J. Org. Chem. **1985**, *50*, 2767-2777

Betweenanenes with Vinylic Heteroatoms. Route to Sulfur Analogues via [2,3]-Sigmatropic Rearrangement

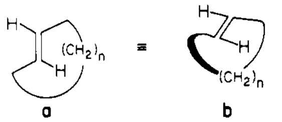
Alex Nickon,* Abimael D. Rodriguez, Rathindra Ganguly, and Vilas Shirhatti

Department of Chemistry, The Johns Hopkins University, Baltimore, Maryland 21218

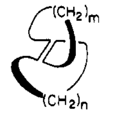
Received December 11, 1984

The goal was to devise routes to double-domed olefins ("betweenanenes") having a heteroatom connected directly to the double bond. Our approach centered on [2,3]-sigmatropic rearrangement of ylides, and specifically we sought to learn if dithioketals could serve as starting points to prepare betweenanenes in which one of the sulfurs is vinylic. Our key test compound was 7-methylene-1,5-dithiaspiro[5.11]heptadecane (**13**), which we synthesized by two schemes. The methylsulfonium salt of **13** was treated with different bases (KO-*t*-Bu, *n*-BuLi, *t*-BuLi, and DBU) to generate a transient sulfur ylide. In all cases the products were those from eliminations and from Stevens-type [1,2] rearrangements. In contrast, when dithioketal **13** was warmed with ethyl diazoacetate–$CuSO_4$, the derived ylide produced the desired betweenanene **35** and its *Z*-isomer **36** in 4:1 ratio. Similarly, with dimethyl diazomalonate and $CuSO_4$, dithioketal **13** afforded the double-domed vinyl sulfide **38** along with its *Z* counterpart **39** in a 5:1 ratio. We also studied 2-methyl-2-(1-methylvinyl)-1,3-dithiane (**42**). This monocyclic substrate also expanded its ring via the [2,3] manner when heated with ethyl diazoacetate or dimethyl diazomalonate. Our findings indicate that the second sulfur in dithioketals does not thwart the [2,3]-sigmatropic rearrangement when ylides are generated with diazoesters. But, eliminations and Stevens-type [1,2] shifts prevailed when strong bases act on a preformed methylsulfonium salt.

The spanning chain in medium-ring *trans*-cycloalkenes (**1**) arches like a dome across one face of the π bond and protects that side from aggression. The degree of shielding (and also the strain in the double bond) should be greatest when the chain is short. An alkene with two such transoid rings (e.g., **2**; called "betweenanenes") is blocked from both top and bottom, so investigations of such encased π units are of interest.[1,4]



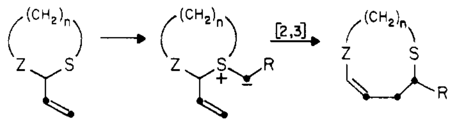
1



2

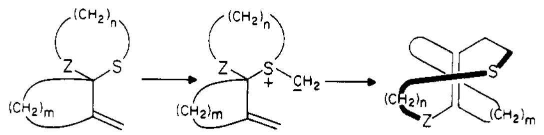
Intriguing situations arise when one or both of the chains contain heteroatoms that might interact with the olefin. As no betweenanenes were known with a heteroatom directly attached to the olefinic carbon, our objective was to synthesize such prototypes. We now report details of a successful route to sulfur analogues.

Our approach was based on earlier research by Vedejs, who developed a way to enlarge, by three carbons, a sulfur-containing ring.[6] Typically, their methodology converts an α-vinyl cyclic sulfide (**3a**) to a transient sulfur ylide (**4a**) that isomerizes to an expanded cycloalkene (**5a**).[7,8] Note that the sulfur in the expanded ring **5a** ends up separated from the alkene by two carbons. Sandri and Fava applied the sequence to a spirocyclic precursor **6a** (n = 3, m = 10) and thereby prepared a [10.7]betweenanene (**8a**, n = 3, m = 10) with an aliphatic sulfur in one chain.[3]



3 4 5

a, Z = CH_2
b, Z = S
c, Z = O



6 7 8

a, Z = CH_2
b, Z = S
c, Z = O

The scope and versatility of the three-atom ring growth would be broadened if dithioketals **3b** could replace monothiaalkanes as ylide precursors and thereby provide access to enlarged cycloalkenes with two distinct types of sulfurs—vinylic and aliphatic (**5b**). Furthermore, if extrapolated to spirocyclics like **6b**, the *gem*-dithia type of precursor might produce betweenanenes **8b** with one sulfur directly bonded to the buried π link. And possibly, monothioketals **3c** (and **6c**) could lead to enol ether analogues **5c** (and **8c**). Our present goal was to learn whether dithioketals could serve as vehicles for generating transient ylides (**4b**). And would such ylides undergo [2,3]-sigmatropic expansion or would the second sulfur promote other fates? We then hoped to apply the notion to spirocyclic analogues like **6b** for entry to betweenanenes with a vinylic heteroatom (**8b**). Because our main thrust involved spirocyclics, we describe first our findings with them. Then we shall turn to our monocyclic model to compare its conduct with our bicyclics as well as with some recent results by Doyle et al., on two closely similar molecules.[9]

Results and Discussion

The pivotal structure in our projected synthesis is an α-methylene dithiaspiro assembly like **6b**, specifically the

---

[1] (a) Marshall, J. A. *Acc. Chem. Res.* **1980**, *13*, 213–218. (b) Marshall, J. A.; Flynn, K. E. *J. Am. Chem. Soc.* **1983**, *105*, 3360–3362.

[2] Nakazaki, M.; Yamamoto, K.; Maeda, M. *J. Org. Chem.* **1980**, *45*, 3229–3232.

[3] (a) Ceré, V.; Paolucci, C.; Pollicino, S.; Sandri, E.; Fava, A. *J. Org. Chem.* **1981**, *46*, 486–490. (b) Ceré, V.; Paolucci, C.; Pollicino, S.; Sandri, E.; Fava, A. *J. Chem. Soc., Chem. Commun.* **1980**, 755–756.

[4] Nickon, A.; Zurer, P. St. J.; Hrnjez, B.; Tino, J. *Tetrahedron* **1983**, *39*, 2679–2690.

[5] Nickon, A.; Rodriguez, A.; Shirhatti, V.; Ganguly, R. *Tetrahedron Lett.* **1984**, *25*, 3555–3558.

[6] For a review, see: Vedejs, E.; Krafft, G. A. *Tetrahedron* **1982**, *38*, 2857–2881.

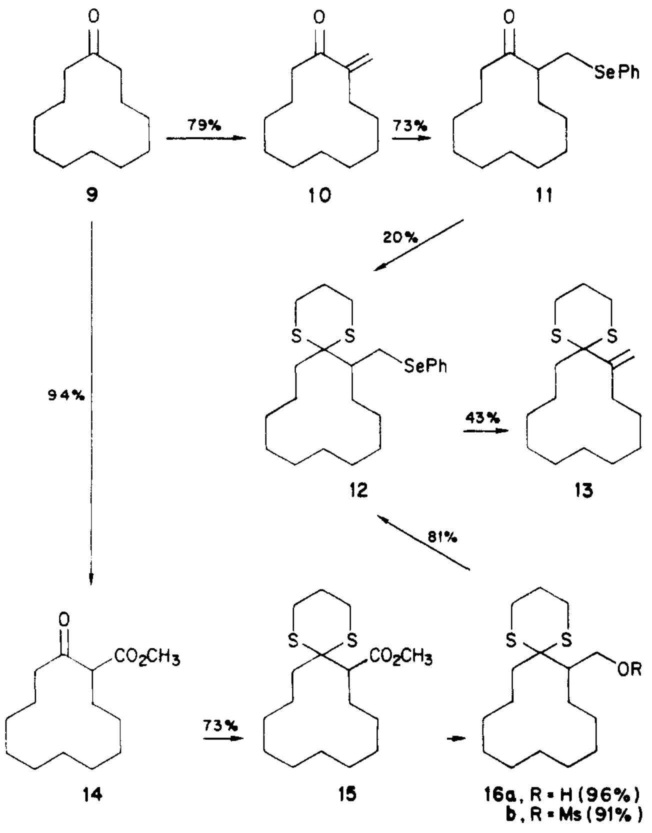
[7] (a) Vedejs, E.; Arco, M. J.; Renga, J. M. *Tetrahedron Lett.* **1978**, 523–526. (b) Vedejs, E.; Hagen, J. P. *J. Am. Chem. Soc.* **1975**, *97*, 6878–6880.

[8] Vedejs, E.; Arco, M. J.; Powell, D. W.; Renga, J. M.; Singer, S. P. *J. Org. Chem.* **1978**, *43*, 4831–4837.

[9] Doyle, M. P.; Griffin, J. H.; Chinn, M. S.; van Leusen, D. *J. Org. Chem.* **1984**, *49*, 1917–1925.

0022-3263/85/1950-2767$01.50/0

Scheme I



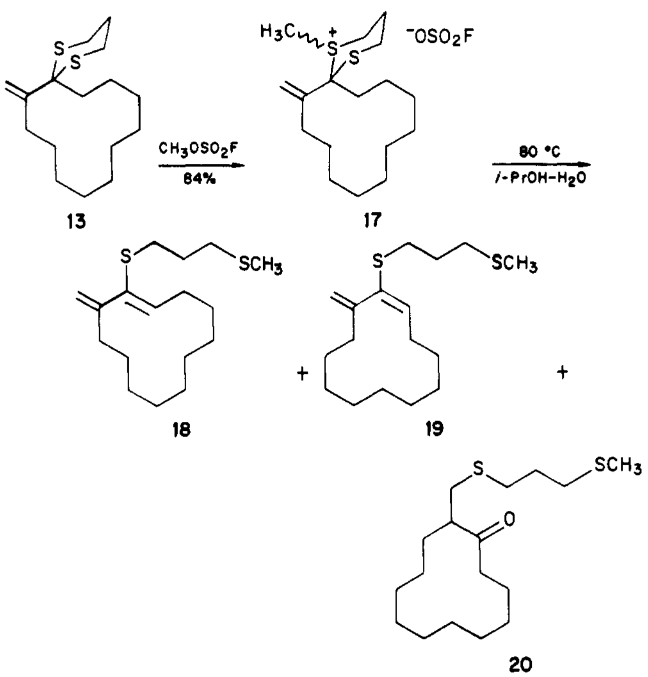
one with $m = 10$ and $n = 3$. Therefore spirocycle **13** became our immediate synthetic objective, and Scheme I displays two routes we developed. Both trails reached the target, but the longer one proved more practicable.

In the first sequence we converted cyclododecanone (**9**) to the 2-methylene ketone **10** by reported methods.[10-12] Next, we protected the exocyclic double bond by conversion to the phenyl selenide **11**, which displayed appropriate spectral characteristics. Treatment of **11** with 1,3-propanedithiol gave the selenide **12** but only in 20% yield.[13] This low yield prompted us to seek an alternative route to **12**. We succeeded through the sequence **9** → **14** → **15** → **16(a,b)** → **12** (Scheme I).

Ketone **9** gave the known[14] 2-methoxycarbonyl derivative **14** by condensation with dimethyl carbonate. With 1,3-propanedithiol, keto ester **14** afforded dithioketal **15**, characterized readily by NMR and analytical data. Reduction with $LiAlH_4$ produced alcohol **16a**, which was converted in turn to its mesylate **16b**. Action by sodium phenylselenate gave **12** identical with the material prepared earlier from **11**.

With a good route to **12** in hand, we next regenerated the exocyclic double bond by oxidative elimination (**12** → **13**). This task was not straightforward; examples of selective oxidation of selenides containing sulfur atoms are relatively sparse and not generally applicable.[15] Typical reagents (H_2O_2 or *m*-chloroperoxybenzoic acid)[16] proved nonselective. Ultimately we obtained an acceptable yield (43–50%) of olefin **13** by action of sodium metaperiodate[17] in dimethyl sulfoxide. The latter solvent proved critical since it dissolved enough of $NaIO_4$ and the selenide **12**. The derived spirocyclic olefin **13** displayed the expected two olefinic hydrogens (^1H NMR) and two olefinic carbons (^{13}C NMR) as well as a C=C stretch at 1625 cm^{-1}.

Scheme II



To set the stage for a [2,3]-sigmatropic rearrangement, we had to transform allyl dithiane **13** to a transient sulfonium ylide. We investigated two different general methods: (A) base treatment of a sulfonium salt; (B) carbenoid addition to sulfur. Each method had a different outcome, so we discuss them separately.

A. Base Treatment of a Sulfonium Salt. We first prepared the *S*-methyl sulfonium salt **17** from **13** by reaction with methyl fluorosulfonate (Scheme II). This methylation is expected to give a mixture of two diastereomers.[3] But the insolubility of **17** in common NMR solvents prevented us from confirming the presence of two epimers at sulfur.[18] On attempted recrystallization, sulfonium salt **17** decomposed. We examined the breakdown products and rationalized them readily in terms of structure **17**. Thus, in refluxing wet 2-propanol, **17** produced a mixture (ca. 1:1) of the conjugated dienes **18** and **19**, along with two minor byproducts, namely ketone **20** and an unidentified oil. Dienes **18** and **19** were not separated from each other, but as a pair they were purified and characterized. Our diene mixture showed two peaks (1:1)

---

(10) Valcavi, U. *Chim. At. Fr M* **1961** *100*; *Chem. Abstr.* **1963**, *58*, P10104*a*.

(11) Van Straten, J. W.; Van Norden, J. J.; Van Schaik, T. A. M.; Franke, G. Th.; De Wolf, W. H.; Bickelhaupt, F. *Recl. Trav. Chim. Pays-Bas* **1978**, *97*, 105–106.

(12) Gras, J. L. *Tetrahedron Lett.* **1978**, 2111–2114.

(13) We tried several other catalysts and reaction conditions (BF_3–CH_2Cl_2; *p*-TsOH-benzene; $AlCl_3$-benzene) but could not raise the yield. Typically, complex mixtures were obtained.

(14) (a) Torri, S.; Okamoto, T.; Ueno, N. *J. Chem. Soc., Chem. Commun.* **1978**, 239–294. (b) Rhoads, S. J.; Gilbert, J. C.; Decora, A. W.; Garland, J. R.; Spangler, R. J.; Urbigkit, M. J. *Tetrahedron* **1963**, *19*, 1625–1644.

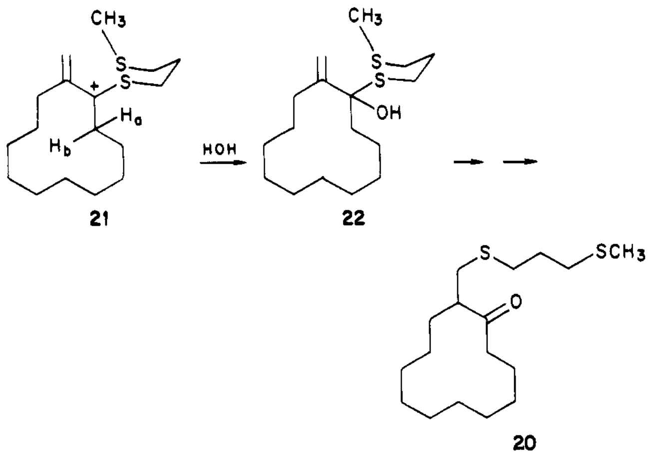
(15) (a) Nicolaou, K. C.; Lysenko, Z. *Tetrahedron Lett.* **1977**, 1257–1260. (b) Nicolaou, K. C.; Barnette, W. E.; Magolda, R. L. *J. Am. Chem. Soc.* **1981**, *103*, 3486–3497.

(16) (a) Jones, D. N.; Mundy, D.; Whitehouse, R. D. *J. Chem. Soc., Chem. Commun.* **1970**, 86–87. (b) Chan, T. H.; Finkenbine, J. R. *Tetrahedron Lett.* **1974**, 2091–2093. (c) Clive, D. L. J.; Denyer, C. V. *J. Chem. Soc., Chem. Commun.* **1973**, 253. (d) Van Ende, D.; Krief, A. *Tetrahedron Lett.* **1975**, 2709–2712. (e) Reich, H. J. *Acc. Chem. Res.* **1979**, *12*, 22–30. (f) Clark, R. D.; Heathcock, C. H. *J. Org. Chem.* **1976**, *41*, 1396–1402. (g) Sharpless, K. B.; Young, M. W. *J. Org. Chem.* **1975**, *40*, 947–949. (h) Grieco, P. A.; Masaki, Y.; Boxler, D. *J. Am. Chem. Soc.* **1975**, *97*, 1597–1599.

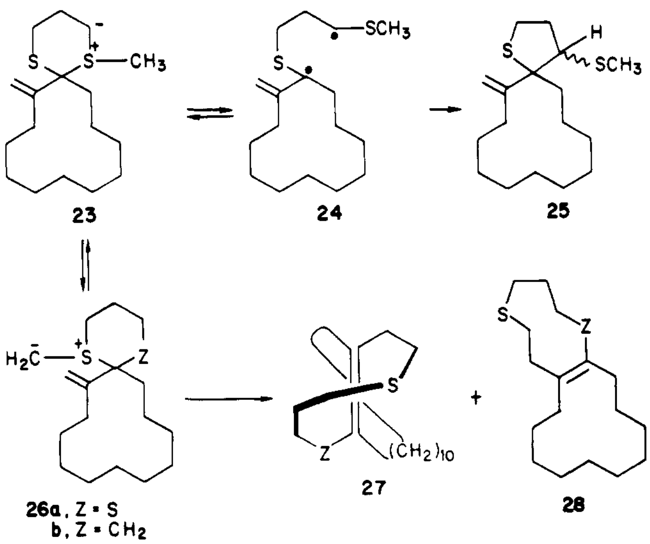
(17) Cinquini, M.; Colonna, S.; Giovini, R. *Chem. Ind.* (*London*) **1969**, 1737.

(18) Ceré, V.; Palucci, C.; Pollicino, S.; Sandri, E.; Fava, A. *J. Org. Chem.* **1978**, *43*, 4826–4831.

Scheme III



Scheme IV

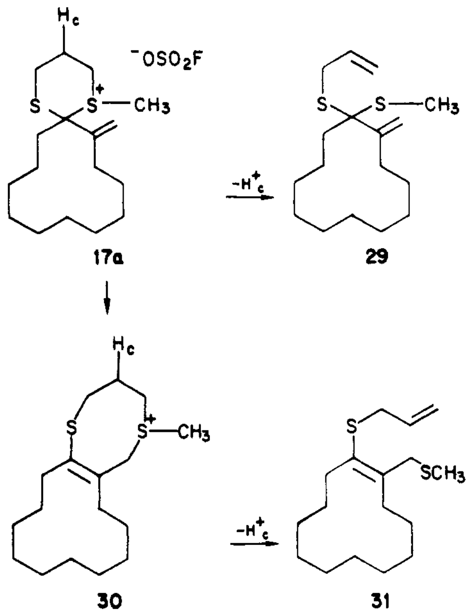


on GLC, absorbed at 260 nm, displayed an SCH_3 singlet, and exhibited ^1H and ^{13}C NMR bands typical of an exocyclic $C{=}CH_2$ and of a trisubstituted alkene. That we are dealing with an *E*–*Z* mixture was supported by the NMR details. For example, each isomer showed its own endocyclic vinyl hydrogen signal (triplet). And ^{13}C NMR revealed eight distinct olefinic carbons, i.e., four from each isomer.[19]

One of the minor byproducts was identified as **20** by elemental analyses and by spectral data. We did not pursue the other minor byproduct but did get it homogeneous and record some spectroscopic data.

Dienes **18** and **19** arise from elimination. For convenience, we may view it as an E1 process via allylic cation **21** followed by loss of H_a or H_b (Scheme III). Ketone **20** is also derivable from cation **21** if we invoke hydrolytic release of a thiol via **22** followed by conjugate addition to the derived enone. Several variants can of course be written, and we do not imply mechanistic veracity to the sequence shown. With sulfonium salt **17** in hand (presumed to be a mixture of diastereomers), we studied its reaction with four different bases, viz., KO-*t*-Bu, *n*-BuLi, DBU,[20] and *t*-BuLi. Each gave a different result and, importantly, none gave products from [2,3]-sigmatropic isomerization of transient ylides.

Scheme V



The first base, KO-*t*-Bu, transformed sulfonium salt **17** into the ring-contracted spiromolecule **25** (Scheme IV). Our structure proof rests on spectroscopic and elemental data. For example, ^1H NMR revealed two olefinic hydrogens and a sharp singlet typical of SCH_3. IR bands at 1635 and 905 cm^{-1} supported the presence of an exocyclic $C{=}CH_2$. Although structure **25** has two chiral centers and could exist as two diastereomers, the experimental data indicate that our compound is a pure, single epimer, but we cannot specify its configuration.

A reasonable path to **25** involves fleeting ylide **23**, homolytic ring scission to **24**, and reclosure to the five-membered cycle. The overall change is akin to a Stevens [1,2] rearrangement, a common fate for ylides derived from monosulfides.[21,22] That KO-*t*-Bu acted on **17** to bring about a [1,2] rather than a [2,3] net change is interesting, because one might expect a hydrogen on CH_3 to be the one most easily abstracted to generate ylide **26a**. This ylide could equilibrate with the other ylide **23**, but **26a** could also have undergone a [2,3]-sigmatropic change to **27a** + **28a** as well as [1,2]-type expansions to a seven-membered ring (not shown). Absence of the [2,3]-sigmatropic path is particularly notable here by contrast to behavior of the monosulfur analogue reported by the researchers in Italy.[3] They generated ylide **26b** by treating its corresponding sulfonium salt with KO-*t*-Bu under the same experimental conditions we used. Their molecule followed the [2,3]-sigmatropic path and gave a 1:1 mixture of **27b** and **28b** in high yield (90%). Evidently, in our dithioketal system **17**, the second sulfur either suppresses formation of the requisite ylide **26a** or diminishes its propensity for [2,3] reorganization. Thus we have before us a major difference between the mono- and disulfur systems.

With *n*-BuLi, sulfonium salt **17** gave the same [1,2]-shift product **25**. In this case we also isolated three minor constituents formed in about equal amounts. We have

---

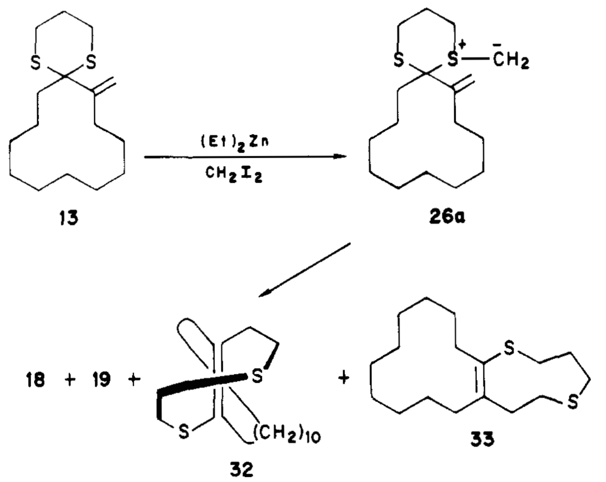
[19] We could not decide rigorously which of our two dienes corresponds to *trans*-alkene **18** and which to *cis*-alkene **19**. To simplify further discussion, we shall presume the isomer with the triplet at δ 6.05 is **18** and that at δ 5.75 is **19**. This choice is tentative and could be reversed.

[20] DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene.

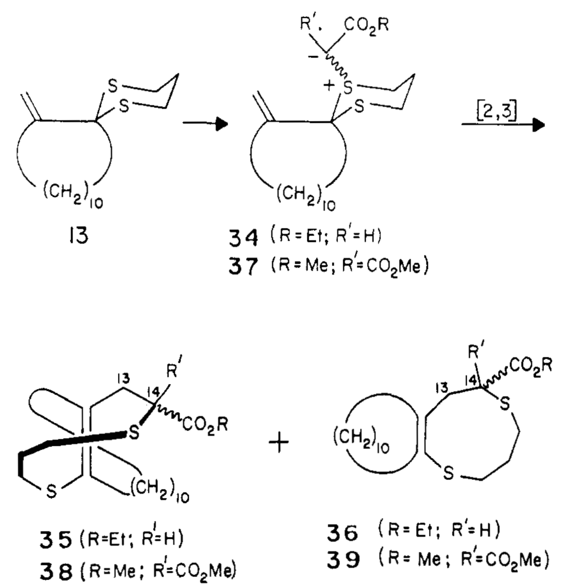
[21] (a) Ando, W. In "The Chemistry of Diazonium and Diazo Groups"; Patai, S., Ed.; Wiley: New York, 1978; Chapter 9, p 341. (b) Ando, W. *Acc. Chem. Res.* **1977**, *10*, 179–185.

[22] Both homolytic and heterolytic mechanisms have been invoked for Stevens rearrangements.[21] Also, see: (a) Jemison, R. W.; Laird, T.; Ollis, W. D.; Sutherland, I. O. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1436–1449, 1450–1457. (b) Doyle, M. P.; Tamblyn, W. H.; Bagheri, V. *J. Org. Chem.* **1981**, *46*, 5094–5102.

Scheme VI



Scheme VII



assigned tentative structures to two of them (**29** and **31**; Scheme V) based upon spectroscopic data (see Experimental Section), but we did not have enough material for full characterization.[23] In **17** (redrawn in Scheme V as **17a**), conventional elimination involving H_c could account for **29**. And **31** might arise by allylic isomerization of **17a** → **30** followed by elimination or perhaps from **29** by allylic shift. But in the main, *n*-BuLi does what KO-*t*-Bu did—promote [1,2] rather than [2,3] rearrangement.

A bulkier alkyllithium, namely *t*-BuLi, gave still different results with **17**. The products were **25**, dienes **18** + **19**,[19] and enone **10**. We presume the enone arose from unchanged sulfonium salt during hydrolytic workup. Thus, eliminations involving hydrogens in the carbocyclic ring vied with the Stevens-type [1,2] process, but again there was no indication of [2,3] ring growth.

The fourth base, DBU gave only dienes **18** + **19** (ratio 3:1). We obtained no evidence for either [1,2]- or [2,3]-type reactions. In summary, the results from the four bases acting on **17** reveal these notable features: (a) There were no [2,3]-type reactions, in marked contrast to known behavior of the corresponding monosulfur analogue.[3] (b) Products arose from eliminations and from [1,2] rearrangements of ylide **23** but not from ylide **26a**.

B. Carbenoid Additions to Sulfur.[21] This approach can produce ylide **26a** directly and so offers an opportunity to learn what fate it chooses. In one procedure we were guided by the recent work of Kosarych and Cohen, who generated the "carbenoid" CH_2 in *homogeneous* solution from diethylzinc and methylene iodide in benzene.[24,25]

The action of Et_2Zn–CH_2I_2 at 70 °C converted our key spiro bicycle **13** to four products and some intractable polymer (Scheme VI). Their adsorption behavior was very similar and required painstaking preparative thin-layer chromatography to separate them into three bands. One band consisted of dienes **18** + **19** (1:1 ratio), confirmed by spectral comparisons and by HPLC peak enhancements.[19]

The other two TLC bands were eluted individually and examined spectroscopically. Their ^{1}H NMR data (see Experimental Section) were consistent with structures **32** and **33**. These assignments are reasonable but not rigorous because all our efforts to obtain completely pure specimens were unsuccessful. Because the four products **18**, **19**, **32**, and **33** are so difficult to separate, this approach to **32** and **33** appeared impracticable for scale-up, unless **18** and **19** could be suppressed. Therefore we repeated the methylidenation of **13** at lower and higher temperatures.

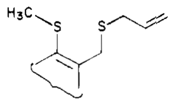
At room temperature we obtained only one product, diene **19**.[19,26] And at 110 °C we again found the four products (**18**, **19**, **32**, and **33**), but the proportion of **32** + **33** relative to **18** + **19** had increased, as judged by ^{1}H NMR. On the other hand, this high-temperature run gave a lower total yield (39%) and more insoluble polymer.

That monoalkenes **32** and **33** from ring growth were not produced at room temperature and only appeared at 70 °C or higher suggests that our dithioketal requires a greater activation energy for [2,3]-sigmatropic rearrangement (relative to competing reactions) than do allylic monosulfides.[24] Our experiments with the four bases discussed earlier were conducted at low temperatures, and no [2,3] process prevailed; yet the Sandri–Fava team observed it with their corresponding monosulfur systems.[3] We are inclined to think that for sulfur ylides generated with strong bases or by Cohen's "carbenoid" methylidenation, the second sulfur works against the [2,3] option.

A second avenue to sulfur ylides involves diazo esters as carbenoid precursors.[21] We generated ylide **34** by decomposing ethyl diazoacetate with $CuSO_4$ in the presence of dithioketal **13**. The reaction produced the ring-enlarged isomers **35** and **36** (total yield 58%) in a 4:1 ratio (Scheme VII). We separated the crystalline *Z*-isomer **36** from oily **35**, which itself consisted of two epimers at C14 ("major" and "minor") in a 3:1 ratio. These epimers behaved so similarly we were not able to separate them, so for C and H analyses we left them as a pair. The physical and chemical properties of **35** agreed with its betweenanene-type structure. For example, in the ^{1}H NMR scan of **35**

---

[23] For the compound we formulate as **31**, our NMR spectra do not rigorously exclude an alternative structure, namely i (*E* or *Z*), but we favor this less on mechanistic grounds.



i

[24] Kosarych, Z.; Cohen, T. *Tetrahedron Lett.* **1982**, *23*, 3019–3022.

[25] (a) Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron* **1968**, *24*, 53–58. (b) Nishimura, J.; Furukawa, J.; Kawabata, N.; Kitayama, M. *Tetrahedron* **1971**, *27*, 1799–1806. (c) Miyano, S.; Hashimoto, H. *J. Chem. Soc., Chem. Commun.* **1971**, 1418–1419.

[26] In separate controls we established that diene **19** was stable for 12 h at 80 °C in benzene and for 4 h at 80 °C in benzene containing diethylzinc. Therefore, it seems unlikely that the *E*–*Z* mixture of **18** + **19** obtained at 70 °C arises from isomerization after the fact. We conclude that elimination to give dienes is more stereoselective near 25 °C than at 70 °C.

the C14 methine H appears in *each* epimer as a doublet of doublets, centered at δ 3.5 (major epimer) and 3.3 (minor epimer). Molecular models indicate that rotation around the C13–C14 bond in **35** is difficult because of rigidity within the transoid nine-membered ring and because serious crowding occurs during such rotation. This situation would accentuate the diastereotopic difference between the two methylene hydrogens at C13 so that each of them splits the C14 methine H characteristically. In contrast, the heterocyclic loop in the corresponding *Z*-isomer **36** is more flexible, and its tertiary hydrogen at C14 appears as a pseudotriplet (centered at δ 4.0) because of similar averaged coupling with each C13 hydrogen.

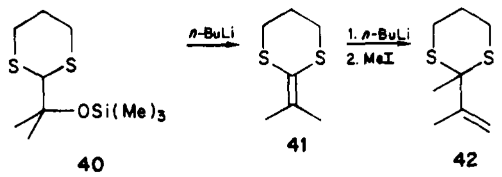
The ^{13}C NMR spectrum of the domed alkene **35** showed the two olefinic carbon signals farther apart (major epimer $\Delta\delta$ 10.8; minor epimer $\Delta\delta$ 8.2) than is the case for the nondomed isomer **36** ($\Delta\delta$ 7.7). Also, the aliphatic carbons as a bunch lie more downfield in **35** (δ 61.53–23.99) than in **36** (δ 61.16–22.15). Both these ^{13}C NMR trends have been noted before for trans–cis pairs of cycloalkenes[18,27-29a] including **27b** and **28b**.[3] However, we shall see later that $\Delta\delta$ for the alkene carbons is not reliable as a structural criterion for domed vs. nondomed pairs.

If the major and minor epimers of **35** enjoy the same olefin geometry and differ only in configuration at C14, they should interconvert through enolization. Indeed, when we treated **35** with NaOEt–EtOH, the initial epimer ratio (3:1) became a final ratio of 1:3, and no new products were produced. In contrast and in accord with our assignments, the *Z*-isomer **36** was unchanged even after prolonged exposure to the same alkaline conditions. Diastereoisomerism is not possible for this *Z* skeleton. These results also established two other facts. First, no $Z \rightleftharpoons E$ isomerization of the double bond took place under the alkaline conditions. Second, the initial 3:1 epimer ratio in **35** from the [2,3]-sigmatropic expansion is governed by kinetic factors and not by thermodynamic stabilities of the two epimers.

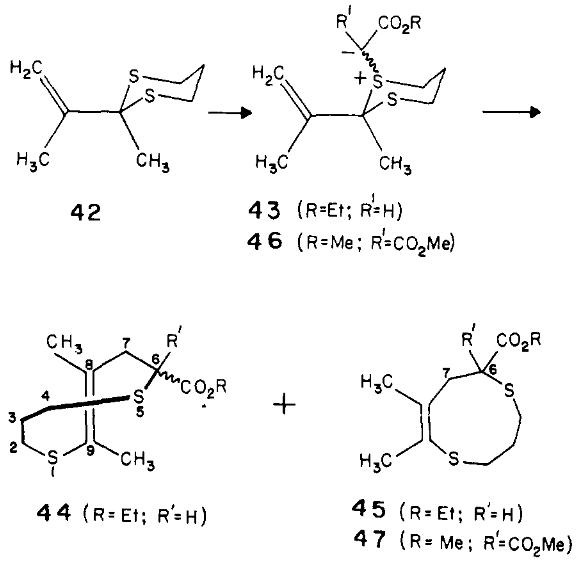
The bis-sulfur structure **35** represents the first case of a betweenanene having a heteroatom attached directly to the hidden double bond. Note that our [2,3] ring-enlargement step (**13** → **34** → **35** + **36**) favored the "transoid" domed product **35** over its "cis" counterpart **36** by a margin of 4:1. This ratio is decidedly more favorable than the 1:1 proportions observed by Sandri, Fava, and co-workers with the corresponding mono-sulfur analogue (i.e., **13** with CH_2 in place of one sulfur).[3] We used the same procedure as they did to generate the stabilized ylide, so the different stereoselectivity in the two systems must be attributed to the second sulfur in our molecule. Other examples are known where relatively minor structural changes markedly affected the olefin geometry in [2,3]-sigmatropic ring expansions.[3,6,29]

Owing to the chiral plane at the alkene unit in **35**, our use of ethyl diazoacetate as the carbenoid source added a second element of chirality, hence the two epimers at C14. To remove that influence, we examined dimethyl diazomalonate as a precursor. Its reaction with **13** gave only two products: the desired betweenanene **38** and its *Z*-counterpart **39** in a 5:1 ratio. They were separated and crystallized, and each was fully characterized spectrally and by elemental analyses. In **38** the two methoxycarbonyl groups are diastereomeric because of the olefin's chiral plane;[1,30] accordingly they exhibited distinct, sharp OCH_3 singlets in the ^1H NMR. In **39**, both ester functions are equivalent, and, in agreement, this isomer showed only one OCH_3 singlet. Likewise, by ^{13}C NMR, **38** was seen to have two different carbonyl carbons whereas **39** had but one. Also, in line with known trends for trans–cis pairs of cycloolefins, the aliphatic carbons in **38** collectively are more downfield (δ 64.56–23.93) than in the *Z*-isomer **39** (δ 61.58–21.80).[18,27-29] But, in contrast to expectations, the alkene carbon signals in **38** fall closer together ($\Delta\delta$ 4.1) than they do in **39** ($\Delta\delta$ 4.9). Consequently, this last spectroscopic criterion is fallible for distinguishing betweenanene and nonbetweenanene isomers.

Scheme VIII



Scheme IX



Finally, we correlated our two betweenanenes **38** and **35** chemically by treating **38** with NaOEt–EtOH. This base effected transesterification and concomitant retro-Claisen condensation to produce **35** as a mixture of the same two C14 epimers already in hand. And, in this experiment the major epimer:minor epimer ratio was virtually identical (1:3) with that obtained earlier by NaOEt equilibration of **35** through enolization.

Our results indicate that stabilized sulfur ylides generated from **13** by thermal decomposition of diazo esters with Cu(II) salts prefer [2,3]-sigmatropic ring expansion over [1,2] Stevens-type rearrangements or 1,2-eliminations. The question arises whether these findings apply to dithioketals in general or only to the specialized bicyclic spiro framework. Therefore, we pursued some parallel experiments with the simple monocyclic substrate **42**.

This compound is known, and we prepared it initially by a published sequence,[31] which did not prove satisfactory. We therefore developed a more efficient route (Scheme VIII). It involves three straightforward steps, proceeds in 92% overall yield, and is easily scaled-up. We

---

[27] Ceré, V.; Pollicino, S.; Sandri, E.; Fava, A. *J. Am. Chem. Soc.* **1978**, *100*, 1516–1520.

[28] Stothers, J. B. "Carbon-13 Nuclear Magnetic Resonance Spectroscopy"; Academic Press: New York, 1972; p 69.

[29] (a) Ceré, V.; Paolucci, C.; Pollicino, S.; Sandri, E.; Fava, A. *J. Org. Chem.* **1979**, *44*, 4128–4135. (b) Ceré, V.; Paolucci, C.; Pollicino, S.; Sandri, E.; Fava, A. *J. Org. Chem.* **1981**, *46*, 3315–3321.

[30] Marshall, J. A.; Flynn, K. E. *J. Am. Chem. Soc.* **1982**, *104*, 7430–7435.

[31] Seebach, D.; Kolb, M. *Justus Liebigs Ann. Chem.* **1977**, 811–829.

added acetone to 2-lithio-1,3-dithiane and directly quenched the intermediate lithium alcoholate with chlorotrimethylsilane.[32] The derived trimethylsilyl ether **40** was carried directly to 2-isopropylidene-1,3-dithiane (**41**) by reaction with *n*-BuLi–THF.[33] Finally, we converted **41** to **42** using a general methylation method.[36]

We treated dithioketal **42** with ethyl diazoacetate and $CuSO_4$ to generate the transient ylide **43** (Scheme IX). The product was a mixture of the dithiacyclononenes **44** and **45**. The ratio of *E* (**44**) to *Z* (**45**) was 4:1. We separated **45** from the (*E*)-olefin **44**, which consisted of a mixture of epimers at C6 in a ratio of 3:1 (major epimer:minor epimer). These epimers exist because of the chiral plane at the transoid dimethylcyclononene unit.[1] We tried in vain to separate these two epimers; so they were characterized as a pair. Spectral, analytical, and chemical properties supported our assigned structures for **44** and **45**.

In the ^1H NMR of **44** (epimeric mixture) the C6 hydrogen in *each* epimer appears as a doublet of doublets, owing to coupling with the adjacent diastereotopic hydrogens at C7. For the major *E* epimer, this pair of doublets centers at δ 3.5, whereas the minor *E* epimer shows the center at δ 3.3. By contrast, the methine H in the pure (*Z*)-olefin **45** is a pseudotriplet at δ 4.0. Evidently, in **45** the C6 H experiences similar averaged coupling with each C7 hydrogen as a result of conformational freedom in the cisoid nine-membered ring. (Recall analogous proton NMR differences exhibited by olefins **35** and **36**.)

Interestingly, in the ^{13}C NMR the (*E*)-alkenes **44** have their olefinic carbon signals further apart (viz., $\Delta\delta$ 13.90 major epimer, $\Delta\delta$ 9.58 minor epimer) than in the (*Z*)-alkene ($\Delta\delta$ 9.23). Also, the aliphatic carbons in (*E*)-**44** collectively fall further downfield (δ 61.52–23.43) than they do in the *Z*-isomer **45** (δ 61.25–18.83). So, in terms of their ^{13}C NMR, these monocyclic (*E*)- and (*Z*)-alkenes with two sulfurs follow the same trends observed with our bicyclic counterparts (**35** and **36**) and with mono-sulfur analogues.[18,27–29a]

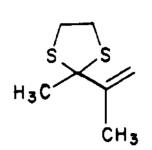
We confirmed our *E* and *Z* assignments for **44** and **45**, respectively, by enolization experiments with NaOEt–EtOH. At room temperature, the major and minor epimers of **44** interconverted; their relative proportions changed from an initial 3:1 to a final 1:3, and no new products were formed. By comparison, our *Z*-isomer **45** was stable to prolonged treatment with NaOEt as expected because diastereoisomerism is not possible.

At this point we call attention to the parallel in behavior between the simple monocyclic system (**42** → **44** + **45**) and the spiro bicyclic one (**13** → **35** + **36**). Both substrates, treated similarly produced (*E*)- and (*Z*)-olefins in a ratio of 4:1. Thus it appears that the two methyl groups in **42** and the large ring in **13** act comparably in their influence (if any) on generation and [2,3]-sigmatropic rearrangement of their corresponding stabilized ylides.[37]

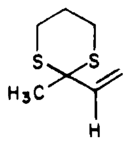
We also conducted ring expansion of **42** via ylide **46** generated in situ from Cu(II)-catalyzed decomposition of dimethyl diazomalonate. The product was the crystalline (*Z*)-alkene **47**; none of the related *E* isomer could be found. In **47** the magnetically equivalent H's at C7 showed up as a singlet (δ 1.6) as did the equivalent OCH_3 groups (δ 3.8), and ^{13}C NMR corroborated the presence of but one type of carbonyl carbon (single peak at δ 169.74). Chemical evidence supported the *Z* geometry. Thus, treatment of **47** with NaOEt-EtOH brought about ester exchange and also removed one CO_2CH_3 group (retro-Claisen condensation). We obtained a single product identical in all respects with (*Z*)-alkene **45** obtained from our other route.

It is worth noting that the transformation of **42** to (*Z*)-alkene **47** without forming an *E* isomer is the only instance in our study where a [2,3]-sigmatropic expansion did not produce both geometric isomers. The reasons for this outcome are not clear, but we refrain from speculation because the yield of **47** was low (36%) and the experimental procedure was not optimized.

We now draw attention to recent independent studies by Doyle and co-workers.[9] Among other things they treated allylic dithioketals with the "carbenoid" delivered in situ when ethyl diazoacetate is decomposed catalytically by $Rh_2(OAc)_4$. They examined **48** and **49**, which resemble closely our model compound **42**. Both of their substrates gave substantial [2,3]-type expansion (as well as some elimination). The heterocyclic cyclooctene ring obtained from **48** was entirely *Z*, and the cyclononene from **49** was an 8.3:1 mixture of *E–Z* isomers. In parallel with our own results with stabilized sulfur ylides, they also found no products from [1,2] Stevens-type processes.



48



49

Experimental Section[38]

General. Melting points and boiling points are uncorrected. NMR spectra refer to $CDCl_3$ solutions. Chemical shifts from 60-MHz spectra are subject to an uncertainty of δ 0.15 because that instrument often showed a drift. ^{13}C NMR were recorded at 20 MHz on a Varian Model CFT-20 or at 30 MHz on a Bruker Model WM-300 spectrometer with Fourier transform and with full proton broad-band noise decoupling. Carbon shifts are expressed relative to tetramethylsilane as δ 0. UV–vis spectra were obtained in anhydrous EtOH or heptane.

GLC refers to analytical gas chromatography with a Perkin-Elmer Model 900 instrument with a flame-ionization detector. To describe GLC conditions, we give the column name followed by temperature and pressure. For temperature programming T_i = initial isothermal time, and programming rate is given in °C/min. Retention times (T_R) are in minutes. The format is as follows: GLC [column name] (temperature, pressure, T_i, programming rate) T_R (integration). The following name code applies: CW 20M, 6 ft 15% Carbowax 20M on Chromosorb W-AW/DMCS, 60–80 mesh; OV 101, 6 ft 3% silicone OV-101 on Chromosorb W-HP, 80–100 mesh; SE-30, 9 ft 1.5% SE-30 on Chromosorb W-HMDS, 80–100 mesh; OV-17, 3 ft 3% OV-17 on Anakrom Q, 80–100 mesh; BBBT, 4 ft 2.5% BBBT on Chromosorb W-HP, 100–200 mesh.

High-pressure liquid chromatography (HPLC) was performed with a Perkin-Elmer liquid chromatograph Model 1220 equipped with a Perkin-Elmer UV detector Model LC-75. To describe HPLC conditions, we designate column, solvent(s), flow rate (mL/min), retention time (T_R) in minutes, integration values, and

---

(32) Chamchaang, W.; Prankprakma, V.; Tarnchompoo, B.; Thebtaranonth, C.; Thebtaranonth, Y. *Synthesis* **1982**, 579–580.

(33) The ketene dithioketal **41** has been prepared by others by less efficient ways.[34,35] It has also been methylated to **42**, but we found the published procedure difficult to reproduce.[31]

(34) Seebach, D.; Kolb, M.; Gröbel, B. T. *Chem. Ber.* **1973**, *106*, 2227–2290.

(35) Jones, P. F.; Lappert, M. F. *J. Chem. Soc., Chem. Commun.* **1972**, 526.

(36) Corey, E. J.; Kozikowski, A. P. *Tetrahedron Lett.* **1975**, 925–928.

(37) As has been suggested by Vedejs[8] and by Cerè et al.,[3] we presume ylides rearrange stereospecifically. On this basis, ylide **34** with an equatorial group on sulfur should give **35**, and the sulfur-axial ylide should lead to **36**. By the same token, equatorial **43** should produce **44**, and axial **43** would give **45**.

(38) For full details on drying solvents, purification of reagents, and modification of published procedures, see: Rodriguez, A. D. Ph.D. Dissertation, The Johns Hopkins University, 1983.

wavelength (λ) in nanometers (nm) as follows: HPLC [column code] (solvent; flow rate) T_R (integration), λ. The column codes are as follows: A, Altex Custom Packed Column/Base Spherisorb Function-CN, 4.6 mm × 25 cm, particle size 5 μm; B, Altex Ultrasphere-Si, 4.6 mm × 25 cm, particle size 5 μm; C, Altex Ultrasphere-ODS, 4.6 mm × 25 cm, particle size 5 μm.

TLC refers to analytical thin-layer chromatography on commercial silica gel GF (250 μm) or commercial alumina GF (250 μm). The term "homogeneous" indicates that under the given TLC conditions the component appeared as a single well-defined spot.

PTLC refers to preparative thin-layer chromatography on plates coated with commercial silica gel GF (2000 μm) or commercial alumina GF (1000 μm). MDPTLC refers to multiple-development preparative thin-layer chromatography conducted as follows: an initial solvent combination was found that gives an R_f value of 0.4–0.5 after one development. The relative proportion of the nonpolar partner in such solvent combination was then doubled, and the plate was developed three or four times, allowing it to dry partially, but not completely, after each development.[39]

Column chromatography was performed on Brinkmann silica gel 60, 70–230 mesh, or on Alumina Woelm N, Activity-I. J. T. Baker silica gel 60, 25–40 mesh, was used for flash chromatography. THF refers to tetrahydrofuran.

2-Methylenecyclododecanone (10). Method A. We first prepared 2-[(diethylamino)methyl]cyclododecanone by modifying the method of Valcavi,[10] mp 47–48 °C (lit.[11] mp 49 °C).

A solution of this Mannich base (2.00 g, 8.35 mmol) and iodomethane (1.91 g, 13.45 mmol) in ethyl acetate (15 mL) was refluxed 30 min. The collected precipitate was washed with small portions of ethyl acetate and was recrystallized from EtOH, mp 249 °C dec (2.95 g, 94%). No melting point or other properties for this methiodide salt were reported.[10,11]

A mixture of the methiodide (4.0 g, 10.5 mmol) and saturated aqueous $NaHCO_3$ solution (10 mL) in CH_3OH (40 mL) was stirred vigorously at 25 °C for 12 h, was diluted with aqueous 10% HCl at 0 °C (pH ~4), and was extracted with petroleum ether. The organic layer was washed with water, dried (Na_2SO_4), and evaporated in vacuo to leave a thick, transparent oil, which solidified at -10 °C. Enone **10** was recrystallized from CH_3OH-H_2O: mp 35 °C; yield 1.75 g, 86%; IR ($CHCl_3$) 1670 (s), 1625 (m), 1470 (s), 1445 (s), 1335 (m), 1288 (m), 935 (s) cm^{-1}; 80-MHz ^1H NMR δ 5.86 (s, 1 H), 5.70 (s, 1 H), 2.9–1.1 (m, 20 H); TLC (silica gel, benzene) [homogeneous]. Anal. Calcd for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.47; H, 11.42.

Method B. A solution of cyclododecanone (5.0 g, 0.027 mol), *s*-trioxane (7.3 g, 0.081 mol), and *N*-methylanilinium trifluoroacetate (15.0 g, 0.0678 mol, mp 65–66 °C; lit.[12] mp 66.5 °C) in dry dioxane (50 mL) was refluxed 3 h. The cooled mixture was diluted with ether, and the organic layer was washed successively with water, $NaHCO_3$ solution, and brine and was dried over Na_2SO_4. Evaporation in vacuo left an oil, which crystallized at −10 °C. Recrystallization from CH_3OH-H_2O gave white needles of pure **10** (4.20 g, 79%) as confirmed by IR, ^1H NMR, and TLC.

2-[(Phenylseleno)methyl]cyclododecanone (11). We were guided by a reported general procedure.[40] A stirred solution of diphenyl diselenide (0.41 g, 1.3 mmol) in ethanol (5 mL) was treated with small batches of sodium borohydride (0.10 g, 2.6 mmol). After 30 min the colorless solution was cooled to 0 °C, and glacial acetic acid (0.26 mL) was introduced. A solution of enone **10** (0.39 g, 2.0 mmol) in ethanol (2 mL) was added, and stirring was continued at 0 °C for 1 h then at 25 °C for another 2 h. The yellow turbid mixture was poured into ice-cold water (50 mL) and was extracted with ether (2 × 25 mL). The combined ether was washed with water, dried over Na_2SO_4, and concentrated in vacuo to leave a yellow oil (0.75 g). This oil was crystallized from a 1:9 mixture of benzene–CH_3OH and from a mixture of CH_3OH-H_2O: off-white needles, mp 46–47 °C; yield 0.50 g, 73%; IR ($CHCl_3$) 2765 (s), 1702 (s), 1470 (s), 1445 (s), 1268 (s), 1042 (s), 845 (s) cm^{-1}. 60-MHz ^1H NMR δ 7.62–7.20 (m, 5 H), 3.40–1.05 (m, 23 H). Anal. Calcd for $C_{19}H_{28}OSe$: C, 64.94; H, 8.03. Found: C, 65.15; H, 8.12.

7-[(Phenylseleno)methyl]-1,5-dithiaspiro[5.11]heptadecane (12). Method 1. A stirred 0 °C solution of phenylseleno ketone **11** (0.70 g, 1.99 mmol) and 1,3-propanedithiol (0.2 g, 2.6 mmol) in acetic acid (10 mL) was treated with boron trifluoride etherate (1.125 g, 7.92 mmol). The mixture was brought to room temperature and stirred 48 h. The solution was diluted with water (10 mL) and was extracted with ether (2 × 20 mL). The ether was washed in turn with water, 10% $NaHCO_3$ solution, and brine, was dried (Na_2SO_4), and was evaporated in vacuo. Chromatography of the oily residue on 50 g of silica gel (2% ether in hexane) gave a viscous oil (0.19 g, 20%). An analytical sample of **12** was prepared by recrystallizations from $CHCl_3$–EtOH: mp 60–60.5 °C; 80-MHz ^1H NMR δ 7.96–7.64 (m, 2 H), 7.65–7.28 (m, 3 H), 4.0–3.8 (dd, 1 H), 3.3–0.80 (m, 28 H); 20-MHz ^{13}C NMR δ 133.28, 128.79, 126.74, 59.61, 43.83, 33.42, 31.22, 26.65, 26.26, 25.87, 25.43, 25.08, 24.90, 23.02, 22.82, 22.69, 22.58, 22.57, 21.03; TLC (silica gel, 10% benzene in petroleum ether) [homogeneous]. Anal. Calcd for $C_{22}H_{34}S_2Se$: C, 59.87; H, 7.77. Found: C, 59.97; H, 7.88.

2-(Methoxycarbonyl)cyclododecanone (14). We modeled our procedure after that of Rhoads et al.[14b] The keto ester **14** was distilled: bp 119 °C (0.47 torr); yield 94%; IR ($CHCl_3$) 1735 (s), 1165 (br) cm^{-1}; 60-MHz ^1H NMR δ 3.65 (s, 3 H, CO_2CH_3), 2.85–2.50 (m, $O{=}CCH_2$), 1.3 (br s).

7-(Methoxycarbonyl)-1,5-dithiaspiro[5.11]heptadecane (15). Keto ester **14** (33.84 g, 0.14 mol) in a 3:1 mixture of acetic acid–THF (90 mL) cooled to 0 °C under argon was treated with 1,3-propanedithiol (15.24 g, 0.14 mol). Then boron trifluoride etherate (28.39 g, 0.20 mol) was slowly added. The solution was stirred at 0 °C for 2 h and then at room temperature for 48 h. During this time, a thick white slurry usually formed. The content was poured into an ice-cold mixture of water and ether. The organic layer was washed in turn with water, aqueous 10% $NaHCO_3$ solution to neutrality, and brine. The ethereal solution was dried over Na_2SO_4, filtered, and evaporated in vacuo at 60 °C for 4–5 h. The white solid **15** was recrystallized twice from heptane: mp 111–112 °C; yield 29.6 g, 73%; IR (KBr) 1730 (s), 1430 (br), 1160 (br) cm^{-1}; 80-MHz ^1H NMR δ 3.75 (s, 3 H, CO_2CH_3), 2.86 (br m, 5 H), 2.50–1.50 (br m, 6 H), 1.35 (br s, 16 H); 20-MHz ^{13}C NMR δ 172.89, 54.19, 51.26, 49.14, 33.08, 25.83, 25.19, 24.63, 22.95, 22.01, 20.76; TLC (silica gel, 6:1 petroleum ether–ether) [homogeneous]. Anal. Calcd for $C_{17}H_{30}O_2S_2$: C, 61.77; H, 9.15. Found: C, 61.92; H, 8.96.

7-(Hydroxymethyl)-1,5-dithiaspiro[5.11]heptadecane (16a). A solution of dithioketal ester **15** (55.45 g, 0.16 mol) in a 14:1 mixture of ether–THF (375 mL) was added slowly over a period of 1 h to a slurry of lithium aluminum hydride (12.71 g, 0.33 mol) in dry ether (450 mL). The mixture was stirred at room temperature for 6 h, and then the excess of $LiAlH_4$ was decomposed by addition of a 50% mixture of ethyl acetate–ether (100 mL) over a period of 30 min. Then the mixture was stirred with 10% HCl (300 mL) for 30 min and was poured into saturated $NaHCO_3$ (100 mL). The organic layer was washed with brine and was dried over Na_2SO_4. Evaporation in vacuo afforded **16a** as a white solid, which was recrystallized from heptane: yield 48.81 g, 96.2%; IR (KBr) 3540–3260 (br), 1430 (br), 1040 (br) cm^{-1}; 80-MHz ^1H NMR δ 3.98 (br s, 2 H, CH_2OH), 3.5–2.5 (br m, 5 H), 2.0 (br m, 5 H), 1.37 (br s, 18 H); 20-MHz ^{13}C NMR δ 62.17, 58.02, 43.92, 33.11, 26.22, 25.54, 25.13, 24.42, 22.85, 22.52, 22.37, 22.20, 20.87, 20.56; TLC (silica gel, 6:1 petroleum ether–ether) [homogeneous]. Anal. Calcd for $C_{16}H_{30}OS_2$: C, 63.52; H, 10.00. Found: C, 63.68; H, 9.76.

7-[((Methylsulfonyl)oxy)methyl]-1,5-dithiaspiro[5.11]heptadecane (16b). A 0 °C solution of dithioketal alcohol **16a** (24.46 g, 0.08 mol) in dry pyridine (100 mL) under nitrogen was treated slowly with methanesulfonyl chloride (10.36 g, 0.09 mol) and stirred for 2 h, during which the ice used for cooling melted. Vigorous stirring was continued at room temperature for 4 h. The mixture was poured into an ice-cold mixture of water and CH_2Cl_2, and the organic layer was washed successively with 10% HCl (2 × 100 mL), saturated $NaHCO_3$ solution (2 × 50 mL), water, and brine and was dried over Na_2SO_4. Evaporation of the solvent in vacuo gave the mesylate **16b**, which was recrystallized twice from ethanol; mp 103–104 °C; yield 28 g, 91%; 80-MHz ^1H NMR δ 4.90 (dd, 1 H), 4.30 (dd, 1 H), 3.08 (s, 3 H, SO_2CH_3), 2.76 (m, 4 H, SCH_2), 2.0 (br m, 5 H), 1.39 (br s, 18 H); 20-MHz ^{13}C NMR δ 72.36, 57.63, 42.44, 37.29, 33.28, 26.29, 26.02, 25.71, 25.40, 25.01, 24.78,

---

[39] Loewenthal, H. J. E. "Guide for the Perplexed Organic Experimentalist"; Heyden & Son: Philadelphia, 1978; pp 93–94.

[40] Miyashita, M.; Yoshikoshi, A. *Synthesis* **1980**, 664–666.

23.70, 23.18, 22.76, 22.52, 20.95; TLC (silica gel, benzene) [homogeneous]. Anal. Calcd for $C_{17}H_{32}O_3S_3$: C, 53.64; H, 8.47. Found: C, 53.57; H, 8.70.

7-[(Phenylseleno)methyl]-1,5-dithiaspiro[5.11]heptadecane (12). Method 2. To a solution of diphenyl diselenide (2.04 g, 6.5 mol) in dry dimethyl sulfoxide (15 mL) was added slowly and in small batches $NaBH_4$ (0.5 g, 13.22 mmol) until the yellow color was discharged completely. (**Caution**! This is a *highly exothermic* reaction with constant evolution of flammable H_2 gas.) A solution of dithioketal mesylate **16b** (3.8 g, 10 mmol) in dry dimethyl sulfoxide (10 mL) was added over a period of 5 min. The resulting solution was heated slowly to 110–120 °C under argon, and stirring was continued another 6 h. The cooled mixture (25 °C) was poured into crushed ice and was extracted with ether, which was washed with water and dried over Na_2SO_4. Concentration in vacuo left a red oily residue, which was purified by flash chromatography on 75 g of silica gel. Elution with petroleum ether first gave starting diphenyl diselenide. Subsequent elution with 10% benzene in petroleum ether gave the TLC-pure phenyl selenide **12** (3.5 g, 81%), identical in all respects (IR, ^1H NMR, TLC) with the sample obtained by method 1.

7-Methylene-1,5-dithiaspiro[5.11]heptadecane (13). A solution of phenylseleno dithiane **12** (43 g, 97.38 mmol) in dry dimethyl sulfoxide (600 mL) was treated with powdered $NaIO_4$ (48 g, 224 mmol) in three batches of 16 g each over a period of 6.5 h. The resulting solution was stirred at room temperature for 3 days, during which a thick, orange slurry formed. The mixture was poured into ice-cold water and was extracted with ether (4 × 400 mL). The ether was washed successively with aqueous 10% $NaHSO_3$ solution (2 × 200 mL), water, and brine, was dried (Na_2SO_4), and was evaporated in vacuo. The brownish solid was recrystallized from ethanol: off-white crystals, mp 107–107.5 °C; yield 12 g, 43%; IR ($CHCl_3$) 1625 (w), 1465 (m), 910 (m) cm^{-1}; 80-MHz ^1H NMR δ 5.75 (m, 1 H), 5.40 (m, 1 H), 2.65 (m, 4 H, SCH_2), 2.4–1.28 (m, 22 H); 20-MHz ^{13}C NMR δ 143.53, 116.91, 60.32, 36.90, 27.53, 26.38, 26.00, 25.57, 25.12, 23.21, 22.57, 22.19, 21.89, 19.03; TLC (silica gel, 3:2 petroleum ether–benzene) [homogeneous]. Anal. Calcd for $C_{16}H_{28}S_2$: C, 67.54; H, 9.92. Found: C, 67.48; H, 9.90.

1-Methyl-7-methylene-1-thionia-5-thiaspiro[5.11]heptadecane Fluorosulfonate (17). A mixture of spiro olefin **13** (0.727 g, 2.55 mmol) and methyl fluorosulfonate (0.29 g, 2.55 mol) in dry CH_2Cl_2 (15 mL) at 0 °C under argon was stirred vigorously for 4 h, during which a white precipitate formed. After addition of petroleum ether (25 mL) the mixture was cooled to −10 °C for 8 h and was filtered with suction, and the white solid was rinsed abundantly with cold 50% CH_2Cl_2–petroleum ether (60 mL). The product (0.851 g, 83.6%) was dried under vacuum at 25 °C overnight: mp 110–112 °C dec (it decomposed on attempted recrystallization so we used it without further purification); IR (KBr) 3025 (m), 1610 (w), 1465 (s), 1440 (s), 1420 (s), 1410 (s), 1320–1200 (br), 1065 (s), 710 (br), 575 (s) cm^{-1}; TLC (silica gel, benzene) [homogeneous].

Thermal Decomposition of Sulfonium Salt 17. Formation of (*E*)- and (*Z*)-3-(Methylthio)propyl 3-Methylene-1-cyclododecen-2-yl Sulfides (18 and 19) and 3-(Methylthio)propyl (2-Oxocyclododecyl)methyl Sulfide (20). A suspension of sulfonium salt **17** (0.85 g, 2.13 mmol) in commercial 2-propanol (70 mL) was heated at 80 °C for 15 min. The white slurry was cooled at 0 °C for 4 h and filtered, and the filtrate was evaporated in vacuo to leave a brown, acrid-smelling oil. It was purified by chromatography on 40 g of silica gel (benzene) to give first a mixture of dienes **18** and **19** in about 1:1 ratio: IR (neat) 3070 (w), 1620 (m), 1465 (s), 1445 (s), 1260 (m), 1250 (m), 905 (s) cm^{-1}; UV (EtOH) λ_{max} 260 nm; 80-MHz ^1H NMR δ 6.05 (t), 5.75 (t), 4.95 (m, 2 H), 2.5 (m, 8 H), 2.05 (s, 3 H), 1.25 (br s, 16 H); 20-MHz ^{13}C NMR δ 150.35, 144.39, 137.32, 136.52, 136.09, 135.62, 117.70, 114.27, 34.26, 33.64, 33.06, 32.99, 31.31, 30.98, 30.33, 29.80 (the remaining resonances appeared between δ 29.53 and 15.57); GLC [OV-17] (150–300 °C, 30 psi, T_i = 2 min, 10 °C/min) T_R = 8.4 and 8.7 min; TLC (silica gel, benzene) [homogeneous]. Anal. Calcd for $C_{17}H_{30}S_2$: C, 68.39; H, 10.13. Found: C, 68.59; H, 10.27.

Further elution gave a TLC-pure colorless oil, which showed a very simple ^1H NMR spectrum with absorptions at δ 3.6 (s, 1 H), 2.6 (m, 7 H), 2.05 (s, 3 H), and 1.35 (br s, 12 H) and also a simple IR spectrum with absorptions at 2920 (s), 2850 (s), 1470 (s), 1440 (s), 1250 (br), and 760 (s) cm^{-1}. This compound was not further characterized.

The material eluted last consisted of a pale yellow oil identified as ketone **20**: IR (neat) 1705 (s), 1470 (s), 1440 (s), 1365 (m), 1250 (m), 730 (m) cm^{-1}; 80-MHz ^1H NMR δ 2.6 (m, 9 H), 2.05 (s, 3 H), 1.75 (m, 6 H), 1.28 (br s, 14 H); TLC (silica gel, benzene) [homogeneous]. Anal. Calcd for $C_{17}H_{32}OS_2$: C, 64.50; H, 10.19. Found: C, 64.47; H, 10.21. Although accurate yields were not obtained, we estimate the product ratio **18** + **19**:unknown:**20** to be roughly 70:10:20.

Reaction of Sulfonium Salt 17 with Potassium *tert*-Butoxide. Formation of 4-(Methylthio)-6-methylene-1-thiaspiro[4.11]hexadecane (25). A mixture of sulfonium salt **17** (0.208 g, 0.52 mmol) and potassium *tert*-butoxide (0.088 g, 0.78 mmol, 1.5 equiv) in a 10:1 mixture of THF–*t*-BuOH (11 mL) under argon was stirred vigorously at −40 °C for 4 h. The mixture was poured into water and was extracted with pentane (3 × 40 mL). The pentane was washed with water and brine, was dried over Na_2SO_4, and was evaporated in vacuo. Purification by PTLC (silica gel, benzene) gave a GLC-pure, white solid (0.117 g, 75.5%), which was crystallized from acetonitrile, mp 83.5–84.5 °C. This ring-contracted olefin **25** could in principle exist as a mixture of diastereoisomers: IR ($CHCl_3$) 3080 (w), 2980 (m), 1635 (w), 1470 (m), 1440 (m), 1275 (m), 905 (m) cm^{-1}; 60-MHz ^1H NMR δ 5.4 (br s, 1 H), 5.1 (br s, 1 H), 3.2 (m, 3 H), 2.8–2.2 (m, 4 H), 2.10 (s, 3 H), 1.8–1.2 (br s, 18 H); GLC [OV-17] (150–300 °C, 30 psi, T_i = 2 min, 10 °C/min) T_R = 9.5 min; TLC (silica gel, benzene) [homogeneous]. Anal. Calcd for $C_{17}H_{30}S_2$: C, 68.39; H, 10.13. Found: C, 68.22; H, 9.90.

Reaction of 17 with *n*-Butyllithium. Formation of 2-Methylene-1-(3-propenylthio)-1-(methylthio)cyclododecane (29) and 1-(3-Propenylthio)-2-[(methylthio)methyl]cyclododecene (31). A suspension of sulfonium salt **17** (0.52 g, 1.33 mmol) in dry THF (50 mL) under argon at −45 °C was treated with 1.5 equiv of 2.5 M *n*-butyllithium in hexane (0.80 mL, 2 mmol) and was stirred vigorously for 3 h. The mixture was poured into water and was extracted with pentane. The combined organic layer was washed with water and brine and was dried over Na_2SO_4. Evaporation in vacuo followed by chromatography of the oily residue (0.34 g) on 20 g of silica gel (15:1 petroleum ether–ether) first eluted a colorless nonpolar oil (25 mg, 7.2%). This oil consisted of three components of about equal abundance, and these were separated by PTLC (silica gel, 3:1 petroleum ether–ether) and analyzed by IR and ^1H NMR. The first component was identified as thioketal **29** on the basis of its spectroscopic properties: IR (neat) 3080 (w), 1635 (m), 1470 (s), 1445 (m), 990 (m), 920 (s), 730 (w) cm^{-1}; 80-MHz ^1H NMR δ 6.05–5.5 (m, 1 H), 5.05 (m, 4 H), 3.2 (dd, 2 H), 2.25 (m, 4 H), 2.0 (s, 3 H), 1.35 (br s, 16 H); TLC (silica gel, 3:1 petroleum ether–benzene) [homogeneous].

The second component is tentatively assigned structure **31** also on the basis of spectroscopy:[23] IR (neat) 3080 (w), 1635 (m), 1470 (s), 1445 (s), 1225 (m), 990 (m), 920 (s), 730 (w) cm^{-1}; 80-MHz ^1H NMR δ 6.05–5.5 (m, 1 H), 5.05 (m, 2 H), 3.6 (s, 2 H), 3.25 (dd, 2 H), 2.35 (m, 4 H), 2.05 (s, 3 H), 1.35 (br s, 16 H); TLC (silica gel, 3:1 petroleum ether–benzene) [homogeneous].

The ^1H NMR spectrum of the third component showed δ 5.3 (s, olefinic), 5.15 (s, olefinic), 3.5–2.5 (m), 2.5–1.5 (m), and 1.3 (br s). IR 3100 (w), 2940 (s), 2920 (s), 2860 (s), 1630 (w), 1470 (s), 1445 (s), 1410 (s), and 900 (s) cm^{-1}. We did not identify this component.

The material eluted second (0.30 g, 77%) was a GLC-pure solid, which was recrystallized from acetonitrile, mp 83–84 °C. It proved to be spiro olefin **25** by IR, ^1H NMR, GLC, and mixture melting point.

Reaction of 17 with *tert*-Butyllithium. A suspension of sulfonium salt **17** (0.10 g, 0.25 mmol) in dry THF (5 mL) at −65 °C under argon was treated with 1.68 equiv of 2.1 M *tert*-butyllithium in pentane (0.20 mL, 0.42 mmol) for 9 h with vigorous stirring. The mixture was poured into water and was extracted with pentane (3 × 40 mL). The combined pentane extract was washed with water and brine, dried (Na_2SO_4), and evaporated in vacuo. Purification of the residue by PTLC (silica gel, benzene) gave four bands, which were isolated and individually analyzed by ^1H NMR, IR, TLC, and GLC. The major product (25 mg, 33%) was **10**. The next two products were dienes **18** and **19** (20 mg, 26%) in a ratio 1:3.3 and together constituted the second major component from the reaction.[19] The fourth product was spiro olefin **25** (16 mg, 21%).

Reaction of 17 with DBU.[20] A suspension of sulfonium salt **17** (0.10 g, 0.25 mmol) in dry CH_3CN (5 mL) under argon at 0 °C was treated with DBU (56.3 mg, 0.37 mmol) and was stirred vigorously for 14 h while the temperature was allowed to rise to 25 °C. The mixture was poured into water and extracted with pentane (3 × 30 mL). The extract was washed with water and brine, was dried over Na_2SO_4, and was evaporated in vacuo. Purification of the residue by PTLC (silica gel, toluene) gave a colorless oil (50 mg, 66%), which proved to be a 3:1 mixture of dienes **18** and **19** by IR, ^1H NMR, TLC, and GLC.[19]

Homogeneous Simmons–Smith Reaction with 13. A. At 70 °C. We modified the general procedure of Kosarych and Cohen.[24] A toluene solution of diethylzinc (0.105 g, 0.85 mmol),[41] spiro olefin **13** (0.20 g, 0.70 mmol), and diiodomethane (0.50 g, 1.86 mmol) in dry benzene (15 mL) under argon was heated at 70 °C for 4 h. The cooled solution (25 °C) was quenched with acetaldehyde (3 mL), was stirred for 15 min, was poured into saturated NH_4Cl solution (40 mL), and was extracted with ether. The ether was washed with water and brine, was dried over Na_2SO_4, and was concentrated in vacuo, first with a water aspirator and then with a mechanical pump, to remove residual diiodomethane and toluene. A small portion of the crude residue purified by MDPTLC (silica gel, 20:1 petroleum ether–ether) gave three fairly well separated bands. The first band (highest R_f) was identified as a 1:1 mixture of dienes **18** and **19** by ^1H NMR, IR, and HPLC (peak enhancement).[19] The second and third bands were also isolated and examined individually. They gave very similar IR spectra, and ^1H NMR showed no olefin H's as expected for **32** and **33**. *Each* showed the following characteristics: IR (neat) 1460 (s), 1445 (s), 1260 (m), 1225 (m), 845 (w), 760 (m) cm^{-1}; 80-MHz ^1H NMR δ 3.0–1.8 (br m, 14 H), 1.25 (br s, 16 H); TLC (silica gel, 20:1 petroleum ether–ether) [homogeneous]; HPLC [C] (heptane; 1.0) T_R = 2.7 min, λ = 260 nm.

B. At Room Temperature. The reaction of **13** with diethylzinc and diiodomethane was conducted in benzene at 23–24 °C. After 2.5 h with vigorous stirring, the solution was quenched and processed as in part A. The sole product was identified as diene **19** (77%) by IR, ^1H NMR, and HPLC.[19]

C. At 110 °C. The mixture was stirred efficiently at 110 °C for 1.5 h and processed as in part A. Analysis of the four products (39%) showed that the proportion of dienes **18** + **19** had diminished and that of **32** + **33** had increased relative to the outcome in part A. The higher temperature also produced more insoluble polymer.

Thermal Stability of Diene 19.[19] A vigorously stirred solution of pure diene **19** (0.043 g, 0.14 mmol) in dry benzene (5 mL) was heated to 80 °C for 12 h. The solution was cooled, and the solvent was evaporated in vacuo. The residue was identified as starting diene by ^1H NMR, IR, and GLC. The oil was redissolved in dry benzene (5 mL), and the solution was closed off under argon. Diethylzinc (0.035 g, 0.28 mmol) was added, and the temperature was raised to 80 °C. After being stirred for 4 h, the cooled solution was poured into water and worked up conventionally with ether. The derived oil proved to be starting material by ^1H NMR, IR, and GLC. A small amount of insoluble polymer was also formed.

Reaction of 13 with Ethyl Diazoacetate. Formation of (*E*)-14-(Ethoxycarbonyl)-15,19-dithiabicyclo[10.7.0]nonadec-1(12)-ene (35; Two Epimers) and (*Z*)-14-(Ethoxycarbonyl)-15,19-dithiabicyclo[10.7.0]nonadec-1(12)-ene (36). A mixture of spiro sulfide **13** (2.06 g, 7.25 mmol) in dry benzene (30 mL), anhydrous copper(II) sulfate (0.4 g, 2.50 mmol), and ethyl diazoacetate (2.05 g, 18 mmol) was stirred under argon for 5 min. The temperature was increased slowly, and the mixture was maintained at 55–60 °C and vigorously stirred for 2 h. (**Caution**! Intense evolution of nitrogen gas started around 40 °C.) The solution was cooled, was diluted with benzene (30 mL), was washed with water and brine, was dried (Na_2SO_4), and was evaporated in vacuo. Chromatography of the oily residue on 120 g of silica gel (benzene) first eluted starting spiro sulfide **13** (0.43 g, 21%) and then a product (1.54 g, 57.5%) that consisted of a mixture of the three isomeric olefins **36** and **35** (both epimers). The ^1H NMR absorption of the CH_2 in the ethyl group appeared at three closely spaced quartets around δ 4.2, suggesting three isomers. This view was confirmed by ^{13}C NMR, which showed six olefinic carbon singlets and three carbonyl carbons. Relative intensities were roughly in a 1:1:3 ratio for the components: IR (neat) 1735 (br), 1460 (s), 1445 (s), 1285 (br), 1160 (br), 1040 (s), 760 (br) cm^{-1}; UV (EtOH) λ_{max} 260, 324 nm; 80-MHz ^1H NMR δ 4.2 (q, 2 H, OCH_2CH_3), 3.6–1.7 (br m, 13 H), 1.7–0.75 (br m, 19 H); 20-MHz ^{13}C NMR δ 172.50, 172.00, 171.82, 144.63, 143.71,143.16, 133.79, 135.54, 135.47, 61.18, 60.89, 51.27, 50.83, 43.55, 38.97, 36.96, 36.63, 35.91, 35.07, 33.25, 32.43, 32.21, 31.56, 31.26 (the remaining resonances fell between δ 29.25 and 14.05); GLC [BBBT] (250 °C, 30 psi) T_R = 20.92 and 30.10 min; HPLC [A] (10:1 heptane–CH_2Cl_2; 2.0) T_R = 6.6 (20%) and 8.8 min (80%), λ = 260 nm; TLC (alumina, 6:1 petroleum ether–ether) R_f 0.68 (minor), 0.60 (major), and 0.55 (minor).

Separation of (*Z*)-Olefin 36 from the Epimeric Mixture of (*E*)-Olefins 35 by MDPTLC. A batch of 325 mg of the mixture of *Z* and *E* sulfide monoesters was divided into four and was loaded and developed on four silica gel plates (12:1 petroleum ether–ether). After one development, the plates were carefully dried and then were multiply developed six times (24:1 petroleum ether–ether). In each plate two well-separated bands were obtained. The fast-moving band [(*Z*)-olefin **36**] was isolated, washed abundantly with CH_2Cl_2, and filtered, and the solvent was evaporated in vacuo to give 65 mg (20%) of a white solid, which was recrystallized from EtOH; beautiful crystals, mp 115–116 °C; IR (CCl_4) 1725 (s), 1465 (m), 1445 (m), 1280 (br), 1160 (br) cm^{-1}; 300-MHz ^1H NMR δ 4.2 (q, 2 H, OCH_2CH_3), 4.0 (t, 1 H, $CHCO_2Et$), 3.3–1.9 (br m, 12 H), 1.9–1.1 (br m, 19 H); 20-MHz ^{13}C NMR δ 172.84, 143.16, 135.47, 61.16, 43.74, 33.43, 31.57, 31.15, 27.64, 27.10, 26.64, 26.08, 25.94, 25.79, 25.55, 24.92, 24.25, 24.03, 23.66, 23.35, 22.15, 14.25; GLC [BBBT] (250 °C, 30 psi) T_R = 29.82 min; HPLC [B] (50% $CHCl_3$–heptane; 2.0) T_R = 1.75 min, λ = 260 nm; TLC (alumina, 6:1 petroleum ether–ether) R_f 0.68 [homogeneous]. Anal. Calcd for $C_{20}H_{34}O_2S_2$: C, 64.82; H, 9.25. Found: C, 64.72; H, 9.23.

The slow-moving band (mixture of epimers of **35**) was isolated, washed abundantly with CH_2Cl_2 and filtered. Evaporation of the solvent in vacuo left a colorless oil (263 mg, 80.8%): IR (CCl_4) 1730 (br), 1445 (m), 1250 (br), 1150 (br), 1040 (m) cm^{-1}; 300-MHz ^1H NMR δ 4.2 (2 closely spaced q, 2 H, OCH_2CH_3), 3.5 (dd, 1 H, $CHCO_2Et$), 3.3–1.8 (br m, includes the methine H of the minor *E* epimer at δ 3.3, 12 H), 1.7–0.9 (br m, 19 H); 20-MHz ^{13}C NMR δ 172.42, 172.23, 144.63, 143.71, 135.54, 133.79, 61.53, 51.54, 51.12, 39.25, 37.21, 36.91, 36.18, 35.32, 32.68, 32.47, 31.44, 29.43, 27.25, 27.01, 26.65, 26.47, 26.05, 25.84, 25.34, 25.06, 24.95, 24.68, 24.32, 23.99, 14.25 (the relative intensities of the four olefinic carbon singlets were roughly in a 3:1:1:3 ratio, and those of the two carbonyl carbon singlets were 1:3); GLC [BBBT] (250 °C, 30 psi) T_R = 21.06 min; HPLC [B] (50% $CHCl_3$–heptane; 2.0) T_R = 1.75 min, λ = 260 nm; TLC (alumina, 6:1 petroleum ether–ether) R_f 0.60 (major) and 0.55 (minor). Anal. Calcd for $C_{20}H_{34}O_2S_2$: C, 64.82; H, 9.25. Found: C, 64.71; H, 9.28.

Equilibration of the (*E*)-Alkene Epimers 35 with NaOEt. A solution of the pure *mixture* of *E* isomers of **35** (ratio is roughly 3:1, but we do not know which isomer is which) (50 mg, 0.13 mmol) in absolute EtOH (2 mL) was treated with NaOEt (17 mg, 0.25 mmol) and stirred vigorously at room temperature for 48 h. The solvent was evaporated in vacuo, and the residue was taken up in ether and then poured into a mixture of brine and ether. The organic layer was passed through a short column of anhydrous Na_2SO_4 and was evaporated in vacuo. The residue was analyzed by ^1H NMR, GLC, and TLC. Only the original two components were present, but their relative intensities had changed from 3:1 to 1:3.

Stability of (*Z*)-Alkene 36 to NaOEt. A solution of pure (*Z*)-alkene **36** (25 mg, 0.06 mmol) in absolute EtOH (2 mL) was treated with NaOEt (9 mg, 0.13 mmol) and stirred at room temperature for 48 h. The solvent was evaporated in vacuo, and the concentrate was worked up conventionally with ether. The ^1H NMR, GLC, and TLC of the residue were identical with those of the starting material. None of the (*E*)-olefin epimers **35** formed during the treatment.

---

[41] Diethylzinc was a 15% solution in toluene supplied by the Aldrich Chemical Co.

Reaction of 13 with Dimethyl Diazomalonate. A mixture of spiro olefin **13** (0.65 g, 2.3 mmol), anhydrous copper(II) sulfate (108 mg, 0.67 mmol), and dimethyl diazomalonate (0.51 g, 3.22 mmol)[42] in dry toluene (8 mL) was heated slowly to 100–110 °C under argon for 24 h. The cooled solution (25 °C) was diluted with benzene (10 mL) and was poured into a mixture of water and benzene. The organic layer was separated, washed with water and brine, dried (Na_2SO_4), and evaporated in vacuo. Chromatography of the oily residue on 40 g of silica gel (benzene) first eluted as a colorless liquid (0.67 g, 71%), a mixture of the two isomeric olefins **38** and **39**. The ^{1}H NMR of the methoxy group appeared as three closely spaced singlets near δ 3.80 in accord with those two types of isomers. The presence of two isomers was further confirmed by ^{13}C NMR, which showed three carbonyl carbons and four olefinic carbon singlets; the relative intensities of the two sets of olefinic carbon singlets corresponded roughly to a 1:5 ratio (i.e., $E{:}Z = 5$): IR (neat) 1730 (br), 1430 (s), 1250 (br), 1030 (s) cm^{-1}; 80-MHz ^{1}H NMR δ 3.81, 3.79, and 3.78 (3 closely spaced s, 6 H, OCH_3), 3.5–1.5 (br m, 12 H), 1.25 (br s, 16 H); 20-MHz ^{13}C NMR δ 170.25, 170.01, 169.79, 142.15, 141.44, 137.34, 137.27, 64.43, 53.68, 53.54, 53.20, 37.29, 35.36, 35.25, 34.79, 32.95, 31.91, 31.40 (the remaining resonances fell between δ 31.11 and 14.14); HPLC [A] (10:1 heptane–CH_2Cl_2; 3.0) $T_R = 6.8$ (84%) and 8.4 min (16%), $\lambda = 260$ nm; TLC (alumina 6:1 petroleum ether–ether) [two closely spaced spots].

Isolation of (*E*)-Alkene 38. After refrigeration for several days, the oily mixture of olefins **38** and **39** (0.67 g) crystallized to give a white semisolid, which was purified by seven successive fractional recrystallizations from EtOH to give pure (*E*)-olefin **38** as white crystals (0.26 g): mp 91–93 °C; IR (CCl_4) 1735 (split), 1435 (s), 1240 (br) cm^{-1}; UV (EtOH) λ_{max} 265 nm; 80-MHz ^{1}H NMR δ 3.81, 3.79 (s, 6 H, OCH_3), 3.5–2.3 (br m, 10 H), 2.0 (m, 2 H), 1.26 (br s, 16 H). 20-MHz ^{13}C NMR δ 170.25, 170.01, 141.44, 137.34, 64.56, 53.80, 53.64, 37.73, 35.53, 35.39, 31.24, 31.09, 30.67, 30.26, 26.67, 26.02, 25.50, 25.14, 25.01, 24.37, 23.93; HPLC [A] (10:1 heptane–CH_2Cl_2; 3.0) $T_R = 6.8$ min, $\lambda = 260$ nm; MS, *m/e* (relative intensity) 415 (86.2), 383 (11.8), 367 (10), 340 (100), 308 (35), 280 (40), 169 (10.6), 106 (15); TLC (alumina, 6:1 petroleum ether–ether) [homogeneous]. Anal. Calcd for $C_{21}H_{34}O_4S_2$: C, 60.83; H, 8.26. Found: C, 61.00; H, 8.40.

Isolation of (*Z*)-Alkene 39 by MDPTLC. All the mother liquors from isolation of (*E*)-olefin **38** by fractional recrystallization were combined, and the solvent was evaporated in vacuo to give a colorless oil (0.31 g), which was then loaded on eight alumina PTLC plates (ca. 38 mg per plate). After initial development (6:1 petroleum ether–ether), the plates were dried and then were multiply developed three times (12:1 petroleum ether–ether). In each plate two well-separated bands were obtained. The *slower moving band* was scraped off each plate, was washed abundantly with CH_2Cl_2, and was filtered, and the solvent was evaporated in vacuo. The white solid **39** (0.085 g) was recrystallized twice from EtOH: mp 112–114 °C; IR (CCl_4) 1725 (s), 1435 (m), 1240 (br) cm^{-1}; UV (EtOH) λ_{max} 256 nm; 80-MHz ^{1}H NMR δ 3.78 (s, 6 H, OCH_3), 2.90 (m, 4 H, SCH_2), 1.68 (m, 8 H), 1.35 (br s, 16 H); 20-MHz ^{13}C NMR δ 169.79, 142.15, 137.27, 61.58, 53.23, 34.85, 32.99, 31.46, 28.26, 26.82, 26.16, 25.75, 25.23, 24.81, 24.66, 23.60, 23.10, 21.80; HPLC [A] (10:1 heptane–CH_2Cl_2; 3.0) $T_R = 8.4$ min, $\lambda = 260$ nm; MS, *m/e* 414 (M); TLC (alumina, 6:1 petroleum ether–ether) [homogeneous]. Anal. Calcd for $C_{21}H_{34}O_4S_2$: C, 60.83; H, 8.26. Found: C, 61.00; H, 8.27.

Isolation of the *faster moving band* led to recovery of more pure (*E*)-olefin **38** (0.175 g) to provide a combined weight of 0.435 g (0.26 + 0.175 g). This total represents about five times that of the isolated (*Z*)-olefin **39** (0.085 g) and agrees with the 5:1 *E*–*Z* ratio established by ^{13}C NMR and HPLC.

Reaction of (*E*)-Alkene 38 with NaOEt. Concomitant Demethylcarboxylation and Transesterification. A solution of pure (*E*)-olefin **38** (0.175 g, 0.42 mmol) in absolute EtOH (10 mL) was treated with NaOEt (0.102 g, 1.50 mmol) and stirred at room temperature for 22 h. The solvent was removed in vacuo on a rotary evaporator. Fresh EtOH (10 mL) was added, and efficient stirring was continued another 2 h. The solution was concentrated in vacuo and the residue was partitioned between water and ether. The ether was washed with water and brine, was dried (Na_2SO_4), and was removed in vacuo. The oily residue (0.096 g, 62%) proved to be a mixture of olefins **35** according to IR, ^{1}H NMR, HPLC, GLC, and TLC comparisons with samples prepared before. The ratio of the two epimers of **35** was very similar to that (1:3) obtained earlier from the epimerization of a 3:1 epimeric mixture of **35**. None of the isomeric (*Z*)-alkene **36** could be detected.

2-[1-((Trimethylsilyl)oxy)-1-methylethyl]-1,3-dithiane (40). To a −30 °C solution of 1,3-dithiane[43] (5.0 g, 0.041 mol) in dry THF (300 mL) under argon was added slowly *n*-butyllithium (0.042 mol, 16.8 mL of a 2.5 M solution in hexane). Stirring was continued vigorously for 30 min, during which the temperature was allowed to come to 0 °C. A solution of dry acetone (2.41 g, 0.041 mol) in THF (50 mL) was added dropwise to the solution of 2-lithio-1,3-dithiane during 40 min, and stirring was continued another 50 min at 0 °C. The solution was cooled to −65 °C, and freshly distilled chlorotrimethylsilane (4.59 g, 0.042 mol) was added at once. Stirring was continued for 3 h, during which the temperature was allowed to rise to −30 °C. The cold bath then was removed, and stirring was continued at room temperature for 1 h. Most of the solvent was evaporated in vacuo, and the concentrate was partitioned between water and ether. The ether was washed successively with water and brine, was dried (Na_2SO_4), and was evaporated in vacuo to give **40** as a colorless oil (10 g, 96%). This new trimethylsilyl ether was pure and was used directly for the next step: IR (neat) 1425 (s), 1380 (s), 1370 (s), 1250 (s), 1220 (s), 1180 (s), 1130 (s), 1050 (br), 965 (s), 915 (m), 850 (br), 790 (m), 755 (br), 690 (m) cm^{-1}; 60-MHz ^{1}H NMR δ 4.0 (s, 1 H), 2.8 (m, 4 H), 2.0 (m, 2 H), 1.4 (s, 6 H), 0.2 (s, 9 H); TLC (silica gel, benzene) [homogeneous].

2-Isopropylidene-1,3-dithiane (41). To a −65 °C solution of **40** (6.5 g, 0.026 mol) in dry THF (150 mL) under argon was slowly added 1 equiv of 2.5 M *N*-butyllithium in hexane (10.6 mL) at the rate of 3–5 mL/min. After 1 h at −65 °C, the CO_2–acetone cold bath was replaced by an ice bath (0 °C), and vigorous stirring was continued for 2 h. After removing most of the solvent in vacuo, we poured the concentrate into water and extracted it with ether (3 × 60 mL). The combined ether was washed with water and brine, was dried (Na_2SO_4), and was evaporated in vacuo. The IR and ^{1}H NMR spectra of the GLC-pure, pale yellow liquid (4.2 g, 100%) agreed with those reported[34] for **41** prepared differently: GLC [OV-17] (100–170 °C, 30 psi, $T_i = 4$ min, 10 °C/min) $T_R = 6.0$ min; TLC (silica gel, 3:2 petroleum ether–benzene) [homogeneous]. We also synthesized **41** by an alternative, published route[34] but found it much less satisfactory.

2-Methyl-2-(1-methylvinyl)-1,3-dithiane (42). The methylation of **41** to **42** has been reported by Seebach and Kolb,[31] but we found their procedure difficult to reproduce. Therefore, we adapted a general technique.[36] A −78 °C solution of 2.5 M *n*-butyllithium (11 mL, 0.027 mol) in dry THF (80 mL) under argon was treated with dry hexamethylphosphoric triamide (14.35 g, 0.080 mol) to give an intense orange solution. A solution of **41** (4.23 g, 0.026 mol) in dry THF (15 mL) was added at once, and the mixture became intense purple. Stirring was continued while the temperature was allowed to rise to −40 °C over a period of 2 h. After a further $^1/_2$ h at −40 °C, the stirred mixture was cooled to −78 °C, and an excess of iodomethane (5.85 g, 0.041 mol) was added to give a colorless clear solution. After 15 min at −78 °C, the temperature was allowed to climb to 0 °C, and the mixture was stirred vigorously another 1 h. Evaporation in vacuo gave a clear concentrate, which was partitioned between water and ether (3 × 100 mL). The ether was washed with water and brine, dried (Na_2SO_4), and was evaporated in vacuo to give a pale yellow residue. Vacuum distillation, bp 51–52 °C (0.1 torr) [lit.[31] bp 50–51 °C (0.1 torr)], afforded **42** as a colorless liquid (4.4 g, 95.6%): IR (neat) 3080 (w), 3000 (w), 2970 (s), 1635 (m), 1450 (s), 1425 (s), 1370 (s), 1280 (s), 1080 (s), 1070 (s), 910 (s), 870 (w), 760 (s) cm^{-1}; 60-MHz ^{1}H NMR δ 5.5 (br s, 1 H), 5.2 (br s, 1 H), 2.8 (m, 4 H), 2.0 (m, 2 H), 2.0 (s, 3 H), 1.8 (s, 3 H); GLC [OV-17] (100–250 °C, 30 psi, $T_i = 4$ min, 10 °C/min) $T_R = 5.2$ min; TLC (silica gel 3:2 petroleum ether–benzene) [homogeneous].

Reaction of 42 with Ethyl Diazoacetate. Formation of

---

(42) Peace, B. W.; Carman, F.; Wulfman, D. S. *Synthesis* **1971**, 658–661.

(43) Corey, E. J.; Seebach, D. *Org. Synth.* **1970**, *50*, 72–74.

(*E*)-2,3-Dimethyl-5-(ethoxycarbonyl)-1,6-dithiacyclonon-2-ene (44; Two Epimers) and (*Z*)-2,3-Dimethyl-5-(ethoxycarbonyl)-1,6-dithiacyclonon-2-ene (45). A mixture of olefin **42** (0.73 g, 4.18 mmol), anhydrous copper (II) sulfate (0.18 g, 1.12 mmol), and ethyl diazoacetate (1.192 g, 10.45 mmol) in dry benzene (15 mL) was stirred under argon at room temperature for 5 min, and the resulting solution was heated to 60 °C for 1 h. **(Caution!** Intense evolution of nitrogen gas began at 35 °C). The mixture was cooled to 25 °C, was diluted with benzene (30 mL), and was partitioned between water and benzene. The organic layer was washed with water and brine, dried (Na_2SO_4), and evaporated in vacuo. Chromatography of the liquid residue on 45 g of silica gel (benzene) first eluted the starting olefin **42** (0.106 g, 14.5%) and then a second component (0.523 g, 56.2%) comprised of a mixture of the isomeric olefins **44** (two epimers) and **45**. The ^{1}H NMR absorption of the ethyl group methylene appeared as three very closely spaced quartets near δ 4.2, as expected for three isomers. Their presence was confirmed by ^{13}C NMR, which showed six olefinic carbon singlets as well as three carbonyl carbons whose relative intensities were roughly in a 1:1:3 ratio: IR (neat) 3000 (w), 2980 (s), 1730 (br), 1440 (br), 1370 (s), 1330 (m), 1280 (br), 1250 (br), 1220 (m), 1160 (br), 1100 (m), 1090 (m), 1040 (s), 870 (w), 850 (w), 755 (w) cm^{-1}; 80-MHz ^{1}H NMR δ 4.2 (q, 2 H, OCH_2CH_3), 3.8–2.5 (br m, 7 H), 2.35 (br s, 5 H), 2.1 (br s, 3 H), 1.3 (t, 3 H); 20-MHz ^{13}C NMR δ 172.85, 172.20, 172.00, 140.37, 138.52, 138.16, 128.94, 128.93, 126.47, 61.52, 61.25, 51.75, 50.28, 43.90, 38.23, 36.62, 36.39, 35.86, 35.57, 33.34, 32.20, 31.94, 31.09 (the remaining resonances fell between δ 29.80 and 14.22); GLC [OV-17] (100–300 °C, 30 psi, T_i = 4 min, 10 °C/min) T_R = 17.29 (20%) and 17.81 min (80%); TLC (silica gel, 6:1 petroleum ether–ether) R_f 0.61 (minor) and 0.48 (major).

Separation of (*Z*)-Olefin 45 and (*E*)-Olefins 44. Column chromatography of the olefinic mixture (0.52 g) on 20 g of silica gel (6:1 petroleum ether–ether) first eluted a colorless oil (0.10 g, 20%), which crystallized upon standing at room temperature, mp 43–45 °C. The GLC-pure white (*Z*)-olefin **45** has the following properties: IR (CCl_4) 2980 (m), 1730 (s), 1450 (m), 1415 (w), 1370 (w), 1340 (w), 1285 (s), 1265 (m), 1160 (br), 1135 (m), 1100 (w), 1040 (m) cm^{-1}; 300-MHz ^{1}H NMR δ 4.2 (q, 2 H, OCH_2CH_3), 4.0 (t, 1 H, $CHCO_2Et$), 3.4–2.7 (br m, 6 H), 2.1 (br s, 3 H), 1.85 (m, 2 H), 1.75 (s, 3 H), 1.3 (t, 3 H, CH_3); 20-MHz ^{13}C NMR δ 172.85, 138.16, 128.93, 61.25, 43.90, 35.86, 33.34, 27.25, 24.02, 23.47, 18.83, 14.29; GLC [OV-17] (100–300 °C, 30 psi, T_i = 4 min, 10 °C/min) T_R = 17.29 min; TLC (silica gel, 6:1 petroleum ether–ether) R_f 0.61 [homogeneous]. Anal. Calcd for $C_{12}H_{20}O_2S_2$: C, 55.35; H, 7.74. Found: C, 55.56; H, 7.85.

The material eluted second (0.42 g, 80%) consisted of a colorless oil comprised of an epimeric mixture of (*E*)-olefins **44**. These epimers were unresolved on GLC and TLC: IR (CCl_4) 2980 (m), 1735 (split), 1440 (br), 1370 (s), 1280 (br), 1250 (br), 1220 (m), 1150 (br), 1085 (m), 1045 (s) cm^{-1}; 300-MHz ^{1}H NMR δ 4.2 (2 closely spaced q, 2 H, OCH_2CH_3), 3.55 (dd, 1 H, $CHCO_2Et$; the major diastereomer), 3.3 (dd, $CHCO_2Et$; the minor diastereomer), 3.2–2.7 (br m, 4 H), 2.4 (m, 2 H), 2.3 (split br s, 3 H), 2.1 (br s, 5 H), 1.3 (2 closely spaced t, 3 H, CH_3); 20-MHz ^{13}C NMR δ 172.20, 172.00, 140.37, 138.52, 128.94, 126.47, 61.52, 51.75, 50.28, 38.23, 36.62, 36.39, 35.82, 35.57, 33.30, 32.20, 31.94, 31.09, 29.80, 28.91, 26.23, 24.96, 23.43, 14.22; GLC [OV-17] (100–300 °C, 30 psi, T_i = 4 min, 10 °C/min) T_R = 17.81 min; TLC (silica gel, 6:1 petroleum ether–ether) R_f 0.48 [homogeneous]. Anal. Calcd for $C_{12}H_{20}O_2S_2$: C, 55.35; H, 7.74. Found: C, 55.53; H, 7.78.

Equilibration of (*E*)-Alkene Epimers of 44 with NaOEt. A solution of (*E*)-alkene **44** (two epimers; initial ratio ca. 3:1) (50 mg, 0.19 mmol) in absolute EtOH (2 mL) was treated with NaOEt (19 mg, 0.28 mmol) and stirred vigorously at room temperature for 48 h. The solvent was evaporated in vacuo, and the concentrate was partitioned between water and ether and worked up conventionally. The GLC and TLC of the residue showed that no new components were present, and specifically no (*Z*)-alkene had formed. A 300-MHz ^{1}H NMR spectrum revealed that the absorptions at δ 3.55 and at 3.3 ascribed to the two epimers of **44** had changed in relative intensity from a starting ratio of ca. 3:1 to a final ratio of ca. 1:3. Similar changes also occurred in the relative intensities of the closely spaced triplets near δ 1.3 (OCH_2CH_3).

Stability of (*Z*)-Alkene 45 to NaOEt. A solution of pure (*Z*)-olefin **45** (25 mg, 0.096 mmol) in absolute ethanol (2 mL) was treated with NaOEt (9 mg, 0.13 mmol) and stirred at room temperature for 48 h. The solvent was evaporated in vacuo, and the concentrate was partitioned between water and ether and worked up. The ^{1}H NMR, GLC, and TLC characteristics of the residue were identical with those of the starting (*Z*)-olefin.

Reaction of 42 with Dimethyl Diazomalonate. Formation of (*Z*)-2,3-Dimethyl-5,5-bis(ethoxycarbonyl)-1,6-dithiacyclonon-2-ene (47). A mixture of alkene **42** (0.718 g, 4.12 mmol), anhydrous copper(II) sulfate (0.104 g, 0.65 mmol), and dimethyl diazomalonate (0.912 g, 5.76 mmol) in dry toluene (8 mL) was heated slowly and then maintained at 110 °C under argon for 24 h. The flask was cooled to room temperature, was diluted with benzene (15 mL), and was partitioned between water and benzene. The organic layer was washed with water and brine, was dried (Na_2SO_4), and was evaporated in vacuo. Chromatography of the liquid residue on 40 g of silica gel (benzene) eluted a TLC-pure colorless oil (0.45 g, 36%), which crystallized on standing at −10 °C. The solid (*Z*)-olefin **47** was purified further by two recrystallizations from heptane, off-white crystals, mp 114–115 °C. The presence of only one isomer was confirmed by ^{13}C NMR, which showed one carbonyl carbon and two olefinic carbon singlets. The ^{1}H NMR of the methoxy groups appeared as one sharp singlet at δ 3.80, also suggesting that only one isomer was present: IR (CCl_4) 3000 (w), 1730 (s), 1435 (s), 1415 (w), 1305 (w), 1240 (br), 1180 (m), 1110 (m), 1000 (br), 750 (br) cm^{-1}; 300-MHz ^{1}H NMR δ 3.8 (s, 6 H, OCH_3), 2.95 (m, 4 H, SCH_2), 2.05 (s, 3 H, CH_3), 1.8 (m, 2 H), 1.65 (s, 2 H), 1.60 (s, 3 H, CH_3); 20-MHz ^{13}C NMR δ 169.74, 136.87, 130.72, 61.48, 53.33, 39.81, 32.95, 26.93, 24.53, 23.58, 19.04; GLC [OV-17] (150–210 °C, 30 psi, T_i = 4 min, 10 °C/min) T_R = 15.28 min; HPLC [A] (50% heptane–benzene; 3.0) T_R = 3.6 min, λ = 260 nm; TLC (silica gel, benzene) [homogeneous]. Anal. Calcd for $C_{13}H_{20}O_4S_2$: C, 51.29; H, 6.62. Found: C, 51.36; H, 6.55.

Reaction of (*Z*)-Alkene 47 with NaOEt. Concomitant Demethylcarboxylation and Transesterification. A solution of pure (*Z*)-olefin **47** (0.183 g, 0.60 mmol) in absolute ethanol (10 mL) was stirred with NaOEt (0.22 g, 3.32 mmol) at room temperature for 17 h. The solvent was removed in vacuo. Fresh ethanol (10 mL) was added, and stirring was continued vigorously at room temperature for 7 h. The solvent was evaporated in vacuo, and the concentrate was partitioned between water and ether and worked up as usual. The GLC-pure residue (0.067 g, 44%) crystallized on standing to a white solid, mp 43–45 °C, which proved to be identical with (*Z*)-olefin **45** by ^{1}H NMR, IR, GLC, TLC, and mixture melting point.

Acknowledgment. This research was supported by the National Science Foundation (Grant CHE-8200803) and the National Institutes of Health (Grant G01ES02300). A.D.R. was recipient of an NSF Minority Graduate Fellowship and a Vernon K. Krieble Fellowship. We thank Carol Lisek for running mass spectra (at the Middle Atlantic Regional Mass Spectrometry Center at the Johns Hopkins University School of Medicine) and Bruce J. Hrnjez for 300-MHz ^{1}H NMR spectra recorded at The Johns Hopkins Baltimore Biomedical NMR Center, operated by L.-S. Kan and staff under the auspices of NIH Grant GM27512. Professor G. H. Posner and Dr. P. Radhakrishnan Iyer gave helpful advice. Joy E. Merrit (Chemical Abstracts Service, The American Chemical Society, Columbus, OH) graciously assisted us on the systematic nomenclature.

Registry No. **9**, 830-13-7; **9** (2-[(diethylamino)methyl]derivative), 96575-34-7; **9** (2-[(diethylamino)methyl]derivative)·MeI, 96555-22-5; **10**, 3045-76-9; **11**, 96555-23-6; **12**, 93390-76-2; **13**, 93390-77-3; **14**, 62939-87-1; **15**, 96555-24-7; **16a**, 93360-01-1; **16b**, 93360-02-2; **17**, 96555-25-8; **18**, 96555-26-9; **19**, 96555-27-0; **20**, 96555-28-1; **25**, 96555-29-2; **29**, 96555-30-5; **31**, 96555-31-6; **32**, 96555-32-7; **33**, 96555-33-8; **35** (isomer 1), 93452-69-8; **35** (isomer 2), 93452-68-7; **36**, 93360-03-3; **38**, 93390-83-1; **39**, 96555-34-9; **40**, 96615-36-0; **41**, 36998-38-6; **42**, 64087-41-8; **44** (isomer 1), 93390-75-1; **44** (isomer 2), 93452-67-6; **45**, 96614-04-9; **47**, 93360-00-0; Me_2CO, 67-64-1; 1,3-dithiane, 505-23-7.