Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron Letters 45 (2004) 6137–6139
Tetrahedron Letters

Stereospecific carbon–carbon bond formation by the reaction of a chiral episelenonium ion with aromatic compounds

Kazuki Okamoto,[a] Yoshiaki Nishibayashi,[a] Sakae Uemura[a] and Akio Toshimitsu[b,*]

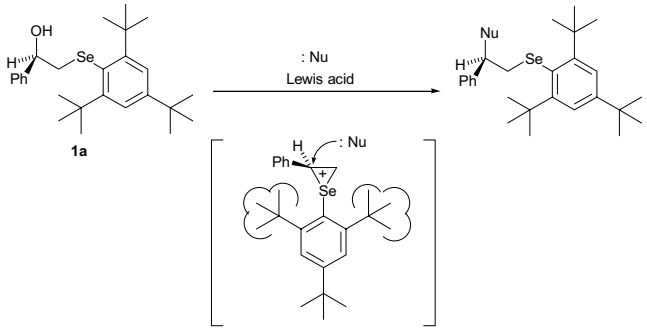
[a]*Department of Energy and Hydrocarbon Chemistry, Graduate School of Engineering, Kyoto University, Yoshida, Sakyo-ku, Kyoto 606-8501, Japan*
[b]*International Innovation Center, Kyoto University, Yoshida, Sakyo-ku, Kyoto 606-8501, Japan*

Received 30 April 2004; revised 9 June 2004; accepted 11 June 2004
Available online 2 July 2004

Abstract—The stereospecific exchange of a hydroxyl group of chiral alcohols bearing a pyridylseleno group on the adjacent carbon atom with aromatic compounds occurred smoothly in the presence of Lewis acid.

Organic reactions via three-membered episelenonium ion intermediate have been widely used in organic syntheses.[1] Most of the examples have been concerned with the reactions of an episelenonium ion intermediate with oxygen- and nitrogen-centered nucleophiles[2] and much less attention has been paid to the reaction with carbon-centered nucleophiles.

Recently we have succeeded in the stereospecific carbon–carbon bond formation by the reactions of a chiral episelenonium ion (an episelenonium ion bearing a chiral carbon in the three-membered ring) with carbon-centered nucleophiles such as alkenyl silyl ethers, trimethylsilyl cyanide, and allyltrimethylsilane by the use of a 2,4,6-tri-*tert*-butylphenylseleno (TTBPSe) group,[3] the role of *tert*-butyl groups being the steric protection of the selenium atom to prevent both the racemization of the chiral carbon atom and the attack of carbon-centered nucleophiles on the selenium atom (Scheme 1).[4] In order to find a new aspect of this chemistry, we have now investigated the reaction of a chiral episelenonium ion with aromatic compounds such as carbon nucleophiles. As a result, we found that (1) a carbon–carbon bond forming reaction proceeds even without the steric protection of the selenium atom, and (2) when a 2-pyridyl group is employed as the substituent on the selenium atom, stereospecificity of the reaction depends greatly on the reactivity of aromatic compounds.

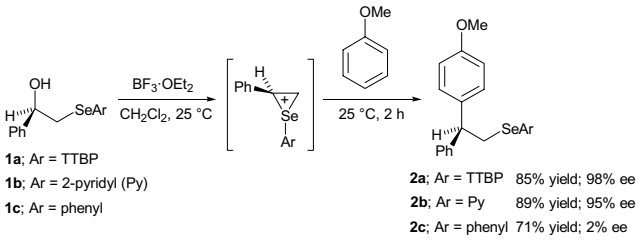


Scheme 1. Reaction of a chiral alcohol bearing a TTBPSe group on the adjacent carbon atom (**1a**) with carbon-centered nucleophile (:Nu) in the presence of Lewis acid.

By the reaction of a chiral alcohol bearing a phenylseleno group on the adjacent carbon atom (**1c**) (>99% ee) with anisole in the presence of trifluoroborane–diethyl ether (Scheme 2), substitution of a hydroxyl group by the aromatic carbon proceeded to afford **2c** in high yield. It should be noted that the substitution occurred selectively at the *para*-position of anisole. Enantiomeric excess of **2c**, on the other hand, was found to be only 2%. These results indicate that the aromatic carbon attacks selectively on the carbon atom of the episelenonium ion bearing a phenyl group on the selenium atom, while the chiral carbon in the episelenonium ion racemizes almost completely during the reaction.

Keywords: Stereospecific reaction.
* Corresponding author. Tel.: +81-7575-39174; fax: +81-7575-39145; e-mail: akiot@iic.kyoto-u.ac.jp

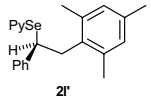
0040-4039/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2004.06.042



Scheme 2. Reactions of chiral alcohols bearing various arylseleno groups on the adjacent carbon atom (**1**) with anisole (10 equiv) in the presence of $BF_3{\cdot}OEt_2$ (10 equiv).[5]

When a chiral alcohol bearing a 2-pyridylseleno group (**1b**) (>99% ee) was used as substrate, the corresponding substituted product (**2b**) was obtained in 89% yield. The enantiomeric excess of **2b** was found to be 95%. It has already been reported that the racemization of the chiral carbon in the episelenonium ion was retarded greatly by changing the substituent on the selenium atom from phenyl to 2-pyridyl group.[6] As expected, the reaction of a chiral alcohol bearing a TTBPSe group on the adjacent carbon atom (**1a**) with anisole afforded the corresponding substituted product (**2a**) in 85% yield with 98% ee.

In order to know the reason for the slight loss of optical purity during the reaction of a chiral episelenonium ion bearing a 2-pyridyl group with anisole described above, the reaction of **1b** with a variety of aromatic compounds was investigated in detail. Typical results are shown in Table 1. The reactions of **1b** with azulene and ferrocene proceeded smoothly to give the corresponding substituted products (**2d** and **2e**) in good yields without the loss of optical purity (runs 1 and 2). By the reaction of **1b** with heterocyclic aromatic compounds such as 2-methylfuran and 2-methylthiophene, the corresponding substituted products (**2f** and **2g**[7]) were obtained in high yields with a slight loss of optical purity (runs 3 and 4). The reactions of **1b** with 1,4-dimethoxybenzene and 1,3,5-trimethoxybenzene were also accompanied by a partial racemization (runs 5 and 6). However, the reactions of **1b** with less reactive aromatic compounds such as toluene, *p*-xylene, and 1,3,5-trimethylbenzene afforded the corresponding substituted products (**2j–l**) in moderate yields with low enantiomeric purity (runs 7–9). Thus, enantiomeric purity of the chiral carbon atom of **2** was found to depend much on the electronic nature of aromatic compounds employed. It should be noted here that, in the reaction of **1b** with 1,3,5-trimethylbenzene, the products were found to be a mixture of regioisomers (**2l** and **2l′**), the ratio of isomers being 2:1.

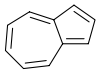
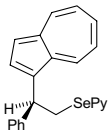
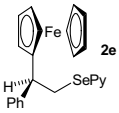
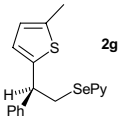
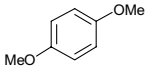
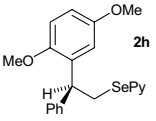
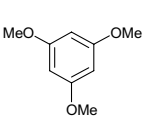
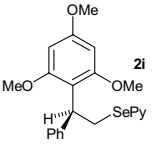
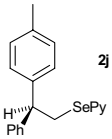
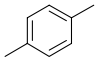
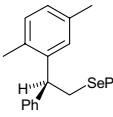
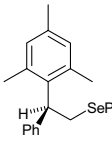


2l′

The stereochemistry of the chiral carbon atoms of the products is considered to be the retention of configuration due to the double inversion during the formation and reaction of the episelenonium ion.[3]

To our knowledge, this is the first example of the stereoselective intermolecular reaction of a chiral episelenonium ion with aromatic compounds, although a

Table 1. Reaction of a chiral alcohol bearing a 2-pyridylseleno group on the adjacent carbon atom (**1b**) with a variety of aromatic compounds (10 equiv) in the presence of $BF_3{\cdot}OEt_2$ (10 equiv)[a]

Run	Aromatic compound	Substituted product **2**	Yield of **2** (%)[b]	ee of **2** (%)[c]
1		 **2d**	51	99
2		 **2e**	27	99
3		 **2f**	66	96
4		 **2g**	87	92
5		 **2h**	66	86
6		 **2i**	66	96
7		 **2j**	35	24
8		 **2k**	49	8
9		 **2l**	57[d]	13

[a] Reactions conditions: **1b** (0.30 mmol), $BF_3{\cdot}OEt_2$ (3.00 mmol), aromatic compound (3.00 mmol), dichloromethane (15 mL) at 25 °C for 2 h under nitrogen atmosphere.
[b] Isolated yield.
[c] Determined by HPLC analysis using chiral columns, Chiralcel OJ or OD.
[d] Other regioisomer (**2l′**) was formed. The isomer ratio of **2l** and **2l′** was 2:1.

stereoselective intramolecular cyclization of the ion with benzene derivatives has been reported by Déziel et al.[8] The reaction described here may provide a new procedure for chiral compounds, which can be used for the preparation of chiral hydrocarbons bearing an aryl group at the asymmetric carbon atom with the predictable configuration. Moreover, our findings should provide a new opportunity to elucidate the mechanism of the racemization of the chiral carbon in episelenonium ion intermediates and to develop a new methodology for the synthetically important carbon–carbon bond forming reactions. Further work is currently in progress aiming at the elucidation of the reaction mechanism and broading the scope of asymmetric synthesis.

Acknowledgements

This work was supported by Grant-in Aid for Scientific Research (No. 14044047) from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

References and notes

1. Wirth, T. *Angew. Chem., Int. Ed.* **2000**, *39*, 3741.
2. For examples, see: (a) Tomoda, S.; Iwaoka, M. *Chem. Lett.* **1988**, 1895; (b) Mihelich, E. D. *J. Am. Chem. Soc.* **1990**, *112*, 8995; (c) Lipshutz, B. H.; Barton, J. C. *J. Am. Chem. Soc.* **1992**, *114*, 1084; (d) Mihelich, E. D.; Hite, G. A. *J. Am. Chem. Soc.* **1992**, *114*, 7318; (e) Déziel, R.; Goulet, S.; Grenier, L.; Bordeleau, J.; Bernier, J. *J. Org. Chem.* **1993**, *58*, 3619; (f) Wirth, T. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1726; (g) Lipshutz, B. H.; Gross, T. *J. Org. Chem.* **1995**, *60*, 3572; (h) Déziel, R.; Malenfant, E. *J. Org. Chem.* **1995**, *60*, 4660; (i) Fukuzawa, S.; Takahashi, K.; Kato, H.; Yamazaki, H. *J. Org. Chem.* **1997**, *62*, 7711; (j) Takada, H.; Nishibayashi, Y.; Uemura, S. *J. Chem. Soc., Perkin Trans. 1* **1999**, *1*, 1511; (k) Back, T. G.; Moussa, Z.; Parvez, M. *J. Org. Chem.* **2002**, *67*, 499; (l) Tiecco, M.; Testaferri, L.; Santi, C.; Tomassini, C.; Marini, F.; Bagnoli, L.; Temperini, A. *Chem. Eur. J.* **2002**, *8*, 1118; (m) Uehlin, L.; Fragale, G.; Wirth, T. *Chem. Eur. J.* **2002**, *8*, 1125; (n) Tiecco, M.; Testaferri, L.; Santi, C.; Tomassini, C.; Marini, F.; Bagnoli, L.; Temperini, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 3131.
3. (a) Toshimitsu, A.; Nakano, K.; Mukai, T.; Tamao, K. *J. Am. Chem. Soc.* **1996**, *118*, 2756; (b) Toshimitsu, A.; Terada, M.; Tamao, K. *Chem. Lett.* **1997**, 733.
4. (a) Clive, D. L. J.; Chittattu, G.; Wong, C. K. *J. Chem. Soc., Chem. Commun.* **1978**, *0*, 441; (b) Rouessac, F.; Zamarlik, H. *Tetrahedron Lett.* **1981**, *22*, 2643; (c) Ley, S. V.; Lygo, B.; Moliness, H.; Morton, J. A. *J. Chem. Soc., Chem. Commun.* **1982**, 1251; (d) Alexander, R. P.; Paterson, I. *Tetrahedron Lett.* **1983**, *24*, 5911.
5. The enantiomeric excess of products slightly decreased when less than 10 equiv of Lewis acid was used.
6. Toshimistu, A.; Ito, M.; Uemura, S. *J. Chem. Soc., Chem. Commun.* **1989**, 530.
7. A typical procedure is as follows. To a solution of (*R*)-2-pyridylseleno-1-phenylethanol (**1b**; 84 mg, 0.30 mmol; >99% ee) and thiophene (295 mg, 3.00 mmol) in dichloromethane (15 mL) was added trifluoroborane–diethyl ether complex (0.90 mL, 3.00 mmol) at 25 °C under nitrogen atmosphere, and then the resulting mixture was stirred at 25 °C for 2 h. The mixture was then quenched with water (10 mL) and extracted with dichloromethane (20 mL × 3). The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, and then concentrated under reduced pressure. Purification of the residue by column chromatography gave **2g** as a pale yellow oil (94 mg, 0.26 mmol; 87% yield; 92% ee). Selected spectroscopic data for **2g**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.40 (3H, s), 3.87 (2H, dd, $J = 7.8$, 2.1 Hz), 4.52 (1H, dd, $J = 7.8$ Hz), 6.57 (1H, d, $J = 3.0$), 6.69 (1H, d, $J = 3.0$), 7.03 (1H, t, $J = 6.0$), 7.21–7.31 (7H, m), 7.41 (1H, t, $J = 7.5$), 8.46 (1H, d, $J = 4.5$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.3, 32.6, 47.4, 120.3, 124.3, 124.6, 125.7, 127.0, 127.7, 128.5, 136.2, 138.5, 143.6, 145.4, 149.6, 155.0 (Found: C, 60.5; H, 4.8; N, 3.9. $C_{18}H_{17}NSSe$ requires C, 60.3%; H, 4.8%; N, 3.9%); $[\alpha]_D$ −22.8 (c 0.5, $CHCl_3$). Enantiomeric excess was determined by HPLC analysis with a Daicel Chiralcel OJ column (eluent: hexane–propan-2-ol = 90:10).
8. Déziel, R.; Malenfant, E.; Thibault, C. *Tetrahedron Lett.* **1998**, *39*, 5493.