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Synthesis of hetero- and carbocycles by nucleophilic substitution at sp² carbon

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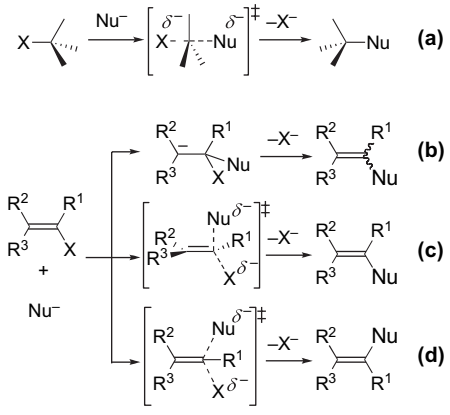
Abstract—Vinylic halides having alcohol, sulfonamide, active methine, and thiol moieties as nucleophiles cyclize to hetero- and carbocycles by intramolecular nucleophilic substitution at the sp² carbon centers. The density functional theory calculations suggest that the cyclization proceeds through S_N2-type substitution (the in-plane vinylic nucleophilic substitution, $S_NV\sigma$), when vinyl halides are substituted with oxygen, nitrogen, and carbon nucleophiles. The substitution with sulfur nucleophiles, in contrast, proceeds through both routes of $S_NV\sigma$ and out-of-plane vinylic nucleophilic substitution ($S_NV\pi$).

1. Introduction

Bimolecular nucleophilic substitution reaction (S_N2) is one of the most fundamental reactions in organic chemistry. A nucleophile (Nu^-) approaches an sp³ carbon from the opposite side of a leaving group (X), and the bond formation (Nu–C) and the bond cleavage (C–X) occur concertedly without any intermediates (Scheme 1a).[1] On the contrary, the nucleophilic substitution on a vinylic sp² carbon is supposed to have many mechanistic possibilities.[2] The most common pathway is an addition–elimination route, in which a nucleophile attacks the π-bond. If the double bond has an electron-withdrawing group, the nucleophilic addition gives a stable anion intermediate and the successive elimination of a leaving group completes the reaction (Scheme 1b). Otherwise, the lifetime of the intermediate becomes short enough and the reaction occurs in one step. It is called as $S_NV\pi$ mechanism because a nucleophile interacts with the π* orbital of the vinylic carbons (Scheme 1c). There is another possibility named $S_NV\sigma$ mechanism where a nucleophile attacks the σ* orbital of C–X bond of a vinylic carbon (Scheme 1d).



Scheme 1. Bimolecular nucleophilic substitution (S_N2) reaction.

The $S_NV\sigma$ mechanism has been considered as an unfavorable process. In-plane attack of nucleophile is undesirable due to steric repulsion,[3] and an early theoretical study also denied the possibility of the $S_NV\sigma$ pathway.[4] However, recent studies suggested the possibilities as follows. Theoretical calculations done by Glukhovtsev show that the in-plane nucleophilic attack of a chlorine ion to chloroethene has about 10 kcal mol^{-1} lower activation energy as compared to the out-of-plane attack.[5] Following this discovery, several theoretical studies have been published on the $S_NV\sigma$ reaction.[6] Furthermore, experimental supports have been provided recently for the substitution reaction at sp² atoms. The substitution reactions of alkenyliodonium salts were found to give the products with inversion of stereochemistry via intermolecular $S_NV\sigma$ mechanism.[7] 2-Bromoallylamines cyclized to aziridines by vinylic substitution and the stereochemistry of the products suggests that the amino group approaches from the backside of the bromo groups.[8] We also previously showed that haloalkenes having an intramolecular hydroxy group gave the corresponding cyclized products, such as benzofurans and dihydrofurans, in good yields.[9] Because intramolecular vinylic substitution is considered to become a powerful tool for the synthesis of cyclic compounds and its mechanistic study is also of interest, we

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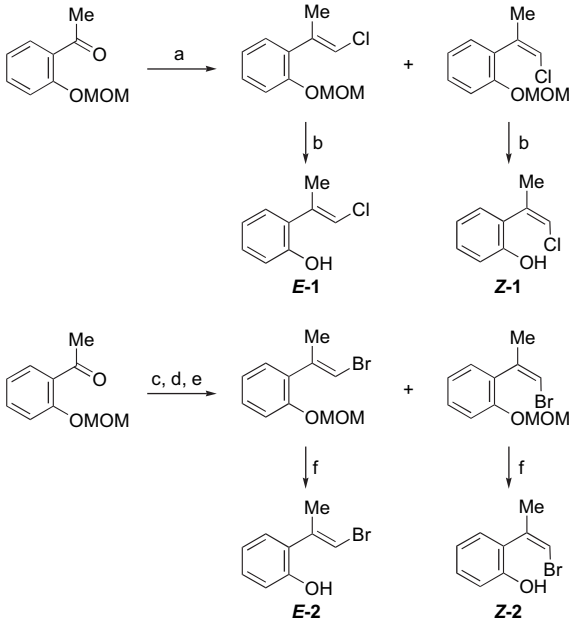
were motivated to investigate the scope and the mechanism of the intramolecular vinylic substitution with various intramolecular nucleophiles.

Here, we wish to report the cyclization of vinyl halides bearing hydroxy, sulfonamide, active methine, and thiol counterparts to clarify the difference between the nucleophilic moieties. Firstly, the preparation of starting materials and the experimental results of the cyclization reactions are described successively, and then these reaction mechanisms are discussed later.

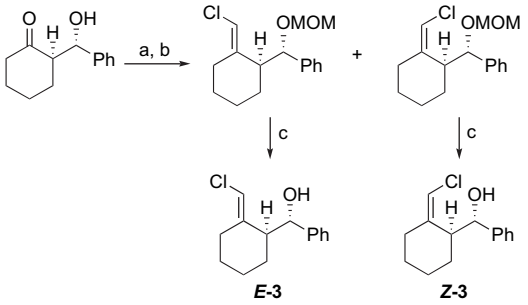
2. Results and discussion

2.1. Preparation of starting materials

Haloalkenes bearing a hydroxy group were prepared as previously described (Schemes 2 and 3).[9]

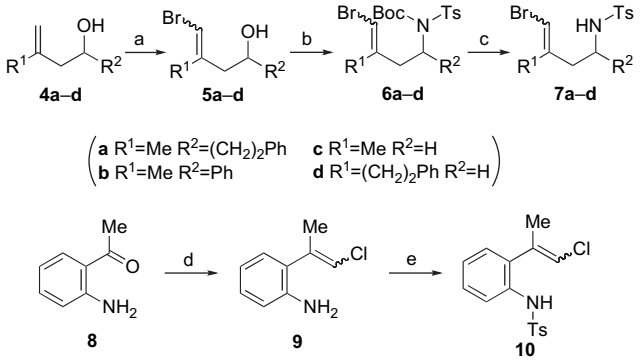


Scheme 2. Preparation of chloroalkenes having an aromatic hydroxy group. Reagents and conditions: (a) Cp_2TiCl_2, Mg, $CHCl_3$, $P(OEt)_3$, MS 4A, THF, rt, 2 h, 31% (*E*-isomer), 35% (*Z*-isomer). (b) HCl aq, THF, rt, 2 h, 99% (*E*-**1**), 81% (*Z*-**1**), 98% (*E*-**2**), 94% (*Z*-**2**). (c) $LiCHBr_2$, THF, −78 °C, 1 h, 66%. (d) Me_3SiCl, imidazole, CH_2Cl_2, rt, 3 h, 92%. (e) *n*-BuLi, THF, −78 °C, 1 h, 40% (*E*-isomer), 27% (*Z*-isomer). (f) HCl aq, THF, rt, 2 h, 98% (*E*-**2**), 94% (*Z*-**2**). Cp=cyclopentadienyl; MOM=methoxymethyl.



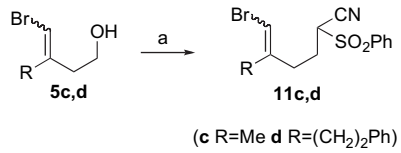
Scheme 3. Preparation of chloroalkenes having an aliphatic hydroxy group. Reagents and conditions: (a) MOMCl, *i*-Pr_2NEt, CH_2Cl_2, rt, overnight, 93%. (b) Cp_2TiCl_2, Mg, $CHCl_3$, $P(OEt)_3$, MS 4A, THF, rt, overnight, 80% (*E*/*Z*-mixture). (c) HCl aq, THF, 60 °C, 7 h, 44% (*E*-**3**), 56% (*Z*-**3**).

Bromoalkenols **5** were synthesized by dibromination of the corresponding alkenols **4** followed by dehydrobromination under basic conditions.[10] Alkenyl bromides bearing nitrogen nucleophiles (**7**) were prepared from the above alcohols **5** by the Mitsunobu reaction with *N*-*tert*-butoxycarbonyl tosylamide.[11] The *tert*-butoxylcarbonyl (Boc) group of **6** was removed under acidic conditions. Halo stylene derivative **10** was prepared from commercially available 2-aminoacetophenone **8** by chloroalkenylation with a Wittig reagent[12] and then sulfonylation of the amino group (Scheme 4).



Scheme 4. Preparation of bromo- and chloroalkenes with nitrogen nucleophilic moieties. Reagents and conditions: (a) Br_2, CCl_4, rt, then KOH, MeOH, rt, 40% (**5a**, *E*/*Z*-mixture, 10:1), 31% (**5b**, *E*/*Z*-mixture, 7:1), 57% (**5c**, *E*-isomer: 49%, *Z*-isomer: 8%, separated), 47% (**5d**, *E*-isomer: 35%, *Z*-isomer: 12%, separated). (b) BocNHTs, diethyl azodicarboxylate, PPh_3, THF, rt, 50% (**6a**, *E*-isomer: 44%, *Z*-isomer: 6%, separated), 72% (**6b**, *E*-isomer: 63%, *Z*-isomer: 9%, separated), 83% (*E*-**6c**), 95% (*E*-**6d**). (c) CF_3CO_2H, CH_2Cl_2, rt, 92% (*E*-**7a**), 77% (*Z*-**7a**), 94% (*E*-**7b**), 84% (*E*-**7c**), 91% (*E*-**7d**). (d) Ph_3PCHCl, THF, rt, 24 h, 70% (**9**, *E*-isomer: 63%, *Z*-isomer: 7%, separated). (e) TsCl, pyridine, CH_2Cl_2, rt, 12 h, 75% (*E*-**10**), 63% (*Z*-**10**). Boc=*tert*-butoxycarbonyl; Ts=*p*-toluenesulfonyl; THF=tetrahydrofuran. For detailed information of *E*/*Z*-separation, see Section 5.

Alkenyl bromides with an active methine moiety (**11**) were prepared from **5** by the Mitsunobu reaction with 2-phenylsulfonylacetonitrile (Scheme 5).[13]

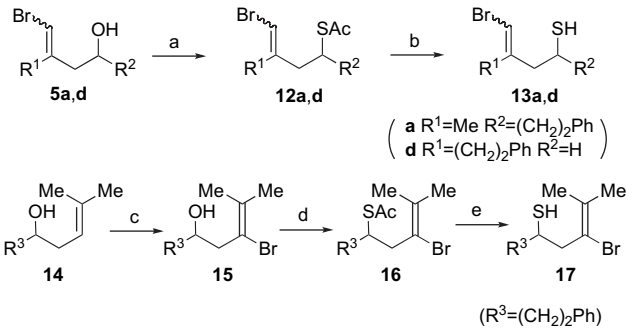


Scheme 5. Preparation of bromoalkene with an active methine part. Reagents and conditions: (a) $NCCH_2SO_2Ph$, azodicarbonyldipiperidine, $P(n\text{-}Bu)_3$, THF, rt, 56% (*E*-**11c**), 41% (*E*-**11d**), 30% (*Z*-**11d**).

Alkenyl bromides having a thiol part **13** and **17** were prepared from bromoalkenyl alcohols **5** and **15**, respectively, by the Mitsunobu reaction with thioacetic acid,[14] followed by the removal of the acetyl group from **12** and **16** under basic conditions (Scheme 6).

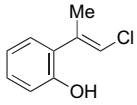
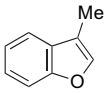
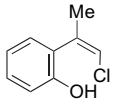
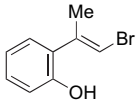
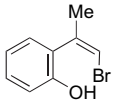
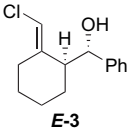
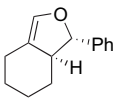
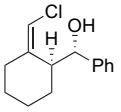
2.2. Cyclization of phenols and alcohols

When chloroalkene *E*-**1** was treated with NaH in dimethylformamide (DMF) at room temperature, benzofuran **18** was obtained in 95% yield (Table 1, entry 1), whereas *Z*-**1** was recovered quantitatively even after heating at 110 °C (entry 2). Under the same reaction conditions (NaH, rt), bromoalkene *E*-**2** was converted to benzofuran **18** in 73%



Scheme 6. Preparation of bromoalkene with homoallylic thiol. Reagents and conditions: (a) AcSH, DIAD, PPh_3, THF, rt, 32% (**12a**), 50% (*E*-**12d**), 46% (*Z*-**12d**). (b) KOH, MeOH, rt, 79% (**13a**), 91% (*E*-**13d**), 76% (*Z*-**13d**). (c) Br_2, CCl_4, rt, then KOH, MeOH, rt, 66%. (d) AcSH, DIAD, PPh_3, THF, rt, 30%. (e) K_2CO_3, MeOH, rt, 65%. Ac=acetyl; DIAD=diisopropyl azodicarboxylate.

Table 1. Cyclization reaction of haloalkenes having a hydroxy group[a]

Entry	Starting material	Product	Temp/°C	Time/h	Yield/%
1	 ***E*-1**	 **18**	rt	13	95
2	 ***Z*-1**	**18**	rt to 110[b]	16[b]	0 (100)[c]
3	 ***E*-2**	**18**	rt	3	73
4	 ***Z*-2**	**18**	rt	144	6 (87)[c]
5	 ***E*-3**	 **19**	80	10	82
6	 ***Z*-3**	**19**	80	10	0[d]

[a] Reactions were carried out in DMF with 1.5 equiv of NaH.
[b] rt, 13 h; 50 °C, 1 h; 80 °C, 1 h; 110 °C, 1 h.
[c] Recovery of the starting material.
[d] A complex mixture.

yield, while *Z*-**2** gave only 6% yield of **18** after a prolonged reaction time along with 87% recovery of *Z*-**2** (entries 3 and 4). An *E*-isomer of chloroalkene having an aliphatic hydroxy group (*E*-**3**) was also cyclized to give dihydrofuran **19** in 82% yield by heating at 80 °C (entry 5). The product **19** was not obtained from *Z*-**3** (entry 6). The possibility of 6π-electrocyclization could be excluded, because the non-conjugated compound *E*-**3** also gave the product **19**.

A mixture of *E*- and *Z*-deuterated chloroalkenes **1D** was treated with NaH in DMF at room temperature. Deuterium remained at 2-position of the resulted benzofuran **18D** and also in the recovered *Z*-isomer *Z*-**1D** as shown in Scheme 7. From these results, we could exclude the intermediacy of allyl chloride and carbene, which is described later (see Section 3.1).

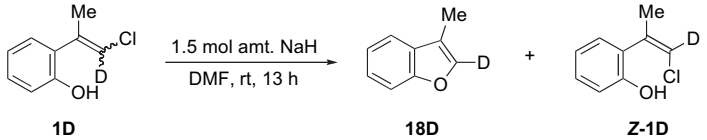
2.3. Cyclization of sulfonamides

Some tosylamides having *E*-haloalkenyl moieties were subjected to the cyclization and the results are listed in Table 2. Homoallylic amide **7a** having an alkyl group at the α-position was treated with various bases in 1,3-dimethyl-2-imidazolidinone (DMI), which was used instead of DMF to ensure the reaction at higher temperature. When sodium hydride was used as a base, dihydropyrrole **20a** was obtained in 76% yield within an hour (entry 1). The treatment with sodium methoxide or potassium carbonate also gave the product in good yield, although the reaction became slower (entries 2 and 3). Compound **7b** having a phenyl group at the α-position gave the corresponding product **20b** at 100 °C in 77% yield (entry 4). The treatment of tosylamides having no α-substituent (**7c** and **7d**) with sodium hydride also gave the cyclization products in good yield (entries 5 and 6). *N*-Tosylanilide **10** was smoothly converted to the corresponding *N*-tosylindole **21** at lower temperature (80 °C) by the treatment of various bases (NaH, NaOMe, and K_2CO_3), in which potassium carbonate gave the best yield of the product (entry 9).

As mentioned above, *E*-bromohomoallylsulfonamides smoothly cyclized to dihydroindole derivatives, whereas the corresponding *Z*-sulfonamide *Z*-**7a** was found to give only 4% yield of the cyclized product even after longer heating. The *Z*-isomer of *N*-tosylanilide **10**, *Z*-**10** gave no cyclization product even after heating at 120 °C for 6 h and was recovered in 95% (Scheme 8).

2.4. Cyclization of active methine compounds

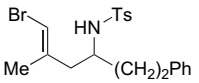
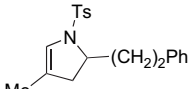
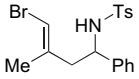
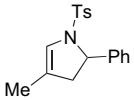
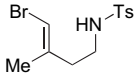
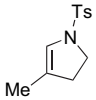
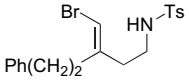
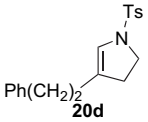
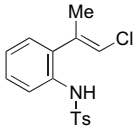
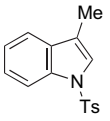
The formation of carbocycles was then examined by using active methine compounds **11c** and **11d** having cyano and phenylsulfonyl groups (Table 3). As compared to the cyclization of sulfonamides, it took longer time to consume the



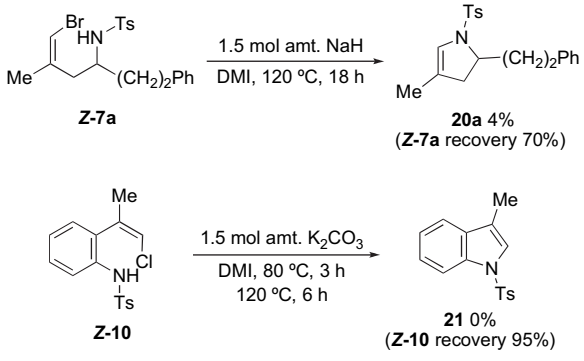
1D (*E*/*Z* = 2.5:1, 93% D) **18D** (78% from *E*, 91% D) ***Z*-1D** (98% recovery, 93% D)

Scheme 7. Reaction of deuterated chloroalkene.

Table 2. Cyclization reaction of bromoalkenes having tosylamide moiety[a]

Entry	Starting material	Product	Base	Temp/°C	Time/h	Yield/%
1	 **7a**	 **20a**	NaH	120	1	76
2	**7a**	**20a**	NaOMe	120	5	87 (10)[b]
3	**7a**	**20a**	K_2CO_3	120	5	80 (15)[b]
4	 **7b**	 **20b**	NaH	100	1.5	77 (10)[b]
5	 **7c**	 **20c**	NaH	120	5	87
6	 **7d**	 **20d**	NaH	120	5	69 (18)[b]
7	 **10**	 **21**	NaH	80	2	77
8	**10**	**21**	NaOMe	80	3	87
9	**10**	**21**	K_2CO_3	80	3	89

[a] Reactions were carried out in DMI with 1.5 equiv of base.
[b] Recovery of the starting material.



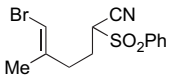
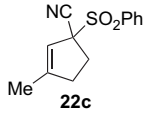
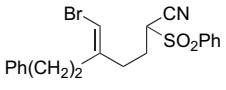
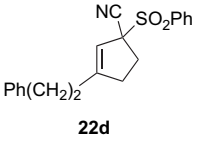
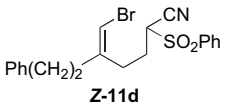
Scheme 8. Reactions of *Z*-isomers.

starting materials, presumably due to the steric hindrance. From *E*-**11c**, cyclopentene **22c** was obtained in a moderate yield (entries 1 and 2). Each of *E*/*Z*-isomers of bromoalkene **11d** was treated independently under the same conditions. Although the *E*-isomer *E*-**11d** was converted to cyclopentene **22d** in 50% yield (entry 3), the *Z*-isomer *Z*-**11d** was recovered in 34% and no cyclized products were detected (entry 4). Thus the cyclization with active methine moiety also revealed to proceed in a stereospecific manner. The moderate yield of the products **22** may originate from the instability of the products under basic conditions.

2.5. Cyclization of thiols

The cyclization of thiols to dihydrothiophene was found to proceed very smoothly as shown in Table 4. When an

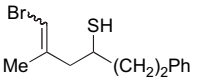
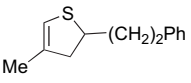
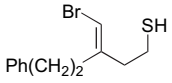
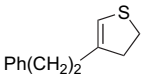
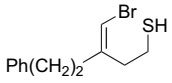
Table 3. Cyclization reaction of bromoalkenes with an active methane moiety[a]

Entry	Starting material	Product	Base	Time/h	Yield/%
1	 ***E*-11c**	 **22c**	NaH	10	61
2			NaOMe	12	71
3	 ***E*-11d**	 **22d**	NaOMe	12	50
4	 ***Z*-11d**	**22d**	NaOMe	12	0 (34)[b]

[a] Reactions were carried out in DMI with 1.5 equiv of base at 102 °C.
[b] Recovery of the starting material.

E/*Z*-mixture (10:1) of thiol **13a** was treated with NaH in DMI, the reaction proceeded even at room temperature, giving dihydrothiophene **23a** in 70% yield (entry 1). Interestingly, in contrast to the previous cyclization of alcohols, amides, and active methine derivatives, the *Z*-isomer was not recovered. This meant that the both stereoisomers could be cyclized to **23a**. To confirm this, each of the *E*- and *Z*-isomer of bromoalkenes **13d** was treated with sodium hydride. The same cyclopentene **23d** was obtained in 34%

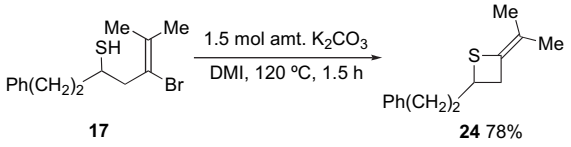
Table 4. Cyclization reaction of bromoalkenes with a thiol moiety[a]

Entry	Starting material	Product	Temp/ °C	Time/ h	Yield/ %
1	 **13a** (*E*/*Z* = 10:1)	 **23a**	rt	9	70
2	 ***E*-13d**	 **23d**	50	6	34
3	 ***Z*-13d**	**23d**	80	4	12

[a] Reactions were carried out in DMI with 1.5 equiv NaH.

and 12% yields, respectively (entries 2 and 3). It is quite noteworthy that the cyclization reaction proceeded from the both isomers.

In addition to the ring closure to five-membered dihydrothiophenes, the formation of four-membered ring was examined (Scheme 9). When thiol **17** was treated with potassium carbonate in DMI at 120 °C, methylenethietane **24** was obtained in 78% yield. The reaction of the corresponding bromohomoallyl alcohol did not give a cyclized product (oxetane) but an allene derivative as a dehydrobromination product. The analogous reaction of tosylamide to give azetidine did not proceed and resulted in the recovery of the tosylamide.



17 **24** 78%

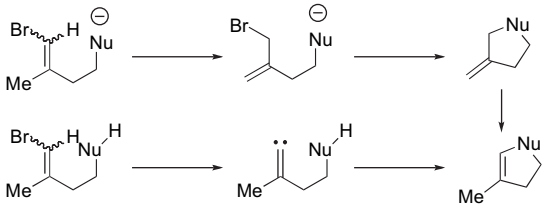
Scheme 9. Formation of thietane.

3. Theoretical study

In order to examine the reaction mechanisms, theoretical calculations were done by using Gaussian program.[15] All calculations were performed at the B3LYP[16]/6-31+G(d) level and the solvent effect was included by using the Onsager continuum model[17] for DMF (ε=37.06) as a solvent. DMI has an almost same dielectric constant (37.60) as DMF. Since DMF and DMI are able to dissolve many salts and tend to surround metal cations rather than nucleophilic anions, the use of free anions as model systems could be approved. Vibrational frequency calculations gave only one imaginary frequency for all transition structures and only harmonic frequencies for the reactants and products. The structures of the reactants and products were obtained by the optimization of the last structures on both sides of IRC (intrinsic reaction coordinate) calculations.[18] Gibbs free energies are calculated at 298.15 K and 1.00 atm. The thermal energy corrections are not scaled, because the scale factors for B3LYP are very close to 1.0.[19]

3.1. Mechanistic possibilities

As mentioned before, vinylic substitution has many mechanistic possibilities. Besides the addition–elimination, $S_NV\sigma$, and $S_NV\pi$ reaction mechanisms,[20] the allylic isomerization and the vinyl carbene formation may be the candidates for the reaction mechanism (Scheme 10).



Scheme 10. Allylic isomerization and carbene insertion.

The stereospecificity observed in the cyclization of alcohols, amides, and active methyne derivative nucleophiles can deny both the allylic isomerization and the carbene formation,[21] because these reactions can proceed from both *E*- and *Z*-isomers. Furthermore, the deuterium-label experiment depicted in Scheme 7 clearly shows the vinylic hydrogen remains intact during the reaction. Accordingly, we discuss here the addition–elimination, $S_NV\sigma$, and $S_NV\pi$ reactions only.

3.2. Cyclization of alcohols

We have already reported the transition structures for the cyclization of the anion *E*-**25** both in the gas phase and in DMF.[9] The in-plane S_N2-type structures *E*-**25-ts** were obtained with the activation energy of 17.1 kcal mol^{-1} in the gas phase and 14.4 kcal mol^{-1} in DMF (Fig. 1a). On the other hand, *Z*-**25** gave the $S_NV\pi$ transition structure *Z*-**25-ts** with the activation energy of 28.9 kcal mol^{-1} (Fig. 1b). The larger activation energy compared to the $S_NV\sigma$ reaction is

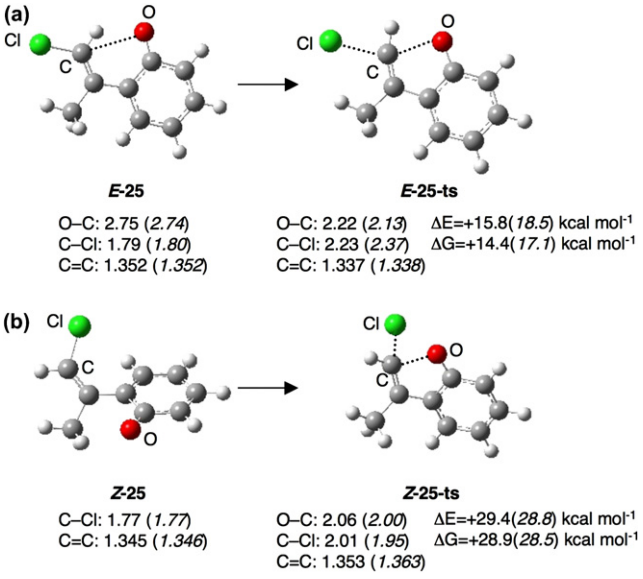


Figure 1. Transition structures for the nucleophilic cyclization of phenoxides **25** [B3LYP/6-31+G(d), SCRF (dipole, solv=DMF)]. Selected bond lengths are shown in Å. The italic numbers are the values in the gas phase.

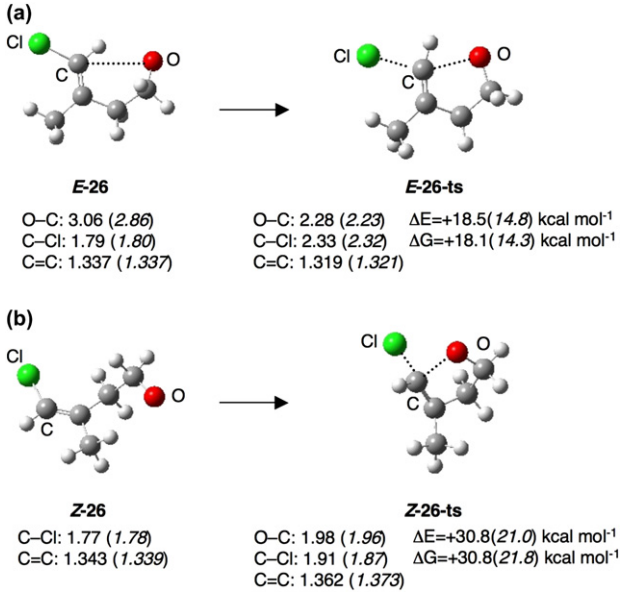


Figure 2. Transition structures for the nucleophilic cyclization of alkoxides **26** [B3LYP/6-31+G(d), SCRF (dipole, solv=DMF)]. Selected bond lengths are shown in Å. The italic numbers are the values in the gas phase.

consistent with the experimental failure of the cyclization of *Z*-**1**.

The cyclization of the anion **26** was also studied. *E*-Isomer *E*-**26** gave the $S_NV\sigma$ transition state *E*-**26-ts** with the activation energy of 18.1 kcal mol^{-1} in DMF (Fig. 2a). It is noteworthy that the activation energy is higher than that in the gas phase (14.3 kcal mol^{-1}). This difference seems to arise from the large stabilization of the unstable oxyanion in a polar solvent. *Z*-Isomer *Z*-**26** gave the $S_NV\pi$ transition structure *Z*-**26-ts** contrastively (Fig. 2b) and the activation energy in DMF is estimated as 30.8 kcal mol^{-1}, which is also higher than that in the gas phase (21.8 kcal mol^{-1}).

3.3. Cyclization of tosylamides

The DFT calculations on the cyclization of the anion *E*-**27c** derived from *E*-isomer *E*-**7c** gave the $S_NV\sigma$ type transition structure *E*-**27c-ts** (Fig. 3a). The nitrogen approached the alkenyl bromide from the backside of the C–Br bond in the plane of the vinylic carbons. The distances of the forming N–C and the breaking C–Br bonds were 2.35 and 2.49 Å, respectively. The length of the C=C double bond was slightly decreased in the transition state, which suggests that the central vinylic carbon has been changed from the sp^2 hybridization into an sp-like state due to the interaction of the nucleophile with the σ* orbital of the C–Br bond. The reaction gave a loose complex of dihydropyrrole **19c** and bromide ion without the formation of any intermediates. The reaction was exothermic and the heat of reaction in the gas phase was estimated as 27.4 kcal mol^{-1}. The activation energies for the transition state were estimated as 26.1 kcal mol^{-1} in the gas phase and 20.5 kcal mol^{-1} in DMF. In the Onsager reaction field, the reactant *E*-**27c** was stabilized by 5.1 kcal mol^{-1} as compared with the gas phase energy, while the transition state *E*-**27c-ts** was stabilized by 10.7 kcal mol^{-1}. Several attempts to obtain an $S_NV\pi$ type transition state from the *E*-isomer failed.

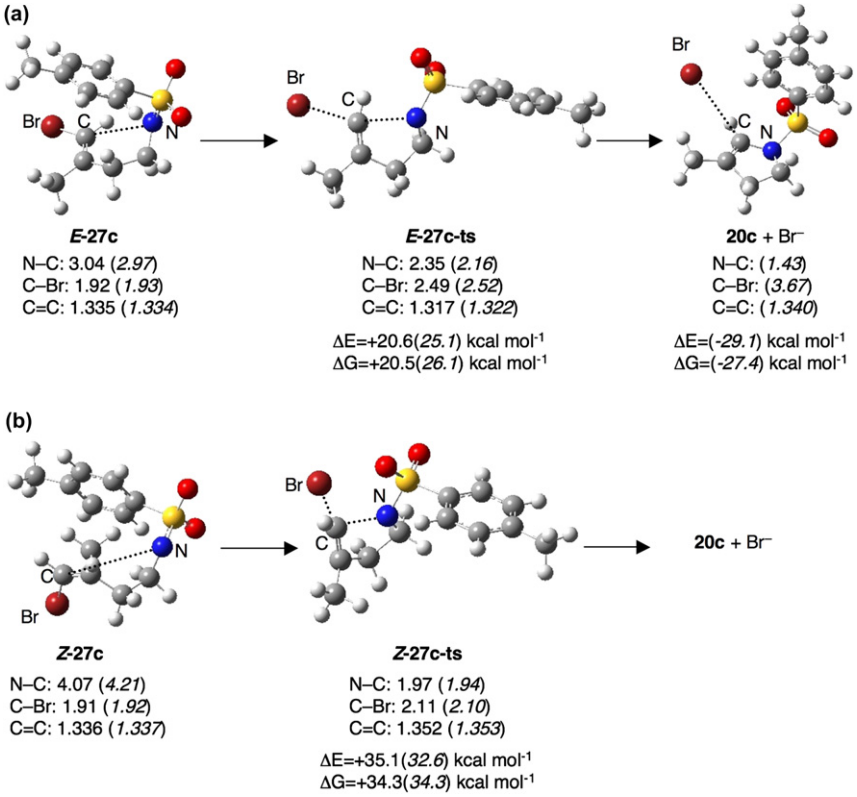


Figure 3. Transition structures for the nucleophilic cyclization of tosylamidates **27** [B3LYP/6-31+G(d), SCRF (dipole, solv=DMF)]. Selected bond lengths are shown in Å. The italic numbers are the values in the gas phase.

On the contrary, the anion *Z*-**27c** derived from *Z*-**7c** gave only the $S_NV\pi$ type transition structure *Z*-**27c-ts** (Fig. 3b). The length of the C=C double bond in the transition state was slightly increased due to the interaction with the π^* orbital. It resembles the addition–elimination pathway, but the bond formation and cleavage were almost simultaneous. The product was the same as that from the *E*-isomer *E*-**27c** with the heat of reaction being 24.6 kcal mol^{-1} in the gas phase. The activation energy of the $S_NV\pi$ reaction was calculated as 34.3 kcal mol^{-1} both in the gas phase and in DMF. The SCRF calculations did not change the activation energy, because both the transition structure *Z*-**27c-ts** and the reactant *Z*-**27c** were stabilized to the same extent (5.6 kcal mol^{-1} compared to the gas phase energy). These values of activation energy are much higher than those of the $S_NV\sigma$ reaction from the *E*-isomer *E*-**27c** and the results are consistent with the experimental results, that is, *Z*-isomer *Z*-**7c** gave only 4% yield of the product **20c**.

Similar results were obtained for the anion **28** derived from phenylene-tethered compound **10**. *E*-Isomer *E*-**28** gave only the $S_NV\sigma$ type transition structure *E*-**28-ts**, which requires the activation energies of 22.1 kcal mol^{-1} in the gas phase and 15.3 kcal mol^{-1} in DMF (Fig. 4a). These values are lower than those of *E*-**27c-ts** and are in accordance with the experimental results that the reaction proceeded at lower temperature (80 °C) compared with the dihydropyrrole synthesis (**7** to **20**, 120 °C). This is probably because the phenylene tether can make reaction centers close to each other. *Z*-Isomer *Z*-**28** gave the $S_NV\pi$ type transition structure *Z*-**28-ts** with the activation energies of 33.7 kcal mol^{-1} in the gas phase and 33.5 kcal mol^{-1} with solvent effect (Fig. 4b). Again, the SCRF model did stabilize the $S_NV\pi$ transition state *Z*-**28-ts** as the same extent as the reactant *Z*-**28**.

3.4. Cyclization with carbanion

For the carbon nucleophiles, the reactant anions *E*-**29c** and *Z*-**29c** derived from *E*-**11c** and *Z*-**11c**, respectively, were placed in the gas phase and in the self-consistent reaction field. In the same as the nitrogen nucleophiles, only the $S_NV\sigma$ type transition structure *E*-**29c-ts** was obtained from the *E*-isomer *E*-**29c**, and the $S_NV\pi$ type *Z*-**29c-ts** from the *Z*-isomer *Z*-**29c** (Fig. 5). The activation energies of the $S_NV\sigma$ type reaction from the *E*-isomer *E*-**29c** were 28.4 kcal mol^{-1} in the gas phase and 23.5 kcal mol^{-1} in DMF, while those of the $S_NV\pi$ type reaction pathway from the *Z*-isomer *Z*-**29c** were 33.2 kcal mol^{-1} in the gas phase and 29.9 kcal mol^{-1} in DMF. Although both the activation energies of the $S_NV\sigma$ and $S_NV\pi$ type reactions were lowered in the SCRF method, the $S_NV\sigma$ reaction still had lower activation energies. These results are in good accordance with the stereospecific formation of **22** from the *E*-isomer in the experiments. Furthermore, the higher activation energy of *E*-**29c-ts** compared with *E*-**27c-ts** may reflect the steric hindrance of the carbon nucleophile and can explain the slow cyclization reaction of **8**.

3.5. Cyclization of thiols

For the cyclization of thiol, *E*-anion *E*-**30a** generated from *E*-**13a** gave the $S_NV\sigma$ transition structure *E*-**30a-ts** (Fig. 6a). The activation energy is 19.6 kcal mol^{-1} in the gas phase. The calculation with SCRF method gave the activation energy of 12.5 kcal mol^{-1}, which is reasonably in agreement with the room temperature reaction of **13a** (*E*/*Z*=10:1). Several attempts to obtain $S_NV\pi$ transition structure from *E*-**30a** were unsuccessful. On the other hand, the $S_NV\pi$ type transition structure *Z*-**30a-ts** was

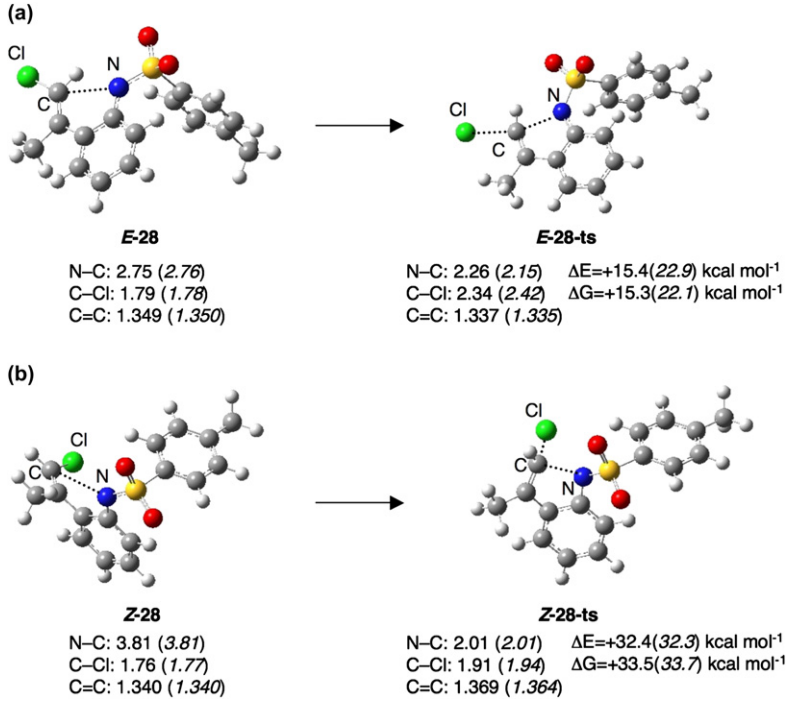


Figure 4. Transition structures for the nucleophilic cyclization of tosylanilidates **28** [B3LYP/6-31+G(d), SCRF (dipole, solv=DMF)]. Selected bond lengths are shown in Å. The italic numbers are the values in the gas phase.

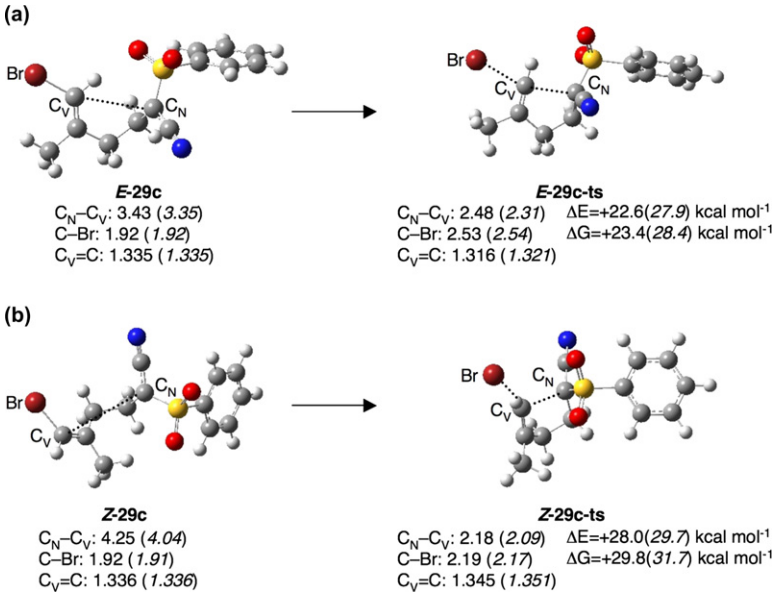


Figure 5. Transition structures for the nucleophilic cyclization of carbanions **29c** [B3LYP/6-31+G(d), SCRF (dipole, solv=DMF)]. Selected bond lengths are shown in Å. The italic numbers are the values in the gas phase.

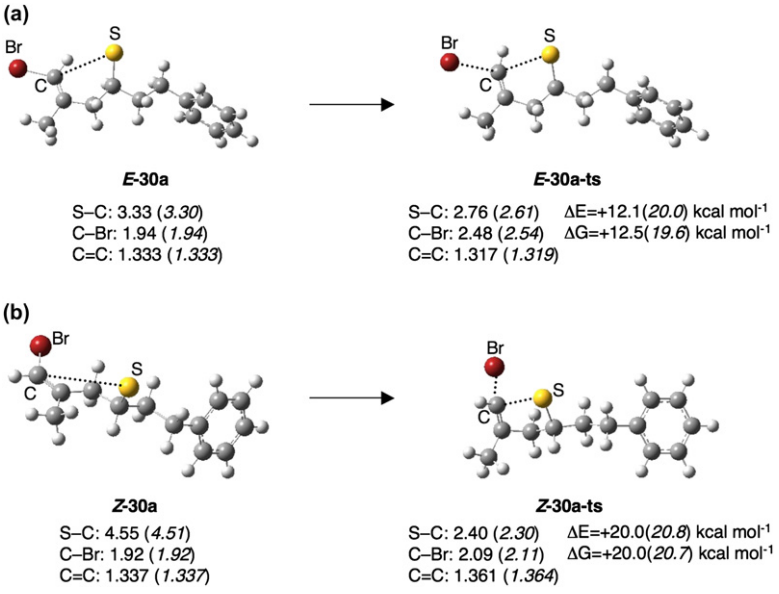


Figure 6. Transition structures for the nucleophilic cyclization of thiolate anions **30a** [B3LYP/6-31+G(d), SCRF (dipole, solv=DMF)]. Selected bond lengths are shown in Å. The italic numbers are the values in the gas phase.

obtained from *Z*-isomer *Z*-**30a** and its activation energies are 20.6 kcal mol^{-1} in the gas phase and 20.0 kcal mol^{-1} in DMF, respectively (Fig. 6b). Since the activation energy of the $S_NV\pi$ reaction is smaller than that of the nitrogen (*E*-**27c-ts**, 20.5 kcal mol^{-1}) and the carbon (*E*-**29c-ts**, 23.4 kcal mol^{-1}) nucleophiles, the cyclization reaction of *Z*-**13a** could also occur. The experimental results obtained from **13a** and **13d** accord with these calculation results although the yields are low.

The transition state structure for the thietane formation from thiol **17** was also studied and only the $S_NV\pi$ type transition structure **31-ts** was obtained instead of the $S_NV\sigma$ type (Fig. 7). The activation energy for **31-ts** was 20.0 kcal mol^{-1}

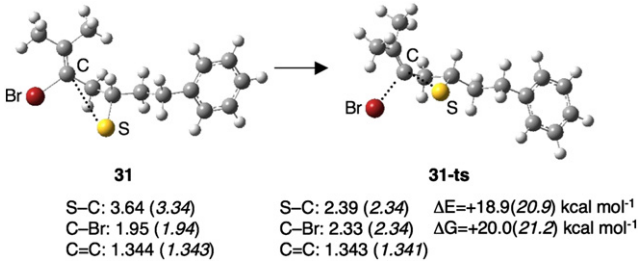


Figure 7. A transition structure for the nucleophilic cyclization of thiolate **31** [B3LYP/6-31+G(d), SCRF (dipole, solv=DMF)]. Selected bond lengths are shown in Å. The italic numbers are the values in the gas phase.

in DMF. Due to the large steric expulsion between the thiolate and the isopropylidene group, the $S_NV\sigma$ reaction became unfavorable. In fact, both the $S_NV\sigma$ and the $S_NV\pi$ transition structures were obtained in the case of the thiolate without the two methyl groups, and they have almost the same activation energies (24.7 kcal mol^{-1} for $S_NV\sigma$ and 24.9 kcal mol^{-1} for $S_NV\pi$) in the gas phase.

4. Conclusion

By the intramolecular vinylic substitution reaction, benzofuran, dihydrofuran, indole, dihydropyrrole, cyclopentene, dihydrothiophene, and thietane derivatives were synthesized from various vinylic halides, which have nucleophilic moieties at the suitable positions. Among the possible reaction mechanisms, fundamentally, the $S_NV\sigma$ reaction pathway was feasible for *E*-isomers and the $S_NV\pi$ pathway for *Z*-isomers. The theoretically predicted activation energies of $S_NV\sigma$ reactions were generally smaller than those of $S_NV\pi$ reactions, although the activation energies for the $S_NV\pi$ reactions of thiols were relatively small, which make the $S_NV\pi$ pathway also possible.

5. Experimental

5.1. General

^1H and ^{13}C NMR spectra were recorded on Bruker DRX500 and AVANCE 500 spectrometers at 500 and 125 MHz, respectively. Chemical shifts were reported in parts per million relative to trimethylsilane (internal standards, δ=0, for ^1H) and solvent peaks (δ=77.0, for ^{13}C). Multiplicities are abbreviated as follows: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br =broad. Infrared spectra were obtained on a Horiba FT-300S spectrometer. High-resolution mass spectra were measured on a JEOL JMS-700P using FAB ionization with *m*-nitrobenzylalcohol (NBA) as a matrix. Elemental analyses were performed at The Elemental Analysis Laboratory, Department of Chemistry, Faculty of Science, The University of Tokyo. All melting points are uncorrected. Flash column chromatography was carried out with PSQ100B silica gel (spherical, neutral, Fuji Silicia Kagaku). Preparative thin layer chromatography (PTLC) was performed on Wakogel B-5F silica gel (Wako Pure Chemical Industries, Ltd.). Dehydrated Et_2O, THF, and CH_2Cl_2 were purchased from Kanto Chemical Co., Inc., and were dried and degassed by Glass Contour solvent dispenser system. MeOH was distilled from a small amount of iodine and magnesium, and stored over MS 3 Å. Dimethylimidazolidinone was purchased from Aldrich Co., Inc., distilled over CaH_2, and stored under argon over MS 4 Å. All reactions were carried out under an argon atmosphere.

5.2. Preparation of starting materials

Preparation of compounds **1**, **2**, and **3** is described in the preceded literature.[9]

5.2.1. 3-Methylene-5-phenylpentan-1-ol (4d). This compound was prepared by using 3-methyl-3-buten-1-ol dianion chemistry described by Chong et al.[22]

To an ice-cold solution of tetramethylethylenediamine (8 mL, 53 mmol) in Et_2O (30 mL) was added *n*-BuLi (40 mmol), and the solution was stirred at room temperature for 1 h. The solution was then cooled (0 °C), and 3-methyl-3-buten-1-ol (2 mL, 20 mmol) was added slowly. The resulting solution was stirred for 6 h at room temperature to give a heterogeneous dark yellow suspension. The slurry was cooled to −78 °C and benzyl bromide (1.2 mL, 10 mmol) in Et_2O (5 mL) was added dropwise. The reaction vessel was allowed to warm up to room temperature and stirred for 6 h. The reaction was quenched with satd NH_4Cl aq and diluted with H_2O. Organic materials were extracted three times by Et_2O and combined organic layer was washed successively with 1 M HCl and brine, dried over $MgSO_4$, and concentrated in vacuo. Purification by column chromatography (hexane/ethyl acetate 4:1 to 2:1 v/v, gradient) gave 3-methylene-5-phenylpentan-1-ol (**4d**, 1.1 g, 6.5 mmol, 65%).

Colorless oil; ^1H NMR (500 MHz, $CDCl_3$) δ 7.30–7.27 (2H, m), 7.20–7.18 (3H, m, overlapped), 4.92 (1H, distorted s), 4.87 (1H, distorted s), 3.72 (2H, t, *J*=6.3 Hz), 2.77 (2H, t, *J*=8.1 Hz), 2.36–2.32 (4H, m, overlapped), 1.50 (1H, br); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.4, 141.8, 128.3, 128.3, 125.9, 112.0, 60.3, 39.3, 37.5, 34.2; IR (ZnSe) 3338, 2935, 1645, 1603, 1496, 1454, 1041, 891, 744, 696 cm^{-1}. Found: C, 81.62; H, 9.23%. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15%.

5.2.2. Typical procedure for the preparation of bromoalkenes with alcohol moiety. 4-Bromo-3-methylbut-3-en-1-ol (**5c**) was prepared as described in the literature,[10] and *E*/*Z*-isomers were separated by column chromatography. Other bromoalkenyl alcohols were synthesized in a similar procedure from corresponding alkenyl alcohols.

To a stirred solution of 5-methyl-1-phenylhex-5-en-3-ol **4a** (3.6 g, 19.0 mmol) in CCl_4 (100 mL) was added a solution of bromine (3.2 g, 20.0 mmol) in CCl_4 (30 mL) at 0 °C. The resulting solution was stirred for 1 h, and the solvent and excess bromine were removed in vacuo. The residual brown oil was treated with 5 M solution of KOH in MeOH (5 mL) at room temperature for 3 h. The reaction mixture was quenched with water, 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 column chromatography (hexane/ethyl acetate 5:1 v/v) to give an *E*/*Z*-mixture (10:1) of **5a** (2.0 g, 7.6 mmol, 40%).

5.2.2.1. 6-Bromo-5-methyl-1-phenylhex-5-en-3-ol (5a). The starting material 5-methyl-1-phenylhex-5-en-3-ol (**4a**) was synthesized from 2-methylallylmagnesium chloride and 3-phenylpropanal.

Pale yellow oil; 10:1 mixture, data for the major isomer (*E*): ^1H NMR (500 MHz, $CDCl_3$) δ 7.30–7.27 (2H, m), 7.22–7.18 (3H, m, overlapped), 6.00 (1H, s), 3.77–3.72 (1H, m), 2.84–2.79 (1H, m), 2.72–2.66 (1H, m), 2.31–2.27 (1H, m), 2.26–2.22 (1H, m), 1.83–1.74 (2H, m, overlapped), 1.80 (3H, s), 1.60 (1H, br); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.7, 138.6, 128.4, 128.4, 125.9, 103.7, 68.1, 46.4, 38.6, 32.0, 19.3; IR (ZnSe) 3388, 2935, 1630, 1603, 1495, 1454,

1288, 1163, 1053, 698 cm^{-1}. Found: C, 57.86; H, 6.46%. Calcd for $C_{13}H_{17}BrO$: C, 58.01; H, 6.37%.

5.2.2.2. 4-Bromo-3-methyl-1-phenylbut-3-en-1-ol (5b). This compound was synthesized from 3-methyl-1-phenylbut-3-en-1-ol (**4b**), which was prepared from 2-methylallylmagnesium chloride and benzaldehyde.

Colorless oil; 7:1 mixture, data for major isomer (*E*): ^1H NMR (500 MHz, $CDCl_3$) δ 7.37–7.22 (5H, m, overlapped), 5.95 (1H, s), 4.73 (1H, dd, *J*=8.7, 4.2 Hz), 2.49 (1H, dd, *J*=14.0, 8.7 Hz), 2.40 (1H, dd, *J*=14.0, 4.2 Hz), 2.36 (1H, br), 1.82 (3H,s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.5, 138.2, 128.4, 127.7, 125.6, 104.2, 71.6, 48.0, 19.3; IR (ZnSe) 3392, 2912, 1630, 1492, 1454, 1286, 1161, 1049, 1026, 756, 696, 532 cm^{-1}. Found: C, 54.56; H, 5.57%. Calcd for $C_{11}H_{13}BrO$: C, 54.79; H, 5.43%.

5.2.2.3. (*E*)-3-(Bromomethylene)-5-phenylpentan-1-ol (*E*-5d). *E*/*Z*-Isomers of **5d** were separable.

Colorless oil; ^1H NMR (500 MHz, $CDCl_3$) δ 7.31–7.28 (2H, m), 7.24–7.19 (3H, m, overlapped), 6.05 (1H, s), 3.69 (2H, t, *J*=6.3 Hz), 2.76 (2H, t, *J*=8.2 Hz), 2.52 (2H, t, *J*=8.2 Hz), 2.34 (2H, t, *J*=6.3 Hz), 1.63 (1H, br); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.5, 141.2, 128.4, 128.3, 126.1, 104.0, 60.1, 39.3, 34.8, 33.2; IR (ZnSe) 3354, 2929, 1624, 1603, 1495, 1454, 1038, 746, 696, 563 cm^{-1}. Found: C, 56.44; H, 6.07%. Calcd for $C_{12}H_{15}BrO$: C, 56.49; H, 5.93%.

5.2.2.4. (*Z*)-3-(Bromomethylene)-5-phenylpentan-1-ol (*Z*-5d). Colorless oil; ^1H NMR (500 MHz, $CDCl_3$) δ 7.29 (2H, dd, *J*=7.5, 7.4 Hz), 7.20 (1H, t, *J*=7.4 Hz), 7.16 (2H, d, *J*=7.5 Hz), 6.03 (1H, s), 3.78 (2H, t, *J*=6.9 Hz), 2.75 (2H, t, *J*=8.0 Hz), 2.57 (2H, t, *J*=6.9 Hz), 2.45 (2H, t, *J*=8.0 Hz), 1.53 (1H, br); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.6, 140.9, 128.4, 128.3, 126.1, 104.1, 60.3, 38.3, 36.1, 34.2; IR (ZnSe) 3342, 2943, 1624, 1603, 1496, 1454, 1041, 746, 698, 561 cm^{-1}. Found: C, 56.51; H, 6.06%. Calcd for $C_{12}H_{15}BrO$: C, 56.49; H, 5.93%.

5.2.2.5. 5-Bromo-6-methyl-1-phenylhept-5-en-3-ol (15). This compound was derived from 6-methyl-1-phenylhept-5-en-3-ol (**14**), which was prepared according to the literature.[23]

Colorless oil; ^1H NMR (500 MHz, $CDCl_3$) δ 7.29–7.27 (2H, m), 7.22–7.17 (3H, m, overlapped), 4.03–3.97 (1H, m), 2.87–2.78 (2H, m, overlapped), 2.72–2.66 (1H, m), 2.55–2.51 (1H, m), 1.90 (3H, s), 1.85–1.79 (2H, m, overlapped), 1.81 (3H, s), 1.75 (1H, br); ^{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.

5.2.3. Typical procedure for the preparation of bromoalkenes with tosylamide moiety. Compounds **7a** and **7b** were prepared from an *E*/*Z*-mixture of **5a** and **5b**, respectively, where *E*-**7c** and *E*-**7d** were derived from isolated *E*-isomers of **5c** and **5d**, respectively.

To an ice-cold solution of 6-bromo-5-methyl-1-phenylhex-5-en-3-ol (**5a**, 97 mg, 0.36 mmol), PPh_3 (0.19 g, 0.72 mmol), and *N*-butoxycarbonyltosylamide (0.15 g, 0.55 mmol) in THF (10 mL) was added dropwise a toluene solution of diethyl azodicarboxylate (40 wt %, ca. 2.2 M, 0.25 mL, 0.54 mmol). The resulting mixture was stirred for 12 h at room temperature and solvents were evaporated under reduced pressure. Residual materials were treated with Et_2O and insoluble compounds were filtered. Filtrate was concentrated in vacuo and subjected to column chromatography (hexane/ethyl acetate 5:1 v/v) to give *E*-**6a** (84 mg, 0.16 mmol, 44%), *Z*-**6a** (10 mg, 0.02 mmol, 6%), and **5a** (26 mg, 0.10 mmol, 27%). *E*/*Z*-Isomers of **6b** were also separated at this step.

E-**6a** (61 mg, 0.12 mmol) was dissolved in CH_2Cl_2 (5 mL) and treated with CF_3COOH (0.09 mL, 0.13 g, 1.17 mmol) at room temperature overnight. The reaction mixture was quenched with $NaHCO_3$ aq and extracted three times with Et_2O. The extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by PTLC (hexane/ethyl acetate 3:1 v/v) to give *E*-**7a** (45 mg, 0.11 mmol, 92%). Contaminant *Z*-isomers could be removed by recrystalization (hexane/CH_2Cl_2).

5.2.3.1. (*E*)-*N*-(6-Bromo-5-methyl-1-phenylhex-5-en-3-yl)-4-methylbenzenesulfonamide (*E*-7a). White powder; mp 113 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.69 (2H, d, *J*=8.3 Hz), 7.29 (2H, d, *J*=8.3 Hz), 7.26 (2H, dd, *J*=7.5, 7.3 Hz), 7.19 (1H, t, *J*=7.3 Hz), 7.05 (2H, d, *J*=7.5 Hz), 5.85 (1H, s), 4.51 (1H, br), 3.33–3.25 (1H, m), 2.63–2.50 (2H, m), 2.43 (3H, s), 2.20 (1H, dd, *J*=13.8, 6.5 Hz), 2.14 (1H, dd, *J*=13.8, 7.4 Hz), 1.82–1.68 (2H, m), 1.40 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.5, 140.9, 137.8, 137.4, 129.7, 128.4, 128.3, 127.2, 126.0, 104.4, 51.0, 43.9, 36.6, 31.4, 21.5, 18.6; IR (ZnSe) 3278, 2924, 1599, 1495, 1456, 1325, 1157, 1092, 920, 814, 771, 700, 665, 550 cm^{-1}. Found: C, 56.76; H, 5.85; N, 3.14%. Calcd for $C_{20}H_{24}BrNO_2S$: C, 56.87; H, 5.73; N, 3.32%.

5.2.3.2. (*Z*)-*N*-(6-Bromo-5-methyl-1-phenylhex-5-en-3-yl)-4-methylbenzenesulfonamide (*Z*-7a). Colorless oil; ^1H NMR (500 MHz, $CDCl_3$) δ 7.72 (2H, d, *J*=8.2 Hz), 7.28–7.24 (4H, m, overlapped), 7.18 (1H, t, *J*=7.4 Hz), 7.07 (2H, d, *J*=7.0 Hz), 5.78 (1H, q, *J*=1.3 Hz), 4.59 (1H, br), 3.50–3.42 (1H, m), 2.69–2.63 (1H, m), 2.60–2.54 (1H, m), 2.42 (3H, s), 2.38 (1H, dd, *J*=13.6, 8.4 Hz), 2.26 (1H, dd, *J*=13.6, 6.5 Hz), 1.84–1.72 (2H, m, overlapped), 1.47 (3H, d, *J*=1.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.3, 141.1, 137.9, 137.7, 129.5, 128.4, 128.3, 127.2, 125.9, 103.9, 51.9, 39.5, 37.0, 31.5, 22.0, 21.5; IR (ZnSe) 3275, 2922, 1599, 1495, 1452, 1323, 1157, 1090, 916, 814, 700, 663, 550 cm^{-1}. HRMS (FAB^+) Found: 422.0779. Calcd for $C_{20}H_{25}BrNO_2S$ ($M+H^+$): 422.0789.

5.2.3.3. (*E*)-*N*-(4-Bromo-3-methyl-1-phenylbut-3-enyl)-4-methylbenzenesulfonamide (*E*-7b). White powder; mp 81 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.55 (2H, d, *J*=8.3 Hz), 7.17–7.14 (3H, m, overlapped), 7.16 (2H, d, *J*=8.3 Hz), 7.08–7.06 (2H, m), 5.88 (1H, s), 5.30 (1H, br), 4.37 (1H, dd, *J*=8.8, 6.3 Hz), 2.49 (1H, dd, *J*=14.1, 8.8 Hz), 2.40 (1H, dd, *J*=14.1, 6.3 Hz), 2.37 (3H, s), 1.55

(3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.1, 140.3, 137.2, 137.0, 129.4, 128.5, 127.5, 127.1, 126.3, 105.2, 55.7, 46.5, 21.4, 18.7; IR (ZnSe) 3276, 2920, 1599, 1456, 1321, 1155, 1092, 1065, 949, 812, 700, 667 cm^{-1}. Found: C, 54.80; H, 5.32; N, 3.37%. Calcd for $C_{18}H_{20}BrNO_2S$: C, 54.83; H, 5.11; N, 3.55%.

5.2.3.4. (*E*)-*N*-(4-Bromo-3-methylbut-3-enyl)-4-methylbenzenesulfonamide (*E*-7c). White powder; mp 74 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (2H, d, J=7.9 Hz), 7.33 (2H, d, J=7.9 Hz), 5.88 (1H, q, J=1.2 Hz), 4.36 (1H, d, J=6.1 Hz), 3.06 (2H, dt, J=6.1, 6.2 Hz), 2.44 (3H, s), 2.26 (2H, t, J=6.2 Hz), 1.67 (3H, d, J=1.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.6, 137.6, 136.8, 129.8, 127.1, 104.1, 40.4, 38.0, 21.5, 18.5; IR (ZnSe) 3278, 2920, 1633, 1599, 1423, 1321, 1153, 1093, 912, 814, 660, 548 cm^{-1}. Found: C, 45.00; H, 5.10; N, 4.22%. Calcd for $C_{12}H_{16}BrNO_2S$: C, 45.29; H, 5.07; N, 4.40%.

5.2.3.5. (*E*)-*N*-(3-(Bromomethylene)-5-phenylpentyl)-4-methylbenzenesulfonamide (*E*-7d). White powder; mp 72 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (2H, d, J=8.2 Hz), 7.31 (2H, d, J=8.2 Hz), 7.28 (2H, dd, J=7.4, 7.3 Hz), 7.20 (1H, t, J=7.4 Hz), 7.14 (2H, d, J=7.3 Hz), 5.92 (1H, s), 4.30 (1H, d, J=6.6 Hz), 3.03 (2H, dt, J=6.6, 6.6 Hz), 2.63 (2H, t, J=8.2 Hz), 2.41 (3H, s), 2.35 (2H, t, J=8.2 Hz), 2.21 (2H, t, J=6.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.7, 140.9, 140.8, 136.7, 129.8, 128.4, 128.3, 127.1, 126.2, 104.9, 40.6, 36.1, 34.2, 33.0, 21.5; IR (ZnSe) 3276, 2925, 1599, 1495, 1454, 1323, 1155, 1093, 814, 698, 661, 550 cm^{-1}. Found: C, 55.82; H, 5.58; N, 3.26%. Calcd for $C_{19}H_{22}BrNO_2S$: C, 55.88; H, 5.43; N, 3.43%.

5.2.4. The preparation of chloroalkenes with tosylanilide moiety. To an ice-cold solution of diisopropylamine (1.43 mL, 10.2 mmol) in THF (50 mL) was added a hexane solution of *n*-BuLi (2.55 M, 4.0 mL, 10.2 mmol). After stirring for 30 min at 0 °C, the reaction mixture was cooled to −78 °C. Chloromethyltriphenylphosphonium chloride (3.53 g, 10.2 mmol) was added and the solution was stirred for 15 min at −78 °C, 15 min at room temperature. The reaction vessel was again cooled to −78 °C and 2-aminacetophenone (0.5 mL, 0.56 g, 4.1 mmol) was added. The resulting solution was allowed to warm up to room temperature and stirred overnight. The reaction mixture was quenched by a saturated NH_4Cl solution, diluted with water, and extracted three times with Et_2O. The ethereal solution was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Residual materials were isolated with column chromatography to give *E*-**9** (0.44 g, 2.6 mmol, 63%) and *Z*-**9** (yield was not determined.). Minor *Z*-isomer *Z*-**9** was collected from several same reactions.

To a mixture of *E*-**9** (0.44 g, 2.6 mmol), 4-dimethylaminopyridine (catalytic amount), and pyridine (0.63 mL, 0.62 g, 7.8 mmol) in CH_2Cl_2 (30 mL) was added tosyl chloride (0.60 g, 3.1 mmol) at 0 °C. After stirring overnight at room temperature, the reaction was quenched with water, extracted three times with CH_2Cl_2. The combined organic layer was washed with brine, dried over $MgSO_4$. CH_2Cl_2 was evaporated in vacuo, and the product *E*-**10** (0.63 g, 75%) was isolated by column chromatography (hexane/ethyl acetate 5:1 v/v).

5.2.4.1. (*E*)-*N*-(2-(1-Chloroprop-1-en-2-yl)phenyl)-4-methylbenzenesulfonamide (*E*-10). White powder; mp 117 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (1H, d, J=8.5 Hz), 7.61 (2H, d, J=8.3 Hz), 7.26–7.29 (1H, m), 7.24 (2H, d, J=8.3 Hz), 7.07–7.10 (1H, m), 6.98 (1H, d, J=7.6 Hz), 6.50 (1H, s), 5.56 (1H, s), 2.39 (3H, s), 1.78 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.1, 136.2, 135.4, 133.5, 132.8, 129.7, 129.0, 128.9, 127.1, 125.0, 121.7, 118.6, 21.5, 18.7; IR (ZnSe) 3271, 1597, 1491, 1398, 1336, 1159, 1092, 912, 812, 758, 663, 543 cm^{-1}. Found: C, 59.64; H, 5.28; N, 4.16%. Calcd for $C_{16}H_{16}ClNO_2S$: C, 59.71; H, 5.01; N, 4.35%.

5.2.4.2. (*Z*)-*N*-(2-(1-Chloroprop-1-en-2-yl)phenyl)-4-methylbenzenesulfonamide (*Z*-10). White powder; mp 88 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (2H, d, J=8.2 Hz), 7.58 (1H, d, J=8.2 Hz), 7.29–7.26 (1H, m), 7.22 (2H, d, J=8.2 Hz), 7.15–7.12 (1H, m), 6.98 (1H, d, J=7.6 Hz), 6.54 (1H, s), 6.18 (1H, s), 2.37 (3H, s), 1.64 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.9, 136.6, 135.9, 132.7, 130.8, 129.6, 128.8, 128.0, 127.3, 125.1, 121.3, 116.3, 23.0, 21.5; IR (ZnSe) 3278, 1599, 1491, 1396, 1336, 1159, 1092, 914, 814, 758, 663, 555 cm^{-1}. Found: C, 59.53; H, 5.19; N, 4.20%. Calcd for $C_{16}H_{16}ClNO_2S$: C, 59.71; H, 5.01; N, 4.35%.

5.2.5. Typical procedure for the preparation of bromoalkenes with active methine moiety. A portion of azodicarbonyldipiperidine (0.35 g, 1.40 mmol) was added to a mixture of (*E*)-3-(bromomethylene)-5-phenylpentan-1-ol (*E*-**5d**, 0.16 g, 0.61 mmol), phenylsulfonylacetonitrile (0.17 g, 0.92 mmol), and tributylphosphine (0.31 mL, 1.23 mmol) in THF (3 mL) at room temperature. After stirring 6 h, the reaction mixture was passed through a Celite pad, and collected solids were washed with Et_2O. The filtrate was concentrated under reduced pressure and purified by column chromatography (hexane/ethyl acetate 5:1 v/v) to give (*E*)-5-(bromomethylene)-7-phenyl-2-(phenylsulfonyl)-heptanenitrile (*E*-**11d**, 0.10 g, 0.25 mmol, 41%).

5.2.5.1. (*E*)-5-(Bromomethylene)-7-phenyl-2-(phenylsulfonyl)heptanenitrile (*E*-11d). Pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (2H, d, J=8.3 Hz), 7.79 (1H, t, J=7.5 Hz), 7.66 (2H, dd, J=8.3, 7.5 Hz), 7.31–7.29 (2H, m), 7.23–7.20 (3H, m, overlapped), 6.08 (1H, s), 3.82 (1H, dd, J=10.9, 4.2 Hz), 2.77–2.72 (2H, m, overlapped), 2.61–2.55 (1H, m), 2.46–2.40 (2H, m, overlapped), 2.40–2.35 (1H, m), 2.28–2.23 (1H, m), 2.05–1.99 (1H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.4, 140.7, 135.4, 135.4, 129.7, 129.6, 128.5, 128.3, 126.3, 113.5, 105.1, 56.5, 34.2, 33.1, 32.8, 24.6; IR (ZnSe) 2924, 1496, 1448, 1331, 1155, 1084, 785, 748, 725, 687, 600 cm^{-1}. HRMS (FAB$^+$) Found: 418.0475. Calcd for $C_{20}H_{21}BrNO_2S$ (M+H$^+$): 418.0476.

5.2.5.2. (*Z*)-5-(Bromomethylene)-7-phenyl-2-(phenylsulfonyl)heptanenitrile (*Z*-11d). Pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (2H, d, J=8.6 Hz), 7.78 (1H, t, J=7.5 Hz), 7.66 (2H, dd, J=8.6, 7.5 Hz), 7.30 (2H, dd, J=7.4, 7.0 Hz), 7.21 (1H, t, J=7.4 Hz), 7.15 (2H, d, J=7.0 Hz), 6.05 (1H, s), 3.89 (1H, dd, J=10.7, 4.1 Hz), 2.77–2.70 (2H, m, overlapped), 2.57–2.47 (2H, m, overlapped), 2.43–2.35 (3H, m, overlapped), 2.11–2.03 (1H, m);

^{13}C NMR (125 MHz, $CDCl_3$) δ 141.5, 140.4, 135.5, 135.4, 129.7, 129.6, 128.6, 128.3, 126.3, 113.8, 105.2, 56.9, 37.6, 34.1, 29.8, 24.3; IR (ZnSe) 2924, 1496, 1448, 1331, 1155, 1084, 789, 748, 725, 687, 598 cm^{-1}. HRMS (FAB$^+$) Found: 418.0459. Calcd for $C_{20}H_{21}BrNO_2S$ (M+H$^+$): 418.0476.

5.2.5.3. (*E*)-6-Bromo-5-methyl-2-(phenylsulfonyl)hex-5-enenitrile (*E*-11c). White powder; mp 75 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (2H, d, J=8.1 Hz), 7.80 (1H, t, J=7.6 Hz), 7.67 (2H, dd, J=8.1, 7.6 Hz), 6.06 (1H, s), 3.85–3.82 (1H, m), 2.49–2.45 (1H, m), 2.42–2.31 (2H, m, overlapped), 2.08–2.01 (1H, m), 1.81 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.0, 135.4, 129.7, 129.6, 129.6, 113.6, 104.4, 56.4, 34.8, 24.5, 18.6; IR (ZnSe) 2922, 1633, 1583, 1448, 1331, 1155, 1084, 785, 750, 719, 687, 588 cm^{-1}. Found: C, 47.63; H, 4.47; N, 4.19%. Calcd for $C_{13}H_{14}BrNO_2S$: C, 47.57; H, 4.30; N, 4.27%.

5.2.6. Typical procedure for the preparation of bromoalkenes with a thiol moiety. To a mixture of (*E*)-3-(bromomethylene)-5-phenylpentan-1-ol (*E*-**5d**, 0.15 g, 0.59 mmol) and triphenylphosphine (0.23 g, 0.88 mmol) in THF (3 mL) was added diisopropyl azodicarboxylate (0.17 mL, 0.88 mmol) over an ice bath. After 10 min, thioacetic acid (0.06 mL, 0.88 mmol) was added and the resulting mixture was stirred for 2 h. Hexane was added to the reaction mixture, which was then filtered, concentrated, purified by column chromatography (hexane/ethyl acetate 10:1 v/v) to give (*E*)-*S*-3-(bromomethylene)-5-phenylpentyl ethanethioate (*E*-**12d**, 0.09 g, 0.30 mmol, 50%).

To a solution of *E*-**12d** (0.09 g, 0.30 mmol) in MeOH (3 mL) was added K_2CO_3 (0.25 g, 1.80 mmol) at room temperature. After 1 h, the reaction mixture was quenched by water, acidified with 1 M HCl aq, and extracted three times with Et_2O. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated in vacuo. Purification on PTLC (hexane/ethyl acetate 10:1 v/v) gave (*E*)-3-(bromomethylene)-5-phenylpentane-1-thiol (*E*-**13d**, 0.07 g, 0.27 mmol, 91%).

5.2.6.1. (*E*)-3-(Bromomethylene)-5-phenylpentane-1-thiol (*E*-13d). Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (2H, dd, J=7.4, 7.4 Hz), 7.24–7.20 (3H, m, overlapped), 6.03 (1H, s), 2.74 (2H, t, J=8.2 Hz), 2.61 (2H, dt, J=7.6, 7.4 Hz), 2.49 (2H, t, J=8.2 Hz), 2.39 (2H, t, J=7.4 Hz), 1.40 (1H, t, J=7.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.4, 141.1, 128.4, 128.3, 126.1, 104.2, 40.5, 34.4, 33.2, 22.6; IR (ZnSe) 2929, 1622, 1603, 1495, 1454, 1271, 1076, 1030, 746, 696 cm^{-1}. HRMS (FAB$^+$) Found: 271.0165. Calcd for $C_{12}H_{16}BrS$ (M+H$^+$): 271.0156.

5.2.6.2. (*Z*)-3-(Bromomethylene)-5-phenylpentane-1-thiol (*Z*-13d). Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (2H, dd, J=7.4, 7.4 Hz), 7.21 (1H, t, J=7.4 Hz), 7.16 (2H, d, J=7.4 Hz), 6.01 (1H, s), 2.74 (2H, t, J=8.0 Hz), 2.66 (2H, dt, J=7.7, 7.8 Hz), 2.57 (2H, t, J=7.8 Hz), 2.43 (2H, t, J=8.0 Hz), 1.46 (1H, t, J=7.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.6, 140.8, 128.5, 128.3, 126.2, 104.1, 38.0, 37.3, 34.1, 21.9; IR (ZnSe) 2925, 1626, 1603, 1496, 1454, 1281, 1076, 1030, 748, 698 cm^{-1}. HRMS (FAB$^+$) Found: 271.0130. Calcd for $C_{12}H_{16}BrS$ (M+H$^+$): 271.0156.

5.2.6.3. 6-Bromo-5-methyl-1-phenylhex-5-ene-3-thiol (13a). Colorless oil; 10:1 mixture, data for the major isomer (*E*): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31–7.28 (2H, m), 7.21–7.18 (3H, m, overlapped), 5.99 (1H, s), 2.98–2.91 (1H, m), 2.89–2.83 (1H, m), 2.74–2.68 (1H, m), 2.46 (1H, dd, J=13.9, 6.2 Hz), 2.31 (1H, dd, J=13.9, 8.4 Hz), 2.00–1.93 (1H, m), 1.76–1.67 (1H, m), 1.72 (3H, s), 1.50 (1H, d, J=5.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.1, 138.8, 128.4, 128.4, 126.0, 104.0, 48.1, 39.5, 37.5, 33.2, 18.6; IR (ZnSe) 2933, 1630, 1603, 1496, 1454, 1377, 1286, 1161, 1030, 748, 698 cm^{-1}. Found: C, 54.66; H, 5.87%. Calcd for $C_{13}H_{17}BrS$: C, 54.74; H, 6.01%.

5.2.6.4. 5-Bromo-6-methyl-1-phenylhept-5-ene-3-thiol (18). Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30–7.27 (2H, m), 7.21–7.18 (3H, m, overlapped), 3.31–3.25 (1H, m), 2.92–2.86 (1H, m), 2.80 (1H, dd, J=14.5, 8.2 Hz), 2.75–2.68 (2H, m, overlapped), 2.05–1.98 (1H, m), 1.91 (3H, s), 1.82 (3H, s), 1.79–1.71 (1H, m), 1.55 (1H, d, J=5.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.4, 133.3, 128.4, 128.4, 125.9, 118.9, 46.7, 39.5, 38.8, 33.5, 25.5, 21.2; IR (ZnSe) 2914, 1655, 1603, 1496, 1454, 1221, 1012, 746, 698 cm^{-1}. Found: C, 56.38; H, 6.69%. Calcd for $C_{14}H_{19}BrS$: C, 56.19; H, 6.40%.

5.3. Typical procedure of the intramolecular vinylic substitution reaction

(*E*)-*N*-(6-Bromo-5-methyl-1-phenylhex-5-en-3-yl)-4-methylbenzenesulfonamide (*E*-**7a**, 45 mg, 0.11 mmol) and NaH (4 mg, 0.16 mmol) were dissolved in DMI (1 mL) and heated at 120 °C for 1 h. The reaction was quenched by water 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 several times with water, then with brine, and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by PTLC using hexane/ethyl acetate (5:1 v/v) as an eluent. 4-Methyl-2-phenethyl-1-tosyl-2,3-dihydro-1*H*-pyrrole (**20a**, 28 mg, 0.08 mmol, 76%) was obtained as colorless oil.

Spectral data of 4-methyl-1-tosyl-2,3-dihydro-1*H*-pyrrole (**20c**)[24] and 3-methyl-1-tosyl-1*H*-indole (**21**)[25] were reported and are in accordance with the data obtained in this work.

5.3.1. 4-Methyl-2-phenethyl-1-tosyl-2,3-dihydro-1*H*-pyrrole (20a). Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (2H, d, J=8.3 Hz), 7.29 (2H, dd, J=7.5, 7.3 Hz), 7.23 (2H, d, J=8.3 Hz), 7.23–7.19 (3H, m, overlapped), 6.01 (1H, q, J=1.3 Hz), 3.68–3.63 (1H, m), 2.81–2.76 (1H, m), 2.66–2.60 (1H, m), 2.41 (3H, s), 2.35–2.28 (1H, m), 2.24–2.17 (1H, m), 2.01–1.95 (1H, m), 1.95–1.87 (1H, m), 1.61 (3H, d, J=1.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.4, 141.5, 133.4, 129.4, 128.5, 128.4, 127.7, 125.8, 124.6, 123.3, 59.9, 40.3, 37.8, 31.1, 21.6, 13.5; IR (ZnSe) 2924, 1597, 1495, 1454, 1346, 1163, 1090, 1030, 982, 814, 700, 667, 592, 548 cm^{-1}. Found: C, 70.14; H, 6.96; N, 3.90%. Calcd for $C_{20}H_{23}NO_2S$: C, 70.35; H, 6.79; N, 4.10%.

5.3.2. 4-Methyl-2-phenyl-1-tosyl-2,3-dihydro-1*H*-pyrrole (20b). White powder; mp 105 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (2H, d, J=8.1 Hz), 7.33–7.26 (5H, m,

overlapped), 7.29 (2H, d, J=8.1 Hz), 6.20 (1H, s), 4.72 (1H, dd, J=10.7, 5.7 Hz), 2.77 (1H, dd, J=16.3, 5.7 Hz), 2.43 (3H, s), 2.29 (1H, dd, J=16.3, 10.7 Hz), 1.65 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.5, 143.0, 133.8, 129.5, 128.5, 127.7, 127.4, 126.2, 124.7, 121.6, 63.2, 44.6, 21.6, 13.4; IR (ZnSe) 2916, 1597, 1495, 1350, 1163, 1090, 1030, 976, 814, 758, 700, 669, 592 cm^{-1}. Found: C, 68.79; H, 6.30; N, 4.35%. Calcd for $C_{18}H_{19}NO_2S$: C, 68.98; H, 6.11; N, 4.47%.

5.3.3. 4-Phenethyl-1-tosyl-2,3-dihydro-1*H*-pyrrole (20d). Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (2H, d, J=8.3 Hz), 7.29 (2H, d, J=8.3 Hz), 7.26 (2H, dd, J=7.3, 7.3 Hz), 7.19 (1H, t, J=7.3 Hz), 7.11 (2H, d, J=7.3 Hz), 6.09 (1H, s), 3.45 (2H, t, J=9.0 Hz), 2.69 (2H, t, J=7.6 Hz), 2.44 (3H, s), 2.34 (2H, t, J=9.0 Hz), 2.30 (2H, t, J=7.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.5, 141.2, 132.5, 129.6, 128.4, 128.1, 127.7, 126.2, 126.0, 124.8, 47.5, 33.9, 32.4, 29.8, 21.6; IR (ZnSe) 2922, 1597, 1495, 1454, 1348, 1161, 1090, 1032, 814, 700, 667, 592 cm^{-1}. HRMS (FAB$^+$) Found: 328.1378. Calcd for $C_{19}H_{22}NO_2S$ (M+H$^+$): 328.1371.

5.3.4. 3-Methyl-1-(phenylsulfonyl)cyclopent-2-enecarbonitrile (22c). White powder; mp 95 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (2H, d, J=7.5 Hz), 7.76 (1H, t, J=7.6 Hz), 7.64 (2H, dd, J=7.6, 7.5 Hz), 5.18 (1H, s), 2.94–2.90 (1H, m), 2.66–2.59 (1H, m), 2.53–2.44 (2H, m, overlapped), 1.89 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.7, 134.9, 134.7, 130.4, 129.3, 117.2, 116.5, 72.9, 36.4, 32.2, 16.8; IR (ZnSe) 1647, 1583, 1446, 1325, 1149, 1086, 725, 688, 594, 559 cm^{-1}. Found: C, 62.95; H, 5.59; N, 5.49%. Calcd for $C_{13}H_{13}NO_2S$: C, 63.13; H, 5.30; N, 5.66%.

5.3.5. 3-Phenethyl-1-(phenylsulfonyl)cyclopent-2-enecarbonitrile (22d). Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (2H, d, J=8.0 Hz), 7.73 (1H, t, J=7.5 Hz), 7.58 (2H, dd, J=8.0, 7.5 Hz), 7.33 (2H, dd, J=7.4, 7.4 Hz), 7.24 (1H, t, J=7.4 Hz), 7.19 (2H, d, J=7.4 Hz), 5.13 (1H, s), 2.97–2.91 (1H, m), 2.82 (2H, t, J=7.7 Hz), 2.75–2.65 (1H, m), 2.57–2.47 (4H, m, overlapped); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.9, 140.5, 134.9, 134.6, 130.3, 129.2, 128.5, 128.2, 126.2, 117.1, 116.2, 72.6, 35.0, 33.3, 32.6, 31.7; IR (ZnSe) 2924, 1641, 1603, 1583, 1446, 1325, 1149, 1084, 725, 688, 594 cm^{-1}. HRMS (FAB$^+$) Found: 338.1193. Calcd for $C_{20}H_{20}NO_2S$ (M+H$^+$): 338.1215.

5.3.6. 4-Methyl-2-phenethyl-2,3-dihydrothiophene (23a). Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29–7.26 (2H, m), 7.20–7.17 (3H, m, overlapped), 5.63 (1H, s), 3.76–3.70 (1H, m), 2.77 (1H, dd, J=16.0, 9.0 Hz), 2.76–2.62 (2H, m, overlapped), 2.36 (1H, dd, J=16.0, 6.4 Hz), 2.03–1.92 (2H, m, overlapped), 1.74 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.5, 131.6, 128.4, 128.3, 125.8, 116.9, 49.3, 45.9, 38.8, 34.2, 17.1; IR (ZnSe) 2924, 1603, 1496, 1454, 1383, 1074, 1030, 742, 698 cm^{-1}. HRMS (FAB$^+$) Found: 205.1076. Calcd for $C_{13}H_{17}S$ (M+H$^+$): 205.1051.

5.3.7. 4-Phenethyl-2,3-dihydrothiophene (23d). Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30–7.27 (2H, m), 7.21–7.17 (3H, m, overlapped), 5.75 (1H, s), 3.23 (2H, t, J=8.7 Hz), 2.77 (2H, t, J=8.0 Hz), 2.68 (2H, t, J=8.7 Hz), 2.42 (2H, t, J=8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.7, 136.7, 128.4, 128.3, 125.9, 117.9, 38.2, 34.5, 33.4, 32.2; IR (ZnSe) 2924, 1603, 1496, 1454, 1232, 1074, 1030, 806, 748, 698 cm^{-1}. HRMS (FAB$^+$) Found: 191.0896. Calcd for $C_{12}H_{15}S$ (M+H$^+$): 191.0895.

5.3.8. 2-Phenethyl-4-(propan-2-ylidene)thietane (24). Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22–7.19 (2H, m), 7.13–7.08 (3H, m, overlapped), 3.49–3.39 (2H, m, overlapped), 2.95–2.92 (1H, m), 2.63–2.57 (1H, m), 2.52–2.46 (1H, m), 2.11–1.97 (2H, m, overlapped), 1.45 (3H, s), 1.39 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.1, 128.4, 128.4, 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%.

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References and notes

1. Hughes, E. D.; Juliusburger, F.; Masterman, S.; Topley, B.; Weiss, J. *J. Chem. Soc.* **1935**, 1525.
2. For reviews, see: (a) Rapport, Z. *Acc. Chem. Res.* **1992**, *25*, 474; (b) Okuyama, T.; Lodder, G. *Advances in Physical Organic Chemistry*; Tidwell, T. T., Richard, J. P., Eds.; Academic: New York, NY, 2002; Vol. 37, pp 1–56; (c) Okuyama, T. *J. Synth. Org. Chem. Jpn.* **2006**, *64*, 348.
3. (a) Miller, S. I.; Yonan, P. K. *J. Am. Chem. Soc.* **1957**, *79*, 5931; (b) Miller, S. I. *Advances in Physical Organic Chemistry*; Gold, V., Ed.; Academic: New York, NY, 1968; Vol. 6, pp 185–332.
4. Kelsey, D. R.; Bergman, R. G. *J. Am. Chem. Soc.* **1971**, *93*, 1953.
5. Glukhovtsev, M. N.; Pross, A.; Radom, L. *J. Am. Chem. Soc.* **1994**, *116*, 5961.
6. (a) Lucchini, V.; Modena, G.; Pasquato, L. *J. Am. Chem. Soc.* **1995**, *117*, 2297; (b) Kim, C. K.; Hyun, K. H.; Kim, C. K.; Lee, I. *J. Am. Chem. Soc.* **2000**, *122*, 2294; (c) Bach, R. D.; Baboul, A. G.; Schlegel, H. B. *J. Am. Chem. Soc.* **2001**, *123*, 5787.
7. (a) Ochiai, M.; Oshima, K.; Masaki, Y. *J. Am. Chem. Soc.* **1991**, *113*, 7059; (b) Okuyama, T.; Takino, T.; Sato, K.; Ochiai, M. *J. Am. Chem. Soc.* **1998**, *120*, 2275; (c) Ochiai, M.; Nishi, Y.; Hirobe, M. *Tetrahedron Lett.* **2005**, *46*, 1863.
8. Shiers, J. J.; Shipman, M.; Hayes, J. F.; Slawin, A. M. Z. *J. Am. Chem. Soc.* **2004**, *126*, 6868.
9. Ando, K.; Kitamura, M.; Miura, K.; Narasaka, K. *Org. Lett.* **2004**, *6*, 2461.
10. Ito, M.; Kobayashi, M.; Koyama, T.; Ogura, K. *Biochemistry* **1987**, *26*, 4745.
11. Henry, J. R.; Marcin, L. R.; McIntosh, M. C.; Scola, P. M.; Harris, G. D., Jr.; Weinreb, S. M. *Tetrahedron Lett.* **1989**, *30*, 5709.

12. Grainger, R. S.; Owoare, R. B. *Org. Lett.* **2004**, *6*, 2961.
13. Lai, J.-Y.; Yu, J.; Hawkins, R. D.; Falck, J. R. *Tetrahedron Lett.* **1995**, *36*, 5691.
14. Moree, W. J.; van der Marel, G. A.; Liskamp, R. J. *J. Org. Chem.* **1995**, *60*, 5157.
15. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03, Revision C.02*; Gaussian: Wallingford, CT, 2004.
16. (a) Becke, A. D. *J. Chem. Phys.* **1992**, *96*, 2155; (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.
17. (a) Onsager, L. *J. Am. Chem. Soc.* **1936**, *58*, 1486; (b) Wong, M. W.; Frisch, M. J.; Wiberg, K. B. *J. Am. Chem. Soc.* **1991**, *113*, 4776.
18. (a) Fukui, K. *Acc. Chem. Res.* **1981**, *14*, 363; (b) Gonzalez, C.; Schelegel, H. B. *J. Chem. Phys.* **1989**, *90*, 2154; (c) Gonzalez, C.; Schelegel, H. B. *J. Phys. Chem.* **1990**, *94*, 5523.
19. (a) Bauschlicher, C. W., Jr.; Partridge, H. *J. Chem. Phys.* **1995**, *103*, 1788; (b) Scott, A. P.; Radom, L. *J. Phys. Chem.* **1996**, *100*, 16502.
20. For the theoretical study on the intramolecular addition–elimination reaction of dihaloalkenes, see: Ando, K. *J. Org. Chem.* **2004**, *69*, 4203.
21. (a) Yanagisawa, H.; Miura, K.; Kitamura, M.; Narasaka, K.; Ando, K. *Helv. Chim. Acta* **2002**, *85*, 3130; (b) Yanagisawa, H.; Miura, K.; Kitamura, M.; Narasaka, K.; Ando, K. *Bull. Chem. Soc. Jpn.* **2003**, *76*, 2009; (c) Ando, K. *J. Org. Chem.* **2006**, *71*, 1837 and references cited therein.
22. Yong, K. H.; Lotoski, J. A.; Chong, J. M. *J. Org. Chem.* **2001**, *66*, 8248.
23. Cheng, H.-S.; Loh, T.-P. *J. Am. Chem. Soc.* **2003**, *125*, 4990.
24. Åhman, J.; Somfai, P. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1079.
25. Yamane, M.; Kubota, Y.; Narasaka, K. *Bull. Chem. Soc. Jpn.* **2005**, *78*, 331.