Epoxyannulation. 4. Reactions of 1,5-, 1,6-, and 1,7-Oxosulfonium Salts

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Received December 9, 1981

Treatment of six 1,5- and 1,6-oxosulfonium salts with potassium *tert*-butoxide affords an oxabicyclo[3.1.0]hexane, an oxabicyclo[4.1.0]heptane, hydrindan oxides, or a decalin oxide in 55–95% yield. The stereoselectivity of this reaction ranges from 75% for the formation of (1α,3α,7α)-2-oxatricyclo[5.3.0.0^{1,3}]decane (**21**) to greater than 99% for (1α,2α,7α)-2-oxatricyclo[4.4.0.0^{1,3}]decane (**14**) and for (1α,2α,8β)-2-oxatricyclo[6.4.0.0^{1,3}]undecane (**25**). Five 1,7-oxosulfonium salts, one 1,8-salt, and one 1,11-salt and base give only elimination products. The sulfonium salt from 2-[3-methyl-5-(ethylthio)-2(*Z*)-pentenyl]cyclopentanone (**29**) provides 3-methylspiro[4.5]dec-2-en-6-one (**30**) in 40% yield. The salt from 2-[3-methyl-5-(ethylthio)-2(*Z*)-pentenyl]cyclohexanone (**32**) yields 38% of 4-methylbicyclo[5.4.0]undeca-1(7),3,5-triene (**33**).

In a preliminary report[2] we described the cyclization of 1,5- and 1,6-oxosulfonium ylides as illustrated in Scheme I. This simultaneous construction of a new carbocyclic ring and an epoxide has been called "epoxyannulation". The details of this previous paper and the reactions of seven 1,7-oxosulfonium ylides are now presented. These results are summarized in Tables I and II.

All of 1,5- and 1,6-oxosulfonium salts that have been examined afforded cyclic epoxides in 55–99% yield (Table I, entries 1–7). Although the product stereochemistry is a function of ring size and ketone structure, one stereoisomer always predominates by more than 3:1. A 2-oxabicyclo[5.1.0]octane was not the major product from any 1,7-oxosulfonium salt. Instead, a spirocyclic ketone, a cycloheptatriene, or a oxodiene was observed (Table I, entries 8–10).

We had anticipated that sulfur ylides might undergo the intramolecular addition depicted in Scheme I. At the onset of our work,[3] numerous related cyclizations had been detailed for phosphorous-stabilized anions.[4] However, the two cases of intramolecular sulfur ylide cyclizations contained aryl groups which limited other reaction pathways[5] and thus the generality of epoxyannulation. Epoxides structurally similar to our expected products had been prepared by intramolecular variants of the Robinson annulation[6] and the Darzens condensation.[7] After completion of our work, we learned of a comparable study obtained by Crandall and Magaha.[8]

General Considerations. The plan outlined in Scheme I requires the preparation of an ω-oxosulfonium salt followed by ring closure of the corresponding ylides. The requisite sulfonium salts can be prepared by S-alkylation of ω-oxosulfides. In turn, the sulfides might be generated by ketone enolate alkylation with either ω-halo thioethers or cyclic sulfonium salts. Although the ω-halo thioethers offer varying chain lengths, these "mustard gas" electrophiles are unstable. Unfortunately, the reaction of stable cyclic sulfonium salts with carbon nucleophiles lacked chemical precedent.[9]

The potential generation of a sulfur ylide in the presence of a ketone followed by epoxyannulation requires a more detailed analysis than suggested by the isolated examples of Newman[5a] snd Cazeau.[5b] The acidity of a hydrogen adjacent to a sulfonium salt is probably comparable to or less than that of a hydrogen adjacent to a carbonyl.[10] Therefore equilibrating base conditions (potassium *tert*-butoxide or phase transfer) should maximize ylide formation. For control of ylide specificity and methylene transfer, all of the S-alkyl groups should have at least comparable substitution patterns. For instance, a dimethylsulfonium salt (Scheme I) might only afford a sulfonium methylide. This ylide would give products other than ring formation.[8,11] The use of auxiliary S groups without α-hydrogens such as phenyl or *tert*-butyl would be ideal; however, these compounds are synthetically inaccessible. The simplest solution is the diethylsulfonium salt (Scheme I).

In principle, generation of the correct ylide should assure epoxyannulation. Although the reactivity and stability of a model ylide, diethylsulfonium ethylide, is the subject of conflicting reports,[12,13] either of its decomposition pathways, elimination or [1,2] migration, possesses a higher activation energy than does carbonyl addition. Ylide cyclization yielding five- and six-membered rings is faster than any intermolecular ylide reaction. To increase the yield of cyclic products from other ω-keto ylides, the rotational entropy of the acyclic unit may be decreased by the insertion of geminal substituents or sp^2 atoms.

The stereochemistry of the newly formed cyclic epoxide results from the geometry of the required *trans*-betaine. The formation of this betaine from a sulfur ylide can be under kinetic control (irreversible carbonyl addition) or thermodynamic control (reversible carbonyl addition), depending upon the ylide substituents (Scheme I, a $\rightleftharpoons$ b). In bimolecular ylide additions, this step has been investigated by analysis of the products from independent be-

(1) Undergraduate Research Participant, 1979–1980.

(2) Garst, M. E.; Johnson, A. T. *Tetrahedron Lett.* **1980**, *21*, 4811–4814.

(3) Garst, M. E. *J. Org. Chem.* **1979**, *44*, 1578–1580.

(4) (a) Becker, K. B. *Helv. Chim. Acta* **1977**, *60*, 68–80, 81–102. (b) Fuchs, P. L. *Tetrahedron Lett.* **1974**, 4055–4058. (b) Büchi, G.; Pawlak, M. *J. Org. Chem.* **1975**, *40*, 100–102. (d) Büchi, G.; Wuest, H. *Helv. Chim. Acta* **1971**, *54*, 1767–1776. (e) Martin, S. F.; Garrison, P. J. *Tetrahedron Lett.* **1977**, 3875–3878. (f) Darling, S. D.; Muralidharan, F. N.; Muralidharan, V. B. *Ibid.* **1979**, 2757–2760 and 2761–2762.

(5) (a) Newman, M. S.; Lee, L.-F. *J. Org. Chem.* **1974**, *39*, 1446. (b) Cazeau, P.; Muckensturm, B. *Tetrahedron Lett.* **1977**, 1493–1494. Gosselck, J.; Winkler, A. *Z. Chem.* **1970**, *10*, 380–381.

(6) Danishefsky, S.; Koppel, G. A. *J. Chem. Soc., Chem. Commun.* **1971**, 367.

(7) White, D. R. *J. Chem. Soc., Chem. Commun.* **1975**, 95–96. McIntosh, J. M.; Khalil, H. *J. Org. Chem.* **1977**, *42*, 2123–2126.

(8) Crandall, J. K.; Magaha, H. S.; Widener, R. K.; Tharp, G. A. *Tetrahedron Lett.* **1980**, *21*, 4807–4810.

(9) For a general discussion of sulfonium salts as leaving groups see: (a) Ingold, C. K. "Structure and Mechanism in Organic Chemistry"; Cornell University Press; Ithaca, NY, 1953; Chapter VII. (b) Stirling, C. J. M. In "The Organic Chemistry of Sulfur"; Oae, S., Ed.; Plenum: New York, 1977; pp 473–526.

(10) Bordwell, F. G.; Branca, J. C.; Johnson, C. R.; Vanier, N. R. *J. Org. Chem.* **1980**, *45*, 3884–3889. These authors have determined that the equilibrium acidity of the (dimethylamino)methyl(phenyloxo)sulfonium cation to be pK_a = 15, which appears to be the only reported value for a sulfonium cation. In this system acetophenone has a pK_a of 24.7.

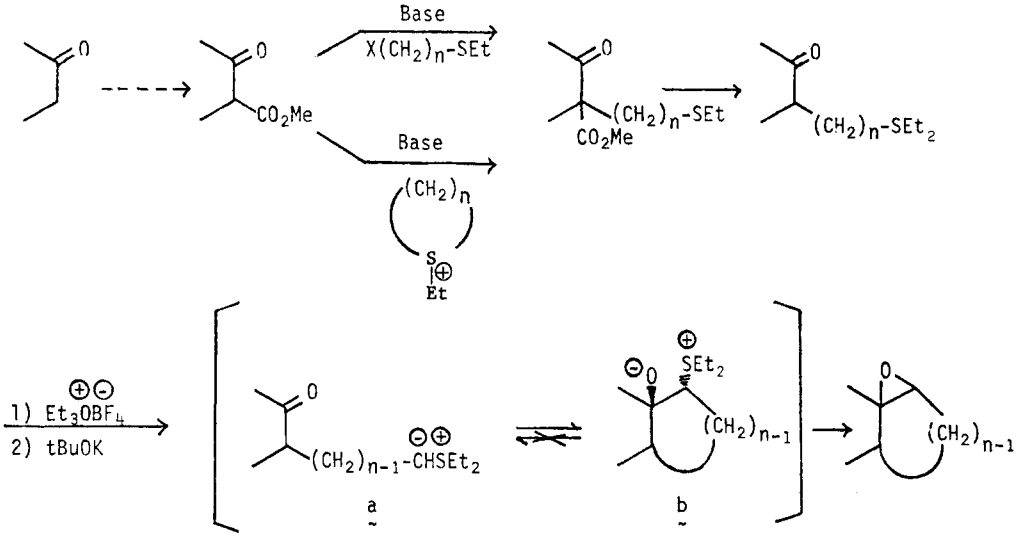
(11) Matthews, R. S.; Meteyer, T. E. *Synth. Commun.* **1972**, *2*, 399–404; *J. Chem. Soc., Chem. Commun.* **1971**, 1576–1577.

(12) Corey, E. J.; Oppolzer, W. *J. Am. Chem. Soc.* **1964**, *86*, 1899–1900.

(13) Franzen, V.; Schmidt, H. J.; Mertz, C. *Chem. Ber.* **1961**, *94*, 2942–2950.

0022-3263/83/1948-0008$01.50/0

Scheme I

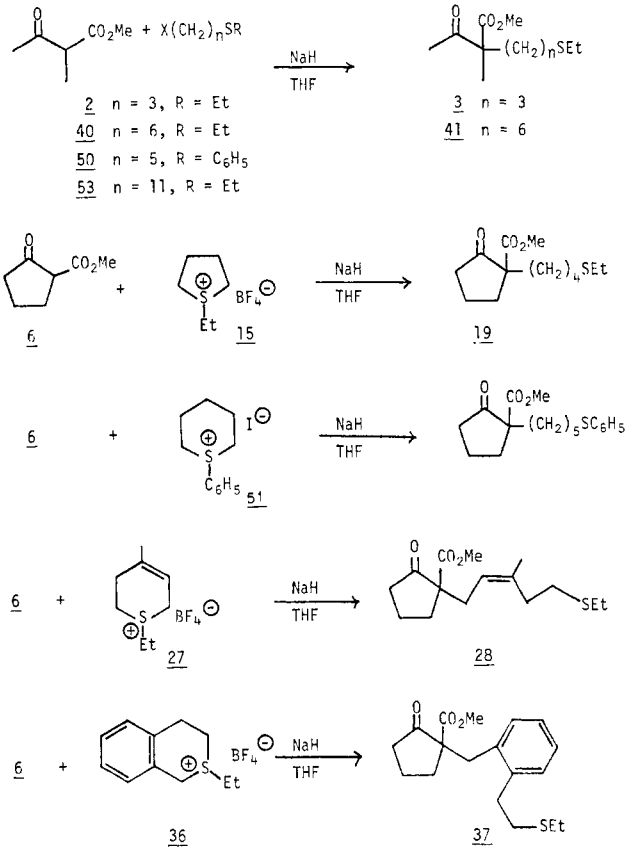


taine generation,[14] from ylide reactions with unhindered enones,[15] and from ylide reactions with 4-*tert*-butylcyclohexanone.[15] All of these tests for reversible carbonyl addition lead to the conclusion that dialkylsulfonium ylides add to the carbonyl group irreversibly. Therefore, intramolecular ylide reactions with diethylsulfonium salts are under kinetic control.

Preparation of Oxo-ω-sulfonium Salts. All of the ω-oxosulfonium salts were prepared by the C-alkylation of β-keto esters with ω-halo sulfides or cyclic sulfonium salts followed by decarboxylation and S-ethylation. Since the final two stages require little discussion, they are presented first. Although four methods for decarboxylation were examined,[16-19] the standard lithium iodide–collidine procedure was the most dependable.[19] Chemoselective S-ethylation was effected by treatment of the sulfide with triethyloxonium fluoborate in methylene chloride. These oily salts were characterized only by NMR spectroscopy and were used directly in the cyclization step.

The synthesis of β-keto esters with ω-thioether appendages had precedent in the alkylation of malonate with 3-bromopropyl ethyl sulfide.[20] With slight modification of these conditions, we observed clean C-alkylation of the sodium enolate of β-keto esters **1**, **6**, and **11** with iodo sulfides (X = I) **2**, **40**, **50**, and **53** (Scheme II and Tables I and II). Although these ω-halo thioethers were unstable to prolonged storage at −30 °C, only 5-iodopentyl phenyl sulfide (**50**) afforded a discrete decomposition product, *S*-phenylthianium iodide (**51**), in quantitative yield. Attempted isolation of 4-chlorobutyl ethyl sulfide[16] provided *S*-ethylthiolanium chloride (**15**). Although these halo

Scheme II



sulfides are reactive alkylating reagents, their instability limits their utility.

We then examined the reactions of cyclic sulfonium salts with carbon nucleophiles. *S*-Ethylthiolanium fluoborate (**15**) and enolates from β-keto esters such as **1** yielded exclusively ring-opened products, i.e., **19**, Scheme II, a process suggested by Eliel et al.[21] Likewise *S*-phenylthianium iodide (**51**) also afforded only the desired thioether (Scheme II).[22] Salt **51** was prepared from 1-(phe-

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(16) Baker, W.; Leeds, W. G. *J. Chem. Soc.* **1948**, 974–980.

(17) Parish, E. J.; Huang, B. S.; Miles, D. H. *Synth. Commun.* **1975**, *5*, 341–346.

(18) Jung, M. E.; Lyster, M. A. *J. Am. Chem. Soc.* **1977**, *99*, 968–969. Ho, T.-L. *Synth. Commun.* **1979**, *9*, 233–235. Coates, R. M.; Sanderfur, L. O.; Smillie, R. D. *J. Am. Chem. Soc.* **1975**, *97*, 1619–1621. These authors imply that indirect formation of a silyl enol ether from a β-keto ester should be possible. Unfortunately we observed sulfur oxidation in competition with ester cleavage.

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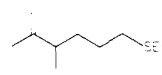
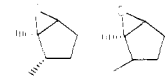
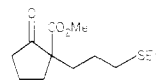
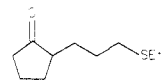
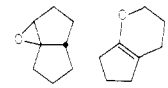
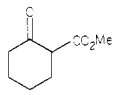
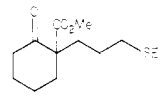
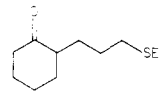
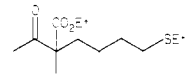
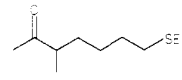
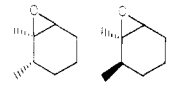
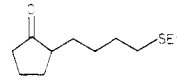
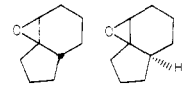
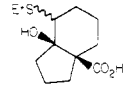
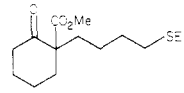
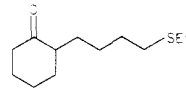
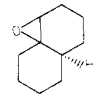
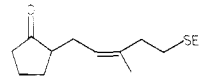
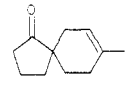
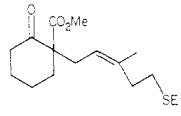
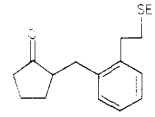
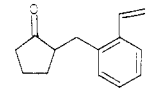
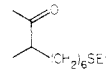
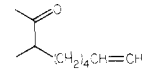
(20) Lee, C.-J.; Serif, G. S. *Biochemistry* **1970**, *9*, 2068–2071.

(21) Eliel, E. L.; Hutchins, R. O.; Mebane, R.; Willer, R. L. *J. Org. Chem.* **1976**, *41*, 1052–1057.

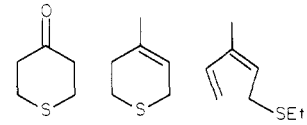
(22) Eliel had shown that *S*-methylthianium fluoborate underwent demethylation with cyanide and phenoxide.[21] We observed similar behavior with *S*-ethylthianium fluoborate. A detailed account of our studies of carbon nucleophiles with sulfonium salt electrophiles will be given: McBride, B. J.; Garst, M. E., *J. Org. Chem.*, accepted for publication.

Table I. Epoxyannulation Reactions

entry	keto ester	sulfur electrophile	alkylation product	annulation precursor	product(s)	product ratio
1	1	2	3	 4	 5	21:79
2	6	2	 7	 8	 9 10	1:1
3	 11	2	 12	 13	 14	
4	1	15	 16	 17	 18	12:88
5	6	15	19	 20	 21	74:26
6				19	 22	
7	11	15	 23	 24	 25	
8	6	27	28	 29	 30	
9	11	27	 31	32	33	
10				34	35	
11	6	36	37	 38	 39	
12	1	40	41	 42	 43	

nylthio)-5-iodopentane rather than by the S-phenylation of tetrahydrothiopyran,[23] a reaction requiring vigorous conditions and affording products which are difficult to purify. Unfortunately, neither of these two routes to **51** is compatible with other functional groups.[24]

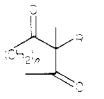
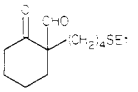
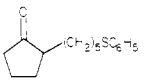
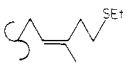
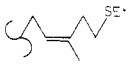
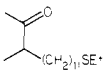
To further extend the S_N2 reactions of cyclic sulfonium salts with carbon nucleophiles, we prepared *S*-ethyl-5,6-dihydro-4-methyl-2(*H*)-thiapyranium fluoborate (**27**) and *S*-ethylisothiochromanium fluoborate (**36**) by well-precedented routes. During the preparation of **27**, some minor modifications were made which improved the large-scale yields of tetrahydro-4(*H*)-thiapyran-4-one (**54**)[25] and 5,6-


54 55 56

dihydro-4-methyl-2(*H*)-thiapyran (**55**).[26] Buffering the

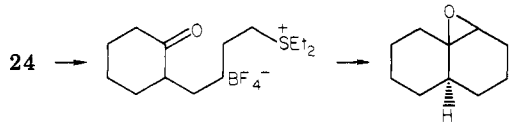
(23) Crivello, J. V.; Lam, J. H. W. *J. Org. Chem.* **1978**, *43*, 3055–3058.
(24) We are currently exploring new arylation procedures: B. J. McBride, unpublished.
(25) Johnson, P. Y.; Berchtold, G. A. *J. Org. Chem.* **1970**, *35*, 584–592.

Table II. Keto Sulfides Affording Complex Mixtures

sulfide	sulfur electrophile	sulfide	sulfur electrophile
			15
T		48	
44, n = 2; R = $(CH_2)_4SEt$	15		50 or 51
		49	
45, n = 3; R = $(CH_2)_4SEt$	15		
46, n = 2; R = 	27		
47, n = 3; R = 	27		53
		52	

solution leading to **54** obviated the high-dilution conditions, while acid-catalyzed dehydration afforded the highest yields of **55**. These activated allylic salts **27** and **36** underwent smooth ring-opening with anions from β-keto esters (Scheme II).[27,28] Treatment of **27** with the anions from 2-methyl-1,3-cyclopentanedione and 2-methyl-1,3-cyclohexanedione gave the expected products **46** and **47** (Table II) accompanied by **56**.[27] These experiments clearly demonstrate the utility of sulfonium salt electrophiles with carbon nucleophiles.[22]

Reactions of 1,5- and 1,6-Oxosulfides. An analysis of the ylide formation problems (vide infra) led us to select thermodynamic or equilibrating reaction conditions for ring closure. Our initial choice of potassium *tert*-butoxide in tetrahydrofuran (THF) as the base–solvent combination did yield epoxides. Below −20 °C the reaction was very slow and above 0 °C noticeably exothermic. With the salt from **24**, these higher initial temperatures afforded a more

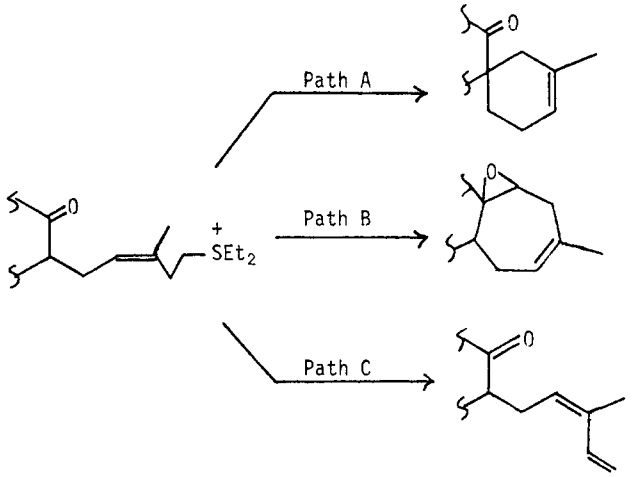


25

complex product mixture containing less epoxide **25**. Attempted use of lithium diisopropylamide–THF with this substrate provided even less of **25**.

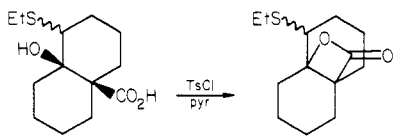
Treatment of a variety of 1,5- and 1,6-oxosulfides with triethyloxonium fluoborate and base has yielded only epoxides. The structure and stereochemistry of the products (Table I, **5**, **9**, **10**, **14**, **18**, **21**, and **25**) could not be unambiguously determined by spectroscopy. Therefore, the epoxides were reduced with lithium aluminum hydride ($LiAlH_4$) to the known tertiary alcohols. Authentic samples of these alcohols were prepared. For example, a mixture of 1,2-dimethylcyclopentanols (**57**) and of the cyclohexanols (**58**) were available in established stereochemical ratios by the method of Ashby[29] and of Ficini,[30]

Scheme III



respectively. In both instances, the $LiAlH_4$ reduction of the epoxide and the Grignard addition provided the same major isomer.[31] The tertiary hydrindanols **59** and **60** and *cis*-1a-decalinol (**61**) were prepared by the stereospecific ozonolysis procedure of Mazur.[32] *trans*-1a-Decalinol (**63**) arose from reduction of *trans*-1,1a,4,4a,5,6,7,8-hexahydronaphthalen-1a-ol (**62**).[33] In the only instance where another type of product was detected (compounds **9** and **10**, Table I, entry 2), those products were characterized as a mixture.[34] Both **9** and **10** exhibited appropriate GC/MS data.

To increase the complexity of the substrates used in epoxyannulation, we examined the reactions of the salts from sulfides **19**, **44**, **45**, and **48**. Salt **19** afforded hydroxy acid **22** in 60% crude yield. Apparently, the oxyanion of the betaine was trapped by the ester, yielding a β-lactone which could suffer S-deethylation. Hydrolysis during the workup would afford **22**. The β-hydroxy acid can be relactonized to afford **64** in 83% yield.[35] Salts from **44**, **45**,



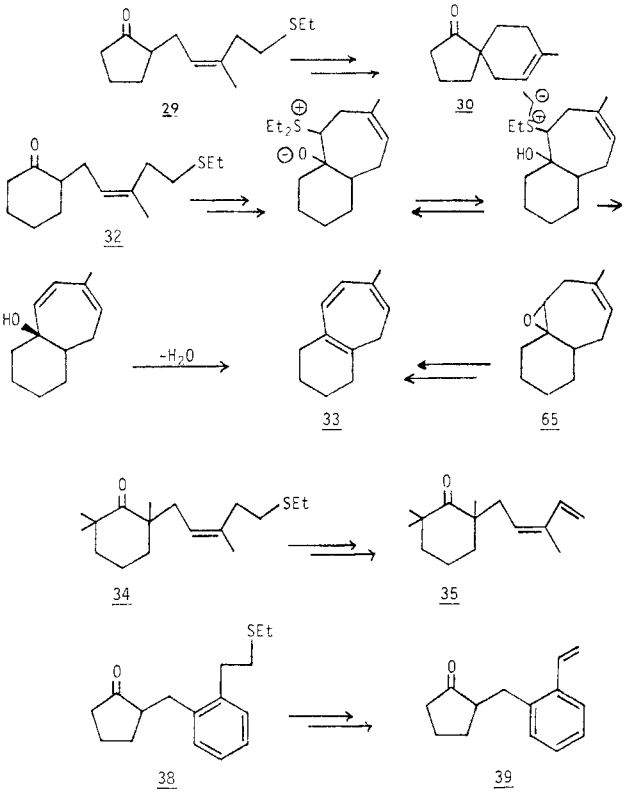
22 **64**

and **48** afforded complex mixtures containing at least four major products other than the expected epoxide.

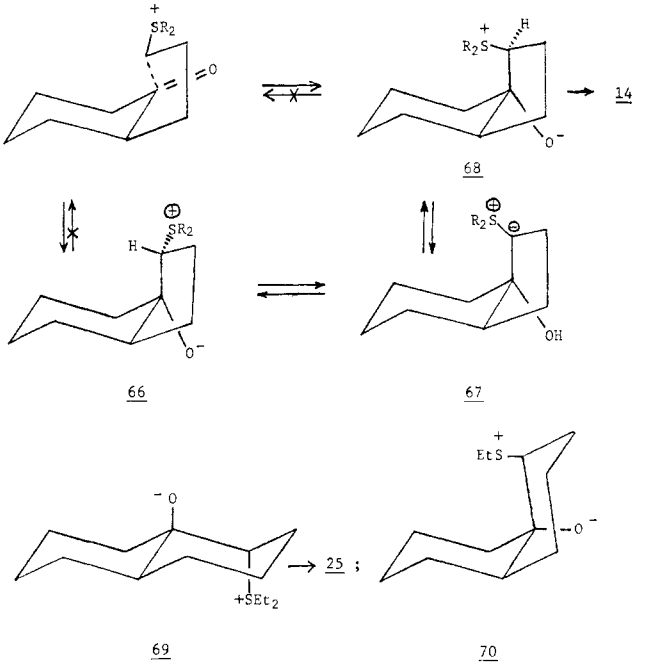
Reactions of 1,7- and Longer Oxosulfides. To evaluate epoxyannulation in 1,7-systems as model reactions for sesquiterpene synthesis, the reactions of 1,7-oxosulfonium salts derived from **29**, **32**, **34**, **38**, **46**, **47**, and **49** were investigated. We anticipated complications because attempted aldol-type formation of seven-membered rings normally gives other condensation products. These epoxyannulation substrates have two new pathways (Scheme III), one of which (spirocyclization mode, path A) could also be applied to terpenoid synthesis. A simple homologue of the thioether **20**, compound **49**, afforded a complex mixture of products possibly containing the desired epoxide but from which spiro[4.5]decan-1-one was the major componant (34%).[8]

(26) Stotter, P. L.; Hornish, R. E. *J. Am. Chem. Soc.* **1973**, *95*, 4444–4446.
(27) These alkylation reactions required benzene as the solvent.
(28) King, J. F.; Tsang, G. T. Y. *J. Chem. Soc., Chem. Commun.* **1979**, 1131–1132.
(29) Laemmle, J.; Ashby, E. C.; Roling, P. V. *J. Org. Chem.* **1973**, *38*, 2526–2534.
(30) (a) Ficini, J.; Maujean, A. *Bull. Soc. Chim. Fr.* **1971**, 219–226. (b) Still, W. C.; MacDonald, T. L. *J. Am. Chem. Soc.* **1975**, *97*, 5280–5281.
(31) In our previous communication these ratios were reversed for **57**.[2]
(32) Varkony, H.; Pass, S.; Mazur, Y. *J. Chem. Soc., Chem. Commun.* **1974**, 437–438.
(33) Staroscik, J.; Rickborn, B. *J. Org. Chem.* **1972**, *37*, 738–740.
(34) Etheridge, S. J. *J. Org. Chem.* **1966**, *31*, 1990–1994.
(35) Wolinsky, L. E.; Faulkner, D. J.; Finer, J.; Clardy, J. *J. Org. Chem.* **1976**, *41*, 697–699.

Scheme IV



Scheme V



To increase the probability of cyclization, as well as the ease of precursor preparation, we examined unsaturated 1,7-oxosulfonium salts. Epoxyannulation products from most of these salts could be used directly in sesquiterpene synthesis. Three of these compounds, **29**, **32**, and **34**, afforded single major products (Scheme IV). Compound **29** affords the spiroannulated product **30** in a modest isolated yield. The identity of **30** was apparent from its spectral data. The formation of **30** can be rationalized by the increased acidity of cyclopentanoid α-hydrogens. Attempted extension of this spirocyclization with **32** led to the formation of **33** as the major product. The identity of **33** was apparent from its spectral data. The expected epoxide (**65**, Scheme IV) might undergo rapid base-catalyzed elimination as reported by Thummel and Rickborn[36] for related epoxides with stronger bases. An alternative pathway to **33** is also outlined in Scheme IV. Formation of a *cis*-betaine, which cannot yield an epoxide, followed by an acid–base reaction would afford a new ylide. Elimination of this ylide and dehydration of the resultant allylic dienol would provide the observed triene. The dehydration is facile in cis-fused tertiary bridgehead alcohols.[37] Yields of **30** and **33** are probably greater than 60%, but substantial amounts of these volatile compounds were lost during purification.

Compound **34** illustrates the third reaction pathway. The elimination product **35** is the only compound detected and isolated in greater than 85% yield. Apparently the carbonyl in **34** is simply too hindered to undergo ylide addition. The other compounds in this series, **38**, **46**, and **47**, afforded four to six products, with only **38** being analyzed in any detail (Table I, entry 11). Although the major product from **38** was elimination product **39**, the carbon NMR spectrum of the crude mixture contained resonances appropriate for the expected epoxide (50.7 and 60.3 ppm). Since less than a 15% yield of this oxirane was realized the product was not further characterized.

Attempted formation of cyclooctanes or cyclotridecanes from **42** (Table I, entry 12) or **52** (Table II) by epoxyannulation gave only elimination products regardless of the base or temperature employed including conditions used for the cyclization of phosphorus ylides.[3,38]

Discussion

To rationalize the stereoselectivity of epoxyannulation, it should be recalled that the betaine is formed by kinetic control and that this betaine must be trans diaxial for epoxide formation as illustrated with betaine **68** in Scheme V. Furthermore, there is no precedent for betaine equilibration via generation of a β-alkoxy ylide (**67**) followed reprotonation (Scheme V),[14] although appropriate experiments have not been completed to eliminate this possibility. In simple intermolecular reactions, unstablized sulfonium ylides and cyclohexanones give products via predominant axial addition;[39] the addition stereochemistry with cyclopentanones has only been determined with the sterically biased 17-oxo steroids.[14,40] This kinetic stereoselectivity has been rationalized by invoking the dipole–dipole interactions of the ylide and carbonyl as well as by using the standard arguments about steric strain, torsional strain, and compression effects of the incoming nucleophile.[41]

The conformational restrictions of the intramolecular reaction are often more important than the considerations of the intermolecular process. Whenever a five-membered ring is formed fused to another small ring (**9** and **14**), cisoid addition is sterically less demanding. Crandall[8] has presented arguments that betaine **68** leads to **14** (Scheme V). This betaine has axial sulfonium salt addition.

(36) Thummel, R. P.; Rickborn, B. *J. Org. Chem.* **1972**, *37*, 4250–4254.
(37) Fort, R. C.; Hornish, R. E.; Liang, G. A. *J. Am. Chem. Soc.* **1970**, *92*, 7558–7564.
(38) (a) Stork, G.; Nakamura, E. *J. Org. Chem.* **1979**, *44*, 4010–4011. (b) Nicolaou, K. C.; Seitz, S. P.; Pavia, M. R.; Petasis, N. A. *Ibid.* **1979**, *44*, 4011–4013.
(39) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353–1364. Stabilized sulfonium ylides often give equatorial addition products, an observation which has been rationalized by reversible carbonyl addition (see ref 14).
(40) All ylides add to the C-17 carbonyl from the α face.
(41) Reference 15, Chapter 2.

Crandall's rationale can be extended to the formation of **9**. The selective generation of epoxide **25** requires equatorial addition to the cyclohexanone as in **69** but not **70**. The preference for axial additions in intermolecular reactions is overcome by the two gauche butane carbon–carbon interactions of **70** which are absent in **69**. This stereochemistry is also observed when the analogous aldol reaction is under kinetically controlled conditions.[42] This cyclohexane analysis, with the assumption that the betaines are formed via chairlike transition states, affords a rationalization for the isomers in **5** and **18**. In both instances, the major betaine has one less gauche butane interaction than the minor isomer.

From several observations, equilibration of the betaine (**66** ⇄ **68**, Scheme V) via ylide formation in these systems seems unlikely. Apparently, only a single instance of sulfonium salt isomerization via a ylide has been documented.[43] Although betaine ylides are common in the phosphorus series,[44] there are no cases of sulfur betaine ylides. Generation of this betaine ylide (**67**) is kinetically less favorable than formation of an ethylidene ylide. Elimination of the ethylidene ylide affords nonepoxide products, as observed with **22**, **33**, **35**, and **39**. Since these products are formed at rates comparable to that of epoxide formation, we conclude that **67** is not formed. Therefore, betaine **68** must be formed exclusively.

*Simple 1,5- and 1,6-oxosulfonium salts, economically prepared via a general route, undergo exclusive epoxyannulation to yield 6-oxabicyclo[3.1.0]hexanes or 7-oxabicyclo[4.1.0]heptanes. The stereoselectivity illustrated by the formation of epoxides **5** and **18** is unparalleled in olefin epoxidation reactions*, a logical pathway to these epoxides.[45] Ylide formation competes with ketone enolization only when the ketone is very acidic and when the epoxyannulation product is strained (**9** and **10**). In these simple systems, other ylide-induced complications were not observed. However, when we attempted to extend epoxyannulation of 1,6-oxosulfonium salts from β-diketones, ylide rearrangement and elimination products predominated even though analogous phosphonium salts cyclize cleanly.[46]

Epoxyannulation leading to larger rings does present difficulties. Again, general syntheses of 1,7-, 1,8- and 1,11-oxosulfonium salts have been developed. The ring opening reaction of 4,5-dihydro-2(*H*)-thiapyrylium salts with carbon nucleophiles makes numerous 1,7-oxosulfonium salts particularly accessible. Treatment of seven 1,7-oxosulfonium salts with base may have afforded epoxyannulation products in two cases, **32** and **38**. If epoxide **65** is formed from **32**, it is not stable to the reaction conditions. The isolated triene **33** is a unique annulation product. Although the epoxide from **38** is apparently formed stereoselectively, the low yield has precluded assignment. With almost all of these compounds including 1,8- and 1,11-oxosulfonium salts, ylide elimination overwhelms epoxyannulation. The salt from cyclopentanone **29** provided spirocycle **30** via enolate displacement of the sulfonium salt. *This highly efficient spirocyclization illustrates the application of a cyclic sulfonium salt as a bis electrophile.* Salts such as **27** allow for the facile introduction of the cis olefin required for spirocyclization.[46] The different products from **29** and **38** indicates that the examination of other sulfonium salts are required to develop this scheme for the synthesis of [4.5] spirocyclic ketones.

3-Iodopropyl ethyl sulfide (**2**) and a ketone enolate can be stereoselectively transformed into an oxabicyclo[3.1.0]hexane. By an analogous sequence, *S*-ethylthiolanium fluoborate (**15**) affords oxabicyclo[4.1.0]heptanes. The stereochemistry of these products is a function of the ketone structure. With certain ketones *S*-ethyl-5,6-dihydro-4-methyl-2(*H*)-thiopyranium fluoborate (**27**) affords spirocyclic ketones or cycloheptatrienes, processes which are now being investigated.

Experimental Section

General Methods. Infrared spectra were recorded on a Beckman IR 18 AX spectrophotometer; bands yielding structural information are reported in reciprocal centimeters with polystyrene calibration. Nuclear magnetic resonance spectra were recorded on a Varian EM 390 at 35 °C in deuteriochloroform, and peak positions are reported in parts per million from tetramethylsilane as an internal standard with a multiplet (m), quartet (q), triplet (t), doublet (d), or singlet (s) designation. Low-resolution mass spectra were obtained from an LKB 9000 at 70- and 16–20-eV ionizing voltages or from a Finigan 4021 GCMS DS system. High-resolution spectra were performed at the California Institute of Technology Analytical Facility or at the Biomedical Mass Spectrometry Resource, Berkeley. Low-resolution spectra were also recorded of compounds for which only high-resolution data has been reported. Samples for low-resolution spectra were introduced by GC and for high-resolution by direct probe; both techniques afforded identical spectra.

GC analysis was performed on a Varian 3700 gas chromatograph with an FID detector outfitted with a 6 ft × 0.25 in. glass column containing the following: (A) 3% HI EFFIC 8BP on 100/120 Chromosorb; (B) 3% OV-225 on 100/120 Chromosorb; (C) 3% DEXIL 300 on 100/120 Supelcoport (Supelco, Inc.); (D) 3% SE-30 on 100/120 Supelcoport.

The term "evaporative distillation" refers to distillation with a Kugelrohr apparatus often at reduced pressure. All boiling points listed refer to the oven temperature during distillation.

The term "standard workup" means that the organic layer was washed with brine, dried over Na_2SO_4, and filtered and the solvent removed on a rotary evaporator at aspirator pressure. The term "base wash" means the organic layer was washed with saturated aqueous Na_2CO_3.

Reagents and Solvents. Tetrahydrofuran (THF) was distilled from sodium–benzophenone[48] immediately prior to use. Hexane was washed with sulfuric acid and distilled from calcium hydride. Dimethyl sulfoxide (Me_2SO) was distilled from calcium hydride at reduced pressure. All amines were distilled from barium oxide and stored over molecular sieves under nitrogen. All organolithium reagents were purchased from Alfa Ventron. All other reagents and solvents were purchased from Aldrich Chemical and Mallinckrodt Chemical, respectively, and were used as received after determining the purity by usual spectroscopic methods. All reactions were magnetically stirred under a nitrogen atmosphere. Keto ester **11** was prepared by the method of Deslongchamps.[49]

General Sulfonium Salt Preparation. A solution of 0.11 mol of freshly prepared triethyloxonium fluoborate (TEOF)[50] in 100 mL of methylene chloride was treated with 0.10 mol of the sulfide. The solution was stirred for 12 h. This solution was treated with 0.2 mol of ethanol, 0.2 mol of sodium bicarbonate, and 0.2 mol of magnesium sulfate. After being stirred for 1 h, the solution was filtered through sodium sulfate and evaporated to afford the salt. The purity was determined by NMR spec-

(42) Marshall, J. A.; Fanta, W. I. *J. Org. Chem.* **1964**, *29*, 2501–2505.
(43) Trost, B. M.; Bogdanowicz, M. J. *J. Am. Chem. Soc.* **1973**, *95*, 5298–5307.
(44) (a) Schlosser, M.; Christmann, K. F. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 126. (b) Corey, E. J.; Yamamoto, H. *J. Am. Chem. Soc.* **1970**, *92*, 6636–6637.
(45) McCurry, P. M., Jr. Ph.D. Thesis, Columbia University, 1970.
(46) Dauben, W. G.; Hart, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 7307–7314.
(47) Marshall, J. A.; Brady, S. F.; Anderson, N. H. *Fortschr. Chem. Org. Naturst.* **1974**, *31*, 283–376.
(48) Seyferth, D.; Spohn, R. J. *J. Am. Chem. Soc.* **1969**, *91*, 3037–3044.
(49) Ruest, L.; Blouin, G.; Deslongchamps, P. *Synth. Commun.* **1976**, *6*, 169–174.
(50) Meerwein, H. "Organic Syntheses"; Wiley: New York, 1973; Collect, Vol. V, pp 1080–1082.

troscopy. This procedure was used to prepare salts **15**, **27**, **36**, and **54**.[51]

***S*-Ethyl-4-methyl-5,6-dihydro-2(*H*)-thiapyrylium Fluoborate (27).** The preparation of tetrahydro-4-thiapyrone (**54**) by the method of Johnson and Berchtold[25] was slightly modified to avoid the slow addition. A solution of 5.10 g (2.00×10^{-2} mol) of *N,N*-dimethyl-4-oxopiperidinium iodide in 50 mL of deionized water and 100 mL of ether was treated with 5.52 g (6.00×10^{-2} mol) of sodium hydrogen sulfide with 5.28 g (2.20×10^{-2} mol) of sodium sulfide. This mixture was heated at reflux for 4 h. Treatment of the resulting mixture according to the standard workup left 1.64 g (70.7%) of tetrahydro-4-thiapyrone.

4-Hydroxy-4-methyltetrahydro-2(*H*)-thiapyran was prepared by the method of Stotter[26] by using methyllithium. A solution of 0.5 g of this alcohol and 0.13 g of *p*-toluenesulfonic acid in 40 mL of toluene was heated at reflux in a Dean–Stark apparatus for 21 h, at which time no alcohol remained. The toluene solution was washed with 10 mL each of saturated sodium bicarbonate (three times), 10% hydrochloric acid (once), and saturated sodium bicarbonate (once). The toluene was dried over $MgSO_4$ and then filtered. TEOF was added until the pungent odor of 5,6-dihydro-4-methyl-2(*H*)-thiapyran disappeared and then 1 g of additional TEOF was added. This suspension was treated with ethanol, sodium bicarbonate and magnesium sulfate and was stirred for 2 h. This suspension was filtered, and the solids were washed with CH_2Cl_2. The pooled filtrates were evaporated to leave a greenish solid (98% yield) which was pure by NMR. Repeated crystallization from ethanol afforded 0.43 g (53%) of **27** as a white solid: mp 81–82 °C; NMR (CD_3NO_2) δ 1.45 (t, J = 9 Hz, 3), 1.79 (br s, 3), 2.53 (m, 2), 3.27 (q, J = 9 Hz, 4), 3.50 (m, 2), 3.70 (m, 2), 5.58 (br s, 1). Anal. Calcd for $C_8H_{15}SBF$: C, 41.74; H, 6.52, S, 13.94. Found: C, 41.83; H, 6.70;, S, 14.28.

The preparation afforded comparable yields on a 0.5-mol scale.

Other routes to precursors of **27** which proved less satisfactory included the Dieckmann condensation of dimethyl 3,3′-thiodipropionate[52] and the preparation of 5,6-dihydro-4-methyl-2-(*H*)-thiapyran from 5,6-dihydro-4-methyl-2(*H*)-pyran by sequential treatment with boron trichloride, mesyl chloride, and disodium sulfide.

ω-Iodo Sulfides. Sulfide **2** was prepared by the method of Lee and Serif[20] in 64% yield. It was stored at −20 °C under N_2.

Sulfides **40**, **50**, and **53** were prepared from 6-chlorohexanol, 5-chloropentanol, and 11-bromoundecanol. A solution of 4 g (10^{-2} mol) of sodium hydroxide in 100 mL of 80% aqueous ethanol was diluted with 100 mL of THF and deoxygenated by bubbling with N_2 for 30 min. To this solution was slowly added 7.2 mL (10^{-2} mol) of ethanethiol. After 30 min this cloudy suspension was treated with 12.2 g (0.09 mol) of 6-chlorohexanol. The solution was stirred for 12 h and processed via the standard workup to leave 10 g of 6-(ethylthio)-1-hexanol: NMR δ 1.2 (t, $J \approx 8$ Hz, 3), 1.5 (m, 8), 2.5 (m, 4), 3.6 (t, $J \approx 8$ Hz, 2).

Conversion of this alcohol to the mesylate was accomplished by the method of Servis:[53] NMR δ 1.2 (t, $J \approx 8$ Hz, 3), 1.5 (m, 8), 2.5 (m, 4), 2.9 (s, 3), 4.1 (t, $J \approx 8$ Hz, 2). Immediate treatment of this mesylate with sodium iodide (20 equiv) in refluxing acetone for 45 h yielded after the usual workup 30% of 6-(ethylthio)-1-iodohexane (**40**): NMR δ 1.2 (t, $J \approx 8$ Hz, 3), 1.5 (m, 8), 2.5 (m, 4), 3.1 (t, $J \approx 8$ Hz, 2). This iodide was stored short periods at −30 °C under N_2.

Similarly prepared were 6-(phenylthio)-1-iodopentane (**50**) [NMR δ 1.6 (m, 6), 2.45 (t, $J \approx 8$ Hz, 2), 2.95 (t, $J \approx 8$ Hz, 2), 7.35 (s, 5)] and 11-(ethylthio)-1-iodoundecane (**53**): NMR δ 1.2 (t, $J \approx 8$ Hz, 3), 1.6 (m, 18), 2.5 (m, 4), 3.6 (t, $J \approx 8$ Hz, 2). On being allowed to stand at room temperature for 2 weeks, 6-(phenylthio)-1-iodopentane (**50**) yielded *S*-phenylthianium iodide (**51**): NMR δ 2.0–2.5 (m, 6), 4–4.5 (m, 4), 7.6 (br s, 3), 8.3 (m, 2).

Preparation of ω-(Thioalkyl)-β-oxo Ester. A 1 M solution of sodium enolate was prepared by addition of the β-oxo ester to 1 equiv of sodium hydride in THF at 0 °C. To this solution at 0 °C was added 0.95 equiv of the sulfonium salt or halide. After 1 h at 0 °C, this solution was heated at reflux for 12 h. The standard workup followed by evaporative distillation afforded the C-alkylated oxo ester.

Ethyl 2-methyl-2-[3-(ethylthio)propyl]acetoacetate (3): 97% yield; IR 1720, 1710 cm^{-1}; NMR δ 1.25 (2 t, $J \approx 8$ Hz, 6), 1.30 (s, 3), 1.90 (m, 4), 2.15 (s, 3), 2.60 (m, 4), 4.25 (q, $J \approx 8$ Hz, 2); mass spectrum, m/z 246 (M^+), 155, 101 (base); HRMS, m/z 228.1211 ($M^+ - 18$; $C_{12}H_{20}O_2S$ requires 228.1238).

Methyl 1-[3-(ethylthio)propyl]-2-oxocyclopentanecarboxylate (7): 58% yield; bp 140 °C (0.33 kPa); IR 1740, 1720 cm^{-1}; NMR δ 1.60 (t, $J \approx 8$ Hz, 3), 1.95 (m, 8), 2.35 (m, 6), 3.70 (s, 3); mass spectrum, m/z 244 (M^+), 167 (base), HRMS, m/z 244.1138 ($C_{12}H_{20}O_3S$ requires 244.1143).

Methyl 1-[3-(ethylthio)propyl]-2-oxocyclohexanecarboxylate (12): 91% yield; bp 166–171 °C (0.33 kPa); IR 1720, 1715 cm^{-1}; NMR δ 1.21 (t, $J \approx 8$ Hz, 3), 1.40–2.15 (m, 10), 2.50 (m, 6), 3.72 (s, 3); mass spectrum, m/z 258 (M^+), 818 (base); HRMS, m/z 258.1286 ($C_{13}H_{22}O_3S$ requires 258.1283).

Ethyl 2-methyl-2-[4-(ethylthio)butyl]acetoacetate (16): 66% yield; IR 1720, 1710 cm^{-1}; NMR δ 1.20 (2 t, $J \approx 8$ Hz, 6), 1.90 (s, 3) 2.2 (m, 6), 2.2 (s, 3), 2.6 (m, 4), 4.2 (q, $J \approx 8$ Hz, 2); HRMS, m/z 246.1289 ($M^+ - 32$; $C_{12}H_{22}O_3S$ requires 246.1289).

Methyl 1-[4-(ethylthio)butyl]-2-oxocyclopentanecarboxylate (19): 88% yield; IR 1750, 1720 cm^{-1}; NMR δ 1.2 (t, $J \approx$ Hz, 3), 2.2 (m, 10), 2.6 (m, 6), 3.7 (s, 3); HRMS, m/z 240.1204 ($C_{13}H_{22}O_3S - 18$ requires 240.1184).

Ethyl 1-[4-(ethylthio)butyl]-2-oxocyclohexanecarboxylate (23): 72% yield; IR 1720, 1715 cm^{-1}; NMR δ 1.2 (2 t, $J \approx 8$ Hz, 6), 1.6 (m, 12), 2.5 (m, 6), 4.2 (q, $J \approx 8$ Hz, 2); HRMS, m/z 272.1464 ($C_{15}H_{26}O_3S$ requires 272.1471).

Methyl 1-[3-methyl-5-(ethylthio)-2(*Z*)-pentenyl]-2-oxocyclopentanecarboxylate (28): 98% yield: bp 50 °C (0.013 kPa); IR 2980, 1760, 1735, 1450, 1335, 1160 cm^{-1}; NMR δ 1.27 (t, J = 12 Hz, 3), 1.71 (s, 3), 2.2 (m, 12), 2.43 (q, J = 12 Hz, 2), 3.68 (s, 3) 5.10 (t, 1); HRMS, m/z 284.144 ($C_{15}H_{24}O_3S$ requires 284.1442).

Methyl 1-[3-methyl-5-(ethylthio)-2(*Z*)-pentenyl]-2-oxocyclohexanecarboxylate (31): 58% yield; IR 2920, 1708, 1170, 1125 cm^{-1}; NMR (CCl_4) δ 1.24 (t, 3), 1.72 (s, 3), 1.70 (m, 6), 2.08–2.68 (m, 10), 3.70 (s, 3), 5.05 (t, 1); HRMS, m/z 298.1593 ($C_{16}H_{26}O_3S$ requires 298.1596).

Methyl 1-[*o*-[2-(ethylthio)ethyl]benzyl]-2-oxycyclopentanecarboxylate (37): 83% yield; IR 1750, 1725 cm^{-1}; NMR (CCl_4) δ 1.23 (t, $J \approx 9$ Hz, 3), 1.42–3.07 (m, 14), 3.68 (s, 3), 7.00 (m, 4).

Ethyl 2-methyl-2-[6-(ethylthio)hexyl]acetoacetate (41): 95% yield; IR 1720, 1710 cm^{-1}; NMR δ 1.20 (t, $J \approx 8$ Hz, 6), 1.30 (s, 3), 1.60 (m, 10), 2.10 (s, 3), 2.60 (m, 4), 4.20 (q, $J \approx 8$ Hz, 2).

Decarboalkoxylation of β-Oxo Esters. Procedure A. A 0.1 M suspension of the β-oxo ester in 6 M hydrochloric acid was heated at reflux for 36 h. The solution was cooled to room temperature, saturated with sodium chloride, and washed with an equal volume of ether (five times). Processing of the ether layer left the product.

Procedure B. The method of Miles[17] was followed.

Procedure C. The method of Elsinger[19] was used.

3-Methyl-6-(ethylthio)-2-hexanone (4). Procedure A: 86% yield (from **3**); IR 1700 cm^{-1}; NMR δ 1.14 (d, $J \approx 8$ Hz, 2), 1.29 (t, $J \approx 8$ Hz, 3), 1.70 (m, 3), 2.15 (s, 3), 2.55 (m, 6); mass spectrum, m/e 174 (M^+), 97 (base); HRMS, m/z 174.1078 ($C_9H_{18}OS$ requires 174.1078).

2-[3-(Ethylthio)propyl]cyclopentanone (8). Procedure A: 75% yield (from **7**); 120 °C (0.43 kPa); IR 1750 cm^{-1}; NMR δ 1.20 (t, $J \approx 8$ Hz, 3), 1.50–2.60 (m, 15); HRMS, m/z 186.1080 ($C_{10}H_{18}OS$ requires 186.1079).

2-[3-(Ethylthio)propyl]cyclohexanone (13). Procedure A: 95% yield (from **12**); IR 1710 cm^{-1}; NMR δ 1.20 (t, $J \approx 8$ Hz, 3), 1.30–2.6 (m, 17); mass spectrum, m/e 200 (M^+ and base); HRMS, m/z 200.1241 ($C_{11}H_{20}OS$ requires 200.1247).

3-Methyl-7-(ethylthio)-2-heptanone (17). Procedure A: 87% yield (from **16**); IR 1715 cm^{-1}; NMR δ 1.00 (d, $J \approx 8$ Hz, 3), 1.20 (t, $J \approx 8$ Hz, 3), 1.5 (m, 6), 2.00 (s, 3), 2.40 (m, 5); HRMS, m/z 216.1540 ($C_{12}H_{24}OS$ requires 216.1533).

2-[4-(Ethylthio)butyl]cyclopentanone (20). Procedure A: 78% yield from **19**; IR 1740 cm^{-1}; NMR δ 1.20 (t, $J \approx 8$ Hz, 3), 1.2–2.2 (m, 12), 2.5 (m, 5); HRMS, m/z 200.1236 ($C_{11}H_{20}OS$ requires 200.1236).

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2-[4-(Ethylthio)butyl]cyclohexanone (24). Procedure A: 72% yield (from **23**); IR 1715 cm^{-1}; NMR δ 1.20 (t, $J \approx 8$ Hz, 3), 1.20–2.60 (m, 19); HRMS, m/z 214.139 ($C_{12}H_{22}OS$ requires 214.139).

2-[3-Methyl-5-(ethylthio)-2(*Z*)-pentenyl]cyclopentanone (29). Procedure C: 90% yield (from **28**); IR 2970, 2935, 1740, 1458 cm^{-1}; NMR δ 1.23 (t, $J = 8$ Hz, 3), 1.72 (s, 3), 1.80–2.70 (m, 15), 5.17 (t, $J = 6$ Hz, 1); HRMS, m/z 226.1392 ($C_{13}H_{22}OS$ requires 226.1392).

2-[3-Methyl-5-(thioethyl)-2(*Z*)-pentenyl]cyclohexanone (32). Procedure C: 85% yield (from **31**); 150 °C (0.013 kPa); IR 2940, 2870, 1715, 1130 cm^{-1}; NMR (CCl_4) δ 1.23 (t, $J = 7$ Hz, 3), 1.73 (s, 3), 1.85–2.68 (m, 17), 5.11 (t, $J = 7$ Hz, 1); HRMS, m/z 240.1548 ($C_{14}H_{24}Os$ requires 240.1548).

2-[3-Methyl-5-(ethylthio)-2(*Z*)-pentenyl]-2,6,6-trimethylcyclohexanone (34). According to the method of Rathke and Millard,[54] **32** was permethylated to give **34**: 94% yield; IR 2975, 2940, 2870, 1692 cm^{-1}; NMR (CCl_4) δ 1.05 (s, 6), 1.09 (s, 3), 1.25 (t, $J = 6.5$ Hz, 3), 1.70 (m, 9), 2.05–2.62 (m, 8), 4.96 (t, $J = 7.5$ Hz, 1); ^{13}C NMR δ 219.27, 135.44, 121.81, 47.62, 43.97, 39.34, 37.13, 36.49, 31.90, 29.47, 27.47, 26.79, 25.56, 25.40, 23.09, 17.46, 14.39; HRMS, m/z 282.2010 ($C_{17}H_{30}OS$ requires 282.2011).

2-[*o*-[2-(Ethylthio)ethyl]benzyl]cyclopentanone (38). Procedure A: 66% yield (from **37**); IR 1730 cm^{-1}; NMR (CCl_4) δ 1.27 (t, $J \approx 9$ Hz, 3), 1.45–3.30 (m, 15), 7.05 (s, 4); HRMS, m/z 262.1393 ($C_{16}H_{22}OS$ requires 262.1391).

3-Methyl-9-(ethylthio)-3-nonanone (42). Procedure A: 71% yield (from **41**); bp 100 °C (0.33 kPa); IR 1700 cm^{-1}; NMR δ 1.0 (d, $J \approx 8$ Hz, 3), 1.2–1.8 (m, 14), 2.0 (s, 2), 2.5 (m, 5); HRMS, m/z 216.1540 ($C_{12}H_{24}OS$ requires 216.1547).

2-[5-(Phenylthio)pentyl]cyclopentanone (49). Procedure A: 75% yield; IR 1745 cm^{-1}; NMR δ 1.0–2.5 (m, 15), 2.9 (t, $J \approx 8$ Hz, 2), 7.2 (s, 5).

2-Methyl-14-(ethylthio)-2-tetradecanone (52). Procedure B: 50% yield; bp 105 °C (0.046 kPa); IR 1715 cm^{-1}; NMR δ 1.2 (t, 3), 1.3 (m, 24), 2.1 (s, 3), 2.6 (m, 4).

Preparation of Epoxides. General Procedure. A 1-M solution of the oxosulfide in methylene chloride was treated with 1.3 equiv of TEOF. This solution was stirred for 12 h. The excess oxonium ion was decomposed by treatment with anhydrous ethanol and sodium bicarbonate. Filtration and evaporation of the solution left the viscous sulfonium salt which was not characterized but checked by NMR spectroscopy.

This oil was suspended in THF (1 M) and cooled to 0 °C. This suspension was treated with 1.5 equiv of a 5 M solution of potassium *tert*-butoxide in THF. The solution was allowed to warm to room temperature and processed as usual by using pentane as an extraction solvent.

3,4-Dimethyl-2-oxabicyclo[3.1.0]hexane (5) was prepared in 80% yield from **4**: NMR δ 1.00 (d, $J = 8$ Hz, 3), 1.25 (s, 3), 1.40–2.00 (m, 5), 3.20 (s, 1); mass spectrum, m/z 112 (M^+), 97 (base), 84, 83; minor isomer not easily detected.

(1α,3α,6α)-2-Oxatricyclo[4.3.1.0^{1,3}]nonane (9) and 2-oxabicyclo[4.3.0]non-1(6)-ene (10)[34] were prepared in 90% yield from **8**: NMR δ 1.4–2.0 (m, 12), 2.0–2.4 (m, 3), 2.5 (m, 6), 3.2 (br s, 1), 3.5 (m, 2); GC/MS (column C), m/z 124 (M^+, first peak), 124 (M^+, second peak).

(1α,3α,6α)-2-Oxatricyclo[4.4.0.0^{1,3}]decane (14) was prepared from **13**: 99% yield; NMR δ 0.85–2.68 (m, 13), 3.23 (s, 1); MS (70 eV), m/z 138 (M^+), 122, 121, 120, 94, 89 (base); HRMS, m/z 138.1033 ($C_9H_{14}O$ requires 138.1022).

3,4-Dimethyl-2-oxatricyclo[5.3.0.0^{1,3}]decane (18) was prepared from **17**: 55% yield; NMR δ 1.05 (d, $J \approx 8$ Hz, 3), 1.25 (s, 3), 1.16 (m, 7), 2.85 (t, $J \approx 3$ Hz, 1); mass spectrum, m/z 126 (M^+).

(1α,3α,7α)-2-Oxatricyclo[5.3.0.0^{1,3}]decane (21) was prepared from **20**: 73% yield; NMR δ 1.0–2.2 (m, 13), 2.85 (t, $J \approx 4$ Hz, 1); mass spectrum (15 eV) m/z 138 (M^+), 120 (base), 109, 97, 92, 91.

3aα-Hydroxy-4α-(ethylthio)octahydroindan-7aα-carboxylic Acid (22). From 1.60 g of keto ester **19** there was obtained 0.66 g of a base-soluble compound and a complex mixture of netural materials. The base-soluble compound was triturated with ethyl acetate to afford 0.16 g (11%) of **22**: IR 3700–2350 (br), 2940, 2590, 1700 (weak), 1660, 1185, 1110, 864 cm^{-1}; NMR δ 1.22 (t, $J = 8$ Hz, 3), 1.35–2.38 (m, 12), 2.58 (q, $J = 8$ Hz, 2), 2.80 (t, $J = 5$ Hz, 1); ^{13}C NMR δ 181.33 (s), 82.92 (s), 55.14 (s), 51.02 (d), 36.13 (t), 32.77 (t), 30.00 (t), 29.58 (t), 27.21 (t), 20.17 (t), 18.86 (t), 15.09 (q); HRMS, m/z 244.1149 ($C_{12}H_{20}O_3S$ requires 244.1144).

According to Faulkner and Wolinsky,[35] a solution of 0.0915 g (3.74×10^{-4} mol) of **22** and 0.21 g (1.13×10^{-3} mol) of *p*-toluenesulfonyl chloride was prepared in 4 mL of pyridine at 0 °C and kept at 0 °C for 2 days. The solution was diluted with ether and washed three times with saturated copper sulfate. Completion of the standard workup on the ether layer provided 0.070 g (83%) of lactone **64**: IR 2935, 2870, 1808, 1160, 1105 cm^{-1}; NMR δ 1.25 (t, $J = 7$ Hz, 3), 1.37–2.30 (m, 12), 2.30–2.90 (m, 3).

(1α,3aα,7β)-2-Oxatricyclo[6.4.0.0^{1,3}]undecane (25) was prepared from **24** in 67% yield; NMR δ 1.0–2.0 (m, 15) and 2.90 (d, $J = 5$ Hz, 1); HRMS, m/z 152.1180 ($C_{10}H_{16}O$ requires 152.1201).

3-Methylspiro[4.5]dec-2-en-6-one (30). From **29** was formed **30**: 40% yield; IR 2950, 1745, 1440, 1150 cm^{-1}; NMR δ 1.62 (s, 3), 1.68–2.07 (m, 6), 2.09–2.32 (m, 6), 5.28 (br s, 1); ^{13}C NMR δ 223.48 (s), 132.97 (s), 118.57 (d), 47.30 (s), 37.62 (t), 33.87 (t), 32.28 (t), 28.33 (t), 26.83 (t), 23.22 (q), 18.73 (t); mass spectrum, m/z 164 (M^+); HRMS, m/z 164.1200 ($C_{11}H_{16}O$ requires 164.1200).

4-Methylbicyclo[5.4.0]undeca-1(7),3,5-triene (33). From **32** was formed **33**: 38% yield; IR 3030, 2960, 1645, 1455, 1440 cm^{-1}; NMR δ 1.68 (br s, 4), 1.80 (s, 3), 2.13 (m, coupled to 5.12, 6), 5.12 (br t, $J = 6$ Hz, 1), 6.13 (s, 2); HRMS, m/z 160.1251 ($C_{12}H_{16}$ requires 160.1255).

2-(3-Methyl-2(*Z*),4-pentadienyl)-2,6,6-trimethylcyclohexanone (35) was obtained from **34**: 86% yield; IR 2980, 2950, 2878, 1696, 1460, 1382, 1268 cm^{-1}; NMR (CCl_4) δ 1.10 (s, 6), 1.13 (s, 3), 1.54–1.85 (m, 9), 2.30–2.50 (m, 2), 4.92–5.26 (m, 3), 6.56 (dd, $J = 9.6$, 2.5 Hz, 1); ^{13}C NMR δ 219.62, 133.49, 126.33, 121.66, 113.66, 65.60, 39.54, 36.70, 36.70, 27.65, 27.01, 25.63, 19.87, 17.64, 15.05; HRMS, m/z 220.1828 ($C_{15}H_{24}O$ requires 220.1827).

1,2-Dimethylcyclopentan-1-ol (57). A solution of 0.100 g of epoxide **5** in 5 mL of Et_2O was treated with $LiAlH_4$ as usual to provide 0.080 g of alcohols **57**, IR 3500 cm^{-1}.

A sample of alcohols **57** was prepared according to Ashby[29] from 2-methylcyclopentanone. This sample contained 1β,2α-dimethylcyclopentan-1-ol and 1β,2β-dimethylcyclopentan-1-ol in a 3:2 ratio.

Analysis of the alcohols **57** from **5** by using GC columns C and D indicated the α to β ratio to be 79:21.

1,2-Dimethylcyclohexan-1-ol (58). A solution of 0.20 g of epoxide **18** was treated with excess $LiAlH_4$ in 5 mL of ether. After being stirred for 16 h, this suspension was treated with an aqueous sodium sulfate paste and filtered. Evaporation of the solvent left 0.19 g (90%) of **58**: IR 3500 cm^{-1}; NMR δ 0.90 (d, $J \approx 8$ Hz, 3), 1.00–1.80 (m, 12).

A sample of alcohols **58** was prepared by treatment of 2-methylcyclohexanone in ether with methyl magnesium bromide according to Ficini and Maujean.[30] The expected product ratio of 85:15 was obtained. The product ratio of the reduction products from **18** was then determined to be 88:12 by using GC columns A and B.

(1α,6β)-Bicyclo[4.3.0]nonan-1-ol (59) and (1α,6α)-Bicyclo[4.3.0]nonan-1-ol (60). A solution of 0.050 g of epoxide **14** was treated with lithium aluminum hydride as before to yield 0.039 g of alcohol **59**, IR 3500 cm^{-1} (weak).

A solution of 0.035 g of epoxide **21** yielded 0.029 g of alcohols **59** and **60**, IR 3500 cm^{-1} (weak).

Ozonolysis of *trans*-octahydroindene and of *cis*-octahydroindene afforded pure samples of **59** and **60**.[32,37] GC analysis using columns C and D indicated that the ratio of **59** to **60** from **21** was 24:76 and that **14** gave **60** in greater than 99% yield: **59**, mass spectrum, m/z 140 (M^+); **60**, mass spectrum, m/z 140 (M^+).

(1α,6β)-Bicyclo[4.4.0]decan-1-ol (63). A solution of 0.041 g of epoxide **25** in 5 mL of ether was treated with excess $LiAlH_4$, quenched with an aqueous sodium sulfate paste, filtered, and processed to leave 0.030 g of **63**: IR 3500 cm^{-1} (weak); NMR δ 1.0–2.1 (m); mass spectrum, m/z (relative intensity) 154 (M^+, 62), 136 (47), 111 (100), 98 (47), 84 (48), 49 (47).

Authentic **63** was prepared by catalytic hydrogenation of *trans*-1a-hydroxy-1,1a,4,4a,5,6,7,8-octahydronaphthalene.[33] Isomer **61** was prepared by the ozonolysis of *cis*-decahydronaphthalene:[32]

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mass spectrum, m/z (relative intensity) 154 (M^+, 62), 136 (70), 111 (58), 74 (75), 59 (94), 31 (100). Analysis by GC on columns A and B indicated the alcohol derived from **25** was >99% of **63**.

Acknowledgment. We are grateful to Professor Bruce Rickborn (UCSB) and Professor Jack Crandall (Indiana University) for helpful discussions. The finnigan GC/MS instrument was purchased with a NIH shared instrument grant (No. GM 27583-01). High-resolution mass spectra were obtained at the Bioorganic, Biomedical Mass Spectrometry Resource (A. L. Burlingame, Director) supported by NIH Grant No. RR00719.

Registry No. **1**, 17094-21-2; **2** (X = Br), 83705-51-5; **3**, 83705-52-6; **4**, 77505-18-1; **5** (isomer 1), 77505-24-9; **5** (isomer 2), 77549-98-5; **6**, 10472-24-9; **7**, 83705-53-7; **8**, 77505-19-2; **9**, 77505-25-0; **10**, 10468-35-6; **11**, 41302-34-5; **12**, 83705-54-8; **13**, 77505-20-5; **14**, 77550-59-5; **15**, 696-98-0; **16**, 83705-55-9; **17**, 77505-21-6; **18** (isomer 1), 34459-06-8; **18** (isomer 2), 32432-88-5; **19**, 83705-56-0; **20**, 77505-22-7; **21** (isomer 1), 77549-99-6; **21** (isomer 2), 77610-39-0; **22**, 83705-57-1; **23**, 83705-58-2; **24**, 77505-23-8; **25**, 77550-66-4; **27**, 83705-60-6; **28**, 83705-61-7; **29**, 83705-62-8; **30**, 83705-63-9; **31**, 83705-64-0; **32**, 83705-65-1; **33**, 83705-66-2; **34**, 83705-67-3; **35**, 83705-68-4; **36**, 83705-70-8; **37**, 83705-71-9; **38**, 83705-72-0; **39**, 83705-73-1; **40** (X = I), 83705-74-2; **41**, 83705-75-3; **42**, 77510-84-0; **43**, 77505-26-1; **50** (X = I), 83705-76-4; **53** (X = I), 83705-77-5; **54**, 1072-72-6; **57**, 19550-45-9; **58**, 5402-29-9; **59**, 13366-91-1; **60**, 13366-92-2; **63**, 1654-87-1; *N,N*-dimethyl-4-oxopiperidinium iodide, 26822-37-7; sodium hydrogen sulfide, 16721-80-5; 4-hydroxy-4-methyltetrahydro-2(*H*)-thiapyran, 38447-82-4; 5,6-dihydro-4-methyl-2(*H*)-thiapyran, 39193-69-6; 6-bromohexanol, 4286-55-9; ethanethiol sodium salt, 811-51-8; 6-(ethylthio)-1-hexanol, 83705-78-6; 6-(ethylthio)-1-hexanol mesylate, 83705-79-7; 5-chloropentanol, 5259-98-3; 11-bromodecanol, 1611-56-9.

Epoxyannulation. 5. Reactions of 1-Butadienylsulfonium Salts

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Received December 9, 1981

Treatment of the lithium enolate from three aldehydes, cycloheptanone, and four unhindered cyclohexanones with (1,3-butadien-1-yl)dimethylsulfonium fluoborate (**1**) provides a 7-oxabicyclo[4.1.0]hept-4-ene stereoselectively in 30–58% yield. These epoxides are accompanied by 2-[2-[(methylthio)methyl]-3-butenyl] ketones. This alkylated ketone is the sole product from the enolates of three hindered cyclic ketones and three acyclic ketones. Five related sulfonium salts, **2**, **21**, **46**, **50**, and **63**, and the enolate from cyclohexanone gave these alkylated ketones accompanied by a 5–40% yield of the epoxyannulated product.

Recently we communicated that certain enolates combine with *S*-(1,3-butadien-1-yl)dimethylsulfonium fluoborate (**1**) to yield 7-oxabicyclo[4.1.0]hept-4-enes.[2] This specific reaction sequence illustrates the more general cyclization of oxo-ω-sulfonium ylides, a process called epoxyannulation. The use of **1** permits the entire epoxyannulation process to be completed in one pot.[3,4] In addition to the full details of our previous study, we are now reporting the reactions of additional enolates with **1** and the reactions of the enolate from cyclohexanone with sulfonium salts **2**, **21**, **46**, **50**, and **63** (Scheme I). *Sulfonium salts **1**, **2**, **46**, and **50** with enolates from unhindered cyclohexanones and cycloheptanones as well as from aldehydes provide epoxyannulation products in modest yet synthetically useful yields (Table I). This one-pot procedure using **1** is the most efficient preparation of these 7-oxabicyclo[4.1.0]hept-4-enes.*

The 7-oxabicyclo[4.1.0]heptene ring is a synthetic precursor for the major structural component of the cytotoxic antibiotics crotopoxide[5a] and triptolide[5b] as well as the arene oxides.[6] Our epoxyannulation protocol provides a single stereoisomer of this system containing functionalized carbons at four of the six atoms in a disposition complementing products from epoxides prepared by Birch reduction–epoxidation,[6] phosphonium ylide condensation–epoxidation,[7] or other epoxyannulation reactions[8] including Robinson annulations.[9]

Results

The reactions of fourteen enolates with sulfonium salts[10] **1**, **2**, **46**, and **50** are summarized in Table I. Unhindered cyclic ketone and aldehyde enolates with **1** in tetrahydrofuran (THF) provide 7-oxabicyclo[4.1.0]hept-4-enes in 30–60% yield, accompanied by a 10–20% yield of 2-[2-[(methylthio)methyl]-3-butenyl] ketones, such as **5**, and by the unreacted carbonyl compound. These butenyl ketones are the major products from acyclic ketone enolates and **1** as well as from all enolates with **2** in *t*-BuOH–THF solvent.

The identity of the epoxides was established by examination of their spectral properties. The NMR spectra of

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