Pergamon

Tetrahedron: *Asymmetry* 9 (1998) 547–550

TETRAHEDRON:
ASYMMETRY

Catalytic asymmetric oxyselenenylation–elimination reactions using chiral selenium compounds

Thomas Wirth,* Sara Häuptli and Michele Leuenberger

Institut für Organische Chemie der Universität Basel, St. Johanns-Ring 19, CH-4056 Basel, Switzerland

Received 7 January 1998; accepted 22 January 1998

Abstract

Only catalytic amounts of chiral selenium reagents are necessary to achieve a sequence of methoxyselenenylation and oxidative β-hydride elimination of alkenes. Performing this reaction with peroxodisulfates and various metal salts led to enantiomeric excesses of up to 75%. © 1998 Elsevier Science Ltd. All rights reserved.

1. Introduction

Very efficient and advanced methods have been established for some synthetic transformations to highly enriched stereoisomers. But only a few useful methods are known for the stereoselective functionalization of unactivated C=C double bonds. With alkenes as substrates, stoichiometric as well as catalytic reactions to optically active products remain to be investigated. Recently we developed a variety of chiral selenium compounds which can be used as efficient stoichiometric reagents for the stereoselective functionalization of alkenes.[1] Herein we report an asymmetric oxyselenenylation–elimination sequence using only catalytic amounts of these chiral selenium compounds.

In the stoichiometric addition reactions mentioned above, the electrophilic selenium triflates are generated from the corresponding diselenides. Because these reaction conditions are incompatible with a subsequent elimination, we used peroxodisulfates for the generation of the selenium electrophiles.[2] An excess of these strong oxidizing reagents is then responsible for the subsequent oxidative elimination reaction.

Electrochemical oxyselenenylation–elimination reactions have also been reported with diphenyl diselenide.[3] Furthermore it is possible to use diselenides with nitrogen-containing substituents in the catalytic conversion of alkenes to allylic ethers.[4] Very recently chiral diselenides have been investigated in catalytic oxyselenenylation–elimination sequences leading to optically active allylic ethers.[5]

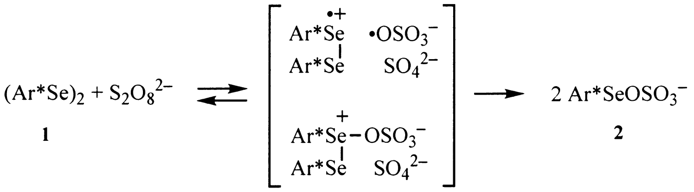
---

* Corresponding author. E-mail: wirth@ubaclu.unibas.ch

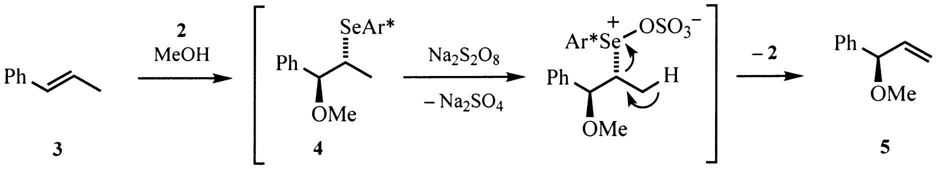
PII: S0957-4166(98)00031-7

2. Results and discussion

The selenium electrophiles are formed from the corresponding diselenides **1** by reaction with peroxodisulfates. This process can be initiated by an electron-transfer or an S_N2 process generating the selenenylsulfates as electrophilic species.[2a] It is likely that in the presence of metal ions the electron-transfer process occurs, as the metal-catalyzed decomposition to the sulfate radical anion and its subsequent chemistry has been investigated intensively.[6]



After formation of the selenenyl sulfate **2** and methoxyselenenylation of the alkene **3**, the selenide **4** is oxidized by the peroxodisulfate (or by the sulfate radical anion derived therefrom). The chiral allylic ether **5** is obtained and the selenenyl sulfate **2** is cleaved off which then can undergo the next addition reaction.

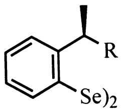


Chiral nitrogen-containing diselenides have been described as useful ligands in various transformations such as the diethylzinc additions to aldehydes[7] and asymmetric hydrosilylation reactions,[8] as well as transfer hydrogenations.[9] We are using chiral diselenides of type **1** for the catalytic oxyselenenylation–elimination reaction with *trans*-β-methylstyrene **3** as alkene.[10] First we employed the reaction conditions reported by Tomoda et al.[4a] using the various diselenides **1** in the catalytic reaction. Table 1 shows that diselenide **1a** yields the product **5** with the highest enantioselectivity (up to 56%).[11] The configuration of the main enantiomer of **5** is always *R* and was confirmed by independent synthesis.[12] Potassium peroxodisulfate seems to be superior to sodium peroxodisulfate as well as ammonium peroxodisulfate.[13]

Table 1
Addition–elimination using diselenides **1**[14]

Entry	Diselenide (10 mol %)	Yield[a] **5** [%]	*ee* **5** [%]
1	**1a**	38	50
2 [b]	**1a**	35	56
3	**1b**	9	18
4	**1c**	46	28
5	**1d**	45	27
6	**1e**	39	30

[a] Determined by GC. [b] $K_2S_2O_8$ used instead of $Na_2S_2O_8$.



	R:
1a:	NMe_2
1b:	NHMe
1c:	NEt_2
1d:	pyrrolidin-1-yl
1e:	$NH\text{-}CO\text{-}NMe_2$

Nitrogen-containing selenium compounds of type **1** and **2** can serve as ligands to metals.[7–9] Furthermore it is known that metal ions can accelerate the decomposition of peroxodisulfates.[6a] Therefore we varied the metal salt added to the reaction and found a strong influence on the stereoselectivity. We additionally found that there is no time-dependence of the enantiomeric excess of **5** during the catalytic reaction. Because of the long reaction times, even in the presence of metal salts, the reactions summarized

Table 2
Addition–elimination sequence with catalytic amounts (10 mol %) of diselenide **1a**[a]

Entry	Metal Salt (10 mol %)	*ee* **5** [%]	Entry	Metal Salt (10 mol %)	*ee* **5** [%]
1	none	51	6	$ZnSO_4$	59
2[b]	$Cu(NO_3)_2$•$3H_2O$	56	7	$PdCl_2$	65
3	$CuCl_2$	46	8	$AgNO_3$	66
4	CuCl	41	9	$Zn(NO_3)_2$•$6H_2O$	69
5	$CuSO_4$	50	10	$Ni(NO_3)_2$•$6H_2O$	71

[a] 1 mmol **3**, 1 mmol $K_2S_2O_8$, 3 ml MeOH, 200 mg molecular sieve 3 Å, r.t., 7 days.

Table 3
Addition–elimination sequence with diselenides **1** in MeOH:H_2O (10:1)[16]

Entry	Diselenide (10 mol %)	Yield[a] **5** [%]	*ee* **5** [%]
1	**1a**	30	58
2[b]	**1a**	15	16
3	**1f**	22	63
4[c]	**1f**	23	75

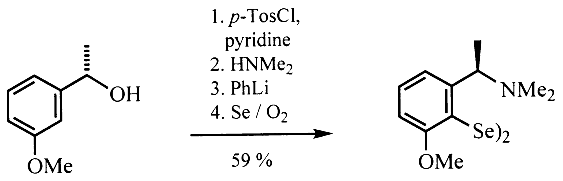
[a] Determined by GC. [b] $(NH_4)_2S_2O_8$ used instead of $K_2S_2O_8$. [c] 3 mL MeOH, 200 mg molecular sieve 3 Å, 7 d.

in Table 2 have been stopped after formation of some product and no yields are given in Table 2. Among the various metal salts investigated we found that nickel nitrate (entry 10) has the strongest influence upon the stereoselectivity, yielding product **5** in 71% *ee*.

Independent preparation of the methoxyselenenylated product **4** and treatment with potassium peroxodisulfate under the reaction conditions showed clearly that the oxidative elimination is very slow. This is probably due to the very bad solubility of peroxodisulfates in organic solvents. After dissolving the peroxodisulfate partially by addition of a small amount of water to the methanolic solution, the elimination reaction was complete within one day.

As can be seen from Table 3, the enantiomeric excess of the product **5** in water-containing catalytic reactions decreases. Using diselenide **1a** the enantiomeric excess drops from 71% *ee* (Table 2, entry 10) to 58% *ee* (Table 3, entry 1). The reasons for this are not clear at present, but with the derivative **1f** the stereoselectivity was improved to 63% *ee* (Table 3, entry 3). Catalytic reaction under anhydrous conditions, however, yielded the product **5** in 75% *ee* (Table 3, entry 4). Although the turnover numbers in the catalytic reaction described are still low, this is to our knowledge the highest enantiomeric excess reported to date for a catalytic asymmetric oxyselenenylation–elimination reaction. The additional methoxy group in the second *ortho*-position to selenium in **1f** may stabilize the selenium cations. After tosylation of the chiral alcohol **6**[15] and subsequent treatment with dimethylamine, the diselenide synthesis of **1f** via the *ortho*-lithiation route was achieved.

Depending on the reaction conditions, side products can be formed which were identified to be benzaldehyde and benzaldehyde dimethyl acetal. It is known that peroxodisulfates can cleave alkenes to aldehydes probably via the 1,2-diols.[17]



6 **1f**

Other alkenes can also be used in the catalytic addition–elimination sequence. While *trans*-β-ethylstyrene[18] gave comparable results, the stereoselectivity with indene is lower (24% *ee*) in the catalytic reaction. We already established the stoichiometric selenenylation reaction to be a useful transformation for natural product synthesis.[19] Currently we are synthesizing modified diselenides and investigating applications of the catalytic alkoxyselenenylation–elimination sequence in total synthesis.

Acknowledgements

This work was supported by the Deutschen Forschungsgemeinschaft, the Schweizer Nationalfonds and the Treubel-Fonds. We thank Prof. B. Giese for his generous support.

References

1. Wirth, T. *Angew. Chem.* **1995**, *107*, 1872–1873; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1726–1728; Wirth, T.; Fragale, G. *Chem. Eur. J.* **1997**, *3*, 1894–1902.
2. (a) Tiecco, M.; Testaferri, L.; Tingoli, M.; Chianelli, D.; Bartoli, D. *Tetrahedron Lett.* **1989**, *30*, 1417–1420; (b) Tiecco, M.; Testaferri, L.; Tingoli, M.; Bagnoli, L.; Santi, C. *J. Chem. Soc., Chem. Commun.* **1993**, 637–639; (c) Tiecco, M.; Testaferri, L.; Tingoli, M.; Bagnoli, L.; Marini, F.; Santi, C.; Temperini, A. *Gazz. Chim. Ital.* **1996**, *126*, 635–643.
3. Torii, S.; Uneyama, K.; Ono, M. *Tetrahedron Lett*. **1980**, *21*, 2653–2654; Torii, S.; Uneyama, K.; Ono, M.; Bannou, T. *J. Am. Chem. Soc*. **1981**, *103*, 4606–4608.
4. (a) Iwaoka, M.; Tomoda, S. *J. Chem. Soc., Chem. Commun*. **1992**, 1165–1167; (b) Kaur, R.; Singh, H. B.; Patel, R. P. *J. Chem. Soc., Dalton Trans.* **1996**, 2719–2726; (c) Fujita, K. *Rev. Heteroatom. Chem.* **1997**, *16*, 101–117.
5. Fujita, K.; Iwaoka, M.; Tomoda, S. *Chem. Lett.* **1994**, 923–926; Wirth, T. *Liebigs Ann./Recueil* **1997**, 2189–2196; Fukuzawa, S.; Takahashi, K.; Kato, H.; Yamazaki, H. *J. Org. Chem.* **1997**, *62*, 7711–7716.
6. (a) House, D. A. *Chem. Rev.* **1962**, *62*, 185–203; (b) Norman, R. O. C.; Storey, P. M.; West, P. R. *J. Chem. Soc. (B)* **1972**, 1087–1095.
7. Wirth, T. *Tetrahedron Lett.* **1995**, *36*, 7849–7852; Wirth, T.; Kulicke, K. J.; Fragale, G. *Helv. Chim. Acta* **1996**, *79*, 1957–1966.
8. Nishibayashi, Y.; Singh, J. D.; Segawa, K.; Fukuzawa, S.; Uemura, S. *J. Chem. Soc., Chem. Commun.* **1994**, 1375–1376; Nishibayashi, Y.; Segawa, K.; Singh, J. D.; Fukuzawa, S.; Ohe, K.; Uemura, S. *Organometallics* **1996**, *15*, 370–379.
9. Nishibayashi, Y.; Singh, J. D.; Arikawa, Y.; Uemura, S.; Hidai, M. *J. Organomet. Chem.* **1997**, *531*, 13–18.
10. Oxygen containing chiral diselenides as developed for the stoichiometric alkoxyselenenylations[1] proved to be less efficient in the catalytic reaction.
11. HPLC conditions: Chiracel OD, 2-propanol:hexane (0.01:99.99), 0.3 ml/min, 220 nm, (*R*)-**5**: t_R=31.0 min, (*S*)-**5**: t_R=40.9 min.
12. Commercially available (*R*)-1-phenyl-2-propen-1-ol was methylated: Kwart, H.; Sarner, S. F.; Slutsky, J. *J. Am. Chem. Soc.* **1973**, *95*, 5234–5242.
13. The use of $Rb_2S_2O_8$ gave no further improvement. Mackenzie, J. E.; Marshall, H. *J. Chem. Soc.* **1908**, *93*, 1726–1739.
14. 1 mmol **3**, 1 mmol $Na_2S_2O_8$, 0.1 mmol $Cu(NO_3)_2 \cdot 3H_2O$, 3 mL MeOH, 200 mg molecular sieve 3 Å, r.t., 7 days.
15. Zhao, M.; King, A. O.; Larsen, R. D.; Verhoeven, T. R.; Reider, P. J. *Tetrahedron Lett.* **1997**, *38*, 2641–2644.
16. 1 mmol **3**, 1 mmol $K_2S_2O_8$, 0.1 mmol $Ni(NO_3)_2 \cdot 6H_2O$, 3 mL MeOH:H_2O (10:1), r.t., 1 day.
17. Andreeva, L. K.; Birger, E. A.; Kheifits, L. A.; *J. Org. Chem. USSR (Engl. Trans.)* **1978**, *14*, 616; Greenspan, F. P.; Woodburn, H. M. *J. Am. Chem. Soc.* **1954**, *76*, 6345–6349.
18. Seebach, D.; Schäfer, H.; Schmidt, B.; Schreiber, M. *Angew. Chem.* **1992**, *104*, 1680–1681; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1587–1588.
19. Wirth, T.; Kulicke, K. J.; Fragale, G. *J. Org. Chem.* **1996**, *61*, 2686–2689; Wirth, T. *Liebigs Ann./Recueil* **1997**, 1155–1158; Wirth, T.; Fragale, G. *Synthesis* **1998**, in press.