Pergamon

Tetrahedron Letters 42 (2001) 1559–1562

TETRAHEDRON LETTERS

Asymmetric methoxyselenenylation of alkyl vinyl ethers: a new route to chiral acetals

Masahiko Uchiyama,* Shinya Satoh and Akihiro Ohta

School of Pharmacy, Tokyo University of Pharmacy and Life Science, 1432-1 Horinouchi, Hachioji, Tokyo 192-0392, Japan

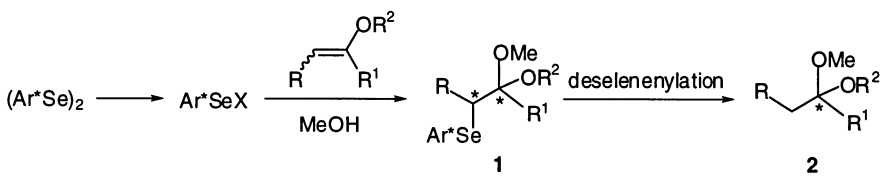
Received 13 November 2000; revised 30 November 2000; accepted 8 December 2000

Abstract—The asymmetric methoxyselenenylation of alkyl vinyl ethers afforded the corresponding chiral acetals with moderate to good diastereoselectivity. This reaction and subsequent deselenenylation provided a new method of preparing enantiomerically enriched acetals in which the acetal carbon was the only stereogenic center.

Oxyselenenylation, the addition reaction of electrophilic organoselenium compounds to alkenes in the presence of oxygen nucleophiles, is a very useful reaction in organic synthesis because it is highly stereoselective and the incorporated organoselenium moiety plays an important role in subsequent functional group manipulations.[1]

The first asymmetric variant to this reaction was reported by Tomoda and co-workers in 1988.[2] After this report, several groups have devised chiral selenium electrophiles for use in asymmetric methoxyselenenylations.[3] Many examples of the reaction using a wide variety of alkenes have also been reported. However, to our knowledge, only one example of the reaction using alkyl vinyl ethers is known,[3f,4] moreover no notice has been taken of its utility value to date.

Asymmetric methoxyselenenylation with alkyl vinyl ethers and subsequent deselenenylation could gave enantiomerically enriched acetals **2** in which the acetal carbon was the only stereogenic center (Scheme 1). Acetals **2** are suitable substrates for a more conclusive mechanistic investigation of the Lewis acid-promoted nucleophilic substitution of acetals. The mechanism of this type of reaction (S_N1 or S_N2), despite the detailed studies by several groups,[5] has not been completely established because in most of these studies the cyclic and acyclic acetals with the stereogenic centers placed away from the acetal carbon were used. In spite of this situation, only a few methods of preparing such acetals as **2** are known,[6,7] and besides, the reported methods are not likely to be applicable to the preparation of varied acetals. For example, Davies and co-workers synthesized some acetals (**2**, R = Ar, R^1 = H, R^2 = Pr^i) using enantiopure (*o*-substituted benzaldehyde) chromium tricarbonyl complexes, and investigated the stereospecificity of their nucleophilic substitution reactions with Me_2CuLi–$BF_3{\cdot}OEt_2$.[5l] However, the acetals used in their study were limited to the benzaldehyde derivatives. Therefore, we undertook to synthesize various types of enantiomerically enriched acetals **2** using the method as shown in Scheme 1. In this paper, we report the asymmetric methoxyselenenylation of alkyl vinyl ethers and its first application to the preparation of an enantiomerically enriched acetal whose acetal carbon only is chiral.



Scheme 1.

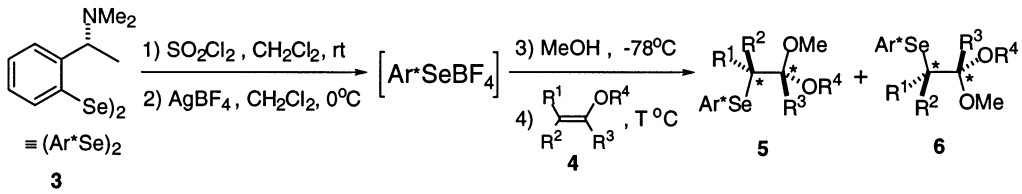
Keywords: chiral selenium compounds; asymmetric methoxyselenenylation; vinyl ethers; chiral acetals.

* Corresponding author. Tel.: +81-426-76-3037; fax: +81-426-76-3040; e-mail: uchiyama@ps.toyaku.ac.jp

0040-4039/01/$ - see front matter
PII: S0040-4039(00)02285-1

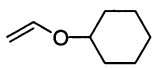
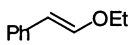
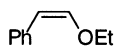
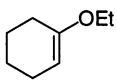
We attempted the asymmetric methoxyselenenylation of alkyl vinyl ethers using the known enantiopure diselenide **3**,[8] which could be easily prepared in a few steps from the commercially available (*R*)-(+)-*N*,*N*-dimethyl-1-phenethylamine. Diselenide **3** was converted to the corresponding electorophilic selenenyl tetrafluoroborate by successive treatment with sulfuryl chloride and silver tetrafluoroborate.[9] The resulting tetrafluoroborate intermediate was then treated with alkyl vinyl ethers **4** to give a mixture of **5** and **6** (Scheme 2). The results of the reactions with alkyl vinyl ethers **4a**–**k**[10] are summarized in Table 1.

All the reactions proceeded regioselectively to afford *anti* addition products[11] **5** and **6** as an inseparable mixture, which were fully characterized by ^{1}H and ^{13}C NMR, and low and high resolution mass spectroscopy. The diastereomeric ratios (drs) were determined by ^{1}H

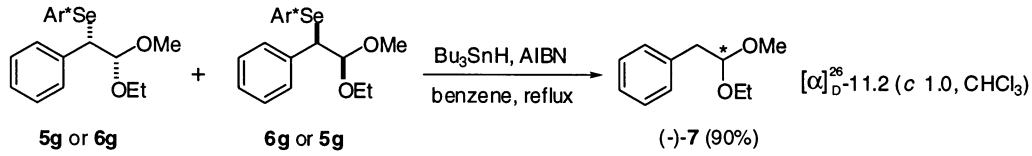


Scheme 2.

Table 1. Asymmetric methoxyselenenylation of various alkyl vinyl ethers

Entry	Substrate 4		Temp.(°C)	Products[a,b]	Yield(%)[c]	dr[d,e,f]
1		**4a**	-78	**5a** + **6a**	92	77 : 23
2		**4b**	-78	**5b** + **6b**	90	79 : 21
3		**4c**	-78	**5c** + **6c**	89	73 : 27
4		**4d**	-78	**5d** + **6d**	92	81 : 19
5		**4e**	-78	**5e** + **6e**	92	75 : 25
6		**4f**	-78	**5f** + **6f**	89	58 : 42
7		**4g**[g]	-78 → -50[h]	**5g** + **6g**	56	90 : 10
8	**4g**[g]		-78 → -20[h]	**5g** + **6g**	80	90 : 10
9		**4h**[i]	-78 → -50[h]	**5h** + **6h**	24[j]	73 : 27
10	**4h**[i]		-78 → -20[h]	**5h** + **6h**	53[j]	73 : 27
11		**4i**	-78	**5i** + **6i**	90	75 : 25
12		**4j**	-78	**5j** + **6j**	87	74 : 26
13		**4k**	-78	**5k** + **6k**	87	62 : 38

[a]Products **5** and **6** could not been separated. [b]**5** and **6** are assumed to be the *anti* addition products on the basis of literature precedents. See ref. 11. [c]Isolated yield. [d]dr = diastereomeric ratio. [e]determined by ^{1}H NMR integration. [f]It has not been established which of the diastereomers was major. [g]*E* : *Z* = 98 : 2. [h]The reaction temperature was raised because the reaction did not proceed at -78°C. [i]*E* : *Z* = > 98 : 2. [j]The products contained a small amount of **5g** or **6g** (major diastereomer in entry 8).



Scheme 3.

NMR integration of the protons of the methoxy group and/or that at the acetal carbon. However, up to now it has not been established which of the diastereomers was major. The reactions with non-substituted alkyl vinyl ethers **4a**–**e** (entries 1–5) proceeded smoothly at −78°C to provide the corresponding acetals in high yields with moderate diastereoselectivities. The alkyl groups in the alkyl vinyl ethers had only a small influence on the diastereoselectivity. Although the reaction with the 1-substituted alkyl vinyl ether **4f** also afforded the acetal products in high yields, the dr was very low (entry 6). With 2-substituted alkyl vinyl ethers **4g** and **4h**, the reactions did not proceed at −78°C. Therefore, the reaction temperature was raised to −50°C to give the corresponding acetals, but whose yields were still low (entries 7 and 9). Raising the reaction temperature further to −20°C improved the chemical yields without the deterioration of drs and the epimerization of the products (entries 8 and 10). The reaction with *trans*-β-ethoxystyrene (**4g**) gave a much better dr than that with *cis*-β-ethoxystyrene (**4h**). This relationship between the regiochemistry of the substrate and the magnitude of the diastereoselectivity is in accord with that reported for the reactions with *trans*- and *cis*-β-methylstyrene.[3a,b] With cyclic vinyl ethers **4i**–**k**, the corresponding acetals were obtained in high yields (entries 11–13). Although the diastereoselectivities in the reactions of **4i** and **4j** were moderate, that of **4k** was rather low.

We next attempted the conversion of the methoxyselenenylation adducts **5g** and **6g** to the acetal whose acetal carbon only was chiral. Treatment of a diastereomeric mixture of **5g** and **6g** (dr = 90:10 or 10:90) with *n*-Bu_3SnH in refluxing toluene afforded the acetal (−)-**7** in 90% yield (Scheme 3). The enantiomeric excess of (−)-**7** was determined to be 74% ee by ^1H NMR spectroscopic analysis upon comparison with authentic racemic **7**[12] using (*R*)-(−)-2,2,2-trifluoro-1-(anthryl)-ethanol as the chiral shift reagent.[6,13] The absolute configuration of (−)-**7** has not been yet established. Although Kirmse and co-workers refer to acetal **7** in non-racemic form in their report, the compound was not specifically purified nor was its optical purity determined.[14] Therefore, we believe that our present report is the first to disclose the practical preparation of optically active **7**.

In summary, we have demonstrated that the asymmetric methoxyselenenylation of alkyl vinyl ethers afforded the corresponding acetals in good chemical yields with moderate to good diastereoselectivity, and also that a diastereomeric mixture of **5g** and **6g** (dr = 90:10 or 10:90) was converted to acetal (−)-**7** with 74% ee. These processes provide a new method of preparing enantiomerically enriched acetals in which the acetal carbon is the only stereogenic center.

References

1. (a) Paulmier, C. *Selenium Reagents and Intermediates in Organic Synthesis*; Pergamon Press: Oxford, 1986; Chapter 7; (b) Back, T. G. In *Organoselenium Chemistry*; Liotta, D., Ed.; Wiley: New York, 1987; Chapter 1; (c) Nicolaou, K. C.; Petasis, N. A. *Selenium in Natural Products Synthesis*; CIS: Philadelphia, 1984.
2. Tomoda, S.; Iwaoka, M. *Chem. Lett*. **1988**, 1895–1898.
3. (a) Fujita, K.; Murata, K.; Iwaoka, M.; Tomoda, S. *Tetrahedron* **1997**, *53*, 2029–2048; (b) Déziel, R.; Malenfant, E.; Thibault, C.; Fréchette, S.; Gravel, M. *Tetrahedron Lett*. **1997**, *38*, 4753–4756; (c) Wirth, T.; Fragale, G. *Chem. Eur. J*. **1997**, *3*, 1894–1902; (d) Santi, C.; Fragale, G.; Wirth, T. *Tetrahedron: Asymmetry* **1998**, *9*, 3625–3628; (e) Fukuzawa, S.; Takahashi, K.; Kato, H.; Yamazaki, H. *J. Org. Chem*. **1997**, *62*, 7711–7716; (f) Back, T. G.; Nan, S. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3123–3124.
4. (a) The asymmetric methoxyselenenylation with silyl enol ethers has been reported, but the products were α-seleno ketones instead of acetals. This precedent study did not aim at the preparation of chiral acetals. See Ref. 3e; (b) The reaction with a vinylic silane has been also reported: Fragale, G.; Wirth, T. *Eur. J. Org. Chem*. **1998**, 1361–1369.
5. (a) Denmark, S. E.; Wilson, T. J.; Almstead, N. G. *J. Am. Chem. Soc*. **1989**, *111*, 9258–9260; (b) Denmark, S. E.; Almstead, N. G. *J. Am. Chem. Soc*. **1991**, *113*, 8089–8110; (c) Denmark, S. E.; Almstead, N. E. *J. Org. Chem*. **1991**, *56*, 6485–6487; (d) Sato, T.; Otera, J. *J. Organomet. Chem*. **1994**, *473*, 55–62; (e) Yamamoto, Y.; Yamada, J. *J. Chem. Soc., Chem. Commun*. **1987**, 1218–1219; (f) Sammakia, T.; Smith, R. S. *J. Am. Chem. Soc*. **1992**, *114*, 10998–10999; (g) Sammakia, T.; Smith, R. S. *J. Am. Chem. Soc*. **1994**, *116*, 7915–7916; (h) Mori, I.; Ishihara, K.; Flippin, L. A.; Nozaki, K.; Yamamoto, H.; Bartlett, P. A.; Heathcock, C. H. *J. Org. Chem*. **1990**, *55*, 6107–6115; (i) Alexakis, A.; Mangeney, P. *Tetrahedron: Asymmetry* **1990**, *1*, 477–511; (j) Matsutani, H.; Ichikawa, S.; Yaruva, J.; Kusumoto, T.; Hiyama, T. *J. Am. Chem. Soc*. **1997**, *119*, 4541–4542; (k) Matsutani, H.; Poras, H.; Kusumoto, T.; Hiyama, T. *J. Chem. Soc., Chem. Commun*. **1998**, 1259–1260; (l) Bull, S. D.; Correia, L. M. A. R. B.; Davies, S. G. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2231–2233; (m) Manju, K.; Trehan, S. *J. Chem. Soc., Chem. Commun*. **1999**, 1929–1930.
6. Davies, S. G.; Correia, L. M. A. R. B. *J. Chem. Soc., Chem. Commun*. **1996**, 1803–1804.

7. For synthesis of an optically active 1-alkoxy-2,2,2-trichloroethyl ester, see: Chênevert, R.; Desjardins, M.; Gagnon, R. *Chem. Lett*. **1990**, 33–34. For syntheses of optically active 1-alkoxyalkyl carboxylates, see: Ref. 5j. For syntheses of optically active 1-alkoxypolyfluoroalkyl sulfonates, see: Ref. 5k.
8. Wirth, T.; Kulicke, K. J.; Fragale, G. *Helv. Chim. Acta* **1996**, *79*, 1957–1966.
9. (a) Schmid, G. H.; Garratt, D. G. *J. Org. Chem*. **1983**, *48*, 4169–4172; (b) Iwaoka, M.; Tomoda, S. *J. Am. Chem. Soc*. **1996**, *118*, 8077–8084; (c) Murata, S.; Suzuki, T. *Chem. Lett*. **1987**, 849–852; (d) See Ref. 3a.
10. Vinyl ethers **4a–e** and **4j–k** were obtained from commercial sources, and some of them were distilled before use. **4f**, **4h** and **4i** were prepared according to the methods described in the literature. For **4f**, see: Hanzlik, R. P.; Hilbert, J. M. *J. Org. Chem*. **1978**, *43*, 610–614. For **4h**, see: Baldwin, J. E.; Walker, L. E. *J. Org. Chem*. **1966**, *31*, 3985–3989. For **4i**, see: Wohl, R. A. *Synthesis* **1974**, 38–39. **4g** was obtained as a mixture of *E*- and *Z*-isomers by the Wittig benzylidenation of ethyl formate and enriched to 98:2 (*E*:*Z*) by column chromatography (silica gel, hexane). Also see: Subramanyam, V.; Silver, E. H.; Soloway, A. H. *J. Org. Chem*. **1976**, *41*, 1272–1273.
11. *Anti* addition is assumed on the basis of literature precedents. (a) Kozikowski, A. P.; Sorgi, K. L.; Schmiesing, R. J. *J. Chem. Soc., Chem. Commun*. **1980**, 477–479. (b) Tiecco, M.; Testaferri, L.; Chianelli, D.; Bartoli, D. *Tetrahedron Lett*. **1989**, *30*, 1417–1420. (c) Kaye, A.; Neidle, S.; Reese, C. B. *Tetrahedron Lett*. **1988**, *29*, 2711–2714. (d) Petrzilka, M.; *Helv. Chim. Acta* **1978**, *61*, 2286–2289.
12. Tiecco, M.; Testaferri, L.; Tingoli, M.; Chianelli, D.; Bartoli, D. *Gazz. Chim. Ital*. **1987**, *117*, 423–427.
13. The enantiomeric excess was determined by recording ^{1}H NMR spectra in benzene-d_6 in the presence of 4 equivalents of (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol.
14. Kirmse, W.; Plath, P.; Schaffrodt, H. *Chem. Ber*. **1975**, *108*, 79–87.