Stereoselective Synthesis of Homochiral Substituted Tetrahydrothiophenes by Electrophile-Promoted Thioetherification

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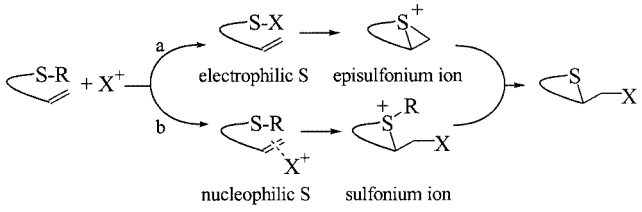
In this paper we study the electrophile-promoted cyclization of 2-sulfanyl-4-penten-1-ol and 1-sulfanyl-4-penten-2-ol derivatives as a way of preparing cyclic sulfides. The reaction is completely chemoselective and always proceeds by activation of the sulfur centre. The reaction of 2-sulfanyl-4-penten-1-ol derivatives proceeds by a 5-*endo* mode. Unsaturated thiol **6** undergoes iodine-promoted cyclothioetherification to give the tetrahydrothiophene **9** in moderate yields and with excellent regio- and stereoselectivity. However, when the reaction starts from the benzyl sulfide **7**, a diastereomeric mixture of **9** and **10** is obtained in good yields. Selenium-promoted cyclization of unsaturated thioacetate **5** provides the selenyltetrahydrothiophene **12** or the sulfanyl acetate **13**, depending on the selenium reagent used. On the other hand, electrophile-induced cyclization of 1-sulfanyl-4-penten-2-ol derivatives **23**–**25** depends on the electrophile used. Iodothioetherification of benzyl sulfide **25** followed by oxidation affords unsaturated sulfone **26** as a result of 6-*endo*-cyclization, dehydroiodination and oxidation. In contrast, selenothiocyclization of **24** with PhSeX results in the formation of the 5-*exo* tetrahydrothiophenes **29/30** and/or **31/32**.

Introduction

Electrophile-promoted cyclization of acyclic alkenes with internal nucleophiles is an important synthetic tool for the construction of a wide range of heterocyclic structures. This strategy has been extensively studied in substrates in which the heteroatom is O or NH,[1] and has been used to synthesise products with interesting biological properties.[2] Less attention has been paid to the synthesis of sulfur analogues by this approach,[3−16] even though replacement of O by S is a well-known strategy in the search for interesting new compounds.

Mechanistically, the overall reaction is believed to proceed as a stepwise addition/dealkylation sequence through a cationic intermediate. Oxygen and nitrogen cyclizations are considered to be kinetically controlled and the regioselectivity can be predicted by use of Baldwin's rules;[17−19] sulfur cyclizations, however, often afford products with different regiochemical outcomes. This difference can be accounted for by the fact that sulfur, which is a third-row element of larger atomic size, greater polarizability and higher nucleophilicity, may allow transition states that are not possible for the smaller second-row elements, and so Baldwin's rules cannot be applied to these systems. Furthermore, sulfur cyclizations are known to be highly reversible and to give products that can further isomerize.[5,9,13,20]

The most widely accepted mechanistic interpretation of sulfur cyclization involves initial generation of a source of a positive sulfur atom (pathway a, Scheme 1), such as sulfanyl halide, followed by intramolecular electrophilic addition of the S atom to the alkene to form episulfonium species. Nucleophilic (S_N2) opening of the episulfonium ion produces the final ring.[3−13] Only a few examples describe the cyclization in the form of an addition of a nucleophilic sulfur group to an electrophilically activated alkene (pathway b).[14−16]



Scheme 1. Proposed mechanisms for the electrophilically induced cyclization of sulfanylalkenes

Turos et al.[3,14] have carried out a systematic study of electrophilic and nucleophilic sulfur cyclizations from unsaturated sulfanyl halides and sulfides, respectively, by modifying the tether between the reactive sites and the type of unsaturated group. On treatment with iodine, thiols − which are prone to oxidation and dimerization − generate the sulfanyl iodide, which undergoes intramolecular addition to the alkene moiety present in the molecule. However,

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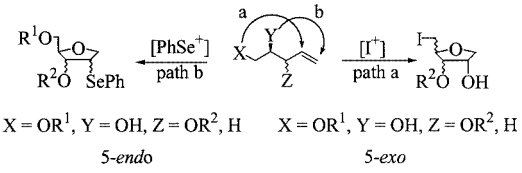
benzyl sulfides are quite resistant to dimerization and oxidation and seem to add to activated alkenes and therefore to react through a nucleophilic pathway (Scheme 1, pathway b).

We have recently shown that the electrophile-promoted cyclization of alkenediols and -triols can be regioselectively controlled, depending on the electrophile (Scheme 2).[22,23] With iodine as an electrophile, 5-*exo* cyclization takes place exclusively by involvement of the primary hydroxy group (path a) even when it is protected. If selenium electrophiles are used, however, the 5-*endo* product (path b) is obtained.



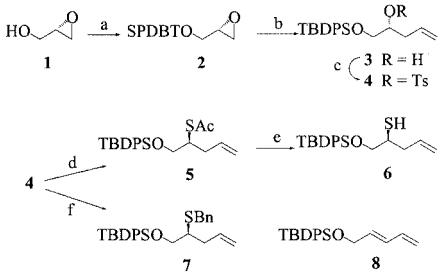
Scheme 2. Chemo- and regioselectivity in the electrophilically induced cyclization of 4-pentene-1,2-diols

We decided to extend our study to electrophilically induced cyclization reactions by replacing the hydroxy groups by sulfur functionalities. In this paper we report cyclizations of differently protected unsaturated sulfanyl alcohol derivatives such as 2-sulfanyl-4-pentenols (Scheme 2; X = OR, Y = SR, Z = H) and 1-sulfanyl-4-penten-2-ols (Scheme 2; X = SR, Y = OR, Z = H) induced by iodine and selenium electrophiles as a procedure for obtaining chiral sulfur-containing heterocycles.

Results and Discussion

We first explored the synthesis and cyclization of 2-sulfanyl-4-penten-1-ol derivatives. Thioacetate **5**, thiol **6** and benzyl sulfide **7** were synthesized and subjected to thiocyclization in order to study the chemo-, regio- and stereoselectivity of the reaction.

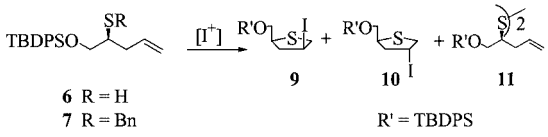
Compounds **5**, **6** and **7** were prepared from enantiopure glycidol (**1**) by a straightforward sequence (Scheme 3). Protection of **1** as a *tert*-butyldiphenylsilyl ether **2** and nucleophilic regioselective ring opening with a higher-order vinylcyanocuprate afforded homoallylic alcohol **3** in an excellent yield.[22] Activation of the hydroxy group as a tosylate **4** and displacement with potassium thioacetate under typical S_N2 conditions gave thioacetate **5** in a 85% yield, which was subjected to oxygen-free hydrolysis to afford labile thiol **6** in a 96% yield. The corresponding benzyl sulfide **7** was also prepared in a 62% yield, together with the elimination product **8** (18%), by displacement of tosylate **4** with sodium benzylsulfide.



a) imidazole, TBDPSCl, DMF, 80%. b) $(CH=CH_2)_2Cu(CN)(MgCl)_2$, ether, 98%. c) TsCl, py, 90%. d) $KSCOCH_3$, DMF, 45°C, 85%. e) $NaOCH_3$, CH_3OH, 96%. f) NaSBn, DMF, 62% (**7**), 18% (**8**).

Scheme 3. Synthesis of 2-sulfanyl-4-penten-1-ol derivatives

The study of the cyclization started with treatment of thiol **6** with iodine in the presence of K_2CO_3 in dichloromethane at −78 °C for 12 h, to afford the 5-*endo* cyclization product **9** in a 41% yield as a single stereoisomer, along with disulfide **11** (Entry 1, Table 1, Scheme 4). The configuration of the product was elucidated by NOE experiments (Figure 1).



Scheme 4. Iodine-induced cyclization of 2-sulfanyl-4-penten-1-ol derivatives

Figure 1. Observed NOE effects in compound **9**

Table 1. Iodine-promoted thiocyclization of compounds **6** and **7**

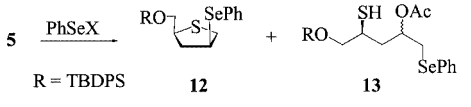
Entry	Substrate	Reagents	Product	Ratio **9/10**	Yield
1	**6**	I_2, K_2CO_3, CH_2Cl_2, −78 °C	**9/10**	100:0	41%[a]
2	**6**	I_2, K_2CO_3, CH_2Cl_2, −20 °C	**9/10**	80:20	40%[a]
3	**6**	I_2, $NaHCO_3$, MeCN	**9/10**	100:0	4%[a]
4	**6**	NIS, K_2CO_3, CH_2Cl_2, −20 °C	**9/10**	90:10	45%[a]
5	**6**	NIS, CH_2Cl_2, −20 °C	**9/10**	90:10	40%[a]
6	**7**	I_2, CH_2Cl_2, 0 °C → room temp.	**9/10**	60:40	77%
7	**7**	I_2, $NaHCO_3$, CH_2Cl_2, 0 °C → room temp.	**9/10**	58:42	75%
8	**7**	I_2, $NaHCO_3$, MeCN	**9/10**	63:37	70%
9	**7**	Br_2, CH_2Cl_2	complex mixture		
10	**7**	NIS, CH_2Cl_2, 0 °C → room temp.	**9/10**	85:15	40%[a]

[a] Variable amounts of disulfide **11** (not quantified) were also recovered.

Carrying out the reaction at −20 °C did not improve the yield and gave a lower stereoselectivity (Entry 2). Replacement of the base (Entry 3) or the electrophilic reagent (Entries 4 and 5) did not cause any significant changes in the yield or **9**/**10** isomer ratio. The *cis* compound **9** was always the major isomer, and variable amounts of disulfide **11** were always obtained as a secondary product. In the iodocyclization of similar diol and triol systems (Scheme 2) we observed that the counter-ion had a decisive role in the cyclization process.[22] Thus, 5-*exo* cyclizations took place in the presence of a nucleophilic counter-ion such as I^-, but there was no reaction when non-nucleophilic counter-ions were used. In contrast, cyclizations from sulfur derivatives **6** and **7** proceeded even in the presence of a non-nucleophilic counter-ion (Entries 4 and 5) and exhibited complete chemoselectivity through involvement of the sulfur atom.

Thiocyclization of benzyl sulfide **7** with iodine afforded the 5-*endo* product as a diastereomeric mixture of tetrahydrothiophenes **9** and **10** (Table 1, Entries 6−8). Under these conditions the yield increased to around 75% but the stereoselectivity decreased (ca. 60:40). Neither base nor solvent seemed to have any influence on the stereochemical outcome of the reaction. The use of bromine as electrophilic reagent (Entry 9) resulted in a complex mixture. Treatment of compound **7** with *N*-iodosuccinimide (NIS) (Entry 10) gave a mixture of diastereomeric tetrahydrothiophenes **9** and **10** in a lower yield (40%) but with a higher stereoselectivity (85:15).

Treatment of thioacetate **5** with iodine gave compound **9** in very low yield (4%). This may be because of its lower nucleophilicity relative to benzyl sulfide **7**. We then decided to explore the selenium-promoted cyclization of **5** (Table 2, Scheme 5). Thus, when PhSeCl/AgOTf was used as an electrophilic system, the 5-*endo* cyclization product **12** was obtained in a 9% yield (Entry 1). Treatment of thioacetate **5** with PhSeCl in dichloromethane increased the yield of **12** to 38%, but compound **13** (10% yield) was also isolated (Entry 2). Use of *N*-phenylselenophthalimide (N-PSP) and camphorsulfonic acid (CSA)[23] in dichloromethane afforded no cyclization product but increased the amount of compound **13** obtained (56%, Entry 3). Formation of **13** is believed to proceed by nucleophilic attack of the thioacetate oxygen atom on the intermediate seleniranium ion.

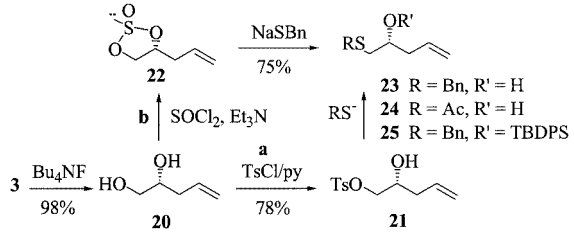


Scheme 5. Selenium-induced cyclization of sulfanylpentenol **5**

As shown above, the thiocyclization reactions were all chemo- and regiospecific, and they all provided the 5-*endo* product by involvement of the sulfur atom; no traces of the 4-*exo* product, or of the 5-*exo* product by involvement of the oxygen atom[22,24] were detected. Both the yield and the stereochemical outcome appeared to depend on the group attached to the sulfur atom.

In contrast to iodocyclization from benzyl sulfide **7**, selenium-promoted thiocyclization of **5** is highly stereoselective. This may be because the congestion of the seleniranium ion is greater than in the alkene−iodine π complex. Nicolaou et al.[7] explained the stereospecificity of an analogous selenium-promoted thiocyclization in terms of the complexation of both the olefin and the sulfur group by selenium prior to seleniranium ion formation. In addition, cyclization from **5** involves initial sulfonium ion formation and subsequent deacylation. Like benzyl sulfide cyclizations, deacylation requires a nucleophilic anion if it is to proceed. This may explain the improved yield in compound **12** when changing from PhSeOTf to PhSeCl, as Cl^- is more nucleophilic than TfO^- and therefore facilitates deacylation. On the other hand, *N*-PSP/CSA gave no cyclization product, perhaps because of the absence of nucleophiles in the medium.

In the light of the results obtained with 2-sulfanyl-4-pentenol derivatives, we decided to explore the preparation and cyclization of primary sulfanyl derivatives, that is, 1-sulfanyl-4-pentenols. Benzyl sulfides **23**/**25** and thioacetate **24** were prepared from enantiopure (*S*)-glycidol and subjected to thiocyclization. Treatment of diol **20** with tosyl chloride in pyridine gave the monotosylated compound **21** in 78% yield. Displacement of the sulfonate group with sodium benzylsulfide or potassium thioacetate afforded the thio derivatives **23** and **25**, respectively, in quantitative yields. Benzyl sulfide **23** was also prepared through the cyclic sulfite derivative **22** and nucleophilic ring opening with sodium benzylsulfide.



Scheme 6. Synthesis of 1-sulfanyl-4-pentene-2-ol derivatives

Table 2. Selenium-promoted thiocyclization of compound **5**

Entry	Substrate	Reagents	Product	Ratio **12**/**13**	Yield
1	**5**	PhSeCl, AgOTf, MeCN	**12**/**13**	100:0	9%
2	**5**	PhSeCl, CH_2Cl_2, −78 °C	**12**/**13**	80:20	38%:10%
3	**5**	*N*-PSP, CSA, CH_2Cl_2	**12**/**13**	0:100	56%

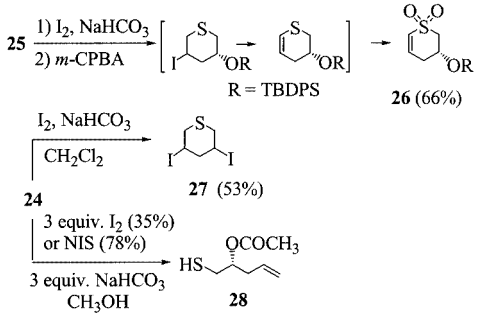
Table 3. Iodocyclization of thioalkenols **23**–**25**

Entry	Substrate	Reagent	Reaction conditions[a]	Product (yield)
1	**23**	I_2	A 4 h at 25 °C	decomposition
2	**23**	Br_2	A 4 h at 25 °C	complex mixture
3	**23**	NIS	− 4 h at 0 °C	decomposition
4	**25**	I_2	A + oxidation *m*CPBA	**26** (66%)
5	**24**	I_2	A 24 h, 0 to 25 °C	**27** (53%)
6	**24**	I_2	B 6 h, −78 to 0 °C	**28** (35%)
7	**24**	I_2	B 16 h, −78 to 25 °C	complex mixture
8	**24**	NIS	B 1 h at −78 °C	**28** (78%)

[a] A: 1.0 equiv. of I_2 or Br_2 in CH_2Cl_2. B: CH_3OH, 3.0 equiv. of $NaHCO_3$.

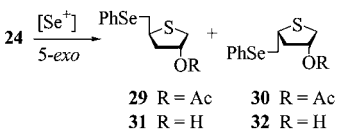
Treatment of benzyl sulfide **23** with iodine under a variety of conditions gave either unchanged starting material or complex mixtures. When bromine or NIS were used, the reaction mixtures were again complex (Entries 2 and 3).

Cyclizations of *tert*-butylsilyl-protected compound **25**, induced by iodine or NIS, also gave decomposition products. Nevertheless, when the reaction was followed by oxidation with *m*CPBA to prevent decomposition, unsaturated sulfone **26** was isolated as a major product (Entry 4). Compound **26** is believed to be formed by 6-*endo* cyclization, dehydroiodination and oxidation of the sulfide to the sulfone.



Scheme 7. Iodine-induced cyclization of 1-sulfanyl-4-pentene-2-ol derivatives **24** and **25**

When thioacetate **24** was treated with iodine (Entry 5), diiodide **27** was formed as a crystalline solid in a 53% yield. This compound is thought to form by 6-*endo* cyclization, acetylation of the hydroxy group, and acetate displacement by iodide generated in situ. When dry deoxygenated methanol was used as a solvent in the treatment of **24** with iodine or NIS, acetate **28** was obtained as a result of an intramolecular transesterification process.



Scheme 8. Selenium-induced cyclization of 1-sulfanyl-4-pentene-2-ol derivative **24**

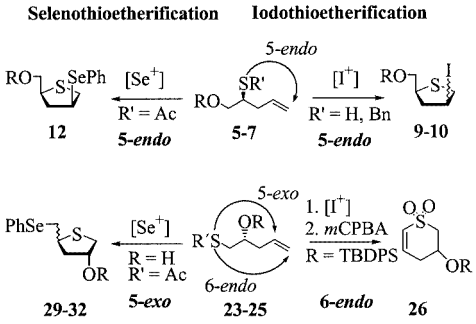
In the light of the results obtained from the cyclization promoted by different iodine electrophiles, we decided to explore the selenothioetherification of thioacetate **24**. Treatment of **24** with 1.1 equiv. of phenylselenyl chloride in dichloromethane (Table 4, Entry 1) provided a 57:43 diastereomeric mixture of tetrahydrothiophenes **29** and **30** in 67% yield. This reaction is thought to proceed through 5-*exo* cyclization followed by acetylation of the hydroxy group by acetyl chloride generated in the course of the reaction. In order to prevent acetylation, the reaction was carried out in methanol (Entry 2), so that compounds **31** and **32** were obtained with better stereoselectivity but in a lower yield (38%). Acid-mediated selenothioetherification with *N*-phenylselenophthalimide and camphorsulfonic acid in dichloromethane (Entry 3) resulted in a 64:36 mixture of acetylated products **29** and **30** in 32% yield. The use of this reagent system in methanol gave the free hydroxy derivatives **31** and **32** with higher stereoselectivity (76:24) and in a higher yield (47%). In summary, selenothioetherification of thioacetate **24** is completely regioselective, and only the 5-*exo* product is formed.

Table 4. [Se^+]-promoted thiocyclization of thioacetate **24**

Entry	Substrate	Reagents	Product	Ratio	Yield
1	**24**	PhSeCl, CH_2Cl_2, room temp.	**29/30**	57:43	67%
2	**24**	PhSeCl, MeOH, room temp.	**31/32**	70:30	38%
3	**24**	*N*-PSP, CSA, CH_2Cl_2, room temp.	**29/30**	64:36	32%
4	**24**	*N*-PSP, CSA, MeOH, room temp.	**31/32**	76:24	47%

Conclusion

In conclusion, unlike the electrophile-promoted cycloetherification of pentene-1,2-diols, electrophile-induced cyclization of 1-sulfanyl- and 2-sulfanylpentenol derivatives always proceeds with complete chemoselectivity, by involvement of the sulfur centre (Scheme 9). Iodine-promoted thiocyclization always undergoes an *endo* cyclization independently of the relative position of the sulfur atom.



Scheme 9. Summary of the reactivity of 1-sulfanyl- and 2-sulfanylpentenol derivatives towards iodo- and selenothioetherification

When the sulfur atom is present at position 2, the cyclization is always 5-*endo*, independently of the electrophile. When the sulfur atom is present at position 1, it is possible to control the regioselectivity depending on the electrophile and the sulfur protecting group; thus, iodine provides the 6-*endo* product while selenium provides the 5-*exo* product.

The stereoselectivity and the yield of the iodine-promoted thiocyclization of derivatives **5**−**7** depend on the group attached to the sulfur atom. Thus, iodocyclization of thiol **6** is highly stereoselective and provides compound **9** in a moderate yield, whereas benzyl sulfide **7** affords a mixture of compounds **9** and **10** with low stereoselectivity and in good yields. Selenium-mediated cyclization of thioacetate **5** affords 5-*endo* selenotetrahydrothiophene **12** in a moderate yield but with excellent stereoselectivity.

Experimental Section

General Remarks: Melting points are uncorrected. Optical rotations were measured at 25 °C in 10-cm cells. ^{1}H and ^{13}C NMR spectra were recorded with 300 and 400 MHz (75.4 and 100.5 MHz) instruments. Coupling constants are given in Hz. Elemental analyses were determined at the Servei de Recursos Científics (Universitat Rovira i Virgili). TLC was carried out on aluminium sheets precoated with silica gel 60 F_{254}. Flash column chromatography was performed with Kieselgel 60 (40−63 microns). Radial chromatography was performed on 1-, 2- or 4-mm silica gel plates, depending on the amount of product. Band separation was monitored by UV. Medium pressure chromatography (MPLC) was performed with silica gel 60 A CC (6−35 microns). All chromatographic solvents were distilled at atmospheric pressure prior to use. Dry solvents were obtained by conventional methods.

(*R*)-1-*O*-(*tert*-Butyldiphenylsilyl)-2-*O*-(*p*-tolylsulfonyl)-4-pentene-1,2-diol (4): *p*-Toluenesulfonyl chloride (2.35 g, 12.38 mmol) was added at 0 °C to alcohol **3** (1.40 g, 4.13 mmol) in anhydrous pyridine (25 mL) and the mixture was kept at 4 °C (refrigerator) for 4 d. The reaction mixture was poured into cold water (100 mL) and extracted with diethyl ether (2 × 50 mL). The combined organic layers were washed with $NaHCO_3$ and brine, and dried with $MgSO_4$. The solvent was removed and the crude product was purified by column chromatography on silica gel in hexane/ethyl acetate (95:5) to afford pure product **4** (1.84 g, 90%) as a viscous liquid. $[\alpha]_D^{25}$ = +8.0 (*c* = 1.32, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 7.75−7.20 (m, 14 H, Ph), 5.58 (dddd, *J* = 7.1, 7.1, 10.1, 17.1 Hz, 1 H, 4-H), 5.08−4.97 (m, 2 H, 5-H), 4.55 (tt, *J* = 4.7, 4.7 Hz, 6.2, 6.2 Hz, 1 H, 2-H), 3.62 (dd, *J* = 4.7, 11.1 Hz, 2 H, 1-H), 2.61−2.42 (m, 2 H, 3-H), 2.40 (s, 3 H), 1.01 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 144.4, 135.5, 135.4, 132.8 (Ph), 132.0 (C-4), 129.7, 129.6, 127.7, 127.6 (Ph), 118.8 (C-5), 81.9(C-2), 63.8 (C-1), 35.5 (C-3), 26.6 (Me), 21.6 (Me), 19.1 (CSi) ppm. $C_{28}H_{34}O_4SSi$ (494.72): calcd. C 67.98, H 6.93, S 6.48; found C 68.22, H 6.94, S 6.46.

(*S*)-2-(Acetylsulfanyl)-1-*O*-(*tert*-butyldiphenylsilyl)-4-penten-1-ol (5): Solid potassium thioacetate (1.42 g, 12.5 mmol) was added to substrate **4** (1.23 g, 2.5 mmol) in anhydrous DMF (15 mL), and the mixture was stirred for 12 h at 45 °C. It was then cooled, diluted with water (75 mL) and extracted with diethyl ether (2 × 25 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, and dried with $MgSO_4$. Removal of the solvent and column chromatography on silica gel in hexane/ethyl acetate (95:5) yielded 0.84 g (85%) of pure product of **5** as a colorless, gummy liquid. $[\alpha]_D^{25}$ = −15.1, (*c* = 1.07, $CHCl_3$). IR: $\tilde{\nu}$ = 1692 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 7.71−7.33 (m, 10 H, Ph), 5.74 (dddd, 1 H, *J* = 7.0, 7.0, 10.1, 17.1 Hz, 4-H), 5.20−5.04 (m, 2 H, 5-H), 3.79 (dd, *J* = 3.7, 9.2 Hz, 1 H, 1-H), 3.76−3.68 (m, 1 H, 2-H), 3.67 (dd, *J* = 5.3, 9.2 Hz, 1 H, 1-H), 2.66−2.53 (m, 1 H, 3-H), 2.46−2.35 (m, 1 H, 3-H), 2.29 (s, 3 H, Me). 1.06 (s, 9 H, Me) ppm. ^{13}C NMR ($CDCl_3$): δ = 195.6 (CO), 135.7, 135.6 (Ph), 134.9 (C-4), 133.3, 129.7, 127.7, 127.6 (Ph), 117.6 (C-5), 64.9 (C-1), 45.6 (C-2), 35.4 (C-3), 30.7 (Me), 26.6 (Me), 19.3 (CSi) ppm. $C_{23}H_{30}O_2SSi$ (398.63): calcd. C 69.30, H 7.58, S 8.04; found C 69.52, H 7.60, S 8.01.

(*S*)-1-*O*-(*tert*-Butyldiphenylsilyl)-2-sulfanyl-4-penten-1-ol (6): Compound **5** (0.199 g, 0.5 mmol) was dissolved in dry methanol (5 mL) and the solution was degassed with argon for 30 min. Sodium methoxide (0.135 g, 2.5 mmol) was added in one portion, and the reaction mixture was stirred under an inert gas. Once the reaction was complete, the mixture was diluted with water (5 mL) and the basic solution was acidified to pH = 4 by addition of 1 N oxalic acid. The aqueous solution was extracted with diethyl ether (2 × 25 mL) and the organic layer was washed with brine and dried with $MgSO_4$. Evaporation of the solvent under reduced pressure gave 0.177 g (96%) of spectroscopically pure, labile thiol **6** as a colorless oil, which was used in the next reaction without further purification. ^{1}H NMR ($CDCl_3$): δ = 7.66−7.22 (m, 10 H, Ph), 5.69 (dddd, 1 H, *J* = 7.0, 7.0, 10.1, 17.0 Hz, 4-H), 5.07−4.98 (m, 2 H, 5-H), 3.62 (dd, *J* = 6.0, 10.1 Hz, 1 H, 1-H), 3.58 (dd, *J* = 6.1, 10.1 Hz, 1 H, 1-H), 2.92 (ddddd, *J* = 1.4, 1.4, 5.3, 7.0, 14.2 Hz, 1 H, 2-H), 2.24 (ddddd, *J* = 1.4, 1.4, 5.3, 7.0, 14.2 Hz, 1 H, 3-H), 2.21 (ddddd, *J* = 1.2, 1.2. 7.0 .8.3, 14.2 Hz, 1 H, 3-H), 1.75 (d, *J* = 7.5 Hz, 1 H, SH), 1.00 (s, 9 H, Me) ppm. ^{13}C NMR ($CDCl_3$): δ = 135.7, 135.7 (Ph), 135.0 (C-4), 133.4, 129.6, 127.6 (Ph), 117.2(C-5), 64.9(C-1), 41.7(C-2), 38.5(C-3), 26.7(Me), 19.2(CSi) ppm.

(*S*)-2-(Benzylsulfanyl)-1-*O*-(*tert*-butyldiphenylsilyl)-4-penten-1-ol (7): Benzylhydrosulfide (0.744 g, 6 mmol) was added at 0 °C to a suspension of sodium metal (0.161 g, 7 mmol) in dry DMF (10 mL). The cooling bath was removed and the mixture was stirred for 1 h at room temperature. A solution of compound **4** (2.5 g, 5 mmol) in dry DMF (10 mL) was added dropwise over 5 min, and stirring was continued at room temperature for a further 2 h. The reaction mixture was poured into water (100 mL) and extracted with diethyl ether (2 × 50 mL). The solvent of the combined organic layers was removed and the resulting crude product was purified by column chromatography on silica gel in hexane/ethyl acetate (95:5) to afford compounds **7** (1.39 g, 62%) and **8** (0.270 g, 18%) as colorless oils. **7:** $[\alpha]_D^{25}$ = −20.7, (*c* = 1.03, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 7.60−7.13 (m, 15 H, Ph), 5.73−5.64 (m, 1 H, 4-H), 5.01−4.92 (m, 2 H, 5-H), 3.67 (dd, *J* = 5.1, 10.5 Hz, 1 H, 1-H), 3.57−3.47 (m, 3 H, SCH_2, 1-H), 2.62 (ddd, *J* = 5.7, 7.2, 12.9 Hz, 1 H, 2-H), 2.47 (ddd, *J* = 6.3, 7.2, 13.5 Hz, 1 H, 3-H), 2.35 (ddd, *J* = 6.3, 7.2, 13.5 Hz, 1 H, 3-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 135.6(Ph), 135.2(C-4), 133.5, 133.4, 129.6, 128.7, 128.4, 127.6, 126.8 (Ph), 116.9 (C-5), 65.9 (C-1), 46.3 (C-2), 35.6 (C-3,SCH_2Ph), 26.8 (CH_3), 19.2(CSi) ppm. $C_{28}H_{34}OSSi$ (446.72): calcd. C 75.35, H 7.62, S 7.17, found C 75.36, H 7.63, S 7.20. **8:** ^{1}H NMR ($CDCl_3$): δ = 7.70−7.38 (m, 10 H, Ph), 6.42−6.27 (m, 1 H), 5.83−5.75 (m, 2 H), 5.21−5.05 (m, 2 H), 4.25 (m, 2 H), 1.05 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 126.6, 135.5, 133.5, 132.8, 130.2, 129.6, 127.6, 116.6, 63.9, 26.7, 19.2 ppm.

Representative Procedure for the Halocyclization of 6 and 7: Potassium carbonate (0.138 g, 1 mmol) and iodine (0.152 g, 0.6 mmol) were added at −78 °C to a solution of homoallylic thiol **6** (0.073 g, 0.2 mmol) in anhydrous CH_2Cl_2 (10 mL), and the reaction mixture

was stirred for 12 h at room temperature, washed with a 10% aq. $Na_2S_2O_3$ solution (10 mL) and brine, and dried with $MgSO_4$. The solvent was evaporated and the resulting crude mass was subjected to radial chromatography on silica gel in hexane to give pure product **9** (0.040 g, 41%) as a colorless oil.

(2*S*,4*S*)-[(2-*tert*-Butyldiphenylsilyloxy)methyl]-4-iodo-tetrahydrothiophene (9): $[\alpha]_D^{25} = +1.3$, ($c = 1.10$, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 7.65−7.25 (m, 10 H), 4.04 (dddd, $J = 6.1, 6.1, 10.9, 12.4$ Hz, 1 H, 4-H), 3.65 (d, $J = 6.1$ Hz, 2 H, 6-H), 3.45 (dddd, $J = 6.1, 6.1, 6.1, 9.4$ Hz, 1 H, 2-H), 3.15 (dd, $J = 6.1, 10.9$ Hz, 1 H, 4-H), 3.07 (dd, 1 H, $J_2 = 10.9, 10.9$ Hz, 5′-H), 2.70 (ddd, $J = 6.1, 6.1, 12.4$ Hz, 1 H, 3-H), 1.82 (ddd, $J = 9.4, 12.4, 12.4$ Hz, 1 H, 3′-H), 0.99 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 135.7, 133.4, 133.3, 129.8, 127.8 (Ph), 67.8 (C-6), 48.9 (C-2), 45.7 (C-3), 41.6 (C-5), 26.7 (Me), 20.2 (C-4), 19.1 (CSi) ppm. $C_{21}H_{27}IOSSi$ (482.49): calcd. C 52.28, H 5.60, S 6.64 found C 52.47, H 5.59, S, 6.65.

(2*S*,4*S*)-[(2-*tert*-Butyldiphenylsilyloxy)methyl]-4-(phenylselenyl)-tetrahydrothiophene (12) and 1,4-Diol Derivative 13: Solid PhSeCl (0.100 g, 0.52 mmol) was added to a cold solution (−78 °C) of homoallylic thioacetate **5** (0.199 g, 0.5 mmol) in anhydrous CH_2Cl_2 (15 mL). The mixture was allowed to warm to room temperature while stirring for 16 h. The reaction mixture was washed with saturated $NaHCO_3$ and brine, and dried with $MgSO_4$. The solvent was removed and the resulting crude mass was purified by column chromatography on silica gel in hexane/ethyl acetate (98:2) to afford products **12** (0.100 g, 38%) and **13** (0.022 g, 10%) (2:1 diastereomeric mixture) as colorless oils. **12:** $[\alpha]_D^{25} = -8.6$, ($c = 0.85$, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 7.65−7.16 (m, 15 H, Ph), 3.63 (dd, $J = 7.0, 9.9$ Hz, 1 H, 6-H), 3.59 (dd, $J = 6.0, 9.9$ Hz, 1 H, 6′-H), 3.56−3.48 (m, 2 H, 4-H, and 2-H), 2.99 (dd, $J = 6.1, 10.6$ Hz, 1 H, 5-H), 2.82 (dd, $J = 10.6, 10.6$ Hz, 1 H, 5′-H), 2.51 (ddd, $J = 5.2, 6.1, 12.6$ Hz, 1 H, 3-H), 1.52 (ddd, $J = 9.3, 12.5, 12.5$ Hz, 1 H, 3′-H), 0.97 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 135.6, 135.1, 133.3, 129.7, 127.1, 127.9, 127.7 (Ph), 68.1 (C-6), 49.3 (C-4), 43.1 (C-2), 40.5 (C-3), 38.1 (C-5), 26.8 (Me), 19.1 (CSi) ppm. $C_{27}H_{32}OSSeSi$ (511.65): calcd. C 63.40, H 6.26, S 6.26; found C 63.51, H 6.25, S 6.24. **13:** Data obtained from the spectra of the diastereomeric mixture: IR: $\tilde{\nu} = 1738\ cm^{-1}(\nu_{CO})$. Major diastereomer: ^1H NMR ($CDCl_3$): δ = 7.66−7.19 (m, 15 H, Ph), 5.14−5.12 (m,1 H, 4-H), 3.74 (dd, $J = 10.5, 5.4$ Hz, 1 H, 1-H), 3.62 (dd, $J = 10.4, 6.6$ Hz, 1 H, 1′-H), 3.04 (dd, $J = 12.9, 5.7$ Hz, 1 H, 5-H), 2.96 (dd, $J = 12.9, 6.0$ Hz, 1 H, 5′-H), 2.86−2.82 (m,1 H, 2-H), 2.36 (dt, $J = 14.7, 5.7, 5.7$ Hz, 1 H, 3-H), **1.9**2 (ddd, $J_{3',3} = 14.7, 7.2, 7.2$ Hz, 1 H, 3′-H), 1.79 (s, 3 H, Me), 1.04 (s, 9 H, Me) ppm. ^{13}C NMR ($CDCl_3$): δ = 170.4 (CO), 135.6−127.1 (CAr), 71.4 (C-4), 66.0 (C-1), 49.3 (C-2), 35.4, (C-5), 31.1 (C-3), 27.6 [Si(*Me*)$_3$], 20.7 (Me), 19.1 (*C*SiMe$_3$) ppm. Minor diastereomer: NMR ($CDCl_3$): δ = 170.4 (CO), 135.6−127.1 (CAr), 70.8 (C-4), 66.9 (C-1), 48.8 (C-2), 35.3 (C-5), 31.5 (C-3), 27.6 [Si(*Me*)$_3$], 20.6 (Me), 19.1 (*C*SiMe$_3$) ppm.

(*R*)-4-Pentene-1,2-diol (20): A tetrabutylammonium fluoride solution in THF (1 M, 28 mL, 28.00 mmol) was added to a cold solution (0 °C) of **3** (8.59 g, 25.26 mmol) in 258 mL of dry THF, and the mixture was stirred at 0 °C for 2 h. The cooling bath was then removed and the mixture was allowed to warm to room temperature and then poured into water/ice. The aqueous solution was extracted with ethyl acetate, and the combined organic layers were dried with magnesium sulfate. The solvent was removed in vacuo and the crude product was chromatographed (diethyl ether/petroleum ether, 20:1) to give compound **20** (2.51 g, 98%) as a pure syrup. $[\alpha]_D^{25} = +3.3$ ($c = 0.25$, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 5.79 (ddt, $J_{4,5;trans} = 17.1$ Hz, $J = 10.2, 5.7, 5.7$ Hz, 1 H, 4-H), 5.10−5.01 (m, 2 H, 5-H, 5′-H), 3.88 (br. s, 2 H, OH), 3.68 (dtd, $J = 7.5, 6.5, 6.5, J_{1,2} = 2.8$ Hz, 1 H, 2-H), 3.56 (dd, $J = 11.5, 2.8$ Hz, 1 H, 1-H), 3.37 (dd, $J = 11.5, 7.5$ Hz, 1 H, 1′-H), 2.18−2.12 (m, 2 H, 3-H, 3′-H) ppm. ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ = 134.2(C-4), 117.8 (C-5), 71.4 (C-2), 66.0 (C-1), 37.6 (C-3) ppm. $C_5H_{10}O_2$ (102.13): calcd. C 58.80; H 9.87; found. C, 59.15; H 9.90.

(*R*)-1-(Tosyloxy)-4-penten-2-ol (21): Tosyl chloride (1.87 g, 9.80 mmol) was added to a cold solution (−10 °C) of compound **20** (1.00 g, 9.80 mmol) in dry pyridine (20 mL). The mixture was allowed to react at −10 °C for 15 h, and then poured into an aqueous HCl solution and extracted with dichloromethane. The combined organic layers were dried with magnesium sulfate and concentrated. Purification of the crude product by column chromatography in hexane-hexane/ethyl acetate (3:1) gave 1.96 g (78%) of compound **21**. $[\alpha]_D^{25} = -9.8$ ($c = 0.94$, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.79 (d, $J = 8.4$ Hz, 2 H, Ph), 7.35 (d, $J = 8.4$ Hz, 2 H, Ph), 5.79−5.69 (m, 1 H, 4-H), 5.12−5.07 (m, 2 H, 5-H, 5′-H), 4.06−4.00 (m, 1 H, 2-H), 3.94−3.90 (m, 2 H, 1-H, 1′-H), 2.63 (br. s, 1 H, OH), 2.45 (s, 3 H, CH_3), 2.26−2.22 (m, 2 H, 3-H, 3′-H) ppm. ^{13}C NMR ($CDCl_3$, 100.5 MHz): δ = 145.0, 132.8 (C-4), 132.2, 129.8, 127.8 (Ph), 118.6 (C-5), 72.9 (C-1), 68.4 (C-2), 37.2 (C-3), 21.5 (CH_3) ppm. $C_{12}H_{16}OS$ (256.32): calcd. C 56.80, H 5.71, S 12.50; found C 56.56, H 5.70, S 12.56.

(3*R*)-4-Allyl-1,3,2-dioxathiolane 2-Oxide (22): An ice/water-cooled solution of diol **20** (0.143 g, 1.40 mmol) and triethylamine (0.780 mL, 5.61 mmol) in dry dichloromethane (6 mL) was added dropwise over a period of 10 min to a solution of thionyl chloride (0.150 mL) in dichloromethane (4 mL). The mixture was stirred at 0 °C for 1 h, monitored by TLC in hexane/ethyl acetate (1:5). The mixture was then diluted with dichloromethane and washed with water (2 × 50 mL) and brine (100 mL). The organic layer was dried with sodium sulfate, filtered and concentrated in vacuo. The crude residue was filtered through a small pad of silica gel to give 0.195 g (94%) of a diastereomeric mixture of compound **22** as an orange syrup. ^1H NMR ($CDCl_3$, 400 MHz): δ = 5.78−5.64 (m, 1 H, 2′-H), 5.17−5.11 (m, 2 H, 3′-Ha, 3′-H^b), 4.97 (q, $J = 6.4$ Hz, 1 H, 4-H), 4.62 (dd, $J = 8.4, 6.4$ Hz, 1 H, 5-H^a), 3.97 (dd, $J = 8.4, 6.4$ Hz, 1 H, 5-H^b), 2.69−2.34 (m, 2 H, 1′-H^a, 1′-H^b) ppm. ^{13}C NMR ($CDCl_3$, 100.5 MHz): δ = δ = 131.6 (C-2′), 119.2 (C-3′), 79.1 (C-4), 70.6 (C-5), 37.5 (C-1′) ppm. ^1H NMR ($CDCl_3$, 400 MHz): δ = 5.78−5.64 (m, 1 H, 2′-H), 5.17−5.11 (m, 2 H, 3′-H^a, 3′-H^b), 4.50−4.29 (m, 2 H, 5-H^a, 5-H^b), 2.69−2.34 (m, 2 H, 1′-H^a, 1′-H^b) ppm. ^{13}C NMR ($CDCl_3$, 100.5 MHz): δ = 131.2 (C-2′), 119.5 (C-3′), 82.5 (C-4), 69.9 (C-5), 36.5 (C-1′) ppm.

(*R*)-1-(Benzylsulfanyl)-4-penten-2-ol (23). Method A (from 22): Sodium benzylsulfide (0.120 g, 0.81 mmol, prepared by treatment of benzylhydrosulfide with 1 equiv. of NaH in diethyl ether for 16 h, filtration and drying under vacuum) and 15-crown-5 (0.160 mL, 0.54 mmol) were added under an inert gas to a solution of **22** (0.80 g, 0.54 mmol) in dry DMF (2 mL). The reaction was monitored by TLC (hexane/ethyl acetate, 2:1). The mixture was diluted with water/ice, and extracted thoroughly with dichloromethane. The combined organic layers were dried with sodium sulfate and concentrated. The resulting crude product was filtered through a small pad of silica gel and then purified by radial chromatography with hexane/dichloromethane (1:1) to give 0.084 g (75%) of compound **23** as a syrup. **Method B (from Tosylate 21):** Sodium benzylsulfide (0.390 g, 2.64 mmol) was added to a solution of tosylate **21** (0.450 g, 1.76 mmol) in dry acetonitrile (14 mL). The mixture was stirred at room temperature for 2 h, filtered through silica gel and concentrated. The resulting residue was purified by column chro-

matography with an elution gradient (hexane, hexane/CH_2Cl_2, 10:1, CH_2Cl_2) to give 0.363 g (99%) of alkenol **23** as a colorless syrup. $[\alpha]_D^{25} = -51.4$ ($c = 0.85$, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.38−7.35 (m, 5 H, Ph), 5.84−5.73 (m, 1 H, 4-H), 5.14−5.09 (m, 2 H, 5-H, 5′-H), 3.74 (s, 2 H, CH_2Bn), 3.72−3.66 (m, 1 H, 2-H), 2.61 (dd, $J = 13.6$, 3.6 Hz, 1 H, 1-H), 2.48 (br. s, 1 H, OH), 2.43 (dd, $J = 14.0$, 8.4 Hz, 1 H, 1′-H), 2.30−2.24 (m, 2 H, 3-H, 3′-H) ppm. ^{13}C NMR ($CDCl_3$, 100.5 MHz): δ = 137.9, 134.0 (C-4), 128.9, 128.6, 127.2 (Ph), 118.1 (C-5), 68.6 (C-2), 40.5 (C-3), 38.3 (C-1), 36.2 (CH_2Bn) ppm. $C_{12}H_{16}OS$ (208.32): calcd. C 69.23, H 7.69, S 15.38; found C 69.45, H 7.70; S 15.43.

(*R*)-1-(Acetylsulfanyl)-4-penten-2-ol (24): Potassium thioacetate (780 g, 6.68 mmol) and 18-crown-6 (1.77 g, 6.68 mmol) were added under an inert gas to a solution of tosylate **21** (1.14 g, 4.45 mmol) in CH_3CN (18 mL). The mixture was stirred for 2.5 h (TLC: hexane/ethyl acetate, 2:1), filtered through silica gel and concentrated. The crude product was purified by radial chromatography with CH_2Cl_2 to give compound **24** in a quantitative yield. $[\alpha]_D^{25} = -32.8$ ($c = 1.06$, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz): δ = 5.86−5.77 (m, 1 H, 4-H), 5.19−5.14 (m, 2 H, 5-H, 5′-H), 3.84−3.78 (m, 1 H, 2-H), 3.14 (dd, $J = 14.0$, 4.0 Hz, 1 H, 1-H), 2.93 (dd, $J = 14.0$, 7.2 Hz, 1 H, 1′-H), 2.45 (br. s, 1 H, OH), 2.38 (s, 3 H, CH_3), 2.36−2.23 (m, 2 H, 3-H, 3′-H) ppm. ^{13}C NMR ($CDCl_3$, 100.5 MHz): δ = 196.3 (CO), 133.7 (C-4), 118.5 (C-5), 69.8 (C-2), 40.6 (C-3), 35.4 (C-1), 30.5 (CH_3) ppm. $C_7H_{12}O_2S$ (160.23): calcd. C 52.50, H 7.50, S 20.00; found C 52.70, H 7.52, S 19.94.

(*R*)-Penten-2-ol Derivative 25: A solution of alkenol **23** (0.198 g, 0.95 mmol), imidazole (0.136 mg, 2.00 mmol) and *tert*-butyldiphenylsilyl chloride (0.370 mL) in DMF (2 mL) was heated at 55 °C for 16 h (TLC: hexane/ethyl acetate, 5:1). The mixture was diluted with CH_2Cl_2 (75 mL) and washed with water (5 × 50 mL) and brine (50 mL). The combined organic layers were dried with magnesium sulfate, filtered and concentrated in vacuo. The resulting residue was filtered through a pad of silica gel and then purified by radial chromatography with hexane to afford 0.344 g (81%) of compound **25**. $[\alpha]_D^{25} = +7.1$ ($c = 0.63$, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.60−7.56 (m, 4 H, Ph), 7.34−7.24 (m, 6 H, Ph), 7.23−7.00 (m, 5 H, Ph), 5.66−5.56 (m, 1 H, 4-H), 4.90−4.83 (m, 2 H, 5-H, 5′-H), 3.80−3.74 (m, 1 H, 2-H), 3.34 (d, $J = 13.2$ Hz, 1 H, CH_2Bn), 3.28 (d, $J = 13.2$ Hz, 1 H, CH_2Bn), 2.45 (dd, $J = 13.2$, 7.2 Hz, 1 H, 1-H), 2.35 (dd, $J = 13.6$, 4.8 Hz, 1 H, 1′-H), 2.31−2.25 (m, 1 H, 3-H), 2.19−2.13 (m, 1 H, 3′-H), 0.96 [s, 9 H, $(CH_3)_3$] ppm. ^{13}C NMR ($CDCl_3$, 100.5 MHz): δ = 138.4, 135.9 (C-4), 134.0, 133.9, 133.8, 129.6, 129.6, 128.7, 128.3, 127.5, 127.4, 126.7 (Ph), 117.7 (C-5), 71.9 (C-2), 39.8 (C-3), 37.4 (C-1), 36.7 (CH_2Bn), 26.9 (CH_3), 19.3 ppm. $C_{28}H_{34}OSSi$ (446.72): calcd. C 75.34, H 7.62, S 7.17; found C 75.46, H 7.59, S 7.20.

3-*O*-(*tert*-Butyldiphenylsilyl)-1,1-dioxo-3,4-dihydro-2*H*-thiopyran-3-ol (26): Iodine (0.033 g, 0.13 mmol) was added under argon to a cold solution (−78 °C) of compound **25** (0.052 g, 0.12 mmol) in dry dichloromethane (1 mL). The mixture was allowed to warm to room temperature, and *m*CPBA (0.074 g, 0.30 mmol) was then added. After 2 h, aqueous Na_2SO_3 (5%, 25 mL) was added. The aqueous layer was extracted with dichloromethane (3 × 50 mL) and the combined organic layers were dried with anhydrous $MgSO_4$ and concentrated. The resulting residue was purified by radial chromatography with an elution gradient (hexane/dichloromethane, 1:1, dichloromethane) to afford 0.037 g (66%) of compound **26** as a syrup. IR: $\tilde{\nu} = 908$ cm^{-1}, 735 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.67−7.62 (m, 4 H, Ph), 7.50−7.35 (m, 6 H, Ph), 6.33 (ddd, 1 H, $J = 10.8$, $J = 4.4$, 2.8 Hz, 6-H), 6.25 (ddd, $J = 10.8$, 5.6, 2.8 Hz, 1 H, 5-H), 4.45 (m, 1 H, 3-H), 3.31 (dddd, $J = 1.2$, 2.4, 3.2, 13.2 Hz, 1 H, 2-H), 3.15 (dd, $J = 11.2$, 13.2 Hz, 1 H, 2′-H), 2.54 (dtt, $J = 5.6$, 5.6, 19.2 Hz, 1 H, 4-H), 2.35 (ddt, $J = 19.2$, 9.2, 2.8 Hz, 1 H, 2.8 Hz, 4′-H), 1.10 [s, 9 H, $(CH_3)_3$] ppm. ^{13}C NMR ($CDCl_3$, 100.5 MHz): δ = 133.7, 135.6 (Ph), 134.2 (C-5), 130.4, 130.2 (Ph), 129.4 (C-6), 128.0, 127.9 (Ph), 65.4 (C-3), 57.9 (C-2), 34.9 (C-4), 26.8 [(CH_3)$_3$CSi], 19.0 [(CH_3)$_3$*C*Si] ppm. $C_{21}H_{26}O_3SSi$ (386.58): calcd. C 65.25, H 6.78, S 8.29; found C 65.00, H 6.80, S 8.31.

3,5-Diiodo-tetrahydrothiopyran (27): Iodine (0.088 g, 0.34 mmol) was added at 0 °C to a solution of compound **24** (0.053 g, 0.33 mmol) in dry dichloromethane (1 mL). The mixture was stirred for 24 h and then decolourized with 5% aq. Na_2SO_3. The aqueous layer was extracted with dichloromethane (3 × 50 mL) and the combined organic layers were dried with anhydrous $MgSO_4$, filtered and concentrated in vacuo. The resulting residue was purified by radial chromatography with an elution gradient (hexane, hexane/dichloromethane, 1:1) to afford 0.062 g (53%) of compound **27** as a solid. M.p. 115−117 °C. EM: *m*/*z* = 354, 227, 127, 99, 67, 46. ^1H NMR (C_6D_6, 400 MHz): δ = 3.68−3.60 (dddd, 2 H, $J = 12.4$, 11.0, 3.6, 4.0 Hz, 3-H, 5-H), 2.61−2.56 (dddd, 1 H, $J = 12.4$, $J = 5.2$, 3.2, $J_{4',2} = 1.6$ Hz, 4′-H), 2.47 (d, $J = 11.0$ Hz, 4 H, 2-H, 6-H), 2.03 (q, $J = 12.4$ Hz, 1 H, 4-H) ppm. ^{13}C NMR ($CDCl_3$, 100.5 MHz): δ = 52.1 (C-4), 37.6 (C-2, C-6), 24.5 (C-3, C-5) ppm.

(*R*)-4-Penten-2-ol Derivative 28: $NaHCO_3$ (0.129 g, 1.54 mmol) and NIS (0.125 g, 0.54 mmol) were added under argon to a cold solution (−78 °C) of compound **24** (0.082 g, 0.51 mmol) in dry and deoxygenated CH_3OH (3 mL). The reaction mixture was stirred at −78 °C for 1 h (TLC: hexane/ethyl acetate, 2:1) and decolourized with Na_2SO_3 (5%), the aqueous layer was extracted with dichloromethane (3 × 50 mL), and the combined organic layers were dried with anhydrous $MgSO_4$, filtered and concentrated. The crude product was chromatographed on silica gel (hexane/ethyl acetate, 5:1) to give acetate **28** (0.064 g, 78%). ^1H NMR ($CDCl_3$, 400 MHz): δ = 5.79−5.67 (m, 1 H, 4-H), 5.17−5.08 (m, 3 H, 5-H, 5′-H, 2-H), 2.89 (dd, $J = 14$, 6.0 Hz, 1 H, 1-H), 2.85 (dd, $J = 14$, 6.8 Hz, 1 H, 1′-H), 2.52−2.30 (m, 2 H, 3-H, 3′-H), 2.05 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100.5 MHz): δ = 170.4 (CO), 132.7 (C-4), 118.5 (C-5), 72.3 (C-2), 42.2 (C-3), 37.3 (C-1), 21.0 (CH_3) ppm.

Selenothioetherification of 24 under Basic Conditions. (3*S*,5*S*)-Tetrahydrothiophen-3-ol Derivative 29 and (3*S*,5*R*)-Tetrahydrothiophen-3-ol Derivative 30: Phenylselenyl chloride (0.075 g, 0.38 mmol) was added to a cold solution (−78 °C) of alkenol **24** (0.058 g, 0.36 mmol) in 11 mL of dry dichloromethane. The course of the reaction was monitored by TLC. The reaction mixture was then washed with saturated $NaHCO_3$ solution and brine. The organic layer was dried with anhydrous $MgSO_4$ and the solvent was removed in vacuo. The resulting residue was purified by MPLC (elution gradient: hexane/ethyl acetate, 20:1, hexane/ethyl acetate, 10:1), to afford a 10:13 diastereomeric mixture of tetrahydrothiophenes **29** and **30** (0.083 g 67%). The single diastereoisomers were separated by radial chromatography with cyclohexane/ethyl acetate (25:1). **29** (higher R_f): $[\alpha]_D^{25} = +18.8$ ($c = 1.00$, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.54−7.51 (m, 2 H, Ph), 7.32−7.26 (m, 3 H, Ph), 5.38 (q, 1 H, J4.8 Hz, 3-H), 3.60 (ddt, $J = 7.2$, 5.2, 8.8 Hz, 1 H, 8.8 Hz, 5-H), 3.20 (d, $J = 7.2$ Hz, 2 H, 6-H), 3.17 (dd, $J = 11.6$, 5.2 Hz, 1 H, 2-H), 3.00 (ddd, $J = 11.6$, 4.4, 0.6 Hz, 1 H, 2′-H), 2.32 (ddd, 1 H, $J = 13.6$, $J = 7.6$, 5.2 Hz, 4-H), 2.14 (dt, $J = 13.6$, 5.2 Hz, 1 H, 5.2 Hz, 4′-H), 2.03 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100.5 MHz): δ = 135.0, 133.4, 129.2, 127.3 (Ph), 76.8 (C-3), 45.5 (C-5), 40.3 (C-4), 36.9 (C-2), 35.7 (C-6), 21.2 (CH_3) ppm. $C_{13}H_{16}O_2SSe$ (315.29): calcd. C 49.52, H 5.08, S 10.16; found C

49.38, H 5.06, S 10.13. **30** (lower R_f): $[\alpha]_D^{25}$ = +17.0 (*c* = 0.350, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.55−7.52 (m, 2 H, Ph), 7.29−7.26 (m, 3 H, Ph), 5.49 (m, 1 H, 3-H), 3.81 (dddd, *J* = 8.4, 6.4, 6.4, 9.6 Hz, 1 H, 5-H), 2.28 (dd, *J* = 12.0, 4.4 Hz, 1 H, 2-H), 3.18 (dd, *J* = 12.0, 6.4 Hz, 1 H, 6-H), 3.14 (dd, *J* = 12.4, 8.0 Hz, 1 H, 6′-H), 2.94 (ddd, *J* = 12.0, 2.4, 1.6 Hz, 1 H, 2′-H), 2.40 (dddd, *J* = 13.6, 5.6, 3.2, 1.6 Hz, 1 H, 4-H), 2.05 (s, 3 H, CH_3), 1.79 (ddd, *J* = 13.6, 9.6, 4.0 Hz, 1 H, 4′-H) ppm. ^{13}C NMR ($CDCl_3$, 100.5 MHz): δ = 133.2, 129.2, 127.3 (Ph), 77.1 (C-3), 46.7 (C-5), 42.0 (C-4), 37.7 (C-2), 33.9 (C-6), 21.2 (CH_3) ppm. $C_{13}H_{16}O_2SSe$ (315.29): calcd. C 49.52, H 5.08, S 10.16; found C 49.61, H 5.10, S 10.15.

Selenothioetherification of 24 under Basic Conditions in Methanol. (3*S*,5*S*)-5-[(Phenylselenyl)methyl]-tetrahydrothiophen-3-ol (31) and (3*S*,5*R*)-5-[(Phenylselenyl)methyl]-tetrahydrothiophen-3-ol (32): Phenylselenyl chloride (68 mg, 0.35 mmol) was added to a cold solution (−78 °C) of alkenol **24** (0.058 g, 0.36 mmol) in 11 mL of dry methanol. The reaction mixture was allowed to warm and stirred for 6 h, and then washed with saturated $NaHCO_3$ solution and brine. The organic layer was dried with anhydrous $MgSO_4$ and the solvent was removed in vacuo. The resulting residue was purified by radial chromatography (elution gradient: hexane, hexane/ethyl acetate, 3:1), to give a 70:30 diastereomeric mixture of tetrahydrothiophenes **31** and **32** (0.034 g, 38%). **31:** ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.44−7.41 (m, 2 H, Ph), 7.18−7.15 (m, 3 H, Ph), 4.42 (m, 1 H, 3-H), 3.51 (m, 1 H, 5-H), 2.94 (dd, *J* = 12.2, 5.2 Hz, 1 H, 2-H), 3.12−3.03 (m, 2 H, 6-H, 6′-H), 2.81 (ddd, *J* = 12.2, 5.2, 1.2 Hz, 1 H, 2′-H), 2.34 (br. s, 1 H, OH), 2.23 (ddd, *J* = 13.2, 7.2, 5.2 Hz, 1 H, 4-H), 1.58 (ddd, *J* = 13.2, 5.6, 1.2 Hz, 1 H, 4′-H) ppm. ^{13}C NMR ($CDCl_3$, 100.5 MHz) 132.9, 129.2, 128.9, 127.0 (Ph), 75.1 (C-3), 45.4 (C-5), 43.2 (C-4), 40.1 (C-2), 36.0 (C-6) ppm. **32:** ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.44−7.41 (m, 2 H, Ph), 7.18−7.15 (m, 3 H, Ph), 4.54 (m, 1 H, 3-H), 3.73 (m, 1 H, 5-H), 3.19 (dd, *J* = 12.0, 8.4 Hz, 1 H, 2-H), 3.12−3.03 (m, 2 H, 6-H, 6′-H), 2.75 (ddd, *J* = 12.0, 1.6, 1.6 Hz, 1 H, 2′-H), 2.27 (br. s, 1 H, OH), 2.23 (dddd, 1 H, *J* = 13.2, 6.4, 2.8, 1.6 Hz, 4-H), 1.58 (ddd, *J* = 13.2, 9.6, 3.6 Hz, 1 H, 4′-H) ppm. ^{13}C NMR ($CDCl_3$, 100.5 MHz): δ = 132.8, 129.4, 128.9, 127.0 (Ph), 75.0 (C-3), 46.0 (C-5), 44.6 (C-4), 40.8 (C-2), 34.7 (C-6) ppm.

Selenothioetherification of 24 under Acidic Conditions. Synthesis of 29/30 and 31/32: *N*-Phenylselenophthalimide (*N*-PSP, 0.105 g, 0.29 mmol) and camphorsulfonic acid (0.047 g, 0.20 mmol) were added to a solution of thioacetate **24** (0.046 g, 0.29 mmol) in 1.5 mL of dichloromethane. The mixture was stirred for 4 h, filtered through a small pad of silica gel and concentrated in vacuo. The residue was purified by radial chromatography (elution gradient: hexane, hexane/ethyl acetate, 3:1) to give a 64.36 mixture of acetylated products **29** and **30** (0.029 g, 32%) and a 26:74 mixture of compounds **31** and **32** (23%).

Selenothioetherification of 24 under Acidic Conditions in Methanol. Synthesis of 31 and 32: *N*-Phenylselenophthalimide (*N*-PSP, 0.098 g, 0.32 mmol) and camphorsulfonic acid (0.044 g, 0.19 mmol) were added to a solution of thioacetate **24** (0.043 g, 0.27 mmol) in 1.5 mL of dichloromethane. The mixture was stirred for 2 h, filtered through a small pad of silica gel and concentrated in vacuo. The residue was purified by radial chromatography (elution gradient: hexane, hexane/ethyl acetate, 3:1) to give a 24:76 mixture of compounds **31** and **32** (0.034 g, 47%).

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