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The Regiochemistry of Cyclization of α-Sulfenyl-, α-Sulfinyl-, and α-Sulfonyl-5-hexenyl Radicals: Procedures Leading to Regioselective Syntheses of Cyclic Sulfones and Sulfoxides

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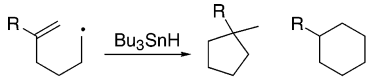
A study of the cyclization of α-sulfenyl-, α-sulfinyl-, and α-sulfonyl-5-hexenyl and 5-methyl-5-hexenyl radicals reveals a unique contrast in the mode of ring closure of the radicals. In the case of the 5-hexenyl radicals, the sulfinyl-substituted species displays unexpected regioselectivity relative to its analogues. Thus, while the α-S- and α-SO_2-5-hexenyl radicals give measurable and increasing quantities of 6-*endo* product, the α-sulfinyl species cyclizes with high selectivity (95.5:4.5) via a 5-*exo* mode. By contrast, ring closure of the 5-methyl-5-hexenyl radicals is found to give substantially the 6-*endo* product in all cases. It is the α-sulfonyl-5-methyl-5-hexenyl radical that now exhibits high regioselectivity (97.5:2.5) for 6-*endo* closure: an illustration of the synthetic value of this observation is the independent synthesis of the model cyclohexyl sulfone **61** in high yield. It is found that ring closure under the conditions employed occurs irreversibly in all cases.

Introduction

Organic synthesis has benefited enormously from reactions involving internal addition of a radical center to a double bond. In particular, cyclization of 5-hexenyl radicals represents a process which, over the years, has provided access to a large number of complex substances.[1] Contrary to predictions based on thermodynamic criteria, cyclization of 5-hexenyl systems, exemplified by **1**, generally gives a product **2** via a predominant 5-*exo* mode of closure,[1c,2] a feature that has been rationalized[3] in terms of stereoelectronic control of the reaction; accordingly, these cyclizations generally lead to cyclopentane derivatives with little of the product **3** arising from 6-*endo* closure observed. Nevertheless, the regiochemistry of ring closure of 5-hexenyl radicals is sometimes governed by other factors besides stereoelectronic control, and elements such as polar and steric effects which normally play a minor role now become more prominent. One illustration involves ring closure of the 5-methyl-hexenyl radical **4**, which yields a 2:3 ratio of the exo/endo products **5/6**, an observation ascribed to the presence of an unfavorable steric effect in the 5-*exo* mode of cyclization.[2a,3,4] On the other hand, ring closure of the 5-carbomethoxy-substituted 5-hexenyl radical **7** gives a 1:6 distribution of the exo/endo products **8** and **9**. This unusual observation has been attributed[5] to the operation of a steric effect along the lines proposed for cyclization of **4**, reinforced by a strong contribution from a polar effect.



1, R=H **2**, R=H **3**, R=H
4, R=Me **5**, R=Me **6**, R=Me
7, R=CO_2Me **8**, R=CO_2Me **9**, R=CO_2Me

The nature and reactivity of a radical center can be altered significantly when adjacent to a heteroatom, and cyclization of 5-hexenyl systems containing an α-heteroatom has been exploited for the synthesis of heterocyclic compounds; extensive studies of hexenyl systems containing first-row atoms such as oxygen and nitrogen have shown that ring closure occurs smoothly. We have demonstrated previously,[6] for example, that rearrangement of α- and β-ammonium-substituted 5-hexenyl radicals provides a convenient entry into novel nitrogen-

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(2) (a) Beckwith, A. L. J.; Blair, I. A.; Phillipou, G. *Tetrahedron Lett.* **1974**, 2251. (b) Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of Radical Reactions−Concepts, Guidelines and Synthetic Applications*; VCH: Weinheim, Germany, 1996.

(3) Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073 and references therein.

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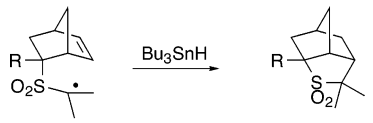
containing heterocycles, including bicyclic compounds of potential physiological interest.

We have recently directed our attention to an analogous study of sulfur-based 5-hexenyl radicals in which the hetero group constitutes part of the hexenyl chain.[7] Our objective was to examine, first, the effect of the longer C−S bonds on the facility, or otherwise, for cyclization of selected 5-hexenyl systems containing α-sulfenyl, sulfinyl, and sulfonyl functional groups and, second, how the presence of these groups might influence the regiochemistry of ring closure. Ultimately, we were keen to determine whether this study may lead to a viable procedure for the efficient synthesis of heterocyclic sulfur compounds.

The number of studies into the behavior of 5-hexenyl radicals with second-row groups α to the radical center is limited. On the basis of all the available evidence, it has been suggested[8] that the cyclization rates of such systems appear to be slower in general than those incorporating first-row elements. Of direct relevance to the work described here are the reports on the ring closure of α-sulfenyl-, sulfinyl-, and sulfonyl-5-hexenyl radicals by Tsai and his colleagues,[9,10d] and by several groups[10a−c] on cyclization of α-sulfonyl-5-hexenyl radicals. However, in all the systems examined the sulfonyl group was located external to the 5-hexenyl chain. Chanon and his colleagues[11] have disclosed that the norbornyl derivative **10** undergoes 5-*exo* ring closure to give **11** with extraordinary rapidity, and it is noteworthy that **10** is the only reported example where the sulfonyl group is part of a 5-hexenyl chain.



10 **11**

According to their σ_I values,[12] SO_2, SO, and S are powerful inductive electron-withdrawing groups, a property that would normally be expected to lead to destabilization of an α radical center. Nonetheless, S exerts a stabilizing influence overall because of a favorable and dominant mesomeric interaction of the lone pair with the radical center. As a matter of interest, while oxygen in $ROCH_2^+$ confers greater thermodynamic stability than S in $RSCH_2^+$ on the adjacent cationic center, the reverse is true for stabilization of radicals. For the α-sulfinyl radical, which is described as being electrophilic, there is some stabilization because of π-conjugation involving the lone pair on sulfur, although Creary[13] has suggested that the sulfinyl group stabilizes free radicals by an acceptor mechanism utilizing sulfur vacant d-orbitals. According to Clark,[14] the α-sulfonyl group is generally accepted to be remarkable for its lack of a stabilizing effect on a radical center. The sulfur atom of a sulfonyl group lacks a lone pair, and it is therefore not surprising that a similar stabilizing phenomenon is not displayed. Bordwell and Liu have suggested[15] that the increasing +ve charge on sulfur also destabilizes the electron-deficient radical. These observations are supported by high-level calculations[16] which demonstrate significant stabilization of $SCH_2^\bullet$ and some stabilization of $SOCH_2^\bullet$, but destabilization of $SO_2CH_2^\bullet$. In a review of the chemistry of α-sulfonyl systems, Paquette[17] has drawn attention to the thermodynamic instability of α-sulfonyl radicals and their associated reactivity with alkenes to generate C−C bonds.

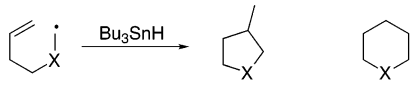
TABLE 1. Products of Ring Closure of Selected 5-Hexenyl Radicals in the Presence of Bu_3SnH

5-hexenyl radical	X	*T* (°C)	5-*exo*	6-*endo*	ref
1	CH_2	70	99	1	2
12	S	80	84	16	this work
15	SO	80	95.5[a]	4.5	this work
18	SO_2	80	76	24	this work
21	$SiMe_2$	80	33	66	20
24	CHMe	80	98	2	23
27	CMe_2	80	100	0	4, 23b
30	O	80	100	0	27d,e
31	$^+NMe_2$	102	100	0	6d,e
32	NCH_2Ph	80	0	0	18

[a] Cis/trans = 3:1

Results and Discussion

The 5-Hexenyl System. The behavior of the series of α-sulfenyl-, α-sulfinyl-, and α-sulfonyl-5-hexenyl systems **12**, **15**, and **18** forms the basis of this report. These radicals have not been studied previously. The results of this investigation are displayed in Table 1, which also contains, for comparison, the products of ring closure of several related systems, including the 2-hetero-substituted 5-hexenyl radicals, **21**, **30**, **31**, and **32**. Of these, the amine **32** is exceptional in that it does not afford ring-closure product at all,[18] which presumably reflects the enhanced thermodynamic stability of the α-amino radical.



12, X=S
15, X=SO
18, X=SO_2
21, X=$SiMe_2$
24, X=CHMe
27, X=CMe_2
30, X=O
31, X=$^+NMe_2$
32, X=$NHCH_2Ph$

13, X=S
16, X=SO
19, X=SO_2
22, X=$SiMe_2$
25, X=CHMe
28, X=CMe_2

14, X=S
17, X=SO
20, X=SO_2
23, X=$SiMe_2$
26, X=CHMe
29, X=CMe_2

The products of ring closure of **12**, **15**, and **18** were identified by comparison with authentic specimens, prepared independently, and the ratios of 5-*exo* to 6-*endo*

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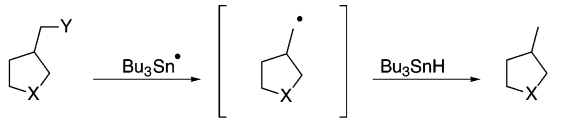
(11) (a) Vacher, B.; Samat, A.; Chanon, M. *Tetrahedron Lett.* **1985**, *26*, 5129. (b) Vacher, B.; Samat, A.; Allouche, A.; Laknifli, A.; Baldy, A.; Chanon, M. *Tetrahedron* **1988**, *44*, 2925. (c) Mattalia, L.-M.; Vacher, B.; Samat, A.; Chanon, M. *J. Am. Chem. Soc.* **1992**, *114*, 4111.
(12) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165; record the following values: SO_2 (σ_I = 0.53), SO (σ_I = 0.52), and S (σ_I = 0.23).

SCHEME 1



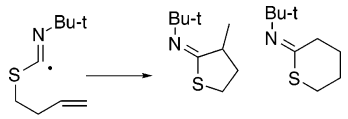
33a, X=S, Y=Br **33**, X=S **13**, X=S
33b, X=S, Y=SePh
34a, X=SO, Y=SePh **34**, X=SO **16**, X=SO
35a, X=SO_2,Y=Br **35**, X=SO_2 **19**, X=SO_2

products were determined by GC analysis with appropriate correction for individual detector response. In addition, the possibility of reversibility of these reactions was tested by generating the 5-*exo* radical precursors **33**, **34**, and **35** independently from their respective precursors and noting their behavior when exposed to tributyltin hydride (Scheme 1). It was observed that reduction gave only the corresponding cyclopentyl derivatives **13**, **16**, and **19**, respectively, demonstrating that none of the cyclization processes involving the sulfur-based radicals **12**, **15**, and **18** was reversible.

To attempt to delineate the factors responsible for cyclization of the substrates described in this work, it is convenient to consider, first, the products of ring closure in the presence of Bu_3SnH of the all-carbon system **1**, along with the species **12** and **30** which incorporate the Group 7 atoms S and O.

It is noteworthy that all three radicals **1**, **12**, and **30** can be classified as having nucleophilic character and, according to Frontier Molecular Orbital Theory,[19] the more favorable interaction in the transition state for ring closure is that between the radical SOMO and the LUMO of the π-bond. For cyclization of radicals incorporating the first-row atoms, viz., **1** and **30**, the transition state best accommodated by the SOMO/LUMO interaction is that involving orbital overlap of the radical center with C5, a process leading to 5-*exo* closure (stereoelectronic effect). The propensity for 5-*exo* closure is further facilitated by the polar effect, inasmuch as the coefficient of the π-LUMO at C5 is larger than the coefficient at C6 and this leads to more favorable overlap in the former case, bearing in mind, as discussed above, that the polar influence is generally considered to be dominated by stereoelectronic considerations. When these factors are taken into account in considering ring closure of the radicals **1** and **30**, it is not surprising that the cyclopentane derivatives predominate and that there are essentially zero amounts of the 6-*endo* products formed.

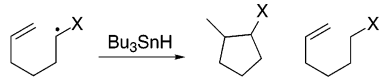
By contrast, the product of closure of the sulfur-substituted 5-hexenyl radical **12** is found to consist of a 5.3:1 mixture of the 5-*exo* and 6-*endo* products **13** and **14**. Clearly, while cyclization of the sulfenyl radical **12** is still strongly in favor of 5-*exo* closure, there is a significant amount of the 6-*endo* product formed. An obvious distinction between the 5-hexenyl systems incorporating the first-row atoms **1** and **30** and the radical **12** is the length of the C−X bonds. We believe that the production of **14** is facilitated by the presence of the longer C−S bond lengths which allow for a competitive pathway via a transition state corresponding to 6-*endo* cyclization. There is supporting evidence for this from studies on the silicon-based radical **21**.[20] Although this system is isoelectronic with the species **1**, it is found that the predominant product of ring closure is **23**, viz., that derived from the 6-*endo* pathway, despite the presence of the two methyl groups attached to silicon which, according to observations on the all-carbon analogue,[2] would be expected to favor 5-*exo* cyclization. The ratio of five- to six-membered-ring products **22** and **23** formed is approximately 1:2. The poor yield of cyclized products derived from the radical **21** has been ascribed not so much to a reluctance for ring closure, but to a very rapid rate of H-abstraction from Bu_3SnH. Interestingly, it has been found[8] that the radical **36** undergoes ring closure overwhelmingly via the 5-*exo* mode; the ratio of the 5-*exo* (**37**) and 6-*endo* (**38**) products, respectively, is 35:1. Perhaps the lesser amount of 6-*endo* product in this case compared with **12** may be the result of a shorter sp^2 C−S bond in the former, in addition to constraints imposed by the N=C moiety.



36 **37** **38**

Accordingly, we are led to conclude that the mode of cyclization of radicals **12** and **21** is influenced not only by stereoelectronic and polar effects, but also by a steric effect arising from the increased C−X bond length (1.87 Å for C−Si; 1.81 Å for C−S),[21] which allows for an easier approach of the radical center to the terminus of the alkene moiety and thus a more ready accommodation of the 6-*endo* transition state. As discussed above in the case of the analogous carbon and oxygen species **1** and **30**, the corresponding transition state is sterically unfavorable and of much higher energy.

It is interesting now to compare the products of cyclization of the α-sulfenyl and α-sulfonyl radicals **12** and **18** examined in this work (Table 1). α-Sulfonyl radicals are electrophilic, kinetically unstable species, which have been shown to be sufficiently reactive to undergo carbon−carbon bond formation with alkenes.[17] As mentioned above, a number of these reactions are found to include ring closure of 5-hexenyl systems.[9,10] The latter, typified by **39** in which the functional group is arranged external to the hexenyl chain, have invariably afforded the 5-*exo* product **40** exclusively.[9]



39a, X=SPh **40a**, X=S
39b, X=SOPh **40b**, X=SO
39c, X=SO_2Ph **40c**, X=SO_2

(13) Creary, X. In *Substituent Effects in Radical Chemistry*; Viehe, H. G., et al., Eds.; Reidel Publishing Co.: New York, 1986; p 245.
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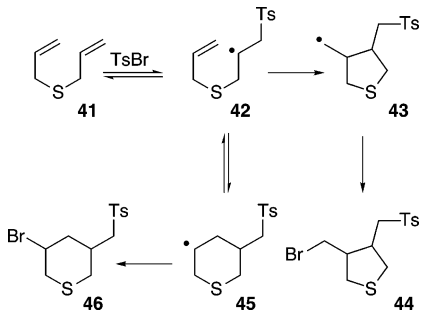
(19) Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; Wiley: London, UK, 1976.

In the study described herein, it can be seen that the ratio of 5-*exo* to 6-*endo* isomers changes from 5.3:1 (**13**/**14**) in the case of the sulfenyl substituent to 3.2:1 (**19**/**20**) for the sulfonyl-substituted radical. It is noteworthy that, while the C−S bond lengths are now comparable, the proportion of 6-*endo* product has increased, which we ascribe to the change from a nucleophilic radical **12** to a strongly electrophilic species **18**. We suggest that this modification is associated with a significant change in the frontier molecular orbital interactions between the radicals and the π system which govern cyclization as discussed below.

For electrophilic radicals, such as the sulfonyl species **18**, a lowered SOMO energy level allows a more attractive interaction with the alkene HOMO. In the type of alkene under study, the magnitude of the HOMO coefficient at the terminal carbon is larger than that at C5 and, accordingly, orbital interaction between the SOMO and C6 is favored leading to a preference for 6-*endo* closure. This occurs despite the presence of the oxygen atoms attached to sulfur which, like *gem*-dimethyl groups attached to the α-carbon, may be expected to favor 5-*exo* attack, although the Thorpe−Ingold effect would be reduced. Thus, 5-*exo* ring closure of **18** would seem to be governed, as before, by stereoelectronic factors leading to 5-exo product, modified by a steric effect associated with the longer C−S bonds acting in concert with a polar effect which together favor 6-*endo* closure. A difficulty with this rationale, however, is that it does not explain the discrepancy in regiochemistry observed between ring closure of the radical **18** and the related α-sulfonyl species **39c**, which gives only the product of 5-*exo* closure **40c**.[9,10] The radical center in **39c** has similar electrophilic character to that in **18**, suggesting that the regiochemistry of its ring closure would be expected to be governed to some extent by polar considerations. It is important to note, however, that the skeletal bond lengths of the hexenyl moiety in **39c** are essentially identical with those in the radical **1**, and we suggest that the polar effect exerts little influence in the cyclization of **39c** and that stereoelectronic factors now appear to be dominant. A similar situation is encountered in the case of the radical **31**. We have observed[6d,e] that, despite its strongly electrophilic nature, **31** undergoes ring closure smoothly with high regioselectivity to give only the product of 5-*exo* cyclization. None of the 6-*endo* isomer was detected. We are forced to conclude, therefore, that the C−X bond length plays a very important role in these cyclizations. The observations of Serra and his colleagues,[22] in which light-induced radical addition of tosyl bromide to **41** to give cyclized material **44** only, presumably via the intermediates **42** and **43**, appear to contradict this conclusion. None of the 6-*endo* isomer **46** was detected. However, it is claimed[22] that the precursor radical **45** is formed reversibly and, accordingly, it is not surprising that the 6-*endo* product is not observed.

Now to the question of the regiochemistry of ring closure of the α-sulfinyl-5-hexenyl radical **15**. Inspection

SCHEME 2



of the data collected in the Table 1 allows a comparison to be made of the products of cyclization of the α-sulfenyl-, α-sulfinyl-, and α-sulfonyl-substituted radicals **12**, **15**, and **18**. These data are intriguing but difficult to rationalize. It is seen that the anticipated progression in the behavior of this series of radicals, discussed above, is not observed. Thus, based on the electronic effect of the sulfinyl group on an adjacent radical center, ring closure of the sulfoxide **15** was expected to yield a mixture of 5-*exo* and 6-*endo* products **16** and **17** intermediate in composition to those formed from the α-S- and α-SO_2-substituted radicals, respectively. The data in Table 1 reveal that, while the ratio of 5-*exo* to 6-*endo* products produced by the α-sulfenyl and α-sulfonyl radicals **12** and **18** decreases from 5.3:1 to 3.2:1, cyclization of the species **15** proceeds with extraordinarily high regioselectivity (21:1), giving 5-*exo* product **16** almost exclusively; little of the product **17** derived from 6-*endo* closure was detected. Indeed, we have shown that the high regioselectivity associated with ring closure of the sulfoxide **15** provides a stereoselective synthesis of the sulfoxide **16** in excellent yield. It is also noteworthy that the cis/trans ratio of sulfoxides **16** is 3:1, in contrast to the situation encountered in the cyclization of the 2-methyl-5-hexenyl radical **24**, which yields a 1:1.8 cis/trans mixture of **25**. Assuming a chairlike transition state, the distribution of diastereomers in the case of ring closure of **15** may reflect the fact that, unlike most substituents, the conformational preference of the sulfinyl oxygen is the axial position.[24] Interestingly, the α-sulfinyl radical **39b** undergoes[9b] ring closure to give only 5-*exo* product **40b** but, once again, this case involves a system in which the functional group is external to the 5-hexenyl chain.

Clearly, our hypothesis that cyclization of the radicals **12** and **18** to give endo product is facilitated, and probably dominated, by the longer C−S bonds no longer holds for closure of the α-sulfinyl radical **15**. We do not have an explanation for the "anomalous" behavior of **15**, although it is relevant that sulfoxides have been found previously to exhibit unexpected properties. The rarely observed conformational preference for axial oxygen cited above[24] is one example. Another, which is more closely related to the current work, is the demonstration by Ueno and his colleauges[25] that the order of elimination from a series of β-organosulfur radicals is $RSO^{\bullet} > RS^{\bullet} > RSO_2^{\bullet}$.

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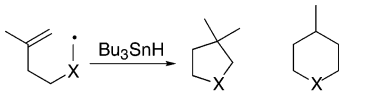
TABLE 2. Exo/Endo Ratios in Ring Closure of Various 2-X-5-Methyl-5-hexenyl Radicals in the Presence of Bu_3SnH

5-hexenyl radical	X	*T* (°C)	5-*exo*	6-*endo*	ref
4	CH_2	80	40	60	4
47	S	80	11	89	this work
50	SO	80	23	77[a]	this work
53	SO_2	80	2.5	97.5	this work
56	$^+NMe_2$	80	74	26	6d,e
57	CMe_2	102	68	32	4
58	O	80	80	20	*b*

[a] Cis/trans = 1.6:1. [b] Smith, T. W.; Butler, G. B. *J. Org. Chem.* **1978**, *43*, 6.

The 5-Methyl-5-hexenyl System. Dramatic effects are observed on the regiochemistry of cyclization of the 5-hexenyl systems bearing a substituent at C5. Reference has already been made to the effect of introducing an alkyl group at C5 which increases the extent of 6-*endo* closure because the rate of 5-*exo* cyclization is greatly reduced.[2a,3,4] It was decided, therefore, to include an analogous study of the systems **47**, **50**, and **53**. The results of the behavior of these radicals toward ring closure are displayed in Table 2, along with corresponding data for several related systems, **4**, **56**, **57**, and **58**, for comparison.



47, X=S
50, X=SO
53, X=SO_2
56, X=$^+NMe_2$
57, X=CMe_2
58, X=O

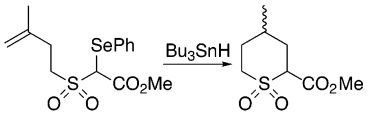
48, X=S
51, X=SO
54, X=SO_2

49, X=S
52, X=SO
55, X=SO_2

Inspection of Table 2 reveals that while the parent system **4** now prefers the 6-*endo* mode of closure, the range of the observed 5-*exo*/6-*endo* ratios is quite extensive.

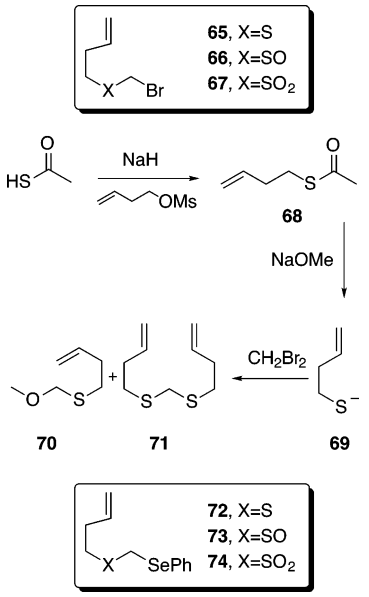
In the case of the sulfenyl and sulfonyl radicals **47** and **53**, it is suggested that the combined effect of the steric factors associated with the presence of the methyl group at C5 and the longer C−S bonds lead to considerably enhanced quantities of 6-*endo* product, the formation of which is reinforced by a contribution from the polar effect. Indeed, we have found that the high regioselectivity associated with ring closure of **53** provides an excellent entry to the cyclohexyl sulfone **55**. The selenide **60** is an additional example that exploits the synthetic utility associated with the high degree of selectivity involved in this kind of cyclization. Bu_3SnH treatment of the substrate **60**, available in an easy 4-step sequence from thioacetic acid (see Scheme 8), affords the sulfone **61** as a mixture of diastereomers in excellent yield. In this case, the presence of the ester function undoubtedly contributes further to the electrophilic nature of the radical center and enhances an already favorable polar effect that promotes 6-*endo* cyclization.It is noteworthy that cyclization of the sulfinyl radical **50** proceeds, as in the case of the 5-hexenyl analogue **15**, in an unexpected fashion—an observation for which we have no satisfactory explanation. We had anticipated that **50** would give an

SCHEME 3

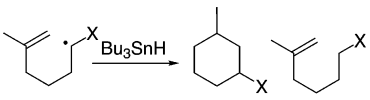


60 **61**

SCHEME 4



exo/endo distribution somewhere between those of the radicals **47** and **53**. Instead, while the 6-*endo* mode of cyclization of the sulfinyl radical **50** is still preferred, significantly more of the 5-*exo* product is obtained from **50** than from either **47** or **53**. Thus, we find that more of the exo product is produced in the case of the sulfinyl radicals **15** and **50** than from the corresponding sulfenyl and sulfonyl radicals. Examination of the related systems **62**−**64,** in which the functional group is external to the hexenyl chain, reveals some interesting contrasts. For example, the α-sulfenyl radical **62** is found to give only the product of reduction.[9a] On the other hand, compared with their unsubstituted analogues **39b** and **39c** each of which ring closes via the 5-*exo* pathway, cyclization of the α-sulfinyl **63** and α-sulfonyl **64** radicals surprisingly exhibits a complete reversal of regioselectivity to afford the 6-*endo* product exclusively.[9b]

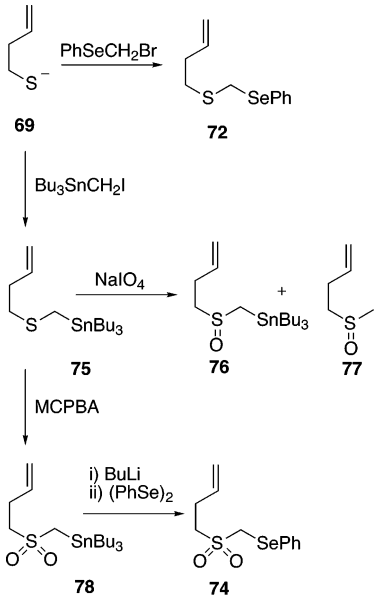


62, X=SPh	0	100
63, X=SOPh	30	70
64, X=SO_2Ph	70	30

Syntheses

Radical Precursors and Reaction Products. The bromides **65**, **66**, and **67** were thought to be the simplest precursors to the 5-hexenyl systems radicals **12**, **15**, and **18**, inasmuch as access to the sulfide **65** would afford a convenient route to the α-sulfinyl and α-sulfonyl bromides by application of selective oxidative procedures. Synthesis of **65** was attempted as outlined in Scheme 4. The thioacetate **68**, generated from commercially available thioacetic acid in reasonable yield (70%) by standard nucleophilic displacement, was con-

SCHEME 5



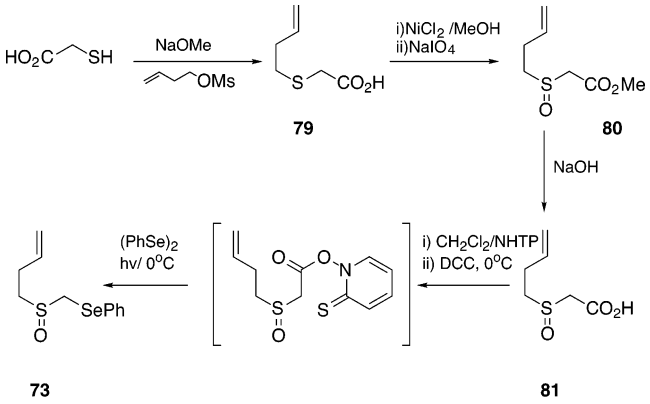
verted into its conjugate base **69**, which was exposed to a 10-fold excess of dibromomethane. Despite the fact that this procedure has been employed successfully for the bromomethylation of amines,[6a−h] in this case it delivered a mixture of products of which the sulfide **70** and disulfide **71** predominated.

Attention was, therefore, directed to the synthesis of the selenides **72**, **73**, and **74** as alternative precursors. In view of the ease of oxidation of selenides, **72** was not expected to provide direct access to the corresponding sulfoxide and sulfone, and alternative strategies would need to be devised for the preparation of **73** and **74**. Although the reaction of phenylselenomethyl bromide with alkoxide ions has been found[26] to give very poor yields of the corresponding selenides, treatment of **69** with $PhSeCH_2Br$ gave the required compound **72** in good yield (70%) (Scheme 5). This is presumably a reflection of the different behavior of the softer base RS^- relative to RO^-, and the success in generating **72** compares with the excellent yields of selenides produced from reaction of (the soft) amines with $PhSeCH_2Br$.[6d,e]

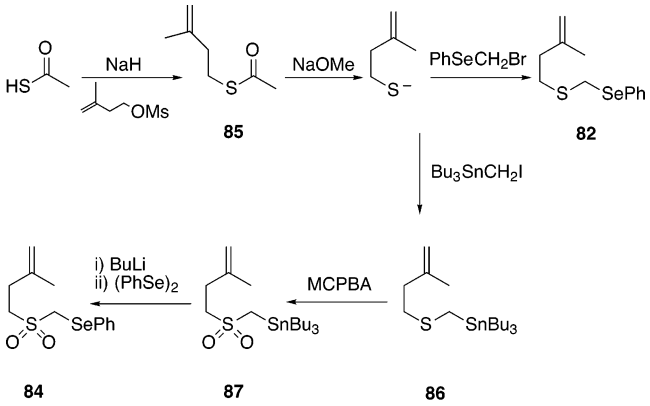
For the synthesis of the selenides **73** and **74**, recourse was made to tin−lithium metathesis exchange in the reaction of stannanes with BuLi described by Still[27a] and exploited for similar work to this by Paquette[27c] and Rawal[27d,e] and their respective colleagues. In a modified approach commencing with **68**, reaction of the derived thiolate **69** with iodomethyltributyltin led to the stannane **75** in 79% yield. Although the conversion of sulfides into sulfoxides can be achieved selectively by reaction with $NaIO_4$, under these conditions **75** gave the desired compound **76** heavily contaminated with destannylated material **77**. On the other hand, treatment of the stannane **75** with *m*-chloroperbenzoic acid afforded a good yield (79%) of the sulfone **78** which, without purification, was converted (74%) into the selenide **74** by reaction with butyllithium followed by diphenyldiselenide.

Access to **73** was provided by recourse to Barton ester methodology (Scheme 6).[28] Mercaptoacetic acid was treated with NaOMe (2 equiv) and the dianion then exposed to 3-butenyl mesylate yielding the acid **79** (95%). Esterification of the latter followed by treatment with $NaIO_4$ afforded the

SCHEME 6



SCHEME 7



sulfoxide **80** (72% overall). Reaction of the derived acid **81** with DCC and 1-hydroxypyridine-2-thione (NHTP) gave the thiohydroxamic ester which, without purification, was treated in situ with $(PhSe)_2$ under illumination to afford the desired sulfoxide **73**.

The corresponding α-sulfenyl-, sulfinyl-, and sulfonyl-5-methyl-5-hexenyl derivatives **82**, **83**, and **84** were earmarked as convenient precursors to the radicals **47**, **50**, and **53** and were synthesized by using similar strategies to those described above for the parent species. The procedures, displayed in Schemes 7 and 8, proceeded as anticipated and require no further elaboration.

It was considered essential to have available all of the potential products of reaction of the selenides with tributyltin hydride, including the unrearranged reduction products. Scheme 9 depicts the routes employed for the synthesis of the products of direct reduction of the radical precursors, viz., **77**, **92**, **93**, **94**, **95**, and **96**. The cyclic products **13**, **14**, **16**, **17**, **19**, and **20** were either commercially available (e.g., **14**) or accessible by standard procedures without incident.

Reversibility Studies. Scheme 10 summarizes the procedures employed to synthesize the substrates **33a**, **33b**, **34a**, and **35a** required for examining whether reduction of the radicals **33**, **34**, and **35** occurs reversibly. The sequence commences with 2-methylenetetrahydrothiophene **97**, which has been referred to previously in the literature only as an uncharacterized product of pyrolysis.[29] The alkene **97**, derived conveniently from 2-methylene-1,4-butanediyl dimesylate, was converted into the alcohol **98** under standard hydroboration/

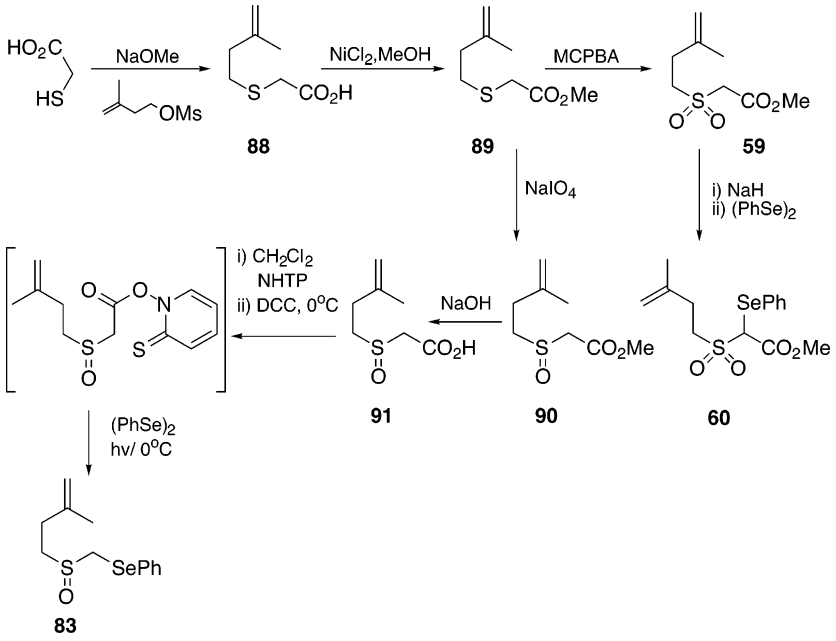
(26) Beckwith, A. L. J.; Pigou, P. E. *Aust. J. Chem.* **1986**, *39*, 77.

(27) (a) Still, W. C.; Mitra, A. *J. Am. Chem. Soc.* **1978**, *100*, 1927. (b) Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481. (c) Friedrich, D.; Paquette, L. A. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1621. (d) Rawal, V. H.; Singh, S. P.; Dufour, C.; Michoud, C. J. *J. Org. Chem.* **1993**, *58*, 7718. (e) Rawal, V. H.; Singh, S. P.; Dufour, C.; Michoud, C. J. *J. Org. Chem.* **1991**, *56*, 5425.

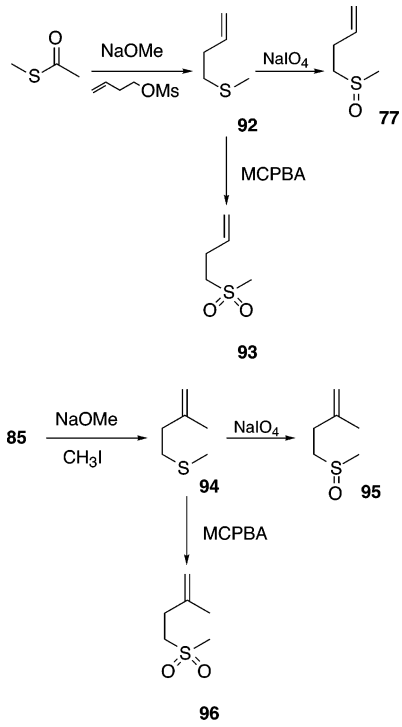
(28) Barton, D. H. R.; Crich, D.; Motherwell, W. B. *Tetrahedron*, **1985**, *41*, 3901. Barton, D. H. R.; Zard, S. Z. *Pure Appl. Chem.* **1986**, *58*, 675. Barton, D. H. R.; Zard, S. Z. *Janssen Chim. Acta* **1987**, *4*, 3. Crich, D. *Aldrichim. Acta* **1987**, *20*, 35. Barton, D. H. R. *Aldrichim. Acta* **1990**, *23*, 3.

(29) Hincelin, O.; Ames, J. M.; Apriyantono, A. A.; Elmore, J. S. *Food Chem.* **1992**, *44*, 381.

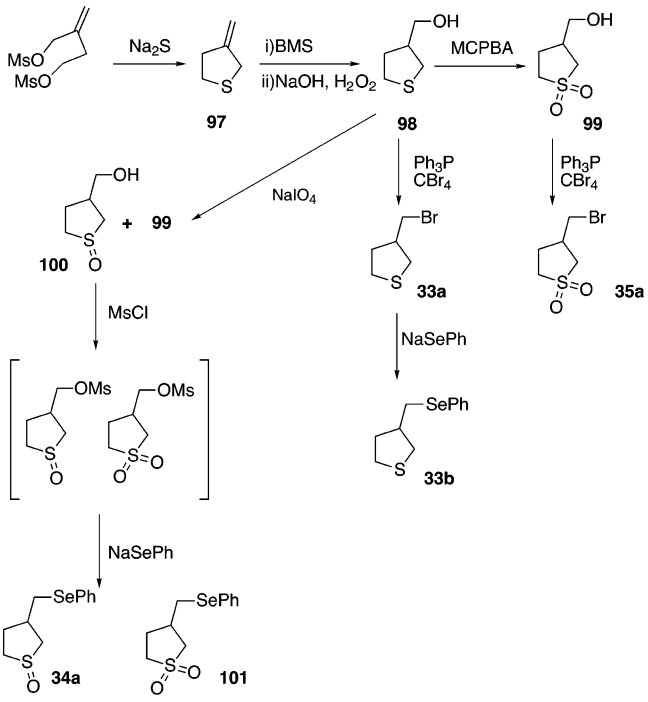
SCHEME 8



SCHEME 9



SCHEME 10



oxidation procedures. Treatment of the latter with triphenylphosphine/CBr_4 led to the required bromide **33a**, which also served as an intermediate to the alternative selenide precursor **33b**. Similar treatment of the sulfone **99**, which was obtained by MCPBA oxidation of **98**, afforded the sulfonyl radical precursor **35a**. Periodate oxidation of the sulfide **98** yielded a mixture of the sulfone **99** and the desired sulfoxide **100**, which were transformed into the corresponding mesylates. The latter, upon treatment with sodium phenylselenide, afforded a mixture of the selenides **34a** and **101**, which could be separated by chromatographic techniques.

As discussed earlier, it was observed that treatment of the precursors with tributyltin hydride, under conditions conductive to reversibility, demonstrated that the radicals were stable to the conditions and reproduced the cyclopentyl derivative completely.

Experimental Section

1-Phenylselenyl-2-sulfenyl-5-hexene (72). 3-Butenyl thioacetate (1.87 g, 7.5 mmol) was added dropwise over 10 min to a solution of sodium methoxide (0.29 g, 12.6 mmol sodium, 10 mL of methanol) at room temperature with stirring. After 90 min, phenylselenylmethyl bromide[30] (1.25 g, 5.0 mmol) in CH_3OH (2 mL) was added and the mixture was stirred for a further 2 h at room temperature. Water (25 mL) was then

(30) Baldwin, J. E.; Adlington, R. M.; Robertson, T. *Tetrahedron* **1989**, *45*, 909.

added and the mixture extracted with ether (2 × 80 mL). The combined ether extracts were washed with water (2 × 50 mL) and then brine (50 mL) before being dried (Na_2SO_4) and evaporated. The crude yellow oil (1.30 g) was chromatographed (hexane followed by hexane/CH_2Cl_2) and distilled (Kugelrohr: 105−110 °C/0.1 mm) to give the title compound **72** as a pale straw-colored oil (1.0 g, 74%): ^{1}H NMR ($CDCl_3$) δ 7.59−7.56 (m, 2H), 7.32−7.27 (m, 3H), 5.89−5.75 (m, 1H), 5.12−5.02 (m, 2H), 4.02 (s, 2H), 2.75 (t, J = 7.5 Hz, 2H), 2.40−2.32 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 136.4, 133.4, 130.1, 129.1, 127.5, 116.1, 33.1, 31.9, 30.3. HRMS (EI) calcd for $C_{11}H_{14}SSe$: 257.9981, found 257.9980.

1-Tributylstannyl-2-sulfenyl-5-hexene (75). 3-Butenyl thioacetate **68** (1.60 g, 12.3 mmol) was added dropwise over 10 min to a stirred solution of sodium methoxide (0.290 g, 12.6 mmol sodium, 20 mL methanol) at room temperature. After 1 h, iodomethyltributyltin[27b] (4.42 g, 10.25 mmol) was added and the mixture was stirred for a further 2 h at room temperature. Water (100 mL) was then added and the mixture extracted with hexane (2 × 150 mL). The organic extracts were washed with water (2 × 100 mL) and then brine (100 mL) before being dried ($MgSO_4$) and evaporated. The crude product was distilled (Kugelrohr:135 °C/0.1 mm) yielding **75** as a colorless oil (3.81 g, 79%): ^{1}H NMR ($CDCl_3$) δ 5.95−5.73 (m, 1H), 5.12−4.96 (m, 2H), 2.60−2.49 (m, 2H), 2.42−2.29 (m, 2H), 1.92 (s, 2H), 1.74 (s, 3H), 1.59−1.21 (m, 12H), 1.10−0.81 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 137.2, 115.4, 37.5, 33.0, 29.0, 27.3, 13.7, 9.4, 8.7. HRMS (EI) calcd for $C_{13}H_{27}SSn$ $(M - C_4H_9)^+$ 335.0856, found 335.0858

1-Phenylselenyl-2-sulfonyl-5-hexene (74). MCPBA (50%, 2.5 g, 7.2 mmol, 1.4 equiv) was added in one portion to a stirred, cold (0 °C) solution of 1-tributylstannyl-3-sulfenyl-5-hexene (**75**) (1.0 g, 2.56 mmol) in CH_2Cl_2 (30 mL) and the mixture was allowed to warm to room temperature overnight. The slurry was then filtered and the precipitate washed with cold CH_2Cl_2 (30 mL). The filtrate was then washed with 3 M NaOH (3 × 30 mL) and brine (50 mL) before being dried (Na_2SO_4). Removal of the solvent in vacuo gave **78** as a colorless oil (0.86 g), which was used without further purification. 2M Butyllithium (1.5 mL, 3.0 mmol) was added to a cold (−78 °C) stirred solution of the crude sulfone (0.86 g, 2.0 mmol) in dry THF (14 mL). After 10 min, a solution of $(PhSe)_2$ (0.93 g, 3.0 mmol) in dry THF (10 mL) was added and the resulting mixture maintained at −78 °C for 20 min before being allowed to warm to room temperature. The reaction was quenched with saturated NH_4Cl (20 mL) then poured into water (60 mL) and extracted with pentane (2 × 50 mL). The organic extracts were washed with water (2 × 80 mL) and then brine (100 mL) before being dried ($MgSO_4$) and evaporated onto silica. Flash chromatography (hexane, hexane/CH_2Cl_2) yielded 1-phenylselenyl-2-sulfonyl-5-hexene (**74**) as a viscous, colorless oil (0.43 g, 74%): ^{1}H NMR ($CDCl_3$) δ 7.71−7.68 (m, 2H), 7.37−7.29 (m, 3H), 5.77−5.64 (m, 1H), 5.10−5.03 (m, 2H), 4.17 (s, 2H), 3.17 (t, J = 8.1 Hz, 2H), 2.53−2.47 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 134.3, 133.7, 129.6, 128.9, 127.8, 117.5, 50.4, 47.7, 26.3. HRMS (EI) calcd for $C_{11}H_{14}O_2SSe$ 289.9880, found 289.9882.

3-Sulfenyl-6-heptenoic Acid (79). Mercaptoacetic acid (1.22 mL, 17.5 mmol) was added dropwise over 10 min to a stirred solution of sodium methoxide (1.0 g, 43.0 mmol of sodium, 25 mL of methanol) at room temperature. After 90 min, 3-butenyl methanesulfonate (2.90 g, 19.3 mmol) in diethyl ether (5 mL) was added and the mixture was stirred overnight at room temperature. The solvent was then removed under reduced pressure and the residue dissolved in 3 M NaOH (35 mL). The resulting solution was washed with CH_2Cl_2 (80 mL), acidified (pH 2) with 10% HCl, and then extracted with CH_2Cl_2 (3 × 50 mL). The combined extracts were dried (Na_2SO_4) and the solvent removed under reduced pressure to yield 3-sulfenyl-6-heptenoic acid (**79**) as a colorless oil (2.43 g, 95%): ^{1}H NMR ($CDCl_3$) δ 11.2 (s, 1H), 5.89−5.76 (m, 1H), 5.14−5.04 (m, 2H), 3.27 (s, 2H), 2.74 (t, J = 7.5 Hz, 2H), 2.42−2.34 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 176.9, 136.0, 116.4, 33.5, 33.1, 32.0 (lit.[33] NMR); LRMS *m*/*z* (% base), 146 (64), 105 (79), 87 (52), 77 (100), 54 (76). HRMS (EI) calcd for $C_6H_{10}O_2S$ (M^+) 146.0402, found 146.0402.

Methyl 3-Sulfinyl-6-heptenoate (80). A mixture of 3-sulfenyl-6-heptenoic acid (**79**) (2.77 g, 19.1 mmol) and $NiCl_2 \cdot 6H_2O$ (10 mol %) in methanol (20 mL) was heated at reflux overnight.[32] After removal of the solvent under reduced pressure, the residue was dissolved in diethyl ether (120 mL) and washed with H_2O (2 × 50 mL) then saturated sodium bicarbonate solution (2 × 40 mL) before being dried (Na_2SO_4). Removal of solvent and distillation of the residue (Kugelrohr: 50 °C/0.1 mm) gave methyl 3-sulfenyl-6-heptenoate as a colorless oil (2.5 g, 83%): ^{1}H NMR ($CDCl_3$) δ 5.86−5.72 (m, 1H), 5.10−5.0 (m, 2H), 3.71 (s, 3H), 3.21 (s, 2H), 2.68 (t, J = 7.3 Hz, 2H), 2.37−2.29 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 170.8, 136.2, 116.2, 52.3, 33.4, 33.2, 31.9 (lit.[33] ^{13}C NMR: NB extra signal reported at 128.2 ppm); LRMS *m*/*z* (% base) 160 (47), 119 (58), 87 (59), 61 (70), 45 (100). Sodium metaperiodate (3.47 g, 16.25 mmol) was added portionwise to a cooled solution (0 °C) of the above ester (2.60 g, 16.25 mmol) in methanol/H_2O (20 mL /15 mL) and the stirred mixture was allowed to warm to room temperature over 2 h. The mixture was then filtered and the precipitate washed with CH_2Cl_2 (40 mL) and solvent removed under reduced pressure. The residue was taken into brine and extracted with CH_2Cl_2 (2 × 80 mL) and dried ($MgSO_4$). Removal of solvent and distillation of the residue (Kugelrohr: 130 °C/0.1 mm) afforded methyl 3-sulfinyl-6-heptenoate (**80**) as a clear colorless oil (2.5 g, 87%): ^{1}H NMR ($CDCl_3$) δ 5.89−5.76 (m, 1H), 5.19−5.08 (m, 2H), 3.77 (s, 3H), 3.70 (d, J = 13.8 Hz, 1H), 3.67 (t, J = 13.8 Hz, 1H), 2.94−2.89 (m, 2H), 2.59−2.51 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 165.4, 134.4, 117.4, 55.6, 52.8, 51.8, 26.4; LRMS *m*/*z* (% base) 177 (23), 122 (17), 90 (13), 55 (100); HRMS (ESI) calcd for $C_7H_{13}O_3S$ (M + H) 177.0585, found 177.0580.

3-Sulfinyl-6-heptenoic Acid (81). NaOH (3 M, 4.5 mL) was added dropwise over 5 min to a stirred cool solution (0 °C) of methyl 3-sulfinyl-6-heptenoate (**80**) (1.6 g, 9.1 mmol) in methanol (15 mL) and the mixture was allowed to warm to room temperature overnight. The majority of the solvent was removed under reduced pressure followed by the addition of water (20 mL) then washed with ether (30 mL) acidified to pH 1−2 with HCl (10%) and extracted with CH_2Cl_2 (2 × 80 mL). After being dried ($MgSO_4$), solvent was removed in vacuo to give **81** as a white solid (mp 52−54 °C) (1.40 g, 88%): ^{1}H NMR ($CDCl_3$) δ 10.6 (br, s, 1H), 5.88−5.75 (m, 1H), 5.20−5.10 (m, 2H), 3.82 (s, 2H), 3.15−2.95 (m, 2H), 2.59−2.51(m, 2H), 3.19−3.03 (m, 2H), 2.49 (t, J = 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 166.6, 134.0, 117.7, 54.4, 50.7, 26.5; HRMS (ESI) calcd for $C_6H_{10}NaO_3S$ $(M + Na)^+$ 185.0249, found 185.0242. Anal. Calcd for $C_6H_{10}O_3S$: C, 44.43; H, 6.21. Found: C, 44.25; H, 6.42.

1-Phenylselenyl-2-sulfinyl-5-hexene (73). Dicyclohexyldicarbodiimide (0.635 g, 3.1 mmol) in CH_2Cl_2 (2 mL) was added dropwise over 5 min to a cold (0 °C) stirred solution of 3-sulfinyl-6-heptenoic acid (**81**) (0.5 g, 3.1 mmol) and 1-hydroxypyridine-2-thione (0.39 g, 3.1 mmol) in CH_2Cl_2 (10 mL). The solution was protected from light and allowed to stir for a further 3 h at 0 °C. Diphenyldiselenide (4.0 g 12.8 mmol, 4.2 equiv) was added in one portion and the mixture was allowed to stir to the exclusion of light for a further 15 min and then irradiated at 0 °C with a 300 W tungsten lamp. After 60 min the mixture was filtered and then concentrated on silica and subjected to flash chromatography (hexane, hexane/CH_2Cl_2, EtOAc) yielding **73** as a colorless solid (200 mg, 24%): ^{1}H NMR ($CDCl_3$) δ 7.65−7.60 (m, 2H), 7.35−7.28 (m, 3H), 5.87−5.74 (m, 1H), 5.16−5.07 (m, 2H), 4.04 (s, 2H), 3.03−2.92 (m, 1H), 2.80−2.71 (m, 1H), 2.56−2.47 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 134.6, 133.6, 129.4, 128.2, 127.9, 116.9, 50.2, 46.4 ($^1J_{^{77}Se-^{13}C}$

(31) Oswald, A. A.; Griesbaum, K.; Thaler, W. A.; Hudson, B. E. *J. Am. Chem. Soc.* **1962**, *84*, 3897.
(32) Ram, R. N.; Charles, I. *Tetrahedron* **1997**, *53*, 7335.
(33) Padwa, A.; Heidelbaugh, T. M.; Kuethe, J. T. *J. Org. Chem.* **1999**, *64*, 2038.

=91 Hz), 26.2; HRMS (ESI) calcd for $C_{11}H_{15}OSSe^+$ $(M + H)^+$: 275.0009, found 275.0008.

3-Methyl-3-butenyl Thioacetate (85). Thioacetic acid (5.2 mL, 73.2 mmol) was added dropwise over 20 min to a stirred slurry of sodium hydride (60%, 2.92 g, 73.2 mmol) in DMF (40 mL) under a nitrogen atmosphere at room temperature. After 60 min, 3-methyl-3-butenyl methanesulfonate (11.0 g, 67.0 mmol) in DMF (10 mL) was added over 20 min. After being stirred for 2 h, the reaction was quenched by the addition of water (80 mL) and then extracted with pentane (2 × 100 mL). The combined organic extracts were washed with water (3 × 50 mL) and then brine (80 mL) before being dried (Na_2SO_4). Evaporation of the solvent and distillation of the residue (Kugelrohr: 85−90 °C/20 mm) yielded **85** as a pale yellow oil (8.64 g, 90%): ^{1}H NMR ($CDCl_3$) δ 4.79−4.77 (m, 1H), 4.73−4.71 (m, 1H), 3.01−2.96 (t, J = 7.5 Hz, 2H), 2.31 (s, 3H), 2.29−2.24 (t, J = 7.5 Hz, 2H), 1.73 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 195.7, 143.4, 111.5, 37.3, 30.6, 27.2, 22.2; HRMS (EI) calcd for $C_7H_{12}OS$ $(M)^+$ 144.0609, found 144.0608.

1-Phenylselenyl-2-sulfenyl-5-methyl-5-hexene (82). 3-Methyl-3-butenyl thioacetate (1.08 g, 7.5 mmol) was treated with sodium methoxide (0.17 g, 7.5 mmol sodium, 10 mL methanol) and phenylselenylmethyl bromide (1.25 g, 5.0 mmol) and worked up as outlined for the preparation of **72**. The crude yellow oil (1.30 g) was chromatographed (hexane, hexane/CH_2Cl_2) and distilled (Kugelrohr: 105−110 °C/0.1 mm) to give **82** as a pale straw-colored oil (1.0 g, 74%): ^{1}H NMR ($CDCl_3$) δ 7.73−7.68 (m, 2H), 7.40−7.29 (m, 3H), 4.81−4.79 (m, 1H), 4.68−4.66 (m, 1H), 4.02 (s, 2H), 2.82−2.76 (t, J = 7.6 Hz, 2H), 2.33−2.28 (t, J = 7.6 Hz, 2H), 1.76 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 143.7, 133.4, 130.2, 129.0, 127.5, 111.4, 37.1, 30.9, 30.4, 22.2; HRMS (EI) calcd for $C_{12}H_{16}SSe$ 272.0138, found 272.0137.

1-Tributylstannyl-2-sulfenyl-5-methyl-5-hexene (86). Treatment of 3-methyl-3-butenyl thioacetate (**85**) (1.86 g, 12.9 mmol) with sodium methoxide (0.32 g, 13.9 mmol sodium, 20 mL of methanol) and then iodomethyltributyltin[27b] (5.0 g, 11.6 mmol) followed by work up along the lines described for the synthesis of **75** and distillation of the product (Kugelrohr: 135 °C/0.1 mm) gave **86** as a colorless oil (4.2 g, 91%): ^{1}H NMR ($CDCl_3$) δ 4.76−4.71 (m, 2H), 2.62−2.57 (m, 2H), 2.34−2.29 (t, J = 7.8 Hz, 2H), 1.94 (s, 2H), 1.74 (s, 3H), 1.59−1.45 (m, 6H), 1.37−1.25 (m, 6H), 0.96−0.87 (m, 15H): ^{13}C NMR ($CDCl_3$) δ 144.5, 110.8, 37.0, 36.5, 29.0, 27.3, 22.3, 13.7, 9.5, 8.9; HRMS (EI) calcd for $C_{14}H_{29}SSn$ $(M - C_4H_9)^+$ 349.1012, found 349.1014.

1-Phenylselenyl-2-sulfonyl-5-methyl-5-hexene (84). Treatment of **86** (2.28 g, 5.63 mmol) with MCPBA (77%, 3.05 g, 9.88 mmol) as employed for the stannane **75** gave 1-tributylstannyl-2-sulfonyl-5-methyl-5-hexene (**87**) as a colorless oil (2.35 g, ∼95%), which was used without further purification. The stannane **87** (3.0 g, 7.5 mmol) in dry THF (25 mL) was treated with 2.5 M butyllithium (3.45 mL, 8.62 mmol) and then $(PhSe)_2$ (2.85 g, 9.15 mmol) in the manner used for the synthesis of **74**. Workup and flash chromatography (hexane, hexane/EtOAc) yielded **84** as a viscous, colorless oil (0.79 g, 35%): ^{1}H NMR ($CDCl_3$) δ 7.73−7.68 (m, 2H), 7.40−7.29 (m, 3H), 4.81−4.79 (m, 1H), 4.68−4.66 (m, 1H), 4.18 (s, 2H), 3.24−3.18 (m, 2H), 2.44−2.39 (m, 2H), 1.70 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 141.2, 134.2, 129.6, 128.9, 127.9, 112.2, 49.7, 47.6, 29.7, 22.2; HRMS (ESI) calcd for $C_{12}H_{17}O_2SSe^+$ $(M + H)^+$ 305.0114, found 305.0109.

3-Sulfenyl-6-methyl-6-heptenoic Acid (88). 3-Methyl-3-butenyl methanesulfonate (12.0 g, 74.0 mmol) in CH_3OH (15 mL) was added to a solution of mercaptoacetic acid (4.8 mL, 69.2 mmol) and sodium methoxide (3.72 g, 161.2 mmol sodium, 100 mL methanol) as performed for the synthesis of **79**. Workup gave **88** as a colorless oil (10.9 g, 98%). A small sample was distilled (Kugelrohr: 100 °C/0.1 mm): ^{1}H NMR ($CDCl_3$) δ 11.0 (s, 1H), 4.79−4.77 (m, 1H), 4.75−4.73 (m, 1H), 3.26 (s, 2H), 2.81−2.75 (t, J = 7.6 Hz, 2H), 2.34−2.29 (t, J = 7.6 Hz, 2H), 1.73 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 176.9, 143.3, 111.7, 37.0, 33.5, 30.8, 22.1; HRMS (ESI) calcd for $C_7H_{12}NaO_2S$ (M + Na) 183.0456, found, 183.0455.

Methyl 3-Sulfenyl-6-methyl-6-heptenoate (89). A mixture of $NiCl_2 \cdot 6H_2O$ (0.9 g, 10 mol %) and 3-sulfenyl-6-methyl-6-heptenoic acid (**88**) (5.6 g, 135 mmol) in methanol (53 mL) was treated as described for the acid **79**. Workup and distillation of the product (Kugelrohr: 95−100 °C/3 mm) gave **89** as a colorless oil (5.3 g, 87%): ^{1}H NMR ($CDCl_3$) δ 4.77 (m, 1H), 4.73 (m, 1H), 3.71 (s, 3H), 3.22 (s, 2H), 2.73 (t, J = 7.6 Hz, 2H), 2.29 (t, J = 7.6 Hz, 2H), 1.72 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 170.8, 143.4, 111.5, 52.3, 37.1, 33.4, 30.7, 22.0; LRMS m/z (% base) 174 (59), 101 (71), 68 (66), 67 (59), 61 (81), 45 (100); HRMS (ESI) calcd for $C_8H_{14}NaO_2S$ (M + Na) 197.0612, found 197.0605. Anal. Calcd for $C_8H_{14}O_2S$: C, 55.14; H, 8.10. Found; C, 55.18; H,7.91.

Methyl 3-Sulfinyl-6-methyl-6-heptenoate (90). Methyl 3-sulfenyl-6-methyl-6-heptenoate (**89**) (3.0 g, 17.22 mmol) in 1:1 methanol/H_2O (30 mL) was treated with sodium metaperiodate (3.88 g, 18.08 mmol) as reported for the synthesis of **80**. Flash chromatography of the product (hexane, CH_2Cl_2, ether) yielded **90** as a clear colorless oil that solidified upon standing (3.1 g, 94%): ^{1}H NMR ($CDCl_3$) δ 4.85−4.83 (m, 1H), 4.80−4.78 (m, 1H), 3.77 (s, 3H), 3.72 (d, J = 13.7 Hz, 1H), 3.68 (t, J = 13.7 Hz, 1H), 2.48 (t, J = 7.8 Hz, 2H), 1.76 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.5, 141.9, 112.3, 55.6, 52.8, 50.9, 30.0, 22.3; HRMS (ESI) calcd for $C_8H_{14}NaO_3S$ (M + Na) 213.0562, found 213.0555.

3-Sulfinyl-6-methyl-6-heptenoic Acid (91). Hydrolysis of methyl 3-sulfinyl-6-methyl-6-heptenoate (**90**) (2.05 g, 10.8 mmol) with 3 M NaOH (5.4 mL) was effected as described for **80**. Workup gave **91** as a clear colorless oil that solidified upon standing (1.65 g, 86%): ^{1}H NMR ($CDCl_3$) δ 10.2 (br s, 1H), 4.86−4.84 (m, 1H), 4.81−4.79 (m, 1H), 3.83 (d, J = 14.4 Hz, 1H), 3.79 (d, J = 14.4 Hz, 1H), 3.19−3.03 (m, 2H), 2.49 (t, J = 7.8 Hz, 1H), 1.77 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 166.6, 141.5, 112.7, 54.1, 49.8, 30.2, 22.2. Anal. Calcd for $C_7H_{12}O_3S$: C, 47.71; H, 6.86. Found: C, 47.74; H, 6.97.

1-Phenylselenyl-2-sulfinyl-5-methyl-5-hexene (83). The acid **91** was exposed to dicyclohexyldicarbodiimide (0.585 g, 2.83 mmol) and 1-hydroxypyridine-2-thione (0.36 g, 2.83 mmol) as outlined above for **81**. After workup, the crude product was subjected to flash chromatography (hexane, hexane/CH_2Cl_2, EtOAc) to give **83** as a colorless solid (370 mg, 45%): ^{1}H NMR ($CDCl_3$) δ 7.63−7.60 (m, 2H), 7.34−7.27 (m, 3H), 4.82−4.80 (m, 1H), 4.74−4.73 (m, 1H), 4.04 (s, 2H), 3.09−2.99 (m, 1H), 2.81−2.71 (m, 1H), 2.46−2.41 (m, 2H), 1.74 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 142.1, 133.7, 129.4, 128.4, 128.0, 111.9, 49.3, 46.5, 29.9, 22.3; HRMS (ESI) calcd for $C_{12}H_{17}OSSe$ $(M + H)^+$ 289.0165, found 289.0163.

2-Sulfinyl-5-hexene (77). 2-Sulfenyl-5-hexene (**92**) (0.34 g, 3.3 mmol) in methanol (5 mL) was treated with sodium metaperiodate (0.75 g, 3.49 mmol) as discussed for the preparation of **80**. Workup gave a pale brown oil (0.31 g, 80%) purification of which by flash chromatography (CH_2Cl_2/ethyl acetate) gave 2-sulfinyl-5-hexene (**77**) as a colorless oil (0.28 g, 72%): ^{1}H NMR ($CDCl_3$) δ 5.90−5.76 (m, 1H), 5.18−5.07 (m, 2H), 2.85−2.67 (m, 2H), 2.58−2.47 (m, 2H), 2.56 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 134.8, 117.1, 53.7, 38.5, 26.6; HRMS (ESI) calcd for $C_5H_{10}NaOS^+$ (M + Na) 141.0350, found 141.0350.

2-Sulfonyl-5-hexene (93). Treatment of 2-sulfenyl-5-hexene (**92**) (0.30 g, 2.9 mmol) in CH_2Cl_2 (20 mL) with MCPBA (50%, 2.22 g, 6.40 mmol) was performed as outlined for oxidation of **75**. Workup and flash chromatography (hexane/CH_2Cl_2) yielded 2-sulfonyl-5-hexene (**93**) as a colorless oil (0.20 g, 51%) that solidified upon standing: ^{1}H NMR ($CDCl_3$) δ 5.92−5.72 (m, 1H), 5.22−5.09 (m, 2H), 3.12−3.05 (m, 2H), 2.90 (s, 3H), 2.66−2.53 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 133.7,117.6, 59.9, 40.8, 26.6; HRMS (EI) calcd for $C_5H_{10}O_2S$ 134.0402, found 134.0401.

2-Sulfinyl-5-methyl-5-hexene (95). Treatment of 2-sulfenyl-5-methyl-5-hexene (**94**) (0.75 g, 6.46 mmol) in methanol (2 mL) with sodium metaperiodate (1.45 g, 6.79 mmol) as described above for **77** and flash chromatography of the

product yielded 2-sulfinyl-5-methyl-5-hexene (**95**) as a colorless oil (0.75 g, 88%): ^{1}H NMR ($CDCl_3$) δ 4.82−4.81 (m, 1H), 4.77−4.76 (m, 1H), 2.88−2.73 (m, 2H), 2.57 (s, 3H), 2.48−2.40 (m, 2H), 1.76 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 142.1, 111.9, 52.6, 38.5, 30.2, 22.4; LRMS *m*/*z* (% base), 133 (6), 115 (18), 69 (58), 41 (100); HRMS (EI) calcd for $C_6H_{12}OS$ 132.0609, found 132.0612.

2-Sulfonyl-5-methyl-5-hexene (96). The sulfide **94** (0.75 g, 6.46 mmol) was treated with MCPBA (50%, 4.42 g, 13.0 mmol) as outlined above for **93**. Flash chromatography (hexane/CH_2Cl_2) and recrystallization (hexane) of the product gave 2-sulfonyl-5-methyl-5-hexene (**96**) (0.85 g, 89%) as colorless plates (mp 52−53 °C): ^{1}H NMR ($CDCl_3$) δ 4.86−4.83 (m, 1H), 4.78−4.76 (m, 1H), 3.16−3.10 (m, 2H), 2.91 (s, 3H), 2.56−2.50 (m, 2H), 1.76 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 141.1, 112.2, 53.0, 40.5, 30.0, 22.1; HRMS (EI) calcd for $C_6H_{12}O_2S$ 148.0558, found 148.0559. Anal. Calcd for $C_6H_{12}O_2S$: C, 48.62; H, 8.16; S, 21.63. Found: C, 48.52; H, 8.34; S, 21.62.

Synthesis of 4-Methylthiapyran 1,1-Dioxide (55). A 0.01 M solution of 1-phenylselenyl-2-sulfonyl-5-methyl-5-hexene (**84**) (0.135 g, 0.43 mmol) in benzene (40 mL) was deoxygenated, heated to reflux (80 °C), and then treated with a solution of Bu_3SnH (0.16 g, 0.54 mmol) in deoxygenated benzene (3 mL) containing a few crystals of AIBN over 15 min. The resulting solution was heated for a further 3 h, cooled, and then quenched with CH_3I and concentrated in vacuo. GCMS analysis of the crude product revealed the presence of 3,3-dimethyltetrahydrothiophene 1,1-dioxide (**54**) in a minute amount (ca. 3%) and a trace of 2-sulfonyl-5-methylhexene (**96**). Flash chromatography on silica (hexane/ether) yielded the sulfone **55** as a colorless solid (0.055 g, 86%), which was identified by comparison of its physical properties with those of the authentic sample.

Methyl 3-Sulfonyl-6-methyl-6-heptenoate (59). Methyl 3-sulfenyl-6-methyl-6-heptenoate (**89**) (3.0 g, 17.22 mmol) was dissolved in CH_2Cl_2 (150 mL), cooled to (0 °C) with stirring, and then treated with MCPBA (11.78 g, 35.65 mmol) as described above. Workup and flash chromatography of the product yielded methyl 3-sulfonyl-6-methyl-6-heptenoate (**59**) as a colorless solid (2.6 g, 74%): ^{1}H NMR ($CDCl_3$) δ 4.87−4.85 (m, 1H), 4.81−4.79 (m, 1H), 3.98 (s, 2H), 3.82 (s, 3H), 3.41−3.36 (m, 2H), 2.58−2.53 (m, 2H), 1.78 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 163.5, 141.0, 112.7, 57.3, 53.2, 51.8, 29.7, 22.1; LRMS *m*/*z* (% base) 206 (M^+) (14), 139 (42), 81 (18), 67 (100), 53 (24), 41 (79); HRMS (ESI) calcd for $C_8H_{14}NaO_4S$ (M + Na) 229.0511, found 229.0507.

Methyl 2-Phenylselenyl-3-sulfonyl-6-methyl-6-heptenoate (60). A mixture of methyl 3-sulfonyl-6-methyl-6-heptenoate (**59**) (140 mg, 0.68 mmol) and $(PhSe)_2$ (320 mg, 1.03 mmol) in dry THF (3 mL) was added to a stirred slurry of 60% sodium hydride (80 mg, 2.0 mmol) in THF (8 mL) at 0 °C. After a further 10 min at 0 °C, the ice bath was removed and the mixture allowed to warm to room temperature and stirred for a further 45 min. The reaction was quenched with H_2O (15 mL) and washed with hexane. After saturation of the aqueous layer with NaCl, the mixture was extracted with EtOAc (2 × 25 mL), then dried ($MgSO_4$) and the solvent removed in vacuo. Chromatography (hexane, hexane/CH_2Cl_2, CH_2Cl_2) of the product yielded methyl 2-phenylselenyl-3-sulfonyl-6-methyl-6-heptenoate (**60**) as a colorless solid (70 mg, 30%): ^{1}H NMR ($CDCl_3$) δ 7.80−7.70 (m, 2H), 7.44−7.32 (m, 3H), 4.85−4.83 (m, 1H), 4.78 (s, 1H), 4.77−4.75 (m, 1H), 3.78 (s, 3H), 3.63−3.39 (m, 2H), 2.55 (t, J = 8.2 Hz, 2H), 1.76 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.5, 141.2, 135.6, 129.8, 129.5, 126.9, 112.2, 63.6 ($^1J_{^{77}Se-^{13}C}$ = 98.8 Hz), 53.6, 48.9, 28.8, 22.3; HRMS (ESI) calcd for $C_{14}H_{18}NaO_4SSe$ (M + Na) 384.9989, found 384.9977.

2-Carboxymethyl-4-methyl-thiopyran 1,1-Dioxide (61). A 0.014 M solution of the ester **60** (50 mg, 0.14 mmol) in benzene (10 mL) was deoxygenated and heated under reflux. Bu_3SnH (51 mg, 0.17 mmol, 1.25 equiv) in benzene (4 mL) containing a small amount of AIBN was added over 15 min and the solution heated for a further 60 min. The mixture was cooled then quenched with CH_3I. The reaction mixture was concentrated giving a diastereomeric mixture (26 mg, ~86%) of 2-carboxymethyl-4-methyl-thiopyran 1,1-dioxide (**61**). HRMS (ESI) calcd for $C_8H_{14}NaO_4S$ (M + Na) 229.0511, found 229.0501. Flash chromatography (hexane, CH_2Cl_2) yielded (i) the minor diastereomer [^{1}H NMR ($CDCl_3$) δ 3.88−3.80 (m, 1H), 3.81 (s, 3H), 3.66−3.56 (m, 1H), 3.01−2.93 (m, 1H), 2.22−2.01 (m, 4H), 1.93−1.79 (m, 1H), 0.99 (d, J = 6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 167.28, 63.51, 53.08, 48.68, 35.27, 31.72, 25.38, 20.89] and (ii) the major diastereomer [^{1}H NMR ($CDCl_3$) δ 3.95−3.87 (m, 1H), 3.84 (s, 3H), 3.17−2.98 (m, 2H), 2.26−1.84 (m, 4H), 1.83−1.70 (m, 1H), 1.07 (d, J = 6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 165.37, 65.10, 53.42, 52.55, 35.69, 31.85, 30.94, 21.33].

3-Methylenetetrahydrothiophene (97). A stirred solution of 2-methyene-1,4-butanediyl dimethanesulfonate[34] (3.25 g, 12.6 mmol) in 95% EtOH (80 mL) was treated with a solution of $Na_2S{\cdot}2H_2O$ (2.95 g, 26.3 mmol) in 95% EtOH (20 mL) as described.[35] Workup gave 3-methylenetetrahydrothiophene (**97**) as a pale-brown oil (1.09 g, 86%): ^{1}H NMR ($CDCl_3$) δ 4.98−4.96 (m, 1H), 4.94−4.92 (m, 1H), 3.45−3.43 (s, 2H), 2.86 (t, J = 6.6 Hz, 2H), 2.65−2.60 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 148.9, 107.3, 36.8, 35.3, 30.5; LRMS *m*/*z* (% base) 100 (M^+) (98), 99 (100), 85 (52), 71 (18), 67 (13); HRMS (EI) calcd for C_5H_8S (M^+) 100.0347, found 100.0346.

3-Hydroxymethyltetrahydrothiophene (98). With use of a modified procedure developed by Brown and associates,[36] a solution of 10 M borane−methyl sulfide complex (0.37 mL, 3.7 mmol) was added dropwise to a cold (0 °C) stirred solution of 3-methylenetetrahydrothiophene (**97**) (350 mg, 3.5 mmol) and stirring continued for 1 h at room temperature. The mixture was then cooled (0 °C) and treated dropwise with 3 M NaOH (1.2 mL) followed immediately by addition of 30% H_2O_2 (0.6 mL). The mixture was allowed to warm to room temperature and stirred for a further 2 h before being quenched by addition of H_2O (3 mL) and then extracted with ether (3 × 30 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ and then dried ($MgSO_4$). Removal of solvent under reduced pressure yielded a straw-colored oil (250 mg, 61%), a portion of which was distilled (Kugelrohr: bp 95−100 °C/1.0 mm) to give the title compound **98** as a clear colorless oil: ^{1}H NMR ($CDCl_3$) δ 3.62−3.52 (m, 2H), 2.92−2.78 (m, 3H), 2.62−2.57 (m, 1H), 2.48 (br s, 1H), 2.45−2.31 (m, 1H), 2.12−2.02 (m, 1H), 1.76−1.64 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 64.3, 40.5, 33.6, 33.2, 30.6; LRMS *m*/*z* (% base) 118 (M^+) (100), 101 (24), 85 (43), 59 (24); HRMS (ESI) calcd for $C_5H_{11}OS$ (M + H) 119.0531, found 119.0529; HRMS (ESI) calcd for $C_5H_{10}NaOS$ (M + Na) 141.0350, found 141.0346.

3-Bromomethyltetrahydrothiophene (33a). Carbon tetrabromide (755 mg, 2.11 mmol) was added slowly to a stirred mixture of triphenylphosphine (555 mg, 2.11 mmol) and 3-hydroxymethyltetrahydrothiophene (**98**) (250 mg, 2.11 mmol) in THF (5 mL) at 0 °C. The reaction was stirred for a further 2 h and then filtered through a sintered glass funnel and concentrated in vacuo. The residue was dissolved in pentane (5 mL) and filtered through a short silica plug giving a colorless oil (245 mg, 64%) of high purity (NMR). Distillation (Kugelrohr: bp 105−110 °C/16 mm) provided the title compound **33a** as a clear colorless oil: ^{1}H NMR ($CDCl_3$) δ 3.48−3.38 (m, 2H), 3.02−2.96 (m, 1H), 2.92−2.87 (m, 2H), 2.71−2.55 (m, 2H), 2.26−2.16 (m, 1H), 1.89−1.76 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 46.4, 35.5, 35.3, 34.9, 30.3; LRMS *m*/*z* (% base) 182 (21), 180 (22), 101 (100), 67 (38), 59 (40); HRMS (ESI) calcd for C_5H_9BrS (M^+) 179.9608, found 179.9602.

3-Phenylselenomethyltetrahydrothiophene (33b). 3-Hydroxymethyltetrahydrothiophene (**98**) (120 mg, 1.02 mmol) in

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THF (5 mL) was converted into 3-bromomethyltetrahydrothiophene as described above. When the reaction was complete (GC), a solution of sodium benzeneselenolate (PhSeNa, 2 equiv), prepared by treatment of diphenyldiselenide in dry ethanol (5 mL/mmol) with $NaBH_4$ (2.2 equiv), was added via cannula and stirring continued for a further 2 h. The reaction was quenched with H_2O (15 mL) and extracted with CH_2Cl_2 (2 × 50 mL), and the extracts dried ($MgSO_4$), and the solvent removed in vacuo. Purification of the residue by chromatography yielded **33b** as colorless solid (60 mg, 23%): ^{1}H NMR ($CDCl_3$) δ 7.52−7.48 (m, 2H), 7.28−7.23 (m, 3H), 3.01−2.95 (m, 3H), 2.88−2.83 (m, 2H), 2.66−2.61 (m, 1H), 2.52−2.39 (m, 1H), 2.22−2.12 (m, 1H), 1.82−1.70 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 132.7, 130.1, 129.1, 127.0, 44.7, 36.63, 36.57, 31.1, 30.4; LRMS (CI) *m/z* 259 (M + H) 181, 101; HRMS (ESI) calcd for $C_{11}H_{14}SSe$ (M^+) 257.9981, found 257.9981.

3-Hydroxymethyltetrahydrothiophene 1,1-Dioxide (99). Treatment of 3-hydroxymethyltetrahydrothiophene (**98**) (0.2 g, 1.7 mmol) with sodium metaperiodate (0.80 g, 3.74 mmol) under conditions employed above and flash chromatography (EtOAc) of the crude product gave the title compound **99** as a colorless oil (90 mg, 36%). ^{1}H NMR ($CDCl_3$) δ 3.78−3.68 (m, 2H), 3.25−3.17 (m, 2H), 3.11−3.01 (m, 1H), 2.97−2.90 (dd, *J* = 9.3, 12.9 Hz, 1H), 2.74−2.62 (m, 1H), 2.37−2.26 (m, 1H), 2.10−1.97 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 64.10, 53.36, 51.58, 38.12, 24.98; LRMS *m/z* (% base) 151 (12), 133 (6), 117 (33), 104 (37), 67 (19), 57 (55), 55 (100). 3-Hydroxymethyltetrahydrothiophene-1-oxide (**100**) (∼1:1 mixture diastereomers); was isolated as minor byproduct. ^{1}H NMR ($CDCl_3$) δ 3.70−3.55 (m, 4H), 3.14−2.96 (m, 5H), 2.86−2.20 (m, 8H), 1.92−1.81 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 64.0, 63.6, 57.1, 55.9, 53.8, 53.6, 43.1, 41.6, 28.1, 27.6; LRMS *m/z* (% base) 135 (99), 117 (33), 104 (37), 88 (97), 67 (46), 63 (85), 55 (100).

3-Bromomethyltetrahydrothiophene 1,1-Dioxide (35a). Carbon tetrabromide (260 mg, 0.72 mmol) was added slowly to a stirred mixture of triphenylphosphine (190 mg, 0.72 mmol) and 3-hydroxymethyltetrahydrothiophene 1,1-dioxide (**99**) (90 mg, 0.6 mmol) in CH_2Cl_2 (3 mL) at 0 °C. The reaction was stirred overnight, after which the solvent was removed and the residue dissolved in ether (5 mL) to which CH_3I (250 uL) was added. After the mixture was filtered through a short silica plug and the solvent evaporated, the crude product was chromatographed (ether) to afford the title compound **35a** as a colorless solid (50 mg, 39%): ^{1}H NMR ($CDCl_3$) δ 3.50−3.48 (m, 2H), 3.32−3.22 (m, 2H), 3.16−3.06 (m, 1H), 2.96−2.78 (m, 2H), 2.48−2.37 (m, 1H), 2.11−1.97 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 55.2, 52.0, 37.9, 34.3, 27.5; LRMS *m/z* (% base) 215 (5), 213 (6), 133 (16), 105 (13), 69 (40), 41 (100); HRMS (ESI) calcd for $C_5H_9BrNaSO_2$ (M + Na) 234.9404, found 234.9404.

3-Phenylselenylmethyltetrahydrothiophene 1-Oxide (34a). Treatment of 3-hydroxymethyltetrahydrothiophene (**98**) (0.24 g, 2.0 mmol) in 1:1 acetone/H_2O (5 mL) with sodium metaperiodate (0.42 g, 2.0 mmol) under conditions employed above afforded a pale brown oil (0.10 g) that was found (NMR analysis) to consist of a mixture of the sulfone **99** and a diastereomeric mixture of the corresponding sulfoxide **100**. The mixture was converted into the corresponding mesylates by treatment with methanesulfonyl chloride (110 mg, 0.97 mmol) and Et_3N (100 mg, 0.97 mmol). After being stirred for 3 h, the mixture was treated with ether (10 mL) and filtered and the solvent removed. The residue was dissolved in THF (3 mL) and treated dropwise with a solution of sodium benzeneselenolate (PhSeNa, 2 equiv), prepared by treatment of $(PhSe)_2$ in dry ethanol (5 mL/mmol) with $NaBH_4$ (2.2 equiv). The mixture was stirred overnight and then worked up in the usual way. Chromatography of the crude product yielded (i) a 1:1 diastereomeric mixture of 3-phenylselenylmethyltetrahydrothiophene 1-oxide (**34a**) (50 mg) [^{13}C NMR ($CDCl_3$) δ 133.05, 132.94, 129.29, 129.25, 129.23, 129.14, 127.44, 127.24, 60.16, 58.57, 54.29, 53.46 ($J_{^{77}Se-^{13}C}$ = 116.4 Hz), 41.88, 40.09, 32.43, 32.01, 31.38, and 31.43; HRMS (ESI) calcd for $C_{11}H_{14}OSSe$ (M^+) 273.9930, found 273.9935] and (ii) 3-phenylselenylmethyltetrahydrothiophene 1,1-dioxide (**101**) (40 mg) as a white solid [^{1}H NMR ($CDCl_3$) δ 7.52−7.49 (m, 2H), 7.31−27 (m, 3H), 3.21−3.17 (m, 2H), 3.08−2.98 (m, 1H), 3.0 (d, *J* = 6.9 Hz, 2H), 2.84−2.76 (m, 1H), 2.72−2.56 (m, 1H), 2.46−2.36 (m, 1H), 1.98−1.84 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 133.2, 129.3, 128.7, 127.7, 56.7, 52.3, 37.2, 31.6, 29.0; LRMS *m/z* (% base) 290 (1), 213 (3), 158 (20), 133 (100), 117 (20), 91 (22), 77 (27), 69 (40); HRMS (ESI) calcd for $C_{11}H_{14}O_2SSe$ (M^+) 289.9879, found 289.9889.

TABLE 3. Products of Ring Closure of the Radicals 12, 15, 18, 47, 50, and 53

precursor	radical	concn (M)	*T* (°C)	acyclic	5-*exo*	6-*endo*
72	**12**	0.01	80	17	70	13
72	**12**	0.05	80	33	57	10
73	**15**	0.5	80	0.5	95[a]	4.5
74	**18**	0.01	80	4	73	23
74	**18**	0.05	80	9	69.5	21.5
82	**47**	0.01	80	38.5	7	54.5
83	**50**	0.01	80	2.5	22.5	76[b]
84	**53**	0.01	80	4	2.5	93.5
84	**53**	0.04	80	9	2.3	88.3

[a] Cis/trans = 3:1. [b] Cis/trans = 1.6:1

Typical Reduction Conditions. Stock solutions of selenophenyl radical precursors were prepared in benzene with the addition of bistributyltin oxide[37] and subjected to standard radical cyclization conditions (catalytic amount of A1BN; 1.2 equiv of Bu_3SnH injected over 2 min; reaction temperature 80 °C; reaction time further 2 h; cooled then quenched with CCl_4, for **72** and **82**, or CH_3I for **73**, **74**, **83**, and **84**). Reaction mixtures were analyzed by GC and calibrated with use of authentic samples of products prepared by standard procedures. The results are collected in Table 3.

Reversibility Experiments: Treatment of 3-Bromomethyltetrahydrothiophene (33a) with Bu_3SnH. Procedure A. A 0.009 M solution of 3-bromomethyltetrahydrothiophene (**33a**) (0.049 mmol) in benzene (5 mL) was deoxygenated and heated under reflux. Bu_3SnH (13 μL, 1.05 equiv) in benzene (250 μL) containing a small amount of AIBN was added over 5 min and the solution heated for a further 60 min. The mixture was cooled and then quenched with CCl_4. GC analysis of the reaction mixture and comparison with authentic samples indicated that it consisted solely of 3-methyltetrahydrothiophene (**33**).

Procedure B. A 0.005 M solution of 3-bromomethyltetrahydrothiophene (**33a**) (0.0048 mmol) in benzene (10 mL) was deoxygenated and heated under reflux. Bu_3SnH (13 μL, 1.05 equiv) in benzene (5 mL) containing a small amount of AIBN was added over 30 min and the solution heated for a further 60 min. The mixture was cooled then quenched with CCl_4. GC analysis in comparison with authentic samples indicated 3-methyltetrahydrothiophene (**33**) to be the sole product. Identical results were obtained when the corresponding selenide (**33b**) was used.

Treatment of 3-Phenylselenomethyltetrahydrothiophene 1-Oxide (34a) with Bu_3SnH. 3-Phenylselenylmethyltetrahydrothiophene-1-oxide (**34a**) (0.004 M, 0.02 mmol) in benzene (5 mL) was treated with Bu_3SnH (6 μL, 1.1 equiv) in benzene (0.25 mL) as described under Procedure A above, and then cooled and quenched with CH_3I. GC analysis showed 3-methyltetrahydrothiophene 1-oxide (**16**) (ca.1:1, diastereomeric mixture) to be the only product.

Treatment of 3-Bromomethyltetrahydrothiophene 1,1-Dioxide (35a) with Bu_3SnH. Procedure A. A 0.01 M solution of 3-bromomethyltetrahydrothiophene 1,1-dioxide (**35a**) (0.05 mmol) in benzene (4.5 mL) was deoxygenated and

(37) Maxwell, B. J.; Smith, B. J.; Tsanaktsidis, J. *J. Chem. Soc., Perkin 2* **2000**, 425.

heated under reflux. Bu_3SnH (13 μL, 1.1 equiv) in benzene (0.5 mL) was added as above. The mixture was cooled and quenched with CH_3I. GC analysis indicated 3-methyltetrahydrothiophene 1,1-dioxide (**19**) to be the sole product.

Procedure B. A 0.005 M solution of 3-bromomethyltetrahydrothiophene 1,1-dioxide (**35a**) in benzene (10 mL) was deoxygenated and heated under reflux. Bu_3SnH (13 μL, 1.1 equiv) in benzene (5 mL) was added. GC analysis indicated 3-methyltetrahydrothiophene 1,1-dioxide (**19**) to be the sole product. Treatment of the selenide (**101**) under the same conditions gave only the sulfone (**19**).

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Supporting Information Available: General experimental methods together with the synthesis of precursors/products **13**, **14**, **16**, **17**, **19**, **20**, **48**, **49**, **51**, **52**, **54**, **55**, **68**, **92**, and **94** and selected NMR spectra for compounds **33a**, **33b**, **34a**, **35a**, **59**, **60**, **61**, **68**, **70**−**75**, **77**, **79**, **80**−**85**, **86**, and **88**−**101**. This material is available free of charge via the Internet at http://pubs.acs.org.

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