$ were distilled immediately prior to use from Na/benzophenone under argon, and $CH_2Cl_2$ was freshly distilled from $CaH_2$ under $N_2$. Thiiranes **22** and **55** were prepared from commercially-available epoxides (Aldrich Chemical Co.) using thiourea in methanol. The glycidol ethers used to make the episulfides **32**, **36**, **42**, **44**, **46**, and **57** were prepared from epibromohydrin and the corresponding alcohol by phase-transfer etherification[26] and purified by bulb-to-bulb distillation at 0.1 Torr using a dry ice trap.

**Representative Procedure for the Preparation of Enyne Precursors.** To a solution of phenylacetylene (2.50 g, 24.5 mmol) in THF (50 mL) at 0 °C was slowly added $CH_3MgBr$ (13.0 mL, 3.0 M in $Et_2O$, 39.0 mmol) and a catalytic amount of CuI. To this mixture was added dropwise allyl bromide (3.5 mL, 39.0 mmol). The reaction mixture was stirred for 6 h, poured into water (100 mL), and extracted with $CH_2Cl_2$ (3 × 50 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and evaporated. Flash chromatography of the crude mixture afforded 2.43 g (70%) of 5-phenylpent-1-en-4-yne as a colorless oil: $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.44–7.42 (m, 2H), 7.30–7.26 (m, 3H), 5.91 (ddt, $J$ = 16.6, 9.8, 5.9 Hz, 1H), 5.39 (d, $J$ = 9.8 Hz, 1H), 3.20 (d, $J$ = 5.9 Hz, 2H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 133.3, 132.0, 128.8, 128.2, 124.2, 116.8, 87.0, 83.5, 24.0.

**6-(Benzyloxy)hex-1-en-4-yne**: 3.16 g (85%) of a colorless oil obtained using an identical procedure starting from 2.92 g

(26) Mouzin, G.; Cousse, H.; Rieu J.-P.; Duflos, A. *Synthesis* **1983**, 117.

of 3-(benzyloxy)-1-propyne[27] and 2.8 mL of allyl bromide; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.38–7.25 (m, 5H), 5.80 (ddt, $J$ = 16.6, 9.8, 5.9 Hz, 1H), 5.34 (d, $J$ = 16.6 Hz, 1H), 5.13 (d, $J$ = 9.8 Hz, 1H), 4.60 (s, 2H), 4.19 (s, 2H), 3.03 (m, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 138.1, 133.0, 129.6, 129.5, 129.4, 116.8, 84.0, 78.5, 72.0, 58.0, 23.5.

**Representative Procedure for the Preparation of Epoxide Precursors.** To a solution of 5-phenylpent-1-en-4-yne (2.43 g, 17.1 mmol) in $CH_2Cl_2$ (100 mL) at 0 °C was added in one portion *m*-CPBA (6.05 g, 50–60%, approximately 17.5 mmol). The reaction mixture was stirred for 16 h and poured into 5% aqueous $NaHSO_3$ solution (50 mL). The mixture was stirred for 8 h until the layers separated, and the organic layer was washed with 5% $NaHCO_3$ solution (100 mL). The aqueous layer was extracted with $CH_2Cl_2$ (3 × 50 mL), and the combined organic layers were dried over anhydrous $MgSO_4$ and evaporated. Flash chromatography of the crude mixture afforded 1.86 g (69%) of 1,2-epoxy-5-phenyl-4-pentyne as a colorless oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.44–7.42 (m, 2H), 7.30–7.26 (m, 3H), 3.20 (m, 2H), 2.85 (m, 2H), 2.70 (m, 2H).

**3-[(*tert*-Butyldimethylsilyl)oxy]-1,2-epoxy-4-pentene**: 1.61 g (75%, 1:1 mixture) prepared from 1.98 g of 3-[(*tert*-butyldimethylsilyl)oxy]-1,4-pentadiene as a colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) (major isomer) $\delta$ 5.82 (ddd, $J$ = 15.6, 10.7, 3.9 Hz, 1H), 5.35 (d, $J$ = 15.6 Hz, 1H), 5.18 (d, $J$ = 10.7 Hz, 1H), 3.88 (m, 1H), 2.88 (m, 1H), 2.78 (m, 1H), 2.60 (m, 1H), 0.90 (s, 9H), 0.07 (s, 3H), 0.04 (s, 3H); (minor isomer): $\delta$ 5.85 (m, 1H) 5.32 (d, $J$ = 15.6 Hz, 1H), 5.18 (d, $J$ = 10.7 Hz, 1H), 4.10 (m, 1H), 2.92 (d, $J$ = 2.9 Hz, 1H), 2.70 (m, 2H), 0.90 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H). Anal. Calcd for $C_{11}H_{22}O_2Si$: C, 61.68; H, 10.28. Found: C, 61.75; H, 10.22.

**3,4-Dihydroxy-1,2-epoxy-5-hexene acetonide**: 1.88 g (85%, 2:1 mixture) prepared from 2.00 g of 3,4-dihydroxy-1,5-hexadiene acetonide as a colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) (mixture of isomers) $\delta$ 6.0 (m) (total 1H), 5.5 (m) (total 1H), 5.35 (m) (total 1H), 4.75 (m) and 4.68 (m) and 4.38 (m) (total 1H), 4.86 (m) and 4.77 (m) (total 1H), 3.05 (m) and 2.98 (m) (total 1H), 2.83 (m) and 2.78 (m) (total 1H), 2.70 (m) and 2.60 (m) (total 1H), 1.56 (s) and 1.42 (s) (total 3H), 1.39 (s, total 3H). Anal. Calcd for $C_9H_{14}O_3$: C, 63.53; H, 8.24. Found: C, 63.59; H, 8.16.

**6-(Benzyloxy)-1,2-epoxy-4-hexyne**: 1.49 g (74%) of a colorless oil obtained from 1.86 g of 6-(benzyloxy)hex-1-en-4-yne; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.38–7.25 (m, 5H), 4.60 (s, 2H), 4.18 (s, 2H), 3.12 (m, 1H), 2.80 (m, 1H), 2.65 (m, 2H), 2.55 (m, 1H). Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.23; H, 6.93. Found: C, 77.28; H, 6.88.

**Representative Procedure for the Preparation of Unsaturated Thiiranes.** To a solution of the above-prepared 1,2-epoxy-5-phenyl-4-pentyne (1.86 g, 11.8 mmol) in MeOH (50 mL) at 0 °C was added in one portion thiourea (2.32 g, 30.5 mmol). The reaction mixture was stirred for 16 h then poured into water (100 mL) and extracted with $CH_2Cl_2$ (3 × 50 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and evaporated. Flash chromatography of the crude mixture gave 1.81 g (88%) of 1,2-epithio-5-phenyl-4-pentyne (**17a**) as a colorless oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.44–7.42 (m, 2H), 7.30–7.26 (m, 3H), 3.15 (dd, $J$ = 5.9, 11.7 Hz, 1H), 2.95 (dd, $J$ = 4.9, 16.6 Hz, 1H), 2.74 (dd, $J$ = 6.8, 16.6 Hz, 1H), 2.58 (m, 1H), 2.36 (m, 1H).

**1,2-Epithio-4-penten-3-ol** (**15a**): 1.14 g (95%, 1:1 mixture of diastereomers) prepared from 1.04 g of 1,2-epoxy-4-penten-3-ol[28] (1:1 mixture) as a colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) (mixture of diastereomers) $\delta$ 5.92 (m, total 1H), 5.36 (dd, $J$ = 15.6, 11.7 Hz) and 5.21 (dd, $J$ = 11.7, 10.7 Hz) (total 1H), 4.21 (m) and 4.11 (m) (total 1H), 3.15 (m, total 1H), 2.40 (m, total 2H), 1.55 (broadened s, total 1H).

**3-(*tert*-Butyldimethylsiloxy)-1,2-epithio-4-pentene** (**15b**): 1.96 g (85%, 1:1 mixture of diastereomers) prepared from 2.14 g of 3-[(*tert*-butyldimethylsilyl)oxy]-1,2-epoxy-4-pentene[29] (1:1 mixture) as a colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) (isomer 1) $\delta$ 5.85 (ddd, $J$ = 15.6, 10.7, 3.9 Hz, 1H), 5.26 (d, $J$ = 15.6 Hz, 1H), 5.15 (d, $J$ = 10.7 Hz, 1H), 3.78 (m, 1H), 2.93 (m, 1H), 2.45 (d, $J$ = 3.9 Hz, 1H), 2.25 (d, $J$ = 3.9 Hz, 1H), 0.90 (s, 9H), 0.06 (s, 3H), 0.02 (s, 3H); (isomer 2) $\delta$ 5.90 (ddd, $J$ = 15.6, 10.7, 3.9 Hz, 1H), 5.26 (d, $J$ = 15.6 Hz, 1H), 5.13 (d, $J$ = 10.7 Hz, 1H), 3.80 (m, 1H), 2.98 (m, 1H), 2.43 (d, $J$ = 3.9 Hz, 1H), 2.21 (d, $J$ = 3.9 Hz, 1H), 0.90 (s, 9H), 0.50 (s, 3H), 0.06 (s, 3H).

**6-(Benzyloxy)-1,2-epithio-4-hexyne** (**17b**): 1.84 g (83%) prepared from 2.05 g of 6-(benzyloxy)-1,2-epoxy-4-hexyne as a colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.38–7.25 (m, 5H), 4.60 (s, 2H), 4.18 (s, 2H), 3.06 (m, 1H), 2.74 (m, 1H), 2.60 (m, 2H), 2.29 (m, 1H).

**1,2-Epithio-5-hexene** (**22**): prepared from 1.50 g of 1,2-epoxy-5-hexene to give 1.72 g (99%) of a crude oil, which upon bulb-to-bulb distillation afforded 0.56 g (32%) of **22** as a colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.89 (m, 1H), 5.03 (AB m, 2H), 2.88 (qd, $J$ = 6.0, 5.6 Hz, 1H), 2.49 (d, $J$ = 5.6 Hz, 1H), 2.26 (m, 2H), 2.15 (d, $J$ = 6.0 Hz, 1H),1.93 (dt, $J$ = 14.8, 6.0 Hz, 1H), 1.53 (dt, $J$ = 14.8, 6.0 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 138.1, 115.8, 36.1, 35.5, 33.7, 26.0.

**3,4-Dihydroxy-1,2-epithio-5-hexene acetonide** (**28:31**): 1.44 g (91%, 2:1 mixture of diastereomers) prepared from 1.45 g of 3,4-dihydroxy-1,2-epoxy-5-hexene acetonide[30] (2:1 mixture) as a colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) (mixture of diastereomers) $\delta$ 5.99 (m) and 5.82 (m) (total 1H), 5.44 (m) and 5.36 (m) (total 1H), 4.63 (m) and 4.38 (m) (total 1H), 3.60 (m, total 1H), 2.90 (m) and 2.80 (m) (total 1H), 2.56 (m) and 2.43 (m) (total 1H), 2.26 (m) and 2.10 (m) (total 1H), 1.56–1.40 (total 6H).

**1,2-Epithio-3-(2-propenyloxy)propane** (**32**): prepared from 1.53 g of 1,2-epoxy-3-(2-propenyloxy)propane to give 1.69 g (97%) of a crude oil, which upon bulb-to-bulb distillation gave 0.89 g (51%) of **32** as a colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.90 (m, 1H), 5.17–5.31 (overlapping m, 2H), 4.03 (AB m, 2H), 3.63 (dd, $J$ = 6.0, 10.8 Hz, 1H), 3.44 (dd, $J$ = 5.6, 10.8 Hz, 1H), 3.06 (ddt, $J$ = 4.8, 5.6, 6.0 Hz, 1H), 2.51 (d, $J$ = 6.0 Hz, 1H), 2.20 (d, $J$ = 4.8 Hz, 1H).

**(*E*)-3-(2-Butenyloxy)-1,2-epithiopropane** (**36a**): prepared from 0.49 g of (*E*)-3-(2-butenyloxy)-1,2-epoxypropane to give 0.36 g (65%) of a crude oil, which upon bulb-to-bulb distillation gave 0.13 g (24%) of **36a** as a colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.73 (m, 1H), 5.57 (m, 1H), 3.95 (app d, $J$ = 6.8 Hz, 2H), 3.62 (dd, $J$ = 6.0, 10.8 Hz, 1H), 3.42 (dd, $J$ = 6.8, 10.8 Hz, 1H), 3.07 (ddt, $J$ = 5.2, 6.0, 6.8 Hz, 1H), 2.51 (d, $J$ = 6.8 Hz, 1H), 2.20 (d, $J$ = 5.2 Hz, 1H), 1.70 (d, $J$ = 6.0 Hz).

**1,2-Epithio-3-[(3-methyl-2-butenyl)oxy]propane** (**36b**): prepared from 2.01 g of 1,2-epoxy-3-[(3-methyl-2-butenyl)oxy]propane to give 2.12 g (95%) of a crude oil, which upon bulb-to-bulb distillation gave 1.09 g (49%) of **36b** as a colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.33 (br t, app $J$ = 8.0 Hz, 1H), 4.00 (app d, $J$ = 6.8 Hz, 2H), 3.62 (d, $J$ = 6.0, 10.8 Hz, 1H), 3.38 (dd, $J$ = 6.8, 10.8 Hz, 1H), 3.06 (dtd, $J$ = 4.8, 6.0, 6.8 Hz, 1H), 2.50 (d, $J$ = 6.0 Hz, 1H), 2.19 (d, $J$ = 4.8 Hz, 1H), 1.73 (s, 3H), 1.66 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 138.0, 121.3, 75.0, 67.8, 32.4, 26.0, 24.1, 18.2.

**1,2-Epithio-3-[(1-methyl-2-propenyl)oxy]propane** (**42a:44a**): prepared from 0.90 g of 1,2-epoxy-3-[(1-methyl-2-propenyl)oxy]propane (1:1 mixture) to give 0.97 g (96%) of a crude oil, which upon bulb-to-bulb distillation gave 0.41 g (41%, 1:1 mixture) of **42a:44a** as a colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) (mixture of diastereomers) $\delta$ 5.73 (m, 1H), 5.12–5.20 (AB m, 2H), 3.89 (br m, total 1H), 3.69 (dd, $J$ = 6.0, 10.8 Hz, 1H, isomer 1), 3.56 (dd, $J$ = 4.8, 10.8 Hz, 1H, isomer 1), 3.41 (dd, $J$ = 6.8, 10.8 Hz, 1H, isomer 2), 3.30 (dd, $J$ = 6.8, 10.8 Hz, 1H, isomer 2), 3.07 (m, total 1H), 2.53 (d, $J$ = 6.0 Hz) and 2.51 (d, $J$ = 4.8 Hz) (total 1H), 2.22 (d, $J$ = 4.8 Hz) and 2.18 (d, $J$ = 6.0 Hz) (total 1H), 1.26 (d, $J$ = 6.8 Hz) and 1.25 (d, $J$ = 6.0 Hz) (total 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 140.6, 140.6, 116.7, 116.6, 73.3, 73.1, 32.7, 24.3, 24.1, 21.5, 21.4.

(27) The preparation of this compound can be found in the Experimental Section of the preceding paper.[3a]

(28) The epoxy alcohol was synthesized from 1,4-pentadien-3-ol by monoepoxidation using 1 molar equiv of *m*-CPBA in $CH_2Cl_2$ at room temperature.

(29) The siloxy diene was obtained by derivatization of 1,4-pentadien-3-ol with $tBuMe_2SiCl$ and pyridine in $CH_2Cl_2$.

(30) This epoxide was prepared by monoepoxidation of the 1,4-diene using 1 molar equiv of *m*-CPBA in $CH_2Cl_2$.

(31) The author has deposited atomic coordinates for **19a** and **33** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

**(*E*)-1,2-Epithio-3-[(1-methyl-2-butenyl)oxy]propane (42b:44b)**: prepared from 1.57 g of (*E*)-1,2-epoxy-3-[(1-methyl-2-butenyl)oxy]propane to give 1.61 g (92%) of a crude oil, which upon bulb-to-bulb distillation gave 0.40 g (23%, 1:1 mixture) of **42b:44b** as a colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.62 (m, total 1H), 5.35 (m, total 1H), 3.87 (br m, total 1H), 3.70 (dd, $J$ = 5.6, 10.8 Hz, 1H, isomer 1), 3.53 (dd, $J$ = 5.6, 10.8 Hz, 1H, isomer 1), 3.37 (dd, $J$ = 6.8, 10.8 Hz, 1H, isomer 2), 3.23 (dd, $J$ = 6.8, 10.8 Hz, 1H, isomer 2), 3.05 (m, total 1H), 2.53 (d, $J$ = 5.6 Hz) and 2.51 (d, $J$ = 6.0 Hz) (total 1H), 2.22 (d, $J$ = 4.8 Hz) and 2.20 (d, $J$ = 6.0 Hz) (total 1H), 1.69 (d, $J$ = 6.0 Hz, total 3H), 1.24 (d, $J$ = 6.8 Hz) and 1.23 (d, $J$ = 6.0 Hz) (total 3H).

**1,2-Epithio-3-(2-propynyloxy)propane (46a)**: prepared from 1.20 g of 1,2-epoxy-3-(2-propynyloxy)propane to give 1.30 g (95%) of a crude oil, which upon bulb-to-bulb distillation gave 0.70 g (50%) of **46a** as a colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.21 (s, 2H), 3.72 (dd, $J$ = 6.0, 10.8 Hz, 1H), 3.56 (dd, $J$ = 6.8, 10.8 Hz, 1H), 3.09 (dddd, $J$ = 4.8, 5.6, 6.0, 6.8 Hz, 1H), 2.52 (d, $J$ = 5.6 Hz, 1H), 2.45 (app t, $J$ = 2.0 Hz, 1H), 2.23 (d, $J$ = 4.8 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 79.7, 75.3, 74.6, 58.5, 31.9, 23.9.

**1,2-Epithio-3-[(3-methyl-2-propynyl)oxy]propane (46b)**: prepared from 3.40 g of 1,2-epoxy-3-[(3-methyl-2-propynyl)oxy]propane to give 3.56 g (93%) of a crude oil, which upon bulb-to-bulb distillation gave 2.26 g (59%) of **46b** as a colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 3.82 (dd, $J$ = 4.9, 9.8 Hz, 1H), 3.43 (dd, $J$ = 6.8, 9.8, 1H), 3.06 (dddd, $J$ = 4.9, 6.8, 6.0, 4.0 Hz, 1H), 2.52 (d, $J$ = 6.0 Hz, 1H), 2.42 (s, 1H), 2.22 (d, $J$ = 4.0 Hz, 1H), 1.46, (s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 86.2, 72.8, 70.7, 32.9, 30.4, 29.0, 28.8, 24.4.

**3-[(1,1-Dimethyl-2-propynyl)oxy]-1,2-epithiopropane (46c)**: prepared from 1.55 g of 3-[(1,1-dimethyl-2-propynyl)-oxy]-1,2-epoxypropane to give 1.68 (97%) of a crude oil, which upon bulb-to-bulb distillation gave 0.47 g (27%) of **46c** as a colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 3.76 (m, 1H), 3.39 (m, 1H), 3.01 (m, 1H), 2.46 (d, $J$ = 6.0 Hz, 1H), 2.41 (s, 1H), 2.17 (d, $J$ = 4.0 Hz, 1H), 1.43 (s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 86.2, 72.8, 70.7, 32.9, 30.4, 29.0, 28.8, 24.4.

**1,2-Epithio-7-octene (55)**: prepared from 1.01 g of 1,2-epoxy-7-octene to give 1.09 g (96%) of a pale yellow oil, which upon bulb-to-bulb distillation gave 0.48 g (42%) of **55** as a colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.83 (m, 1H), 4.95–5.05 (AB m, 2H), 3.63 (dd, $J$ = 6.0, 10.8 Hz, 1H), 3.50 (t, $J$ = 6.8 Hz, 2H), 3.42 (dd, $J$ = 6.8, 10.8 Hz, 1H), 3.07 (qd, $J$ = 6.0, 6.8 Hz, 1H), 2.52 (d, $J$ = 6.0 Hz, 1H), 2.21 (d, $J$ = 6.0 Hz, 1H), 2.13 (q, $J$ = 6.8 Hz, 2H), 1.70 (quintet, $J$ = 6.8 Hz, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 138.7, 115.4, 75.8, 70.9, 32.4, 30.4, 29.1, 24.0.

**1,2-Epithio-3-(4-pentenyloxy)propane (57)**: prepared from 0.98 g of 1,2-epoxy-3-(4-pentenyloxy)propane to give 1.07 g (98%) of a pale yellow oil, which upon bulb-to-bulb distillation gave 0.38 g (35%) of **57** as a colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.81 (m, 1H), 5.00 (AB m, 2H), 3.62 (dd, $J$ = 5.6, 10.8 Hz, 1H), 3.52 (AB m, 2H), 3.42 (dd, $J$ = 6.8, 10.8 Hz, 1H), 3.07 (dtd, $J$ = 5.6, 6.0, 6.8 Hz, 1H), 2.52 (d, $J$ = 6.0 Hz, 1H), 2.21 (d, $J$ = 6.0 Hz, 1H), 2.14 (td, $J$ = 6.8, 8.0 Hz, 2H), 1.67 (tt, $J$ = 6.8, 8.0 Hz, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 138.7, 115.4, 75.8, 70.9, 32.4, 30.4, 29.1, 24.0.

**Representative Procedure for the Halocyclization Reaction with Subsequent Sulfonylation.** To a solution of 1,2-epithio-5-phenyl-4-pentyne (**17a**, 1.40 g, 8.0 mmol) in $CH_2Cl_2$ (50 mL) at rt was added $I_2$ (2.06 g, 8.1 mmol). The reaction mixture was stirred for 4 h and poured into 5% aqueous $NaHSO_3$ solution (25 mL). The aqueous layer was extracted with $CH_2Cl_2$ (3 × 50 mL), and the combined organic layers were dried over anhydrous $MgSO_4$ and evaporated. Flash chromatography of the crude mixture afforded 3.27 g (95%) of 2,3-dihydro-4-iodo-2-(iodomethyl)-5-phenylthiophene (**18a**) as a colorless oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.45–7.56 (m, 5H), 4.0 (m, 1H), 3.37–3.52 (m, 3H), 3.17 (dd, $J$ = 3.9, 17.6 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 140.0, 135.5, 132.5, 129.9, 129.8, 129.6, 72.5, 55.8, 49.2. Anal. Calcd for $C_{11}H_{10}SI_2$: C, 30.84; H, 2.34; S, 7.48. Found: C, 30.75; H, 2.42; S, 7.40.

To a solution of **18a** (3.20 g, 7.5 mmol) in $CH_2Cl_2$ (75 mL) at rt was added in one portion *m*-CPBA (6.5 g, 50–60%, approximately 18.8 mmol). The reaction mixture was stirred for 12 h and poured into 5% aqueous $NaHSO_3$ solution (75 mL). The mixture was stirred for 8 h until the layers separated, and the organic layer was washed with 5% $NaHCO_3$ solution (50 mL). The aqueous layer was extracted with $CH_2Cl_2$ (3 × 50 mL), and the combined organic layers were dried over anhydrous $MgSO_4$ and evaporated. Flash chromatography of the crude mixture provided 2.24 g (90%) of **19a** as colorless crystals: mp 152–155 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.45–7.56 (m, 5H), 6.18 (dd, $J$ = 2.0, 4.9 Hz, 1H), 5.83 (d, $J$ = 2.0 Hz, 1H), 3.91 (d, $J$ = 2.0 Hz, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 147.5, 144.2, 131.0, 130.0, 129.8, 129.7, 115.5, 114.0, 42.9. HRMS (EI) $m/z$ calcd for $C_{11}H_9O_2SI$ 331.9369, found 331.9368. Anal. Calcd for $C_{11}H_9O_2SI$: C, 39.76; H, 2.71; S, 9.64. Found: C, 39.77; H, 2.69; S, 9.63.

**19b**: 0.394 g (90%) obtained by oxidation of 0.550 g of **18b**, which was prepared in 95% yield from 0.267 g of **17b**; colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.26–7.42 (m, 5H), 6.10 (d, $J$ = 2.0 Hz, 1H), 5.77 (dd, $J$ = 2.0, 8.8 Hz, 1H), 4.61 (s, 2H), 4.42 (s, 2H), 3.80 (d, $J$ = 2.0 Hz, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 138.0, 134.2, 131.0, 129.1, 129.0, 128.6, 117.6, 107.8, 73.5, 65.5, 60.8. Anal. Calcd for $C_{13}H_{13}O_3SI$: C, 41.49; H, 3.46; S, 8.51. Found: C, 41.52; H, 3.45; S, 8.55.

**26:27** for X = Br: 1.17 g (95%, 1:1 mixture) obtained from 0.460 g of **22**; recrystallization of this mixture from $CH_2Cl_2$–hexane gave a colorless crystalline solid; mp 54–60 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.37 (broadened t, $J$ = 8.8 Hz, 1H for isomer **26**), 3.94 (dd, $J$ = 3.9, 6.8 Hz, 1H for isomer **27**), 3.72 (m, total 2H), 3.51 (m, total 3H), 3.30 (m, total 3H), 2.50–2.40 (m, total 2H), 2.18 (m, total 1H), 2.05–1.95 (m, total 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 63.5, 60.5, 57.4, 40.6, 30.2, 26.9, 26.1, 25.7, 25.0. Anal. Calcd for $C_6H_{10}O_2SBr_2$: C, 23.53; H, 3.27; S, 10.46. Found: C, 23.50; H, 3.31; S, 10.50.

**33** for X = Br: 0.991 g (80%) isolated from 0.500 g of **32**; colorless solid; mp 110–113 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.51 (dd, $J$ = 3.0, 12.6 Hz, 2H), 3.90 (dd, $J$ = 2.9, 10.7 Hz, 2H), 3.82 (dd, $J$ = 9.8, 12.8 Hz, 2H), 3.45 (tt, $J$ = 3.0, 10.7 Hz, 2H), 3.30 (t, $J$ = 10.7 Hz, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 70.5, 63.5, 21.8; IR (neat film) 1136, 1115, 1296, 1329 cm$^{-1}$; MS (CI, isobutane) $m/z$ (relative intensity) 323.0 (8, M + 1), 161.0 (13), 154.1 (100), 136.1 (11). Anal. Calcd for $C_6H_{10}O_3SBr_2$: C, 22.36; H, 3.11; S, 9.94. Found: C, 22.40; H, 3.06; S, 9.99.

**33** for X = I: 0.218 mg (31%) isolated from 0.220 g of **32**; white solid (decomposed upon warming); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.48 (dd, $J$ = 3.9, 12.7 Hz, 2H), 3.72 (overlapping m, 4H), 3.32 (t, broadened, apparent $J$ = 11.4 Hz, 2H), 3.07 (t, $J$ = 11.3 Hz, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 72.5, 63.0, −10.0.

**34**: 0.049 g (10%) isolated from 0.220 g of **32**; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 6.27 (s , 1H), 5.93 (s, 1H), 4.42 (d, $J$ = 12.8 Hz, 2H), 4.24 (dd, $J$ = 4.9, 12.7 Hz, 1H), 3.65 (d, apparent $J$ = 6.8 Hz, 1H), 3.26 (overlapping m, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 144.0, 125.0, 72.4, 71.0, 65.0, −10.0.

**35**: 0.135 mg (50%) isolated from 0.220 g of **32**; colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 6.21 (s, 2H), 5.80 (s, 2H), 4.58 (s, 4H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 147.6, 122.4, 71.1. Anal. Calcd for $C_6H_8O_3S$: C, 45.00; H, 5.00; S, 20.00. Found: C, 44.77; H, 5.09; S, 19.83.

**37a**: 0.288 g (95%) obtained from 0.130 g of **36a**; colorless solid; mp 60–63 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.60 (dd, $J$ = 3.9, 12.7 Hz, 1H), 4.50 (dd, $J$ = 3.9, 12.7 Hz, 1H), 4.30 (qd, $J$ = 6.8, 10.8 Hz, 1H), 3.90 (dd, 3.8, 10.8 Hz, 1H), 3.70 (overlapping m, 2H), 3.46 (tt, $J$ = 3.9, 11.7 Hz, 1H), 3.35 (dt, $J$ = 3.9, 10.8 Hz, 1H), 3.32 (q, $J$ = 10.7 Hz, 1H), 2.06 (d, $J$ = 6.8 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 72.9, 70.7, 68.6, 64.2, 40.2, 26.8, 20.2; IR (neat film) 1312, 1123, 1202 cm$^{-1}$; MS (CI, isobutane) $m/z$ (relative intensity) 337 (100, M + 1), 257 (21), 111 (11). Anal. Calcd for $C_7H_{12}O_3SBr_2$: C, 25.00; H, 3.57; S, 9.52. Found: C, 24.86; H, 3.63; S, 9.59.

**37b**: 0.358 g (34%) obtained from 0.475 g of **36b**; colorless solid; mp 104–105 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.80 (dd, $J$ = 3.9, 11.7 Hz, 1H), 4.50 (dd, $J$ = 2.9, 11.8 Hz, 1H), 4.07 (t, $J$ = 11.7 Hz, 1H), 3.88 (dd, $J$ = 2.9, 11.8 Hz, 1H), 3.70 (t, $J$ = 11.8 Hz, 1H), 3.57 (dd, $J$ = 3.0, 10.8 Hz, 1H), 3.46 (dddd, $J$ = 2.9, 3.9, 10.8, 11.7 Hz, 1H), 3.27 (t, $J$ = 10.8 Hz, 1H), 2.25 (s, 3H),1.94 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 72.8, 71.8, 71.0, 65.1, 61.8, 36.7, 31.3, 20.3; IR (neat film) 1123, 1306, 1375

$cm^{-1}$; MS (CI, isobutane) $m/z$ (relative intensity) 351 (25, M + 1), 271 (100), 185 (1), 129 (21). Anal. Calcd for $C_8H_{14}O_3SBr_2$: C, 27.43; H, 4.00; S, 9.14. Found: C, 27.40; H, 4.11; S, 9.07.

**38**: 0.434 g (54%) obtained from 0.475 g of **36b**; colorless solid; mp 79–81 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 4.53 (dd, $J$ = 3.9, 12.7 Hz, 1H), 4.17 (dd, $J$ = 3.0, 12.8 Hz, 1H), 4.00 (dd, $J$ = 10.7, 12.7 Hz, 1H), 3.94 (dd, $J$ = 3.9, 10.7 Hz, 1H), 3.70 (overlapping m, 2H), 3.47 (tt, $J$ = 3.0, 10.8 Hz, 1H), 3.38 (t, $J$ = 10.7 Hz, 1H), 1.95 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 131.8, 121.5, 70.9, 70.7, 68.6, 63.9, 23.9, 21.2; IR (neat film) 1117, 1138, 1298, 1325 $cm^{-1}$; MS (CI, isobutane) $m/z$ (relative intensity) 271.0 (99, M + 1), 269.0 (100, M + 1), 255.1 (16). Anal. Calcd for $C_8H_{13}O_3SBr$: C, 35.69; H, 4.83; S, 11.90. Found: C, 35.66; H, 4.82; S, 11.93.

**43a**: 0.201 g (23%) obtained from 0.375 g of a 2:1 mixture of **42a**:**44a**; colorless solid; mp 60–63 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 4.50 (dd, $J$ = 3.9, 12.7 Hz, 1H), 3.99 (dd, $J$ = 5.8, 9.5 Hz, 1H), 3.88 (dd, $J$ = 3.9, 10.7 Hz, 1H), 3.77 (overlapping m, 2H), 3.53 (dd, $J$ = 4.9, 11.7 Hz, 1H), 3.45 (tt, $J$ = 3.9, 10.8 Hz, 1H), 3.30 (t, $J$ = 10.8 Hz, 1H), 3.15 (td, $J$ = 4.9, 9.8 Hz, 1H), 1.46 (d, $J$ = 5.9 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 77.5, 69.3, 68.0, 63.3, 20.6, 19.5, 19.1; IR (neat film) 1123, 1287, 1319 $cm^{-1}$; MS (CI, isobutane) $m/z$ (relative intensity) 339.1 (65, M + 1), 337.1 (100, M + 1), 335.0 (60, M + 1), 257.1 (49), 255.0 (48), 175.1 (41), 114.1 (20). Anal. Calcd for $C_7H_{12}O_3SBr_2$: C, 25.00; H, 3.57; S, 9.52. Found: C, 25.03; H, 3.59; S, 9.63.

**43b**: 0.352 g (75%) obtained from 0.212 g of a 2:1 mixture of **42b**:**44b**; colorless solid; mp 119–122 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 4.81 (dd, $J$ = 6.8, 11.7 Hz, 1H), 4.30–4.22 (m, 2H), 3.96 (t, $J$ = 12.0 Hz, 1H), 3.90 (dd, $J$ = 4.0, 10.8 Hz, 1H), 3.48 (m, 2H), 3.32 (t, $J$ = 10.8 Hz, 1H), 2.13 (d, $J$ = 6.8 Hz, 3H), 1.52 (d, $J$ = 6.8 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 75.0, 70.4, 64.1, 62.5, 43.0, 27.2, 20.5, 11.4; IR (neat film) 1134, 1317 $cm^{-1}$. Anal. Calcd for $C_8H_{14}O_3SBr_2$: C, 27.43; H, 4.00; S, 9.14. Found: C, 27.50; H, 4.01; S, 9.17.

**45a**: 0.262 g (30%) obtained from 0.375 g of a 2:1 mixture of **42a**:**44a**; colorless solid; mp 107–110 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 4.53 (broadened m, 1H), 4.29–4.22 (m, 2H), 3.90 (d, $J$ = 7.8 Hz, 1H), 3.84 (dd, $J$ = 3.0, 9.8 Hz, 1H), 3.45 (overlapping m, 3H), 3.28 (broadened m, 1H), 1.50 (d, $J$ = 6.8 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 77.5, 69.3, 68.0, 63.3, 20.6, 19.5, 19.1; IR (neat film) 1107, 1121, 1319 $cm^{-1}$; MS (CI, isobutane) $m/z$ (relative intensity) 337.0 (18, M + 1), 257.0 (24), 255.0 (24), 175.1 (100), 114.1 (69). Anal. Calcd for $C_7H_{12}O_3SBr_2$: C, 25.00; H, 3.57; S, 9.52. Found: C, 24.96; H, 3.63; S, 9.67.

**45b**: 0.047 g (10%) obtained from 0.212 g of a 2:1 mixture of **42b**:**44b**; nearly colorless solid; mp 56–59 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 4.84–4.81 (m, 1H), 4.57–4.49 (m, 1H), 4.21–4.15 (m, 1H), 3.97–3.81 (m, 2H), 3.45–3.37 (m, 1H), 3.32 (t, $J$ = 10.8 Hz, 1H), 2.84 (d, $J$ = 8.8 Hz, 1H), 1.91 (d, $J$ = 6.8 Hz, 3H), 1.50 (d, $J$ = 6.8 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 78.2, 71.5, 69.4, 63.4, 35.0, 27.2, 20.6, 20.5; IR (neat film) 1140, 1319 $cm^{-1}$. Anal. Calcd for $C_8H_{14}O_3SBr_2$: C, 27.43; H, 4.00; S, 9.14. Found: C, 27.36; H, 4.08; S, 9.17.

**47a**: 0.264 mg (33%) obtained from 0.247 g of **46a**; colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.92 (s, 1H), 4.62(AB q, 2H), 4.44 (d, $J$ = 12.7 Hz, 1H), 4.24 (d, $J$ = 12.7 Hz, 1H), 3.63 (m, 1H), 3.24 (m, 2H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 201.4, 145.0, 96.3, 72.4, 70.8, 65.5; IR (neat film) 1645, 1317, 1125 $cm^{-1}$; MS (CI, isobutane) $m/z$ (relative intensity) 414.9 (100, M + 1), 287.0 (32), 223.0 (7). Anal. Calcd for $C_6H_8O_3SI_2$: C, 17.39; H, 1.93; S, 7.73. Found: C, 17.46; H, 1.99; S, 7.82.

**47b**: 0.424 g (71%) obtained from 0.198 g of **46b**; colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 4.77 (d, $J$ = 13.6 Hz, 1H), 4.68 (d, $J$ = 13.7 Hz, 1H), 4.37 (dd, $J$ = 2.0, 12.7 Hz, 1H), 4.15 (dd, $J$ = 5.9, 12.7 Hz, 1H), 3.70 (dd, $J$ = 2.0, 9.8 Hz, 1H), 3.26 (m, 2H), 1.57 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 137.3, 118.6, 80.4, 70.7, 66.1, 32.9, −7.2; MS (CI, isobutane) $m/z$ (relative intensity) 428.7 (97, M + 1), 300.9 (100), 111.1 (47). Anal. Calcd for $C_7H_{10}O_3SI_2$: C, 19.63; H, 2.34; S, 7.48. Found: C, 19.56; H, 2.45; S, 7.28.

**47c**: 0.214 g (40%) obtained from 0.189 g of **46c**; colorless solid; mp 179–181 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.20 (s, 1H), 4.40 (dd, $J$ = 4.9, 13.7 Hz, 1H), 4.00 (dd, $J$ = 5.9, 12.7 Hz, 1H), 3.63 (dd, $J$ = 3.9, 10.8 Hz, 1H), 3.55 (dt, $J$ = 3.9, 5.9 Hz, 1H), 3.30 (dd, $J$ = 10.8, 11.8 Hz, 1H), 1.77 (s, 3H), 1.75 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 90.1, 80.9, 64.1, 63.8, 44.8, 26.8, 26.1, −4.7; IR (neat film) 1362, 1304, 1121 $cm^{-1}$; MS (CI, isobutane) $m/z$ (relative intensity) 443.0 (100, M + 1), 375.1 (12), 259.1 (7). Anal. Calcd for $C_7H_{10}O_3SI_2$: C, 19.00; H, 2.26; S, 7.24. Found: C, 19.16; H, 2.32; S, 7.35.

**48a**: 0.072 mg (13%) obtained from 0.247 g of **46a**; colorless solid; mp 112–116 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 6.24 (s,-1H), 5.86 (s,1H), 5.30 (s,1H), 4.71 (s, 1H), 4.58 (s, 1H), 4.24 (s, 1H), 3.57 (s, 1H); $^{13}C$ NMR (75 MHz, $CDCl_3$) 201.4, 122.9, 94.2, 72.4, 71.0, 1.1; IR (neat film) 1642, 1312, 1127, 1088 $cm^{-1}$. Anal. Calcd for $C_6H_7O_3SI$: C, 25.17; H, 2.45; S, 11.19. Found: C, 25.04; H, 2.49; S, 11.08.

**48b**: 0.100 g (24%) obtained from 0.198 g of **46b**; colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 6.29 (s, 1H), 5.88 (s, 1H), 4.77 (s, 2H), 4.54 (s, 2H), 3.19 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) 146.6, 140.9, 123.4, 116.2, 79.8, 70.7, 32.7. Anal. Calcd for $C_7H_9O_3SI$: C, 28.00; H, 3.00; S, 10.67. Found: C, 27.88; H, 3.11; S, 10.85.

**48c**: 0.087 g (23%) obtained from 0.189 g of **46c**; colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.08 (s, 1H), 6.23 (d, $J$ = 2.0 Hz, 1H), 5.76 (s, 1H), 5.29 (s, 1H), 4.80 (d, $J$ = 2.0 Hz, 1H), 1.75 (s, 3H), 1.63 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 145.4, 140.2, 120.5, 89.3, 63.2, 25.3; IR (neat film) 1364, 1308, 1128 $cm^{-1}$. Anal. Calcd for $C_8H_{11}O_3SI$: C, 30.57; H, 3.50; S, 10.19. Found: C, 30.36; H, 3.46; S, 10.33.

The following compounds were obtained according to the halogenation procedure described above, except for the omission of the $m$-CPBA oxidation.

**2-Hydroxy-1-(iodomethyl)-3-butenyl disulfide (16a)**: 0.493 g (98%) obtained from 0.240 g of **15a** as a slightly discolored oil; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 5.90 (m, total 2H), 5.40 (m, total 4H), 4.60 (broadened s, total 2H), 3.60 (m, total 4H), 3.18 (m, total 2H), 3.05–3.20 (m, total 2H). Anal. Calcd for $C_{10}H_{16}O_2S_2I_2$: C, 24.69; H, 3.29; S, 13.17. Found: C, 24.66; H, 3.31; S, 13.14.

**2-[(*tert*-Butyldimethylsilyl)oxy]-1-(iodomethyl)-3-butenyl disulfide (16b)**: 0.346 mg (97%) obtained from 0.230 g of **15b** as a slightly discolored oil; $^1H$ NMR (400 MHz, $CDCl_3$) (isomer 1) $\delta$ 5.78 (m, total 2H), 5.25 (m, total 4H), 4.49 (m, total 2H), 3.65 (m) and 3.52 (m) (total 2H), 3.40 (m, total 2H), 2.90 (m, total 2H), 0.90 (s, total 18 H), 0.10 (s) and 0.05 (s) (total 6H); (isomer 2) $\delta$ 5.98 (m, total 2H), 5.28 (m, total 4H), 4.58 (m, total 2H), 3.70 (m) and 3.52 (m) (total 4H), 2.98 (m) and 2.80 (m) (total 2H), 0.90 (s, total 18H), 0.16 (s, total 6H), 0.06 (s, total 6H). Anal. Calcd for $C_{22}H_{44}Si_2O_2S_2I_2$: C, 36.97; H, 6.16; S, 8.96. Found: C, 36.77; H, 6.02; S, 9.14.

**5-[(Benzyloxy)methyl]-2,3-dihydro-4-iodo-2-(iodomethyl)thiophene (18b)**: 0.550 g (95%) prepared from 0.267 g of **17b** as a colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.38–7.25 (m, 5H), 4.55 (s, 2H), 4.25 (s, 2H), 3.96 (m, 1H), 3.41 (m, 1H), 3.32-3.18 (m, 2H), 2.97 (m, 1H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 139.6, 138.0, 129.6, 129.5, 129.3, 128.5, 74.0, 73.0, 70.1, 53.5, 48.3. Anal. Calcd for $C_{13}H_{14}OSI_2$: C, 33.05; H, 2.97; S, 6.78. Found: C, 33.11; H, 2.91; S, 6.82.

**2,5-Bis(bromomethyl)tetrahydrothiophene (24:25)**: 0.224 mg (93%, 1:1 mixture) obtained from 0.100 g of **22** as a pale yellow oil; $^1H$ NMR (400 MHz, $CDCl_3$) (mixture of isomers) $\delta$ 4.35 (broadened t, $J$ = 8.8 Hz) (isomer **25**), 3.67 (m, total 3H), 3.52 (m, total 2H), 3.38 (m, total 2H), 3.10 (m, total 2H), 2.96 (m, total 1H), 2.88 (m, total 1H), 2.40 (m, total 1H), 2.20–2.05 (m, total 6H).

**29:30**: 0.172 g (97%, 2:1 mixture) obtained from 0.075 g of **28**. A purified sample of **29** gave the following data: pale yellow oil; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 4.80 (d, $J$ = 2.0 Hz, 2H), 3.60 (m, 2H), 3.45 (dd, $J$ = 9.6, 10.0 Hz, 2H), 3.29 (dd, $J$ = 9.6, 10.0 Hz, 2H), 1.51 (s, 3H), 1.36 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 112.5, 83.6, 56.0, 30.4, 26.2, 25.5; HRMS (EI) $m/z$ calcd for $C_9H_{14}O_2SI_2$ 439.8805, found 439.8817; HRMS (CI, isobutane) $m/z$ calcd for $C_9H_{15}O_2SI_2$ (M + 1) 440.8882, found 440.8917.

A purified sample of **30** gave the following data: pale yellow oil; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 4.77 (m, 2H), 3.75 (dd, $J$ = 5.2, 10.8 Hz, 2H), 3.43 (dd, $J$ = 4.8, 9.6 Hz, 2H), 3.22 (dd, $J$ = 9.6, 10.8 Hz, 2H), 1.54 (s, 3H), 1.36 (s, 3H); $^{13}C$ NMR (75 MHz,

$CDCl_3$) δ 112.9, 88.8, 55.5, 30.0, 27.6, 25.4; HRMS (CI, isobutane) *m/z* calcd for $C_9H_{15}O_2SI_2$ (M + 1) 440.8882, found 440.8915.

**1-(Bromomethyl)-6-heptenyl disulfide (56)**: 0.540 g (72%) obtained from 0.48 g of **55**; colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.87–5.76 (m, 2H), 5.06–4.96 (m, 4H), 3.77–3.68 (m, 6H), 3.56–3.41 (m, 6H), 3.24–3.20 (m, 2H), 2.15–2.10 (m, 4H), 1.74–1.65 (m, 4H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 138.7; 138.7, 115.5; 115.4, 71.1, 70.3, 54.0, 53.9, 32.8, 30.4, 30.3, 28.9, 28.9.

**1-(Bromomethyl)-2-(4-pentenyloxy)ethyl disulfide (58)**: 0.487 g (85%) obtained from 0.380 g of **57**; colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$) (mixture of diastereomers) δ 5.82 (m, 2H), 5.00 (AB m, 4H), 3.72 (m, 8H), 3.50 (m, 4H), 3.22 (m, 2H), 2.12 (m, 4H), 1.68 (m, 4H); $^{13}C$ NMR (75 MHz, $CDCl_3$) (mixture of diastereomers) δ 138.7 and 138.7, 115.5 and 115.4, 71.1 and 71.1, 70.3 and 70.3, 54.0 and 53.9, 32.8 and 32.8, 30.4 and 30.3, 28.9 and 28.9; MS (EI) *m/z* (relative intensity) 478 (6, $M^+$), 476 (8, $M^+$), 474 (4, $M^+$), 393 (25), 391 (40), 389 (22), 239 (27), 237 (26), 159 (96), 127 (100), 125 (78); MS (CI, isobutane) *m/z* (relative intensity) 479 (57, $M^+$), 477 (100, $M^+$), 475 (49, $M^+$).

**Supporting Information Available:** Copies of $^1H$ and selected $^{13}C$ NMR spectra (93 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead for ordering information.

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