Intramolecular Cyclization Reaction *via* a Sterically Protected Episelenonium Ion Intermediate

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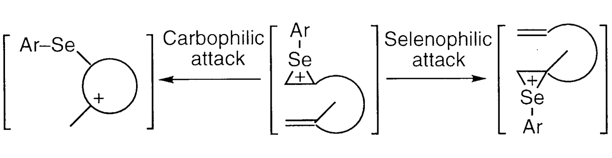
Steric protection of the selenium atom in the episelenonium ion intermediate by the bulky 2,4,6-tri-*tert*-butylphenyl (TTBP) group has been utilized in the selective formation of carbocyclic compounds from the substrate bearing a β-oxyselenide unit and a double bond in the same molecule.

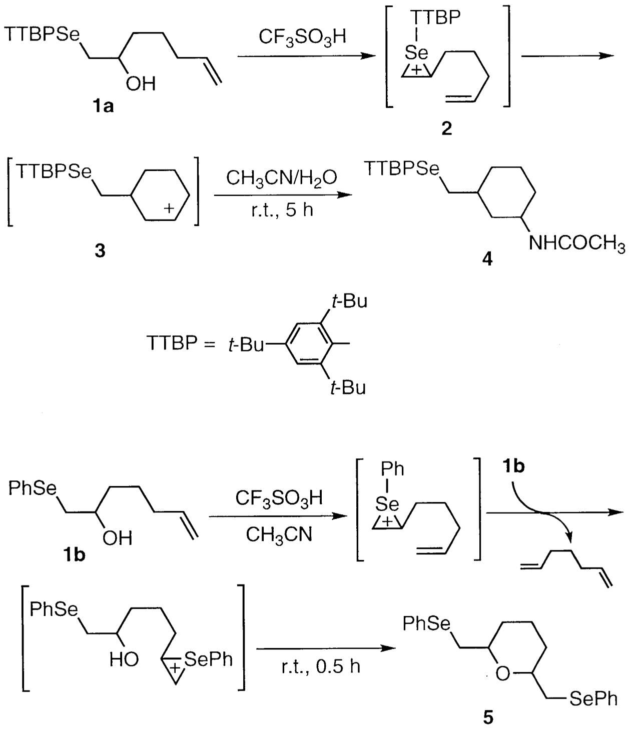
We have already reported that steric protection of the selenium atom in the episelenonium ion intermediate by the bulky 2,4,6-tri-*tert*-butylphenyl (TTBP) group prevents selenophilic attack by nucleophiles.[1] As a result, racemization of the chiral carbon in the three-membered ring is suppressed and carbon–carbon bond formation products are obtained selectively by reactions with carbon nucleophiles such as alkenyl silyl ethers, allyltrimethylsilane, and trimethylsilyl cyanide. These findings lead us to the working hypothesis that this steric protection is also effective in preventing a kinetically favored intramolecular selenophilic attack by a double bond which would induce migration of the arylseleno group to the double bond (Scheme 1). We report herein that, in a reaction *via* the intermediate bearing the protected episelenonium ion and a double bond in the same molecule, the double bond selectively attacks the carbon atom of the ion to afford a cyclized carbocation, which is trapped by an external nucleophile or undergoes deprotonation, depending on reaction conditions. It is confirmed that, in a similar reaction without the steric protection, the traditional phenylseleno group migrates to the double bond even in an intermolecular fashon. These results represent another example of the importance of the TTBPSe group in organoselenium chemistry.

Scheme 1.



From the reaction of the olefinic alcohol **1a** bearing the TTBPSe group with trifluoromethanesulfonic acid and water in acetonitrile as solvent, the cyclohexane derivative **4** bearing the acetylamino and TTBPSe-methyl groups was produced as a mixture of stereoisomers (1:1) in 72% total yield (Scheme 2). The result indicates that the double bond attacked the carbon atom of the TTBP-bearing episelenonium ion intermediate **2** selectively, due to steric protection, to afford the cyclohexyl carbocation **3**, which was trapped by the nitrile to give the amide **4**. In order to demonstrate the cyclization of the same carbon framework without steric protection, the olefinic alcohol bearing the phenylseleno group **1b** was subjected to the same reaction conditions as described above. As shown in Scheme 2, the cyclic ether bearing two phenylseleno groups **5** was obtained, indicating that the phenylseleno group migrated to the double bond of another molecule.[2]

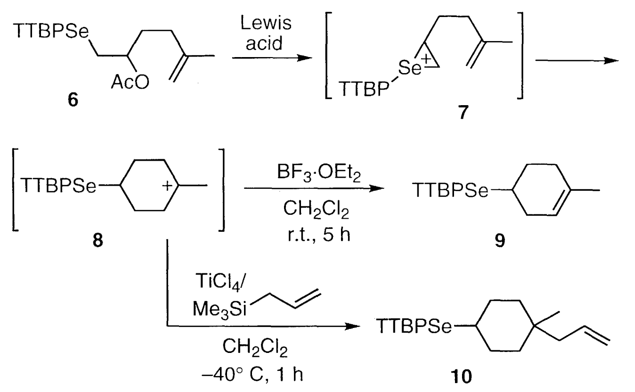
Scheme 2.



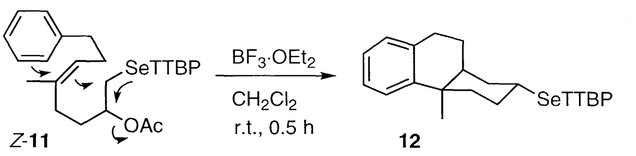
In order to examine whether the steric protection prevents the intramolecular migration of the TTBPSe group during the cyclization reaction, we carried out two types of cyclization reactions using a substrate bearing one methyl group at the double bond **6**. In the two types of reactions shown in Scheme 3, only the products from the tertiary cyclohexyl carbocation **8** were obtained; namely, the olefin **9** (80%) formed by the deprotonation of the cation and **10** (88%; as a mixture of trans and cis isomers (2.5:1)) produced by the trap of the cation with allylsilane. None of the isomers of **9** or **10** were detected among the products.[3] It should be noted that the terminal carbon atom of the double bond attacked the primary carbon atom of the episelenonium ion. The regioselectivity of ring opening of the ion is different from the usual case,[1] presumably because the formation of a six-membered ring is favored in the cyclization reaction induced by the episelenonium ion intermediate. In all reactions in Schemes 2 and 3, cyclization reactions afforded six-membered rings despite the differences in the number of carbon atoms between the episelenonium ion and the nucleophile.

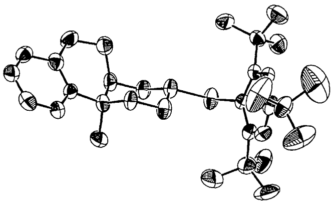
The episelenonium ion bearing the TTBP group was also utilized in the construction of a bicyclic system from the substrate *Z*- and *E*-**11**[4] bearing a β-oxyselenide unit, a double bond, and a phenyl group at suitable positions, as shown in Scheme 4. In a manner similar to the reactions shown in Scheme 3, the first cyclization reaction selectively afforded a tertiary cyclohexyl

Scheme 3.

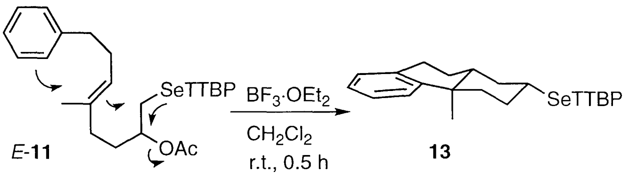


Scheme 4.





Crystal structure of **12**.[7]



carbocation which was trapped effectively by the intramolecular phenyl group, giving the bicyclic products **12** and **13**,[5] respectively, in 72% and 53% yields.[6] The TTBPSe group occupies the equatorial position of the chair cyclohexane ring in both **12** and **13** (confirmed by the coupling constants of the vicinal protons in ^{1}H NMR spectra in combination with X-ray crystallographic analysis[7]) as a result of the trans ring-opening of the episelenonim ion intermediate by the double bond. The selective formation of the cis-fused bicyclic system **12** from *Z*-**11** and the trans-fused system **13** from *E*-**11** can be explained by the anti addition of the episelenonium ion and the phenyl group to the double bond.

As shown in typical examples, the TTBPSe group is valuable in the selective construction of cyclic compounds induced by the episelenonium ion intermediate.

References and Notes

1 A. Toshimitsu, K. Nakano, T. Mukai, and K. Tamao, *J. Am. Chem. Soc.*, **118**, 2756 (1996).

2 The migration of the phenylseleno group to the carbon atom of other (intra- or inter-molecular) double bond has been reported: See for example; T. Kametani, H. Kurobe, and H. Nemoto, *J. Chem. Soc., Perkin Trans. 1,* **1981**, 756; W. P. Jackson, S. V. Ley, and J. A. Morton, *Tetrahedron Lett.*, **22**, 2601 (1981); F. Rouessac and H. Zamarlik, *Tetrahedron Lett.*, **22**, 2643 (1981); A. Rouessac and F. Rouessac, *Tetrahedron*, **37**, 4165 (1981); T. Kametani, H. Kurobe, H. Nemoto, and K. Fukumoto, *J. Chem. Soc., Perkin Trans. 1,* **1982**, 1085; A. Toshimitsu, T. Kusumoto, and S. Tanimoto, *Bull. Inst. Chem. Res., Kyoto Univ.*, **70**, 270 (1992).

3 This result seems to indicate that the TTBPSe group does not migrate to the other double bond during the reaction. However, the possibility of the migration has not yet been completely ruled out, since it is possible that, under the equilibrium of two episelenonium ion intermediates (**7** and its isomer), only **7** affords the cyclized product due to the stability of tertiary carbocation.

4 Starting materials *Z*- and *E*-**11** were prepared by the Wittig reaction using triphenyl(3-phenylpropyl)phosphonium chloride and 5-acetoxy-6-(2,4,6-tri-*tert*-butylphenylseleno)-2-hexanone. The *E* and *Z* isomers were separated by medium pressured column chromatography and assigned by the NOE measurement.

5 The bicyclic product from each substrate was confirmed to consist of one stereoisomer. Their ^{13}C NMR (67.94 MHz) spectra are as follows: **12**; 25.2(t), 26.7(q), 29.2(t), 30.3(t), 31.3(q), 33.1(q), 34.5(t), 34.8(s), 36.6(s), 37.9(t), 39.0(s), 41.5(d), 44.9(d), 121.8(d), 125.2(d), 125.8(d), 126.1(s), 126.6(d), 128.9(d), 135.5(s), 146.2(s), 148.9(s), and 155.2(s); **13**; δ 21.8(q), 25.4(t), 28.4(t), 29.2(t), 31.4(q), 33.1(q), 34.8(t), 34.9(s), 36.5(s), 38.7(t), 39.0(s), 43.1(d), 47.3(d), 121.7(d), 124.5(d), 125.4(s), 125.5(d), 128.3(d), 129.2(d), 135.3(s), 147.4(s), 149.1(s), and 155.5(s).

6 Side products were monocyclic olefins formed by the deprotonation of the cation. Total yields of the regioisomeric olefins were 18% from *Z*-**11** and 35% from *E*-**11**, tetra-substituted olefin being the major isomer in both cases.

7 Crystals of **12** were obtained by recrystallization from 2-propanol. The result of the X-ray crystallographic analysis in Scheme 4 was drawn at the 30% probability level. All hydrogen atoms are omitted for clarity.