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Asymmetric [2,3] Sigmatropic Rearrangement *via* Chiral Selenoxide with Sharpless Oxidants

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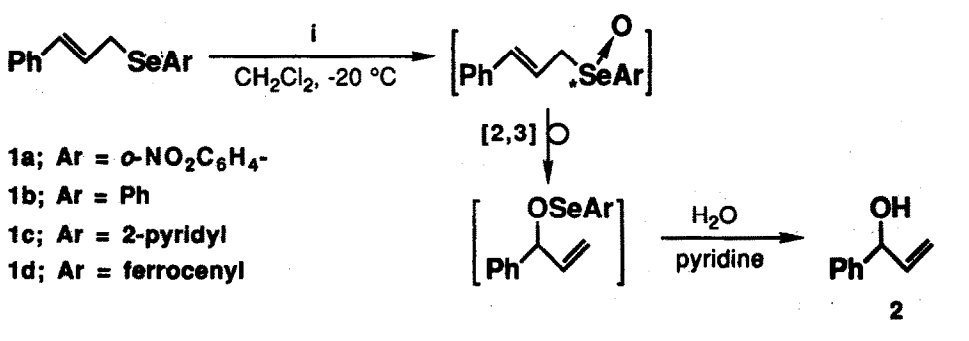
Abstract: The Sharpless oxidation of some aryl cinnamyl selenides afforded a chiral 1-phenyl-2-propen-1-ol *via* asymmetric [2,3] sigmatropic rearrangement in a moderate to high enantiomeric excess (up to 92% e.e.). The enantioselectivity was found to be enhanced remarkably by the introduction of the *o*-nitro group to an arylseleno moiety of the substrate and the use of diisopropyl tartrate (DIPT) ligand in the Sharpless oxidant. In the rearrangement step two possible transition states (TS_{exo} and TS_{endo}) are conceivable in which TS_{endo} was revealed to be more stable by 4.2 kcal/mol than TS_{exo} from the extend-Hückel calculation.

Asymmetric synthesis using organoselenium compound is of current interest and it surely presents a new trend in the field of organoselenium chemistry.[1] Although there are many reports on the isolation of chiral stable selenoxides, its application to asymmetric induction is only limited to a few examples of [2,3] sigmatropic rearrangement[2,3] and asymmetric selenoxide elimination[4] and yet only low to moderate stereoselectivities were achieved in these reactions. We now describe a facile and a highly enantioselective [2,3] sigmatropic rearrangement to afford an allylic alcohol up to 92% e.e., which is the highest value in the asymmetric reactions using organoselenium compounds, to the best of our knowledge, except for the example of asymmetric oxidation of selenides to selenoxides.[2b]

Scheme 1



1a; Ar = *o*-$NO_2C_6H_4$-
1b; Ar = Ph
1c; Ar = 2-pyridyl
1d; Ar = ferrocenyl

i, **1**: $Ti(OPr^i)_4$: tartrate: Bu^tOOH = 1 : 1 : 2 : 1.1

Aryl cinnamyl selenides (**1**) prepared from cinnamyl bromide and the corresponding diaryl diselenide[5] were oxidized with some Sharpless reagents[6] at -20 °C for 5 min (Scheme 1). After the addition of pyridine and water, the mixture was stirred at -20 °C for 15 min and then at room temperature for 6 h. The crude product was extracted with dichloromethane and purified by medium-pressure column chromatography (Kieselgel 60, eluent: 5 % ethyl acetate/hexane). The e.e. and the configuration of the product, 1-phenyl-2-propen-1-ol (**2**), was determined by HPLC using a Daicel Chiralcel OJ column and by comparison with the authentic sample prepared by the reported method.[2b,7] Typical results are summarized in Table 1.

Table 1 Asymmetric synthesis of 1-phenyl-2-propen-1-ol (**2**) by Sharpless oxidation of aryl cinnamyl selenides (**1**) in CH_2Cl_2 at -20 °C.[a]

Run	Substrate Ar	Tartrate[b]	Yield[c] (%)	e.e.[d] (%)	Config.[e]
1	a	(+)-DIPT	42	92	*R*
2	a	(+)-DCHT	35	61	*R*
3	a	(+)-DET	43	41	*R*
4	b	(+)-DIPT	41	69	*R*
5[f]	b	(+)-DIPT	21	42	*R*
6	b	(-)-DIPT	65	61	*S*
7	b	(+)-DCHT	42	43	*R*
8	b	(+)-DET	46	10	*R*
9	b	(+)-BINOL[g]	16	7	*S*
10	c	(+)-DIPT	10	31	*R*
11	d	(+)-DIPT	10	25	*R*

[a] Selenide (0.15 mmol), $Ti(OPr^i)_4$ (0.15 mmol), tartrate (0.3 mmol), *tert*-butyl hydroperoxide (0.17 mmol), CH_2Cl_2 (2 ml) in the presence of molecular sieves 4A. [b] DIPT: diisopropyl tartrate, DCHT: dicyclohexyl tartrate, DET: diethyl tartrate. [c] Isolated yield. [d] Determined by HPLC using a Daicel Chiralcel OJ column. [e] Determined by comparison with the authentic sample prepared by the reported method.[2b,7] [f] $ClCH_2CH_2Cl$ was used as solvent instead of CH_2Cl_2. [g] 2 Eq. of (+)-binaphthol was used instead of tartrate.[12]

As to the aryl groups of the substrates, they showed a remarkable effect upon the e.e. of the produced allylic alcohol **2**. The introduction of the *o*-nitro group (**a**) to an arylseleno moiety enhanced remarkably the enantioselectivity with all types of tartrate of Sharpless reagents (runs 1-3), while phenyl (**b**), 2-pyridyl (**c**), and ferrocenyl (**d**) groups gave low to moderate e.e. value. The chiral selenoxide, the key intermediate in this asymmetric induction, is easy to racemize even in the presence of a trace of moisture[1a,2] and the rate of racemization is accelerated by the acid.[1a,8] Since the titanium complex of the Sharpless oxidant tends to promote the racemization of the chiral selenoxide intermediate as a Lewis acid catalyst,[9] the following two factors of the *o*-nitro group may be considered to minimize the racemization of the selenoxide intermediate to give a high enantioselectivity.[4] One is the steric effect to stabilize the chiral selenoxide and the other is the electronic effect to accelerate the sigmatropic rearrangement.[10] However, the fact that the 2-pyridyl selenide (**1c**) having a

strong electron-withdrawing character gave lower stereoselectivity than the phenyl selenide (**1b**) eliminates the importance of the electronic factor. Namely, the large steric effect of *o*-nitro group is much important for obtaining a high enantioselectivity.

The type of a tartrate ligand of Sharpless reagent also strongly affected the stereoselectivity; the diisopropyl tartrate (DIPT) was revealed to be most effective to obtain a high e.e. (runs 1 and 4), the effectiveness being followed by dicyclohexyl tartrate (DCHT)[11] (runs 2 and 7) and diethyl tartrate (DET) (runs 3 and 8). This order may be determined by the asymmetric oxidation ability to produce a chiral selenoxide with a high e.e. as well as the Lewis acid ability to racemize the produced chiral selenoxide.[9] In the case of the substrate **1a** (runs 1-3), the e.e. values are considered to reflect the asymmetric oxidation ability of the three types of Sharpless oxidants, because the racemization of the selenoxide may be prevented by the above-mentioned substituent effect of the *o*-nitrophenyl group. Using (-)-DIPT instead of (+)-DIPT, the allylic alcohol of opposite configuration was obtained (run 6). The binaphthol, which is a useful ligand for the asymmetric oxidation of sulfide to sulfoxide,[12] was not effective in this case.

This reaction involves the following two successive asymmetric inductions; *i.e.*, asymmetric oxidation of the selenide to the selenoxide followed by the asymmetric [2,3] sigmatropic rearrangement. The following three factors are required to achieve the highly asymmetric induction to an allylic alcohol from the chiral oxidant: a highly stereoselective oxidation of the selenide to the selenoxide, a very slow racemization of the resulted chiral selenoxide intermediate, and a complete asymmetric induction from the selenoxide to an allylic alcohol *via* [2,3] sigmatropic rearrangement. Thus, in this asymmetric induction, Sharpless reagents may oxidize the selenides highly enantioselectively in the case of using DIPT as a ligand and the racemization of the resulted selenoxides is prevented by the rapid [2,3] sigmatropic rearrangement[4b,10] to some extent and almost completely by the steric effect of *o*-nitro group as discussed above. For the step of [2,3] sigmatropic rearrangement, two possible transition states may be considered.[2b] Figure 1 illustrates the two transition states (TS_{exo} and TS_{endo})[2b] for the case of the selenoxide intermediate having *S* configuration. In the TS_{exo} leading to *S* allylic alcohol, some steric interaction is expected between *ortho*-proton of the arylseleno moiety and a vinylic proton at the benzylic

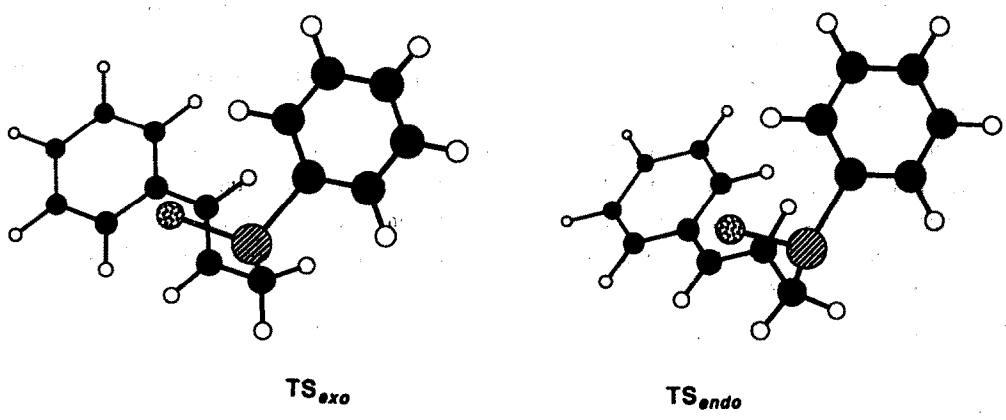


Figure 1. Possible two transition states of [2,3] sigmatropic rearrangement of the selenoxide intermediate.

position. Therefore, the TS_{endo} leading to *R* allylic alcohol may be favored conformationally. Actually, the TS_{endo} is revealed to be 4.2 kcal/mol more stable than the TS_{exo} from our extend-Hückel calculation. The steric interaction, in the case of **1a** as a substrate, was increased between the *o*-nitro group and the vinylic proton in the TS_{exo} transition state, leading to an increase of the stereoselectivity. The *R* configuration of the resulted allylic alcohol shows that the configuration of the intermediate obtained by using (+)-DIPT as a chiral auxiliary should be *S*.

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