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Nucleophilic substitution reaction at an sp^2 carbon of vinyl halides with an intramolecular thiol moiety: synthesis of thio-heterocycles

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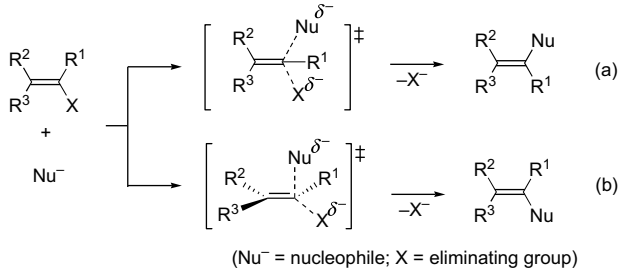
ABSTRACT

This article presents a full account of intramolecular vinylic substitution reactions of bromoalkenes having an acetylthio moiety, which give sulfur-containing heterocycles such as dihydrothiophene, tetrahydrothiopyran, and 2-alkylidenethietane derivatives. The reaction pathways of the substitution reactions were investigated by theoretical and experimental studies.

1. Introduction

Concerted nucleophilic substitution at an sp^3 carbon, typically bimolecular nucleophilic substitution (S_N2) reaction, is one of the most fundamental reactions in organic chemistry, giving a substitution product with inversion of the configuration.[1] For such a concerted bimolecular nucleophilic substitution at a vinylic (sp^2) carbon are proposed two possible mechanisms, namely, in-plane vinylic nucleophilic substitution ($S_NV\sigma$) and out-of-plane vinylic nucleophilic substitution ($S_NV\pi$).[2] In the $S_NV\sigma$ mechanism, a nucleophile attacks to the σ^* orbital of C–X bond and the substitution occurs with inversion of the configuration (Scheme 1a). In the $S_NV\pi$ mechanism, a nucleophile interacts with the π^* orbital of the vinylic carbon and gives a substitution product with retention of the configuration (Scheme 1b). However, both $S_NV\sigma$ and $S_NV\pi$ mechanisms were so far considered as unfavorable processes at unactivated vinylic carbons.[3]



Scheme 1.

Recent theoretical studies have provided some information on these substitution reactions at unactivated vinylic carbons.[4] For example, Glukhovtsev et al. showed that the activation energy (32.6 kcal mol^{-1}) of the $S_NV\sigma$ reaction of vinyl chloride with a chloride ion is about 10 kcal mol^{-1} lower than that of $S_NV\pi$ (42.7 kcal mol^{-1}). Lee reported that in vinylic substitution of chloroethene by HO^- and HS^-, $S_NV\pi$ pathway is favored, whereas the $S_NV\sigma$ pathway is preferred in the nucleophilic attack with Cl^- and Br^-. However, the estimated activation energies of both reaction pathways in these theoretical studies are so high that the substitution reactions hardly proceed under mild reaction conditions.

There are few reports on substitution reactions at unactivated sp^2 carbons, which were proposed to proceed via the $S_NV\sigma$ mechanism.[5] The substitution reaction of alkenyliodonium salts was found to give the products with inversion of the stereochemistry.[6] 2-Bromoallylamines cyclized to aziridines by base treatment and the stereospecificity of the cyclization suggests that the amino group approaches from the backside of the bromine atom.[7]

We also showed that haloalkenes bearing intramolecular alcohol, sulfonamide, active methine, and thiol moieties at suitable positions cyclized to the corresponding 5-membered products by

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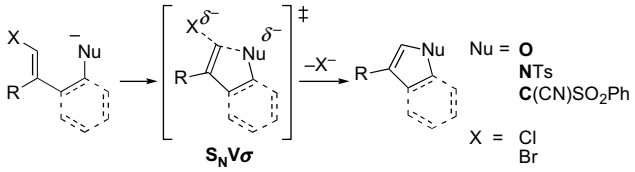
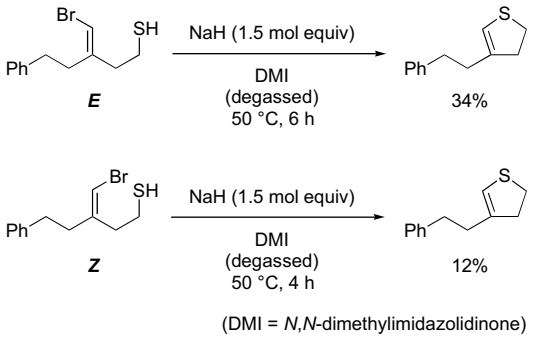
intramolecular vinylic substitution.[8] The cyclizations with *O*,*N*,*C*-nucleophiles proceeded only from the *E*-isomers, with the *Z*-isomers giving no cyclization products with recovery of the starting haloalkenes (Scheme 2). This stereospecificity is consistent with our theoretical studies by DFT calculations, namely, that reactions proceed via the $S_NV\sigma$ mechanism.



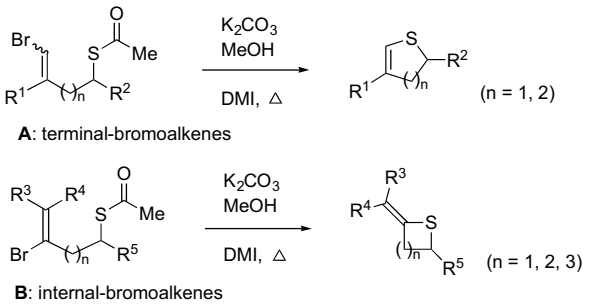
Scheme 2.

However, the cyclization reaction with a thiol moiety exhibited contrasting phenomena with the above nucleophiles, that is, the cyclization proceeded with both *E*- and *Z*-isomers (Scheme 3), which meant $S_NV\pi$ as a possible reaction pathway for the *Z*-isomer. The calculation also suggested relatively small activation energies for the $S_NV\pi$ pathway. In addition, 4-membered ring compounds, 2-alkylidenethietanes could be prepared by the cyclization of *S*-acetyl 3-bromo-3-alkenethiols.[9]



Scheme 3.

As the nucleophilic vinylic substitution with thiol moieties exhibited unique characters, we have studied it in detail. This article presents a full account of intramolecular vinylic substitution reactions of terminal-bromoalkenes **A** and internal bromoalkenes **B** having an acetylthio moiety, which gives sulfur-containing heterocycles such as dihydrothiophene, tetrahydrothiopyran, and 2-alkylidenethietane derivatives (Scheme 4).

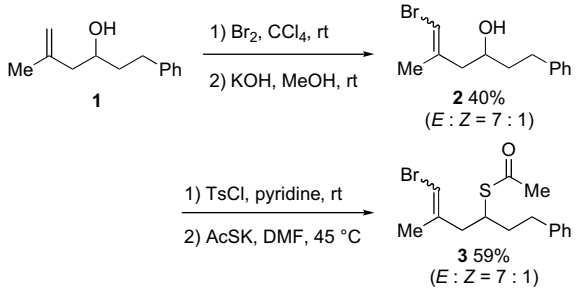


Scheme 4.

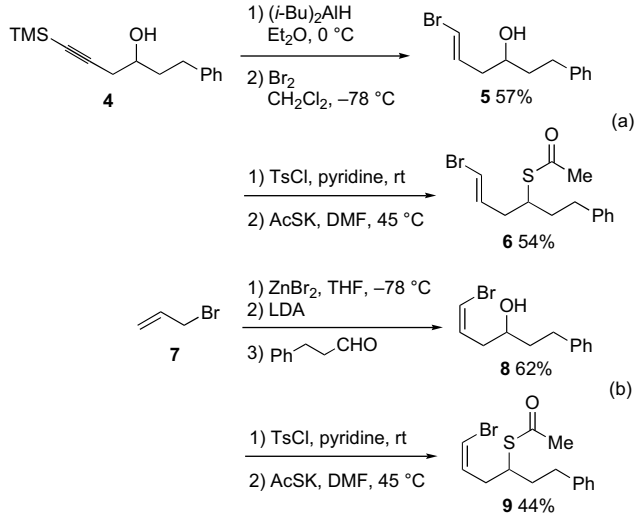
2. Results and discussion

2.1. Preparation of bromoalkenes

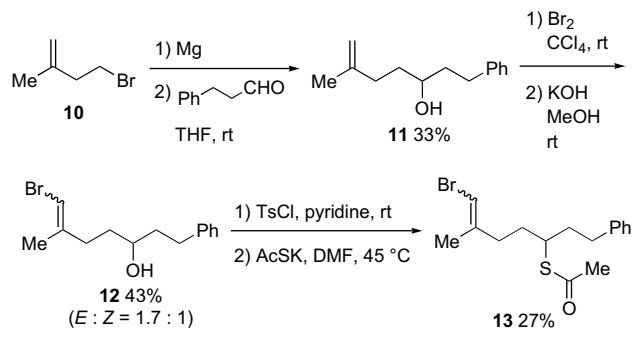
For 5-membered ring formation from terminal-bromoalkenes **A**, 4-bromo-3-alkenyl thioacetates **3**, **6**, **9** were prepared as shown in Schemes 5 and 6. Dibromination of alkenol **1**[10] followed by dehydrobromination under basic conditions[11] gave bromoalkenol **2**, which was converted into thioacetate **3** by tosylation of **2** and successive substitution with potassium thioacetate (Scheme 5). cis-Reduction of alkyne **4**[12] with DIBAL[13] followed by treatment of the resulting vinylsilane with Br_2[14] provided *E*-bromoalkenol **5** (Scheme 6a). The corresponding *Z*-isomer **8** was prepared by the reaction of 3-phenylpropanal and allylzinc reagent (Scheme 6b).[15] These bromoalkenols **5** and **8** were transformed into thioacetates **6** and **9** via their tosylates, respectively. 5-Bromo-4-alkenyl thioacetate **13** for 6-membered ring formation was also synthesized as shown in Scheme 7. The reaction of 3-methyl-3-butenylmagnesium bromide and 3-phenylpropanal gave alkenol **11**. Introduction of a bromine atom onto alkene **11** followed by the sequence of tosylation and substitution with potassium thioacetate led to **13**.



Scheme 5.

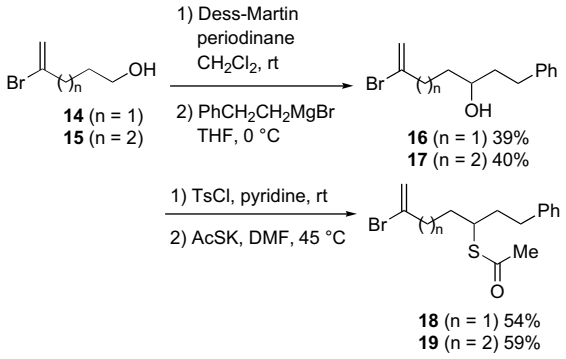


Scheme 6.

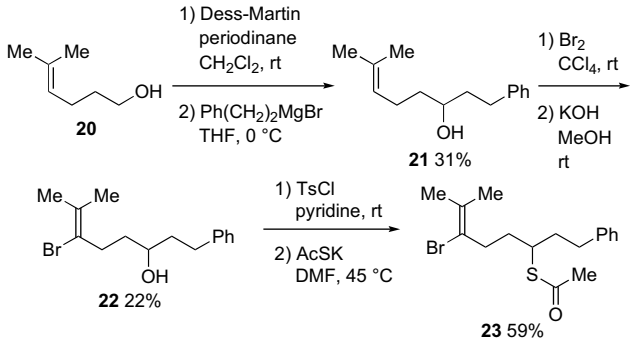


Scheme 7.

The preparation internal bromoalkenes **B** for 5- and 6-membered ring cyclization are summarized in Schemes 8 and 9. Starting from known bromoalkenols **14**[16] and **15**,[17] oxidation followed by alkylation with phenethylmagnesium bromide gave **16** and **17**, which were converted to thioacetates **18** and **19**, respectively. In a similar procedure, 5-methyl-4-hexen-1-ol (**20**)[18] was converted into thioacetate **23**.



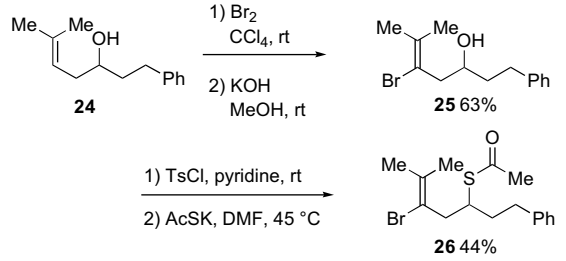
Scheme 8.



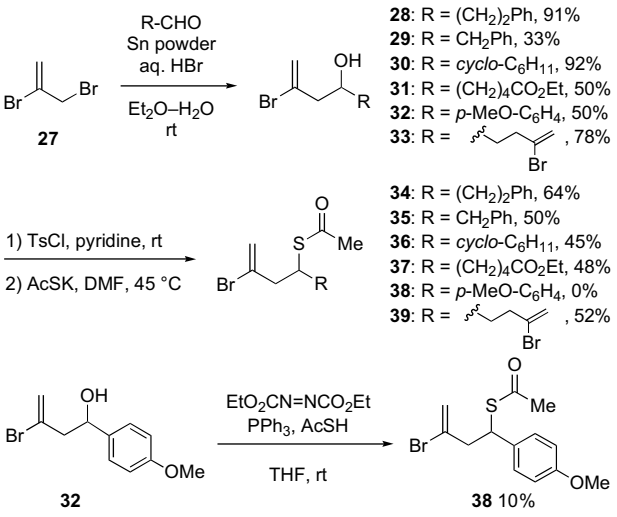
Scheme 9.

To examine 4-membered ring (2-alkylidenethietanes) formation, γ-bromo-γ-alkenyl thioacetates were prepared as shown in Schemes 10–13. Dibromination of the known homoallylic alcohol **24**[19] and successive dehydrobromination gave 3-bromo 4,4-dimethyl homoallylic alcohol **25**, which was converted into thioacetate **26** (Scheme 10). 3-Bromo homoallylic alcohols **28**–**33** were synthesized by the reaction of 2,3-dibromopropene (**27**) with aldehydes in the presence of tin powder,[20] and were converted into the corresponding thioacetates **34**–**39** by tosylation and substitution of tosylates with potassium thioacetate or by Mitsunobu reaction with thioacetic acid[21] (Scheme 11).

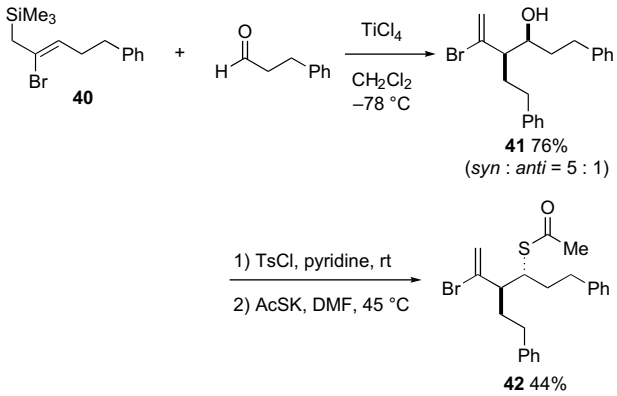
For the preparation of β-substituted homoallylic alcohol **41**, (*Z*)-β-bromoallylsilane **40** reacted with 3-phenylpropanal to afford **41** with *syn*-selectivity (Scheme 12).[22] Tosylation of **41** followed by substitution with potassium thioacetate gave thioacetate **42** having *anti*-stereochemistry.



Scheme 10.

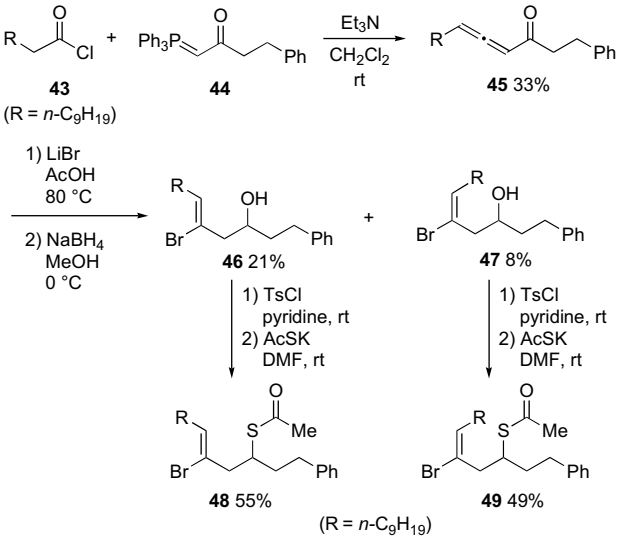


Scheme 11.



Scheme 12.

Both *E*- and *Z* bromoalkenyl thioacetates were prepared from undecanoyl chloride (**43**) and phosphorus ylide **44**.[23] The resulting allene **45** was treated with LiBr in acetic acid,[24] and then reduced with $NaBH_4$, giving a *Z* and *E* mixture of homoallylic alcohols **46** and **47** (Scheme 13). After chromatographic separation of the isomers,



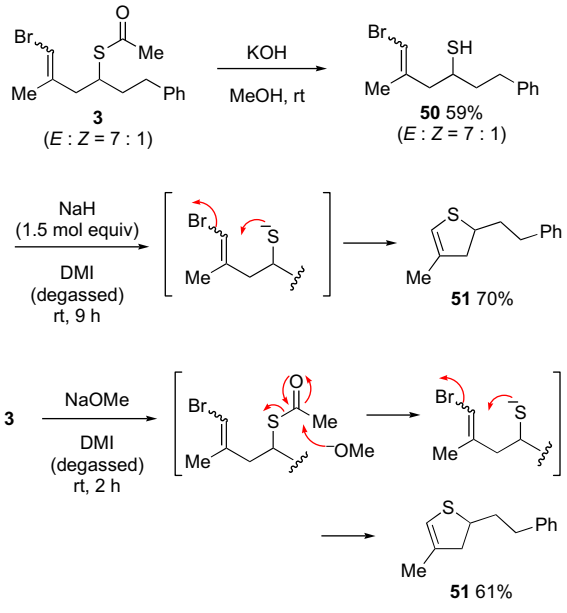
Scheme 13.

thioacetates **48** and **49** were obtained by tosylation followed by substitution with potassium thioacetate (Scheme 13).[25]

2.2. Intramolecular vinylic substitution reactions

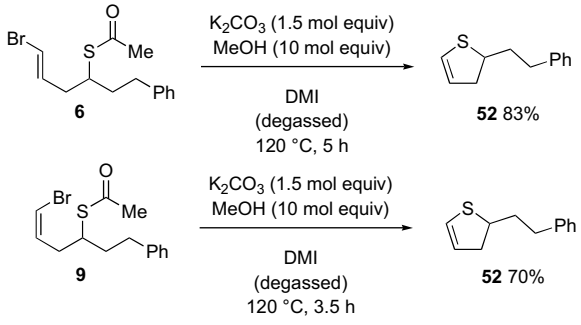
*2.2.1. Reactions of terminal-bromoalkenes **A***

When an *E*/*Z*-mixture (7:1) of thiol **50** prepared from thioacetate **3** was treated with NaH in *N*,*N*′-dimethylimidazolidin-2-one (DMI), the cyclization proceeded even at room temperature, giving dihydrothiophene **51** in 70% yield (Scheme 14). However, thiol **50** was found not to be stable enough because it was easily oxidized to the corresponding disulfide. We envisaged that thioacetate **3** could be used directly instead of thiol **50** for this intramolecular substitution reaction. As expected, treatment of thioacetate **3** with 1.5 mol equiv of NaOMe at room temperature in DMI gave dihydrothiophene **51** in 61% yield (Scheme 14).



Scheme 14.

Interestingly, the *Z*-isomer of **50** was not recovered in these reactions, which meant that both the *E*- and *Z*-stereoisomers were cyclized to **51**. To confirm this, the reactions of *E*- and *Z*-bromoalkenes **6** and **9** were examined independently (Scheme 15). It is noteworthy that dihydrothiophene **52** was obtained in 83% and 70% yields from both stereoisomers **6** and **9**, respectively by treatment with K_2CO_3 and MeOH in DMI at 120 °C.[26]



Scheme 15.

To get more information on these vinylic substitution reactions, we carried out theoretical calculations using the Gaussian program.[27] All calculations were performed at the B3LYP[28]/6-31+G(d) level and the solvent effect was included by using the Onsager continuum model[29] for DMF (ε=37.06) as a solvent.[30] For the cyclization of the thiolate anion from **3**, *E*-anion *E*-**53** generated from *E*-**3** gave the $S_NV\sigma$ transition structure *E*-**53**-ts (Fig. 1). The activation energy is 19.6 kcal mol^{-1} in the gas phase and 12.5 kcal mol^{-1} in DMF, respectively. On the other hand, the $S_NV\pi$ transition structure *Z*-**54**-ts was obtained from *Z*-isomer *Z*-**3** and its activation energies are 20.7 kcal mol^{-1} in the gas phase and

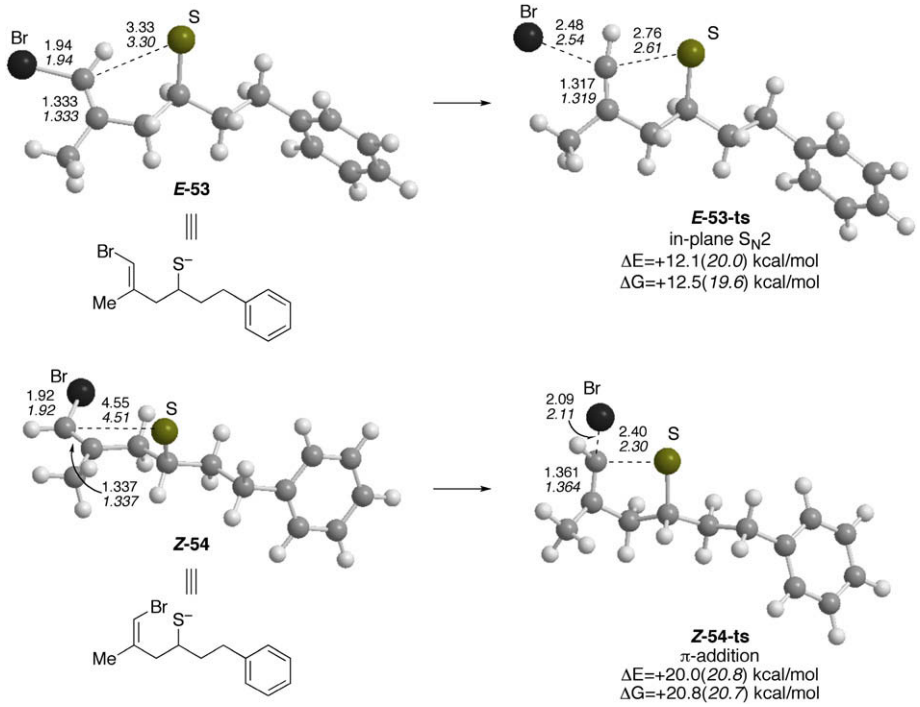
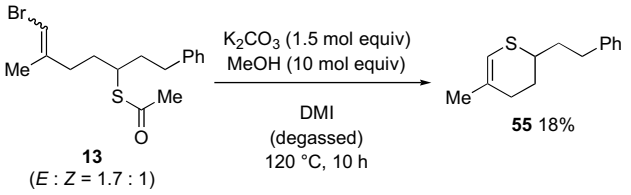


Figure 1. Transition structures for the nucleophilic cyclization of thiolate anion *E*-**53** and *Z*-**54** [B3LYP/6-31+G(d), SCRF (dipole, solv=DMF)]. Selected bond lengths are shown in Å. The italic numbers are the values in the gas phase.

20.8 kcal mol^{-1} in DMF, respectively (Fig. 1). Thus, the calculation also suggested that each stereoisomer can cyclized through the $S_NV\sigma$ or $S_NV\pi$ transition states, because their activation energies are low enough to undergo substitution under the presented reaction conditions.

This intramolecular nucleophilic substitution was next applied to 6-membered ring formation using bromoalkene **13**. However, the yield of the cyclized product, tetrahydrothiopyran **55** was low (18%), and we couldn't confirm whether the substitution reaction proceeded from the *E*-isomer or both stereoisomers (Scheme 16).

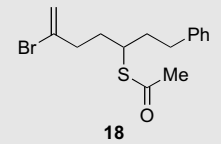
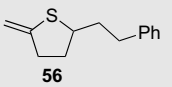
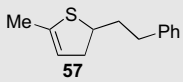
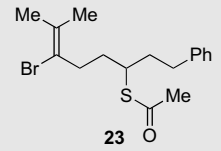
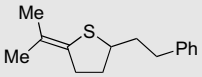
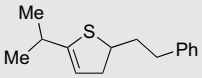
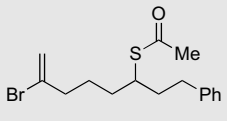
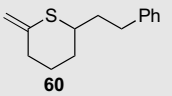
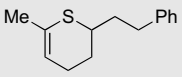
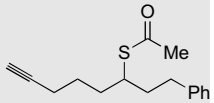


Scheme 16.

2.2.2. *Reactions of internal-bromoalkenes **B***

As well as terminal-bromoalkenes **A**, substitution reactions of internal-bromoalkenes **B** with a thiolate anion were found to proceed as shown in Table 1. Formation of a 5-membered ring from thioacetate **18** afforded an inseparable mixture of 2-methylenetetrahydrothiophene **56** and 2,3-dihydrothiophene **57** in 85% yield (**56**/**57**=3:1) (Table 1, entry 1). It was found that 2-methylenetetrahydrothiophene **56** gradually isomerized to 2,3-dihydrothiophene **57** at room temperature during flash chromatography on silica gel. The reaction of thioacetate **23** having an isopropylidene moiety gave tetrahydrothiophene **58** and dihydrothiophene **59** in 59% and 10% yield, respectively (entry 2). Formation of a 6-membered ring was also examined with thioacetate **19**, affording an inseparable mixture of tetrahydrothiopyran **60** and dihydrothiopyran **61** in 31% yield along with 19% yield of dehydrobromination product **62** (entry 3). Tetrahydrothiopyran **60** also slowly isomerized to dihydrothiopyran **61** during flash column chromatography on silica gel.

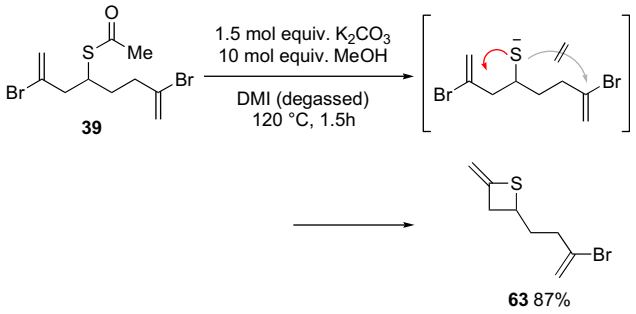
Table 1
Cyclization of internal bromoalkenes **B** with a thiolate anion[a]

Entry	Thioacetate	Conditions	Product (yield/%)[b]
1	 **18**	120 °C, 7 h	 **56**  **57** (85) (**56** : **57** = 3 : 1)
2	 **23**	120 °C, 8 h	 **58** (59)  **59** (10)
3	 **19**	120 °C, 7 h	 **60**  **61** (31) (**60** : **61** = 2.5 : 1)  **62** (19)

[a] Reactions were carried out in degassed DMI with 1.5 mol equiv of K_2CO_3 and 10 mol equiv of MeOH.
[b] Isolated yield.

According to the above results, it was found that 5-membered ring formation proceeded more smoothly than that of 6-membered with both terminal-bromoalkenes **A** and internal-bromoalkenes **B**. Galli and Mandolini reported the kinetics of ring-closure reactions of 1,1-bis(ethoxycarbonyl)cycloalkanes from the anions derived from diethyl (ω-bromoalkyl)malonates by intramolecular nucleophilic substitution at an sp^3 carbon, which showed that the order of ring-closing rate was 5>6>4 membered ring formation.[31] However, in the case of the intramolecular nucleophilic substitution with *S*-nucleophile at an sp^2 carbon, there was no precedent on the reaction rate of ring-closures.

Next we tried a competitive reaction among 5 versus 4-membered ring formation using thioacetate **39**. Surprisingly, the reaction of thioacetate **39** gave only the 4-membered ring product, methylidenethiethane **63**, in 87% yield without forming the 5-membered ring compound (Scheme 17).



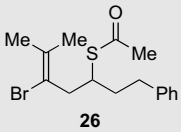
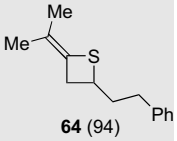
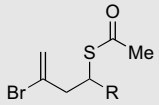
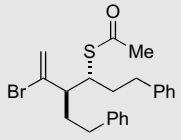
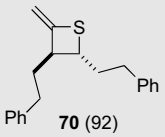
Scheme 17.

This alkylidenethietane formation[32] prompted us to investigate the scope and limitations, the results of which are summarized in Table 2. When thioacetate **26** was treated with 1.5 mol equiv of K_2CO_3 and 10 mol equiv of MeOH at 120 °C in degassed DMI, thietane **64** was obtained in 94% yield (Table 2, entry1). Thioacetate derivatives **34**–**37** bearing primary and secondary alkyl groups at C(4)-position cyclized to give 2-methylenethietanes **65**–**68** in good yields (entries 2–5). Benzylic thioacetate **38** was cyclized to thietane **69** in moderate yield, due to the concurrent elimination of thioacetic acid forming a conjugated diene as a side product (entry 6). 3,4-Disubstituted 2-methylenethietane **70** was also formed in 92% yield (entry 7).

The theoretical calculation of the cyclization of thiolate anion **71** from thioacetate **34** revealed that both $S_NV\sigma$ and $S_NV\pi$ transition states (Fig. 2) have reasonable activation energies (22.4 kcal mol^{-1} for $S_NV\sigma$, 18.2 kcal mol^{-1} for $S_NV\pi$ in DMF) to undergo substitution reactions.

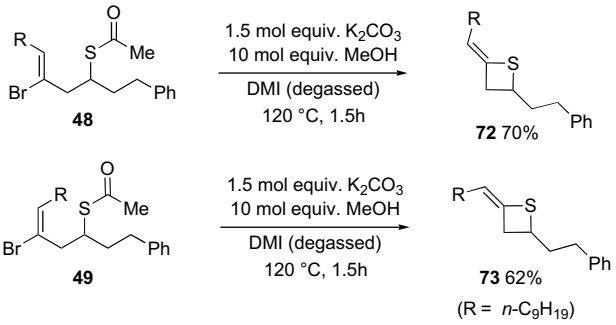
We were motivated to investigate the mechanism of this thiethane formation by experimental evidence. As we could not judge from the above results which is the real reaction course, the $S_NV\pi$

Table 2
Synthesis of 2-alkylidenethietanes[a]

Entry	Thioacetate	Conditions	Thietane (yield/%)[b]
	 **26**	120 °C, 3 h	 **64** (94)
1			
2	**34**: R=$(CH_2)_2Ph$	120 °C, 1.5 h	**65** (93)
3	**35**: R=CH_2Ph	120 °C, 3 h	**66** (92)
4	**36**: R=*cyclo*-C_6H_{11}	120 °C, 3 h	**67** (85)
5[c]	**37**: R=$(CH_2)_4CO_2Et$	120 °C, 10 h	**68** (67)
6	**38**: R=*p*-MeO-C_6H_4	120 °C, 2 h	**69** (30)
7	 **42**	120 °C, 1.5 h	 **70** (92)

[a] Reactions were carried out in degassed DMI with 1.5 mol equiv of K_2CO_3 and 10 mol equiv of MeOH.
[b] Isolated yield.
[c] 10 mol equiv of EtOH was used instead of MeOH.

or/and $S_NV\sigma$ mechanism. It would be confirmed by examining the stereochemical outcomes of the thiethane formation, that is, inversion of configuration should be ovserved for $S_NV\sigma$ and retention should be for $S_NV\pi$. The cyclization reactions of *E* and *Z* thioaetates **48** and **49** were examined, giving thietanes **72** in 70% yield and **73** in 62% yield, respectively, with complete retention of their configurations (Scheme 18).[33] Thus, the thietane formation proceeds with retention of the configuration, namely by the $S_NV\pi$ mechanism.



Scheme 18.

3. Conclusions

By the nucleophilic intramolecular substitution reactions of bromoalkenes bearing an acetylthio moiety, several kinds of sulfur-containing heterocycles could be synthesized. The experimental and theoretical studies revealed that the vinylic substitution reactions with *S*-nucleophiles could proceed in either $S_NV\sigma$ or $S_NV\pi$ mechanisms. The present methods would provide unique synthetic routes for a variety of heterocycles.

4. Experimental

4.1. General

^1H NMR (500, 400 and 300 MHz) spectra were recorded on Bruker AVANCE 500, 400 and 300 and JEOL AL 400 spectrometers in $CDCl_3$ [using tetramethylsilane (for ^1H, δ=0) as internal standard]. ^{13}C NMR (125, 100 and 75 MHz) spectra were recorded on Bruker AVANCE 500, 400 and 300, and JEOL AL 400 spectrometers in $CDCl_3$ [using $CDCl_3$ (for ^{13}C, δ=77.00) as internal standard]. The following abbreviations were used to explain the multiplicities: s=singlet, d=doublet, t=triplet, q=quartet, br=broad. IR spectra were recorded on a Horiba FT 300-S by the ATR method and a Shimazu IR Prestige-21 FT-IR Spectrometer. High-resolution mass spectra were obtained with a JEOL MS-700P mass spectrometer and a Finnigan

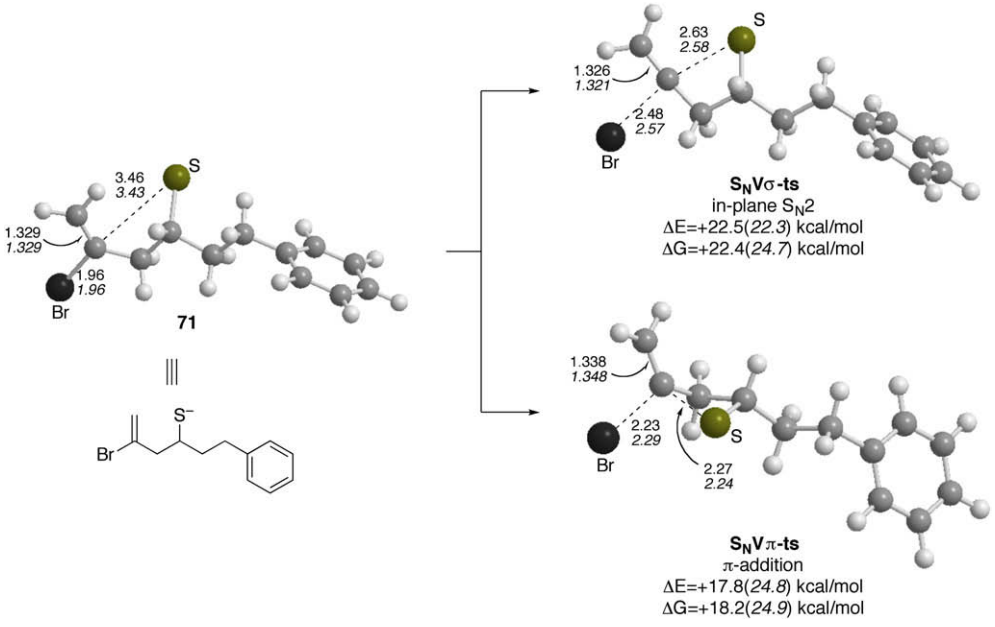


Figure 2. Transition structures for the nucleophilic cyclization of thiolate anion **71** [B3LYP/6-31+G(d), SCRF (dipole, solv=DMF)]. Selected bond lengths are shown in Å. The italic numbers are the values in the gas phase.

MAT 95 XP mass spectrometer (Thermo Electron Corporation) and Q-Tof Premier. Elemental analyses were carried out at the Elemental Analysis Laboratory, Department of Chemistry, Faculty of Science, The University of Tokyo. Melting points are uncorrected and were recorded on a Buchi B-54 melting point apparatus. Flash column chromatography was performed using Merck silica gel 60 with distilled solvents, and preparative thin-layer chromatography was carried out using Wakogel B-5F. Dry tetrahydrofuran (THF), diethyl ether (Et_2O), and dichloromethane (CH_2Cl_2) were taken from a solvent purification system (PS-400-5, Innovative Technology Inc.). 1,3-Dimethyl-2-imidazolidinone (DMI) and *N*,*N*-dimethylformamide (DMF) were distilled from calcium hydride (CaH_2) and stored over molecular sieves 4 Å (MS 4 Å). Ethanol (EtOH) was distilled from sodium and stored over molecular sieves 3 Å (MS 3 Å). Methanol was distilled from a trace amount of iodine and magnesium, and stored over MS 3 Å. Triethylamine and pyridine were distilled from CaH_2 and stored over KOH.

4.2. Preparation of starting materials

4.2.1. 6-Bromo-5-methyl-1-phenylhex-5-en-3-ol (**2**) (Scheme 5)

To a stirred solution of 5-methyl-1-phenylhex-5-en-3-ol (**1**)[10] (5.98 g, 31.4 mmol) in CCl_4 (150 mL) was added a solution of bromine (1.7 mL, 33.0 mmol) in CCl_4 (50 mL) at 0 °C, and the mixture was stirred for 2 h. The reaction was quenched with saturated $Na_2S_2O_3$ solution at 0 °C, and the organic materials were extracted two times with CH_2Cl_2. The combined extracts were washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The residual brown oil was treated with a 5 M solution of KOH in MeOH (37 mL) at room temperature for 4 h. The reaction mixture was quenched with water and extracted three times with Et_2O. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel, hexane/EtOAc=8:1) to give an *E*/*Z*-mixture (7:1) of **2** (3.40 g, 12.6 mmol) in 40% yield.

Pale yellow oil (*E*/*Z*=7:1); R_f=0.23 (silica gel, hexane/EtOAc=8:1); data for the major isomer (*E*): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.31 (2H, m), 7.18–7.23 (3H, m), 6.00–6.01 (1H, m), 3.74–3.76 (1H, m), 2.66–2.84 (2H, m), 2.22–2.29 (2H, m), 1.81 (3H, d, *J*=0.8 Hz), 1.75–1.78 (2H, m), 1.55 (1H of –OH, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.7, 138.7, 128.5, 128.4, 125.9, 103.7, 68.2, 46.5, 38.6, 32.0, 19.3; IR (NaCl): 3447, 3063, 3015, 2940, 2918, 2862, 1628, 1603, 1495, 1454, 1437, 1288, 1217, 1053, 756 cm^{-1}; HRMS (ESI) found: 291.0366, calcd for $C_{13}H_{17}OBrNa$ (M+Na$^+$): 291.0360.

4.2.2. S-6-Bromo-5-methyl-1-phenylhex-5-en-3-yl ethanethioate (**3**) (Scheme 5)

To a stirred solution of 6-bromo-5-methyl-1-phenylhex-5-en-3-ol (**2**) (1.21 g, 4.5 mmol) in pyridine (17 mL) was added *p*-toluenesulfonyl chloride (2.56 g, 13.4 mmol) at 0 °C, and the mixture was stirred at room temperature overnight. The reaction mixture was poured into cold water (150 mL) and extracted three times with Et_2O. The combined extracts were washed with aqueous HCl (1 M) and brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel, hexane/EtOAc=12:1) to give tosylate (1.42 g, 3.4 mmol) in 75% yield.

To a stirred solution of tosylate (1.38 g, 3.3 mmol) in DMF (36 mL) was added potassium thioacetate (2.15 g, 18.8 mmol), and the mixture was stirred at 45 °C for 1 d. The reaction was quenched with water at 0 °C, and the organic materials were extracted three times with Et_2O. The combined extracts were washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel, hexane/EtOAc=50:1) to give *S*-6-bromo-5-methyl-1-phenylhex-5-en-3-yl ethanethioate (**3**) (830 mg, 2.5 mmol) in 78% yield. Yellow oil (*E*/*Z*=7:1); R_f=0.48 (silica gel, hexane/EtOAc=8:1); data for the major isomer (*E*): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.30 (2H, m), 7.14–7.21 (3H, m), 5.93–5.94 (1H, m), 3.64–3.71 (1H, m), 2.58–2.80 (2H, m), 2.38–2.40 (2H, m), 2.35 (3H, s), 1.89–1.95 (1H, m), 1.77 (3H, d, *J*=1.2 Hz), 1.73–1.83 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.4, 141.2, 138.7, 128.5, 128.4, 126.1, 103.9, 44.2, 41.8, 35.6, 33.1, 30.9, 18.8; IR (NaCl): 3063, 3026, 2938, 2916, 2855, 1694, 1682, 1495, 1454, 1354, 1288, 1113, 953, 748, 700 cm^{-1}; HRMS (ESI) found: 349.0224, calcd for $C_{15}H_{19}OSBrNa$ (M+Na$^+$): 349.0238.

4.2.3. (E)-6-Bromo-1-phenylhex-5-en-3-ol (**5**)[12] (Scheme 6a)

To a stirred solution of 1-phenyl-6-(trimethylsilyl)hex-5-yn-3-ol (**4**)[12] (770 mg, 3.1 mmol) in Et_2O (5 mL) was added DIBAL–H in heptane (1.0 M in heptane) (8.1 mL, 8.1 mmol) at 0 °C, and the mixture was stirred at room temperature overnight. The reaction mixture was quenched with methanol (30 mL) and saturated sodium potassium tartrate solution (30 mL), and the organic materials were extracted three times with Et_2O. The combined organic extracts were washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel, hexane/EtOAc=20:1) to afford the (*Z*)-1-phenyl-6-trimethylsilyl-hex-5-en-3-ol (500 mg, 2.0 mmol) as colorless oil in 64 % yield.

To a stirred solution of (*Z*)-1-phenyl-6-trimethylsilanyl-hex-5-en-3-ol (290 mg, 1.2 mmol) in CH_2Cl_2 (4 mL) was added bromine (60 μL, 1.2 mmol) at −78 °C. The reaction mixture was quenched with saturated $Na_2S_2O_3$ solution and the organic materials were extracted three times with CH_2Cl_2. The combined organic extracts were washed with brine, dried over Na_2SO_4, and filtered. The filtrate was cooled to −20 °C prior to addition of TBAF (610 mg, 2.3 mmol). The mixture was stirred at −20 °C for 40 min. The reaction mixture was concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel, hexane/EtOAc=8:1) to afford (*E*)-6-bromo-1-phenylhex-5-en-3-ol (**5**) (270 mg, 1.1 mmol) in 90% yield.

Yellow oil; R_f=0.50 (silica gel, hexane/EtOAc=8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.32 (2H, m), 7.20–7.21 (3H, m), 6.12–6.25 (2H, m), 3.65–3.72 (1H, m), 2.77–2.84 (1H, m), 2.65–2.72 (1H, m), 2.16–2.31 (2H, m), 1.75–1.81 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.7, 134.0, 128.5, 128.4, 126.0, 107.0, 69.7, 40.9, 38.4, 32.0; IR (NaCl): 3375, 3360, 3061, 3026, 2932, 2860, 1620, 1603, 1495, 1454, 1433, 1275, 1242, 1179, 1084, 1049, 941, 910, 735, 700 cm^{-1}; HRMS (EI) found: 254.0303, calcd for $C_{12}H_{15}OBr$ (M$^+$): 254.0301.

4.2.4. (E)-S-6-Bromo-1-phenylhex-5-en-3-yl ethanethioate (**6**) (Scheme 6a)

This compound was synthesized from (*E*)-6-bromo-1-phenylhex-5-en-3-ol (**5**) according to the same procedure as for **3**.

Yellow oil; yield 54% (2 steps); R_f=0.52 (silica gel, hexane/EtOAc=10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.31 (2H, m), 7.15–7.22 (3H, m), 6.08–6.18 (2H, m), 3.57–3.63 (1H, m), 2.71–2.78 (1H, m), 2.59–2.66 (1H, m), 2.37–2.42 (2H, m), 2.36 (3H, s), 1.79–1.97 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.3, 141.2, 134.0, 128.5, 128.4, 126.1, 107.1, 43.1, 38.5, 35.6, 33.2, 30.9; IR (NaCl): 3061, 3026, 2924, 2857, 1694, 1618, 1495, 1454, 1435, 1352, 1132, 1113, 945, 750, 700 cm^{-1}; HRMS (EI) found: 312.0090, calcd for $C_{14}H_{17}OBrS$ (M$^+$): 312.0178.

4.2.5. (Z)-6-Bromo-1-phenylhex-5-en-3-ol (**8**)[12] (Scheme 6b)

To a stirred solution of *i*-Pr_2NH (5.6 mL, 40.0 mmol) in anhydrous THF (40 mL) was added dropwise *n*-BuLi (1.6 M in hexane) (25.2 mL, 40.0 mmol) at 0 °C, and the reaction mixture was stirred at 0 °C for 30 min before being transferred into the other flask.

To a stirred solution of $ZnBr_2$ (2.25 g, 10.0 mmol) and allyl bromide (**7**) (1.7 mL, 20.0 mmol) in THF (80 mL) was added the preformed LDA (40.0 mmol) at −78 °C, and the mixture was stirred for around 25 min at −78 °C. Then hydrocinnamaldehyde (1.0 mL, 8.0 mmol) was added. The reaction mixture was allowed to proceed for 4 h at −78 °C. Then the reaction was quenched with aqueous

HCl (1 M) and the organic materials were extracted three times with Et_2O. The combined organic extracts were washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel, hexane/ether=10:1) to afford (*Z*)-6-bromo-1-phenylhex-5-en-3-ol (**8**) (1.26 g, 5.0 mmol) in 62% yield.

Pale yellow oil; R_f=0.45 (silica gel, hexane/EtOAc=4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.31 (2H, m), 7.20–7.21 (3H, m), 6.30 (1H, ddd, *J*=1.4, 1.5, 7.0 Hz), 6.21 (1H, ddd, *J*=7.0, 7.0, 7.0 Hz), 3.76–3.82 (1H, m), 2.77–2.85 (1H, m), 2.66–2.74 (1H, m), 2.42–2.46 (2H, m), 1.79–1.85 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.8, 130.9, 128.5, 128.4, 125.9, 110.1, 70.1, 38.6, 37.7, 32.0; IR (NaCl): 3374, 3082, 3061, 3024, 2928, 2860, 1622, 1603, 1495, 1454, 1314, 1277, 1080, 1055, 1032, 746, 700, 675 cm^{-1}; HRMS (EI) found: 254.0300, calcd for $C_{12}H_{15}OBr$ (M^+): 254.0301.

4.2.6. (*Z*)-*S*-6-Bromo-1-phenylhex-5-en-3-yl ethanethioate (**9**) (Scheme 6b)

This compound was synthesized from (*Z*)-6-bromo-1-phenylhex-5-en-3-ol (**8**) according to the same procedure as for **3**.

Pale yellow oil; yield 44% (2 steps); R_f=0.50 (silica gel, hexane/EtOAc=8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25–7.30 (2H, m), 7.16–7.20 (3H, m), 6.27 (1H, ddd, *J*=1.3, 1.4, 7.0 Hz), 6.10 (1H, ddd, *J*=7.0, 7.0, 7.0 Hz), 3.65–3.72 (1H, m), 2.72–2.80 (1H, m), 2.62–2.70 (1H, m), 2.53–2.59 (2H, m), 2.35 (3H, s), 1.82–2.02 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 141.3, 131.3, 128.5, 128.4, 126.0, 110.1, 43.0, 35.9, 35.2, 33.2, 30.8; IR (NaCl): 3084, 3061, 3026, 2922, 2857, 1690, 1622, 1603, 1497, 1454, 1352, 1283, 1132, 1111, 953, 750, 700 cm^{-1}; HRMS (EI) found: 312.0164, calcd for $C_{14}H_{17}OBrS$ (M^+): 312.0178.

4.2.7. 6-Methyl-1-phenylhept-6-en-3-ol (**11**) (Scheme 7)

To a stirred suspension of magnesium (300 mg, 12.4 mmol) in anhydrous THF (20 mL) was added 4-bromo-2-methylbut-1-ene (**10**) (1.68 g, 11.3 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 4 h. The resulting Grignard reagent was added dropwise via a cannula to a solution of hydrocinnamaldehyde (1.5 mL, 11.3 mmol) in anhydrous THF (20 mL) at 0 °C, and the reaction mixture was stirred overnight. The reaction was quenched with saturated NH_4Cl solution at 0 °C, and the organic materials were extracted three times with Et_2O. The combined extracts were washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel, hexane/EtOAc=10:1) to give 6-methyl-1-phenylhept-6-en-3-ol (**11**) (760 mg, 3.7 mmol) in 33% yield.

Pale yellow oil; R_f=0.22 (silica gel, hexane/EtOAc=6:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24–7.30 (2H, m), 7.18–7.21 (3H, m), 4.70–4.71 (2H, m), 3.63–3.66 (1H, m), 2.76–2.83 (1H, m), 2.63–2.71 (1H, m), 2.04–2.20 (2H, m), 1.76–1.84 (2H, m), 1.72–1.74 (3H, m), 1.56–1.71 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 142.2, 128.4 (overlapped), 125.8, 110.2, 71.3, 39.1, 35.3, 34.1, 32.1, 22.5; IR (NaCl): 3358, 3063, 3026, 2934, 2859, 1649, 1495, 1454, 1373, 1088, 1057, 1030, 887, 746, 698 cm^{-1}; HRMS (ESI) found: 227.1428, calcd for $C_{14}H_{20}ONa$ ($M+Na^+$): 227.1412.

4.2.8. 7-Bromo-6-methyl-1-phenylhept-6-en-3-ol (**12**) (Scheme 7)

This compound was synthesized from 6-methyl-1-phenylhept-6-en-3-ol (**11**) according to the same procedure as for **2**.

Yellow oil (*E*/*Z*=1.7:1); yield 43%; R_f=0.23 (silica gel, hexane/EtOAc=8:1); data for *E*/*Z*-isomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20–7.31 (5H, m), 5.91–5.93/5.87–5.88 (1H, m), 3.61–3.63 (1H, m), 2.64–2.84 (2H, m), 2.19–2.36 (2H, m), 1.56–1.83 (7H, m), 1.40 (1H of –OH, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.1/141.9, 141.5/141.3, 128.49/128.44, 128.39/128.44, 126.0/125.9, 101.5/101.0, 70.7/70.8, 39.2/39.0, 35.2/30.6, 34.5/34.3, 32.0/32.1, 19.2/22.1; IR (NaCl): 3383, 3026, 2934, 2859, 1632, 1603, 1495, 1454, 1375, 1283, 1088, 1030, 746, 700 cm^{-1}; HRMS (ESI) found: 305.0691, calcd for $C_{14}H_{19}OBrNa$ ($M+Na^+$): 305.0517.

4.2.9. *S*-7-Bromo-6-methyl-1-phenylhept-6-en-3-yl ethanethioate (**13**) (Scheme 7)

This compound was synthesized from 7-bromo-6-methyl-1-phenylhept-6-en-3-ol (**12**) according to the same procedure as for **3**.

Pale yellow oil (*E*/*Z*=1.7:1); yield 27%; R_f=0.50 (silica gel, hexane/EtOAc=8:1); Data for *E*/*Z*-isomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.30 (2H, m), 7.15–7.21 (3H, m), 5.89–5.90/5.87–5.88 (1H, m), 3.51–3.59 (1H, m), 2.59–2.79 (2H, m), 2.36/2.35 (3H, s), 2.11–2.34 (2H, m), 1.81–2.05 (2H, m), 1.78–1.79/1.77–1.78 (3H, m), 1.65–1.77 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.6/195.7, 141.4/141.6, 140.9/140.8, 128.44/128.47, 128.42/128.37, 126.04/125.98, 101.8/101.3, 43.8/44.1, 36.6/36.4, 33.18/33.21, 33.0/35.5, 31.7/31.8, 30.88/30.89, 19.2/22.1; IR (NaCl): 3063, 3026, 2934, 2855, 1694, 1632, 1603, 1497, 1454, 1352, 1287, 1132, 1111, 953, 748, 700 cm^{-1}; HRMS (ESI) found: 363.0391, calcd for $C_{16}H_{21}OSBrNa$ ($M+Na^+$): 363.0394.

4.2.10. 6-Bromo-1-phenylhept-6-en-3-ol (**16**) (Scheme 8)

To a stirred solution of 4-bromopent-4-en-1-ol (**14**)[16] (2.07 g, 12.6 mmol) in anhydrous CH_2Cl_2 (50 mL) was added Dess–Martin periodinane (8.30 g, 20.8 mmol) in one portion at room temperature, and the reaction mixture was stirred at room temperature overnight. Then the reaction was quenched with saturated $Na_2S_2O_3$ solution, and the organic materials were extracted three times with CH_2Cl_2. The combined extracts were washed with saturated $NaHCO_3$ solution, water and brine, dried over Na_2SO_4, and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel, hexane/EtOAc=15:1) to give 4-bromopent-4-enal (1.39 g, 8.5 mmol) in 68% yield.

To a stirred solution of 4-bromopent-4-enal (1.27 g, 7.8 mmol) in anhydrous THF (10 mL) was added phenethylmagnesium bromide (0.7 M in THF) (11.0 mL, 7.8 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 4 h. Then the reaction was quenched with saturated NH_4Cl solution, and the organic materials were extracted three times with Et_2O. The combined extracts were washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel, hexane/EtOAc=15:1) to give 6-bromo-1-phenylhept-6-en-3-ol (**16**) (1.20 g, 4.5 mmol) in 57% yield.

Pale yellow oil; R_f=0.40 (silica gel, hexane/EtOAc=4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18–7.31 (5H, m), 5.60 (1H, d, *J*=1.3 Hz), 5.41 (1H, d, *J*=1.3 Hz), 3.67–3.68 (1H, m), 2.52–2.76 (4H, m), 1.66–1.86 (4H, m), 1.42 (1H of –OH, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.8, 134.3, 128.5, 128.4, 125.9, 116.9, 70.2, 39.2, 37.8, 35.7, 32.0; IR (NaCl): 3364, 3026, 2922, 2857, 1630, 1495, 1454, 1435, 1082, 1057, 1030, 887, 746, 698 cm^{-1}; HRMS (ESI) found: 291.0364, calcd for $C_{13}H_{17}ONaBr$ ($M+Na^+$): 291.0360.

4.2.11. 7-Bromo-1-phenyloct-7-en-3-ol (**17**) (Scheme 8)

This compound was synthesized from 5-bromohex-5-en-1-ol (**15**)[17] according to the same procedure as for **16**.

Pale yellow oil; yield 40%; R_f=0.18 (silica gel, hexane/EtOAc=6:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20–7.31 (5H, m), 5.56 (1H, d, *J*=1.1 Hz), 5.40 (1H, d, *J*=1.1 Hz), 3.64–3.66 (1H, m), 2.64–2.84 (2H, m), 2.42–2.46 (2H, m), 1.44–1.82 (6H, m), 1.41 (1H of –OH, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.0, 134.3, 128.42, 128.39, 125.9, 116.7, 71.0, 41.2, 39.1, 36.1, 32.0, 23.9; IR (NaCl): 3377, 3026, 2940, 2860, 1632, 1603, 1495, 1454, 1429, 1123, 1090, 887, 746, 700 cm^{-1}; HRMS (ESI) found: 305.0523, calcd for $C_{14}H_{19}ONaBr$ ($M+Na^+$): 305.0517.

4.2.12. *S*-6-Bromo-1-phenylhept-6-en-3-yl ethanethioate (**18**) (Scheme 8)

This compound was synthesized from 6-bromo-1-phenylhept-6-en-3-ol (**16**) according to the same procedure as for **3**.

Pale yellow oil; yield 54% (2 steps); R_f=0.53 (silica gel, hexane/EtOAc=10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16–7.30 (5H, m), 5.56

(1H, d, J=1.4 Hz), 5.40 (1H, d, J=1.4 Hz), 3.54–3.61 (1H, m), 2.45–2.79 (4H, m), 2.36 (3H, s), 1.80–2.00 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.4, 141.4, 133.4, 128.45, 128.38, 126.0, 117.2, 43.3, 38.8, 36.9, 33.4, 33.2, 30.8; IR (NaCl): 3026, 2924, 2857, 1694, 1682, 1630, 1497, 1454, 1427, 1352, 1113, 953, 889, 748, 700 cm^{-1}; HRMS (ESI) found: 349.0245, calcd for $C_{15}H_{19}ONaSBr$ (M+Na$^+$): 349.0238.

4.2.13. S-7-Bromo-1-phenyloct-7-en-3-yl ethanethioate (**19**) (Scheme 8)

This compound was synthesized from 7-bromo-1-phenyloct-7-en-3-ol (**17**) according to the same procedure as for **3**.

Pale yellow oil; yield 59% (2 steps); R_f=0.59 (silica gel, hexane/EtOAc=8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16–7.30 (5H, m), 5.56 (1H, d, J=0.9 Hz), 5.40 (1H, d, J=0.9 Hz), 3.56–3.60 (1H, m), 2.60–2.78 (2H, m), 2.40–2.43 (2H, m), 2.36 (3H, s), 1.84–1.98 (2H, m), 1.59–1.70 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.8, 141.6, 134.1, 128.43, 128.39, 126.0, 117.0, 43.9, 40.9, 36.7, 33.5, 33.2, 30.9, 24.9; IR (NaCl): 3026, 2938, 2859, 1692, 1628, 1495, 1454, 1352, 1115, 953, 887, 748, 700 cm^{-1}; HRMS (ESI) found: 363.0404, calcd for $C_{16}H_{21}ONaSBr$ (M+Na$^+$): 363.0394.

4.2.14. 7-Methyl-1-phenyloct-6-en-3-ol (**21**)[34] (Scheme 9)

This compound was synthesized from 4-bromo-5-methylhex-4-en-1-ol (**20**)[18] according to the same procedure as for **16**.

Pale yellow oil; Yield: 31% (2 steps); R_f=0.37 (silica gel, hexane/EtOAc=7:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27–7.30 (2H, m), 7.18–7.22 (3H, m), 5.12–5.15 (1H, m), 3.63–3.67 (1H, m), 2.77–2.83 (1H, m), 2.65–2.71 (1H, m), 2.03–2.17 (2H, m), 1.72–1.83 (2H, m), 1.70 (3H, s), 1.62 (3H, s), 1.47–1.59 (3H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.2, 132.2, 128.44, 128.41, 125.8, 124.1, 71.3, 39.2, 37.5, 32.1, 25.7, 24.4, 17.7; IR (NaCl): 3350, 3026, 2965, 2924, 2857, 1603, 1495, 1454, 1375, 1111, 1080, 1059, 1030, 984, 746, 698 cm^{-1}; HRMS (EI) found: 218.1675, calcd for $C_{15}H_{22}O$ (M$^+$): 218.1665.

4.2.15. 6-Bromo-7-methyl-1-phenyloct-6-en-3-ol (**22**) (Scheme 9)

This compound was synthesized from 7-methyl-1-phenyloct-6-en-3-ol (**21**) according to the same procedure as for **2**.

Yellow oil; yield: 22%; R_f=0.28 (silica gel, hexane/EtOAc=8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.32 (2H, m), 7.17–7.22 (3H, m), 3.63–3.65 (1H, m), 2.76–2.83 (1H, m), 2.67–2.73 (1H, m), 2.57–2.65 (2H, m), 1.79–1.85 (2H, m), 1.59–1.70 (2H, m), 1.86 (3H, s), 1.77 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.0, 130.7, 128.5, 128.4, 125.9, 121.3, 70.4, 39.3, 36.0, 33.9, 32.1, 25.4, 20.3; IR (NaCl): 3404, 3024, 2922, 2859, 1495, 1454, 1217, 1009, 756, 700, 667 cm^{-1}; HRMS (ESI) found: 319.0650, calcd for $C_{15}H_{21}OBrNa$ (M+Na$^+$): 319.0673.

4.2.16. S-6-Bromo-7-methyl-1-phenyloct-6-en-3-yl ethanethioate (**23**) (Scheme 9)

This compound was synthesized from 6-bromo-7-methyl-1-phenyloct-6-en-3-ol (**22**) according to the same procedure as for **3**.

Yellow oil; yield 59%; R_f=0.71 (silica gel, hexanes/EtOAc=8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.30 (2H, m), 7.17–7.21 (3H, m), 3.52–3.59 (1H, m), 2.63–2.76 (2H, m), 2.55–2.60 (2H, m), 2.35 (3H, s), 1.72–1.99 (4H, m), 1.85 (3H, s), 1.74 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.6, 141.6, 131.0, 128.42, 128.40, 126.0, 120.6, 43.6, 37.1, 35.0, 33.3, 33.1, 30.8, 25.4, 20.3; IR (NaCl): 3024, 2918, 2857, 1692, 1497, 1454, 1352, 1111, 953, 748, 700 cm^{-1}; HRMS (ESI) found: 377.0560, calcd for $C_{17}H_{23}OSBrNa$ (M+Na$^+$): 377.0551.

4.2.17. 5-Bromo-6-methyl-1-phenylhept-5-en-3-ol (**25**) (Scheme 10)

This compound was synthesized from 5-methyl-4-hexen-1-ol (**24**)[19] according to the same procedure as for **2**.

Colorless oil; Yield 63%; R_f=0.28 (silica gel, hexane/EtOAc=5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27–7.29 (2H, m), 7.22–7.17 (3H, m), 3.97–4.03 (1H, m), 2.78–2.87 (2H, m), 2.66–2.72 (1H, m), 2.51–2.55 (1H, m), 1.90 (3H, s), 1.79–1.85 (2H, m), 1.81 (3H, s), 1.75 (1H of –OH, br s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.9, 133.8, 128.4, 128.3, 125.8, 117.5, 69.7, 45.4, 38.0, 32.1, 25.6, 20.9; IR (ZnSe) 3388, 2918, 1653, 1603, 1496, 1454, 1223, 1043, 933, 746, 698 cm^{-1}; HRMS (FAB$^+$) found: 283.0693, calcd for $C_{14}H_{20}BrO$ (M+H$^+$): 283.0698.

4.2.18. S-5-Bromo-6-methyl-1-phenylhept-5-en-3-yl ethanethioate (**26**) (Scheme 10)

This compound was synthesized from 5-bromo-6-methyl-1-phenylhept-5-en-3-ol (**25**) according to the same procedure as for **3**.

Pale yellow oil; yield 44% (2 steps); R_f=0.68 (silica gel, hexane/EtOAc=8:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26–7.29 (2H, m), 7.16–7.20 (3H, m), 3.87–3.93 (1H, m), 2.87 (1H, dd, J=7.4, 14.7 Hz), 2.75–2.81 (2H, m), 2.61–2.68 (1H, m), 2.34 (3H, s), 1.99–2.06 (1H, m), 1.82–1.90 (1H, m), 1.87 (3H, s), 1.77 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.3, 141.5, 133.3, 128.3 (overlapped), 125.9, 118.0, 43.9, 42.3, 35.2, 33.2, 30.8, 25.5, 21.0; IR (ZnSe) 2918, 1687, 1603, 1496, 1454, 1352, 1111, 951, 748, 698, 631 cm^{-1}; HRMS (FAB$^+$) found: 341.0573, calcd for $C_{16}H_{22}BrOS$ (M+H$^+$): 341.0575.

4.2.19. 5-Bromo-1-phenylhex-5-en-3-ol (**28**) (Scheme 11)

To a stirred suspension of tin powder (1.59 g, 13.4 mmol) and 2,3-dibromopropene (**27**) (5.34 g, 26.7 mmol) in Et_2O/H_2O (1:1, 36 mL) were added a few drops of an aqueous HBr solution and hydrocinnamaldehyde (1.20 g, 8.9 mmol), and the reaction mixture was stirred at room temperature for 8 h. The organic materials were extracted three times with Et_2O. The combined extracts were washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel, hexane/EtOAc=8:1) to give 5-bromo-1-phenylhex-5-en-3-ol (**28**) (2.06 g, 8.1 mmol) in 91% yield.

Colorless oil; R_f=0.33 (silica gel, hexane/EtOAc=5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.31 (2H, m), 7.17–7.21 (3H, m), 5.70 (1H, ddd, J=0.8, 0.8, 1.6 Hz), 5.54 (1H, d, J=1.6 Hz), 3.95–4.01 (1H, m), 2.84 (1H, ddd, J=7.6, 7.8, 13.6 Hz), 2.71 (1H, ddd, J=7.6, 8.6, 13.6 Hz), 2.52–2.67 (2H, m), 1.97 (1H of –OH, br s), 1.79–1.85 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.8, 130.5, 128.5, 128.4, 125.9, 119.8, 68.6, 49.4, 38.0, 32.0; IR (NaCl): 3392, 3061, 3024, 2939, 2858, 1629, 1602, 1494, 1452, 1078, 1053, 891, 746, 700 cm^{-1}; HRMS (ESI) found: 277.0229, calcd for $C_{12}H_{15}OBrNa$ (M+Na$^+$): 277.0204.

4.2.20. 4-Bromo-1-phenylpent-4-en-2-ol (**29**) (Scheme 11)

This compound was synthesized from 2,3-dibromopropene (**27**) and 2-phenylacetaldehyde according to the same procedure as for **28**.

Colorless oil; Yield 33%; R_f=0.27 (silica gel, hexane/EtOAc=8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.37 (2H, m), 7.26–7.29 (3H, m), 5.74 (1H, d, J=1.1 Hz), 5.57 (1H, d, J=1.1 Hz), 4.19–4.22 (1H, m), 2.88 (1H, dd, J=4.6, 13.6 Hz), 2.76 (1H, dd, J=8.4, 13.6 Hz), 2.61 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9, 130.5, 129.4, 128.6, 126.6, 119.7, 70.0, 48.6, 42.8; IR (NaCl): 3398, 3062, 3026, 2937, 2857, 1629, 1602, 1494, 1454, 1078, 1043, 891, 746, 700 cm^{-1}; HRMS (ESI) found: 263.0050, calcd for $C_{11}H_{13}ONaBr$ (M+Na$^+$): 263.0047.

4.2.21. 3-Bromo-1-cyclohexylbut-3-en-1-ol (**30**)[35]

This compound was synthesized from 2,3-dibromopropene (**27**) and cyclohexanecarbaldehyde according to the same procedure as for **28**.

Colorless oil; yield 92%; R_f=0.40 (silica gel, hexane/EtOAc=8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.69 (1H, s), 5.53 (1H, s), 3.68–3.72 (1H, m), 2.60 (1H, dd, J=2.4, 14.4 Hz), 2.48 (1H, dd, J=9.6, 14.4 Hz), 1.66–1.84 (6H, m), 1.36–1.44 (1H, m), 1.10–1.25 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.5, 119.5, 72.9, 46.4, 42.9, 29.1, 27.9, 26.4, 26.2, 26.1.

*4.2.22. Ethyl 8-bromo-6-hydroxynon-8-enoate (**31**) (Scheme 11)*

This compound was synthesized from 2,3-dibromopropene (**27**) and ethyl 6-oxohexanoate according to the same procedure as for **28**.

Colorless oil; yield 50%; R_f=0.30 (silica gel, hexane/EtOAc=2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.69 (1H, d, J=1.2 Hz), 5.54 (1H, d, J=1.2 Hz), 4.13 (2H, q, J=7.2 Hz), 3.94–3.96 (1H, m), 2.48–2.58 (2H, m), 2.30–2.34 (2H, m), 1.81 (1H of –OH, br s), 1.64–1.71 (2H, m), 1.43–1.56 (3H, m), 1.38–1.43 (1H, m), 1.26 (3H, t, J=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 130.5, 119.5, 68.7, 60.3, 49.4, 35.9, 34.2, 25.1, 24.8, 14.3; IR (ZnSe) 3446, 2979, 2937, 2912, 2866, 1732, 1631, 1373, 1184, 1155, 1093, 1029, 887, 862 cm^{-1}; HRMS (FAB$^+$) found: 279.0584, calcd for $C_{14}H_{20}BrO$ (M+H$^+$): 279.0518.

*4.2.23. 3-Bromo-1-(4-methoxyphenyl)but-3-en-1-ol (**32**) (Scheme 11)*

This compound was synthesized from 2,3-dibromopropene (**27**) and 4-methoxybenzaldehyde according to the same procedure as for **28**.

Colorless oil; yield 50%; R_f=0.23 (silica gel, hexane/EtOAc=4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (2H, ddd, J=2.0, 2.4, 8.8 Hz), 6.89 (2H, ddd, J=2.0, 2.4, 8.8 Hz), 5.66 (1H, d, J=1.6 Hz), 5.52 (1H, d, J=1.6 Hz), 4.97–5.01 (1H, m), 3.81 (3H, s), 2.85 (1H, dd, J=8.8, 14.4 Hz), 2.73 (1H, dd, J=3.6, 14.4 Hz), 2.02 (1H of –OH, br s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1, 134.9, 130.1, 127.1, 119.8, 113.8, 71.2, 55.2, 51.1; IR (ZnSe) 3397, 2908, 2835, 1610, 1510, 1464, 1302, 1244, 1174, 1105, 1032, 891, 829 cm^{-1} found: C, 51.20; H, 5.16%, calcd for $C_{14}H_{18}S$: C, 51.38; H, 5.10%.

*4.2.24. 2,7-Dibromoocta-1,7-dien-4-ol (**33**)[36] (Scheme 11)*

This compound was synthesized from 2,3-dibromopropene (**27**) and 4-bromopent-4-enal according to the same procedure as for **28**.

Colorless oil; Yield 78%; R_f=0.41 (silica gel, hexane/EtOAc=8:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.71 (1H, d, J=1.4 Hz), 5.63 (1H, d, J=1.4 Hz), 5.56 (1H, d, J=1.6 Hz), 5.43 (1H, d, J=1.6 Hz), 3.96–3.98 (1H, m), 2.53–2.66 (4H, m), 1.67–1.84 (3H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.0, 130.2, 119.9, 117.0, 67.9, 49.5, 37.7, 34.6.

*4.2.25. S-5-Bromo-1-phenylhex-5-en-3-yl ethanethioate (**34**) (Scheme 11)*

This compound was synthesized from 5-bromo-1-phenylhex-5-en-3-ol (**28**) according to the same procedure as for **3**.

Pale yellow oil; yield 64% (2 steps); R_f=0.69 (silica gel, hexane/EtOAc=5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26–7.30 (2H, m), 7.16–7.20 (3H, m), 5.61 (1H, d, J=1.7 Hz), 5.49 (1H, d, J=1.7 Hz), 3.83–3.88 (1H, m), 2.69–2.80 (3H, m), 2.63–2.69 (1H, m), 2.35 (3H, s), 1.98–2.05 (1H, m), 1.81–1.91 (1H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.0, 141.3, 130.5, 128.4, 128.3, 126.0, 119.3, 46.2, 42.3, 35.3, 33.0, 30.8; IR (ZnSe) 3026, 2937, 2923, 2858, 1689, 1627, 1602, 1496, 1454, 1425, 1354, 1111, 953, 893, 748, 700, 631 cm^{-1}; found: C, 53.74; H, 5.41%, calcd for $C_{14}H_{18}S$: C, 53.68; H, 5.47%.

*4.2.26. S-4-Bromo-1-phenylpent-4-en-2-yl ethanethioate (**35**) (Scheme 11)*

This compound was synthesized from 4-bromo-1-phenylpent-4-en-2-ol (**29**) according to the same procedure as for **3**.

Pale yellow oil; yield 50% (2 steps); R_f=0.62 (silica gel, hexane/EtOAc=8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.32 (2H, m), 7.23–7.26 (3H, m), 5.64 (1H, s), 5.52 (1H, s), 4.01–4.08 (1H, m), 2.98 (1H, dd, J=7.2, 14.0 Hz), 2.91 (1H, dd, J=7.6, 14.0 Hz), 2.7 (2H, m), 2.28 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.9, 138.1, 130.6, 129.3, 128.3, 126.6, 119.4, 45.0, 43.8, 40.0, 30.7; IR (NaCl): 3064, 3030, 2960, 2923, 2857, 1690, 1631, 1598, 1496, 1454, 1425, 1361, 1188, 1174, 1095, 937, 893, 767, 700, 665 cm^{-1}; HRMS (EI) found: 297.9922, calcd for $C_{13}H_{15}OSBr$ (M$^+$): 298.0022.

*4.2.27. S-3-Bromo-1-cyclohexylbut-3-enyl ethanethioate (**36**) (Scheme 11)*

This compound was synthesized from 3-bromo-1-cyclohexylbut-3-en-1-ol (**30**) according to the same procedure as for **3**.

Pale yellow oil; yield 45% (2 steps); R_f=0.67 (silica gel, hexane/EtOAc=5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.62 (1H, d, J=1.6 Hz), 5.49 (1H, d, J=1.6 Hz), 3.84–3.88 (1H, m), 2.75 (1H, dd, J=6.2, 14.8 Hz), 2.62 (1H, dd, J=8.8, 14.8 Hz), 2.34 (3H, s), 1.64–1.77 (6H, m), 0.95–1.26 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.0, 131.2, 118.8, 47.9, 43.9, 40.9, 30.7, 30.5, 28.7, 26.26, 26.25, 26.21; IR (NaCl): 2926, 2850, 1693, 1627, 1448, 1425, 1352, 1195, 1128, 1078, 950, 736, 632 cm^{-1}; HRMS (ESI) found: 291.0421, calcd for $C_{12}H_{20}OSBr$ (M+H$^+$): 291.0418.

*4.2.28. Ethyl 6-(acetylthio)-8-bromonon-8-enoate (**37**) (Scheme 11)*

This compound was synthesized from ethyl 8-bromo-6-hydroxynon-8-enoate (**31**) according to the same procedure of synthesis **3**.

Pale yellow oil; yield 48% (2 steps); R_f=0.48 (silica gel, hexane/acetone=5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.62 (1H, d, J=1.6 Hz), 5.49 (1H, d, J=1.6 Hz), 4.13 (2H, q, J=7.0 Hz), 3.80 (1H, ddd, J=4.8, 7.6, 14.8 Hz), 2.69 (1H, ddd, J=7.6, 14.8, 24.4 Hz), 2.32 (3H, s), 2.30 (1H, dd, J=7.6, 7.6 Hz), 1.55–1.73 (5H, m), 1.38–1.51 (3H, m), 1.48 (3H, t, J=7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.0, 173.4, 130.6, 119.2, 60.3, 46.3, 42.4, 34.2, 33.2, 30.8, 26.2, 24.7, 14.3; IR (ZnSe) 2981, 2937, 2912, 2862, 1732, 1693, 1628, 1250, 1182, 1115, 1032, 953, 893, 633 cm^{-1}. Found: C, 46.33; H, 6.27%. Calcd for $C_{14}H_{18}S$: C, 46.29; H, 6.28%.

*4.2.29. S-3-Bromo-1-(4-methoxyphenyl)but-3-enyl ethanethioate (**38**) (Scheme 11)*

To a stirred solution of triphenyl phosphine (1.98 g, 7.5 mmol) in THF (19 mL) was added diethyl azodicarboxylate (ca. 2.2 mol L^{-1} in toluene, 3.4 mL, 40.4 mmol) at 0 °C and the reaction mixture was stirred at 0 °C for 10 min. A solution of ethyl 8-bromo-6-hydroxynon-8-enoate (**32**) (970 mg, 3.8 mmol) and thioacetic acid (540 μL, 7.6 mmol) in 10 mL of THF was added dropwise over 10 min at 0 °C, and the reaction mixture was stirred for 12 h at room temperature. The solution was concentrated, and the residue was purified by flash column chromatography (silica gel, hexane/methylene chloride=2:1). Further purification was conducted by gel permeation chromatography (GPC, $CHCl_3$) to give *S*-3-bromo-1-(4-methoxyphenyl)but-3-enyl ethanethioate (**38**) (119 mg, 0.38 mmol) in 10% yield.

Colorless oil; yield 10%; R_f=0.46 (silica gel, hexane/EtOAc=4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (2H, d, J=8.6 Hz), 6.83 (2H, d, J=8.6 Hz), 5.46 (1H, d, J=1.6 Hz), 5.38 (1H, d, J=1.6 Hz), 4.90 (1H, dd, J=6.8, 8.8 Hz), 3.78 (3H, s), 2.93–3.05 (2H, m), 2.30 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.1, 158.8, 132.0, 129.9, 128.8, 119.5, 113.9, 55.2, 47.4, 45.7, 30.5; IR (ZnSe) 2956, 2835, 1689, 1610, 1512, 1458, 1423, 1354, 1304, 1252, 1178, 1130, 1107, 1036, 947, 895, 837, 785, 631 cm^{-1}; Anal. calcd for $C_{14}H_{18}S$: C, 49.53%; H, 4.80%, found: C,49.76%; H, 4.92%.

*4.2.30. S-2,7-Dibromoocta-1,7-dien-4-yl ethanethioate (**39**) (Scheme 11)*

This compound was synthesized from ethyl 2,7-dibromoocta-1,7-dien-4-ol (**33**) according to the same procedure as for **3**.

Yellow oil; yield 52% (2 steps); R_f=0.68 (silica gel, hexane/EtOAc=8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.65 (1H, s), 5.60 (1H, s), 5.52 (1H, d, J=1.5 Hz), 5.42 (1H, d, J=1.5 Hz), 3.77–3.84 (1H, m), 2.66–2.79 (2H, m), 2.50–2.56 (2H, m), 2.33 (3H, s), 1.97–2.05 (1H, m), 1.74–1.83 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.8, 133.1, 130.3, 119.6, 117.4, 46.4, 41.6, 38.7, 32.0, 30.8; IR (NaCl): 2916, 1695, 1628, 1425, 1352, 1184, 1111, 951, 889, 625 cm^{-1}; HRMS (ESI) found: 362.9066, calcd for $C_{10}H_{14}ONaSBr_2$ (M+Na$^+$): 362.9030.

4.2.31. (3S,4R*)-5-Bromo-4-phenethyl-1-phenylhex-5-en-3-ol (**41**)[22] (Scheme 12)*

To a stirred solution of bromoallylsilane **40**[22] (677 mg, 2.3 mmol) and 3-phenylpropionaldehyde (360 μL, 2.7 mmol) in CH_2Cl_2 (23 mL) was added $TiCl_4$ (1 M in CH_2Cl_2) (2.5 mL, 2.5 mmol) at −78 °C, and the reaction mixture was stirred for 5 min. The reaction was quenched with saturated $NaHCO_3$ solution, and the organic materials were extracted three times with EtOAc. The combined extracts were washed with brine and dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel, hexane/EtOAc=8:1) to give the *syn*-diastereomer **41** as well as the *anti*-diastereomer in 5:1 ratio (624 mg, 1.7 mmol) in 76% yield.

Colorless oil; R_f=0.38 (silica gel, hexane/EtOAc=8:1); data for the major isomer (*syn*): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27–7.32 (4H, m), 7.20–7.22 (6H, m), 5.70 (1H, d, *J*=1.5 Hz), 5.61 (1H, d, *J*=1.5 Hz), 3.60–3.68 (1H, m), 2.80–2.90 (1H, m), 2.60–2.78 (2H, m), 2.39–2.50 (1H, m), 2.21–2.28 (1H, m), 2.04–2.13 (1H, m), 1.87–1.97 (1H, m), 1.78–1.85 (1H, m), 1.64–1.74 (1H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.87, 141.85, 135.6, 128.49, 128.48, 128.45 (overlapped), 128.40, 125.9, 119.7, 72.8, 55.4, 36.6, 33.1, 32.0, 30.5; IR (NaCl): 3404, 3084, 3026, 2949, 2922, 2860, 1666, 1622, 1602, 1496, 1454, 1253, 1130, 1080, 1049, 908, 748, 698 cm^{-1}; HRMS (EI) found: 358.0804, calcd for $C_{20}H_{23}OBr$ (M^+): 358.0927.

4.2.32. S-(3R,4R*)-5-Bromo-4-phenethyl-1-phenylhex-5-en-3-yl ethanethioate (**42**) (Scheme 12)*

This compound was synthesized from ethyl (3*S**,4*R**)-5-bromo-4-phenethyl-1-phenylhex-5-en-3-ol (**41**) according to the same procedure as for **3**.

Pale yellow oil; yield 44% (2 steps); R_f=0.51 (silica gel, hexanes/EtOAc=8:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26–7.32 (4H, m), 7.13–7.23 (6H, m), 5.71 (1H, d, *J*=1.5 Hz), 5.65 (1H, d, *J*=1.5 Hz), 3.75–3.82 (1H, m), 2.60–2.75 (4H, m), 2.44–2.52 (1H, m), 2.37 (3H, s), 1.74–2.09 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.4, 141.5, 141.4, 135.1, 128.49, 128.45, 128.42 (overlapped), 126.03, 126.00, 120.4, 51.8, 47.0, 34.7, 33.2, 33.1, 32.7, 30.8; IR (NaCl): 3061, 3026, 2927, 2858, 1693, 1681, 1622, 1602, 1494, 1454, 1352, 1130, 1111, 1029, 952, 898, 748, 700, 626 cm^{-1}; HRMS (ESI) found: 417.0882, calcd for $C_{22}H_{26}OSBr$ ($M+H^+$): 417.0888.

*4.2.33. 1-Phenylpentadeca-4,5-dien-3-one (**45**) (Scheme 13)*

To a stirred solution of phosphorous ylide **44** (10.2 g, 25.0 mmol) in CH_2Cl_2 (50 mL) was added Et_3N (3.5 mL, 25.0 mmol) at 0 °C. After stirring for 5 min at 0 °C, a solution of undecanoyl chloride (**43**) (6.66 g, 32.5 mmol) in CH_2Cl_2 (15 mL) was added dropwise at 0 °C, and the reaction solution was stirred at room temperature overnight. After evaporation of the solvent, the residue was treated with 80 mL of Et_2O and then filtered. This process was repeated five times until no further triphenylphosphine oixde precipitated. After concentration, the crude product was purified by flash column chromatography (silica gel, hexane/EtOAc=15:1) to afford 1-phenylpentadeca-4,5-dien-3-one (**45**) (2.46 g, 8.3 mmol) in 33% yield.

Colorless oil; R_f=0.56 (silica gel, hexane/EtOAc=12:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.30 (2H, m), 7.17–7.21 (3H, m), 5.73–5.76 (1H, m), 5.56–5.61 (1H, m), 2.90–2.92 (4H, m), 2.10–2.16 (2H, m), 1.21–1.46 (14H, m), 0.88 (3H, t, *J*=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.9, 200.6, 141.2, 128.5, 128.4, 126.1, 97.4, 95.7, 40.6, 31.9, 30.6, 29.5, 29.4, 29.3, 29.2, 28.9, 27.8, 22.7, 14.1; IR (NaCl): 2924, 2853, 1946, 1871, 1724, 1680, 1454, 1155, 746, 698 cm^{-1}; HRMS (ESI) found: 321.2080, calcd for $C_{21}H_{30}ONa$ ($M+Na^+$): 321.2189.

*4.2.34. (Z)-5-Bromo-1-phenylpentadec-5-en-3-ol (**46**) and (E)-5-bromo-1-phenylpentadec-5-en-3-ol (**47**) (Scheme 13)*

To a stirred solution of 1-phenylpentadeca-4,5-dien-3-one (**45**) (2.93 g, 9.8 mmol) in glacial acetic acid (23 mL) was added LiBr (1.02 g, 11.8 mmol) under N_2, and the reaction mixture was stirred at refluxed for 6.5 h. The reaction mixture was quenched with H_2O and then extracted five times with Et_2O. The combined organic layer was washed subsequently with saturated NH_4Cl solution, dried over $MgSO_4$, and concentrated in vacuo. The crude product was treated with $NaBH_4$ (371 mg, 9.8 mmol) in MeOH (30 mL) at 0 °C, and the reaction mixture was stirred at 0 °C for 5 min. The reaction was quenched with water at 0 °C, and the organic materials were extracted three times with CH_2Cl_2. The combined extracts were washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. The resulting residue was purified by flash column chromatography (silica gel, hexane/EtOAc=15:1) to afford (*Z*)-5-bromo-1-phenylpentadec-5-en-3-ol (**46**) (792 mg, 2.1 mmol) in 21% yield and (*E*)-5-bromo-1-phenylpentadec-5-en-3-ol (**47**) (299 mg, 0.79 mmol) in 8% yield, respectively.

*4.2.34.1. (Z)-5-Bromo-1-phenylpentadec-5-en-3-ol (**46**).* Pale yellow oil; R_f=0.53 (silica gel, hexane/EtOAc=10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18–7.30 (5H, m), 5.77 (1H, dd, *J*=6.8, 6.8 Hz), 3.94–4.00 (1H, m), 2.51–2.85 (4H, m), 2.15–2.19 (2H, m), 1.78–1.82 (2H, m), 1.71 (1H of –OH, d, *J*=2.8 Hz), 1.26–1.41 (14H, m), 0.88 (3H, t, *J*=6.9 Hz); ^{13}C NMR (100Mz, $CDCl_3$) δ 141.9, 132.5, 128.4 (overlapped), 125.8, 123.6, 68.5, 49.6, 37.9, 32.0, 31.9, 31.4, 29.5, 29.4, 29.3, 29.2, 28.4, 22.7, 14.1; IR (NaCl): 3377, 3026, 2924, 2853, 1657, 1603, 1495, 1454, 1435, 1076, 1049, 1030, 746, 698 cm^{-1}; HRMS (ESI) found: 403.1617, calcd for $C_{21}H_{33}OBrNa$ ($M+Na^+$): 403.1612.

*4.2.34.2. (E)-5-Bromo-1-phenylpentadec-5-en-3-ol (**47**).* Pale yellow oil; R_f=0.61 (silica gel, hexane/EtOAc=10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18–7.31 (5H, m), 6.04 (1H, dd, *J*=6.7, 6.7 Hz), 3.97–4.02 (1H, m), 2.68–2.88 (3H, m), 2.46–2.49 (1H, m), 2.04–2.10 (2H, m), 1.78–1.85 (2H, m), 1.26–1.37 (14H, m), 0.88 (3H, t, *J*=6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.9, 136.1, 128.5 (overlapped), 125.9, 121.0, 69.2, 43.6, 38.0, 32.2, 31.9, 30.0, 29.5, 29.4, 29.3, 29.24, 29.16, 22.7, 14.1; IR (NaCl): 3410, 3026, 2924, 2853, 1715, 1495, 1454, 1435, 1078, 1053, 1030, 746, 698 cm^{-1}; HRMS (ESI) found: 403.1639, calcd for $C_{21}H_{33}OBrNa$ ($M+Na^+$): 403.1612.

*4.2.35. (Z)-S-5-Bromo-1-phenylpentadec-5-en-3-yl ethanethioate (**48**) (Scheme 13)*

This compound was synthesized from (*Z*)-5-bromo-1-phenylpentadec-5-en-3-ol (**46**) according to the same procedure as for **3**.

Pale yellow oil; yield 55% (2 steps); R_f=0.64 (silica gel, hexane/EtOAc=10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15–7.29 (5H, m), 5.68 (1H, dd, *J*=6.9, 6.9 Hz), 3.85–3.92 (1H, m), 2.61–2.80 (4H, m), 2.34 (3H, s), 1.82–2.17 (4H, m), 1.26–1.37 (14H, m), 0.88 (3H, t, *J*=6.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.1, 141.5, 132.0, 128.4, 128.3, 125.9, 124.0, 46.4, 42.8, 35.3, 33.0, 31.9, 31.3, 30.8, 29.53, 29.45, 29.3, 29.2, 28.3, 22.7, 14.1; IR (NaCl): 2924, 2853, 1694, 1497, 1454, 1352, 1115, 951, 910, 748, 735, 698 cm^{-1}; HRMS (ESI) found: 461.1609, calcd for $C_{23}H_{35}OSBrNa$ ($M+Na^+$): 461.1484.

*4.2.36. (E)-S-5-Bromo-1-phenylpentadec-5-en-3-yl ethanethioate (**49**) (Scheme 13)*

This compound was synthesized from (*E*)-5-bromo-1-phenylpentadec-5-en-3-ol (**47**) according to the same procedure as for **3**.

Pale yellow oil; yield 49% (2 steps); R_f=0.68 (silica gel, hexanes/EtOAc=10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17–7.30 (5H, m), 5.96 (1H, dd, *J*=7.6, 7.6 Hz), 3.87–3.90 (1H, m), 2.63–2.77 (4H, m), 2.35 (3H, s), 1.82–2.09 (4H, m), 1.26–1.36 (14H, m), 0.89 (3H, t, *J*=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.1, 141.4, 135.5, 128.4, 128.3, 126.0, 121.3, 43.2, 40.4, 35.3, 33.2, 31.9, 30.8, 30.0, 29.5, 29.4, 29.3, 29.2, 29.1, 22.7, 14.1; IR (NaCl): 2924, 2853, 1694, 1497, 1454, 1130, 1113, 951, 910, 748, 698 cm^{-1}; HRMS (ESI) found: 461.1606, calcd for $C_{23}H_{35}OSBrNa$ ($M+Na^+$): 461.1484.

4.3. Intramolecular vinylic substitution reactions

4.3.1. 4-Methyl-2-phenethyl-2,3-dihydrothiophene (**51**) (Scheme 14)

To a stirred solution of *S*-6-bromo-5-methyl-1-phenylhex-5-en-3-yl ethanethioate (**3**) (48 mg, 0.15 mmol) in degassed DMI (7 mL) was added NaOMe (16 mg, 0.29 mmol), and the reaction mixture was stirred at room temperature for 2 h. The reaction was quenched with pH 9 phosphate buffer solution and Et_2O was added. The layers were separated and the aqueous layer was extracted three times with Et_2O. The combined organic layer was washed three times with water, then with brine, and dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by PTLC using hexane/EtOAc=30:1 as an eluent to give 4-methyl-2-phenethyl-2,3-dihydrothiophene (**51**) (18 mg, 0.09 mmol) in 61% yield.

Colorless oil; R_f=0.76 (silica gel, hexane/EtOAc=8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18–7.31 (5H, m), 5.65 (1H, s), 3.73–3.77 (1H, m), 2.63–2.82 (3H, m), 2.37 (1H, dd, J=6.3, 16.0 Hz), 1.92–2.05 (2H, m), 1.76 (3H, d, J=0.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6, 131.7, 128.5, 128.4, 125.9, 117.0, 49.4, 46.0, 38.9, 34.2, 17.1; IR (NaCl): 3061, 3024, 2957, 2924, 2909, 2851, 2828, 1603, 1495, 1454, 1445, 1435, 1234, 1030, 802, 748, 698 cm^{-1}; HRMS (EI) found: 204.0969, calcd for $C_{13}H_{16}S$ (M^+): 204.0967.

4.3.2. 2-Phenethyl-2,3-dihydrothiophene (**52**) (Scheme 15)

To a stirred solution of (*E*)-*S*-6-bromo-1-phenylhex-5-en-3-yl ethanethioate (**6**) (53 mg, 0.17 mmol) and degassed MeOH (70 μL, 1.7 mmol) in degassed DMI (8 mL) were added K_2CO_3 (35 mg, 0.25 mmol), and the reaction mixture was stirred at 120 °C for 5 h. The reaction was quenched with pH 9 phosphate buffer solution at 0 °C, and the organic materials were extracted three times with Et_2O. The combined extracts were washed with H_2O and brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by PTLC using hexane/EtOAc=50:1 as an eluent to give 2-phenethyl-2,3-dihydrothiophene (**52**) (27 mg, 0.14 mmol) in 83% yield.

Colorless oil; R_f=0.61 (silica gel, hexane/EtOAc=10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.31 (2H, m), 7.18–7.21 (3H, m), 6.12–6.14 (1H, m), 5.53–5.56 (1H, m), 3.71–3.79 (1H, m), 2.83–2.91 (1H, m), 2.63–2.79 (2H, m), 2.47–2.53 (1H, m), 1.92–2.06 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.5, 128.5, 128.4, 125.9, 125.0, 121.4, 49.4, 41.4, 38.6, 34.3; IR (NaCl): 3061, 3024, 2928, 2833, 1734, 1601, 1497, 1452, 1244, 1043, 1030, 910, 789, 748 cm^{-1}; HRMS (EI) found: 190.0805, calcd for $C_{12}H_{14}S$ (M^+): 190.0811.

The compound 2-phenethyl-2,3-dihydrothiophene (**52**) was also synthesized from (*Z*)-*S*-6-bromo-1-phenylhex-5-en-3-yl ethanethioate (**9**) according to the above procedure.

4.3.3. 5-Methyl-2-phenethyl-3,4-dihydro-2H-thiopyran (**55**) (Scheme 16)

This compound was synthesized from *S*-7-bromo-6-methyl-1-phenylhept-6-en-3-yl ethanethioate (**13**) according to the same procedure as for **52**.

Pale yellow oil; yield 18%; R_f=0.61 (silica gel, hexane/EtOAc=10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27–7.30 (2H, m), 7.18–7.21 (3H, m), 5.69 (1H, s), 2.95–3.00 (1H, m), 2.77–2.83 (1H, m), 2.68–2.74 (1H, m), 2.03–2.10 (3H, m), 1.88–1.93 (2H, m), 1.76–1.82 (1H, m), 1.72 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.7, 128.5, 128.4 (overlapped), 125.9, 111.4, 38.6, 37.2, 33.1, 30.0, 28.4, 25.0; IR (NaCl): 3061, 3024, 2959, 2922, 2849, 2833, 1634, 1603, 1495, 1445, 1265, 1030, 831, 797, 739, 698 cm^{-1}; HRMS (EI) found: 218.1123, calcd for $C_{14}H_{18}S$ (M^+): 218.1124.

4.3.4. 2-Methylene-5-phenethyltetrahydrothiophene (**56**) and 5-methyl-2-phenethyl-2,3-dihydrothiophene (**57**) (Table 1, entry 1)

These compounds were synthesized in a mixture (**56**:**57**=3:1) from *S*-6-bromo-1-phenylhept-6-en-3-yl ethanethioate (**18**) according to the same procedure of synthesis **52**. 2-Methylene-5-phenethyltetrahydrothiophene (**56**) gradually tautomerized to give 5-methyl-2-phenethyl-2,3-dihydrothiophene (**57**) at room temperature.

*4.3.4.1. Compound **56**.* Colorless oil; mixture (**56**/**57**=3:1); R_f=0.28 (silica gel, pure hexane); data for the major isomer **56**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.30 (2H, m), 7.18–7.21 (3H, m), 4.96–4.97 (1H, m), 4.89–4.90 (1H, m), 3.55–3.62 (1H, m), 2.59–2.76 (4H, m), 2.14–2.21 (1H, m), 1.88–2.07 (2H, m), 1.68–1.77 (1H, m).

*4.3.4.2. Compound **57**.* Colorless oil; yield: 85%; R_f=0.28 (silica gel, pure hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27–7.30 (2H, m), 7.18–7.19 (3H, m), 5.17–5.18 (1H, m), 3.74–3.79 (1H, m), 2.83–2.87 (1H, m), 2.71–2.76 (1H, m), 2.62–2.68 (1H, m), 2.44–2.49 (1H, m), 1.96–2.06 (2H, m), 1.94 (3H, d, J=1.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.6, 136.7, 128.5, 128.4, 125.9, 116.9, 50.6, 42.0, 38.9, 34.3, 16.7; IR (NaCl): 3063, 3021, 2928, 2857, 1713, 1497, 1454, 1358, 1217, 1094, 1030, 756, 700 cm^{-1}; HRMS (EI) found: 204.0971, calcd for $C_{13}H_{16}S$ (M^+): 204.0967.

4.3.5. 2-Phenethyl-5-(propan-2-ylidene)tetrahydrothiophene (**58**) and 5-isopropyl-2-phenethyl-2,3-dihydrothiophene (**59**) (Table 1, entry 2)

These separated compounds **58** and **59** were synthesized from *S*-6-bromo-7-methyl-1-phenyloct-6-en-3-yl ethanethioate (**23**) according to the same procedure as for **52**.

*4.3.5.1. Compound **58**.* Colorless oil; yield 59%; R_f=0.45 (silica gel, hexane/EtOAc=10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17–7.30 (5H, m), 3.44–3.51 (1H, m), 2.63–2.76 (3H, m), 2.41–2.48 (1H, m), 2.15–2.22 (1H, m), 1.85–2.04 (2H, m), 1.73 (3H, s), 1.71 (3H, s), 1.68–1.77 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6, 132.9, 128.5, 128.4, 125.9, 118.3, 50.0, 38.1, 36.8, 35.1, 32.8, 23.4, 21.4; IR (NaCl): 3061, 3024, 2922, 2851, 1655, 1603, 1495, 1452, 1369, 1236, 1032, 748, 698 cm^{-1}; HRMS (ESI) found: 233.1357, calcd for $C_{15}H_{21}S$ ($M+H^+$): 233.1364.

*4.3.5.2. Compound **59**.* Colorless oil; yield 10%; R_f=0.59 (silica gel, hexane/EtOAc=10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17–7.30 (5H, m), 5.19–5.21 (1H, m), 3.67–3.74 (1H, m), 2.82–2.88 (1H, m), 2.62–2.77 (2H, m), 2.43–2.56 (2H, m), 1.91–2.03 (2H, m), 1.13 (6H, d, J=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.3, 141.7, 128.5, 128.4, 125.9, 113.2, 49.4, 41.6, 38.7, 34.3, 30.6, 22.3; IR (NaCl): 3024, 2963, 2930, 2855, 1707, 1497, 1452, 1215, 1030, 756 cm^{-1}; HRMS (EI) found: 232.1273, calcd for $C_{15}H_{20}S$ (M^+): 232.1280.

4.3.6. 2-Methylene-6-phenethyltetrahydro-2H-thiopyran (**60**), 6-methyl-2-phenethyl-3,4-dihydro-2H-thiopyran (**61**) and S-1-phenyloct-7-yn-3-yl ethanethioate (**62**) (Table 1, entry 3)

These compounds were synthesized in a mixture (**60**/**61**=2.5:1) and **62** from *S*-7-bromo-1-phenyloct-7-en-3-yl ethanethioate (**19**) according to the same procedure of synthesis **52**. 2-Methylene-6-phenethyltetrahydro-2*H*-thiopyran (**60**) gradually tautomerized to give 6-methyl-2-phenethyl-3,4-dihydro-2*H*-thiopyran (**61**) at room temperature.

*4.3.6.1. Compound **60**.* Pale yellow oil; mixture (**60**/**61**=2.5:1); R_f=0.60 (silica gel, pure hexane); data for the major isomer **60**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17–7.29 (5H, m), 5.14–5.15 (1H, m), 5.05–5.06 (1H, m), 2.69–2.85 (2H, m), 2.13–2.55 (3H, m), 1.91–2.05 (1H, m), 1.89–2.05 (4H, m), 1.62–1.72 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.7, 128.5, 128.4, 127.8, 125.9, 116.3, 40.4, 37.5, 32.9, 28.7, 23.9, 23.6; IR (NaCl): 3061, 3024, 3011, 2928, 2914, 2841, 1713, 1495, 1452, 1447, 1435, 1217, 1115, 754, 698 cm^{-1}; HRMS (EI) found: 218.1125, calcd for $C_{14}H_{18}S$ (M^+): 218.1124.

*4.3.6.2. Compound **61**.* Pale yellow oil; yield 31%; R_f=0.60 (silica gel, pure hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17–7.29 (5H, m), 5.47–5.50 (1H, m), 3.04–3.10 (1H, m), 2.69–2.85 (2H, m), 2.13–2.24 (2H, m), 1.89–2.05 (3H, m), 1.87 (3H, d, J=1.3 Hz), 1.62–1.71 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.7, 128.5, 128.4, 127.8, 125.9, 116.3, 40.4, 37.5, 32.9, 28.7, 23.9, 23.6; IR (NaCl): 3061, 3024, 3011, 2928, 2914, 2841, 1713, 1495, 1452, 1447, 1435, 1217, 1115, 754, 698 cm^{-1}; HRMS (EI) found: 218.1125, calcd for $C_{14}H_{18}S$ (M^+): 218.1124.

*4.3.6.3. Compound **62**.* Colorless oil; yield 19%; R_f=0.55 (silica gel, hexane/EtOAc=10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.36 (2H, m), 7.08–7.21 (3H, m), 3.56–3.60 (1H, m), 2.71–2.78 (1H, m), 2.61–2.68 (1H, m), 2.35 (3H, s), 2.18–2.22 (2H, m), 1.77–1.99 (4H, m), 1.52–1.73 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.7, 141.6, 128.42, 128.38, 126.0, 84.0, 68.7, 43.9, 36.9, 34.0, 33.2, 30.8, 25.6, 18.2; IR (NaCl): 3294, 3026, 2940, 2859, 1688, 1497, 1454, 1354, 1113, 953, 748, 700 cm^{-1}; HRMS (EI) found: 260.1238, calcd for $C_{16}H_{20}OS$ (M^+): 260.1229.

*4.3.7. 2-(3-Bromobut-3-enyl)-4-methylenethietane (**63**) (Scheme 17)*

This compound was synthesized from *S*-2,7-dibromoocta-1,7-dien-4-yl ethanethioate (**39**) according to the same procedure as for **52**.

Colorless oil; yield 87%; R_f=0.65 (silica gel, hexane/EtOAc=20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.57 (1H, d, J=1.4 Hz), 5.41 (1H, d, J=1.4 Hz), 4.96 (1H, d, J=1.9 Hz), 4.72 (1H, d, J=1.9 Hz), 3.61–3.68 (2H, m), 3.15–3.18 (1H, m), 2.37–2.47 (2H, m), 2.12–2.19 (1H, m), 2.00–2.07 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.5, 132.9, 117.4, 103.8, 43.5, 39.1, 37.1, 36.6; IR (NaCl): 2918, 2853, 1715, 1628, 1443, 1428, 1360, 1215, 1115, 889, 758, 665 cm^{-1}; HRMS (EI) found: 217.9811, calcd for $C_8H_{11}BrS$ (M^+): 217.9759.

*4.3.8. 2-Isopropylene-4-phenethylthietane (**64**) (Table 2, entry 1)*

This compound was synthesized from *S*-5-bromo-6-methyl-1-phenylhept-5-en-3-yl ethanethioate (**26**) according to the same procedure as for **52**.

Colorless oil; yield 94%; R_f=0.37 (silica gel, hexane/acetone=19:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19–7.22 (2H, m), 7.08–7.13 (3H, m), 3.39–3.49 (2H, m), 2.92–2.95 (1H, m), 2.63–2.57 (1H, m), 2.46–2.52 (1H, m), 1.97–2.11 (2H, m), 1.45 (3H, s), 1.39 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.1, 128.48, 128.43, 125.9, 120.9, 120.0, 40.8, 40.7, 36.5, 33.5, 18.4, 17.7; IR (ZnSe) 2908, 1691, 1603, 1496, 1446, 1369, 1030, 748, 698 cm^{-1}; found: C, 76.75; H, 8.21%, calcd for $C_{14}H_{18}S$: C, 77.01; H, 8.31%.

*4.3.9. 2-Methylene-4-phenethylthietane (**65**) (Table 2, entry 2)*

This compound was synthesized from *S*-5-bromo-1-phenylhex-5-en-3-yl ethanethioate (**34**) according to the same procedure as for **52**.

Pale yellow oil; yield 93%; R_f=0.55 (silica gel, hexane/acetone=19:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (2H, dd, J=7.3, 7.5 Hz), 7.14–7.21 (3H, m), 4.94 (1H, ddd, J=2.0, 2.0, 2.2 Hz), 4.71 (1H, ddd, J=2.2, 2.4, 2.4 Hz), 3.60–3.65 (1H, m), 3.58 (1H, dddd, J=2.0, 2.2, 7.1, 7.6 Hz), 3.14 (1H, dddd, J=2.0, 2.4, 7.1, 14.8 Hz), 2.62–2.68 (1H, m), 2.53–2.59 (1H, m), 2.07–2.20 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.0, 141.0, 128.4 (overlapped), 126.0, 103.5, 43.5, 40.3, 37.9, 33.5; IR (ZnSe) 3026, 2917, 2852, 1631, 1496, 1454, 1120, 1076, 1030, 831, 748, 698, 650 cm^{-1}; HRMS (FAB^+) found: 191.0867, calcd for $C_{12}H_{15}S$ ($M+H^+$): 191.0816.

*4.3.10. 2-Methylene-4-benzylthietane (**66**) (Table 2, entry 3)*

This compound was synthesized from *S*-4-bromo-1-phenylpent-4-en-2-yl ethanethioate (**35**) according to the same procedure as for **52**.

Colorless oil; yield 92%; R_f=0.57 (silica gel, hexane/acetone=19:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29–7.33 (2H, m), 7.23–7.26 (1H, m), 7.19–7.22 (2H, m), 4.99 (1H, ddd, J=2.0, 2.0, 2.2 Hz), 4.75 (1H, ddd, J=2.2, 2.4, 2.4 Hz), 3.94–3.87 (1H, m), 3.63–3.56 (1H, m), 3.30–3.23 (1H, m), 3.16 (1H, dd, J=6.8, 14.0 Hz), 3.09 (1H, dd, J=8.4, 14.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.5, 138.6, 128.6, 128.5, 126.7, 103.6, 44.7, 43.3, 39.1; IR (NaCl): 3026, 2914, 2835, 1633, 1496, 1452, 1120, 1072, 1030, 831, 750, 721 cm^{-1}; HRMS (EI) found: 176.0653, calcd for $C_{11}H_{12}S$: 176.0654.

*4.3.11. 2-Methylene-4-cyclohexylthietane (**67**) (Table 2, entry 4)*

This compound was synthesized from *S*-3-bromo-1-cyclohexylbut-3-enyl ethanethioate (**36**) according to the same procedure as for **52**.

Colorless oil; yield 85%; R_f=0.58 (silica gel, hexane/acetone=19:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.91 (1H, ddd, J=2.0, 2.0, 2.2 Hz), 4.69 (1H, ddd, J=2.2, 2.4, 2.4 Hz), 3.47–3.54 (1H, m), 3.33–3.39 (1H, m), 3.19–3.25 (1H, m), 1.60–1.75 (5H, m), 1.52–1.57 (1H, m), 1.10–1.26 (3H, m), 0.76–0.87 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.2, 103.0, 45.3, 44.2, 42.0, 29.9, 28.8, 26.1, 25.75, 25.73; IR (NaCl): 2922, 2852, 1631, 1448, 1124, 825, 748, 651 cm^{-1}; HRMS (EI) found: 168.0970, calcd for $C_{10}H_{16}S$: 168.0976.

*4.3.12. Ethyl 5-(2-methylenethietan-4-yl)pentanoate (**68**) (Table 2, entry 5)*

This compound was synthesized from ethyl 6-(acetylthio)-8-bromonon-8-enoate (**37**) according to the same procedure as for **52**.

Pale yellow oil; yield 67%; R_f=0.56 (silica gel, hexane/acetone=5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.92–4.93 (1H, m), 4.68–4.69 (1H, m), 4.11 (2H, q, J=7.2 Hz), 3.56–3.66 (2H, m), 3.07–3.15 (1H, m), 2.27–2.31 (2H, m), 1.74–1.90 (2H, m), 1.58–1.69 (2H, m), 1.26–1.30 (2H, m), 1.24 (3H, t, J=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 140.9, 103.4, 60.2, 43.7, 38.4, 38.4, 34.2, 26.8, 24.5, 14.3; IR (ZnSe) 2979, 2935, 2856, 1732, 1633, 1373, 1234, 1180, 1120, 1030, 831, 650 cm^{-1}; HRMS (FAB^+) found: 215.1080, calcd for $C_{11}H_{18}O_2S$ ($M+H^+$): 215.1028.

*4.3.13. 2-Methylene-4-(p-methoxyphenyl)thietane (**69**) (Table 2, entry 6)*

This compound was synthesized from *S*-3-bromo-1-(4-methoxyphenyl)but-3-enyl ethanethioate (**38**) according to the same procedure as for **52**.

Colorless oil; yield 30%; R_f=0.37 (silica gel, hexane/acetone=19:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (2H, dd, J=2.8, 11.6 Hz), 6.83 (2H, dd, J=2.8, 11.6 Hz), 6.20–6.23 (1H, m), 5.56 (1H, ddd, J=2.4, 2.8, 3.2 Hz), 4.88 (1H, dd, J=7.6, 9.6 Hz), 3.79 (3H, s), 3.15 (1H, dddd, J=2.4, 2.8, 9.6, 16.4 Hz), 2.88 (1H, dddd, J=2.4, 2.8, 7.6, 16.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.7, 135.4, 128.0, 125.5, 120.5, 113.8, 55.3, 52.4, 43.9; IR (ZnSe) 2999, 2952, 2931, 2906, 2833, 1610, 1583, 1509, 1458, 1302, 1246, 1176, 1109, 1034, 831, 769, 671, 650 cm^{-1}; HRMS (FAB^+) found: 193.0686, calcd for $C_{11}H_{12}OS$ ($M+H^+$): 193.0609.

4.3.14. (3R,4R*)-2-Methylene-3,4-diphenethylthietane (**70**) (Table 2, entry 7)*

This compound was synthesized from *S*-(3*R**,4*R**)-5-bromo-4-phenethyl-1-phenylhex-5-en-3-yl ethanethioate (**42**) according to the same procedure as for **52**.

Colorless oil; yield 92%; R_f=0.51 (silica gel, hexane/acetone=19:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.35 (4H, m), 7.15–7.26 (6H, m), 5.00 (1H, dd, J=2.0, 2.1 Hz), 4.74 (1H, dd, J=2.1, 2.2 Hz), 3.32–3.42 (2H, m), 2.59–2.68 (3H, m), 2.50–2.57 (1H, m), 2.07–2.18 (2H, m), 1.93–2.01 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 141.5, 141.0, 128.5 (overlapped), 128.4, 128.3, 126.1, 126.0, 102.7, 56.0, 45.5, 40.0, 36.4, 33.8, 32.4; IR (NaCl): 3024, 2929, 2852, 1627, 1602, 1494, 1452, 1126, 1074, 1030, 833, 748, 698 cm^{-1}; HRMS (ESI) found: 295.1485, calcd for $C_{20}H_{23}S$ ($M+H^+$): 295.1520.

*4.3.15. (Z)-2-Decylidene-4-phenethylthietane (**72**) (Scheme 18)*

This compound was synthesized from (*Z*)-*S*-5-bromo-1-phenylpentadec-5-en-3-yl ethanethioate (**48**) according to the same procedure as for **52**.

Colorless oil; yield: 70%; R_f=0.93 (silica gel, hexane/EtOAc=10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17–7.29 (5H, m), 5.18–5.20 (1H, m), 3.69–3.75 (1H, m), 2.82–2.88 (1H, m), 2.63–2.77 (2H, m), 2.45–2.49 (1H, m), 2.23–2.26 (2H, m), 1.92–2.03 (2H, m), 1.26–1.54 (14H, m), 0.88 (3H, t, *J*=6.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.3, 141.7, 128.5, 128.4, 125.9, 115.4, 49.8, 41.7, 38.8, 34.3, 31.9, 31.3, 29.6, 29.4, 29.3, 29.1, 28.7, 22.7, 14.1; IR (NaCl): 3024, 2924, 2853, 1497, 1437, 1260, 1030, 908, 735, 698 cm^{-1}; HRMS (EI) found: 316.2216, calcd for $C_{21}H_{32}S$ (M^+): 316.2219.

*4.3.16. (E)-2-Decylidene-4-phenethylthietane (**73**) (Scheme 18)*

This compound was synthesized from (*E*)-*S*-5-bromo-1-phenylpentadec-5-en-3-yl ethanethioate (**49**) according to the same procedure as for **52**.

Colorless oil; yield 62%; R_f=0.93 (silica gel, hexane/EtOAc=10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15–7.30 (5H, m), 5.00–5.04 (1H, m), 3.49–3.68 (2H, m), 3.02–3.05 (1H, m), 2.53–2.69 (2H, m), 2.07–2.21 (2H, m), 1.85–1.90 (2H, m), 1.20–1.30 (14H, m), 0.88 (3H, t, *J*=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.1, 128.50, 128.46, 128.43, 126.0, 120.1, 41.1, 40.6, 38.5, 33.6, 31.9, 29.64, 29.61, 29.5, 29.4, 29.2, 28.2, 22.7, 14.1; IR (NaCl): 3024, 2922, 2851, 1663, 1603, 1454, 1302, 1240, 908, 698 cm^{-1}; HRMS (EI) found: 316.2229, calcd for $C_{21}H_{32}S$ (M^+): 316.2219.

*4.3.17. (E)-1-(4-Bromobut-3-enyl)naphthalene (**74**) (Ref. 26)*

This compound was synthesized from 1-(but-3-ynyl)naphthalene (**77**) according to the reported method.[37]

Colorless oil; yield 48%; R_f=0.54 (silica gel, hexane/Et_2O=50:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73–8.00 (3H, m), 7.30–7.55 (4H, m), 6.27–6.34 (1H, m), 6.08–6.11 (1H, m), 3.18 (2H, t, *J*=7.8 Hz), 2.48–2.53 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.3, 136.9, 134.0, 131.7, 128.9, 127.0, 126.2, 126.0, 125.6, 125.5, 123.5, 105.1, 34.0, 32.2; IR (NaCl): 3063, 3009, 2940, 2870, 2249, 1620, 1597, 1508, 1458, 1438, 1396, 1250, 1215, 934, 907, 799 cm^{-1}; HRMS (ESI) found: 283.0076, calcd for $C_{14}H_{13}BrNa$ (M+Na^+): 283.0098.

*4.3.18. (Z)-1-(4-Bromobut-3-enyl)naphthalene (**75**) (Ref. 26)*

This compound was obtained from 1-(4,4-dibromobut-3-enyl)naphthalene according to the reported method.[38]

Colorless oil; yield 74%; R_f=0.54 (silica gel, hexane/Et_2O=50:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73–8.11 (3H, m), 7.34–7.54 (4H, m), 6.18–6.25 (2H, m), 3.20 (2H, d, *J*=7.8 Hz), 2.62–2.73 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.2, 134.0, 133.9, 131.9, 128.9, 127.0, 126.1, 126.0, 125.6, 125.5, 123.7, 108.6, 31.4, 30.8; IR (NaCl): 3044, 3005, 2936, 2866, 1620, 1597, 1508, 1458, 1439, 1396, 1304, 1288, 1250, 1022, 795 cm^{-1}; HRMS (ESI) found: 283.0114, calcd for $C_{14}H_{13}BrNa$ (M+Na^+): 283.0098.

*4.3.19. S-1,5-Diphenylpentan-3-yl ethanethioate (**76**) (Ref. 26)*

This compound was prepared from 1,5-diphenylpentan-3-ol[39] by following the same procedure as for **3**.

Pale yellow oil; yield 38% (2 steps); R_f=0.63 (silica gel, hexane/EtOAc=8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.30 (4H, m), 7.15–7.21 (6H, m), 3.60–3.66 (1H, m), 2.61–2.78 (4H, m), 2.38 (3H, s), 1.85–2.02 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.7, 141.6, 128.45, 128.40, 126.0, 44.2, 36.9, 33.2, 30.9; IR (NaCl): 3059, 3024, 2932, 2855, 1690, 1601, 1493, 1454, 1354, 1111, 953, 748 cm^{-1}; HRMS (ESI) found: 299.1477, calcd for $C_{19}H_{23}OS$ (M+H^+): 299.1470.

*4.3.20. 1-(But-3-ynyl)naphthalene (**77**) (Ref. 26)*

This compound was synthesized from 1-(4,4-dibromobut-3-enyl)naphthalene according to the reported method.[40]

Colorless oil; yield 99%; R_f=0.35 (silica gel, pure hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76–8.14 (3H, m), 7.38–7.55 (4H, m), 3.34 (2H, t, *J*=9.7 Hz), 2.64 (2H, dt, *J*=3.2, 9.7 Hz), 2.08 (1H, t, *J*=3.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.3, 133.9, 131.6, 128.9, 127.3, 126.2, 126.1, 125.6, 125.5, 123.4, 83.9, 69.2, 32.1, 19.9; IR (NaCl): 3294, 3048, 2932, 2870, 2118, 1597, 1508, 1458, 1431, 1396, 1250, 1018, 795 cm^{-1}; HRMS (ESI) found: 181.1025, calcd for $C_{14}H_{13}$ (M+H^+): 181.1017.

*4.3.21. (Z)-2-Decylidene-4-phenethylthietan-1,1-dioxide (**78**) (Ref. 33)*

To a stirred solution of (*Z*)-2-decylidene-4-phenethylthietane (**72**) (79 mg, 0.25 mmol) in CH_2Cl_2 (10 mL) was added *m*-CPBA (231 mg, 1.0 mmol) and $NaHCO_3$ (63 mg, 0.75 mmol), and the reaction mixture was stirred at room temperature overnight. The reaction was quenched with saturated $Na_2S_2O_3$ solution, and the organic materials were extracted three times with CH_2Cl_2. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel, hexane/EtOAc=6:1) to give (*Z*)-2-decylidene-4-phenethylthietan-1,1-dioxide (**78**) (70 mg, 0.20 mmol) in 81% yield.

Pale yellow oil; yield 81%; R_f=0.49 (silica gel, hexane/EtOAc=6:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.32 (2H, m), 7.21–7.24 (3H, m), 6.17–6.18 (1H, m), 3.12–3.20 (1H, m), 2.79–2.91 (3H, m), 2.32–2.41 (4H, m), 1.87–1.96 (1H, m), 1.57–1.65 (2H, m), 1.26–1.38 (12H, m), 0.88 (3H, t, *J*=6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 140.3, 129.9, 128.6, 128.5, 126.3, 57.2, 33.0, 31.8, 31.3, 30.3, 29.4, 29.22, 29.18, 29.1, 27.3, 24.0, 22.6, 14.1; IR (NaCl): 2924, 2853, 1736, 1651, 1603, 1497, 1454, 1437, 1292, 1138, 1119, 912, 750, 735, 700 cm^{-1}; HRMS (ESI) found: 371.2214, calcd for $C_{21}H_{32}O_2NaS$ (M+Na^+): 371.2015.

*4.3.22. (E)-2-Decylidene-4-phenethylthietan-1,1-dioxide (**79**) (Ref. 35)*

This compound was synthesized from (*E*)-2-decylidene-4-phenethylthietane (**73**) according to the same procedure as for **78**.

Pale yellow oil; yield 85%; R_f=0.61 (silica gel, hexane/EtOAc=6:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29–7.32 (2H, m), 7.19–7.24 (3H, m), 6.29–6.33 (1H, m), 4.07–4.12 (1H, m), 2.70–2.88 (3H, m), 2.35–2.44 (1H, m), 2.26–2.32 (1H, m), 2.02–2.09 (3H, m), 1.26–1.45 (14H, m), 0.88 (3H, t, *J*=6.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.3, 140.1, 132.4, 128.6, 128.5, 126.4, 72.6, 33.4, 31.8, 31.5, 29.4, 29.3, 29.24, 29.16, 28.5, 28.0, 24.0, 22.6, 14.1; IR (NaCl): 2926, 2855, 1738, 1680, 1603, 1497, 1454, 1300, 1150, 1128, 912, 750, 735, 700 cm^{-1}; HRMS (ESI) found: 371.1992, calcd for $C_{21}H_{32}O_2NaS$ (M+Na^+): 371.2015.

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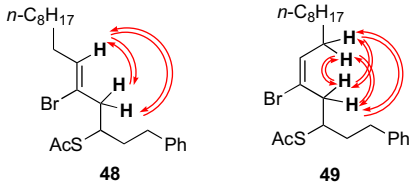

26. To check the *E*,*Z*-isomerization of bromoalkenes **6** and **9** in Scheme 15, *E*- and *Z*-bromoalkenes **74** and **75** were treated with thioacetate **76**, K_2CO_3 and MeOH under the same reaction conditions as those in Scheme 15. *E*-Bromoalkene **74** was recovered in 81% yield without contamination of *Z*-bromoalkene **75**. Although *Z*-bromoalkene **75** was also recovered in 27% without the isomerization, alkyne **77** was isolated in 50% yield. Based on these observations, the possibility of bromoalkene isomerization–substitution sequence was excluded from the cyclizations of both **6** and **9** in Scheme 15. In the cyclization of *Z*-bromoalkene **9**, an alternative mechanism such as formation of alkyne followed by cyclization to dihydrothiophene **52** might be proposed. However, the cyclization of an *E*/*Z*-mixture of bromoalkene **3**, which has no possibility of alkyne formation, gave dihydrothiophene **51** without recovery of the *Z*-isomer. Moreover, the alkyne formation is slower as compared with the cyclization. Accordingly, nucleophilic substitution pathway is most likely for the reaction mechanism of the cyclization of both bromoalkenes **6** and **9** as shown in Scheme 15. For a report of the formation of dihydrothiophenes from sulfur–alkyne cyclizations, see: McDonald, F. E.; Burova, S. A.; Huffman, L. G., Jr. *Synthesis* **2000**, *7*, 970.
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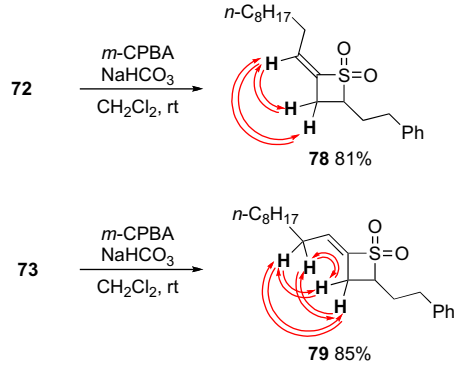

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