The First Example of Asymmetric Selenoxide Elimination: Application to the Synthesis of Chiral Allenes

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The Sharpless oxidation of *o*-nitrophenyl vinyl selenides affords chiral allenes *via* asymmetric selenoxide elimination in moderate enantiomeric excess and in a good chemical yield.

Asymmetric synthesis of allenes with high optical yields is of current interest.[1] Except for a few examples,[2] however, most of the stereochemical methods have been through propynyl rearrangement, namely, the chirality in the carbon adjacent to the acetylene group was induced into the allenic skeleton. We now describe a new methodology for chiral allene synthesis *via* double asymmetric induction, asymmetric oxidation of selenide with Sharpless reagent followed by asymmetric selenoxide elimination. Although several examples of the asymmetric synthesis of stable chiral selenoxides[3] are known, there are no reports on enantioselective eliminations of chiral selenoxides.

The *o*-nitrophenyl vinyl selenides 1 (Ar = *o*-NO$_2$C$_6$H$_4$)† synthesised according to Back's method[4] were oxidized with either Sharpless[5] or modified Sharpless[6] reagent at −20 °C to

† The compounds 1a, b and c (Ar = X) are new, and all gave satisfactory spectral and combustion data. ^{1}H NMR (270 MHz, CDCl$_3$); 1a (Ar = x): δ 7.30–8.29 (8H, m), 6.56 (1H, t, *J* 7.3), 4.09 (2H, s), 2.47 (3H, s), 2.29 (2H, dt, *J* 7.3, 7.7), 1.43 (2H, tq, *J* 7.7, 7.3), 0.90 (3H, t, *J* 7.3); 1b (Ar = x): δ 7.30–8.28 (8H, m), 6.52 (1H, t, *J* 7.3), 4.10 (2H, s), 2.46 (3H, s), 2.29 (2H, q, *J* 7.3), 1.23–1.39 (10H, m), 0.86 (3H, m); 1c (Ar = x): δ 7.30–7.69 (8H, m), 7.12 (1H, s), 4.17 (2H, s), 2.48 (3H, s).

Table 1 Asymmetric synthesis of allenic sulfones^a

Run	Substrate 1 Ar	R	Conditions t/day (T/°C)	Yield^b (%)	$[\alpha]_D^{32c}$ (°)	E.e.^{d} (%)	Config.^{e}
1	x	a	16 (0)	72	-26.21^f	21	R
2^g	x	a	19 (0), 4 (room temp.)	42	$+1.75^f$	1	S
3	x	b	17 (0)	72	-16.68	18	R
4	x	c	18 (0)	78	$+12.73$	10^h	S
5^g	x	c	18 (0)	32^i	-9.22^i	16^h	R
6	y	a	1 (-20), 3 (room temp.)	73	$+1.31^f$	1	S
7	y	b	9 (0)	70	$+3.99$	2	S
8	y	c	7 (0)	86	$+3.37$	2^h	S

^{a} All the reactions were carried out in the presence of 4 Å molecular sieves except runs 2 and 5. ^{b} Isolated yield. ^{c} In CHCl$_3$. ^{d} Determined by HLPC using a Daicel Chiralcel OF column unless otherwise mentioned. ^{e} See ref. 9. ^{f} A value of $[\alpha]_D^{25}+55°$ was reported for this product.[10] ^{g} In the presence of 1 equiv. of H$_2$O to the substrate. ^{h} Determined by ^{1}H NMR using tris[heptafluoropropylhydroxy-methylene-($+$)-camphorato]europium(III). ^{i} The value for crude product.

1a; R = n-C$_3$H$_7$
1b; R = n-C$_7$H$_{15}$
1c; R = Cl

Ar = o-NO$_2$C$_6$H$_4$ (**x**) or Ph (**y**)

RCH=C=CHTs

2
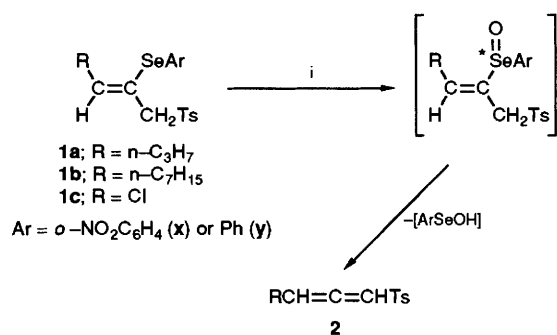
Scheme 1 *Reagents and conditions*: i, **1**: Ti(OPr^i)$_4$: ($+$)-diethyl tartrate: Bu^{t}OOH = 1:1:2:1 in CH$_2$Cl$_2$, (Ts = p-MeC$_6$H$_4$SO$_2$)

room temperature for several days in dichloromethane to afford chiral allenes **2** in moderate enantiomeric excess (e.e.) and in good chemical yields (Scheme 1). The compounds **2** were isolated and purified by column chromatography (Florisil 100–200 mesh). Typical results and reaction conditions are summarised in Table 1. The e.e. of allenic sulfones was determined by either HPLC using a Daicel Chiralcel OF column or by ^{1}H NMR using a chiral shift reagent. It was improved remarkably by the introduction of the o-nitro substituent into the phenyl moiety of the selenide as shown in Table 1. Although the exact nature of the effect of the o-nitro group is not yet clear, two possible reasons are as follows: (i) the chiral selenoxide was more stabilized by the steric effect[7] and (ii) the elimination step was accelerated by the electronic effect.[8] In the presence of water (runs 2 and 5), the reaction proceeded more slowly and the e.e. of the allenic sulfones was

lower than we expected.‡ It is worth noting, however, that the configuration of the predominant allenes was the reverse of that obtained in the absence of water (compare runs 1 and 4 with runs 2 and 5, respectively).

Further studies to find the optimum conditions for obtaining higher enantiomeric excess are now in progress.

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‡ In the asymmetric oxidation of sulfides to sulfoxides with Sharpless reagent, the stereoselectivity of the reaction was increased remarkably by the addition of the equivalent amount of water; see ref. 6. In our selenide case, however, the propensity of selenoxides to form hydrates may be a rationale for this phenomenon.