Conformational Effects on the 2,3-Sigmatropic Shift of Sulfur-Stabilized Ylides and Enolates Involving Bicyclic Transition States

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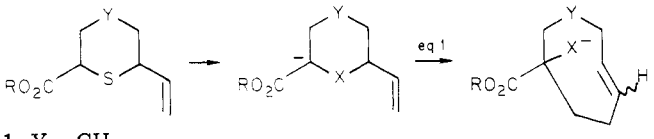
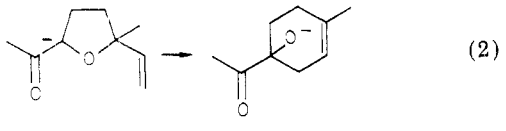
The enolate anions of 2-(carboethoxy)-6-vinylthiane (1) or of 2-(carboethoxy)-8-vinylthiacyclooct-4-ene (2) or the corresponding sulfone **27** do not undergo an anionic 2,3-sigmatropic shift at temperatures up to 50 °C. Double-bond migration is the only observable process with 1 or **27**. The ylide **29** obtained from **1** by S methylation and deprotonation does rearrange to a cycloheptene derivative **30**, which can be considered as the product of a 2,3 shift (50%). However, two diastereomeric cyclopentane derivatives **31** are also formed by a Stevens rearrangement (25%). An analogous ylide **37** derived from **2** gives a Stevens product cycloheptene derivative **38** and ylide fragmentation products, the triene esters **39** and **40**. No 2,3 shift is observed with **37**. The reluctance of these ylides to undergo a 2,3 shift is attributed to conformational and transannular destabilization of the necessary bicyclic transition states. A similar barrier apparently prevents rearrangement of 3,6-divinyl-1,2-dithiane (**15**) to products of a 2,3 shift. The synthesis of **2** involves 3-carbon ring expansion of 2,5-divinyltetrahydrothiophene (**8**), which in turn is made by ionic cyclization of sulfide alcohol **18**. Condensation of the anion of allyl tetrahydropyranyl sulfide with 5-bromopent-2-en-1-ol gives **18**, the product of α alkylation, without detectable amounts of γ alkylation.

Cyclic sulfides of variable ring size are now easily available by the "ring-growing" technique (2,3-sigmatropic ring expansion).[1] In this paper, we consider the possibility that modified 2,3-sigmatropic shifts (eq 1) might be useful for conversion of sulfides such as **1** or **2** into carbocycles. One example of the closely analogous rearrangement of an oxygen-containing ring is already known[2] (eq 2).



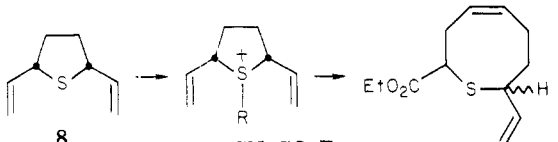
1, Y = CH_2
2, Y = $CH{=}CHCH_2$

X = S, SO_2, $^+SCH_3$



(2)

A synthesis of 1 is described in Scheme I. Alkylation of methyl (thiomethyl)acetate enolate affords the alcohol **4** which can be converted into iodide **6** from the mesylate **5** and sodium iodide. Precedented ionic cyclization[3] then gives the desired cyclic sulfide 1 as a mixture of separable diastereomers. A potential route to **7** by similar alkylation of the methyl thioglycolate dianion[4] was also considered.

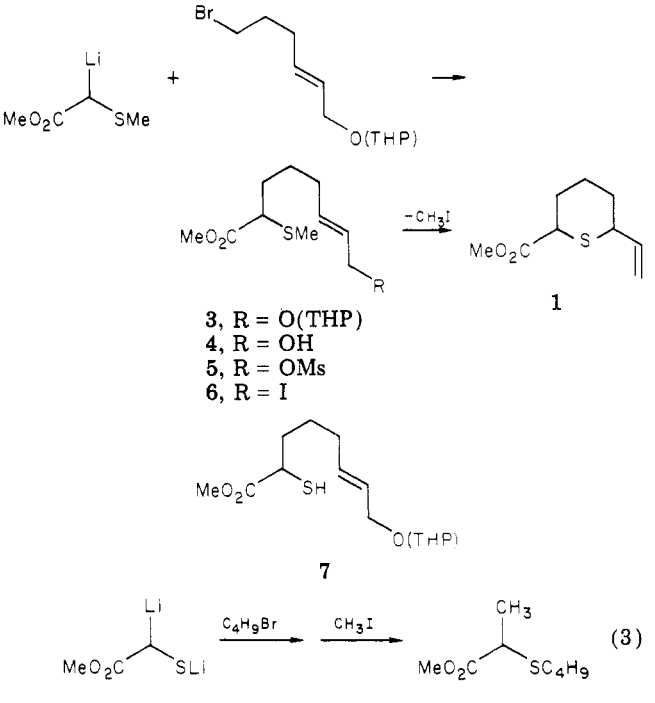


8

9, R = CH_2CO_2Et
10, R = $^-CHCO_2Et$

2

Scheme I



3, R = O(THP)
4, R = OH
5, R = OMs
6, R = I

7

(3)

However, a model study (eq 3, Scheme I) shows that the dianion reacts preferentially at sulfur and not at carbon.

The eight-membered sulfide **2** (eq 4) is available by ring expansion of α,α'-divinyltetrahydrothiophene (**8**) via sulfonium salt **9** and ylide **10**. Under carefully controlled conditions, **2** can be obtained without difficulty as a mixture of diastereomers in 61% yield. Two different syntheses of **8** are described in Schemes II and III.

In the first route (Scheme II), we encountered considerable difficulty in cleavage of the dithiocarbonate **13** to allylic bis(mercaptan) **14**. Various hydrolytic or reductive cleavage methods gave complex product mixtures. Even under the best cleavage conditions with aminoethanol as the nucleophile, the mercaptan **14** was heavily contaminated with allylic isomers having terminal sulfhydryl groups as evidenced by NMR integration of the vinyl region. The mixture of mercaptans was converted directly into the surprisingly stable disulfide **15** (epimer mixture,

(1) (a) E. Vedejs and J. P Hagen, *J. Am. Chem. Soc.*, **97**, 6878 (1975); (b) E. Vedejs, M. J. Arco, and J. M. Renga, *Tetrahedron Lett.*, 523 (1978); (c) E. Vedejs, M. J. Mullins, J. M. Renga, and S. P. Singer, *ibid.*, 519 (1978); (d) E. Vedejs, J. P. Hagen, B. L. Roach, and K. L. Spear, *J. Org. Chem.*, **43**, 1185 (1978); (e) R. Schmid and H. Schmid, *Helv. Chim. Acta*, **60**, 1361 (1977); (f) V. Ceré, S. Pollicino, E. Sandri, and A. Fava, *J. Am. Chem. Soc.*, **100**, 1516 (1978); *Chim. Ind. (Milan)*, **59**, 459 (1977); (g) B. Hasiak, *C. R. Hebd. Seances Acad. Sci., Ser. C*, **282**, 1003 (1976).

(2) A. F. Thomas and R. Dubini, *Helv. Chim. Acta*, **57**, 2084 (1974).

(3) E. Vedejs, M. J. Arco, D. W. Powell, J. M. Renga, and S. P. Singer, *J. Org. Chem.*, **43**, 4831 (1978); see also ref 1c.

(4) K. Tanaka, N. Yamagishi, R. Tanikaga, and A. Kaji, *Chem. Lett.*, 471 (1977).

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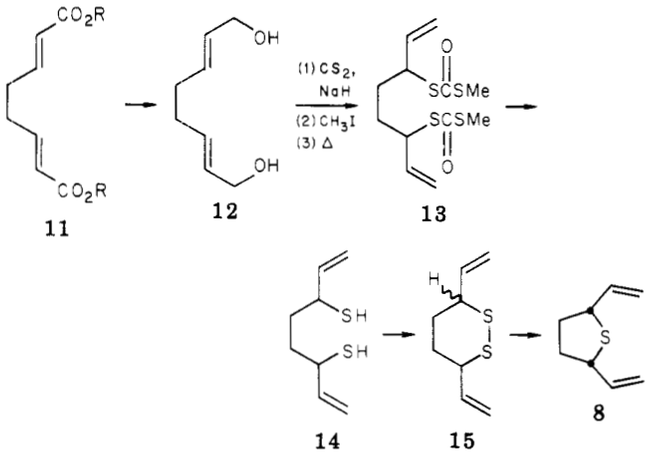
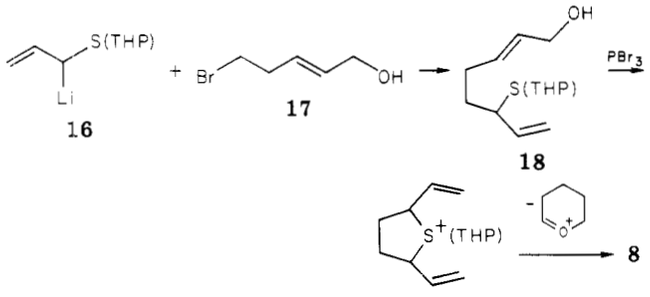
Scheme II



Scheme III

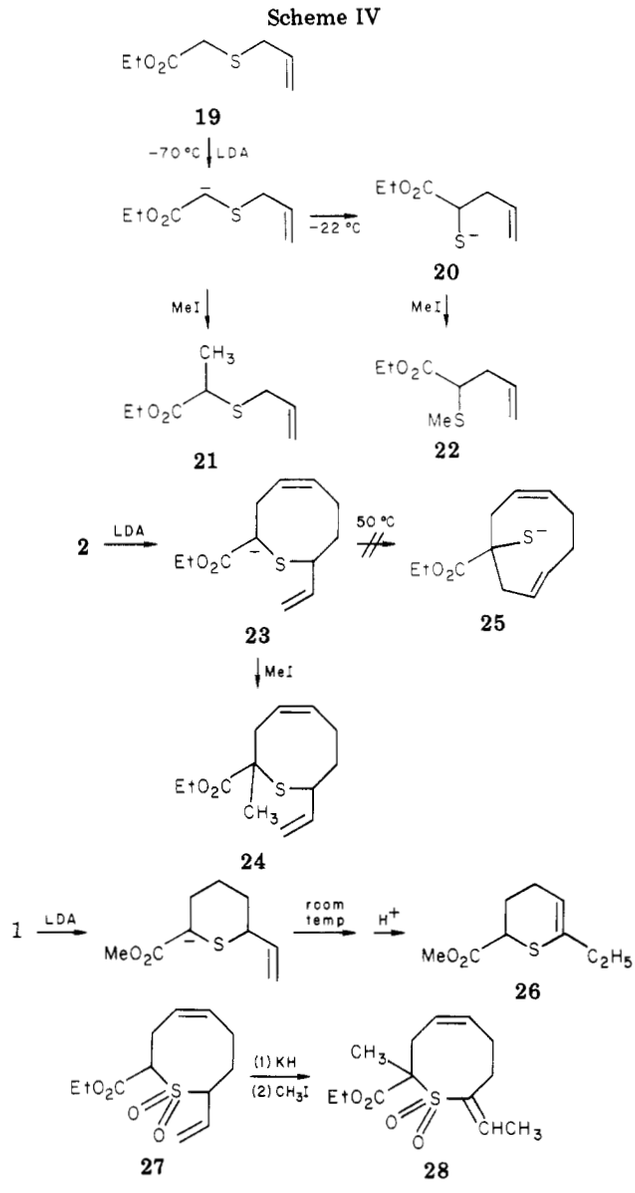


20–30% from **13**) by oxidation with diethyl azodicarboxylate.[5] When heated with hexamethylphosphorous triamide, **15** gave a single diastereomer of the tetrahydrothiophene **8** (60%).[6] Assignment of *cis*-divinyl stereochemistry to **8** is based on the NMR spectrum of the derived salt **9** which clearly retains a plane of symmetry.

In view of the difficulties encountered in Scheme II, a shorter synthesis of **8** was developed to allow easier scale up (Scheme III). The anion **16** of allyl tetrahydropyranyl sulfide (3 equiv) reacted with bromo alcohol **17** to give the sulfide alcohol **18** (75% isolated). None of the γ-alkylated sulfide was detected in the crude product.[7] The last step, cyclization of **18** to **8**, was accomplished by treatment of **18** with PBr_3. Although the yield of **8** is only 30%, the overall sequence of Scheme III is conveniently short and product isolation is not difficult.

With **1** and **2** in hand, we proceeded to examine the prospects for electrocyclic sulfur extrusion. An anionic 2,3-sigmatropic shift was first tested in an acyclic model system to define the temperature and time factors required for rearrangement.[8] Thus, treatment of **19** with LDA at −22 °C for 1 h resulted in partial rearrangement to **20** (see Scheme IV). Upon addition of methyl iodide to the mixture of anions at −22 °C, the corresponding methylation products **21** and **22** were isolated in 30 and 70% yield, respectively. The half-life for the anionic 2,3 shift was

Scheme IV



therefore less than 1 h at −22 °C. However, similar treatment of **2** with LDA and CH_3I gave exclusively the unrearranged C-methylated product **24**. Even after the anion **23** was heated to 50 °C in THF, methylation gave **24** (low material balance) and none of the sulfide derived from rearranged anion **25**. Similar experiments with the six-membered ring system **1** at 0 °C or below again gave only unrearranged products. Under more forcing conditions (>20 °C, added HMPT, etc.), the only observable process was migration of the double bond into the ring to give **26**, after quenching with dilute acid. The eight-membered sulfone **27** also failed to rearrange to carbocyclic products under a variety of basic conditions. An exocyclic double bond isomer **28** was the sole new product of these experiments.

In view of the failure of anionic 2,3-sigmatropic shifts to occur in either ring size, we were surprised to find that the ylide **29** derived from **1** did rearrange at 20 °C to the desired cycloheptene carboxylate **30** (50%). Two diastereomeric vinyl cyclopentanecarboxylates **31** were also formed (25%). For purposes of characterization, both **30** and **31** have been prepared by independent routes as shown in Scheme V. The key steps in the alternate synthesis of **30** are the conversion of methyl thiacyclooct-3-ene-2-carboxylate (**32**) into **34** by Ramberg–Backlund

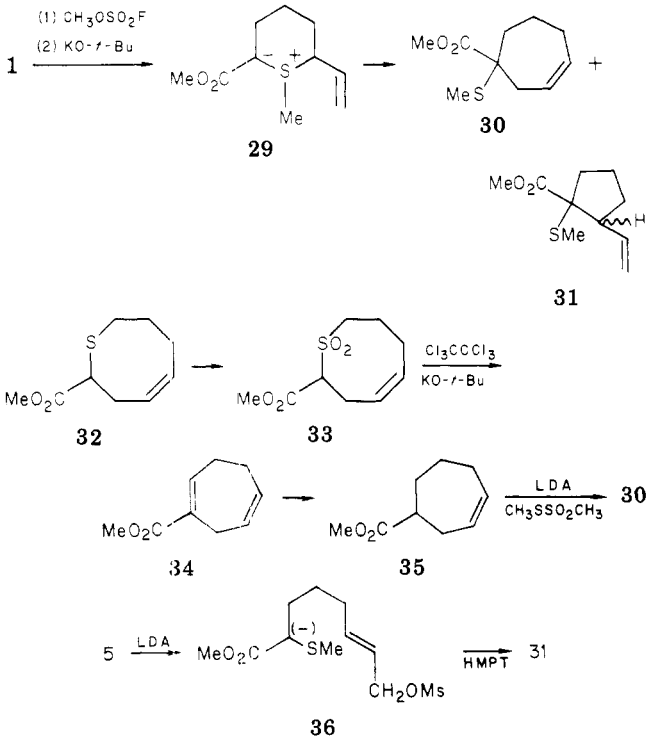
(5) T. Mukaiyama and K. Takahashi, *Tetrahedron Lett.*, 5907 (1968).

(6) Previous examples of disulfide desulfurization occur with inversion of stereochemistry: D. N. Harpp and J. G. Gleason, *J. Am. Chem. Soc.*, **93**, 2437 (1971).

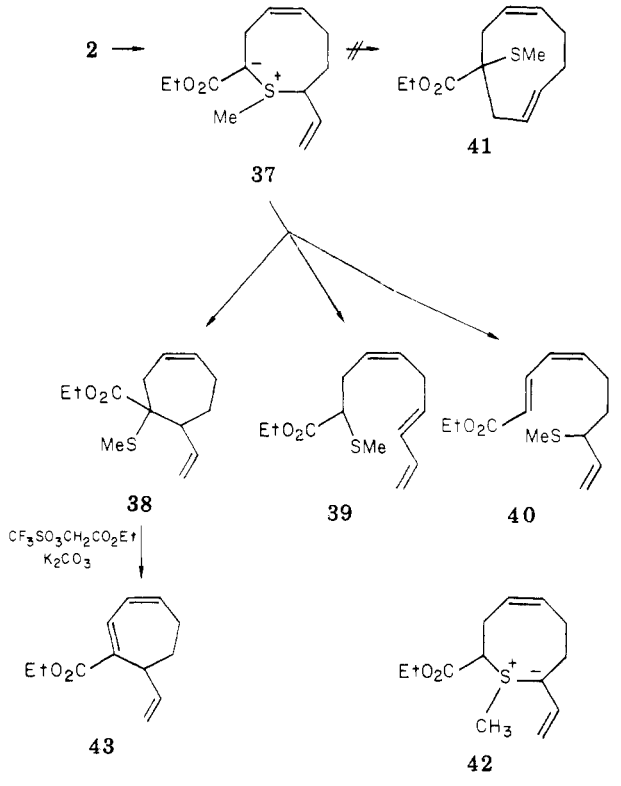
(7) Anions derived from simple allyl alkyl sulfides usually give mixtures of α- and γ-alkylation products: J. Hartmann, R. Muthukrishnan, and M. Schlosser, *Helv. Chim. Acta*, **57**, 2261 (1974); J. F. Biellman and J. B. Ducep, *Tetrahedron Lett.*, 5629 (1968); T. Nakai, H. Shiono, and M. Okawara, *ibid.*, 4027 (1975). The favorable influence of chelating heteroatom functionality attached to sulfur on the α:γ ratio is suggested in the work of K. Hirai and Y. Kishida, *Tetrahedron Lett.*, 2743 (1972).

(8) For an analogous rearrangement of an allylic sulfide enolate, see J. E. Baldwin and N. R. Tzodikov, *J. Org. Chem.*, **42**, 1878 (1977).

Scheme V



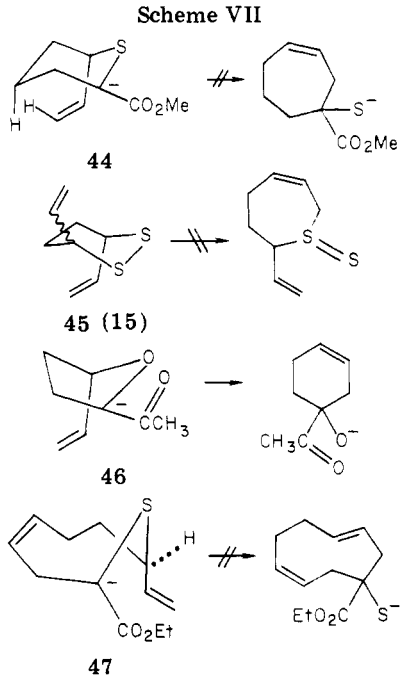
Scheme VI



sulfur extrusion,[9] and subsequent selective reduction to **35**, using Semmelhack's copper hydride reagent.[10] The cyclopentane **31** was prepared by the base-induced cyclization of mesylate **5**. The intermediate enolate **36** could conceivably have closed directly to ylide **29**, by analogy to the recent report by Reich et al. that certain α-sulfenyl enolates undergo competitive C and S alkylation.[11] However, **36** apparently behaves in an unexceptional manner since the ratio of diastereomers **31** is different from that obtained from **29**. Furthermore, none of the seven-membered ring **30** is formed from the enolate cyclization.

In the eight-membered series, the analogous ylide **37** also rearranged at room temperature. A carbocyclic product **38** and two isomeric triene esters **39** (major) and **40** (minor) were isolated, but no trace of **41**, the hypothetical product of a 2,3-sigmatropic shift, was found. In support of the structural assignment, NMR spectra of **39** and **40** at 270 MHz clearly show seven vinylic protons. The NMR spectrum of **38** establishes the presence of a contiguous chain of eight proton-bearing carbons in the correct sequence. Further evidence for the assigned structure is based on transformation of **38** into **43** by treatment with the alkylating agent $CF_3SO_3CH_2CO_2C_2H_5$ *in the presence* of K_2CO_3 (Scheme VI).[12] This reaction generates an intermediate ylide which fragments cleanly to **43** at 20 °C. Attempts to perform the alkylation prior to addition of base (according to the standard method)[12] failed because the intermediate sulfonium salt is unstable at room temperature.

Scheme VII



Discussion

The enolate $EtO_2CCH(Li)SCH_2CH{=}CH_2$ derived from **19** rearranges by a 2,3-sigmatropic shift at −22 °C. In contrast, the analogous cyclic enolates prepared from **1** or **2** are stable at −22 °C and do not undergo a 2,3 shift up to 50 °C. We suggest that the thermal barrier is due to unfavorable steric interactions in the bicyclic transition states required for concerted rearrangement. In the six-membered ring case, reasonable five-center overlap is possible only in conformations having an axial vinyl group in the severely hindered cisoid rotamer form (**44**) (see Scheme VII). A transoid vinyl rotamer cannot be involved in a concerted rearrangement because this would require a trans double bond in the cycloheptene product. Undoubtedly, a similar effect is responsible for the remarkable

(9) E. Vedejs and S. P. Singer, *J. Org. Chem.*, **43**, 4884 (1978).
(10) M. F. Semmelhack, R. D. Stauffer, and A. Yamashita, *J. Org. Chem.*, **42**, 3180 (1977).
(11) H. J. Reich and M. L. Cohen, *J. Am. Chem. Soc.*, **101**, 1307 (1979); see also B. M. Trost and Y Tamaru, *ibid.*, **99**, 3101 (1977).
(12) E. Vedejs and D. A. Engler, *Tetrahedron Lett.*, 3487 (1976).

stability of the dithiane **15** (Scheme II). Analogous acyclic diallyl disulfides undergo a reversible 2,3-sigmatropic shift in the vicinity of room temperature, and desulfurization with triphenylphosphine intercepts the thiosulfoxide valence-bond tautomer.[13] However, **15** survives unchanged at 150 °C and reaction with triphenylphosphine at lower temperatures gives none of the desulfurization product. Transition state **45** would be necessary for concerted rearrangement, but the thermal barrier is apparently prohibitive.

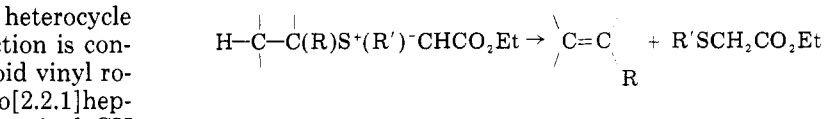
As mentioned previously, one example of an anionic 2,3-sigmatropic shift is known (eq 2) where a heterocycle is converted into a carbocycle.[2] If this reaction is concerted, then bicyclic transition state **46** (cisoid vinyl rotamer) is required. We note that the bicyclo[2.2.1]heptane-like geometry of **46** encounters less severe vinyl–CH interactions than does **44**.

In the conformationally more flexible eight-membered ring system, a pseudoaxial vinyl group is still required for good overlap with the enolate π system. However, the cisoid vinyl rotamer is no longer necessary because the hypothetical carbocyclic product (nine-membered ring) can accommodate a trans double bond. Structure **47** depicts one of several enolate conformations which appears to have a reasonable transition-state geometry for a 2,3 shift. Since rearrangement is not observed, steric interactions between the pseudoaxial vinyl group and transannular C–H bonds must be substantial even for the transoid vinyl orientation. Analogous observations have been reported by Thies et al. for Cope or Claisen rearrangements involving bicyclo[*n*.2.2] transition states.[14] Medium sized ring substrates (n = 4–6) having one endocyclic double bond and one conformationally mobile alkenyl substituent prefer to rearrange by a 1,3 shift rather than by the symmetry-allowed 3,3 shift. These results have been attributed to transannular destabilization of bicyclic transition states.[14]

Before considering the relatively complicated behavior of sulfur ylides **29** and **37**, we shall summarize the important intramolecular processes which are available to analogous ester-stabilized ylides. First of all, it is well-known that acyclic allylsulfonium ylides rearrange by a symmetry-allowed *concerted* reaction (2,3-sigmatropic shift).[15] We have used this reaction extensively for construction of medium-ring sulfides from monocyclic ylides as illustrated by the synthesis of **2** from **9**.[1,3]

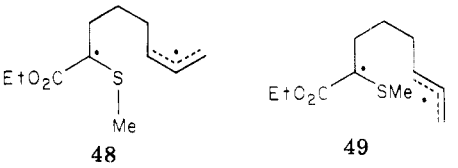
A second important reaction of certain stabilized sulfur ylides is the Stevens rearrangement.[16] For convenience, we shall classify this reaction as any 1,2 migration of a carbon substituent from ylide sulfur to ylide carbon where the rearrangement does not involve a cyclic 6π electron transition state. Isolated cases are known where the Stevens rearrangement competes to a minor extent with a 2,3-sigmatropic shift, generally in molecules where the cyclic transition state for the 2,3 shift is impeded by steric or conformational factors.[15,1d] Baldwin has shown that Stevens rearrangement of sulfur ylides occurs by both intramolecular (major) and intermolecular (minor) pathways.[17] The latter path has all of the characteristics of a homolytic fragmentation–recombination process, while the intramolecular component can be rationalized by recombination of short-lived caged radical pairs. Other mechanisms for the intramolecular Stevens rearrangement have not been ruled out, and a recent study by Closs et al. involving stabilized ammonium ylides points out that a short-lived radical pair mechanism cannot readily be distinguished from a concerted symmetry-forbidden process.[18]

A third option which is well established for certain ester-stabilized ylides is fragmentation to an alkene:[12]



The reaction is rapid at room temperature if R is an unsaturated group, e.g., ester, cyano, etc. In all reported cases where a cyclic transition state for fragmentation is possible, olefin formation occurs faster than Stevens rearrangement. However, a 2,3-sigmatropic shift is much faster than fragmentation to alkene in a number of examples where both reactions appear geometrically feasible according to molecular models.[1,3]

The most important conclusion to be drawn from our study of ylides **29** and **37** is that geometrical factors interfere with the concerted 2,3-sigmatropic shift. As a result, competing reactions such as Stevens rearrangement or fragmentation to alkenes become unusually significant. The desired carbocycle **30** is in fact the major product from the six-membered ylide **29** and may well be formed by a concerted 2,3 shift. However, the five-membered ring side products **31** are undoubtedly formed by a Stevens rearrangement. If the latter process involves a radical pair, one could also explain the formation of **30** by a nonconcerted mechanism. It would be necessary to postulate formation of a cisoid diradical **48** which could give either



48 **49**

30 or **31**. This situation is conceivable but certainly not appealing. There is no reason to expect a cycloheptene to form faster than a cyclopentane from diradical **48**, nor is there any good argument which explains preferential formation of cisoid **4**, rather than transoid **49**. The latter, of course, can only reclose to give the minor products **31**.

In the eight-membered ring system, no sign of any product of a 2,3 shift has been found. In addition to Stevens product **38**, ylide **37** gives two acyclic dienes **39** and **40**. The major diene **39** can be recognized as the product of intramolecular fragmentation of ylide **37** while the trace component **40** is derived similarly from ylide isomer **42**. Equilibration of ylides such as **37** and **42** by proton transfer has literature precedent.[1d,3]

Both ylides **29** and **37** encounter the same steric barriers to a concerted 2,3-sigmatropic shift as do the analogous enolate anions. It is possible that in larger, more flexible ring systems the desired 2,3 shifts might take place efficiently. However, the reaction is not generally useful for conversion of sulfur heterocycles into carbocycles. Other

(13) G. Hofle and J. E. Baldwin, *J. Am. Chem. Soc.*, **93**, 6307 (1971).
(14) R. W. Thies and R. E. Bolestra, *J. Org. Chem.*, **41**, 1233 (1976); R. W. Thies and E. P. Seitz, *ibid.*, **43**, 1050 (1978).
(15) J. E. Baldwin and R. E. Hackler, *J. Am. Chem. Soc.*, **91**, 3646 (1969).
(16) Reviews: T. S. Stevens, *Prog. Org. Chem.*, **7**, 48 (1968); R. A. W. Johnstone, *Mech. Mol. Migr.*, **2**, 249 (1969); S. H. Pine, *Org. React.*, **18**, 403 (1970); U. Schöllkopf, *Angew. Chem., Int. Ed. Engl.*, **9**, 763 (1970).
(17) J. E. Baldwin, W. F. Erickson, R. E. Hackler, and R. M. Scott, *Chem. Commun.*, 576 (1970).
(18) O. H. Dolling, G. L. Closs, A. H. Cohen, and W. D. Ollis, *J. Chem. Soc., Chem. Commun.*, 545 (1975).

methods for achieving this goal have been developed in our laboratory and will be described in due course.

Experimental Section

NMR spectra were recorded on a Jeol MH100 instrument unless specified otherwise. Dry THF was obtained by refluxing over sodium–benzophenone and distilling prior to use. Standard LDA solution was prepared and titrated as described previously.[19] All melting points are uncorrected (microscope–hot-stage apparatus).

4-Bromo-1-butanol. To refluxing THF (1.35 L) was added 48% HBr (906 g, 5.37 mol of HBr) dropwise over a 3.75-h period. The reaction was refluxed a further 1.25 h, and then cooled, neutralized with $NaHCO_3$, partitioned with water, washed with brine, and dried over $MgSO_4$. Concentration yielded 314.2 g (38%) of product: bp 73–74 °C (3.1 mm).

4-Bromobutanal. In a 5-L, three-necked flask fitted with a mechanical stirrer and nitrogen inlet was placed pyridinium chlorochromate (PCC, 484.4 g, 2.247 mol) in CH_2Cl_2 (2.5 L). To this was added 4-bromo-1-butanol (229 g, 1.5 mol) in CH_2Cl_2 (900 mL) over several minutes. Intermittent cooling was required to prevent reflux of solvent. After 35 min the mixture was diluted with one volume of pentane and the solvent decanted off. The residual black sludge was rinsed twice with pentane. The combined pentane washings were filtered through Celite. The solvent was removed and the residue filtered through a short dry plug of silica gel (200 g, 60–200 mesh, pentane eluant) yielding 140 g (62%) of aldehyde: bp 35–40 °C (0.07 mm); NMR (CCl_4) δ 9.76 (1 H, s), 3.44 (2 H, t, J = 7 Hz), 2.64 (2 H, t, J = 7 Hz), 2.15 (2 H, quintet, J = 7 Hz); IR (neat) 2730 (w), 1730 (s) cm^{-1}.

Ethyl 6-Bromohex-2-enoate. In a three-necked, 2-L flask fitted with a nitrogen inlet and mechanical stirrer was placed sodium hydride (14.7 g, 0.35 mol, 57% oil dispersion). The hydride was washed several times with dry hexane by decantation, and dry THF (600 mL) was added by cannula. Triethyl phosphonoacetate (57.9 mL, 0.291 mol) was then added, and the resultant solution was stirred at room temperature until gas evolution ceased. A solution of freshly distilled 4-bromobutanal (48.8 g, 0.323 mol stored at −78 °C until used) in THF (50 mL) was added rapidly to the phosphonate at −30 °C by cannula. The reaction was stirred 5 min at −30 °C and then warmed to 20 °C for 1 h. Water was added to the resulting suspension, the phases were separated, and the ether layer was washed with brine and then dried over $MgSO_4$. The solvent was removed and the residue (73.6 g) was passed through a plug of silica gel (50 g, 60–200, hexane eluant). After solvent removal (aspirator), the crude oil was distilled to give 41.8 g (65%) of product: bp 71–75 °C (0.25–0.3 mm); NMR (CCl_4) δ 6.8 (1 H, ddd, J = 15.5, 13.5, 7 Hz), 5.76 (1 H, dt, J = 15.5, 1.5 Hz), 4.1 (2 H, q, J = 7 Hz), 3.4 (2 H, t, J = 7 Hz), 2.4 (2 H, q, J = 7 Hz), 2.02 (2 H, quintet, J = 7 Hz); IR ($CDCl_3$) 1775 (w), 1710 (s), 1655 (m), 1440 (m), 1375 (m), 1275 (s), 1205 (s), 1040 (m), 980 (m) cm^{-1}; m/e 222.00741 (m/e calcd for $C_8H_{13}BrO_2$ 222.00797).

6-Bromohex-2-enol. Ethyl 6-bromohex-2-enoate (263 mg, 1.19 mmol) in hexane (1 mL, dried with NaH) was treated at 0 °C under a nitrogen flow with diisobutylaluminum hydride (3 mL of a 1 M solution in hexane, Aldrich). After 10 min of stirring, 10% HCl (0.55 mL) and hexane (10 mL) were added. After 5 min $MgSO_4$ (1.1 g) was added, and the mixture was stirred vigorously for 5 min, filtered, and evaporated to give crude product (200 mg, crude yield 94%) which was used without further purification. For purposes of characterization, a sample was distilled: bp 60–71 °C (0.23 mm); NMR ($CDCl_3$) δ 5.58 (2 H, m), 4.0 (2 H, m), 3.36 (2 H, t, J = 7 Hz), 2.6 (1 H, s), 2.16 (2 H, m), 1.92 (2 H, quintet, J = 6 Hz); IR (neat) 3360 (s), 1670 (w), 1440 (m), 1245 (m), 1205 (m), 1095 (m), 1005 (s), 975 (s) cm^{-1}; m/e 179.99721 (m/e calcd for $C_6H_{11}BrO$ 179.99741).

6-Bromohex-2-enyl Tetrahydropyranyl Ether. Dihydropyran (9.23 mL, 0.101 mol) was combined with 6-bromohex-2-enol (16.4 g, 0.092 mol) in CCl_4 (20 mL), and a catalytic quantity of p-toluenesulfonic acid (ca. 10 mg) was added. After 2 h at 20 °C a few drops of triethylamine were added and the mixture was evaporated (aspirator). Filtration with hexane through a short silica gel plug (60–200 mesh) yielded 24.1 g (99%) of product. This material was used without further purification: NMR (CCl_4) δ 5.58 (2 H, m), 4.53 (1 H, m), 4.5–5.58 (3 H, m), 3.4 (1 H, m), 3.38 (2 H, t, J = 7 Hz), 2.4–2.1 (2 H, m), 2.1–1.75 (2 H, m), 1.8–1.3 (6 H, m); IR (neat) 1440 (m), 1350 (m), 1260 (m), 1205 (m), 1135 (s), 1120 (s), 1070 (s), 1025 (s), 970 (m), 905 (m), 870 (m), 815 (m) cm^{-1}; m/e 265.06231 (m/e calcd for $C_{11}H_{20}BrO_2$ 265.06274).

Methyl 2-(Methylthio)-8-hydroxyoct-6-enoate (4). In a 250-mL flask at −78 °C (nitrogen flow) was placed diisopropylamine (11.82 mL, 84.4 mmol), and n-butyllithium (54.1 mL, 1.53 M in hexane) was added dropwise, with stirring. Dry THF (43 mL) was added and the solution was warmed to −23 °C. HMPT (35 mL, dried and distilled from sodium) was added and methyl (methylthio)acetate (6.33 mL, 59.1 mmol) was introduced by syringe. The solution was stirred 10 min at −23 °C and neat 6-bromohex-2-enyl tetrahydropyranyl ether (15.54 g, 59.1 mmol) was added. The mixture was stirred 1 h at −23 °C and 10 min at 0 °C and then quenched with water. The mixture was diluted with ether and extracted (three 10-mL portions of 10% HCl and then 10 mL of saturated $NaHCO_3$). After the mixture was dried over $MgSO_4$ and the solvent removed 16.59 g of crude **3** was obtained. To this residue was added methanol (20 mL) and p-toluenesulfonic acid (682 mg, 4 mmol). After 1 h at 20 °C, triethylamine (556 μL, 4 mmol) was added and the solvent removed (aspirator). The residue was dissolved in ether, extracted (two 10-mL portions of 10% HCl, two 10-mL portions of saturated $NaHCO_3$), and dried ($MgSO_4$). Removal of solvent gave 12.02 g of material. Distillation gave a forerun of 6-bromohex-2-enol (1.67 g, 12.5%) and the desired **4**: 4.7 g; 35%; bp 139 °C (0.25 mm); NMR (CCl_4) δ 5.55 (2 H, m), 3.95 (2 H, m), 3.68 (3 H, s), 3.04 (1 H, t, J = 7 Hz), 2.72 (1 H, s), 2.06 (3 H, s), 2.2–1.2 (6 H, m); IR (neat) 3800 (s), 1735 (s), 1675 (w), 1580 (s), 1440 (s), 1345 (m), 1260 (s), 1200 (s), 1165 (s), 975 (s), 905 (w), 760 (m) cm^{-1}; m/e 218.09766 (m/e calcd for $C_{10}H_{18}O_3S$ 218.09716).

Conversion of 4 into 1. Alcohol **4** (19.3 g, 0.087 mol) was dissolved in dry ether (100 mL). To this at 0 °C was added methanesulfonyl chloride (7.54 mL, 0.0974 mol) and triethylamine (18.6 mL, 0.133 mol). After 10 min at 0 °C the mixture was filtered and the solvent removed (aspirator). The residue containing **5** was dissolved in CH_3CN (100 mL), and sodium iodide (26.7 g, 0.178 mol) was added. After 10 min at room temperature the mixture was diluted with ether and filtered, and solvents were removed (aspirator) to give crude iodide **6**. The oily product was dissolved in CH_3CN (200 mL) and refluxed 1 h. After the mixture had cooled the solvent was removed and the residue partitioned between ether and 10% HCl. The ether phase was washed with saturated $NaHCO_3$ and then saturated $Na_2S_2O_3$ and dried, (Na_2SO_4) and solvent was removed. Distillation gave a diastereomeric mixture of **1** (39% on alcohol, 45% on crude mesylate). Separation was achieved by preparative TLC (Merck PF254, eluant 50% EtO/hexane), R_f(A) 0.47 and R_f(B) 0.53, or by GLPC (5 ft × $^1/_4$ in. column, 20% SE 30 on 60/80 Chromosorb P, 135 °C, flow rate 67 mL/min), T_R(A) = 32 min, T_R(B) = 25.4 min, and A/B = 1.44.

A: NMR (CCl_4) δ 5.7 (1 H, ddd, J = 17, 10, 7 Hz), 5.1 (2 H, m), 3.67 (3 H, s), 3.5 (1 H, dd, J = 10.5, 2.5 Hz), 3.32 (1 H, m), 2.3–1.3 (6 H, m); IR (CCl_4) 1745 (s), 1632 (w), 1440 (m), 1360 (w), 1315 (m), 1265 (m), 1220 (m), 1195 (m), 1163 (m), 1030 (w), 1020 (w), 990 (w), 950 (w), 925 (m) cm^{-1}; m/e 186.07099 (m/e calcd for $C_9H_{14}O_2S$ 186.07145).

B: NMR (CCl_4) δ 5.68 (1 H, ddd, J = 17, 10, 7 Hz), 5.1 (2 H, m), 3.68 (3 H, s), 3.6 (1 H, m), 3.36 (1 H, m), 2–1.4 (6 H, m); IR (neat) 1735 (s), 1635 (w), 1440 (m), 1365 (w), 1328 (m), 1250 (m), 1220 (s), 1195 (s), 1165 (s), 1130 (m), 1100 (w), 1070 (w), 995 (m), 925 (m), 845 (w) cm^{-1}; m/e 186.07102 (m/e calcd for $C_9H_{14}O_2S$ 186.07145).

Alkylation of the Methyl Thioglycolate Dianion. The dianion was formed by addition of neat methyl thioglycolate (179 μL, 2 mmol, Aldrich, distilled) to a mixture of LDA (6.7 mL of a 0.74 M solution in THF/hexane)[19] and HMPT (2 mL, distilled from sodium) at −45 °C under nitrogen. After 10 min at −45 °C, the dianion was alkylated with butyl bromide (118 μL, 1.1 mmol). After 0.5 h, methyl iodide (380 μL, 6.1 mmol) was added. After 5 min, the reaction was extracted with 10% HCl, and the organics were dried ($MgSO_4$) and concentrated (aspirator) to give 240 mg

(19) E. Vedejs, D. A. Engler, and J. E. Telschow, J. Org. Chem., 43, 188 (1978).

(68%) of methyl 2-(butylthio)propionate: NMR (CCl_4) δ 3.7 (3 H, s), 3.24 (1 H, q, J = 7 Hz), 2.56 (2 H, m), 1.6–1.1 (4 H, m), 1.36 (3 H, d, J = 7 Hz), 0.9 (3 H, t, J = 6 Hz). No evidence for SCH_3 signals was found.

2,6-Octadiene-1,8-diol (12). Diisobutylaluminum hydride (DIBAL) (100 mL, 1.1 M in hexane, 0.11 mol) was cooled to 0 °C under N_2. A solution of dimethyl 2,6-octadienoate (**11**)[20] (5.0 g, 0.025 mol) in 30 mL of dry ether was added over a 30-min period, with rapid stirring, after which the mixture was stirred at 0 °C for an additional 30 min. The reaction mixture was then allowed to warm to room temperature, cooled back down to 0 °C and quenched with methanol. Careful addition of 25 mL of 10% HCl gave a white gelatinous precipitate. More ether was added along with Filter Cel, and the mixture was stirred for several minutes and filtered. The aqueous and organic layers were separated and the organic layer was dried over anhydrous sodium sulfate. Removal of the solvent under vacuum afforded 3.1 g of pure diol: 90%; bp 105–110 °C (0.05 mm); IR (neat) 3450, 2975, 1650, 1050 cm^{-1}; NMR ($CDCl_3$) δ 5.6 (4 H, m), 4.05 (4 H, m), 2.80 (2 H, br s), 2.05 (4 H, m).

Conversion of Diol 12 into Dithiolcarbonate 13. The diol **12** (4.0 g, 0.028 mol) in 30 mL of ether was slowly dripped into a flask containing a suspension of sodium hydride (1.44 g, 0.06 mol) in 50 mL of dry ether at room temperature. The mixture was then heated to reflux for 12 h. Carbon disulfide (5.3 g, 0.07 mol) was then added and reflux continued for 24 h. To the resulting yellow mixture was added methyl iodide (8.5 g, 0.06 mol), and reflux was continued for 3 h. The reaction mixture was cooled and the white precipitate (NaI) was filtered off and washed with ether. The combined organic layers were washed with 25 mL of water and dried over anhydrous sodium sulfate. The solvent was removed under vacuum, affording 7.33 g of the bis(xanthate) (91%) as a yellow oil: IR (CCl_4) 2975, 1650, 1217, 1080 cm^{-1}; NMR ($CDCl_3$) δ 5.80 (4 H, m), 5.08 (4 H, d, J = 7 Hz), 2.60 (6 H, s), 2.25 (4 H, m). The bis(xanthate) was heated (neat) at 130 °C under a N_2 atmosphere for 90 min. The resulting oil was chromatographed on silica gel (dry column, eluant 30% ether–hexane), affording a 70% yield (5.1 g) of rearranged **13**: IR (CCl_4) 3090, 3015, 2975, 1710, 1658, 873 cm^{-1}; NMR ($CDCl_3$) δ 5.78 (2 H, ddd, J = 15.5, 8, 2.5 Hz), 5.25 (4 H, m), 4.20 (2 H, m), 2.40 (6 H, s), 1.78 (4 H, m).

Conversion of 13 into 3,6-Divinyl-1,2-dithiane (15). Aminoethanol (0.213 g, 3.5 mmol) was added to a flask containing the dithiolcarbonate **13** (0.543 g, 1.68 mmol) and 5 mL of dry hexane. The two-phase system was stirred rapidly at room temperature under a flow-through N_2 system for 24 h. The hexane layer was decanted from a thick sticky precipitate. The precipitate was washed with several 5-mL portions of hexane, and the combined organic layers were evaporated (aspirator), affording 0.284 g of crude **14** which was used in subsequent steps without further purification. The dimercaptan was unstable to silica gel, and attempted distillation led to much decomposition.

A dry flask under a N_2 atmosphere was charged with 1.5 mL of dry ether and the dimercapto compound **14** (137 mg, 0.78 mmol). Diethyl azodicarboxylate (140 mg, 0.79 mmol) in 5 mL of ether was added at room temperature. The mixture was then refluxed for 36 h. The ether was removed, leaving behind an orange oily residue. This oil was chromatographed on silica gel (eluant 3% ether–hexane), affording a single major zone which proved to be a mixture of the cis and trans isomers of 3,6-divinyl-1,2-dithiane (**15**). These isomers were separated by using high-pressure liquid chromatography (reverse phase on a 4-ft column packed with C-18 Bondapak, eluant 90% methanol–water, recycle mode, flow rate 6 mL/min): IR (CCl_4) 3050, 2960, 2800, 1600, 1410, 1390, 910 cm^{-1}; NMR ($CDCl_3$) isomer A, δ 6.05 (2 H, ddd, J = 15.5, 8.8, 2 Hz), 5.05 (4 H, m), 3.22 (2 H, m), 1.72 (4 H, m); isomer B, δ 5.75 (2 H, ddd, J = 15.5, 8.9, 2 Hz), 5.24 (4 H, m), 3.50 (2 H, m), 2.4–1.8 (2 H, m); m/e 172.0385 (m/e calcd for $C_8H_{12}S_2$ 172.03771).

***cis*-2,5-Divinyltetrahydrothiophene (8).** Hexamethylphosphorous triamide (HMPT) (81 mg, 0.5 mmol) in 5 mL of dry ethyl acetate was added all at once to a flask containing the divinyldithiane **15** (65 mg, 0.38 mmol) in 1 mL of dry ethyl acetate. The mixture was stirred and refluxed under N_2 for 16 h. The solvent was then removed under vacuum and the yellow oily residue was chromatographed on silica gel (eluant 4% ether–hexane). The divinyltetrahydrothiophene **8** was the only significant zone (32 mg, 60%): IR (CCl_4) 3040, 2940, 1600, 1420, 1390, 970, 900 cm^{-1}; NMR ($CDCl_3$) δ 5.8 (2 H, ddd, J = 15.5, 8, 2 Hz), 5.05 (4 H, m), 4.0 (2 H, m), 2.05 (4 H, m); m/e 140.06597 (m/e calcd for $C_8H_{12}S$ 140.06646).

Pyrolysis of 3,6-Divinyl-1,2-dithiane (15). Two clean, dry NMR tubes were flushed with nitrogen and 0.3 mL of dry decalin was added to each. Isomers A and B (30 mg) of **15** were dissolved in two dry NMR tubes under N_2. Both tubes were then heated to 150 °C for 45 min. NMR and TLC analysis of the pyrolized material showed only unchanged starting material in both cases. The experiment was repeated in deuteriobenzene, using an 80 °C bath. Triphenylphosphine (44 mg) was added to each NMR tube and heating was maintained for 30 min. No change was found by NMR or TLC. A similar experiment in benzonitrile at 150 °C gave only an uncharacterizable tar.

Allyl Tetrahydropyranyl Sulfide. To a flask containing 200 mL of methylene chloride was added allyl mercaptan (150 g, 0.2 mol, 70% pure, Aldrich) and dihydropyran (16.8 g, 0.2 mol). Toluenesulfonic acid (100 mg, 0.5 mmol) was then added and the mixture stirred at room temperature for 12 h. The solvent was removed under vacuum and the residue was distilled, affording 25.2 g of product: bp 55–60 °C (2.5 mm); 81%; NMR (CCl_4) δ 5.87 (1 H, m), 5.14 (2 H, m), 4.95 (1 H, m), 4.10 (1 H, m), 3.5 (1 H, m), 3.2 (2 H, t, J = 8 Hz), 2.2–1.5 (6 H, m); IR (CCl_4) 2690, 2880, 1635, 1265, 1190, 1040 cm^{-1}; m/e 158.07654 (m/e calcd for $C_8H_{14}OS$ 158.07670.

Alkylation of Allyl Tetrahydropyranyl Sulfide. Preparation of 18. A flask containing allyl tetrahydropyranyl sulfide (3.67 g, 2.3 mmol) in THF (60 mL) was cooled to −20 °C and *n*-butyllithium (15.5 mL, 1.48 M solution in hexane, 23 mmol) was added. After 30 min a solution of 5-bromo-2-penten-1-ol[21] (1.28 g, 7.75 mmol) in THF (10 mL) was dripped in over a 15-min period. The reaction was stirred at −20 °C for 60 min and was then quenched with glacial acetic acid. The mixture was warmed to room temperature and water (75 mL) was added. After extraction with ether (three 50-mL portions), the organic layers were dried over $MgSO_4$ and the solvent was removed under vacuum. The residue was purified by high-pressure liquid chromatography, using the Waters Prep LC 500 with a silica column (Prep Pack) (27% ethyl acetate–hexane, 250 mL/min). After removal of solvent under vacuum, the pure alcohol **18** was obtained: 1.4 g; 5.7 mmol; 75%; IR (CCl_4) 3410 (s), 2905 (s), 2845 (s), 1640 (w), 1250 (s), 1180 (s), 1170 (s), 1120 (s) cm^{-1}; NMR (CCl_4) δ 5.70 (3 H, m), 5.15 (2 H, m), 4.90 (1 H, m), 4.05 (3 H, m), 3.7–3.2 (2 H, m), 3.0 (1 H, br s), 2.15 (2 H, m), 1.65 (8 H, m); m/e 242.13376 (m/e calcd for $C_{13}H_{22}O_2S$ 242.13405).

2,5-Divinyltetrahydrothiophene (8) from 18. The alcohol **18** (10.0 g, 41.3 mmol) and anhydrous potassium carbonate (12.0 g, 86.8 mmol) were suspended in 250 mL of dry CH_3CN and cooled to −20 °C under N_2. A solution of PBr_3 (3.9 g, 14.4 mmol) in 25 mL of dry CH_3CN was dripped in over 15 min. After 1 h at −20 °C the mixture was warmed to 25 °C and stirred for 30 h. Water (300 mL) was then added and the product was extracted with three 100-mL portions of pentane. The pentane was distilled through a Vigreux column. The crude divinyltetrahydrothiophene was then bulb-to-bulb distilled in a closed system at 40 °C (0.1 mm) affording **8** (1.7 g, 12 mmol, 30%), identical with material prepared from **15**.

Sulfonium Salt 9. 2,5-Divinyltetrahydrothiophene (240 mg, 1.7 mmol) was added to a flame-dried flask containing 2 mL of dry acetonitrile under N_2. (Carboethoxy)methyl trifluoromethanesulfonate (920 mg, 3.5 mmol) was added and the mixture was stirred for 4 h. The solvent was removed under vacuum and the dark oil recrystallized from ethyl acetate–ether, affording white crystalline **9**: 460 mg; 67%; mp 58–59 °C; NMR (CD_3CN) δ 6.1 (2 H, m), 5.7 (4 H, m), 4.5 (2 H, s), 4.35 (2 H, m), 2.45 (4 H, m), 1.27 (3 H, m).

2-(Carboethoxy)-8-vinylthiacyclooct-4-ene (2). A 25-mL, three-necked flask was charged with the salt **9** and 10 mL of dry

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(21) J. K. Sutherland, G. Pratt, R. Battaglia, and J. J. S. Bajorek, *J. Chem. Soc., Perkin Trans. 1*, 1243 (1974).

THF under N_2. Then potassium *tert*-butoxide was dissolved in 5 mL of THF in an addition funnel, and the solution was added to the stirred salt solution over several minutes. After 3 h at 25 °C, the reaction was quenched with 3 drops of glacial acetic acid. The solvent was removed under vacuum and the residue was extracted with 15 mL of 50% ether–hexane. The extract was concentrated (aspirator) to a volume of ca. 1 mL and passed through a silica gel plug (1 × 3 cm) with 50% ether–hexane to give 335 mg of crude product. This material was then separated by using high-pressure liquid chromatography (Waters Porasil A silica gel packing, 8-ft. column, 1% ethyl acetate–hexane). Two major components and four minor unidentified components were obtained. The major components (61%, variable ratio) proved to be the diastereomers of the desired **2**. Isomer A: IR (CCl_4) 3010, (m), 2980 (s), 2935 (s), 1735 (s), 1635 (w), 1250 (s), 1150 (s), 1035 (m), 915 (s) cm^{-1}; NMR ($CDCl_3$) δ 5.85 (3 H, m), 5.05 (2 H, m), 4.20 (2 H, q, J = 7 Hz), 3.80 (1 H, m), 3.50 (1 H, t, J = 4.5 Hz), 2.75 (2 H, m), 2.4–1.6 (4 H, m), 1.30 (3 H, t, J = 7 Hz); m/e 226.10275 (m/e calcd for $C_{12}H_{18}O_2S$ 226.10245). Isomer B: IR (CCl_4) 3060 (w), 2960 (s), 2910 (s), 2840 (m), 1730 (s), 1630 (w), 1450 (m), 1360 (m), 1335 (m), 1275 (s), 1240 (s), 1145 (s), 1130 (s), 1025 (s), 905 (s) cm^{-1}; m/e 226.10275 (m/e calcd for $C_{12}H_{18}O_2S$ 226.10245).

Rearrangement of Ethyl (Allylthio)acetate (19) into 20. Isolation of 21 and 22. A dry 10-mL, two-necked flask under nitrogen was charged with dry tetrahydrofuran (5 mL) and ethyl (allylthio)acetate (**19**) (100 mg, 0.62 mmol) and cooled to −23 °C. Lithium diisopropylamide (0.68 mL, 1 M in THF) was added and the mixture was stirred at −23 °C for 60 min. The reaction was then quenched with methyl iodide (96 mg, 0.68 mmol), the mixture was stirred for 5 min, and water (5 mL) was added. After the solution had warmed to room temperature, water was added and the layers were separated. The aqueous layer was extracted with ether (three 5-mL portions), and the combined organic layers were washed with water (10 mL) and brine (10 mL) and were then dried over $MgSO_4$. The solvent was removed under vacuum and the oily residue was passed through a silica gel (60–200 mesh) plug (5% ether–hexane), affording 103 mg of a mixture of ethyl 2-(methylthio)-4-pentenoate (**22**) [63%; NMR (CCl_4) δ 5.7 (1 H, m), 5.1 (2 H, m), 4.15 (2 H, q, J = 7.5 Hz), 3.1 (1 H, t, J = 8.0 Hz), 2.45 (2 H, m), 2.05 (3 H, s), 1.23 (3 H, t, J = 7.5 Hz)] and ethyl 2-(allylthio)propionate (**21**) [27%; NMR (CCl_4) δ 5.6 (1 H, m), 5.0 (2 H, m), 4.0 (2 H, q, J = 7.7 Hz), 3.1 (2 H, d, J = 8 Hz), 3.05 (1 H, m), 1.2 (6 H, m).

Attempted Rearrangement of 1 by an Anionic 2,3 Shift. A solution of **1** (99 mg, 0.533 mmol) in dry THF (1 mL) was added to LDA (1.63 mL, 0.72 M in THF–hexane) at −70 °C (N_2 flow). After 20 min at −70 °C, the solution was warmed to 0 °C for 2 h. Addition of 5% HCl and a standard aqueous ether workup gave recovered starting material. A similar experiment was performed by using HMPT (0.5 mL), THF (1 mL), and LDA as before. After 12 h at 20 °C, the reaction was quenched with dilute acid and worked up (pentane vs. H_2O) to give a dark oil. Preparative TLC (silica gel PF 254), using 40% ether–hexane as eluant, gave isomer **26** (38 mg, R_f 0.6). Characterization of **26**: NMR ($CDCl_3$) δ 5.64 (1 H, m), 3.8 (3 H, s), 3.78 (1 H, m), 2.5–1.2 (4 H, m), 1.78 (2 H, q, J = 8 Hz), 1.1 (3 H, t, J = 8 Hz); IR ($CDCl_3$) 1735 (s), 1640 (w), 1440 (m) cm^{-1}; m/e 186.07135 (m/e calcd for $C_9H_{14}O_2S$ 186.07145).

Conversion of 1 into 30 and 31 by a 2,3 Shift. Methyl fluorosulfonate (209 μL, 2.59 mmol) was added to 2-(carbomethoxy)-6-vinylthiane (0.377 g, 2.07 mmol) in methylene chloride (1 mL). After 1.5 h at room temperature, ether was added to precipitate salt and the solvents were removed under reduced pressure. The dark brown oil thus obtained was carried on without further purification. To the crude salt (~2.07 mmol; vide supra) was added dry THF (4 mL). The oil only partially dissolves. Then, potassium *tert*-butoxide (4.35 mL of a 0.5 M solution in THF) was added dropwise at room temperature under nitrogen. After 30 min at room temperature, the material was quenched with acetic acid and concentrated to an oil under reduced pressure. The residue was passed through a silica gel (60–200 mesh) plug with ether to yield 305 mg (74%) of crude product. Analysis by GLPC on a 10 ft × $^1/_4$ in. column (8% FFAP on Chrom A coated with disilazane at 140 °C, flow 100 mL/min) gave peaks at 13.3, 15.3, and 23.1 min in 1:2:6.1 ratio. The isolated components in order of increasing retention time were as follows. **31**, isomer A: 270-MHz NMR ($CDCl_3$) δ 5.74 (1 H, ddd, J = 17.1, 10.2, 8.3 Hz), 5.05 (2 H, m), 3.70 (3 H, s), 2.75 (1 H, dt, J = 4.8, 7.4 Hz), 2.4 (1 H, m), 2.15 (1 H, m), 2.11 (3 H, s), 1.86 (3 H, m), 1.68 (1 H, m); IR (CCl_4) 1733 (s), 1640 (w), 1438 (m), 1245 (s), 912 (m) cm^{-1}; m/e 200.0869 (m/e calcd for $C_{10}H_{16}O_2S$ 200.08709). **31**, isomer B (retention time 15.3 min): 270-MHz NMR ($CDCl_3$) δ 6.0 (1 H, ddd, J = 17.1, 10.3, 7.7 Hz), 5.1 (2 H, m), 3.75 (3 H, s), 3.1 (1 H, q, J = 7.35 Hz), 2.38 (1 H, m), 2.05 (3 H, s), 2.0–1.6 (5 H, m); IR (CCl_4) 1735 (s), 1640 (w), 1438 (m), 1245 (s), 912 (m) cm^{-1}; m/e 200.0872 (m/e calcd for $C_{10}H_{16}O_2S$ 200.08709). Cycloheptene derivative **30**: 270-MHz NMR ($CDCl_3$) δ 5.93 (1 H, m), 5.73 (1 H, m), 3.74 (3 H, s), 2.66 (1 H, ddd, J = 14.3, 8, 2 Hz), 2.55 (1 H, ddt, J = 13.4, 6.3, 2 Hz), 2.42 (1 H, ddt, J = 14.3, 4.8, 0.7 Hz), 2.14 (3 H, m), 2.07 (3 H, s), 1.78 (2 H, m); IR ($CDCl_3$) 1725 (s), 1440 (m), 1305 (m), 1260 (m), 1245 (m), 1225 (m), 1200 (m), 1165 (m), 855 (m) cm^{-1}; m/e 200.0877 (m/e calcd for $C_{10}H_{16}O_2S$ 200.08709).

Independent Synthesis of Epimers 31. To LDA (1.8 mL of a 0.74 M solution in THF hexane) was added HMPT (0.57 mL, distilled from CaH_2). The mesylate **5** (195 mg, 0.659 mmol) in THF (2 mL) was then added to the cooled solution (−25 °C) by a motor-driven syringe over a 40-min period. The reaction was then diluted with ether and washed with three 10-mL portions of 10% HCl and 10 mL of saturated $NaHCO_3$. Drying ($MgSO_4$) and solvent removal (aspirator) gave 87 mg of crude product. Preparative TLC (silica gel PF 254) gave two bands with 15% acetone/hexane, R_f 0.44 and 0.26. The upper band proved to be a mixture of epimers **31** (26 mg, 20%) by GLPC comparison with epimers **31** derived from the ylide rearrangement. Analysis on a 10 ft × $^1/_4$ in. column (8% FFAP on Chrom A at 162 °C flow of 100 mL/min) gave peaks at 6.1 and 6.9 min in a relative ratio of 4:1. The ratio of these same compounds derived from the ylide reaction was 1:2. The TLC zone at R_f 0.26 was not characterized. However, comparison to an authentic sample on VPC showed that this material was not the cycloheptane derivative **30**.

Sulfone 33 from Methyl Thiacyclooct-4-ene-1-carboxylate.[1d] To sulfide **32** (315 mg, 1.7 mmol) in CH_2Cl_2 (8 mL) was added MCPBA (722 mg, 3.56 mmol, 85%) at 0 °C. After 1 h at 0 °C, the reaction mixture was allowed to warm to room temperature. After 0.5 h, extraction with saturated $NaHCO_3$ and saturated Na_2SO_3, drying ($MgSO_4$), and solvent removal (aspirator) gave 349 mg of crude sulfone. Preparative TLC (SiO_2, eluant 40% ethyl acetate–hexane) gave a band (R_f 0.29, 237 mg, 64%) of pure sulfone: mp 96–97 °C (ethyl acetate, hexane); NMR ($CDCl_3$) δ 5.75 (2 H, m), 3.9 (2 H, m), 3.76 (3 H, s), 3.2–1.6 (7 H, m); IR (neat) 1735 (s), 1435 (m), 1305 (s), 1215 (m), 1193 (m), 1165 (m), 1145 (m), 1110 (s), 780 (w), 748 (w), 723 (w) cm^{-1}; m/e 218.0610 (m/e calcd for $C_9H_{14}O_4S$ 218.06126).

Ramberg–Backlund Synthesis of Methyl Cyclohepta-1,5-dienecarboxylate (34). To NaH (washed four times with dry hexane under nitrogen) was added the sulfone **33** (86 mg, 0.394 mmol) in THF (4 mL) at 0 °C. Another 4 mL of THF was added. After 0.5 h of stirring at 0 °C, hexachloroethane (103 mg, 0.433 mmol) was added in one portion in 1 mL of THF. After 5 h of stirring at room temperature, the reaction was quenched with ice, partitioned between hexane and water, washed with saturated NaCl, and dried on $MgSO_4$. Solvent removal by aspirator followed by distillation (Kugelrohr) gave the diene ester **34**: 42 mg; 70%; NMR ($CDCl_3$) 7.05 (1 H, q, J = 7 Hz), 5.6 (2 H, m), 3.68 (3 H, s), 3.19 (2 H, m), 2.5–2.1 (4 H, m); IR (neat) 1710 (s), 1645 (w), 1435 (m), 1310 (m), 1265 (s), 1220 (m), 1195 (m), 1120 (m), 780 (m), 730 (w), 720 (w) cm^{-1}; m/e 152.0839 (m/e calcd for $C_9H_{12}O_2$ 152.08372).

Methyl Cyclohept-3-enecarboxylate (35). To CuBr in a dry flask flushed with N_2 was added THF (2 mL) and Red-al (Aldrich, 0.29 mL of a 3.5 M solution) at 0 to −5 °C. After 0.5 h at 0 °C, the mixture was cooled to −78 °C and 2-butanol (275 mL, 3 mmol) was added. Within 3 min the diene ester **34** (31 mg, 0.204 mmol) in 0.4 mL of THF was added. After 10 min at −78 °C, the mixture was warmed to −20 °C. After 1 h it was quenched (2 mmol of H_2O) and poured into 12 mL of saturated NH_4Cl, and the organic layer was separated. The organic layer was washed two times with water and then dried over $MgSO_4$. Solvent removal gave product **35** (20 mg, 64%) which was carried on without further purification: NMR ($CDCl_3$) δ 5.7 (2 H, m), 3.64 (3 H, s), 2.6–1.4 (9 H, m); IR

($CDCl_3$) 1730 (s) cm^{-1}; *m/e* 154.0991 (*m/e* calcd for $C_9H_{14}O_2$ 154.09937).

Sulfenylation of 35. Independent Synthesis of 30. To the ester **35** (18 mg, 0.117 mmol) in THF (0.5 mL) at −78 °C was added LDA (0.4 mL of a 0.7 M solution in THF–hexane).[19] A blood red color appeared. Within 5 min neat $CH_3SSO_2CH_3$ (19 μL, 0.204 mmol) was added. At once the color changed to yellow. After 10 min the reaction mixture was warmed to 0 °C, quenched with 10% HCl, and extracted with ether, and the ether extract was washed with saturated NaCl and dried ($MgSO_4$). Solvent removal gave a yellow odorous oil which was subjected to preparative TLC (SiO_2, eluant 25% acetone in hexane). The fastest moving band (3 mg, 12%, R_f 0.5 in 1:2 actone–hexane) had properties identical wiih those of **30** obtained by ylide rearrangement. No attempt was made to optimize the sulfenylation.

Rearrangement of Ylide 37 to 38, 39, and 40. The sulfide **2** (50 mg, 0.22 mmol) was mixed with 0.5 mL of dry CH_2Cl_2 and methyl fluorosulfonate (76 mg, 0.66 mmol) under N_2, and the mixture was stirred at 25 °C for 8 h. The solvent was removed under vacuum and the dark residue (54 mg) was washed with three 2-mL portions of 50% ether–hexane. Repeated attempts failed to crystallize the salt. The salt was mixed with 0.5 mL of dry THF and cooled to 0 °C under N_2. Potassium *tert*-butoxide (28 mg, 0.25 mmol) in 0.5 mL of dry THF was added and the mixture was stirred at 0 °C for 30 min and at 25 °C for an additional 90 min. Hexane (1 mL) and 1 mL of water were added, and the organic layers were separated and dried over $MgSO_4$. The residue was filtered through a silica gel plug (10% ether–hexane), affording 35 mg of crude material. This mixture was separated into three components, **38**, **39**, and **40**, by preparative TLC (10% ether–hexane, R_f 0.4 (12 mg), 0.38 (14 mg), 0.29 (3 mg)).

38: IR (CCl_4) 2960 (s), 2910 (m), 2840 (s), 1725 (m), 1440 (m), 1370 (m), 1340 (m), 1110 (s) cm^{-1}; NMR ($CDCl_3$) δ 6.21 (1 H, m), 5.85 (1 H, m), 5.71 (1 H, m), 5.25 (2 H, m), 4.21 (2 H, m), 3.20 (1 H, m), 2.6–1.6 (6 H, m), 2.0 (3 H, s), 1.29 (3 H, t, J = 7 Hz); *m/e* 240.11815 (*m/e* calcd for $C_{13}H_{20}S_2S$ 240.11840).

39: IR (CCl_4) 2940 (m), 2900 (s), 2840 (m), 1725 (s), 1460 (w), 1360 (w), 1150 (m), 1085 (w), 900 (s) cm^{-1}; NMR ($CDCl_3$) δ 6.31 (1 H, dt, J = 15, 8 Hz), 6.07 (1 H, m), 5.67 (1 H, m), 5.49 (2 H, m), 5.2–4.9 (2 H, m), 4.19 (2 H, q, J = 7.5 Hz), 3.2 (1 H, t, J = 7 Hz), 2.87 (m, 2 H), 2.64 (1 H, m), 2.44 (2 H, m), 2.15 (3 H, s), 1.29 (3 H, t, J = 7.5 Hz); *m/e* 240.11840 (*m/e* calcd for $C_{13}H_{20}O_2S$ 240.11861).

40: IR (CCl_4) 2950 (m), 2900 (m), 2840 (m), 1715 (s), 1630 (w), 1300 (w), 1260 (s), 1150 (m), 1110 (m), 900 (w) cm^{-1}; NMR (CCl_4) δ 7.45 (1 H, dd, J = 16, 11 Hz), 6.1 (1 H, t, J = 11 Hz), 5.75 (1 H, d, J = 16 Hz), 5.55 (2 H, m), 5.0 (2 H, m), 4.15 (2 H, q, J = 7 Hz), 2.9 (1 H, m), 2.4 (2 H, m), 1.95 (3 H, s), 1.7 (2 H, m), 1.3 (3 H, t, J = 7 Hz).

1-(Carboethoxy)-7-vinyl-1,3-cycloheptadiene (43). The cycloheptene derivative **38** (12 mg, 0.05 mmol) was mixed with dry K_2CO_3 (ca. 20 mg) and (carboethoxy)methyl trifluoromethanesulfonate (105 mg, 0.4 mmol) in 0.5 mL of dry CH_3CN at room temperature under a N_2 atmosphere. The mixture was allowed to stir 48 h at room temperature. Dimethylamine (2 mL, 25% in water) was added to destroy excess alkylating agent, and 5 mL of hexane was added after 5 min. The organic layer was separated and washed with three 5-mL portions of water. The organic layer was then dried over $MgSO_4$ and the solvent removed under vacuum. The crude material was purified by preparative TLC (10% ether–hexane). Two closely spaced bands were obtained at ca. R_f 0.3 ± 0.05. The less polar band contained starting **38** (2 mg) (R_f 0.31) and the more polar band contained product **43** (30 mg, 38% on the basis of recovered **38**): IR (CCl_4) 2990 (m), 2970 (m), 2940 (m), 1719 (s), 1265 (s), 1220 (m), 1100 (w) cm^{-1}; NMR ($CDCl_3$) δ 7.16 (1 H, d, J = 7.8 Hz), 6.05 (1 H, m), 5.8 (1 H, m), 5.6 (1 H, m), 5.06 (1 H, dd, J = 10, 1.3 Hz), 4.82 (1 H, dd, J = 17.2, 1.5 Hz), 4.18 (2 H, q, J = 7 Hz), 3.97 (1 H, m), 2.38 (2 H, m), 2.38 (1 H, m), 1.85 (1 H, m), 1.28 (3 H, t, J = 7 Hz); *m/e* 192.1146 (*m/e* calcd 192.1150).

Attempted Anionic 2,3-Sigmatropic Shift of 2-(Carboethoxy)-8-vinylthiacyclooct-4-ene (2) with LDA. Isolation of 24. A dry 10-mL flask under a nitrogen atmosphere was charged with 5 mL of dry THF, 2-(carboethoxy)-8-vinylthiacyclooctene (**2**) (30 mg, 0.13 mmol), and dry HMPA (hexamethylphosphoric triamide, 0.3 mL, 0.52 mmol). Then LDA (0.52 mmol in THF) was added dropwise with rapid stirring. After 60 min, methyl iodide (74 mg, 0.52 mmol) was added and the mixture was stirred for an additional 15 min. Hexane (10 mL) and water (10 mL) were added. The layers were separated and the aqueous layer was extracted with hexane (three 5-mL portions). The combined organic layers were washed with water and saturated sodium chloride solution and dried over $MgSO_4$. The solvent was removed under vacuum and the residue put through a silica gel plug (10% ether–hexane), affording only 2-methyl-2-(carboethoxy)-8-vinylthiacyclooct-4-ene (**24**) (23 mg, 74%, 0.09 mmol, R_f 0.35 5% Et_2O–hexane). An analogous reaction was run except the reaction mixture was also heated to reflux for 15 min prior to addition of methyl iodide. Extensive degradation was apparent, and TLC analysis indicated the presence of **2** (trace), **24**, and polar base-line material. Characterization of **24**: IR (CCl_4) 3060 (w), 2900 (s), 2915 (s), 2850 (m), 1730 (s), 1628 (w), 1440 (w), 1365 (m), 1270 (s), 1235 (s), 1140 (s), 1125 (m), 1025 (s) cm^{-1}; NMR ($CDCl_3$) δ 5.8 (3 H, m), 5.05 (2 H, m), 4.15 (2 H, q, J = 8 Hz), 3.80 (1 H, m), 2.70 (2 H, m), 2.4–1.6 (4 H, m), 1.4 (3 H, s), 1.2 (3 H, t, J = 8 Hz); *m/e* 240.11792 (*m/e* calcd for $C_{13}H_{20}O_2S$ 240.11839).

Attempted Rearrangement of 2-(Carboethoxy)-8-vinylthiacyclooct-4-ene (2) with KH. A dry 10-mL flask under a nitrogen atmosphere was charged with 5 mL of dry THF and potassium hydride (71 mg, 22.5% in mineral oil, 0.40 mmol). Then HMPA (0.25 mL, 0.43 mmol) was added, followed by 2-(carboethoxy)-8-vinylthiacyclooct-4-ene (30 mg, 0.13 mmol) in 2 mL of dry THF. The mixture was stirred at room temperature for 45 min. Then methyl iodide (57 mg, 0.4 mmol) was added and the mixture stirred for an additional 15 min. Hexane (10 mL) was then added, followed by water (10 mL). The layers were separated and the aqueous layer was extracted with hexane (three 5-mL portions), and the combined organic layers were washed with water and saturated sodium chloride solution and dried over $MgSO_4$. The solvent was removed under vacuum and the residue put through a silica gel plug (10% ether–hexane), affording only 2-(carboethoxy)-2-methyl-8-vinylthiacyclooct-4-ene (25 mg, 0.1 mmol, 75%). An analogous reaction was run with the reaction mixture being heated to 50 °C for 30 min (in addition to 60 min at room temperature), and only starting material and the above product were detected by TLC analysis.

2-(Carboethoxy)-1,1-dioxo-8-vinylthiacyclooct-4-ene (27). The sulfide **2** (50 mg, 0.22 mmol) was dissolved in 2 mL of CH_2Cl_2 (passed through silica gel prior to use), and the solution was placed in a cool water bath under N_2. Then MCPBA (*m*-chloroperbenzoic acid) (83 mg, 0.48 mmol) was added all at once and the mixture allowed to stir for 75 min. The white precipitate was filtered off and washed with 5 mL of CH_2Cl_2. The filtrate was then washed with 10 mL of saturated sodium bicarbonate solution, dried over $MgSO_4$, and filtered. The solvent was removed under vacuum, affording 56 mg of crude material. This residue was purified by using preparative thin-layer chromatography (silica gel, 50% ether–hexane, R_f 0.31), affording 32 mg of sulfone **27** as a pale yellow oil, 56%: IR (CCl_4) 2900 (s), 1732 (s), 1645 (w), 1300 (s), 1250 (s), 1150 (s), 1090 (s), 1000 (s) cm^{-1}; NMR (CCl_4) δ 5.80 (3 H, m), 5.35 (2 H, m), 4.30 (1 H, m), 4.20 (2 H, q, J = 8 Hz), 3.85 (1 H, dd, J = 6, 4 Hz), 3.2–2.0 (6 H, m), 1.30 (3 H, t, J = 8 Hz); *m/e* 258.09258 (*m/e* calcd for $C_{12}H_{18}O_4S$ 258.09238).

Attempted Rearrangement of Sulfone 27 with KH. The sulfone **27** (32 mg, 0.124 mmol) was dissolved in 1 mL of dry THF and the mixture cooled to 0 °C under N_2. The potassium hydride (Ventron, 22 mg of a 22% suspension in mineral oil, 4.9 mg of KH, 0.125 mmol) was added by syringe and the mixture stirred at 0 °C for 30 min. Methyl iodide (17.6 mg, 0.124 mmol) was added and the mixture stirred at 0 °C for 15 min, followed by warming to 25 °C over another 15 min. The solution was diluted with ether (2 mL) and water (2 mL). The organic layer was separated and the aqueous layer extracted with two 2-mL portions of ether. The combined organic layers were dried over $MgSO_4$ and the solvent was removed under vacuum, leaving 42 mg of oily residue. Preparative TLC (1:1 ether–hexane) gave methylated starting material (2-(carboethoxy)-2-methyl-1,1-dioxo-8-vinylthiacyclooct-4-ene) [R_f 0.35; 9 mg (27%); IR (CCl_4) 2980 (m), 2920 (m), 1735 (s), 1635 (w), 1460 (w), 1295 (s), 1275 (m), 1130 (m), 1090 (m) cm^{-1}; NMR (CCl_4) δ 5.7 (3 H, m), 5.2 (2 H, m), 4.45 (1 H, m), 4.15 (2 H, q, J = 7 Hz), 2.7 (2 H, m), 2.15 (4 H, m), 1.55 (3 H, s), 1.25 (3 H, t, J = 7 Hz); *m/e* 272.10853 (*m/e* calcd for

$C_{13}H_{20}O_4S$ 272.10850)] and the double-bond isomer **28** [R_f 0.26; 13 mg; 38%; IR (CCl_4) 2965 (s), 2955 (s), 2900 (s), 2880 (s), 2840 (s), 1730 (s), 1635 (w), 1460 (s), 1370 (m), 1320 (m), 1300 (s), 1240 (m), 1130 (m), 1110 (m), 1085 (m), 1010 (m) cm^{-1}; NMR (CCl_4) δ 6.75 (1 H, q, J = 6.5 Hz), 5.7 (2 H, m), 4.2 (2 H, q, J = 7 Hz), 2.5 (6 H, m), 1.9 (3 H, d, J = 6.5 Hz), 1.55 (3 H, s), 1.3 (3 H, t, J = 7 Hz); m/e 272.10772 (m/e calcd for $C_{13}H_{20}O_4S$ 272.10850)].

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Registry No. 1 isomer A, 71031-77-1; 1 isomer B, 71031-78-2; 2 isomer A, 71031-79-3; 2 isomer B, 71031-80-6; 4, 71031-81-7; 5, 71031-82-8; 6, 71031-83-9; 8, 71031-84-0; 9, 71031-86-2; 11, 26505-44-2; 12, 70475-68-2; 13, 71031-87-3; 14, 71031-88-4; 15 isomer A, 71031-89-5; 15 isomer B, 71031-90-8; 17, 53799-54-5; 18, 71031-91-9; 19, 15224-05-2; 21, 71031-92-0; 22, 71031-93-1; 24, 71031-94-2; 26, 71031-95-3; 27, 71031-96-4; 28, 71031-97-5; 30, 71031-98-6; 31 isomer A, 71031-99-7; 31 isomer B, 71032-00-3; 32, 71032-01-4; 33, 71032-02-5; 34, 71032-03-6; 35, 71032-04-7; 37, 71032-05-8; 38, 71032-06-9; 39, 71032-07-0; 40, 71032-08-1; 43, 71032-09-2; 4-bromo-1-butanol, 33036-62-3; 4-bromobutanal, 38694-47-2; ethyl 6-bromo-hex-2-enoate, 71032-10-5; 6-bromohex-2-enol, 71032-11-6; 6-bromohex-2-enyl tetrahydropyranyl ether, 71032-12-7; methyl (methylthio)acetate, 16630-66-3; methyl thioglycolate, 2365-48-2; methyl 2-(butylthio)propionate, 71032-13-8; carbonodithioic acid *O,O'*-2,6-octadiene-1,8-diyl *S,S'*-dimethyl ester, 71032-14-9; allyl tetrahydropyranyl sulfide, 56393-74-9; allyl mercaptan, 870-23-5; (carboethoxy)methyl trifluoromethanesulfonate, 61836-02-0; 2-(carboethoxy)-2-methyl-1,1-dioxo-8-vinylthiacyclooct-4-ene, 71032-15-0; dihydropyran, 25512-65-6.

Cyclization and Allylic Rearrangement in Solvolyses of Monoterpenoids

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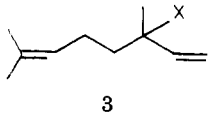
Hydrolysis and methanolysis of chlorides, phosphates, and pyrophosphates are examined. Solvolyses of geranyl derivatives give predominantly acyclic primary and tertiary substitution products, and the S_N1 reaction involves extensive allylic delocalization in the forming carbocation. Cyclic products formed with π participation predominate in solvolyses of neryl derivatives, but acyclic product formation involves allylic delocalization. The conformational requirements for π participation and allylic delocalization are different, and the rates, products, and kinetic secondary hydrogen isotope effects can be explained in terms of the initial state conformations and the transition state geometries. Decrease of solvent polarity favors elimination over substitution, and increasing nucleophilicity of the solvent favors formation of primary over tertiary products, but $LiClO_4$ has the opposite effect. These differences appear to depend upon the lifetime of the carbocation and its attaining the most stable conformation.

There has been considerable interest in mechanisms of solvolyses of the open chain monoterpenoid neryl (**1**) and geranyl (**2**) derivatives. Neryl derivatives readily give cyclic products, whereas predominantly open chain products are formed from geranyl derivatives.[1-9] At the simplest level, observations have been rationalized in terms of π participation in reactions of neryl derivatives (Scheme I).[10] Linalyl derivatives (**3**) are the most important substitution



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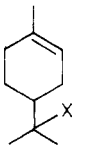
products in solvolyses of **2**. These reactions have also been considered as models for the biosynthesis of cyclic monoterpenes, and in some biological systems neryl, but not geranyl, pyrophosphate is a precursor of monocyclic terpenoids.[9,11,12] The nonbiological reactions have all the characteristics of S_N1 reactions, but the partial product specificity shows that the intermediate carbocations, or their ion pairs, do not undergo rapid trans-cis interconversion by rotation about the allylic double bond of the cation.

Scheme I is inadequate in that some acyclic products are always formed in solvolyses of neryl substrates (**1**), and some cyclic products are generally formed in solvolyses of geranyl substrates (**2**),[2-8] although terpinyl derivatives (**4**)



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are the predominant products in solvolyses of **1**.

Not only is the specificity incomplete, but the rates of solvolyses of neryl and geranyl substrates are often very similar despite product and kinetic isotope evidence for π participation in solvolyses of neryl substrates.[3-8] It is necessary to include additional steps to those shown in

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