the possible fabrication of superlattices.

Summary

Cyclooctatraene can now be polymerized to give high-quality films with iodine-doped conductivities in the metallic regime. Physical and spectral characteristics indicate that polycyclooctatetraene *is* polyacetylene. The one outstanding feature of poly-COT films is an extremely smooth surface, understood to be a consequence of polymerization conditions.

In addition to polymerizing cyclooctatetraene neat on a variety of substrates, highly lustrous films can also be produced at a slower rate by centrifugal compression of polymer during polymerization of a dilute solution of COT. Furthermore, during the liquid stage of neat polymerizations, the polymer can be painted onto substrates, a significant advance in the processability of polyacetylene.

Cyclooctatetraene is endowed with a rich history of chemistry[33]—its derivatives are varied and plentiful. As evidenced by the example of bromocyclooctatetraene, metathesis polymerization of the readily available mono- and polyhalogenated COT derivatives is expected to yield a series of novel polyacetylene analogues.

An advantage of this polymerization methodology lies in the variety of copolymers that can be prepared.[41] Depending on the relative reactivities of cycloolefins, random or block copolymers are formed. The COD/COT random copolymerizations produce materials having varied degrees of $p\pi$–$p\pi$ conjugation, determined by mole fraction COT. *This approach* to the synthesis of polyene sequences spanning the range of conjugations lengths maintains a high degree of experimental control. We are currently addressing research toward both nonlinear optical properties and electronic conduction as a function of conjugation length. Continued investigation into these new materials should lead to a greater understanding of finite conjugation sequences and conducting polymers in general.

Acknowledgment. We appreciate financial support of the National Science Foundation through Grant CHE8520517 and acknowledge the NSF Southern Californian Regional NMR facility for the CP-MAS ^{13}C spectrum. We thank Scott Virgil for his assistance and helpful instruction during catalyst preparation. F.L.K. gratefully acknowledges NSF for a graduate fellowship.

Registry No. 1, 101249-40-5; **2**, 86993-74-0; (COT)(1,5-cyclooctadiene) (copolymer), 116531-80-7; (COT)(norbornene) (block copolymer), 116531-81-8; I_2, 7553-56-2; BrCOT, 116531-82-9; cyclooctatetraene, 629-20-9; benzene, 71-43-2; cyclooctatetraene (homopolymer), 30374-82-4; cyclooctatetraene (SRU), 116531-79-4.

Supplementary Material Available: Raman, solution NMR, DSC, and IR spectra (9 pages). Ordering information is given on any current masthead page.

Lipoxygenase Inhibitors from the Essential Oil of Garlic. Markovnikov Addition of the Allyldithio Radical to Olefins[1a]

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Contribution from the Department of Chemistry, State University of New York at Albany, Albany, New York 12222, Institute of Environmental Medicine, New York University Medical Center, New York, New York 10016, and Department of Chemistry, University of Ottawa, Ottawa, Ontario, Canada K1N 6N5. *Received October 8, 1987. Revised Manuscript Received June 27, 1988*

Abstract: Brief pyrolysis of diallyl disulfide (**2**) at 150 °C affords diallyl trisulfide (**3**), thioacrolein dimers 3-vinyl-4*H*-[1,2]-dithiin (**4**) and 2-vinyl-4*H*-[1,3]-dithiin (**5**), diallyl sulfide (**6**), diallyl tetrasulfide (**7**), 6-methyl-4,5,8,9-tetrathiadodeca-1,11-diene (**8**), a mixture of 2- and 3-(2′,3′-dithia-5′-hexenyl)-3,4-dihydro-2*H*-thiopyran (**9** and **10**), and 4,5,9,10-tetrathiatrideca-1,12-diene (**11**, minor). Further heating resulted in loss or gain of sulfur, disproportionation, and cyclization affording 6- and 7-methyl-4,5,8-trithiaundeca-1,10-diene (**12** and **13**), 5-methyl-4,7-dithiadeca-1,9-diene (**14**), 7- and 8-methyl-4,5,6,9,10-pentathiatrideca-1,12-diene (**15** and **16**), 2- and 3-(2′-thia-4′-pentenyl)-3,4-dihydro-2*H*-thiopyran (**17** and **18**), 2- and 3-(2′,3′,4′-trithia-6′-heptenyl)-3,4-dihydro-2*H*-thiopyran (**19** and **20**), 4,5,9-trithiadodeca-1,11-diene (**21**), 4-methyl-1,2,3-trithiolane (**22**), 5-methyl-1,2,3,4-tetrathiane (**23**), *cis*/*trans*-3,7- and *cis*/*trans*-3,8-dimethyl-1,2,5,6-tetrathiacyclooctane (**24** and **25**), 2-(2′-[3′,4′-dihydro-2*H*-thiopyranyl])-4*H*-[1,3]-dithiin (**26**), bis[2-(3,4-dihydro-2*H*-thiopyranyl)methyl] sulfide (**27**), bis[3-(3,4-dihydro-2*H*-thiopyranyl)methyl] sulfide (**28**), 2-(3,4-dihydro-2*H*-thiopyranyl)methyl 3-(3,4-dihydro-2*H*-thiopyranyl)methyl sulfide (**29**), bis[2-(3,4-dihydro-2*H*-thiopyranyl)methyl] disulfide (**30**), bis[3-(3,4-dihydro-2*H*-thiopyranyl)methyl] disulfide (**31**), and 2-(3,4-dihydro-2*H*-thiopyranyl)methyl 3-(3,4-dihydro-2*H*-thiopyranyl)methyl disulfide (**32**). We have also detected many of these products in commercial samples of the essential oil of garlic. They are postulated to account for the antioxidant and lipoxygenase inhibitory activity of this oil. A general mechanism is proposed for formation of these products based on C–S homolysis of diallyl disulfide and reversible terminal and internal addition of the allyldithio radical to diallyl disulfide. Intramolecular hydrogen atom abstraction–fragmentation of the intermediate formed by internal (Markovnikov) addition of the allyldithio radical is favored, affording thioacrolein and the 1-(allyldithio)-2-propylthio radical. Pyrolysis of neat diallyl sulfide in a sealed tube at 200 °C affords **17** and **18**.

While the first detailed chemical report of the preparation and analysis of the essential oil of garlic (*Allium sativum*) appeared in 1844,[2] it is likely that many centuries earlier alchemists and pharmacists distilled garlic bulbs to produce potions for a plethora of ailments.[3] The 1844 paper attributes garlic's appeal to the presence of a "sulfur-containing, liquid body, the so-called garlic oil. All that is known about the material is limited to some meager facts about the pure product which is obtained by steam distillation of bulbs of *Allium sativum*. Since sulfur bonding has been little investigated so far, a study of this material promises to supply

(1) (a) Portions of this work have been presented at the 11th International Congress of Heterocyclic Chemistry, Heidelberg, West Germany, Aug 16, 1987, and the Third Chemical Congress of North America, Toronto, Canada, June 5–10, 1988 (Abstract ORGN 417). (b) SUNY—Albany. (c) NYU. (d) University of Ottawa.

(2) Wertheim, T. *Justus Liebigs Ann. Chem.* **1844**, *51*, 289.

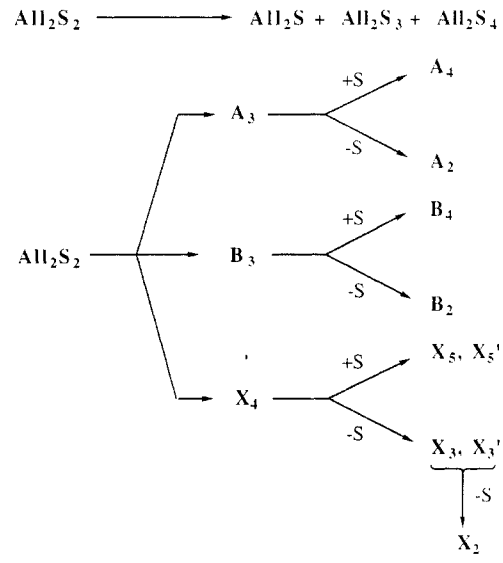
(3) (a) Block, E. *Sci. Am.* **1985**, *252*. 114. (b) Block, E. In *Folk Medicine: The Art and the Science*; Steiner, R. P., Ed.; American Chemical Society: Washington, DC, 1986; pp 125–137.

0002-7863/88/1510-7813$01.50/0

useful results for science."[2] Today the steam-distilled oil is an item of commercial importance for use in both food and health products. In contrast to the room-temperature extract of garlic, which consists predominantly of allicin (CH_2=$CHCH_2S(O)SCH_2CH$=CH_2 (**1**), allyl 2-propenethiosulfinate), a thermally unstable antibacterial substance, along with minor amounts of other dialkyl thiosulfinates (RS(O)SR'; R and R' are variously allyl, methyl, and propyl) and more complex sulfinyl components, including the antithrombotic material ajoene ((*E*/*Z*)-4,5,9-trithiadodeca-1,6,11-triene 9-oxide),[4] the essential oil of garlic is reported to consist primarily of diallyl, dimethyl, and allyl methyl sulfide, disulfide, and trisulfide and a few minor components including those containing an *n*-propyl group,[5] all formed by thermal decomposition of **1** and its homologues. The overall ratio of alkyl residues is ca. 85:13:2 allyl:methyl:*n*-propyl; diallyl disulfide represents 30–50% of the total mixture.[5b] A recent review[6] notes that "the volatiles which have been identified in garlic oils are surprisingly few.... It might be expected that the investigation of the volatiles from garlic oil, essences, and flavorings using modern techniques, such as HPLC or capillary GC–MS, would considerably extend the list of components...." While the essential oil lacks most of the antibacterial and antithrombotic activity of the room-temperature extract, it appears to possess equally interesting antitumor and antioxidant properties among other types of biological activity.[7,8] Garlic oil and some of its components inhibit lipoxygenase (LO), one of the enzymes involved in arachidonic acid metabolism, which may be related to its biological properties.[9a]

In connection with our interest in the organosulfur chemistry of plants of the *Allium* family,[3,4] we have assayed garlic essential oil preparations using the inhibition of soybean lipoxygenase to determine the compounds that may be responsible for their biological activities. We report that (1) the LO-inhibitory activity of garlic oil increases upon heating and concentration;[9b,c] (2) temperature-programmed capillary GC–MS analysis of garlic essential oil reveals a group of previously unknown higher boiling cyclic and acyclic organosulfur compounds, which we have isolated and identified and whose LO-inhibitory activity we have measured; (3) most of these same compounds are generated upon heating pure samples of diallyl disulfide;[10] and (4) the formation of these new compounds is best explained by a remarkable sequence involving *C–S homolysis of* diallyl disulfide, addition of the allyldithio radical in *Markovnikov fashion* to diallyl disulfide, *intramolecular hydrogen atom abstraction–fragmentation* of the radical adduct to produce thioacrolein, and finally *Diels–Alder addition of thioacrolein as a heterodiene* to diallyl sulfide, disulfide, and trisulfide.

Scheme I



Our work, which clarifies the surprisingly complex processes occurring upon heating allylic disulfides, is germane to the chemistry of vulcanized rubber with its polysulfide bridges linking allylic positions.[11d] Our discovery that thioacrolein functions quite nicely as a 4π component in the Diels–Alder reaction has stimulated a broad study, reported separately, of applications of this little used reagent in heterocycle synthesis.[12a]

Product Isolation and Characterization and Initial Mechanistic Observations

We find that the LO-inhibitory activity of commercial garlic oil (IC_{50} = 50 μg/mL) increases upon concentration (IC_{50} = 2 μg/mL), upon heating at 150 °C in the absence of oxygen (IC_{50} = 4 μg/mL), and particularly upon heating followed by concentration (IC_{50} = 0.3 μg/mL); similarly, heating and concentrating diallyl disulfide (**2**, All_2S_2),[12b] itself inactive, gave active material (IC_{50} = 1 μg/mL). Analysis of heated All_2S_2 on both 50- and 5-m capillary GC columns at oven temperatures up to 180 °C showed a characteristic series of peaks of significantly longer retention times than for the known garlic oil constituents diallyl polysulfides, $(CH_2$=$CHCH_2)_2S_n$ (n = 1–4). These same GC peaks were present at low levels in samples of commercial garlic oil that had been concentrated below 90 °C. Heating the garlic oil enhanced these peaks. Field desorption mass spectrometry of the heated (150 °C), concentrated All_2S_2 indicated major molecular ions of *m*/*e* 144, 178, 218, and 252, intermediate intensity ions of *m*/*e* 290, 292, 324, and 358, and weak ions of *m*/*e* 186, 210, 212, 216, 250, 258, 284, and 294. Under identical conditions a commercial sample of garlic essential oil displayed many of these same molecular ions (*m*/*e* 144, 178, 210, 216, 218, 250, and 252) along with additional ions at *m*/*e* 120, 152, 242, and 274, among others. By GC–MS the *m*/*e* 178 and 144 compounds were identified, respectively, as diallyl trisulfide (**3**, All_2S_3)

(4) Block, E.; Ahmad, S.; Catalfamo, J. L.; Jain, M. K.; Apitz-Castro, R. *J. Am. Chem. Soc.* **1986**, *108*, 7045. Block, E.; Ahmad, S.; Jain, M. K.; Crecely, R. W.; Apitz-Castro, R.; Cruz, M. R. *J. Am. Chem. Soc.* **1984**, *106*, 8295.

(5) (a) Guenther, E. *The Essential Oils*; Van Nostrand: New York, 1952; Vol. 6, p 67. (b) Vernin, G.; Metzger, J.; Fraisse, D.; Scharff, C. *Planta Med.* **1986**, 96.

(6) Fenwick, G. R.; Hanley, A. B. *CRC Crit. Rev. Food Sci. Nutr.* **1985**, *22*, 199, 273; **1986**, *23*, 1.

(7) Amonkar, S. V.; Banerji, A. *Science (Washington, D.C.)* **1971**, *174*, 1343. Bordia, A.; Bansal, H. C. *Lancet* **1973**, 1491. Bordia, A. K.; Joshi, H. K.; Sanadhya, Y. K.; Bhu, N. *Atherosclerosis* **1977**, *28*, 155. Bordia, A. *Atherosclerosis* **1978**, *30*, 355. Vanderhoek, J. Y.; Makheja, A. N.; Bailey, J. M. *Biochem. Parmacol.* **1980**, *29*, 3169. Naito, S.; Yamaguchi, N.; Yokoo, Y. *Nippon Shokuhin Kogyo Gakkaishi* **1981**, *28*, 291, 465. Belman, S. *Carcinogenesis* **1983**, *4*, 1063. Belman, S.; Block, E.; Barany, G. *Proc. Am. Assoc. Cancer Res.* **1986**, *27*, 140. Sparnins, V. L.; Mott, A. W.; Barany, G.; Wattenberg, L. W. *Nutr. Cancer* **1986**, *8*, 211. Perchellet, J.-P.; Perchellet, E. M.; Abney, N. L.; Firnstein, J. A.; Belman, S. *Cancer Biochem. Biophys.* **1986**, *8*, 299. Belman, S.; Block, E.; Perchellet, J.-P.; Perchellet, E. M.; Fischer, S. M. *Proc. Am. Assoc. Cancer Res.* **1987**, *28*, 166. Wargovich, M. J. *Carcinogenesis* **1987**, *8*, 487. Sparnins, V. L.; Barany, G.; Wattenberg, L. W. *Carcinogenesis* **1988**, *9*, 131. Wargovich, M. J.; Stephens, L. C.; Gray, K. *Proc. Am. Assoc. Cancer Res.* **1988**, *29*, 136.

(8) Granroth, B. *Ann. Acad. Sci. Fenn., Ser. A2* **1970**, *154*, 1.

(9) (a) Ajoene has IC_{50} = 1.6 and 5.1 μM toward 5-lipoxygenase and cyclooxygenase, respectively: Wagner, H.; Wierer, M.; Fessler, B. *Planta Med.* **1987**, *53*, 305. (b) The commercially available soybean 15-lipoxygenase enzyme is used in our study. (c) S. Belman and G. Barany originally observed that aged or heated garlic oil component allyl methyl trisulfide showed increased LO inhibition compared to a freshly synthesized sample.

(10) It has been noted[8] that "diallyl disulfide is slowly decomposed even at room temperature.... At 100 °C...at least 25 different reaction products were revealed by gas chromatography, the true number being still greater" and that "allylic compounds may undergo changes on the heating of garlic-spiced foods, but the chemistry and possible physiological importance of these changes do not so far appear to have been investigated".

(11) (a) An analogous mechanism has been proposed for the decomposition of allyl *tert*-butyl peroxide[11b] although it has been suggested that "C–H α to O–O is not particularly activated toward free radical attack".[11c] (b) Hiatt, R.; Nair, V. G. K. *Can. J. Chem.* **1980**, *58*, 450. (c) Hiatt, R. R. In *Frontiers of Free Radical Chemistry*; Pryor, W. A., Ed.; Academic: New York, 1980; p 225. (d) Porter, M. In *Perspectives in the Organic Chemistry of Sulfur*; Zwanenburg, B., Klunder, A. J. H., Eds.; Elsevier: Amsterdam, 1987; pp 267–283.

(12) (a) Block, E.; Grisoni, S.; Iyer, R.; Zhao, S.-H., manuscript submitted. (b) In this paper we use the shorthand notation "All" to represent the allyl group.

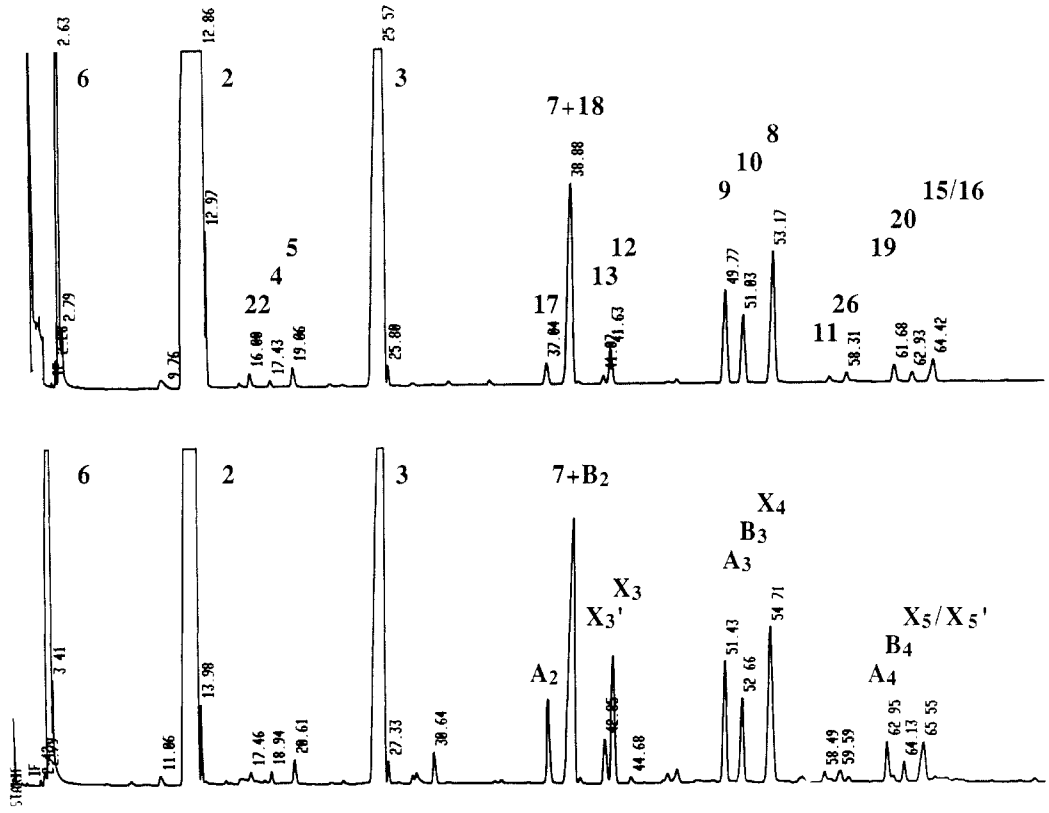
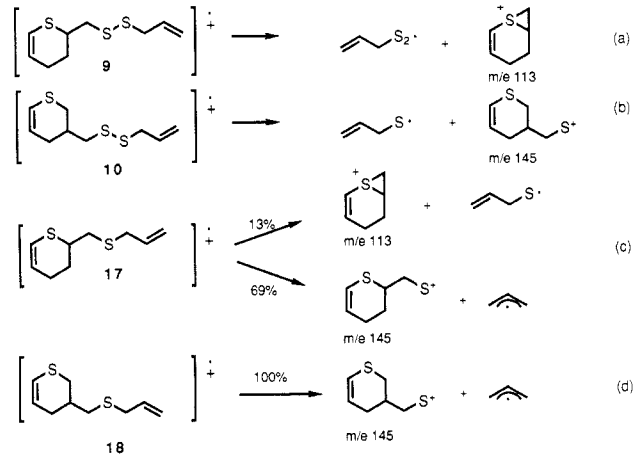


Figure 1. GC traces of pyrolysis of neat diallyl disulfide at 80 °C for 2 days (top) and 10 days (bottom) as described in Table I. Structure numbers corresponding to each peak are given in the upper trace. The "ABX" labeling used in Scheme I appears in the bottom trace.

and a mixture of the known[4,13] thioacrolein dimers 3-vinyl-4*H*-[1,2]-dithiin (**4**) and 2-vinyl-4*H*-[1,3]-dithiin (**5**), while the *m/e* 210 compound was characterized as diallyl tetrasulfide. The *m/e* 120 and 152 compounds, found only in garlic oil, were identified as allyl methyl disulfide and trisulfide, respectively; none of the other GC peaks correspond to known compounds.[14]

While the large number of unknown components present at low concentrations in garlic oil and in the All_2S_2 pyrolysate presents formidable identification problems, examination by GC and GC–MS of the time dependence of product formation on heating All_2S_2 leads to considerable simplification. Heating pure All_2S_2 for <10 min at 150 °C or for 2 days at 80 °C affords significant quantities of diallyl sulfide (**6**, All_2S), All_2S_3, and diallyl tetrasulfide (**7**, All_2S_4) (5:5:1 ratio) and lesser quantities of three other longer retention time compounds, A_3, B_3 (both *m/e* 218), and X_4 (*m/e* 252) (3:2:5 ratio; Figure 1 (top) and Scheme I).[15] Continued heating of the All_2S_2 sample (20 min at 150 °C or 10 days at 80 °C; Figure 1 (bottom)) leads to gradual, simultaneous formation of new sets of four intermediate retention time compounds, A_2, B_2 (both *m/e* 186), X_3, and X_3' (both *m/e* 220) (ratio ca. 6:4:3:9), four long retention time compounds, A_4, B_4, X_5, and X_5' (ratio 2:1:3 for A_4:B_4:(X_5 + X_5')), and small amounts of a short retention time compound, X_2 (*m/e* 188). From GC–MS analysis as well as from data presented below on triphenylphosphine desulfurization of A_3, B_3, and X_4 and addition of sulfur to A_2, B_2, X_2, X_3, and X_3', it became clear that compounds A_2, B_2, and X_3/X_3' are related to A_3, B_3, and X_4, respectively, by each having *one less* sulfur atom while compound X_2 has *two less* sulfur atoms than X_4; similarly compounds A_4, B_4, and X_5/X_5' each have *one more* sulfur atom than A_3, B_3, and X_4, respectively.

Scheme II



Compounds X_4, A_3, and B_3 could be isolated by preparative HPLC and characterized spectroscopically, and through synthesis (see below), as 6-methyl-4,5,8,9-tetrathiadodeca-1,11-diene (**8** = X_4) (*m/e* 252) and 2- and 3-(2′,3′-dithia-5′-hexenyl)-3,4-dihydro-2*H*-thiopyran (**9** = A_3 and **10** = B_3, respectively; *m/e* 218) (see Table I). The identification of **8** by ^1H and ^{13}C NMR spectroscopy, mass spectrometry, and elemental analysis was straightforward. NMR spectroscopy indicated the presence of a $-CH(CH_3)CH_2-$ unit together with $CH_2{=}CHCH_2S_m-$ and $CH_2{=}CHCH_2S_n-$ groups. Synthesis established that in the latter groups, $m = n = 2$. The identification of **9** and **10** was facilitated by 2D HOMCOR and HETCOR NMR studies (see Supplementary Material). Both compounds show a total of nine ^{13}C NMR signals, four olefinic (3 CH, 1 CH_2) and five aliphatic (4 CH_2, 1 CH). Compound **9** shows a more deshielded CH (38.4 ppm; C2, α to S) than **10** (31.4 ppm; C3, β to S) along with a uniquely deshielded CH_2 (22.2 ppm; C3). Analysis of the mass spectra of **9** and **10** shows that although both have an M^+ peak at *m/e* 218, their fragmentation patterns are vastly different. The base peak of **9**, *m/e* 113 (C_6H_9S), results from loss of $AllS_2^{\bullet}$, with

(13) Bock, H.; Mohmand, S.; Hirabayashi, T.; Semkow, A. *Chem. Ber.* **1982**, *115*, 1339. Vedejs, E.; Eberlein, T. H.; Varie, D. L. *J. Am. Chem. Soc.* **1982**, *104*, 1445. Beslin, P. *J. Heterocycl. Chem.* **1983**, *20*, 1753.

(14) The *m/e* 242 and 274 ions may correspond to diallyl pentasulfide (All_2S_5) and diallyl hexasulfide (All_2S_6). The former compound appears to have the same GC retention time as the compound of mass *m/e* 218 (**10**; see below) as indicated by GC–MS analysis of various mixtures.

(15) All of these products are also slowly formed at 50 °C, 2 weeks being required to give comparable results to 2 days at 80 °C.

Table I. Diallyl Disulfide Pyrolysis Products

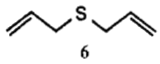
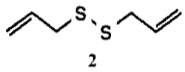
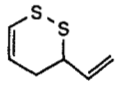
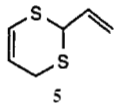
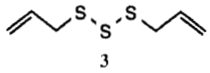
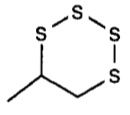
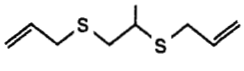
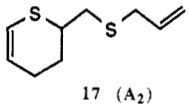
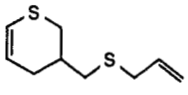
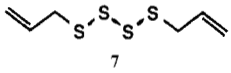
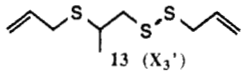
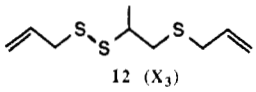
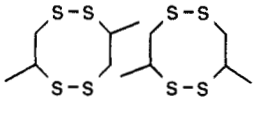
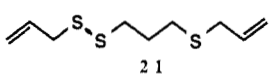
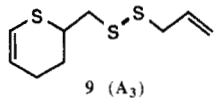
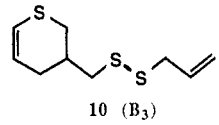
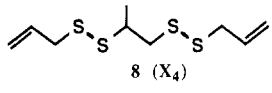
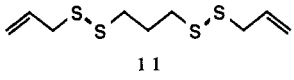
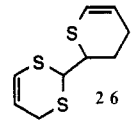
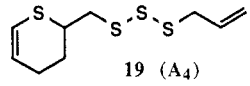
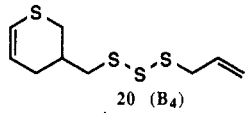
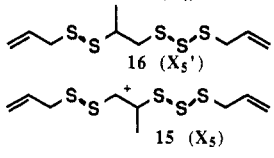
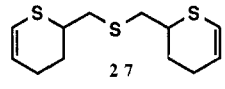
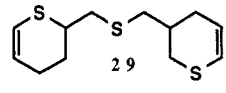
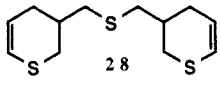
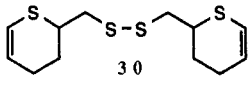
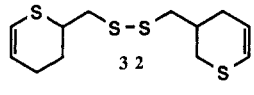
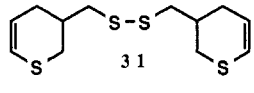
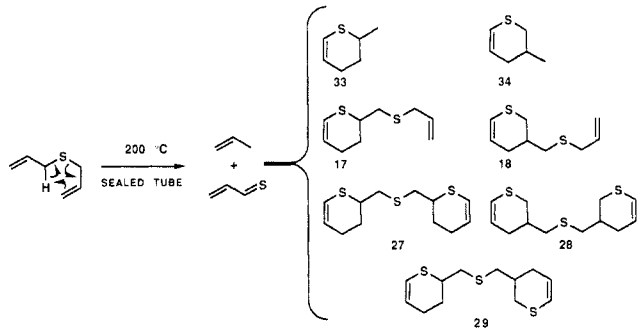
entry #	compound	GC RT, min[a] (%[d],%[e])[f]	MW	MS[b] m/e (rel. intensity)	^{13}C NMR ($CDCl_3$)[c] δ
1	 6	3 (13%; 20%)	114	116 (M^++2, 1%), 114 (M^+, 20%), 99 (17%), 81 (11%), 73 (42%), 45 (100%), 41 (60%)	134.4 (=CH), 116.8 (=CH_2), 33.3 (CH_2)
2	 2	13 (64%, 38%)	146	148 (M^++2, 0.3%), 146 (M^+, 3%), 113 (4%), 105 (4%), 81 (10%), 73 (5%), 64 (4%), 45 (27%), 41 (100%)	133.4 (=CH), 118.3 (=CH_2), 42.2 (CH_2)
3	 2 2	16 (0.12%, 0.68%)	138	140 (M^++2, 10%), 138 (M^+, 64%), 73 (58%), 64 (46%), 45 (69%), 41 (100%)	
4	 4	17 (0.05%, 0.11%)	144	146 (M^++2, 3%), 144 (M^+, 20%), 112 (6%), 111 (33%), 97 (41%), 85 (16%), 79 (31%), 72 (36%), 45 (100%), 41 (27%)	136.5 (CH, C6), 126.6 (CH, C7), 126.0 (CH, C5), 117.5 (CH_2, C8), 44.0 (CH, C3), 30.6 (CH_2, C4)
5	 5	19 (0.17%, 0.29%)	144	146 (M^++2, 3.5%), 144 (M^+, 38%), 111 (33%), 103 (13%), 97 (14%), 85 (12%), 72(98%), 71 (100%), 45 (96%), 41 (34%)	134.3 (CH, C6), 122.2 (CH, C5), 118.3 (CH, C7), 117.2 (CH_2, C8), 45.1 (CH, C2), 25.1 (CH_2, C4)
6	 3	26 (14%, 18%)	178	180 (M^++2, 0.6%), 178 (M^+, 4%), 137 (4%), 113 (58%), 73 (84%), 64 (8%), 45 (69%), 41 (100%)	132.6 (=CH), 119.0 (=CH_2), 41.6 (CH_2)
7	 2 3	29 (tr, 0.42%)	170	172 (M^++2, 14%), 170 (M^+, 76%), 138 (7%), 128 (44%), 106 (35%), (89%), 45 (64%), 41(100%)	
8	 14 (X_2)	30 (tr, 0.45%)	188	188 (M^+, .2%), 147 (17%), 115 (18%), 101 (11%), 73 (38%), 59 (33%), 45 (46%), 41 (100%)	134.7, 134.4 (CH, C2/C9), 117.1, 116.8 (CH_2, C10/C1), 38.5 (CH, C5), 37.9 (CH_2, C6), 35.5, 34.0 (CH_2, C8/C3), 20.2 (CH_3, C11)
9	 17 (A_2)	37 (0.22%, 1.45%)	186	188 (M^++2, 1%), 186 (M^+, 12%), 145 (69%), 113 (13%), 111 (37%), 99 (78%), 85 (28%), 79 (51%), 65 (56%), 45 (100%), 41 (76%)	134.1, 120.7, 118.7 (=CH), 117.4 (=CH_2), 39.2 (CH), 35.6, 35.2, 27.3, 22.6 (CH_2)
10	 18 (B_2)	40[g]	186	188 (M^++2, 0.6%), 186 (M^+, 5%), 145 (100%), 113 (2%), 111 (23%), 99 (46%), 79 (40%), 73 (21%), 65 (27%), 45 (75%), 41 (66%)	134.3, 120.0, 119.2 (=CH), 117.1 (=CH_2), 35.8, 35.1 (CH_2), 31.9 (CH), 30.1, 29.6 (CH_2)
11	 7	40 (2.8%, 5.5%)[g]	210	212 (M^++2, 0.6%), 210 (M^+, 3%), 146 (13%), 105 (7%), 81 (5%), 73 (24%), 64 (10%), 45 (38%), 41 (100%)	132.5 (=CH), 119.5 (=CH_2), 42.0 (CH_2)
12	 13 (X_3')	41 (0.08%, 0.86%)	220	220 (M^+, 0.075%), 115 (40%), 73 (50%), 59 (18%), 41 (100%)	
13	 12 (X_3)	42 (0.4%, 2.2%)	220	220 (M^+, 0.25%), 179 (2%), 115 (69%), 73 (76%), 45 (50%), 41 (100%)	134.3 (CH, C2), 133.3 (CH, C10), 118.6 (CH_2, C1), 117.4 (CH_2, C11), 45.6 (CH, C6), 43.0 (CH_2, C3), 37.3, 35.5 (CH_2, C7/C9), 19.4 (CH_3)
14	 24 25	47 (tr, tr)	212	214 (M^++2, 10%), 212 (M^+, 53%), 138 (58%), 106 (47%), 73 (63%), 64 (42%), 45 (55%), 41 (100%)	49-45.3 (CH_2), 45.3-44 (CH), 24-18 (CH_3)
15	 2 1	48 (tr, tr)	220	220 (M^+, 0.07%), 179 (12%), 147 (97%), 106 (66%), 105 (61%), 73 (89%), 41 (100%)	134.3 (CH, C11), 133.5 (CH, C2), 118.5 (CH_2, C12), 117.0 (CH_2, C1), 42.2 (CH_2, C10), 37.5 (CH_2, C7), 34.7 (CH_2, C3), 29.1 (CH_2, C5), 28.5 (CH_2, C6)
16	 9 (A_3)	50 (1.1%, 2.3%)[h]	218[h]	220 (M^++2, 1%), 218 (M^+, 6%), 177 (2%), 145 (5%), 113 (100%), 85 (33%), 79 (65%), 41 (50%)	132.3 (CH, C2), 119.8 (CH, C3), 117.7 (CH_2, C12), 117.5 (CH, C11), 42.7 (CH_2, C10), 41.2 (CH_2, C7), 37.5 (CH, C6), 25.6 (CH_2, C4), 21.2 (CH_2, C5)

Table I (Continued)

entry #	compound	GC RT, min[a] (%[d],%[e])[f]	MW	MS[b] m/e (rel. intensity)	^{13}C NMR ($CDCl_3$)[c] δ
17	 10 (B_3)	51 (0.8%, 1.4%)	218	220 (M^++2, 0.8%), 218 (M^+, 5%), 179 (6%), 177 (39%), 145 (100%), 113 (4%), 99 (33%), 45 (54%), 41 (54%)	133.4 (CH, C2), 119.7 (CH, C3), 119.3 (CH, C11), 118.6 (CH_2, C12), 43.8 (CH_2, C10), 42.2 (CH_2, C7), 31.4 (CH, C5), 29.7 (CH_2, C6), 29.1 (CH_2, C4)
18	 8 (X_4)	53 (1.7%, 3.4%)	252	252 (M^+, 0.14%), 211 (0.42%), 179 (1%), 147 (25%), 73 (70%), 45 (36%), 41 (100%)	132.4, 132.3 (CH, C2/C11), 117.7 (CH_2, C1/C12), 44.4 (CH_2, C7), 43.7 (CH, C6), 42.0, 41.2 (CH_2, C3/C10), 18.0 (CH_3, C13)
19	 11	57 (tr, tr)	252	252 (M^+, 0.11%), 211 (12%), 179 (25%), 106 (37%), 73 (100%)	133.5 (=CH), 118.5 ($=CH_2$), 42.26 (CH_2-CH=), 37.14 (SCH_2), 28.28 (CH_2)
20	 26	58 (0.09%, 0.2%)	216	218 (M^++2, 10%), 216 (M^+, 54%), 144 (28%), 117 (59%), 111 (100%), 83 (80%), 73 (83%), 71 (79%)	121.9, 121.7, 119.6, 119.6, 119.3, 119.2, 117.10, 117.05 (=CH), 48.7, 48.2, 36.4, 36.3 (CH), 29.0, 28.5, 27.5, 27.3, 26.5, 26.0 (CH_2)
21	 19 (A_4)	62 (0.2%, 0.7%)	250[i]	218 (0.6%), 177 (0.8%), 145 (77%), 113 (41%), 111 (28%), 99 (15%), 85 (17%), 79 (25%), 73 (12%), 45 (95%), 41 (94%), 39 (100%)	132.6 (CH), 120.8 (CH), 119.3 (CH_2), 118.5 (CH), 43.4 (CH_2), 41.6 (CH_2), 38.1 (CH), 26.5 (CH_2), 22.0 (CH_2)
22	 20 (B_4)	63 (0.1%, 0.25%)	250[i]	218 (0.5%), 177 (6%), 147 (10%), 146 (11%), 145 (100%), 113 (5%), 111 (17%), 99 (27%), 73 (15%), 45 (68%), 41 (65%), 39 (77%)	
23	 16 (X_5') 15 (X_5)	65 (0.3%, 0.5%)	284[i]	major: 179 (41%), 138 (9%), 137 (17%), 105 (10%), 104 (7%), 73 (69%), 64 (13%), 41 (100%) minor: 219 (1%), 179 (41%), 138 (9%), 137 (16%), 105 (11%), 73 (69%), 64 (12%), 41 (100%)	133.3 (=CH), 132.6 (=CH), 119.3 ($=CH_2$), 118.8 ($=CH_2$), 45.7 (CH), 45.4* (CH_2), 45.1 (CH_2), 44.4* (CH), 43.0* (CH_2), 42.2 (CH_2), 41.7 (CH_2), 41.6* (CH_2), 19.2* (CH_3), 18.9 (CH_3)(* = major isomer)
24	 27	76 (tr, tr)	258	260 (M^++2, 3%), 258 (M^+, 20%), 146 (11%), 145 (11%), 113 (84%), 112 (100%), 99 (81%), 79 (91%)	
25	 29	77 (tr, tr)	258	260 (M^++2, 3%), 258 (M^+, 21%), 146 (36%), 113 (58%), 112 (69%), 99 (68%), 97 (46%), 79 (100%), 65 (40%)	
26	 28	78 (tr, tr)	258	258 (M^+, 9%), 146 (78%), 112 (59%), 79 (100%)	
27	 30	85 (tr, tr)	290	292 (M^++2, 2%), 290 (M^+, 9%), 145 (16%), 113 (100%), 85 (27%), 79 (56%), 45 (43%), 41 (34%)	
28	 32	86 (tr, tr)	290	292 (M^++2, 4%), 290 (M^+, 24%), 145 (100%), 113 (96%), 85 (45%), 79 (82%), 45 (79%), 41 (50%)	
29	 31	87 (tr, tr)	290	290 (M^+, 12%), 145 (100%), 113 (6%), 99 (29%), 45 (44%), 41 (27%)	

[a] GC analysis performed on a 30-m 0.35-mm capillary column of cross-linked 5% phenylmethylsilicone temperature programmed from 50 °C (after 5 min) to 195 °C at 2 °C/min; injector 200 °C. [b] GC–MS obtained with a Hewlett-Packard 5970 mass-selective detector interfaced to a Hewlett-Packard GC with a 12-m capillary column of cross-linked methylsilicone gum; all spectra were identical with GC–MS of synthetic material. [c] Obtained with a Varian XL-300 NMR spectrometer. [d] 80 °C, 2 days. [e] 80 °C, 10 days. [f] 150 °C, 3.5 min: **6** (5.7%), **2** (88.9%), **5** (0.03%), **4** (0.08%), **3** (3.6%), **17** (0.03%), **7** (0.2%), **13** (0.01%), **12** (0.06%), **9** (0.31%), **10** (0.18%), **8** (0.55%), **26** (0.06%), **19** (0.019%), **20** (0.017%), **15**/**16** (0.04%); 80 °C, 1 day: **6** (4%), **2** (85.2%), **5** (0.25%), **4** (0.54%), **3** (8.2%), **7** (0.38%), **9** (0.23%), **10** (0.12%), **8** (0.16%); 50 °C, 7 days: **6** (3%), **2** (84.2%), **5** (0.3%), **4** (0.7%), **3** (9.7%), **7** (0.47%), **9** (0.33%), **10** (0.18%), **8** (0.18%), **26** (0.17%). [g] While **7** and **18** are not separable on this column, they can be separated on a 50-m OV101 capillary column. [h] On the basis of an *m/e* 242 peak that was sometimes found along with the fragment ions assigned to **9**, it is suggested that All_2S_5 is a minor product with GC retention time identical with that of **9**. This suggestion is consistent with the retention time predicted for All_2S_5 based upon retention times of homologues **6**, **2**, **3**, and **7**. [i] Parent ions could not be detected for this compound.

Scheme III



stabilization of the resulting carbocation by the β sulfur (Scheme IIa) while the base peak of **10**, *m/e* 145 ($C_6H_9S_2$), results from loss of AllS$^\bullet$ (Scheme IIb). Furthermore, the base peak of one compound is present to the extent of <10% abundance in the mass spectrum of the other.

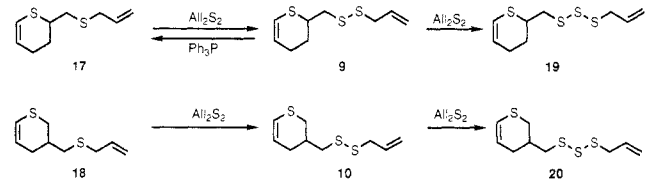
A second, minor, *m/e* 252 isomer, 4,5,9,10-tetrathiatrideca-1,12-diene (**11**), was also identified by GC and GC–MS following preparation of an authentic sample (see below). The **8**:**9**:**10**:**11** ratio was 20:10:7:1. Further heating resulted in loss or gain of sulfur[16] from **8**–**10**, affording 6- and 7-methyl-4,5,8-trithiaundeca-1,10-diene (**12** = X_3 (major) and **13** = X_3' (minor), respectively), 5-methyl-4,7-dithiadeca-1,9-diene (**14** = X_2), 7- and 8-methyl-4,5,6,9,10-pentathiatrideca-1,12-diene (**15** = X_5 (major) and **16** = X_5' (minor), respectively, *m/e* 284), 2- and 3-(2′-thia-4′-pentenyl)-3,4-dihydro-2*H*-thiopyran (**17** = A_2 and **18** = B_2, respectively), and 2- and 3-(2′,3′,4′-trithia-6′-heptenyl)-3,4-dihydro-2*H*-thiopyran (**19** = A_4 and **20** = B_4, respectively; *m/e* 250[17]). Synthesis of the above compounds is given below. A trace amount of 4,5,9-trithiadodeca-1,11-diene (**21**) from loss of sulfur from **11** was also detected.

Other new compounds present in pyrolysis mixtures in low concentrations and identified (or tentatively identified) by comparison with GC and/or GC–MS properties of authentic synthetic materials include 4-methyl-1,2,3-trithiolane (**22**), 5-methyl-1,2,3,4-tetrathiane (**23**), *cis*/*trans*-3,7- and *cis*/*trans*-3,8-dimethyl-1,2,5,6-tetrathiacyclooctane (**24** and **25**, respectively), 2-(2′-[3′,4′-dihydro-2*H*-thiopyranyl])-4*H*-[1,3]-dithiin (**26**; diastereoisomers), bis[2-(3,4-dihydro-2*H*-thiopyranyl)methyl] sulfide (**27**), bis[3-(3,4-dihydro-2*H*-thiopyranyl)methyl] sulfide (**28**), 2-(3,4-dihydro-2*H*-thiopyranyl)methyl 3-(3,4-dihydro-2*H*-thiopyranyl)methyl sulfide (**29**), bis[2-(3,4-dihydro-2*H*-thiopyranyl)methyl] disulfide (**30**), bis[3-(3,4-dihydro-2*H*-thiopyranyl)methyl] disulfide (**31**), and 2-(3,4-dihydro-2*H*-thiopyranyl)methyl 3-(3,4-dihydro-2*H*-thiopyranyl)methyl disulfide (**32**).

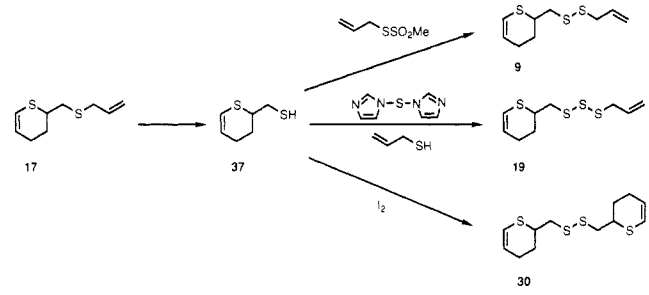
Product Synthesis and Mechanisms for Heterocycle Formation

Heterocyclic Compounds 4, 5, 9, 10, 17, 18, 19, 20, and 26–32. Thioacrolein Formation and Trapping. Mechanistic studies on the origin of the thiopyran heterocycles led to development of syntheses. A remarkable mixture of products is formed when All_2S is heated overnight in a sealed tube at 200–210 °C (Scheme III). On the basis of the extensive high-temperature chemistry of All_2S,[18] we surmise that thioacrolein formed via retroene reaction

Scheme IV



Scheme V



undergoes Diels–Alder reactions with propylene, All_2S and **17** and **18** giving the indicated products. For preparative purposes, All_2S is heated at 200 °C in a sealed tube for 1.5 h, affording a 3:2 mixture of **17** and **18** (the same ratio as found in garlic oil) in 64% yield based on unrecovered All_2S. The same products are formed more slowly at 150 °C. Compounds **17** and **18** can be separated by HPLC and fully characterized by NMR (see below) and mass spectroscopic methods. While the *m/e* 145 fragment resulting from loss of the allyl radical dominates the mass spectra of both **17** and **18**, the *m/e* 113 thiiranium ion is also a significant fragment from **17** but not from **18** (Scheme IIc,d).

If All_2S is heated at 200 °C in a sealed tube for 12 h, the most volatile fraction of the distillate contains a mixture of All_2S and 2- and 3-dihydro-2*H*-thiopyran (**33** and **34**) in a ratio of 1.3:1. Kugelrohr distillation of the less volatile product affords **17** and **18** in a ratio of 1.3:1 in 21% yield. The distillation residue contains small quantities of thioacrolein–All_2S double Diels–Alder adducts bis[2-(3,4-dihydro-2*H*-thiopyranyl)methyl] sulfide (**27**), bis[3-(3,4-dihydro-2*H*-thiopyranyl)methyl] sulfide (**28**), and 2-(3,4-dihydro-2*H*-thiopyranyl)methyl 3-(3,4-dihydro-2*H*-thiopyranyl)methyl sulfide (**29**). These compounds are also formed when All_2S is heated with excess **17**/**18** at 200 °C for 1 h. Compounds **33** and **34** can be separated by HPLC and characterized spectroscopically. Alternatively, the mixture of All_2S, **33**, and **34** can be directly oxidized to the corresponding sulfones All_2SO_2 and 2- and 3-methyl-3,4-dihydro-2*H*-thiopyran 1,1-dioxide (**35** (major) and **36** (minor), respectively). The assignment of **35** (and therefore **33**) as the major regioisomer is consistent with the appearance of an aliphatic α-sulfonyl CH carbon[19a] in the ^{13}C NMR (APT) spectrum of **35** at 54.3 ppm (CH_2 carbons at 27.6 and 24.2 ppm); **36** shows an α-sulfonyl CH_2 carbon[19a] at 56.8 ppm (aliphatic CH carbon at 27.9 ppm, second CH_2 carbon at 32.9 ppm).

Treatment of **17** with All_2S_2 as a sulfur source affords **9** and minor amounts of **19**; similarly, treatment of **18** with All_2S_2 affords **10** and minor amounts of **20**. Treatment of **9** with triphenyl-

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(17) (a) While the expected parent ions at *m/e* 250 were absent under electron impact GC–MS analysis of All_2S_2 pyrolysates, field desorption mass spectrometry of pyrolysates showed ions corresponding to *m/e* 250 while chemical ionization (methane) mass spectrometry showed $M^+ + 1$ ions at *m/e* 251. (b) The difficulty of obtaining molecular ions for polysulfur compounds has been noted; FAB techniques have proven useful in these cases: Singh, P. K.; Field, L.; Sweetman, B. J. *J. Org. Chem.* **1988**, *53*, 2608.

(18) Giles, H. G.; Marty, R. A.; de Mayo, P. *Can. J. Chem.* **1976**, *54*, 537. Bock, H.; Mohmand, S.; Hirabayashi, T.; Semkow, A. *J. Am. Chem. Soc.* **1982**, *104*, 312. Martin, G.; Ropero, M.; Avila, R. *Phosphorus Sulfur* **1982**, *13*, 213.

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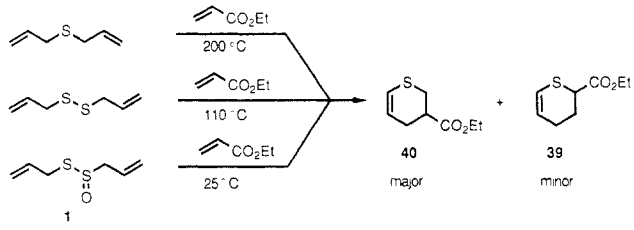
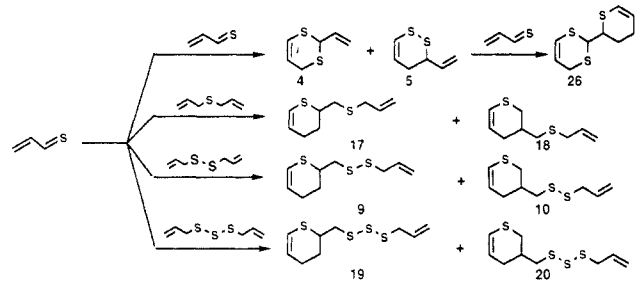
Scheme VI



Scheme VII



phosphine at 70 °C for 1 h results in complete conversion to **17** (Scheme IV). Reductive cleavage of **17** with sodium in liquid ammonia affords 2-(mercaptomethyl)-3,4-dihydro-2*H*-thiopyran (**37**, Scheme V). Compound **37** reacts with allyl methanethiosulfonate affording **9**, reacts with thiobis(imidazole)/2-propenethiol affording **19**, and undergoes oxidation affording **30**. Reductive cleavage of mixtures of **17** and **18** gave mixtures of **37** and 3-(mercaptomethyl)-3,4-dihydro-2*H*-thiopyran (**38**), which upon oxidation afforded disulfides **30–32**.

Comparison of the ^{13}C and ^{1}H NMR spectra of **17**, **9**, and **19** is informative. The $CH_2S_nCH_2$ ^{13}C NMR shifts of **17** (n = 1), **9** (n = 2), and **19** (n = 3) increase from 35.6/35.2 to 42.7/41.2 to 43.4/41.6 ppm, respectively, while the ^{1}H NMR shifts of the $-SCHCH_2S_n-$ methylene protons increase from 2.70 to 2.93/2.94 to 3.09/3.17 ppm, respectively. Barany[19b] reports ^{13}C and ^{1}H NMR deshielding with increasing n in CH_3S_n- and $-CH_2S_n-$. In a further comparison of the ^{1}H NMR spectra of **17**, **9**, and **19**, the $SCH_cCH_aH_bS_n-$ group shows the largest difference between H_a and H_b in the case of **19** (n = 3; δ_a = 3.09, δ_b = 3.17, J_{ab} = 14.1 Hz, J_{ac} = 8.7 Hz, and J_{bc} = 6.5 Hz by LAOCON simulation). The ^{1}H NMR spectrum of **17** shows no separation of H_a and H_b while the spectrum of **9** shows a tight doublet of doublets for H_a and H_b (δ_a = 2.94, δ_b = 2.93, J_{ac} = 6 Hz, J_{bc} = 8.5 Hz), intermediate between the cases of **17** and **19**. Enhancement of the diastereotopic character of the $-CH_2SSS-$ protons compared to the $-CH_2SS-$ protons apparently has not been previously noted. Such an effect, most likely associated with the trisulfide chain conformation, might be useful in interpreting NMR spectra of complex natural trisulfides such as the calichemicins/esperamycins.[19c]

If a mixture of All_2S and an excess of a dienophile such as ethyl acrylate is heated at 200 °C, then the major product isolated in 30% yield is a 1:4 regioisomeric mixture of the thioacrolein–ethyl acrylate Diels–Alder adducts, 2- and 3-carboethoxy-3,4-dihydro-2*H*-thiopyran (**39** (minor) and **40** (major), respectively) (Scheme VI). Structural assignments are supported by ^{13}C NMR studies, analogous to those described above for **35** and **36**, on the sulfones corresponding to **39** and **40**. These reactions and those shown in Scheme III are notable as the first examples of formation of Diels–Alder adducts of thioacrolein with dienophiles, e.g., where thioacrolein functions as a heterodiene.[19d] The scope and full mechanistic aspects of this and related synthetically useful reactions will be presented separately.[12a]

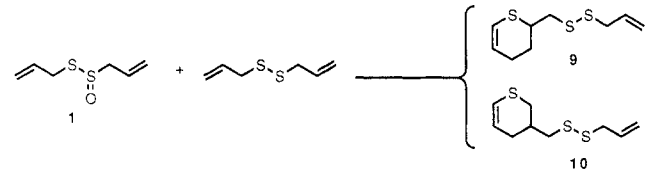
The above results are consistent with a mechanism for formation of the heterocycles in garlic oil involving addition of thioacrolein to All_2S, All_2S_2, and All_2S_3 (Scheme VII). Additional support for this mechanism comes from the following experiments. (1) Heating a 1:1 mixture of All_2S_3 and All_2S_2 at 150 °C for 0.5 h gives predominantly **15**, **16**, **19**, and **20**, together with **8–10** with only minor amounts of **17** and **18**. (2) Heating a 3:1 All_2S–All_2S_2 mixture at 150 °C for 0.5 h gives predominantly **17** and **18** with only minor amounts of **9** and **10**. Since neat All_2S is stable under these conditions, an alternative lower temperature source of thioacrolein is required (see below). (3) Briefly heating a mixture of allicin (**1**) and All_2S_2 at 100 °C gives **9** and **10** with negligible **8** (Scheme VIII). Under these conditions neat All_2S_2 undergoes little decomposition by itself. We have previously indicated that **1** decomposes to thioacrolein under mild conditions;[4] thioacrolein from **1** can be trapped with excess ethyl acrylate at room temperature, affording 1:5 **39**:**40** (Scheme VI). (4) If a mixture of All_2S_2 and excess ethyl acrylate is heated at 110 °C for several hours, a 1:5 **39**:**40** mixture is formed (Scheme VI), a result consistent with the intermediacy of thioacrolein. (5) The 3,4-dihydro-2*H*-thiopyrans formed in reactions involving olefins CH_2=CHX (Scheme IX) are formed in 2-substituted:3-substituted ratios of (1.3–2):1 when X = CH_2Y [Y = H (**33**/**34**), SAll (**17**/**18**), SSAll (**9**/**10**), and n-C_3H_7 (**42**/**43**)] and ratios of 1:(4–5) when X = CO_2Et (**39**/**40**). The regioselectivity seen in the Diels–Alder reaction of thioacrolein with the electron-rich and electron-deficient dienophiles CH_2=$CHCH_2Y$ and CH_2=$CHCO_2Et$, respectively, is in accord with expectations based on HOMO–LUMO interactions and will be discussed more fully elsewhere.[12a] (6) The involvement of thioacrolein is also indicated by the formation of the thioacrolein dimers **4** and **5** (Scheme VII). In addition, a product corresponding to a *trimer* of thioacrolein **26** is also detected. NMR analysis (including 2D HOMCOR studies; see Supplementary Material) shows **26** to be a single regioisomer but a mixture of diastereomers.

While the above observations are consistent with the intermediacy of thioacrolein, it is possible that a *second* reactive heterodiene, thioacrolein *S*-sulfide, CH_2=CHCH=S=S (**41**), may also play a role in diallyl disulfide chemistry, particularly at lower temperatures (see below).

Treatment of 1,2-propanedithiol with thiobis(imidazole)[19e] gives 5-methyl-1,2,3-trithiolane (**22**) in 33% yield while oxidation of 1,2-propanedithiol with iodine according to the procedure of Musker[19f] affords a mixture of *cis*/*trans*-3,7- and *cis*/*trans*-3,8-dimethyl-1,2,5,6-tetrathiacyclooctane (**24** and **25**, Scheme X). The spectroscopic and chromatographic properties of the above synthetic compounds were identical with those of the components of the All_2S_2 pyrolysis (see Table I and Experimental Section).

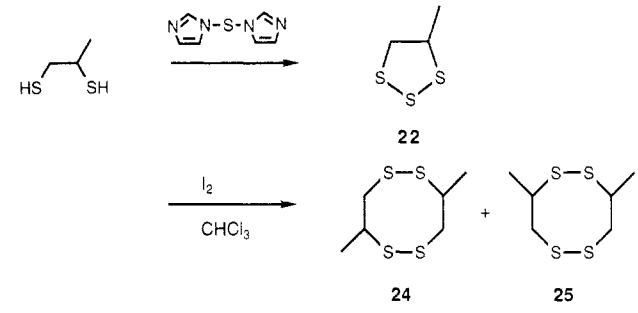
Acyclic Compounds 8 and 11–16. Syntheses of **8** and **11–16** are given in Scheme XI. Spectroscopic and chromatographic properties of the above synthetic alicyclic compounds are identical with those of the components of the All_2S_2 pyrolysis (see Table I and Experimental Section).

Scheme VIII

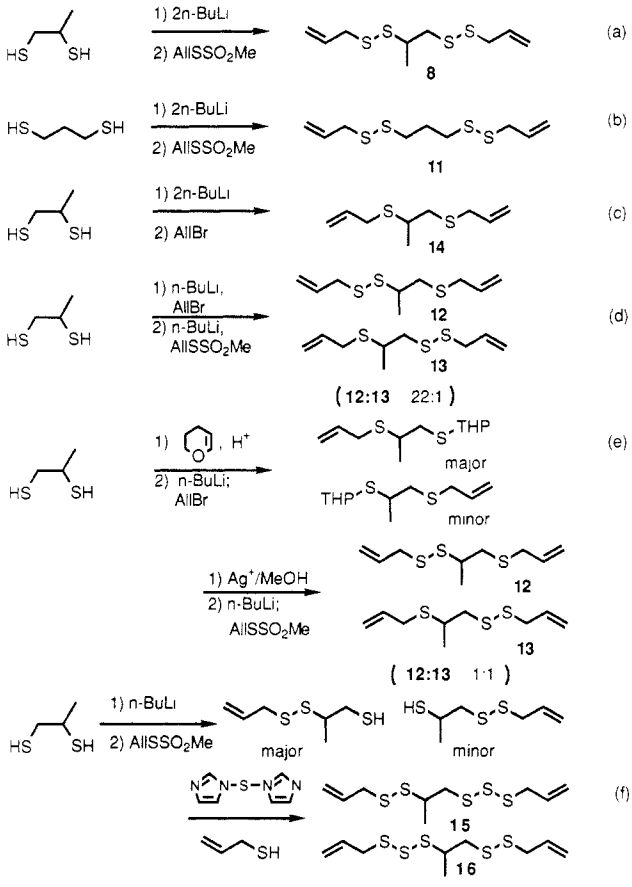


Scheme IX

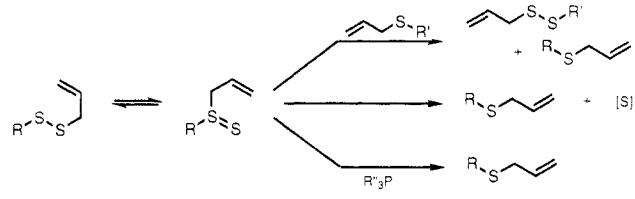
Scheme X



Scheme XI



Scheme XII

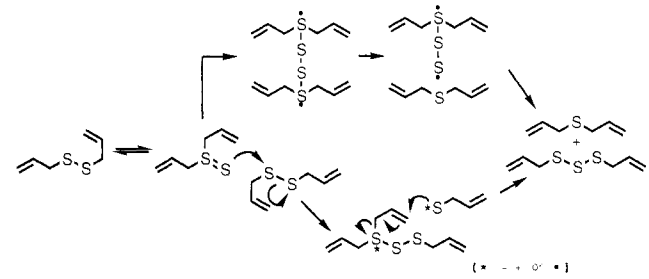


Mechanisms for Primary Processes

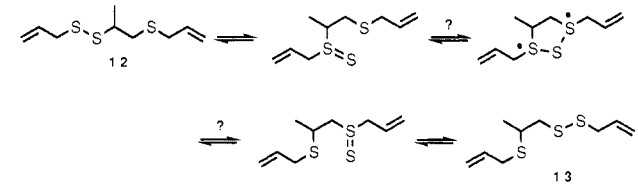
While we have suggested a possible mechanism for formation of dihydrothiopyrans such as **9** and **10**, we have not indicated how compound **8** might be formed nor how thioacrolein is generated from All_2S_2 at 50–150 °C. More generally, we need to consider what occurs first when All_2S_2 is heated. Consideration of the literature as well as the results of some exploratory experiments suggests that this small molecule has a myriad of intra- and intermolecular reaction pathways available: [2,3]-sigmatropic processes, intermolecular sulfurization–desulfurization reactions, and free radical reactions.

[2,3]-Sigmatropic Processes and Allylic Desulfurization and Sulfurization. The pioneering research of Barnard, Baldwin, Mislow, and others[16] has demonstrated that allylic disulfides and trisulfides exist in equilibrium at room temperature with thiosulfoxides formed by facile [2,3]-sigmatropic processes (Scheme XII). The disulfide form is favored since thiosulfoxides have never been directly detected.[16d] At elevated temperatures allylic disulfides can transfer sulfur to allylic sulfides. Some allylic disulfides appear to lose sulfur, affording sulfides even at room temperature. Loss of sulfur from allylic disulfides and trisulfides is particularly favorable in the presence of phosphines. Thiosulfoxides are postulated as intermediates in all of these processes. It is unlikely that *unimolecular* loss of atomic sulfur occurs from thiosulfoxides, or related species such as thiocarbonyl *S*-sulfides, due to the high energy of ^1S. On the basis of the above, All_2S_2 should be capable of directly or indirectly transferring sulfur to a second molecule of All_2S_2, affording All_2S and All_2S_3 via some

Scheme XIII



Scheme XIV



type of bimolecular process involving the corresponding thiosulfoxide form and ionic, radical, or, less likely, diradical species (Scheme XIII). Similar processes should be available to unsymmetrical allylic disulfides such as **8–10** and many of the other compounds described here.

Careful examination of the products formed upon *brief* heating of All_2S_2 (see footnote *f*, Table I) reveals that *twice* as much All_2S_3 is formed as All_2S. It is known that allylic trisulfides undergo [2,3]-sigmatropic rearrangement *10 times more slowly* than allylic disulfides.[19g] We propose that All_2S undergoes sulfurization back to All_2S_2 more rapidly than All_2S_3 undergoes loss of sulfur, resulting in an initial buildup of All_2S_3 compared to All_2S. However, the All_2S concentration increases rapidly and eventually exceeds that of All_2S_3.

We find that disproportionation of All_2S_2 to All_2S and All_2S_3 is much slower in dilute solution than with neat All_2S_2, which is consistent with bimolecular (or higher order) processes for intermolecular sulfur transfer. In view of Mislow's statement[16] that "there appear to exist pathways for the direct transfer of sulfur from disulfides to monosulfides" and his suggestion that "S_8 is not an intermediate in the sulfur transfer reaction", it was of interest to determine if pathways exist for the transfer of sulfur from an allylic disulfide group to a different allylic sulfide group *in the same molecule*, e.g., Scheme XIV. With pure or enriched samples of **12** and **13** in hand, we subjected them separately to pyrolysis. Careful studies showed that interconversion could not be detected under a range of conditions, indicating that there are no intramolecular pathways for allylic disulfide–sulfide interchange, at least in simple acyclic systems. The following additional observations were made based on experiments performed with synthetic **8**, **12**, **13**, and **14**: (1) Heating **14** with sulfur in DMSO at 90 °C for several days led to the gradual formation of **12** and **13** as determined by GC and GC–MS. After 1 week the composition was 63% **14**, 18% **12**, and 8% **13**. (2) Heating **8** with triphenylphosphine in benzene at 60 °C for 0.5 h gives a mixture of **12** (major), **13**, and **14**; desulfurization of **8** with triphenylphosphine also occurs at room temperature. We also find that heating a sample of bis(disulfide) **11** at 150 °C leads to formation of **21** and 4,8-dithiaundeca-1,10-diene, in addition to All_2S_n.

During the early stages of pyrolysis of All_2S_2 the **12**:**13** ratio is considerably greater than that found from desulfurization of **8** (e.g., pyrolysis of All_2S_2 at 65 °C for 3.5 days gives a product showing 10:1 **12**:**13**), requiring that there be an additional mechanism for formation of **12** from All_2S_2 than simply sulfur loss from **8**. This will be discussed below.

Thermochemistry of Diallyl Disulfide. In addition to [2,3]-sigmatropic rearrangement affording thiosulfoxides, a second parallel process likely to occur with All_2S_2 is homolytic bond cleavage. Indeed if a 10:1 mixture of diallyl disulfide and bis(2-methylallyl) disulfide is heated in the dark at 105 °C, formation of *both* All_2S/All_2S_3 and allyl 2-methylallyl disulfide is observed

at comparable apparent rates. Since disulfide interchange (RSSR + R′SSR′ ⇌ RSSR′) is known to occur thermally via a homolytic S_H2 process, it can be concluded that homolytic processes are at least as important in the pyrolysis of All_2S_2 as intermolecular processes involving sulfur exchange from thiosulfoxides.

The predominance of the allyl cation over the allylthio cation in the mass spectrum of diallyl disulfide along with the fact that thermolysis of di-*tert*-butyl disulfide results in preferential C–S cleavage[20] suggested that cleavage of the C–S bond in diallyl disulfide might also be favored. In order to obtain quantitative information on the bond dissociation energies in diallyl disulfide, a mass spectroscopic appearance energy study was performed.

The homolytic bond dissociation energies (BDE) for the S–S and C–S bonds in All_2S_2 were calculated by using the equations

$$\text{BDE(allyl-S—S-allyl)} = 2\Delta H_f(\text{allyl—S}^\bullet) - \Delta H_f(\text{allyl-SS-allyl})$$

$$\text{BDE(allyl-SS—allyl)} = \Delta H_f(\text{allyl—SS}^\bullet) + \Delta H_f(\text{allyl}^\bullet) - \Delta H_f(\text{allyl-SS-allyl})$$

The heats of formation of the allyl—S$^\bullet$ and allyl—SS$^\bullet$ radicals were measured by using the appearance energies (AE) for the ionic reactions $R_1R_2 + e^- \rightarrow R_1^+ + R_2^\bullet + 2e^-$, for which $AE(R_1^+) \geq \Delta H_f(R_1^+) + \Delta H_f(R_2^\bullet) - \Delta H_f(R_1R_2)$. The inequality in this equation can be minimized provided that certain conditions are met: the ionic reaction should be a single-bond rupture and also the reaction of minimum energy in order to avoid uncertainties resulting from the effects of kinetic shift and reverse activation energy. With these precautions, and using an energy-resolved electron beam, good values for the heats of formation of radicals and other species can be obtained.[21]

In the present work we have measured appearance energies for the following processes:

$$\text{allyl-SS—}t\text{-Bu} + e^- \rightarrow t\text{-Bu}^+ + \text{allyl—SS}^\bullet + 2e^- \qquad AE = 9.20 \text{ eV}$$

$$\text{allyl-S—}t\text{-Bu} + e^- \rightarrow t\text{-Bu}^+ + \text{allyl—S}^\bullet + 2e^- \qquad AE = 9.70 \text{ eV}$$

The heat of formation of t-Bu$^+$ is well established at 166 kcal mol^{-1}.[22] The heats of formation of the allyl–sulfur derivatives can be reliably calculated by using the additivity scheme of Benson,[23] whereupon ΔH_f(allyl-SS—t-Bu) = −8.7 kcal mol^{-1} and ΔH_f(allyl-S—t-Bu) = −11.2 kcal mol^{-1}. From these data we get

$$\Delta H_f(\text{allyl—SS}^\bullet) = AE(1) - \Delta H_f(t\text{-Bu}^+) + \Delta H_f(\text{allyl-SS—}t\text{-Bu}) = 37.5 \text{ kcal mol}^{-1}$$

$$\Delta H_f(\text{allyl—S}^\bullet) = AE(2) - \Delta H_f(t\text{-Bu}^+) + \Delta H_f(\text{allyl-S—}t\text{-Bu}) = 46.5 \text{ kcal mol}^{-1}$$

These radical heats of formation, together with ΔH_f(allyl) = 39 kcal mol^{-1} [24] and ΔH_f(allyl-SS-allyl), calculated[23] as +30.9 kcal mol^{-1}, give the following bond dissociation energies:

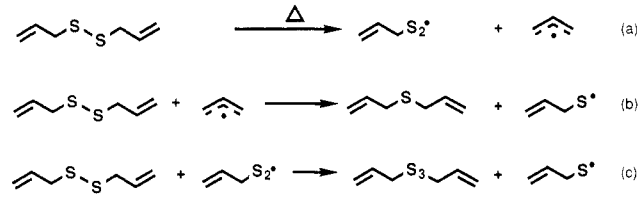
$$D(\text{allyl-SS—allyl}) = 46 \text{ kcal mol}^{-1}$$

$$D(\text{allyl-S—S-allyl}) = 62 \text{ kcal mol}^{-1}$$

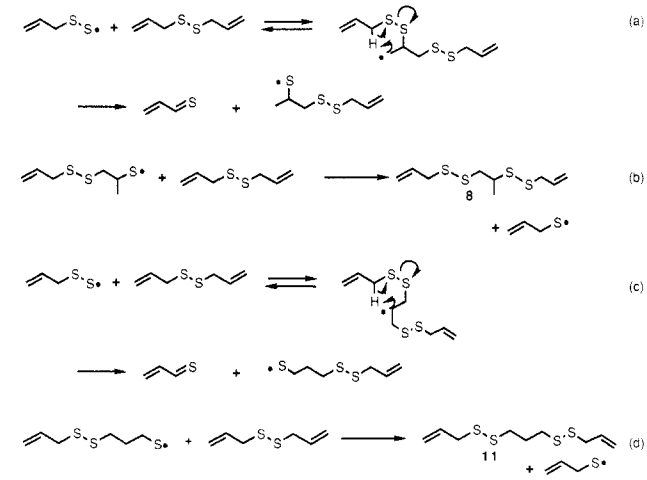
These results show that the allylic C–S bond is weaker than the S–S bond by some 16 kcal mol^{-1}, which should be decisive for the mode of thermal dissociation.

Allylic trisulfides present an interesting case vis-à-vis bond homolysis: the estimated S–S bond energy (46 kcal mol^{-1})[25] in these compounds should be very similar to the C–S bond energy so that *both* S–S and C–S homolysis should occur. Finally, *since allylic C–S$_n$ bonds are common in vulcanized rubber, homolytic cleavage of C–S bonds may represent an important mode of initiation of thermal degradation of these materials at temperatures above 100 °C!*

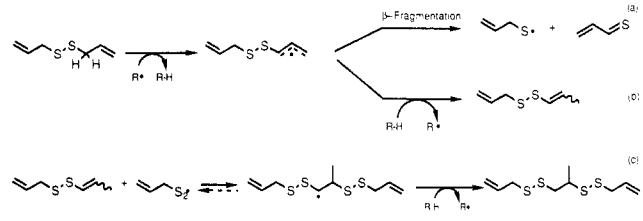
Scheme XV



Scheme XVI



Scheme XVII



Reactions of Radicals with All_2S_2 and Formation of Primary Products. Let us assume that upon thermolysis of All_2S_2, homolytic cleavage of the C–S bond predominates (Scheme XV, step a). Additional routes to All_2S and All_2S_3 can be proposed (steps b and c) paralleling known S_H2 reactions.[26] Two distinct sets of reactions can be postulated to explain preferred formation of **8**.

The first proposal (Scheme XVI) involves comparison of steps a, b and c, d. If, in the intramolecular hydrogen atom abstraction–fragmentation processes (steps a and c), the primary radical intermediate from internal radical addition (step a) is substantially more reactive than the secondary radical intermediate from terminal addition (step c), then formation of **8** (steps a and b) will be favored over formation of **11** (steps c and d) despite a more favorable equilibrium in step c compared to step a. In both steps a and c it is assumed that the equilibria lie far to the left because of the stability of the dithio radicals.[26] The net result of sequence a, b is Markovnikov addition of the allyldithio radical to All_2S_2, a process opposite to that typically encountered in *intermolecular* radical addition to simple olefins.[27a] The key role of *intramolecular* step a in favoring Markovnikov rather than anti-Markovnikov radical addition is reminiscent of the kinetic preference of many intramolecular radical cyclizations for Markovnikov rather than

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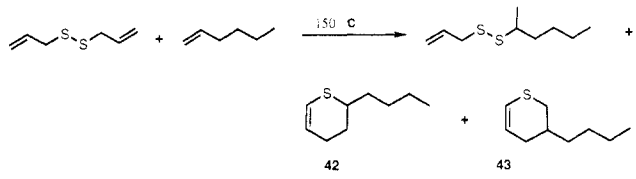
Scheme XVIII

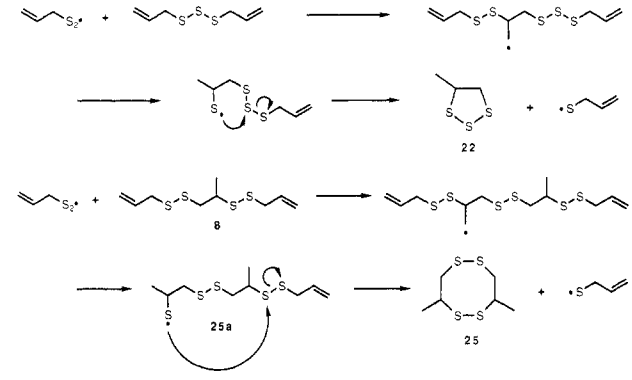


anti-Markovnikov orientation.[27b] The observation that **8** rather than **12** is a primary product suggests that in the case of All_2S_2 an S_H2 process (e.g., step b) is more favorable than an S_H2' (allylic reversal) process.[27c]

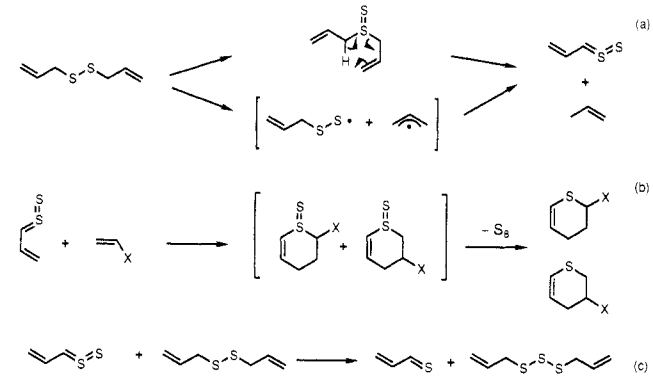
The second proposal (Scheme XVII) involves *intermolecular* hydrogen atom abstraction followed by β fragmentation of the intermediate allyl radical, generating thioacrolein. A parallel process involves radical-catalyzed double-bond isomerization of All_2S_2 to allyl 1-propenyl disulfide followed by allyldithio radical addition to the conjugated double bond, ultimately affording **8**.

The set of reactions in Scheme XVI or XVII can be applied to the major primary products All_2S and All_2S_3 accounting for a portion of the initially formed **12** and **15**, and in particular explaining the high ratio of **12**:**13** at very short reaction times (before **8** begins to accumulate and decompose). The similar apparent rates of formation of many of the products reflect the fact that these products arise by reaction of reactive intermediates with compounds formed via [2,3]-sigmatropic rearrangement of allylic disulfides and trisulfides and that the [2,3] processes should have similar rate constants. Which of the above processes leading to **8** and thioacrolein is more likely? Scheme XVI is more attractive than Scheme XVII because in the former process both thioacrolein and the immediate precursor of **8** are formed in the same step while in the latter process *two different reactions* are required. The observation that the ratio of **8**:(**9** + **10**) is close to 1:1 under all conditions examined is in better agreement with generation of precursors to **8**–**10** in a single step. Several other observations also provide support for the proposal of Scheme XVI: (1) Products **4**, **5**, and **8**–**32** are absent in samples of All_2S_2 subjected to UV irradiation (which should generate the allylthio radical rather than the allyldithio radical[28]). The allylthio radical produced photochemically would have been expected to abstract a hydrogen atom from All_2S_2, initiating the chemistry of Scheme XVII.[29a] That this did not occur argues against the proposal of Scheme XVII. The allylthio radical cannot initiate the reactions of Scheme XVI. (2) Pyrolysis of a 5:1 mixture of 1-hexene and All_2S_2 at 150 °C affords allyl 2-hexyl disulfide[29b] and 2- and 3-butyl-3,4-dihydro-2*H*-thiopyran (**42**, **43**; 2:1) with only minor quantities of allyl 1-hexyl disulfide[29b] (Scheme XVIII). Markovnikov (internal) allyldithio radical addition to 1-hexene analogous to steps a and b of Scheme XVI is postulated. Copyrolysis of 1-hexene and All_2S at 200 °C (1.5 h) affords **42** and **43** (2:1). These experiments are consistent with the proposal of Scheme XVI. (3) When a mixture of All_2S_2 and compound **8** is heated at 150 °C, 3,7- and 3,8-dimethyl-1,2,5,6-tetrathiacyclooctane (**24**/**25**) are formed. We have already noted that **24**/**25** is also found in minor amounts in the All_2S_2 pyrolysates. We suggest that **25** arises by cyclization of a radical such as **25a** by an intramolecular S_H2 process (Scheme XIX); **24** would be formed by an analogous process. A similar mechanism explains formation of **22**.

Scheme XIX



Scheme XX



One observation is more difficult to explain. Experiments reveal that All_2S and All_2S_2 react poorly with thioacrolein generated from sources such as **1** at temperatures below 100 °C, although efficient trapping occurs with the more reactive dienophile ethyl acrylate under these same conditions. The activation energy for the Diels–Alder reaction of thioacrolein with electron-rich dienophiles may therefore be higher than that for reaction with electron-deficient dienophiles. Nonetheless, the ratio of the thioacrolein-derived primary products **9** and **10** to the S_H2-derived **8** during the early stages of reaction *increases* rather than decreases at 50 °C compared to 150 °C (see footnote *f*, Table I)! This observation suggests that there may be an intermediate *in addition to thioacrolein* that generates 3,4-dihydro-2*H*-thiopyrans at low temperatures. One possibility would be thioacrolein *S*-sulfide,[30a] $CH_2{=}CHCH{=}S{=}S$ (**41**), which could be formed and could react as suggested in Scheme XX. At higher temperatures **41** could transfer sulfur to All_2S_2, etc., producing thioacrolein.

The above mechanisms explain the formation of many of the components of the All_2S_2 pyrolysate and garlic essential oil. Disulfide interchange[30b] of the various unsymmetrical disulfides or addition of thioacrolein to these compounds affording mixtures of isomers could account for some of the additional, presently unidentified constituents. As already noted, garlic essential oil has methylthio and propylthio groups in addition to allylthio residues, explaining the greater complexity of this material compared to the diallyl disulfide pyrolysate.

Lipoxygenase-Inhibitory Activity of Isolated Garlic Oil Components and Their Synthetic Homologues

The components of garlic oil that we have thus far isolated and characterized display IC_{50} values toward the soybean 15-lipoxygenase enzyme ranging from 8–37 μM for **8**–**11** to >250 μM (inactive) for diallyl polysulfides; the synthetic model compound 4,8,9,13-tetrathiahexadeca-1,15-diene has IC_{50} = 2 μM (0.6 μg/mL; see Table II). From the data in Table II it is seen that the LO-inhibitory activity increases with molecular weight up to a point and that such changes as introduction of additional un-

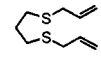
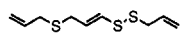
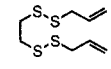
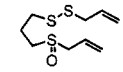
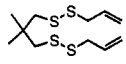
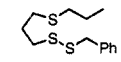
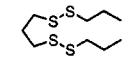
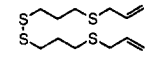
(27) (a) For another example of a sulfur-centered radical giving the product of Markovnikov addition, see: Russell, G. A.; Ngoviwatchai, P.; Tashtoush, H.; Hershberger, J. *Organometallics* **1987**, *6*, 1414. (b) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon–Carbon Bonds*; Pergamon: Oxford, 1986. (c) Hall, D. N.; Oswald, A. A.; Griesbaum, K. *J. Org. Chem.* **1965**, *29*, 3829.

(28) Rosenfeld, S. M.; Lawler, R. G.; Ward, H. R. *J. Am. Chem. Soc.* **1972**, *94*, 9255. Byers, G. W.; Gruen, H.; Giles, H. G.; Schott, H. N.; Kampmeier, J. A. *J. Am. Chem. Soc.* **1972**, *94*, 1016. Burkey, T. J.; Hawari, J. A.; Lossing, F. P.; Lusztyk, J.; Sutcliffe, R.; Griller, D. *J. Org. Chem.* **1985**, *50*, 4966.

(29) (a) Balla, R. J.; Weiner, B. R.; Nelson, H. H. *J. Am. Chem. Soc.* **1987**, *109*, 4804 and references therein. (b) Identified through comparison with authentic samples

(30) (a) For a recent example of another thiocarbonyl *S*-sulfide, see: Huisgen, R.; Rapp, J. *J. Am. Chem. Soc.* **1987**, *109*, 902. (b) Field, L. In *Organic Chemistry of Sulfur*; Oae, S., Ed.; Plenum: New York, 1977; p 303.

Table II. Inhibition of Soybean 15-Lipoxygenase by Garlic Oil Components and Synthetic Homologues

entry #	Compound[a]	IC_{50} (μM)	entry #	Compound[a]	IC_{50} (μM)
1	AllSAll (6)	1800	18		43
2	AllSSMe	860			
3	AllSSAll (2)	514	19		37
4	AllSSSMe	425	20		25
5	AllSSSAll (3)	289			
6	14 (X_2)	319	21		21
7	12 (X_3)	31	22		10
8	8 (X_4)	28			
9	15/16 (X_5/X_5')	20	23		9
10	11	8	24		8
11	17/18 (A_2, B_2)	>650			
12	9 (A_3)	29	25	n-$C_{14}H_{30}$	4[c]
13	10 (B_3)	37	26		2
14	19 (A_4)	51	27	EOG[d]	≈250
15	21	29	28	EOG, heated[e]	≈25
16	30	14	29	EOG, conc.[f]	≈10
17	ajoene[b]	90	30	EOG, heated/conc.[g]	≈2

[a] Structures for numbered compounds may be found in Table I. Synthesis of the compounds in entries 18–24 and 26 are given in the Supplementary Material: entry 18, 4,8-dithiaundeca-1,10-diene; entry 19, 4,5,9-trithiadodeca-1,6,11-triene; entry 20, 4,5,8,9-tetrathiadodeca-1,11-diene; entry 21, 4,5,9-trithiadodeca-1,11-diene 9-oxide; entry 22, 7,7-dimethyl-4,5,9,10-tetrathiatrideca-1,12-diene; entry 23, 1-phenyl-2,3,7-trithiadecane; entry 24, 1,5,9,10-tetrathiatridecane; entry 26, 4,8,9,13-tetrathiahexadeca-1,15-diene. [b] (*E*/*Z*)-4,5,9-trithiadodeca-1,6,11-triene 9-oxide; found in garlic extracts rather than in garlic essential oil; see ref 4. [c] See ref 31. [d] Commercial essential oil of garlic. [e] Commercial essential oil of garlic heated at 150 °C. [f] Commercial essential oil of garlic concentrated under vacuum. [g] Commercial essential oil of garlic heated at 150 °C and then concentrated under vacuum.

saturation (entry 19) including a phenyl group (entry 23) or a sulfoxide group (entry 21), removal of all unsaturation (entry 24), or addition of central geminal methyl groups (to bring the sulfur atoms together through the Thorpe–Ingold effect) have only minor influence. Since *n*-alkanes also show LO inhibition,[31] the activity of the garlic oil components and homologues may be attributed primarily to lipophilic interactions. Nonetheless, the ability of these organosulfur compounds to also bind to the LO iron[32] merits further study. It would also be worthwhile to examine the inhibition of *5-lipoxygenase* by the garlic oil constituents since ajoene inhibits this enzyme to a greater degree than the 15-lipoxygenase enzyme.[9a]

Conclusions

We conclude that the formation of the complex mixture of acyclic and heterocyclic polysulfides in the essential oil of garlic is a consequence of the action of heat during the steam distillation process on the allicin and diallyl disulfide forming thioacrolein and allyldithio radicals. Obviously any culinary procedure that exposes garlic or garlic-spiced food to heat could also generate the types of compounds described herein with possible health benefits associated with the antioxidant or lipoxygenase-inhibitory activity. Our results also indicate that unusual chemistry can still be discovered from the simplest of molecules and that careful scrutiny of commonplace naturally derived products continues to reward the examiner with unexpected and sometimes far-reaching bonuses.

Experimental Section

Appearance Energy Measurements. The appearance energies of *tert*-butyl and allyl ions were measured by using an electrostatic monochromator coupled to a quadrupole mass spectrometer.[33] The initial portions of the ionization energy curves were scanned repeatedly over a range of 0.8 eV, starting at an energy just below the onset. The data were analyzed with a microcomputer data system.[34] The resolved electron beam was of the order of 2×10^{-8} A, with an energy dispersion (FWHM) of about 0.08 eV.

Pyrolysis of Diallyl Disulfide (2) and Isolation of 8, 9, 10, 12, 17, and 18. Commercial **2** (ICN) was freed from diallyl sulfide (**6**) by pumping at room temperature/0.1–0.2 mm for 4 h; **2** was then subjected to repetitive bulb-to-bulb distillation at high vacuum to leave behind diallyl trisulfide (**3**). The so-purified **2** (10 g) of purity >95% sealed under vacuum in a glass tube was immersed in an oil bath (preheated to 150 °C) and heated for 40 min. Bulb-to-bulb distillation at room temperature/0.01 mm removed **6**, **2**, and some **3** (4.3 g), leaving behind a golden brown liquid (5.10 g), which was subjected to flash column chromatography (175 g of silica gel, 1100 mL of hexane/CH_2Cl_2). Using 98:2 hexane/CH_2Cl_2, **2**, **3**, and **6** appeared first followed (at 300 mL of elution) by compound **8** and then closely by **9** and **10**. After 440 mL of total eluent, the polarity was gradually increased in successive stages of 4%, 8%, 12%, and 15% CH_2Cl_2 in hexane to elute the remaining more polar components. Preparative HPLC of the various flash chromatography fractions gave the following compounds:

8 (98% pure by GC, 0.25 g, 5% isolated yield based on unrecovered **2**): chromatographically and spectroscopically identical with synthetic **8** (see below).

9 (95% pure by GC, 0.12 g, 2% isolated yield based on unrecovered **2**): MS *m*/*e* 218 (M^+, 5%), 177 (2%), 145 (5%), 113 (100%), 99 (12%), 85 (33%), 79 (65%), 67 (23%), 45 (48%), 41 (50%); ^{13}C NMR δ 132.93 (CH), 120.75 (CH), 118.70 (CH_2), 118.56 (CH), 43.74 (CH_2), 38.44 (CH), 35.85 (CH_2), 26.55 (CH_2), 22.20 (CH_2); ^1H NMR δ 6.03, (d, J = 10.5 Hz, 1 H), 5.93–5.80 (m, 1 H), 5.74 (dt, J = 10.5, 4 Hz, 1 H), 5.25–5.10 (m, 2 H), 3.45–3.30 (m, including d, J = 7 Hz, 3 H), 2.94 (d, J = 6 Hz, 1 H), 2.93 (d, J = 8.5 Hz, 1 H), 2.23–2.13 (m, 3 H), 1.98–1.83 (m, 1 H).

10 (94% pure by GC, 0.11 g, 2% isolated yield based on unrecovered **2**): MS *m*/*e* 218 (M^+, 5%), 177 (39%), 145 (100%), 113 (4%), 111 (32%), 99 (32%), 85 (23%), 79 (32%), 73 (16%), 71 (15%), 67 (13%), 45 (54%), 41 (54%); ^{13}C NMR δ 133.43 (CH), 119.70 (CH), 119.26 (CH), 118.60 (CH), 43.83 (CH_2), 42.16 (CH_2), 31.41 (CH), 29.65 (CH_2), 29.12 (CH_2); ^1H NMR δ 6.01 (d, 1 H, J = 10 Hz), 5.87 (ddt, 1 H, J = 17, 10, and 7 Hz), 5.69 (dt, 1 H, J = 10 and 4 Hz), 5.21 (d, 1 H, J = 17 Hz), 5.16 (d, 1 H, J = 10 Hz), 3.33 (d, 2 H, J = 7 Hz), 3.05–2.97 (m, 2 H), 2.81–2.70 (m including d, 3 H, J = 6 Hz), 2.39–2.32 (m, 2 H).

12 (98% pure by GC, 0.020 g, 0.35% isolated yield based on unrecovered **2**): chromatographically and spectroscopically identical with synthetic **12** (see below).

17 (97% pure by GC, 0.030 g, 0.53% isolated yield based on unrecovered **2**): chromatographically and spectroscopically identical with synthetic **17** (see below).

18 (78% pure by GC, 0.020 g, 0.35% isolated yield based on unrecovered **2**): chromatographically and spectroscopically identical with synthetic **18** (see below).

GC Analysis of Commercial Garlic Oil Samples. Three different commercial samples of garlic oil (said by the distributors to be variously of Italian, Mexican, or Egyptian origin) were obtained and subjected to analysis by GC (isothermal conditions, 160 °C) and GC–MS. Each was found to contain All_2S_2 (**2**), $AllS_3Me$, All_2S_3 (**3**), All_2S_4 (**7**), **8**, **9**, and

(31) It has been found (Belman, S. unpublished results) that normal alkanes from octane to octadecane inhibit the 15-soybean lipoxygenase; maximum inhibition is obtained with tetradecane (IC_{50} = 4 μM). The inhibitory site for the sulfanes is likely to be the same as that for the alkanes.

(32) (a) For a discussion of the role of iron in LO enzymes, see: Corey, E. J. In *Stereochemistry of Organic and Bioorganic Transformations*; Bartmann, W., Sharpless, K. B., Eds.; VCH Verlagsgesellschaft mbH: Weinheim, 1987; pp 1–12 and references therein. (b) Also see: Nelson, M. J. *J. Am. Chem. Soc.* **1988**, *110*, 2985. (c) For iron–polythioether complexes, see: Olmstead, M. M.; Musker, W. K.; Kessler, R. M. *Acta Crystallogr. Sect. C* **1984**, *C40*, 1172. Wieghardt, K.; Kuppers, H.-J.; Weiss, J. *Inorg. Chem.* **1985**, *24*, 3067.

(33) Maeda, K.; Semeluk, G. P.; Lossing, F. P. *Int. J. Mass Spectrom. Ion Phys.* **1968**, *1*, 395.

(34) Lossing, F. P.; Traeger, J. C. *Int. J. Mass Spectrom. Ion Phys.* **1976**, *19*, 9.

10, in addition to a number of other components, in the proportions indicated for each sample: (1) **2**, 54%; $AllS_3Me$, 19%; **3**, 17%; **7**, 5%; **8**, 0.11%; **9**, 0.07%; **10**, 0.04%. (2) **2**, 45%; $AllS_3Me$, 19%; **3**, 21%; **7**, 7%; **8**, 0.06%; **9**, 0.07%; **10**, 0.02%. (3) **2**, 58%; $AllS_3Me$, 16%; **3**, 15%; **7**, 5%; **8**, 0.03%; **9**, 0.03%; **10**, 0.01%. Heating these samples of garlic oil enhanced the peaks due to **8**, **9**, and **10** as well as the other minor peaks.

6-Methyl-4,5,8,9-tetrathiadodeca-1,11-diene (8). A solution of propane-1,2-dithiol (2.16 g, 20 mmol) in dry THF (40 mL) was treated with *n*-butyllithium (1.6 M, 25 mL, 40 mmol) with stirring at 0 °C. After 0.5 h the mixture was cooled to −17 °C and treated with allyl methanethiosulfonate (6 g, 40 mmol) in dry THF (25 mL). The mixture was warmed to room temperature during 5 h and then poured with vigorous stirring onto a mixture of hexane and water (120 mL apiece). The organic phase was separated, washed with water (4 × 50 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo, affording a light yellow oil (4.4 g) that was a mixture of diallyl disulfide and the title compound (ca. 29 % yield by GC). The diallyl disulfide was removed by pumping at high vacuum and the residue was chromatographed four times (TLC, silica gel, 10:1.5 hexane/CH_2Cl_2), giving an analytically pure (>97%) sample of the title compound: GC RT (160 °C) 15.37 min; ^1H NMR δ 5.93–5.78 (m, 2 H), 5.25–5.14 (m, 4 H), 3.35 (d, 2 H, J = 7.3 Hz), 3.34 (d, 2 H, J = 7.3 Hz), 3.10 (m, 2 H), 2.66 (dd, 1 H, J = 13.0, 9.0 Hz), 1.37 (d, 3 H, J = 6 Hz); ^{13}C NMR δ 132.38 (CH), 132.27 (CH), 117.66 (CH_2), 44.37 (CH_2), 43.69 (CH), 42.01 (CH_2), 41.17 (CH_2), 17.97 (CH_3); MS m/e 252 (M^+, 1%), 147 (48%), 105 (27%), 73 (100%). Anal. Calcd for $C_9H_{16}S_4$: C, 42.82; H, 6.39; S, 50.79. Found: C, 42.96; H, 6.50; S, 51.11.

Pyrolysis of 6-Methyl-4,5,8,9-tetrathiadodeca-1,11-diene (8). Samples of neat **8** were sealed in capillary tubes and heated in an oil bath at 150 °C for time periods ranging from 2 to 30 min. Analysis by GC indicated formation of compounds **12**, **13**, **15**, and **16**. For example, after 30 min the product composition was as follows: **8**, 30%; **12**, 6%; **13**, 12%; **15**/**16**, 4%.

2-(2′,3′-Dithia-5′-hexenyl)-3,4-dihydro-2*H*-thiopyran (9). Sodium (70 mg, 3 mmol) was added to liquid ammonia (3 mL) at −50 °C, the blue mixture was stirred for 20 min, and then ether (2 mL) and a solution of **17** (180 mg, 1 mmol) in ether (2 mL) were added with stirring. After 15 min at −40 °C and 15 min at 0 °C, allyl methanethiosulfonate (600 mg, 43 mmol) in ether (8 mL) was added, and the mixture was allowed to warm to 25 °C during 2 h. After hydrolysis at 0 °C with 10% NH_4Cl and extraction with ether, the organic layer was washed with water, dried (Na_2SO_4), and concentrated. Flash chromatography (silica gel, hexane, hexane + 1% ether) afforded **9** (70 mg, 33% yield) with chromatographic and spectroscopic properties identical with those of the compound isolated above from pyrolysis of diallyl disulfide.

4,5,9,10-Tetrathiatrideca-1,12-diene (11). As in the synthesis of **8**, the title compound was prepared from 1,3-propanedithiol: GC RT 21 min (180 °C); MS m/e 252 (M^+, 0.11%), 211 (12%), 179 (25%), 106 (37%), 73 (100%); ^1H NMR δ 5.86 (ddt, 2 H, J = 17, 10, 7 Hz), 5.20 (d, 2 H, J = 17 Hz), 5.16 (d, 2 H, J = 10 Hz), 3.33 (d, 4 H, J = 7 Hz), 2.79 (t, 4 H, J = 7 Hz), 2.08 (quint, 2 H, J = 7 Hz); ^{13}C NMR δ 133.47 (=CH), 118.50 (=CH_2), 42.26 (CH_2CH=), 37.14 (SCH_2), 28.28 (CH_2). Anal. Calcd for $C_9H_{16}S_4$: C, 42.82; H, 6.39. Found: C, 42.61; H, 6.37.

6- and 7-Methyl-4,5,8-trithiaundeca-1,10-diene (12 and 13, Respectively). A solution of propane-1,2-dithiol (1.08 g, 10 mmol) in dry THF (25 mL) was treated with *n*-butyllithium (1.6 M, 5 mL, 8 mmol) with stirring at −30 °C under argon. After 0.25 h in the mixture was cooled to −78 °C and treated with allyl bromide (1 g, 8.3 mmol) in dry THF (10 mL). The mixture was warmed to 0 °C during 3 h. The mixture was then cooled to −30 °C and treated with 6.3 mL of *n*-butyllithium (1.6 M, 10 mmol). After 0.25 h at −30 °C the mixture was cooled to −78 °C and treated with allyl methanethiosulfinate (1.52 g, 10 mmol) in dry THF (10 mL). The mixture was warmed to 25 °C during 5 h and was then poured with vigorous stirring onto a mixture of hexane and water (100 mL apiece). The organic phase was separated, washed with water (3 × 50 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo, affording a light yellow oil (1.6 g) that was a crude mixture of the title compounds. Low-boiling contaminants were removed by pumping at high vacuum at 22 °C for 3 h. The residue was chromatographed three times (TLC, silica gel, 10:1 hexane/CH_2Cl_2), giving an analytically pure (>96%) sample of the title compounds as a 12:1 mixture (0.9 g, 51%). Anal. Calcd for $C_9H_{16}S_3$: C, 49.09; H, 7.27. Found: C, 48.81; H, 7.55.

If the reaction was stopped after the addition of the allyl bromide and purified by extraction into 2% NaOH solution followed by acidification, extraction (CH_2Cl_2), drying ($MgSO_4$), and concentration in vacuo, a 6:1 mixture of >98% purity could be isolated of 4-thiahept-6-ene-2-thiol (CH_2=$CHCH_2SCH_2CH(SH)CH_3$) as the major product and 2-methyl-3-thiahex-5-ene-1-thiol (CH_2=$CHCH_2SCH(CH_3)CH_2SH$) as the minor product. The identification follows from the δ 1.9 doublet for the SH group in the major product and a very weak δ 1.65 triplet for the minor product. The mixture showed GC RT (160 °C) 3.05 (84%) and 3.07 min (14%); IR 2530 cm^{-1} (w, SH). Treatment of this mixture with 1 equiv of *n*-butyllithium followed by allyl methanethiosulfinate and the usual workup gave a 22:1 mixture of **12** and **13**.

Treatment of 1,2-propanedithiol (11.9 g, 0.11 mol) with 3,4-dihydro-2*H*-pyran (8.4 g, 0.1 mol) and pyridinium *p*-toluenesulfonate (2.52 g, 0.01 mol) in CH_2Cl_2 (100 mL) for 10 h followed by washing with 10% NaOH (4 × 100 mL) and brine (4 × 100 mL), drying ($MgSO_4$), and pumping at high vacuum for 6 h afforded 9 g of a crude product that analyzed for a 3.6:1 mixture of the mono-THP-protected isomers of 1,2-propanedithiol. A portion (1.9 g) of this material upon sequential treatment at −30 °C with *n*-butyllithium followed by allyl bromide gave a crude product whose IR spectrum showed C=C but not SH absorption. This crude product (1.6 g) was dissolved in MeOH (25 mL) and treated with silver nitrate (1.2 g, 7.22 mmol) in water (5 mL) at 25 °C followed by brief heating on a steam bath. Filtration gave a gray solid, which was suspended in $CHCl_3$ and treated with H_2S. The solution was filtered and concentrated, the residue was dissolved in pentane and extracted with 2% NaOH, the basic solution was acidified and extracted with CH_2Cl_2, and the organic layer was dried and concentrated to afford in a low yield a 1:1.6 mixture of 4-thiahept-6-ene-2-thiol (CH_2=$CHCH_2SCH_2CH(SH)CH_3$) as the minor product and 2-methyl-3-thiahex-5-ene-1-thiol (CH_2=$CHCH_2SCH(CH_3)CH_2SH$) as the major product. Treatment of this mixture with 1 equiv of *n*-butyllithium followed by allyl methanethiosulfinate and the usual workup gave a 1:1 mixture of **12** and **13**.

12: ^1H NMR δ 5.91–5.73 (m, 2 H), 5.22–5.11 (m, 4 H), 3.34 (d, J = 7 Hz, 2 H), 3.16 (d, J = 7 Hz, 2 H), 3.00–2.90 (m, 2 H), 2.54–2.46 (m, 1 H), 1.36 (d, J = 7 Hz, 3 H); ^{13}C NMR δ 134.27 (CH), 133.27 (CH), 118.57 (CH_2), 117.35 (CH_2), 45.62 (CH), 43.03 (CH_2), 37.26 (CH_2), 35.48 (CH_2), 19.43 (CH_3); MS m/e 220 (M^+, 0.25%), 115 (69%), 73 (76%), 45 (50%), 41 (100%).

5-Methyl-4,7-dithiadeca-1,9-diene (14). 1,2-Propanedithiol (1.0 g, 0.009 mol) was added to sodium ethoxide (2.2 equiv) prepared by adding sodium (0.46 g, 0.019 mol) to ethanol (10 mL). After the thiolate solution was stirred for 20 min, allyl bromide (2.0 equiv, 2.18 g, 0.018 mol) was added. The cloudy reaction mixture was diluted with ether (100 mL) and washed with water (5 × 60 mL). The organic phase was then dried ($MgSO_4$), the solvent was removed in vacuo, and the residue was distilled at 0.04 mm, giving a colorless oil (0.5 g, 30% yield) 98% pure by GC (RT 4.53 min): MS m/e 188 (M^+, 0.6%), 147 (45%), 115 (47%), 101 (30%), 73 (100%), 59 (86%); ^1H NMR δ 5.89–5.72 (m, 2 H), 5.17–5.06 (m, 4 H), 3.19 (d, 2 H, J = 7.40 Hz), 3.14 (d, 2 H, J = 6.70 Hz), 2.88–2.77 (m, 2 H), 2.49 (dd, 1 H, J = 8 and 12 Hz), 1.34 (d, 3 H, J = 6.78 Hz); ^{13}C NMR δ 134.69 (CH), 134.45 (CH), 117.13 (CH_2), 116.83 (CH_2), 38.54 (CH), 37.87 (CH_2), 35.50 (CH_2), 33.96 (CH_2), 20.19 (CH_3). Anal. Calcd for $C_9H_{16}S_2$: C, 57.39; H, 8.56. Found: C, 57.47; H, 8.62.

7- and 8-Methyl-4,5,6,9,10-pentathiatrideca-1,12-diene (15 and 16). A solution of 1,2-propanedithiol (3 g, 28 mmol) in dry THF (40 mL) was treated with *n*-butyllithium (2.5 M, 8 mL, 20 mmol) with stirring at −30 °C under argon. After 20 min the mixture was cooled to −70 °C and treated with allyl methanethiosulfonate (3.1 g, 20 mmol) in dry THF (20 mL). After 30 min the reaction mixture is poured into 1:2 water/hexane, and the organic layer is washed with water, dried ($MgSO_4$), and concentrated in vacuo. Kugelrohr distillation (110 °C/0.1 mm) of the residue gave a mixture (1.12 g, 31% yield) of 2-methyl-3,4-dithiahept-6-ene-1-thiol (CH_2=$CHCH_2SSCH(CH_3)CH_2SH$) and 4,5-dithiaoct-6-ene-2-thiol (CH_2=$CHCH_2SSCH_2CH(SH)CH_3$): MS (major) m/e 180 (M^+, 1%), 106 (3%), 77 (5%), 76 (5%), 75 (100%), 74 (7%), 73 (12%), 71 (3%), 64 (7%), 59 (7%), 58 (3%); (minor) m/e 180 (M^+, 1%), 106 (4%), 97 (4%), 77 (5%), 76 (5%), 75 (100%), 74 (7%), 73 (13%), 71 (3%), 64 (6%), 61 (8%), 59 (7%), 58 (4%); ^1H NMR mixture δ 5.91–5.75 (m, 1 H), 5.50–5.12 (m, 2 H), 3.33 (d, J = 7 Hz, 2 H), 3.30–3.10 (h, J = 7 Hz, 1/3 H), 3.00–2.80 (m, 2 H), 2.70–2.58 (m, 2/3 H), 1.87 (d, J = 6 Hz, 1/3 H), 1.58 (t, J = 8 Hz, 2/3 H), 1.38 (d, J = 7 Hz, 1 H), 1.33 (d, J = 7 Hz, 2 H); ^{13}C NMR (major) δ 133.15 (CH), 118.59 (CH_2), 48.44 (CH), 42.85 (CH_2), 30.65 (CH_2), 18.67 (CH_3); (minor) δ 133.25 (CH), 118.63 (CH_2), 50.13 (CH_2), 42.17 (CH_2), 34.45 (CH), 23.22 (CH_3); MS (major) m/e 180 (M^+, 1%), 106 (3%), 77 (5%), 76 (5%), 75 (100%), 74 (7%), 73 (12%), 71 (3%), 64 (7%), 59 (7%), 58 (3%); (minor) m/e 180 (M^+, 1%), 106 (4%), 97 (4%), 77 (5%), 76 (5%), 75 (100%), 74 (7%), 73 (13%), 71 (3%), 64 (6%), 61 (8%), 59 (7%), 58 (4%); IR 2970, 2920, 1640, 1460, 1420, 1375, 1120, 990, 920 cm^{-1}.

In a three-necked, round-bottom flask (trimethylsilyl)imidazole (380 mg, 2.7 mmol) in hexane (1 mL) was added to sulfur dichloride (140 mg, 1.35 mmol) in hexane (0.5 mL). After 20 min at room temperature, the mixture was cooled to 0 °C and a mixture of 2-methyl-3,4-dithiahept-6-ene-1-thiol, 4,5-dithiaoct-6-ene-2-thiol (120 mg, 0.67 mmol), 2-propenethiol (150 mg, 2.0 mmol), and hexane (2 mL) was added. After

1 h at room temperature, the mixture was filtered through Celite and concentrated in vacuo. Flash chromatography (hexane/1% ether) gave a mixture of the title compounds as a colorless oil (90 mg, 73% yield): ^{1}H NMR δ 5.90–5.73 (m, 2 H), 5.25–5.08 (m, 4 H), 3.60–3.10 (m, including two d at 3.45 and 3.29 with J = 7.5 Hz, 6 H), 2.85–2.65 (m, 1 H), 1.38 (d, J = 7 Hz, 1 H), 1.33 (d, J = 7 Hz, 2 H); ^{13}C NMR δ 133.26 (CH), 132.57 (CH), 119.31 (CH_2), 118.77 (CH_2), 45.65 (CH), 45.38 (CH_2)*, 45.12 (CH_2), 44.41 (CH)*, 43.03 (CH_2)*, 42.19 (CH_2), 41.71 (CH_2), 41.58 (CH_2)*, 19.20 (CH_3)*, 18.92 (CH_3) (the asterisk indicates bands associated with the major isomer); MS (major) m/e 179 (41%), 138 (9%), 137 (17%), 105 (10%), 104 (7%), 75 (6%), 74 (9%), 73 (69%), 71 (6%), 64 (13%), 59 (10%), 47 (10%), 46 (7%), 45 (39%), 42 (7%), 41 (100%), 39 (61%), 38 (8%); (minor) m/e 219 (1%), 179 (41%), 138 (9%), 137 (16%), 105 (11%), 74 (12%), 73 (69%), 71 (6%), 64 (12%), 59 (10%), 47 (9%), 46 (7%), 45 (40%), 42 (6%), 41 (100%), 40 (9%), 39 (62%), 38 (8%).

2-(2′,3′,4′-Trithia-6′-heptenyl)-3,4-dihydro-2*H*-thiopyran (19). In a three-necked, round-bottom flask that had been flame dried and purged with argon, sulfur dichloride (125 mg, 1.2 mmol) in hexane (2 mL) was introduced and cooled under argon to 0 °C. At this temperature (trimethylsilyl)imidazole (335 mg, 2.4 mmol) in hexane (2 mL) was added followed 20 min later by a mixture of crude 2-(mercaptomethyl)-3,4-dihydro-2*H*-thiopyran (**37**, prepared from **17** as described below; 100 mg, 0.6 mmol), 2-propenethiol (135 mg, 1.8 mmol), and 2:1 hexane/ether (3 mL). After 3 h at 25 °C, the mixture was filtered through Celite and concentrated in vacuo. Flash chromatography (hexane/2% CH_2Cl_2) gave the title compound as a colorless oil (85 mg, 56% yield): ^{1}H NMR δ 6.01 (d, J = 10 Hz, 1 H, H6), 5.88 (ddt, J = 17, 10, 7 Hz, 1 H, H12), 5.75 (dt, J = 10, 4 Hz, 1 H, H5), 5.30–5.18 (m, 2 H, H13), 3.62–3.45 (m with d, J = 7 Hz, 3 H, H11, H2), 3.17 (dd, J = 14.06, 6.46 Hz, 1 H, H7), 3.09 (dd, J = 14.06, 8.67 Hz, 1 H, H7′), 2.30–2.10 (m, 3 H, H4, H3), 2.05–1.90 (m, 1 H, H3′); ^{13}C NMR δ 132.60 (CH, C12), 120.79 (CH, C6), 119.32 (CH_2, C13), 118.48 (CH, C5), 43.43, 41.58 (CH_2, C11/C7), 38.07 (CH, C2), 26.52 (CH_2, C4), 22.01 (CH_2, C3).

Additional Syntheses of 9, 10, 19, and 20. When a 9:1 **17**:**18** mixture was mixed with diallyl disulfide (**2**; 0.8 equiv) and heated at 150 °C for 2 h, analysis by GC and GC–MS indicated the presence of a 9:1 **9**:**10** mixture and **19**. When the same experiment was repeated with a 1:3 **17**:**18** mixture, a 1:3 **9**:**10** product mixture was formed along with **20**.

2-Methyl- and 3-Methyl-3,4-dihydro-2*H*-thiopyran (33 and 34, Respectively) and Their *S*,*S*-Dioxides (35 and 36), 2- and 3-(2′-Thia-4′-pentenyl)-3,4-dihydro-2*H*-thiopyran (17 and 18), Bis[2-(3,4-dihydro-2*H*-thiopyranyl)methyl] Sulfide (27), Bis[3-(3,4-dihydro-2*H*-thiopyranyl)-methyl] Sulfide (28), and 2-(3,4-Dihydro-2*H*-thiopyranyl)methyl 3-(3,4-Dihydro-2*H*-thiopyranyl)methyl Sulfide (29). In a thick glass round-bottomed flask with a long neck and a pressure valve, diallyl sulfide (30.0 g, 0.263 mol) was introduced, degassed, and pyrolyzed in a oil bath at 200 °C for 12 h. (*Caution*! On some occasions tubes have exploded due to buildup of internal pressure. The reaction mixture should be no more than one-third the tube volume. The reaction must be carried out in a hood behind a safety shield.) After cooling to room temperature, the crude mixture was distilled and the first fraction (100–150 °C; 1.5 g), containing 50% of regioisomers **33** and **34** in a ratio of 1.3:1 (2.5% yield) and 50% of the starting material, was collected. The adducts can be separated by flash chromatography (petroleum ether, bp <60 °C).

33: MS m/e 114 (M^+, 75%), 99 (100%), 85 (29%), 81 (27%), 79 (16%), 73 (13%), 72 (47%), 71 (36%), 65 (23%), 60 (23%), 59 (16%), 58 (14%), 55 (8%), 54 (9%), 53 (12%).

34: MS m/e 114 (M^+, 67%), 99 (82%), 85 (16%), 81 (11%), 79 (9%), 73 (13%), 72 (100%), 71 (42%), 69 (9%), 68 (17%), 67 (13%), 65 (15%), 58 (9%), 55 (12%), 53 (9%), 51 (10%).

As it was difficult to separate **33** and **34** from the solvent, the crude distillate was directly oxidized with peracetic acid (6.6 g of 35% peracid, 26 mmol) in dichloromethane (10 mL) for 13 h at 25 °C. After neutralization with Na_2CO_3 (6 g), filtration through Celite–$MgSO_4$, and concentration, 1.3 g of a mixture of three sulfones was obtained. Separation by flash chromatography (ether/pentane, 1/1 and then 2/1) gave 270 mg of diallyl sulfone, 220 mg of 2-methyl-3,4-dihydro-2*H*-thiopyran *S*,*S*-dioxide (**35**), a colorless solid, mp 78–79 °C, and 120 mg of 3-methyl-3,4-dihydro-2*H*-thiopyran *S*,*S*-dioxide (**36**), a colorless oil. **35**: ^{1}H NMR ($CDCl_3$) δ 6.46 (m, 1 H), 6.37 (m, 1 H), 3.17 (m, 1 H), 2.38 (m, 2 H), 2.19 (m, 2 H), 1.41 (d, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 138.7 (CH), 129.0 (CH), 54.3 (CH), 27.6 (CH_2), 24.2 (CH_2), 11.0 (CH_3); IR (neat) 3050, 2950, 1630, 1460, 1430, 1310, 1280, 1180, 1120, 1040 cm^{-1}; GC–MS m/e 146 (M^+, 16%), 129 (100%), 104 (39%), 98 (50%), 97 (44%), 81 (60%), 80 (45%), 79 (72%), 67 (79%), 65 (38%), 56 (47%), 55 (59%), 53 (55%). **36**: ^{1}H NMR ($CDCl_3$) δ 6.47 (ddd, J = 2.5, 5, and 11 Hz, 1 H), 6.39 (d, J = 11 Hz, 1 H), 3.17 (d, J = 13 Hz, 1 H), 2.90 (t, J = 13 Hz, 1 H), 2.63 (m, 1 H), 2.45 (dt, J = 5 and 19 Hz, 1 H), 1.98 (dd, J = 10.5 and 19 Hz, 1 H), 1.17 (d, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 137.8 (CH), 129.0 (CH), 56.8 (CH_2), 32.9 (CH_2), 27.9 (CH), 20.7 (CH_3); IR (neat) 3060, 2980, 2950, 1630, 1470, 1440, 1420, 1360, 1300, 1260, 1130 cm^{-1}; GC–MS m/e 146 (M^+, 16%), 129 (59%), 117 (49%), 104 (39%), 101 (46%), 97 (63%), 81 (60%), 79 (80%), 67 (79%), 65 (44%), 56 (50%), 55 (100%), 53 (61%).

Kugelrohr distillation (110 °C/0.2 mm) of the remaining nonvolatile liquid material gave 1.3:1 **17**:**18** (5.1 g, 21% yield). The regioisomers were separated by HPLC (hexane). The distillation residue contains minor amounts of bis[2-(3,4-dihydro-2*H*-thiopyranyl)methyl] sulfide (**27**), bis[3-(3,4-dihydro-2*H*-thiopyranyl)methyl] sulfide (**28**), and 2-(3,4-dihydro-2*H*-thiopyranyl)methyl 3-(3,4-dihydro-2*H*-thiopyranyl)-methyl sulfide (**29**). These same three compounds could also be produced by heating a 1:3 mixture of **2** and **17**/**18** at 200 °C for 1.5 h. The identification of **27**–**29** follows from the following experiments. If a 9:1 **17**:**18** mixture and diallyl sulfide (2 equiv) are heated at 200 °C for 2 h, analysis of the product by GC indicates formation of a 1.6:1 **27**:**29** mixture; the analogous experiment using a 1:3 **17**:**18** mixture affords a 3:10:4 **27**:**29**:**28** mixture.

In an alternative procedure diallyl sulfide was heated at 200 °C for 1.5 h. Flash distillation at 0.1 mm led to recovery of 64% of the original diallyl sulfide. Kugelrohr distillation of the residue afforded 17% of a 1.8:1 **17**:**18** mixture (46% yield based on unrecovered diallyl sulfide).

17: ^{1}H NMR δ 6.00 (d, J = 10.0 Hz, 1 H, H6), 5.90–5.70 (m, 2 H, H5, H10), 5.15–5.06 (m with d, J = 14.0 Hz, 2 H, H11), 3.25–3.15 (m with d, J = 7.0 Hz, 3 H, H2, H7), 2.70 (d, 2 H, J = 7 Hz, 2 H, H9), 2.20–2.10 (m, 3 H, H3a, H4), 1.90–1.80 (m, 1 H, H3b); ^{13}C NMR δ 134.11 (CH), 120.72 (CH), 118.70 (CH), 117.38 (CH_2), 39.15 (CH), 35.60 (CH_2), 35.20 (CH_2), 27.32 (CH_2), 22.60 (CH_2); MS m/e 186 (M^+, 15%), 145 (91%), 113 (14%), 111 (49%), 99 (100%), 79 (63%), 73 (20%), 65 (64%).

18: ^{1}H NMR δ 6.01 (d, J = 10.0 Hz, 1 H, H6), 5.85–5.66 (m, 2 H, H5, H10), 5.13–5.07 (m, 2 H, H11), 3.14 (d, J = 7.5 Hz, 2 H, H9), 2.99 (br d, J = 13.0 Hz, 1 H, H2eq), 2.71 (dd, J = 12.0, 8.0 Hz, 1 H, H2ax), 2.53 (dd, J = 7.0, 3.5 Hz, 2 H, H7), 2.33 (br d, J = 18 Hz, 1 H, H4a), 2.14 (m, 1 H, H3), 1.94 (m with d, 1 H, H4b); ^{13}C NMR δ 134.30 (CH), 119.90 (CH), 119.15 (CH), 117.10 (CH_2), 35.78 (CH_2), 35.09 (CH_2), 31.89 (CH), 30.03 (CH_2), 29.55 (CH_2); MS m/e 186 (M^+, 5%), 145 (100%), 111 (23%), 99 (44%), 79 (36%).

17 + 18: Anal. Calcd for $C_9H_{14}S_2$: C, 58.01; H, 7.57. Found: C, 57.79; H, 7.48.

27: GC RT 76 min; MS m/e 260 (M^+ + 2, 3%), 258 (M^+, 20%), 146 (11%), 145 (11%), 113 (84%), 112 (100%), 99 (81%), 79 (91%).

28: GC RT 77 min; MS m/e 260 (M^+ + 2, 3%), 258 (M^+, 21%), 146 (36%), 113 (58%), 112 (69%), 99 (68%), 97 (46%), 79 (100%), 65 (40%).

29: GC RT 78 min; MS m/e 258 (M^+, 9%), 146 (78%), 112 (59%), 79 (100%).

Copyrolysis of Diallyl Disulfide/Diallyl Sulfide (2/6) and Diallyl Disulfide/Diallyl Trisulfide (2/3). Samples of disulfide and monosulfide in varying ratios (1:1, 1:3, 1:5) were sealed in capillary tubes and heated in an oil bath at 150 °C, and the product composition was checked by GC at different time intervals. A time of 5 min was taken as the standard, this being representative of the chemistry occurring on initial thermolysis of the diallyl disulfide. In all cases, increasing the percentage of All_2S resulted in preferential formation of the secondary products (**12**, **13**, **17**, and **18**) over the primary products (**8**–**10**). The addition of monosulfide inhibits the formation of **7**–**10**, **15**/**16**, **19**, and **20**. These latter peaks (**15**/**16**, **19**, and **20**) are enhanced on heating disulfide and trisulfide (150 °C, 5 min) while formation of compounds **8**–**10**, and **12**, **13**, **17**, and **18** is inhibited.

Copyrolysis of Diallyl Disulfide (2) and 2- and 3-(2′-Thia-4′-pentenyl)-3,4-dihydro-2*H*-thiopyran (17 and 18). A 1:3 mixture of diallyl disulfide (**2**) and **17**/**18** was sealed in a capillary tube and heated in an oil bath at 150 °C for 1.5 h. GC and GC–MS analysis of the pyrolysate indicated the presence of compounds **9** and **10**. Similar results were obtained upon heating a 1:1 mixture of **2** and **17**/**18**.

Copyrolysis of Allicin (1) and Diallyl Disulfide (2). A 1:4 mixture of allicin (**1**) and diallyl disulfide (**2**) was sealed in a capillary tube and heated in an oil bath at 100 °C for 15 min. GC analysis indicated the presence, among other products, of **9** (0.22%) and **10** (0.26%) but little **8**.

2- and 3-(Mercaptomethyl)-3,4-dihydro-2*H*-thiopyran (37, and 38). Ammonia (25 mL) was liquefied in a three-necked, round-bottomed flask that had been flame dried, purged with argon, and cooled to −50 °C. Finely cut sodium (0.87 g, 0.037 mol), rinsed in hexane and wiped dry, was added to the reaction flask. The solution turned blue and became viscous. The flask was warmed to −5 °C, and anhydrous ether (10 mL) was syringed into the flask, followed by addition of the cyclic sulfide mixture (**17**, **18**) in anhydrous ether (10 mL). After 0.5 h the reddish-orange reaction was quenched with cold water (5 mL), keeping the flask chilled. After 10 min of stirring, a few drops of 10% H_2SO_4 was carefully

added while the flask was cooled at 0 °C. The whitish-yellow slurry was stirred at room temperature for an additional 0.5 h. The reaction mixture was diluted with ether (100 mL), and the organic phase was washed with water (5 × 50 mL). The ethereal layer was dried ($MgSO_4$) and the solvent was removed in vacuo to give a colorless oil (0.35 g, 20% yield). The crude thiol mixture was purified by preparative TLC (silica gel, 30% CH_2Cl_2/hexane) and showed the following: ^{13}C NMR δ 120.76 (CH), 119.70 (CH), 119.23 (CH), 118.39 (CH), 42.54 (CH), 35.32 (CH), 29.33 (CH_2), 29.22 (CH_2), 29.02 (CH_2), 26.57 (CH_2), 22.09 (CH_2). There should be 12 lines (6 lines for each regioisomer). There are in fact only 11 lines, indicating coalescence of two closely spaced CH_2 carbons (presumably 29.33 ppm, which is particularly intense). The ^1H NMR spectrum shows a closely spaced dd pattern in the olefinic region with a coupling constant of 6.0 Hz due to the cis coupling of the olefinic protons; the remainder of the spectrum of the mixture is complex. MS: a *m/e* 146 (M^+, 37%), 112 (14%), 99 (100%), 97 (16%), 79 (20%), 65 (47%); b *m/e* 146 (M^+, 76%), 112 (36%), 99 (57%), 97 (58%), 85 (42%), 79 (100%).

2-(Mercaptomethyl)-3,4-dihydro-2*H*-thiopyran (37). Following the above procedure, a pure sample of sulfide **17** (200 mg, 1.1 mmol) was reduced with sodium (90 mg, 3.8 mmol) to afford 100 mg of a mixture of **37** (ca. 66 mg, 40% yield) and diallyl disulfide (ca. 26 mg). Compound **37**: MS *m/e* 146 (M^+, 29%), 112 (14%), 99 (100%), 97 (16%), 85 (16%), 79 (25%), 71 (22%), 65 (61%), 59 (12%), 58 (15%), 47 (24%), 45 (83%), 41 (26%); ^1H NMR δ 5.99 (d, J = 10 Hz, 1 H, H6), 5.74 (dt, J = 10, 4 Hz, 1 H, H5), 3.15 (dq, J = 3, 7 Hz, 1 H, H2), 2.87–2.67 (m, 2 H, H7), 2.25–2.10 (m, 3 H, H4/H3), 2.0–1.85 (m, 1 H, H3′), 1.63 (t, J = 8 Hz, 1 H, SH); ^{13}C NMR δ 120.61 (CH, C6), 118.49 (CH, C5), 42.46 (CH, C2), 29.19 (CH_2, C7), 26.47 (CH_2, C4), 21.99 (CH_2, C3); IR 2920, 2870, 1610, 1430, 1120 cm^{-1}.

Bis[2-(3,4-dihydro-2*H*-thiopyranyl)methyl] Disulfide (30), Bis[3-(3,4-dihydro-2*H*-thiopyranyl)methyl] Disulfide (31), and 2-(3,4-Dihydro-2*H*-thiopyranyl)methyl 3-(3,4-Dihydro-2*H*-thiopyranyl)methyl Disulfide (32). Procedure 1. Iodine (0.35 g, 0.0013 mol) in ethanol (20 mL) was added to an ethanolic solution (15 mL) of thiols **37/38** (0.2 g, 0.0013 mol) at 0 °C. After stirring for 1 h at room temperature, the reaction mixture was diluted with ether (80 mL), and the organic phase was washed with $Na_2S_2O_3$ (4 × 50 mL) to remove excess iodine. The combined organic layers were dried ($MgSO_4$) and the solvent was removed in vacuo to give a pale yellow oil (0.28 g, 74% yield). Purification by preparative TLC (20% CH_2Cl_2/hexane) gave a mixture of the title disulfides **30**, **31**, and **32** (0.19 g, 50% yield), 91% pure by GC.

30: GC RT 85 min; MS *m/e* 292 (M^+ + 2, 2%), 290 (M^+, 9%), 145 (16%), 113 (100%), 85 (27%), 79 (56%), 45 (43%), 41 (34%).

32: GC RT 86 min; MS *m/e* 292 (M^+ + 2, 4%), 290 (M^+, 24%), 145 (100%), 113 (96%), 85 (45%), 79 (82%), 45 (79%), 41 (50%).

31: GC RT 87 min; MS *m/e* 290 (M^+, 12%), 145 (100%), 113 (6%), 99 (29%), 45 (44%), 41 (27%).

Procedure 2. A 9:1 **17**:**18** sulfide mixture in ether was added to sodium and liquid ammonia at −50 °C. After 15 min at −40 °C and 15 min at 0 °C, iodine was added and the mixture was stirred for 3 h and then quenched by washing with 20% $Na_2S_2O_3$ solution and extracting the resulting disulfides into hexane. Analysis by GC indicated the presence of a 5:1 **30**:**32** mixture.

Procedure 3. A 1.6:1 **17**:**18** sulfide mixture in ether was reduced with sodium–liquid ammonia, the reduction product oxidized with iodine, and the reaction mixture worked up as in procedure 2. Analysis by GC indicated the presence of a 3:4:1 **30**:**32**:**31** mixture.

4,5,9-Trithiadodeca-1,11-diene (21). As in the synthesis of **12**/**13**, the title compound was prepared from 1,3-propanedithiol: MS *m/e* 220 (M^+, 0.07%), 179 (13%), 147 (100%), 106 (68%), 105 (63%), 73 (92%); ^1H NMR δ 6.10–5.25 (m, 2 H), 5.20–4.75 (m, 4 H), 3.25 (d, 2 H, J = 7 Hz), 3.05 (d, 2 H, J = 7 Hz), 2.85–2.25 (m, 4 H), 2.15–1.60 (m, 2 H); ^{13}C NMR δ 134.30 (C2), 133.48 (C11), 118.47 (C1), 117.04 (C12), 42.22 (C3), 37.48 (C6), 34.69 (C10), 29.11 (C8), 28.45 (C7).

4-Methyl-1,2,3-trithiolane (22). In a three-necked, round-bottom flask a solution of (trimethylsilyl)imidazole (2.8 g, 20 mmol) in hexane (10 mL) was added to sulfur dichloride (1.03 g, 10 mmol) in hexane (10 mL). After 30 min at 25 °C, 1,2-propanedithiol (1.08 g, 10 mmol) in hexane (40 mL) was added over the course of 15 min. After 3 h at 25 °C the reaction mixture was filtered through Celite and concentrated. Flash chromatography (silica gel, hexane/ether, 95/5) afforded the title compound (0.45 g, 33% yield) as an unstable oil, which above 0 °C decomposed to a compound of molecular weight 212. The title compound shows the following: MS *m/e* 138 (M^+, 72%), 96 (18%), 74 (64%), 73 (63%), 64 (52%), 59 (34%), 46 (26%), 45 (76%), 41 (100%); ^1H NMR δ 3.3 (m, 3 H), 1.35 (d, J = 6 Hz, 3 H).

***cis*/*trans*-3,7- and *cis*/*trans*-3,8-Dimethyl-1,2,5,6-tetrathiacyclooctane (24 and 25).** A solution of 1,2-propanedithiol (1.08 g, 10 mmol) in chloroform (25 mL) and a solution of iodine (2.66 g, 10.5 mmol) in chloroform (85 mL) were added simultaneously at room temperature to a solution of triethylamine (2.22 g, 22 mmol) in chloroform (50 mL). After 5 h the reaction mixture was washed sequentially with water, 0.1 M H_2SO_4, and water, dried (Na_2SO_4), and concentrated. After flash chromatography (hexane/1% ether), a mixture of the expected isomers was isolated as a colorless oil (0.8 g, 75%) yield: ^1H NMR δ 3.6–3.0 (m, 5 H), 3.0–2.7 (m, 1 H), 1.45–1.25 (m, 6 H); ^{13}C NMR δ 49–45.3 (CH_2), 45.3–44 (CH), 24–18 (CH_3); IR (KBr film) 2970, 2920, 1450, 1400, 1380, 1140 cm^{-1}; MS *m/e* 214 (M^+ + 2, 10%), 212 (M^+, 53%), 138 (58%), 106 (47%), 73 (63%), 64 (42%), 45 (55%), 41 (100%).

2- and 3-Carboethoxy-3,4-dihydro-2*H*-thiopyran (39 and 40). Procedure 1. A mixture of diallyl sulfide (4.0 g, 0.035 mol) and ethyl acrylate (17.5 g, 0.175 mol) was placed in a long-necked Pyrex round-bottom flask fitted with a Teflon vacuum stopcock plug (ACE Glass Catalog no. 8193). The mixture was placed under vacuum and heated for 5 h at 210 °C. After removal of volatiles in vacuo, the brown reaction mixture weighed 18.8 g. The mixture still contained unreacted ethyl acrylate along with desired product and polymeric material. Kugelrohr distillation of 4.0 g of this material gave 1.6 g of distillate, which by GC showed primarily ethyl acrylate and small amounts of allyl sulfide. The orange, viscous distillation residue contained a 1:4 **39**:**40** mixture. Flash chromatography of 2.0 g of this mixture (silica gel, 1% Et_2O/99% 1:1 pentane and 2,2-dimethylbutane) afforded product after 450 mL of elution, at which point a more polar solvent (2% Et_2O; 650 mL) was used. The GC trace of the purified fractions showed 88% of **40** and 8% of **39** (30% yield after chromatography based on diallyl sulfide); GC RT (conditions A): **40**, 29.17 min; **39**, 28.62 min. It was not possible to completely separate **39** from **40** by flash chromatography.

40: ^1H NMR δ 6.06–6.02 (d, J = 10.5 Hz, 1 H, H6), 5.80–5.73 (ddd, J = 3.5, 5.5, 10.5 Hz, 1 H, H5), 4.15 (q, J = 7.0 Hz, 2 H, CH_3CH_2), 3.01 (d, J = 7.0 Hz, 2 H, H2), 2.96–2.87 (m, 1 H, H3), 2.42–2.35 (m, 2 H, H4), 1.28 (t, J = 7.0 Hz, 3 H, CH_3); ^{13}C NMR δ 173.84 (C), 119.85 (CH), 119.01 (CH), 60.84 (CH_2), 38.79, 27.31, 26.43, 14.16 (CH_3); MS *m/e* 172 (M^+, 53%), 99 (44%), 97 (45%), 98 (100%), 65 (26%), 55 (8%). Anal. Calcd for $C_8H_{12}O_2S$: C, 55.79; H, 7.02. Found: C, 55.59; H, 7.21.

2- and 3-Carboethoxy-3,4-dihydro-2*H*-thiopyran (39 and 40). Procedure 2. Allicin (**1**, 95%; 1.7 g, 10 mmol), ethyl acrylate (4.0 g, 40 mmol), and chloroform (2 mL) were placed in a round-bottomed flask. After 16 h at room temperature, the volatile compounds were pumped away and the crude material was purified by flash chromatography on silica gel (hexane/ether, 98/2), affording a 1:5 **39**:**40** mixture (0.59 g, 34 % yield).

2- and 3-Carboethoxy-3,4-dihydro-2*H*-thiopyran 1,1-Dioxide. To a stirred solution of a mixture of **39** and **40** (0.28 g, 1.62 mmol) in CH_2Cl_2 (20 mL) was added 2.2 equiv of 35% peracetic acid (0.774 g, 3.56 mmol). The reaction mixture was refluxed for 28 h. The organic phase was washed with saturated $NaHCO_3$ (50 × 40 mL), the aqueous phase was back-extracted with CH_2Cl_2, and the combined organic layers were washed with cold water (50 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography (CH_2Cl_2) afforded the title mixture as a colorless oil (0.25 g, 75%): GC RT (conditions A) 50.72 min (23%, minor) and 53.38 min (56%, major); IR (neat) 1315–1320, 1135–1140 cm^{-1} (SO_2); MS *m/e* 204 (M^+, 3%), 130 (100%), 176 (4%), 66 (92%); ^1H NMR ($CDCl_3$) (major) δ 6.39 (s, 2 H), 4.15 (q, J = 7 Hz, 2 H), 3.50 (d, J = 13 Hz, 1 H), 3.38 (tdd, J = 2, 4.5, and 12 Hz, 1 H), 3.12 (t, J = 13 Hz, 1 H), 2.71 (ddd, J = 2, 4.5, and 21 Hz, 1 H), 2.39 (dd, J = 11 and 21 Hz, 1 H), 1.23 (t, J = 7 Hz, 3 H); (minor) δ 6.42 (m, 1 H), 6.33 (d, J = 11 Hz, 1 H), 4.25 (q, J = 7 Hz, 2 H), 3.94 (dd, J = 8 and 4 Hz, 1 H), 2.50 (m, 3 H), 2.30 (m, 1 H), 1.28 (t, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) (major) δ 170.40 (C), 136.18 (CH), 130.03 (CH), 61.97 (CH_2), 51.65 (CH_2), 37.95 (CH), 27.67 (CH_2), 14.10 (CH_3); (minor) δ 164.2 (C), 139.0 (CH), 129.4 (CH), 63.4 (CH), 62.6 (CH_2), 23.7 (2 CH_2), 14.0 (CH_3).

2-Hexanethiol. In a three-necked flask fitted with a reflux condenser were placed 2-hexanone (0.1 mol, 10.0 g), 1,2-ethanedithiol (0.1 mol, 9.4 g), and 0.28 g of *p*-toluenesulfonic acid monohydrate in 100 mL of toluene. The mixture was refluxed overnight. The reaction mixture was cooled and transferred to a separatory funnel. The workup involved washing the organic phase with water and removal of toluene in vacuo. Flash distillation of the residue (0.05 torr) gave 14.5 g (82.4% yield) of the ethylene dithioketal of 2-hexanone: 99% pure by GC; MS *m/e* 176 (M^+, 9%), 161 (4%), 121 (8%), 120 (6%), 119 (100%), 74 (11%), 61 (11%), 59 (43%), 55 (12%). The above thioketal (10.01 g, 0.056 mol) in anhydrous ether (170 mL) was placed in a 500-mL three-necked flask, fitted with a three-way outlet for argon flow and then treated with 3 equiv of *n*-BuLi (1.6 M, 106.25 mL, 0.17 mol), which was added by syringe over a period of 10 min. The temperature of the reaction flask was maintained between 0 and −10 °C. The light yellow reaction mixture was warmed to room temperature and stirred overnight. Workup in-

volved addition of cold water (50 mL), keeping the reaction flask chilled at 0 °C. The resulting solution was poured into water (100 mL) and taken up in a separatory funnel. The organic phase was separated and washed with water (4 × 100 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was removed in vacuo to give an oil (3.55 g, 55% yield). The crude product was 74% pure by GC and verified by GC–MS to have $M^+ = 118$ corresponding to the 2-hexanethiol. Washing the crude product with 10% NaOH yielded the thiol of higher purity (GC: conditions B, 2.72 min, 82%); MS *m/e* 118 (M^+, 22%), 85 (24%), 84 (25%), 69 (39%), 61 (100%), 60 (29%), 56 (66%).

6-Methyl-4,5-dithia-1-decene. 2-Hexanethiol (0.47 g, 0.004 mol) was added to a stirred ice cold solution of sodium ethoxide prepared from sodium (0.12 g, 0.005 mol) and absolute ethanol (10 mL). After the thiolate was stirred for 30 min at room temperature, allyl methanethiosulfonate (0.004 mol, 0.61 g) was added and the reaction was stirred for 3 h. The orange-brown reaction mixture was diluted with ether (60 mL), and the organic phase was washed with water (4 × 60 mL), dried ($MgSO_4$), and concentrated in vacuo, giving a pale yellow oil. Preparative TLC (silica gel, 10% CH_2Cl_2/hexane) followed by preparative HPLC (hexane) gave the title compound (0.028 g, 4% yield): MS *m/e* 190 (M^+, 30%), 106 (100%), 85 (17%), 73 (16%), 57 (29%), 55 (29%); ^1H NMR δ 5.89–5.78 (m, 1 H), 5.17 (d, 1 H, J_{trans} = 17 Hz), 5.13 (d, 1 H, J_{cis} = 8.5 Hz), 3.31 (d, 2 H, J = 7.3 Hz), 2.83 (q, 1 H, J = 6.6 Hz), 1.38–1.31 (m, 6 H), 1.30 (d, 3 H, J = 6.9 Hz), 0.91 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 133.56 (CH), 118.19 (CH_2), 46.31 (CH_2), 43.09 (CH_2), 35.87 (CH_2), 29.24 (CH_2), 22.57 (CH_2), 20.76 (CH_3), 13.99 (CH_3).

2- and 3-(*n*-Butyl)-3,4-dihydro-2*H*-thiopyran (42 and 43). A mixture of diallyl sulfide (2.0 g, 0.017 mol) and 1-hexene (10.0 g, 0.119 mol) was sealed in a Pyrex glass tube under vacuum and heated in an oil bath (preheated) at 200 °C for 1.5 h. The tube was then chilled and opened. After removal of 1-hexene in vacuo, unreacted diallyl sulfide was distilled over (0.1 Torr) to give 2.08 g of crude residue (76% crude yield). Preparative TLC of 200 mg of this residue (silica gel, 5% CH_2Cl_2/hexane) gave 40 mg of the title compounds (1.84:1 **42:43**, 20% overall yield) along with some **17**/**18**: GC RT (conditions A) 22.36 min (56%), 23.48 min (30%); MS (major) *m/e* 156 (M^+, 29%), 101 (17%), 99 (100%), 85 (19%), 73 (16%), 72 (15%), 65 (33%), 55 (19%); (minor) *m/e* 156 (M^+, 52%), 109 (32%), 99 (61%), 85 (37%), 72 (100%), 71 (33%), 67 (35%), 65 (37%), 55 (39%); ^1H NMR δ 6.05–5.98 (d, 1 H, J = 9.8 Hz), 5.71 (m, 1 H), 3.12–3.02 (ddt, 2/3 H, J = 3, 7, 9.5 Hz), 2.82–2.71 (m, 1/3 H), 2.61 (dd, 1/3 H, J = 10, 12 Hz), 2.26–1.98 (m, 2 H), 1.95–1.65 (m, <2 H), 1.45–1.25 (m, 4 H), 0.91 (t, 3 H, J = 7.0 Hz); ^{13}C NMR δ 120.85 (CH), 120.68 (CH), 119.31 (CH), 118.90 (CH), 40.40 (CH), 35.56 (CH_2), 32.44 (CH_2), 31.06 (CH_2), 30.35 (CH_2), 29.72 (CH_2), 29.19 (CH_2), 28.95 (CH_2), 28.91 (CH_2), 23.66 (CH_2), 22.79 (CH_2), 22.58 (CH_2), 14.06 (CH_3), 14.00 (CH_3).

2- and 3-(*n*-Butyl)-3,4-dihydro-2*H*-thiopyran 1,1-Dioxide. Peracetic acid (35%; 1.85 g, 4.2 mmol) was added dropwise to a solution of the above prepared **42** and **43** (0.65 g, 4.2 mmol) in chloroform (15 mL). After 10 h at 25 °C the reaction mixture was neutralized with sodium carbonate (1.8 g), filtered, and concentrated. Flash chromatography (silica gel, hexane/ethyl acetate, 85/15) of the crude mixture afforded 200 mg of the major isomer of the title compound, 80 mg of a mixture of isomers, and 180 mg of the minor isomer contaminated with an unknown compound (50% overall yield of title compounds). 2-(*n*-Butyl)-3,4-dihydro-2*H*-thiopyran 1,1-dioxide: MS *m/e* 188 (M^+, 3%), 171 (22%), 132 (21%), 123 (17%), 121 (13%), 106 (21%), 89 (12%), 81 (100%), 80 (12%), 79 (28%), 67 (98%), 65 (12%), 55 (53%), 54 (15%), 53 (20%); ^1H NMR δ 6.40–6.35 (m, 2 H), 2.95 (t + m, J = 8 Hz, 1 H), 2.40–2.05 (m, 5 H), 1.60–1.30 (m, 5 H), 0.91 (t, J = 7 Hz, 3 H); ^{13}C NMR δ 138.28 (CH), 129.79 (CH), 59.23 (CH_2), 28.54 (CH_2), 25.44 (CH_2), 25.40 (CH_2), 24.56 (CH_2), 22.45 (CH_2), 13.71 (CH_3).

Reaction of Diallyl Disulfide with 1-Hexene. A mixture of 1-hexene (2.5 g, 0.03 mol) and diallyl disulfide (0.5 g, 0.003 mol) was sealed under vacuum in a glass tube and heated at 150 °C for 1.5 h. The tube was chilled and then carefully opened, and the unreacted 1-hexene was removed in vacuo to give a pale yellow oil (0.43 g). GC analysis showed three major sets of peaks, which were identified by GC–MS to be the unreacted diallyl disulfide ($M^+ = 146$), a diallyl disulfide–1-hexene adduct ($M^+ = 190$), and the regioisomeric thioacrolein–1-hexene adducts, respectively. The crude material was chromatographed (silica gel, 10% CH_2Cl_2/hexane) to give a colorless oil (0.060 g, 10% yield), identical in its chromatographic behavior and mass spectrum with authentic 6-methyl-4,5-dithia-1-decene.

Lipoxygenase Assay. To the blank and sample cuvettes in a Beckman DK-2A recording spectrophotometer was added 0.1 M Tris (1.0 mL; pH 8.5) at 18 °C, followed by addition of inhibitors in ethanol (10 μL). Type V soybean lipoxygenase (Sigma, St. Louis, MO) (1 nM, final concentration) was added as a solution in buffer (10 μL) to the sample and buffer alone to the blank. After a 5-min equilibration period an ethanolic solution of linoleic acid (Sigma; 25 μL; 110 μM, final concentration) was added to both cuvettes and the absorbance at 234 nm was recorded as a function of time. The rates were measured from the initial slopes of the linear portions of the curves.

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Supplementary Material Available: HOMCOR and HETCOR NMR spectra for **9**, HOMCOR spectrum for **10**, HOMCOR spectrum for **26**, pyrolysis of diallyl disulfide in solution, copyrolysis of diallyl disulfide/dimethallyl disulfide, and syntheses of 4,8-dithiaundeca-1,10-diene, 1-phenyl-2,3,6-trithiadecane, 4,8,9,13-tetrathiahexadeca-1,15-diene, (*E,Z*)-4,5,9-trithiadodeca-1,6,11-triene(deoxyajoene), 4,5,8,9-tetrathiadodeca-1,11-diene, 4,5,9-trithiadodeca-1,11-diene 9-oxide, 7,7-dimethyl-4,5,9,10-tetrathiatrideca-1,12-diene, and 4,5,9,10-tetrathiatridecane (11 pages). Ordering information is given on any current masthead page.