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The Organoselenium-Mediated Reduction of α,β-Epoxy Ketones, α,β-Epoxy Esters, and Their Congeners to β-Hydroxy Carbonyl Compounds: Novel Methodologies for the Synthesis of Aldols and Their Analogues

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Abstract: Novel methods for the reduction of α,β-epoxy ketones, α,β-epoxy esters (glycidic esters), and their congeners to β-hydroxy carbonyl compounds (aldols) by the use of organoselenium reagents are described. The reagents, a sodium phenylseleno(triethyl)borate complex Na[PhSeB(OEt)$_3$] easily prepared by reduction of (PhSe)$_2$ with $NaBH_4$ in EtOH and benzeneselenol (PhSeH) generated *in situ* from the borate complex by addition of acetic acid, have been demonstrated to serve as excellent reducing agents for these transformations. The organoselenium-mediated reduction of α,β-epoxy carbonyl compounds regiospecifically occurs at the α-carbon to produce a wide variety of cyclic (intramolecular) aldols as well as acyclic (intermolecular) ones in excellent yields. Quantitative mechanistic studies have revealed that the organoselenium-mediated reduction proceeds via an α-substitution process in contrast to the common electron transfer reducing agents. © 1997 Elsevier Science Ltd.

Since Sharpless reported a novel method for the conversion of epoxides to allylic alcohols by the use of an organoselenium reagent phenylselenide anion ($PhSe^-$),[1] a variety of organoselenium reagents have been prepared and widely used in organic synthesis.[2] At present, organoseleniums have been used for effecting a wide variety of synthetic transformations such as olefin synthesis via selenoxide fragmentation, carbon-carbon bond forming reactions, radical reactions, annulation reactions, [2,3]sigmatropic rearrangements, epoxidation, etc.[2] Most of organoselenium reagents have been used so far, however, for introducing selenium functionality into substrates, i.e. for *selenenylation*, and their use in the direct conversion of functionalities *without selenenylation* have not been focused, although a few examples of reductive elimination of *vic*-dihalides[3] and α-halo ketones[4] with selenium reagents have been reported.

We have investigated new synthetic reactions utilizing the remarkably soft nucleophilicity of organoselenium reagents and already reported the novel organoselenium-mediated reduction of α,β-epoxy ketones[5] and α,β-epoxy esters (glycidic esters)[6] to the corresponding β-hydroxy carbonyl compounds (aldols). These methods provide powerful tools in organic synthesis including natural product synthesis[7] since a variety of cyclic (intramolecular) aldols as well as acyclic (intermolecular) ones are obtainable in a regiospecific manner and high yields.

In this paper, we describe the organoselenium-mediated reduction methodology in detail which involves the characterization of selenium reagents, stoichiometry, the reaction mechanism, and experimental details. In connection with this research, it was necessary to clarify the structure of phenyl selenide anion generated by reduction of diphenyl diselenide (PhSe)$_2$ with $NaBH_4$ in EtOH. Therefore we set out the

structure determination of this reagent.

The Structure of the Phenylselenide Anion Generated by Reduction of $(PhSe)_2$ with $NaBH_4$ in EtOH

The reagent phenylselenide anion ($PhSe^-$) readily prepared by reduction of $(PhSe)_2$ with $NaBH_4$ in EtOH has been widely used in organic synthesis as the most common organoselenium reagent since the Sharpless protocol (Eq. 1).[1] Despite of its widespread use, however, the structure of this selenide anion had remained unclear until Liotta successfully prepared uncomplexed sodium benzeneselenolate (PhSeNa) by reduction of $(PhSe)_2$ with sodium metal in THF (Eq. 2)[8] and discovered notable discrepancies between both the reagents (Eqs. 1 and 2).[9] As a consequence, they proposed the structure of a borane complex $Na[(PhSe)BH_3]$ for the former species (Eq. 3).[8,9]

$$(PhSe)_2 + 2\,NaBH_4 \xrightarrow{EtOH} 2\,PhSe^- \qquad \text{Eq. 1}$$

$$(PhSe)_2 + 2\,Na \xrightarrow{THF} 2\,PhSeNa \qquad \text{Eq. 2}$$

$$(PhSe)_2 + 2\,NaBH_4 \xrightarrow{EtOH} 2\,Na[(PhSe)BH_3] + H_2 \qquad \text{Eq. 3}$$

However, we proved that the structure of the phenylselenide anion generated by Eq. 1 was not the borane complex $Na[(PhSe)BH_3]$ previously proposed but a sodiumphenylseleno(triethyl)borate complex $Na[PhSeB(OEt)_3]$ which is generated according to Eq. 4.[10]

$$(PhSe)_2 + 2\,NaBH_4 + 6\,EtOH \xrightarrow{EtOH} 2\,Na[PhSeB(OEt)_3] + 7\,H_2 \qquad \text{Eq. 4}$$

In order to confirm the stoichiometry, we measured a quantity of hydrogen evolved by Eq. 1 and exactly seven molar equivalents of hydrogen was captured, being consistent with Eq. 4. Fortunately, the borate complex $Na[PhSeB(OEt)_3]$ could be isolated as white solids in high yield by removal of the solvent (EtOH) and its ^1H-NMR spectrum revealed two signals due to ethoxy protons at δ 1.24 ppm (br t, J=7 Hz) and 3.70 ppm (br s, $W^1/_2$=24 Hz), respectively, besides aromatic protons. These results clearly demonstrate the structure of the triethylborate complex generated by Eq. 4. Formation of the borate complex was also supported by the notable difference between the two selenium reagents, the borate complex $Na[PhSeB(OEt)_3]$ and the uncomplexed PhSeNa, in the reduction of α,β-epoxy ketones (*vide post*).

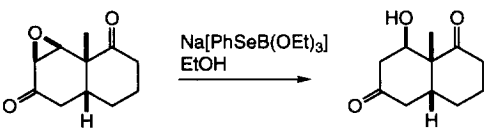
Regiospecific Reduction of α,β-Epoxy Ketones to β-Hydroxy Ketones (Aldols) by Organoselenium Reagents

Aldols have played extremely important roles in organic chemistry, *inter alia* in synthetic organic chemistry, and their synthetic importance has still been increased. Although the directed aldol reaction has made remarkable progress during the last two decades,[11] alternative synthetic methods via reductive cleavage of α,β-epoxy ketones have been focused as well because the latters provide not only intermolecular (acyclic) aldols but also intramolecular (cyclic) ones, which are often difficult to obtain by conventional aldol reactions. Hence a variety of methods and reagents for the reductive cleavage of α,β-epoxy ketones to β-hydroxy ketones have been reported.[12] Most of them have, however, a serious disadvantage of

accompanying dehydration product(s) or synthetic limitations.

We focused on the use of organoselenium reagents for this particular transformation since they act as extremely soft but potent nucleophiles. Because of non-precedents for the reduction of α,β-epoxy ketones with organoseleniums, we initially investigated the reaction of epoxy ketone **1** as a model compound (**Scheme 1**)[5]. Thus treatment of **1** with 3 equiv. of the borate complex Na[PhSeB(OEt)$_3$] in EtOH at 5 - 10 °C resulted in a rapid reaction with the formation of the β-hydroxy ketone **2** (76%) along with $(PhSe)_2$ (90%) (**Table 1**, entry 2). Since the reaction media was presumed to be basic due to alkoxides generated from $NaBH_4$ and EtOH which may cause side reactions, 0.5 equiv. of AcOH was added as a scavenger of alkoxides giving rise to 95% yield of the product (entry 3). Notably, neither selenenylated ketone nor dehydration product was formed in these reactions. Interestingly, use of 1.5 equiv. of the selenium reagent afforded a mixture of **2** (42%) and the starting material (40%), whereupon any selenenylated ketones were not detected (entry 1). On the other hand, the use of 3 equiv. of benzeneselenol (PhSeH) instead of the borate complex, *which can be conveniently generated in situ by simply adding AcOH to an ethanolic solution of the borate complex*,[13] also furnished **2** as the sole product in 95% yield (entry 4). Consequently, both the selenium reagents Na[PhSeB(OEt)$_3$] and PhSeH were found to be highly effective for the conversion of **1** into **2**.

Scheme 1



1 **2**

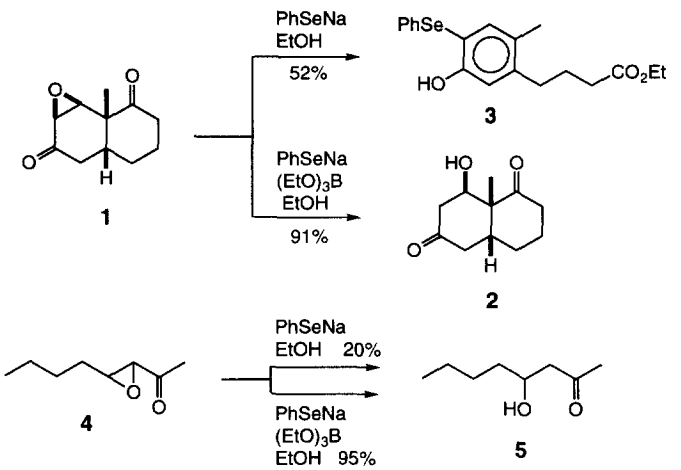
Table 1. Reduction of Epoxy Dione **1** to β-Hydroxy Dione **2**

entry	Na[PhSeB(OEt)$_3$] (equiv)	AcOH (equiv)	yield (%)
1	1.5	0	42
2	3	0	76
3	3	0.5	95
4	3	4	95

In order to get informations regarding the reaction mechanism as well as the reactive species of the organoselenium-mediated reduction, we in turn compared the behavior of two selenium reagents, the borate complex Na[PhSeB(OEt)$_3$] and uncomplexed PhSeNa prepared by Eq. 2, in the reaction of the epoxy ketone **1**.[10] As a result, the following notable discrepancy was observed between both the reactions (**Scheme 2**). The reaction of **1** with the borate complex Na[PhSeB(OEt)$_3$] in EtOH solely produced **2** in excellent yield as already described, while treatment of **1** with 3 equiv. of uncomplexed PhSeNa in EtOH yielded an unexpected aromatic compound **3**[14] as the major product (52%) and did not form the reduction product **2** at all. Although these results were rather surprising, we assumed that such difference may be due to the intermediacy of triethyl borate ($(EtO)_3B$). Indeed, addition of 3 equiv. of $(EtO)_3B$ to the latter reaction dramatically changed the reaction path and produced the β-hydroxy ketone **2** as the sole product in 91% yield (**Scheme 2**). Similarly, on treatment of acyclic epoxy ketone **4** with the combination of

uncomplexed PhSeNa and $(EtO)_3B$ in EtOH, β-hydroxy ketone **5** was exclusively formed in 95% yield exactly as the reaction with the borate complex $Na[PhSeB(OEt)_3]$ (*vide post*), whereas the use of uncomplexed PhSeNa alone resulted in a poor yield of the product (20%).[10] A lower yield of the latter reaction is probably due to the generation of sodium ethoxide which might cause side reactions such as dehydration, the retrograde aldol reaction, Michael reaction, etc. In fact, many products were observed in the latter reaction. These outcomes not only demonstrate that $(EtO)_3B$ plays a crucial role as a scavenger of ethoxide ion generated *in situ* but also support that the structure of selenide anion prepared by Eq. 1 is the borate complex $Na[PhSeB(OEt)_3]$, as already mentioned.

Scheme 2



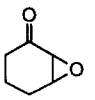
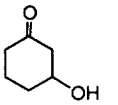
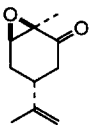
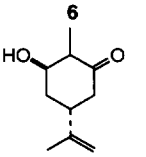
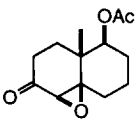
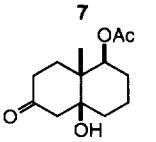
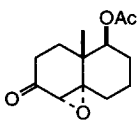
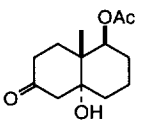
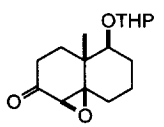
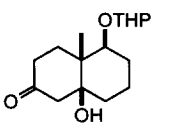
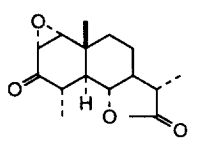
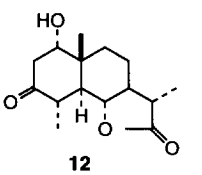
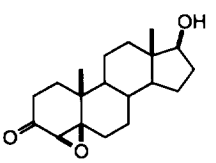
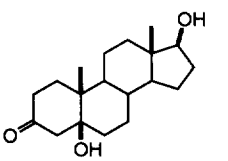
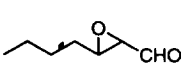
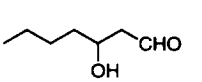
With the optimum conditions in hand, various epoxy ketones including cyclic and acylic ones were examined. The results are summarized in **Table 2**. As seen from **Table 2**, in all cases, the regioselective reduction of epoxy ketones occurred regardless of the stereochemistry and substitution pattern of an epoxide giving the corresponding aldols in excellent yields.

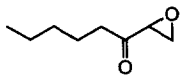
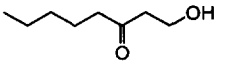
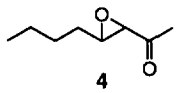
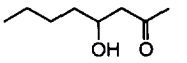
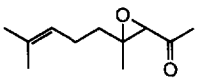
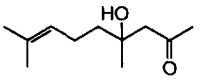
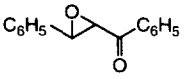
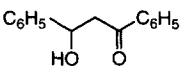
The organoselenium-mediated reduction methodology has the following synthetic advantages.

1) The reaction is very rapid and usually completed within 5-10 min at room temperature.
2) Regardless of the stereochemistry and substitution pattern of an epoxide, the reductive cleavage occurs regioselectively at the α-carbon.
3) Non- or negligible formation of enones (dehydration products).
4) A wide variety of intramolecular and intermolecular aldols bearing primary, secondary, or tertiary hydroxyl group(s) are obtainable in excellent yields.
5) Various functional groups in the substrate are compatible with the reaction conditions.
6) After the reaction, most of the selenium reagent (>90%) is recovered as $(PhSe)_2$ which is reusable.

Synthetic potential of the organoselenium-mediated reduction method is exemplified by the reductive cleavage of epoxy ketone **11** (**Table 2**, entry 6) which was employed as a key step in the synthesis of an eudesmanolide arsantin (**12**) by Yamakawa *et. al.*[15] For this particular transformation, they surveyed typical reducing agents and observed that the reduction of **11** with chromium (II) acetate gave a poor yield of the product **12** (17%) after prolonged reaction time (57 h), while the use of zinc in refluxing EtOH (1.5 h)

Table 2. Reduction of α,β-Epoxy Ketones with $Na[PhSeB(OEt)_3]$ (3 equiv) in EtOH in the Presence of AcOH (0.5 equiv).

entry	substrate	temp °C	time min	product	yield (%)[a]
1		5	10	 **6**	84
2		5	10	 **7**	82 (15)[b]
3		r t	10	 **8**	91 (5)
4		r t	10	 **9**	90 (6)
5		r t	10	 **10**	86 (6)
6	 **11**	r t	30	 **12**	92
7		r t	10	 **13**	88 (6)
8		5	10	 **14**	85

9		r t	10	 **15**	88[c]
10	 **4**	5	10	 **5**	100
11	 d)	5	10	 **16**	89
12		r t	10	 **17**	95

a) Values in parentheses show yields of an α,β-unsaturated ketone.

b) The yield was determined by ^{1}H NMR.

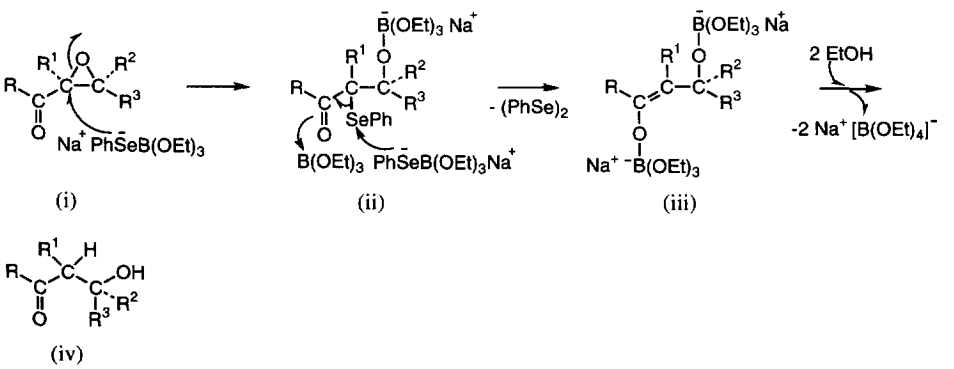
c) β-Phenylseleno substitution product was also formed in 6% yield.

d) A 11: 8 mixture of *cis*- and *trans*-epoxy ketones.

resulted in formation of a mixture of **12** (53%) and an enone (20%). Eventually they concluded that the latter conditions gave the best results. To evaluate the present method, we examined the reaction of **11** with the borate complex Na[PhSeB(OEt)$_3$] in EtOH and found that the reaction was completed in 30 min at room temperature giving rise to **12** as the single product in 92% yield (entry 6). In this case, enone was not detected at all. These results substantiate that the selenium reagent is much superior to the commonly used reducing agents such as chromium (II) and zinc in terms of the reaction time and yield.

Based on the stoichiometry of selenium reagents required for reduction, we propose the following reaction mechanism for the organoselenium-mediated reduction (**Scheme 3**). Initially, a substitution reaction occurs at the α-carbon of epoxy ketone (i) to form an α-phenylseleno ketone (ii), then the second selenium reagent attacks on the selenium atom of the α-phenylseleno substituent giving a borane enolate (iii), which is finally protonated to yield a β-hydroxy ketone (iv). As already discussed, (EtO)$_3$B plays a key role as a scavenger of ethoxide ion in these reactions. The rate-determining step is probably the initial

Scheme 3



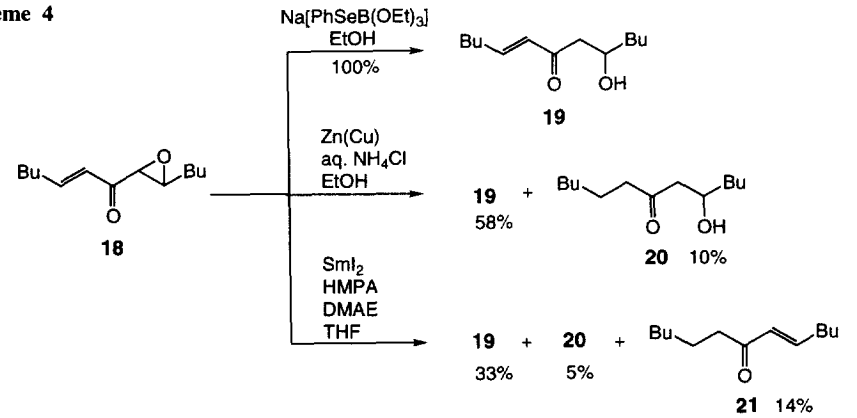
phenylseleno substitution process because any α-phenylseleno ketones were not detected in these reactions, even when less equivalent of a selenium reagent was employed only the product and the starting material were obtained (Table 1, entry 1). The proposed mechanism was eventually confirmed by the reductive cleavage of glycidic esters (*vide post*).

Chemoselective Reduction of an α,β–Epoxy Ketone Function Coexisting with an Enone System

A characteristic feature of the organoselenium-mediated reduction is that the reaction proceeds via an α-substitution process as shown in Scheme 3, which is markedly contrast to the mechanism of the electron transfer reducing agents such as chromium (II) salts, zinc, SmI_2, etc. Therefore the organoselenium-mediated reduction method should allow the chemoselective reduction of an α,β-epoxy ketone function coexisting with an enone system, which may be inaccessible with the common electron transfer reducing agents.

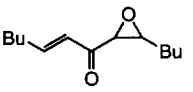
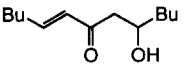
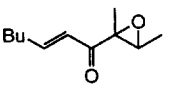
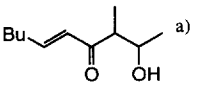
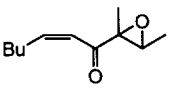
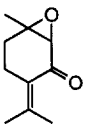
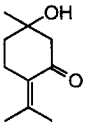
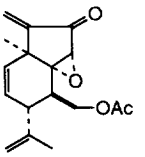
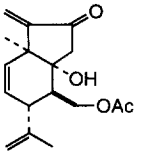
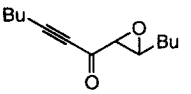
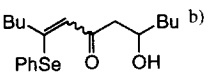
In order to probe the chemical behavior of such a system, epoxy enone **18** was chosen as a model compound and investigated under various conditions (**Scheme 4**).[16] Upon treatment of **18** with 3 equiv. of $Na[PhSeB(OEt)_3]$ in EtOH (r. t., 10 min) β-hydroxy enone **19** was formed quantitatively as expected, while reduction of **18** with Zn(Cu) / aq. NH_4Cl in EtOH (80 °C, 15 min) afforded a mixture of **19** and a saturated compound **20** in 58 and 10% yields, respectively. On the other hand, the reaction of **18** with SmI_2 / HMPA / 2-dimethylaminoethanol (DMAE) in THF yielded a mixture of **19**, **20**, and **21** in 33, 5, 14% yields, respectively. These results obviously demonstrate that the typical electron transfer reducing agents are not effective for the chemoselective reduction of an epoxy ketone function in these systems.

Scheme 4



To illustrate the generality of this method, various α,β-epoxy enones were examined and the results are summarized in Table 3. As seen from Table 3, the chemoselective reduction of an epoxy ketone moiety occurred in all cases giving the corresponding β-hydroxy enone in high yield. Under these conditions, the double bond of an enone moiety remained intact, although isomerization of a *Z*-enone to *E*-isomer was observed (entry 3). It is important to point out here that *prior to workup of the reaction passing oxygen into the reaction mixture is critical for this particular transformation* to prevent the conjugate addition of PhSeH generated by hydrolysis of the excess selenium reagent to an enone. A few minute passing through a needle from an oxygen balloon is sufficient (see Experimental). By such manipulations, the excess selenium

Table 3. Reduction of Epoxy Enones with $Na[PhSeB(OEt)_3]$ (3 equiv) in EtOH in the Presence of AcOH (0.5 equiv).

entry	substrate	time min	product (s)	yield (%)
1		10	 **19**	89
2		25	 a) **22**	83
3		25	**22**	82
4		10	 **23**	97
5		10		92
6	 **24**	15	 b) **25**	90

a) A 1 : 1 diastereoisomeric mixture.

b) A 17 : 1 mixture of *Z*- and *E*-isomers.

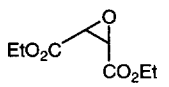
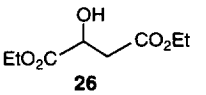
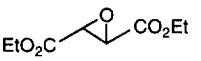
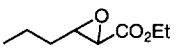
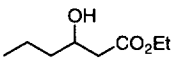
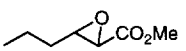
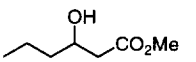
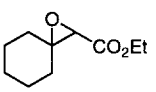
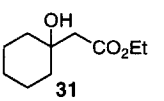
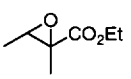
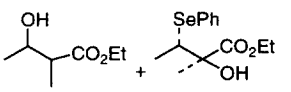
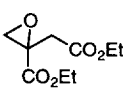
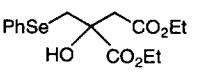
reagent is rapidly converted to inactive diphenyl diselenide. We have confirmed that aqueous workup without oxygen treatment produced a considerable amount of β-hydroxy-β'-phenylseleno ketone. This type of reactions are very useful for the synthesis of natural products. In fact, we have achieved the stereoselective total synthesis of picrotoxinin by employing the transformation of entry 5 as a key step.[7a] Interestingly, in contrast to epoxy enones, an epoxy ynone **24** was found to accompany the reduction of an epoxy ketone moiety with the conjugate addition of phenylselenide anion to the triple bond resulting in formation of **25** (*Z*- and *E*-isomers = 17 : 1) (entry 6).

Reduction of α,β-Epoxy Esters (Glycidic Esters) to β-Hydroxy Esters

In turn, the organoselenium-mediated reduction was extended to glycidic esters.[6] Although a variety of

methods and reagents for the reductive cleavage of α,β-epoxy ketones have been developed, only a limited number of reagents for that of glycidic esters are known.[12a,17] We assumed that the selenium reagents should act as reducing agents for glycidic esters as well and a number of substrates with various alkyl substituents were examined using Na[PhSeB(OEt)$_3$]. The results are summarized in Table 4.

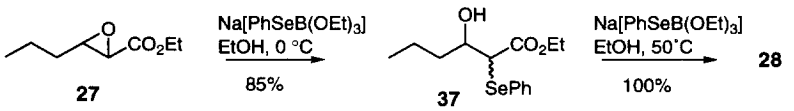
Table 4. Reduction of Glycidic Esters with Na[PhSeB(OEt)$_3$] (3 equiv) in EtOH.

entry	substrate	temp °C	time min	product(s)	yield (%)
1		0	10	 **26**	86
2		0	10	**26**	83
3	 **27**	50	20	 **28**	91
4	 **29**	50	45	 **30**	80
5		50	45	 **31**	97
6	 **32**	50	90	 **33** (4 : 5) **34**	90
7	 **35**	20	35	 **36**	82

Same as the reduction of epoxy ketones, brief treatment of diethyl *cis*-and *trans*-epoxy succinates with Na[PhSeB(OEt)$_3$] (3 equiv) in EtOH produced hydroxy succinate (**26**) in high yields, respectively (entries 1 and 2). Similarly, epoxy ester **27** was reduced at 50 °C to afford β-hydroxy ester **28** as the sole product in 91% yield (entry 3). On the other hand, the corresponding methyl ester **29** was transformed into β-hydroxy ester **30** by using Na[PhSeB(OMe)$_3$] to avoid ester exchange (entry 4) which was prepared by reduction of (PhSe)$_2$ with NaBH$_4$ in MeOH. Meanwhile, as in the case of epoxy ketones, the use of PhSeH generated from the borate complex was also found to produce the β-hydroxy esters in excellent

yields. Thus a variety of α-unsubstituted glycidic esters were efficiently and regioselectively reduced to β-hydroxy esters using Na[PhSeB(OEt)$_3$] or PhSeH (entries 1-5). However epoxy ester **32** bearing an α-alkyl substituent sluggishly reacted to afford a 4 : 5 mixture of β-hydroxy ester **33** and a β-phenylseleno substitution product **34** (entry 6), and an α-alkyl-β-unsubstituted glycidic ester **35** yielded only a β-substitution product **36** (entry 7). Consequently glycidic esters bearing an α-alkyl substituent were found to have synthetic limitations. During the studies of glycidic esters, we could get conclusive evidence regarding the reaction mechanism. Namely, on treatment of **27** with the borate complex at room temperature instead of 50 °C, it was observed on TLC that an α-phenylseleno substitution product was initially formed and the reduction product **28** was gradually increased at the expense of the former. In fact, treatment of **27** with 1.2 equiv. of Na[PhSeB(OEt)$_3$] in EtOH at 0 °C produced only the intermediate α-phenylseleno-β-hydroxy ester **37** as a diastereoisomeric mixture, which was subsequently converted to the β-hydroxy ester **28** quantitatively by further treatment with the selenium reagent at 50 °C (**Scheme 5**). These outcomes are consistent in the reaction mechanism shown in **Scheme 3**.

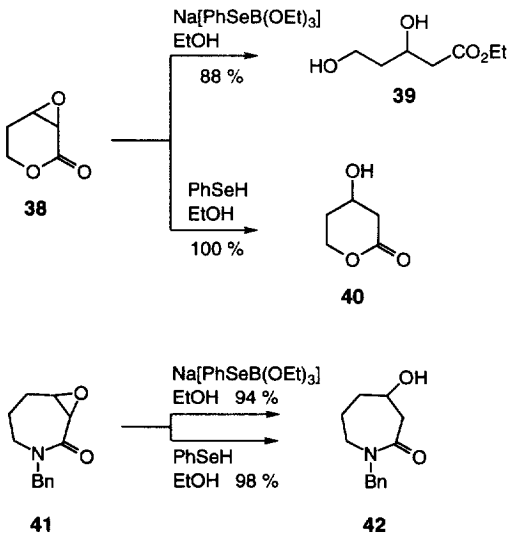
Scheme 5



Reduction of an α,β-Epoxy δ-Valerolactone and α,β-Epoxy ε-Caprolactam

We also investigated the reduction of α,β-epoxy-δ-valerolactone **38** and obtained the following notable results. The reaction of **38** with 3 equiv. of Na[PhSeB(OEt)$_3$] in EtOH solely produced dihydroxy ester **39** in high yield, the product concomitant with lactone cleavage, while treatment of **38** with PhSeH generated *in situ* exclusively afforded β-hydroxy-δ-valerolactone **40** in quantitative yield (**Scheme 6**). Thus depending on a selenium reagent employed, different types of products are obtainable in high yields. On the other hand, α,β-epoxy-ε-caprolactam **41** was found to react with both the selenium reagents to give the

Scheme 6



same β-hydroxy-ε-caprolactam **42** in excellent yields (**Scheme 7**), though the reductive cleavage of epoxy lactams has scarcely been known. These transformations provide useful means in organic synthesis including natural product synthesis.

In conclusion, the organoselenium-mediated reduction methodologies discussed here are applicable to a wide variety of substrates such as α,β-epoxy ketones, α,β-epoxy enones, glycidic esters, α,β-epoxy lactones, and α,β-epoxy lactams and various types of aldols and their congeners are obtainable in high yields. Further, in view of ready accessibility of starting materials, rapid reaction with high regioselectivity, simple manipulations, and mild conditions compatible with polyfunctional groups, these methods provide powerful tools in organic synthesis including natural product synthesis.[18]

Experimental

Melting points were determined on a Mitamura Riken MP-A melting point apparatus and are uncorrected. IR spectra were recorded on a Jasco A-3 spectrophotometer as liquid film unless otherwise noted. ^{1}H NMR spectra were measured at 90 MHz in a JEOL FX-90Q spectrometer in $CDCl_3$. Merck silica gel 60 (230-400 mesh) was employed for flash column chromatography and Merck silica gel 60 (70-230 mesh) for preparative thin-layer chromatography.

The Quantity of Hydrogen Evolved by Reduction of $(PhSe)_2$ with $NaBH_4$ in EtOH.

In a 20 mL two-necked flask were placed $NaBH_4$ (38 mg, 1 mmol) and EtOH[19] (5 mL) and the mixture was stirred for 5 min under nitrogen to dissolve the hydrides. The flask was then equipped with a test tube containing $(PhSe)_2$ (168 mg, 0.53 mmol) using a short vinyl tube, and another neck was connected with a vinyl tube whose outlet was inserted into a 100 mL bottom up messcylinder filled up with water which was placed in a deep Petri dish held with water up to its half level. The $(PhSe)_2$ in a test tube was added in small batches to the methanolic solution of $NaBH_4$ and hydrogen vigorously evolved was collected in the messcylinder. The total volume of hydrogen was 86 mL (3.8 mmol, 7.2 molar equivalent to $(PhSe)_2$).

Sodium Phenylseleno(triethyl)borate Complex $Na[PhSeB(OEt)_3]$.

According to the protocol of Sharpless,[1] $NaBH_4$ (38 mg, 1 mmol) was added in batches to a mixture of $(PhSe)_2$ (156 mg, 0.5 mmol) and EtOH[19] (2 mL) at room temperature. After evolution of hydrogen ceased, the resulting faint yellow solution was evaporated *in vacuo* to leave light yellow solid, sodium phenylseleno(triethyl)borate $Na[PhSeB(OEt)_3]$, (280 mg, 86%): ^{1}H NMR 3.70 (br s, 2H, $W_{1/2}$ = 24 Hz), 1.24 (br, t, 3H, J = 7 Hz). The complex appeared stable under an argon atmosphere, though it was susceptible to air (oxygen).

Reduction of Epoxy Dione 1 with Selenium Reagents.

(a) With 1.5 equiv of $Na[PhSeB(OEt)_3]$. To s solution of epoxy dione **1** (21 mg, 0.11 mmol) in EtOH (0.8 mL) was added under nitrogen an ethanolic solution of $Na[PhSeB(OEt)_3]$, prepared by reduction of $(PhSe)_2$ (25 mg, 0.081 mmol) with $NaBH_4$ (6.2 mg, 0.16 mmol) in EtOH[19] (1.2 mL), at room temperature. After it was stirred for 8 min, the reaction mixture was diluted with AcOEt (10 mL) and washed with saturated brine. Aqueous washes were extracted with AcOEt. The combined organic layers were

concentrated *in vacuo*, and the residue was purified by florisil column chromatography (AcOEt-hexane (1:4 - 1:1)) affording 8.5 mg of the starting material and 9 mg (42%) of **2** as an oil.

(b) With 3 equiv of Na[PhSeB(OEt)$_3$]. According to the above procedure, reduction of **1** (21 mg, 0.11 mmol) was carried out at 10 °C using 3 equiv of the selenium reagent (0.32 mmol). After purification by florisil column chromatography, 16 mg (76%) of **2** was obtained.

(c) With 3 equiv of PhSeNa in the Presence of 0.5 equiv of AcOH. According to the procedure of Liotta,[15] a mixture of $(PhSe)_2$ (234 mg, 0.75 mmol) and sodium (38 mg, 1.65 mmol) in dry THF (1 mL) was stirred at reflux under argon for 3.5 h. The resulting orange solution was evaporated *in vacuo* to leave orange solids which was dissolved in EtOH (3 mL) containing AcOH (15 μL, 0.25 mmol). The brownish mixture was added under argon to a solution of **1** (97 mg, 0.5 mmol) in EtOH (4 mL) at room temperature. After it was stirred for 10 min, the reaction mixture was diluted with AcOEt (20 mL) into which oxygen was passed from a balloon through a needle for 5 min. The mixture was washed twice with half-saturated brine and saturated brine, and concentrated. The yellow residue was purified by silica gel flash chromatography (hexane-AcOEt (3:1 - 1:2)) to give **3** (95 mg, 52%) as a yellow oil: ^{1}H NMR 7.39 (s, 1H), 7.20 (s, 5H), 6.87 (s, 1H), 6.20 (s, 1H, -OH), 4.14 (q, 2H, J = 7.2 Hz), 2.75-2.20 (m, 4H), 2.23 (s, 3H), 2.15-1.75 (m, 2H), 1.27 (t, 3H, J = 7.2 Hz); IR 3400, 3050, 1730, 1605, 1578, 1480, 1024, 735 cm^{-1}. Anal. Calcd for $C_{19}H_{22}O_3Se$: C, 60.47; H, 5.88. Found: C, 60.76; H, 6.13. This compound crystallized on standing in the refrigerator, mp 37-39 °C.

(d) With 3 equiv of PhSeNa and $(EtO)_3B$ in the presence of 0.5 equiv of AcOH. To a solution of PhSeNa (1 mmol) in EtOH (3 mL), prepared from $(PhSe)_2$ (145 mg, 0.46 mmol) and sodium (23 mg, 1 mmol) as mentioned above, was added $(EtO)_3B$ (135 mg, 0.93 mmol) and AcOH (10 μL, 0.16 mmol). Then the mixture was added under argon to a solution of **1** (61 mg, 0.31 mmol) in EtOH (1 mL) at room temperature. After it was stirred for 10 min, the reaction mixture was diluted with AcOEt, into which oxygen was passed for 5 min. Similar workup as mentioned above afforded 55 mg (91%) of **2**.

Reduction of 4 with Selenium Reagents.

According to the procedure (c) and (d) for the reaction of **1**, epoxy ketone **4** (72 mg, 0.5 mmol) was treated with PhSeNa (1.5 mmol) in EtOH (4 mL) and PhSeNa / $(EtO)_3B$ (1.5 mmol each) in EtOH (4 mL) to give 15 mg (21%) and 69 mg (95%) of **5**, respectively.

General Procedure for the Reduction of α,β-Epoxy Ketones to β-Hydroxy Ketones.

Procedure A: With 3 equiv of Na[PhSeB(OEt)$_3$] in the Presence of 0.5 equiv of AcOH.

The reaction should be performed in a well-ventilated hood since hydrogen and noxious vapors are liberated. $NaBH_4$ (57 mg, 1.5 mmol) was added under nitrogen in small batches to a mixture of $(PhSe)_2$ (234 mg, 0.75 mmol) in EtOH[19] (4 mL) with stirring at room temperature. After vigorous evolution of hydrogen ceased and the $NaBH_4$ was thoroughly consumed, the faint yellow solution of Na[PhSeB(OEt)$_3$] was cooled to 0 °C in an ice bath, to which AcOH (15 μL, 0.25 mmol) was added via a microsyringe. The resulting mixture was stirred for 5 min in the cold, and then added to a solution of an α,β-epoxy ketone (0.5 mmol) in EtOH (3 mL) under nitrogen (or a solution of epoxy ketone may be added to the selenium reagent). The mixture was stirred at 5-20 °C for 8-30 min depending on a substrate (Table 1). The reaction mixture was diluted with AcOEt, into which oxygen was passed for 5 min to convert the remaining selenium reagent to $(PhSe)_2$. The mixture was then washed twice with half-saturated brine and aqueous washes were

extracted once with AcOEt. The combined organic layers were concentrated *in vacuo* and the residue was purified by florisil or silica gel column chromatography using hexane-AcOEt (1:1 - 1:3) as eluent. $(PhSe)_2$ was readily eluted with hexane.

Procedure B: With 3 equiv of PhSeH Generated from Na[PhSeB(OEt)$_3$] *in situ*.

Reaction was performed exactly according to the procedure A except that 4 equiv of AcOH was employed instead of 0.5 equiv in the former procedure. It should be noted that *passing of oxygen on workup is critical to avoid handling the malodorous PhSeH as well as for the ready isolation of product.*

8β-Hydroxy-*cis*-8a-methyl-3,4,4a,7,8,8a-hexahydronaphthalen-1,6(2*H*,5*H*)-dione (2): A colorless oil; ^{1}H NMR 3.76-3.20 (m, 2H), 3.00-1.40 (m, 11H), 1.56 (s, 3H); IR 3480, 1705, 1420, 1140 cm^{-1}. Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.51; H, 8.40.

4-Hydroxyoctan-2-one (5): A colorless oil; ^{1}H NMR 4.00 (br m, 1H), 3.04 (d, 1H, J = 3.6 Hz, -OH), 2.61 (d, 1H, J = 13.0 Hz), 2.52 (dd, 1H, J = 13.0, 3.6 Hz), 2.18 (s, 3H), 1.56-1.13 (m, 6H), 0.90 (br t, 3H); IR 3400, 1705, 1360, 1163 cm^{-1}. Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.37; H, 11.25.

3-Hydroxycyclohexanone (6): A colorless oil; ^{1}H NMR 4.40-4.00 (br s, 1H), 3.00-1.50 (m, 9H); IR 3410, 1705, 1065 cm^{-1}.

(3*R*,5*R*)-3-Hydroxy-2-methyl-5-(1-methylethenyl)cyclohexanone (7): This compound was highly susceptible to silica gel and readily dehydrated by silica gel to give carvone. The product was an inseparable 6:1 mixture of **7** and carvone. ^{1}H NMR 4.76 (br s, 2H), 4.44-4.20 (br s, 1H); IR 3470, 3085, 1714, 1665, 896 cm^{-1}.

5β-Acetoxy-8aβ-hydroxy-4aβ-methyl-3,4,4a,5,6,7,8,8a-octahydronaphthalen-2-one (8): mp 161-165 °C; ^{1}H NMR 5.20 (dd, 1H, J = 7.5, 4.5 Hz), 2.90-1.96 (m, 5H), 2.12 (s, 3H), 1.92-1.28 (m, 8H), 1.14 (s, 3H); IR (KBr) 3400, 1721, 1698, 1255 cm^{-1}. Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.70; H, 8.56.

5β-Acetoxy-8aα-hydroxy-4aβ-methyl-3,4,4a,5,6,7,8,8a-octahydronaphthalen-2-one (9): mp 156-157 °C (acetone-hexane); ^{1}H NMR 5.25-4.99 (m, 1H), 2.67 (d, 1H, J = 16.2 Hz), 2.52-1.44 (m, 12H), 2.05 (s, 3H), 1.25 (s, 3H); IR (KBr) 3380, 1728, 1700, 1250 cm-1. Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 65.01; H, 8.36.

8aβ-Hydroxy-4aβ-methyl-3,4,4a,5,6,7,8,8a-octahydro-5β-(tetrahydropyran-2-yl)oxy-naphthalen-2-one (10): A diastereoisomeric mixture; ^{1}H NMR 4.72 (br s, 2H), 4.20-3.20 (m, 9H), 2.80-2.20 (m, 4H), 2.20-1.10 (m, 8H), 1.36 and 1.28 (s each, 3H in total); IR 3450, 1711, 1030 cm^{-1}. Anal. Calcd for $C_{16}H_{26}O_4$: C, 68.05; H, 9.28. Found: C, 68.09; H, 9.57.

[3*S*-(3α,3aα,5aβ,6α,9α,9aα,9bβ)]-6-Hydroxy-3a,5,5a,6,7,9,9a,9b-octahydro-3,5a,9-trimethylnaphto[1,2-*b*]furan-2,8 (3*H*,4*H*)-dione (12): Colorless prisms, mp 177-180 °C (EtOH-hexane); ^{1}H NMR 4.00 (t, 1H, J = 10 Hz), 3.82 (dd, 1H, J = 5.6, 2.8 Hz), 2.84 (dd, 1H,J = 15.6, 3.6 Hz), 2.70-1.30 (m, 9H), 1.26 (d, 3H, J = 6.3 Hz), 1.22 (d, 3H, J = 6.5 Hz), 1.18 (s, 3H); IR (KBr) 3500, 1768, 1708, 1145, 987 cm^{-1}. Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 67.46; H, 8.02.

5β,17β-Dihydroxyandrostan-3-one (13): Colorless crystals; mp 187-189 °C (acetone-hexane); ^{1}H NMR 3.80-3.52 (m, 1H), 3.13 (s, 1H), 2.96 (s, 1H), 2.44-1.10 (m, 21H), 1.01 (s, 3H), 0.77 (s, 3H); IR (KBr) 3440, 1705 cm^{-1}. Anal. Calcd for $C_{19}H_{30}O_3$: C, 74.47; H, 9.38. Found: C, 74.57; H, 9.61.

3-Hydroxyheptanal (14): An oil; ^{1}H NMR 9.85 (t, 1H, J = 1.4 Hz), 4.10-3.70 (br, 1H), 2.66 (d, 1H, J = 1.8 Hz), 2.60 (t, 1H, J = 1.8 Hz), 2.40 (br s, 1H), 2.00-1.30 (m, 6H), 0.92 (br t, 3H, J = 5.5 Hz); IR 3380, 2710, 1720 cm^{-1}. This compound readily formed intermolecular hemiacetals on standing.

1-Hydroxyoctan-3-one (15): A colorless oil; ^{1}H NMR 4.00-3.70 (m, 2H), 2.66 (t, 2H, J = 5.5 Hz), 2.44 (t, 2H, J = 7.2 Hz), 2.65-2.45 (br, 1H), 1.90-1.04 (m, 6H), 0.89 (t, 3H, J = 5.8 Hz) IR 3420, 1710, 1380, 1053 cm^{-1}. Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H,11.18. Found: C, 66.53; H, 11.44.

4-Hydroxy-4,8-dimethyl-7-nonen-2-one (16): A colorless oil; ^{1}H NMR 5.08 (tt, 1H, J = 7.2, 1.4 Hz), 3.69 (s, 1H), 2.61 (s, 2H), 2.18 (s, 3H), 2.20-1.85 (m, 2H), 1.67 (br s, 3H), 1.60 (br s, 3H), 1.64-1.38 (m, 2H), 1.22 (s, 3H); IR 3450, 1700, 1375 cm^{-1}. Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94. Found: C, 71.45; H, 11.15.

3-Hydroxy-3-phenylpropiophenone (17): Colorless crystals; mp 41-42 °C (ether-hexane); ^{1}H NMR 8.08-7.80 (m, 2H), 7.70-7.20 (m, 8H), 5.34 (t, 1H, J = 6.3 Hz), 3.60 (br s, 1H), 3.36 (d, 2H, J= 6.3 Hz); IR (KBr) 3470, 3075, 3050, 1680, 1604, 1583, 1453, 705, 694 cm^{-1}. Anal. Calcd for $C_{15}H_{14}O_2$: C, 79.71; H, 6.44. Found: C, 79.62; H, 6.24.

Reduction of 5,6-Epoxy-8-tridecen-7-one (18).

(a) With Zn(Cu). To a solution of **18** (31 mg, 0.18 mmol) in EtOH (1.2 mL) was added a mixture of Zn(Cu) (95 mg, 0.73 mmol), ammonium chloride (20 mg, 0.37 mmol), and water (50 μL) which were well agitated beforehand by a spatula, and the resulting mixture was stirred for 15 min at 80 °C. The mixture was diluted with AcOEt (20 mL) and inorganic materials were filtered off. The filtrate was washed with water and saturated brine, and evaporated. The residue was purified by preparative TLC (hexane-AcOEt (6:1)) to give 18 mg (58%) of **19** and 3 mg (10%) of **20**. **20:** ^{1}H NMR 4.00 (br s, 1H), 3.30-2.75 (br, 1H), 2.70-2.20 (m, 4H), 1.80-1.00 (m, 14H), 0.90 (t, 3H, J = 5.4 Hz), 0.88 (t, 3H, J = 5.4 Hz); IR 3400, 1705, 1160 cm.$^{-1}$

(b) With SmI_2. A solution of SmI_2 (0.43 mmol) in THF (0.5 mL), prepared according to the procedure of Inanaga,[17b] was cooled to -90 °C to which a mixture of **18** (39 mg, 0.18 mmol), HMPA (167 mg, 0.93 mmol), *N,N'* -dimethylethanolamine (33 mg, 0.37 mmol) in dry THF (0.5 mL) was added under argon. After it was warmed to -70 °C over 10 min, the reaction was quenched with a pH 8 phosphate buffer solution. The mixture was diluted with AcOEt (20 mL) and washed twice with half-saturated brine. Evaporation of the solvent left an oil which was purified by preparative TLC (hexane-AcOEt (6:1)) to give 13 mg (33%) of **19**, 2 mg (5%) of **20**, and 5 mg (14%) of **21**. **21:** ^{1}H NMR 6.84 (dt, 1H, J = 16.0, 7.2 Hz), 5.86 (dt, 1H, J = 16.0, 1.4 Hz), 2.50-2.00 (m, 4H), 1.80-1.10 (m, 12H), 0.92 (t, 6H, J = 6.1 Hz); IR 1655, 1623 cm^{-1}.

Reduction of α,β-Epoxy-α',β'-unsaturated Ketones.

Reaction was carried out according to the procedure A. When PhSeH (procedure B) is employed for these substrates, conjugate addition of PhSeH to an enone moiety and reduction of an epoxy ketone concomitantly occurs.

5-Hydroxy-8-tridecen-7-one (19): A colorless oil; ^{1}H NMR 6.86 (dt, 1H, J = 16.6, 7.2 Hz), 6.10 (dt, 1H, J= 16.6, 1.4 Hz), 4.04 (br m, 1H), 3.28 (br s, 1H, -OH), 2.76 (dd, 1H, J = 14.4, 1.7 Hz), 2.56 (dd, 1H, J = 14.4, 5.4 Hz), 2.40-2.10 (m, 2H), 1.70-1.00 (m, 10H), 0.90 (t, 6H, J = 7.2 Hz); IR 3430,

1658, 1622, 980, 730 cm^{-1}. Anal. Calcd for $C_{13}H_{24}O_2$; C, 73.53; H, 11.39. Found: C, 73.41; H, 11.36.

2-Hydroxy-3-methyl-5-decen-4-one (22): A 1:1 diastereomeric mixture; ^1H NMR 6.91 (dt, 1H, *J* = 16.2, 7.2 Hz), 6.14 and 6.12 (dt each, 1H in total, *J*= 16.2, 1.4 Hz), 4.24-3.76 (m, 1H), 3.14 and 3.04 (br s each, 1H in total), 3.00-2.60 (m, 1H), 2.40-2.04 (m, 2H), 1.70-1.20 (m, 4H), 1.20-1.04 (m, 6H), 1.04-0.76 (m, 3H); IR 3400, 1652, 1620, 912, 730 cm^{-1}. Anal. Calcd for $C_{11}H_{20}O_2$: C,71.69; H, 10.94. Found: C,71.32; H,11.00.

5-Hydroxy-5-methyl-2-(1-methylethylidene)cyclohexanone (23): Colorless crystals; mp 72-73 °C (ether-hexane); ^1H NMR 2.58 (m, 2H), 2.50 (br s, 2H), 2.45 (s, 1H, -OH), 2.00 (s, 3H), 2.00-1.60 (m, 2H), 1.82 (s, 3H), 1.32 (s, 3H); IR (KBr) 3390, 1670, 1630, 1120 cm^{-1}. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.16; H, 9.41.

5-Hydroxy-9-phenylseleno-8-tridecen-7-one (25): A 17:1 mixture of *Z*- and *E*-isomers. **25 (*Z*):** A yellow oil; ^1H NMR 7.75-7.50 (m, 2H), 7.45-7.15 (m, 3H), 6.64 (s, 1H), 4.12 (br m, 1H), 3.32 (br s, 1H, -OH), 2.70 (dd, *J* = 17.3, 1.0 Hz), 2.60 (dd, 1H, *J* = 17.3, 4.3 Hz), 2.26 (d, 1H, *J* = 6.1 Hz), 2.16 (d, 1H, *J* = 7 Hz), 1.70-0.90 (m, 10H), 0.90 (t, 3H, *J* = 6.8 Hz), 0.66 (t, 3H, *J* = 5.8 Hz); IR 3420, 3050, 1642, 1530, 1142, 785, 695 cm^{-1}. Anal. Calcd for $C_{19}H_{28}O_2$: C, 62.12; H, 7.68. Found: C, 62.28; H, 7.52. **25 (*E*):** ^1H NMR 7.70-7.50 (m, 2H), 7.50-7.20 (m, 3H), 5.82 (s, 1H), 3.95 (br m, 1H), 3.20 (br s, 1H, -OH), 2.92 (d, 1H, *J* = 7.0 Hz), 2.82 (d, 1H, *J* = 7.0 Hz), 2.40 (d, *J* = 13 Hz), 2.28 (dd, 1H *J* = 13, 5.4 Hz), 1.80-1.00 (m, 10H), 1.10-0.70 (br t, 6H, *J* = 6.5 Hz); IR 3450, 1665, 1560, 740, 693 cm^{-1}.

Reduction of Glycidic Esters.

The reaction was carried out with 3 equiv of the borate complex $Na[PhSeB(OEt)_3]$ in EtOH at the temperature and reaction time indicated in Table 4. The products were purified by silica gel column chromatography or preparative TLC using hexane-AcOEt (5:1-1:1).

Diethyl hydroxy succinate (26): A colorless oil; ^1H NMR 4.50 (t, 1H, *J* = 5.4 Hz), 4.26 (q, 2H, *J* = 7.2 Hz), 4.18 (q, 2H, *J* = 7.2 Hz), 3.34 (br, 1H, -OH), 2.88 (d, 1H, *J* = 7.8 Hz), 2.76 (dd, 1H, *J* = 7.8, 1.4 Hz), 1.31 (t, 3H, *J* = 7.8 Hz), 1.28 (t, 3H, *J* = 7.8 Hz); IR 3460, 1730, 1180, 1105, 1025 cm^{-1}.

Ethyl 3-hydroxyhexanoate (28): A colorless oil; ^1H NMR 4.17 (q, 2H, *J* = 7.2 Hz), 4.00 (br m, 1H), 2.97 (d, 1H, *J* = 4.3 Hz, -OH), 2.50 (d, 1H, *J* = 12.6 Hz), 2.36 (dd, 1H, *J* = 12.6, 4.7 Hz), 1.70-1.10 (m, 4H), 1.27 (t, 3H, *J* = 7.2 Hz), 0.95 (m, 3H); IR 3450, 1733, 1180, 1020 cm^{-1}.

Methyl 3-hydroxyhexanoate (30): A colorless oil; 4.02 (br m, 1H), 3.72 (s, 3H), 2.92 (d, 1H, *J* = 4.3 Hz, -OH), 2.48 (d, 1H, *J* = 11.0 Hz), 2.40 (dd, 1H, *J* = 11.0, 4.3 Hz). 1.60-1.10 (m, 4H), 0.94 (br t, 3H, *J* = 5.8 Hz); IR 3450, 1737, 1170 cm^{-1}.

Ethyl 1-(hydroxy)cyclohexyl Acetate (31): A colorless oil; ^1H NMR 4.16 (q, 2H, *J* = 7.2 Hz), 3.44 (s, 1H, -OH), 2.46 (s, 2H), 1.90-1.00 (m, 10H), 1.28 (t, 3H, *J* = 7.2 Hz); IR 3500, 1715, 1190, 1175, 727 cm^{-1}. Anal. Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.44; H, 10.04.

Ethyl 3-hydroxy-2-methylbutanoate (33): A 5:3 diastereomeric mixture; ^1H NMR 4.17 (q, 2H, *J* = 7.5 Hz), 4.20-3.70 (m, 1H in total), 2.74 (br, 1H, -OH), 2.70-2.30 (m, 1H in total), 1.40-1.10 (m, 9H in total); IR 3420, 1724, 1185 cm^{-1}.

Ethyl 2-hydroxy-2-methyl-3-phenylselenobutanoate (34): A colorless oil; ^1H NMR 7.70-7.48 (m, 2H), 7.36-7.16 (m, 3H), 4.22 (q, 2H, *J* = 7.2 Hz), 3.43 (q, 1H, *J* = 7.0 Hz), 3.42 (s, 1H, -OH),

1.60 (s, 3H), 1.45 (d, 3H, J = 7.0 Hz), 1.29 (t, 3H, J = 7.2 Hz); IR ($CHCl_3$) 3500, 3050, 1730, 1580, 1250, 1104, 1023, 740, 693 cm^{-1}. Anal. Calcd for $C_{13}H_{18}O_3Se$: C, 51.83; H, 6.02: Found: C, 51.52; H, 5.73.

Diethyl 2-hydroxy-2-phenylselenomethyl succinate (36): Colorless crystals ; mp 44-45 °C; ^1H NMR 7.66-7.36 (m, 2H), 7.35-7.10 (m, 3H), 4.12 (q, 4H, J = 7.2 Hz), 3.96 (br s, 1H, -OH). 3.27 (s, 2H), 2.92 (d, 1H, J = 15.5 Hz), 2.87 (d, 1H, J = 15.5 Hz), 1.23 (t, 3H, J = 7.2 Hz), 1.17 (t, 3H, J = 7.2 Hz); IR ($CHCl_3$) 3490, 3050, 1730, 1580, 740, 690 cm^{-1}. Anal. Calcd for $C_{15}H_{20}O_5Se$: C, 50.14; H, 5.61. Found: C, 50.42; H, 5.78.

Reaction of Ethyl 2,3-Epoxyhexanoate (27) with 1.2 equiv of Na[PhSeB(OEt)$_3$].

To an ethanolic solution of Na[PhSeB(OEt)$_3$] (0.6 mmol) in EtOH (1.5 mL) was added under nitrogen at 0 °C a solution of **27** (79 mg, 0.5 mmol) in EtOH (1.5 mL). After it was stirred for 10 min at the same temperature, the reaction mixture was diluted with AcOEt (20 mL) into which oxygen was passed for 5 min. The mixture was washed with water and saturated brine, and concentrated. The residue was purified by preparative TLC (hexane-AcOEt) (5:1)) to afford 114 mg (74%) of the major isomer of ethyl 3-hydroxy-2-phenylselenohexanoate (**37**) and 17 mg (11%) of its minor isomer. The major product: ^1H NMR 7.70-7.50 (m, 2H), 7.40-7.10 (m, 3H), 4.12 (q, 2H, J =7.2 Hz), 3.96 (br m, 1H), 3.60 (d, 1H, J = 5.8 Hz), 2.88 (br d, 1H, J = 7 Hz, -OH), 1.90-1.20 (m, 4H), 1.19 (t, 3H), 0.91 (br t, 3H, J = 6.1 Hz); IR 3450, 3050, 1720, 1580, 1022, 740, 690, cm^{-1}. The minor isomer: ^1H NMR 7.74-7.50 (m, 2H), 7.44-7.15 (m, 3H), 4.12 (q, 2H, J = 7.0 Hz), 3.95 (m, 1H), 3.60 (d, 1H, J = 4.0 Hz), 3.28 (br s, 1H, -OH), 1.90-1.20 (m, 4H), 1.18 (t, 3H, J = 7.0 Hz), 0.92 (br t, 3H, J = 6.5 Hz); IR 3500, 3050, 1723, 1710, 1578, 1020, 740, 690 cm^{-1}. Reduction product **28** was not detected at all under these conditions.

A diastereomeric mixture of **37** (131 mg, 0.43 mmol) was further treated with an ethanolic solution of the borate complex (0.43 mmol) in EtOH (1.5 mL) at 50 °C for 20 min under nitrogen to afford 68 mg (100%) of **28** after purification.

Reduction of α,β-Epoxy-δ-valerolactone (38).

(a) With Na[PhSeB(OEt)$_3$]. To a solution of **38** (50 mg, 0.44 mmol) in EtOH (1.5 mL) was added a solution of Na[PhSeB(OEt)$_3$] (1.32 mmol) in EtOH (2 mL) under nitrogen. After it was stirred for 30 min at room temperature, the reaction mixture was diluted with AcOEt (20 mL) into which oxygen was passed for 5 min, then evaporated *in vacuo*. The residue was purified by flash column chromatography (CH_2Cl_2-acetone (4:1)) to give 62.5 mg (88%) of **39**: A colorless oil; ^1H NMR 4.18 (q, 2H, J = 7.2 Hz), 4.44-4.10 (m, 1H), 4.14-3.80 (br s, 1H, -OH), 3.82 (t, 2H, J = 6.1 Hz), 3.34 (br, 1H, -OH), 2.50 (d, 2H, J = 7.2 Hz), 1.74 (q, 2H, J = 5.4 Hz), 1.25 (t, 3H, J = 7.2 Hz); IR 3350, 1720, 1055 cm^{-1}. Anal. Calcd for $C_7H_{14}O_4$: C, 51.84; H, 8.70. Found: C, 51.53; H, 8.85.

(b) With PhSeH. According to the procedure B, an ethanolic solution of PhSeH (1.32 mmol) was prepared by addition of AcOH (0.1 mL, 1.76 mmol) to a solution of Na[PhSeB(OEt)$_3$] (1.32 mmol) in EtOH (2 mL) at 0 °C under nitrogen. The mixture was then added to a solution of **38** (50 mg, 0.44 mmol) in EtOH (1.5 mL) and stirred for 30 min at room temperature. The reaction mixture was diluted with AcOEt (20 mL) into which oxygen was passed for 5 min, then evaporated *in vacuo*. The residue was purified by flash chromatography (CH_2Cl_2-acetone (4:1)) to afford 52 mg (100%) of 3-hydroxy-δ-valerolactone (**40**) as a

colorless oil: ^{1}H NMR 4.76-4.06 (m, 3H), 3.60 (br, 1H, -OH), 2.76 (dd, 1H, J = 18.0, 5.4 Hz), 2.66 (dd, 1H, J = 18.0, 5.0 Hz), 2.40-1.60 (m, 2H); IR 3365, 1720, 1255, 1060 cm^{-1}.

Reduction of α,β-Epoxy-ε-Caprolactam (41).

(a) With Na[PhSeB(OEt)$_3$]. To a solution of α,β-epoxy-ε-caprolactam (**41**) (43 mg, 0.20 mmol) in EtOH (1 mL) was added a solution of Na[PhSeB(OEt)$_3$] (0.6 mmol) in EtOH (1 mL) under nitrogen. After it was stirred for 30 min at room temperature, the reaction mixture was diluted with AcOEt (20 mL) into which oxygen was passed for 5 min, then evaporated *in vacuo*. The residue was purified by silica gel column chromatography (AcOEt-EtOH (5:1)) to give 41.6 mg (94%) of **42**: Colorless crystals; mp 89 - 90 °C; ^{1}H NMR 7.27 (s, 5H), 4.59 (s, 2H), 4.20-3.60 (m, 2H), 3.29 (br, t, 2H, J = 4.4 Hz), 2.91 (dd, 1H, J = 16.2, 9.7 Hz), 2.90 (d, 1H, J = 4.4 Hz), 2.00 - 1.20 (m, 4H); IR (KBr) 3350, 3050, 1620, 1490, 1440, 1355, 1050, 730, 700 cm^{-1}. Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.20; H, 7.82; N, 6.39. Found: C, 71.03; H, 7.84; N, 6.34.

(b) With PhSeH. An ethanolic solution of PhSeH (0.6 mmol) was prepared by addition of AcOH (47 μL, 0.82 mmol) to a solution of Na[PhSeB(OEt)$_3$] (0.6 mmol) in EtOH (1.2 mL) at 0 °C under nitrogen. The mixture was then added to a solution of **41** (44.5 mg, 0.21 mmol) in EtOH (1.2 mL) and stirred for 30 min at room temperature. The reaction mixture was diluted with AcOEt (20 mL) into which oxygen was passed for 5 min, then evaporated. The residue was purified by silica gel chromatography (AcOEt-EtOH (5:1)) to give 44 mg (98%) of **41** as colorless crystals.

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Reference and Notes

1 K. B. Sharpless and R. F. Lauer, *J. Am. Chem. Soc.*, **1973**, *95*, 2697.

2 H. J. Reich, *Acc. Chem. Res.*, **1979**, *12*, 22; D. L. J. Clive, *Tetrahedron*, **1978**, *34*, 1049; H. J. Reich, In "Oxidation in Organic Chemistry", W. Trahanovsky, Ed., Academic Press, New York, 1978, Part C, 1; D. Liotta, *Acc. Chem. Res.*, **1984**, *17*, 28; C. Paulmier, "Selenium Reagents and Intermediates in Organic Synthesis", Organic Chemistry Series, J. E. Baldwin, Ed., Pergamon Press, New York, 1986, Vol 4.

3 M. Sevrin, J. N. Denis, and A. Krief, *Tetrahedron Lett.*, **1980**, *21*, 1877.

4 R. Seshadri, W. J. Pegg, and M. Israel, *J. Org. Chem.*, **1981**, *46*, 2596.

5 M. Miyashita, T. Suzuki, and A. Yoshikoshi, *Tetrahedron Lett.*, **1987**, *28*, 4293.

6 M. Miyashita, M. Hoshino, T. Suzuki, and A. Yoshikoshi, *Chem. Lett.*, **1988**, 507.

7 (a) M. Miyashita, T. Suzuki, and A. Yoshikoshi, *J. Am. Chem. Soc.*, **1989**, *111*, 3728; (b) M. Miyashita, T. Suzuki, and A. Yoshikoshi, *Chem. Lett.*, **1987**, 2387; (c) M. Miyashita, M. Hoshino, and A. Yoshikoshi, *Chem. Lett.*, **1990**, 791.

8 D. Liotta, W. Markiewicz, and H. Santiesteban, *Tetrahedron Lett.*, **1977**, 4365.

9 D. Liotta, U. Sunay, H. Santiesteban, and W. Markiewicz, *J. Org. Chem.*, **1981**, *46*, 2605.

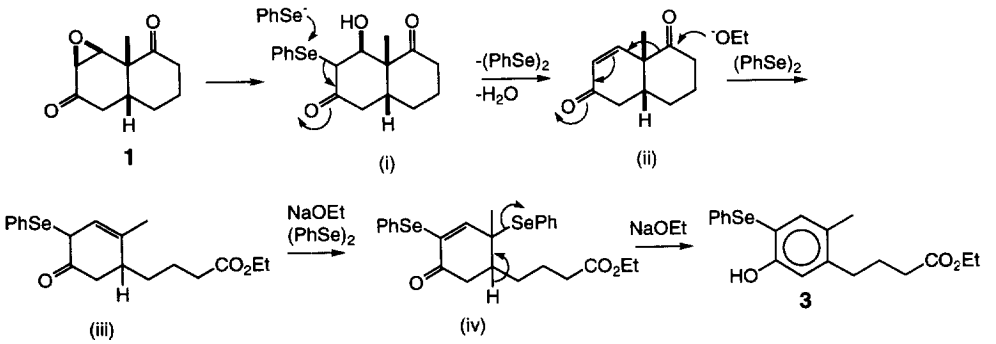
10 M. Miyashita, M. Hoshino, and A. Yoshikoshi, *Tetrahedron Lett.*, **1988**, *29*, 347.

11 T. Mukaiyama, *Org. React.*, **1982**, *28*, 203; M. Braun, *Angew. Chem. Int., Ed. Engl.*, **1987**, *26*, 24; I. Paterson, *Chem. Ind.*, **1988**, 390; E. R. Brukhant, J. J. Doney, G. A. Slough, J. M. Stack, C. H. Heathcock, and R. G. Bergman, *Pure Appl. Chem.*, **1988**, *60*, 1; "Comprehensive Organic Synthesis", B. M. Trost, I. Fleming, Ed., Vol. 2, C. H. Heathcock, Ed., C. H. Heathcock, pp 133-238; B. M. Kim, S. F. Williams, and S. Masamune, pp 239-276.

12 (a) NaTeH: A. Osuka, K. Taka-oka, and H. Suzuki, *Chem. Lett.*, **1984**, 271; (b) SmI_2: G. A. Molander and G. Hahn, *J. Org. Chem.*, **1986**, *51*, 2596; (c) $Pd(0)/HCO_2H/Et_3N$: S. Torii, H. Okumoto, S. Nakayasu, and T. Kotani, *Chem. Lett.*, **1989**, 1975; (d) Electroreduction: T. Inokuchi, M. Kusumoto, and S. Torii, *J. Org. Chem.*, **1990**, *55*, 1548; (e) Zn: L. F. Fieser, *J. Am. Chem. Soc.*, **1953**, *75*, 4395; (f) $Cr(OAc)_2$: C. H. Robinson and R. Handerson, *J. Org. Chem.*, **1972**, *37*, 565; (g) Al(Hg): E. J. Corey, H. E. Ensley, *J. Org. Chem.*, **1973**, *38*, 3187; G. R. Weihe and T. C. McMorris, *J. Org. Chem.*, **1978**, *43*, 3942; (h) NaI: H. Paulsen, K. Ererstein, and W. Koebernick, *Tetrahedron Lett.*, **1974**, 4377. (e) Electricreduction: E. L. Shapiro, M. Gentles, P Kabasakalian, and A. Magatti, *J. Org. Chem.*, **1981**, *46*, 5017; (g) Li/ liq. NH_3: J. D. McChesney and T. N. Thompson, *J. Org. Chem.*, **1985**, *50*, 3473.

13 M. Miyashita and A. Yoshikoshi, *Synthesis*, **1980**, 664.

14 This aromatic compound was probably derived via ene-dione (ii) since the latter afforded the same compound **3** in a similar yield on treatment with EtONa and $(PhSe)_2$ in EtOH.



15 K. Yamakawa and K. Nishitani, *Chem. Pharm. Bull.*, **1976**, *24*, 2810.

16 M. Miyashita, T. Suzuki, and A. Yoshikoshi, *Tetrahedron Lett.*, **1989**, *30*, 1819.

17 (a) E. Bartmann, *Angew. Chem. Int. Ed. Engl.*, **1986**, *25*, 653; (b) K. Otsubo, J. Inanaga, and M. Yamaguchi, *Tetrahedron Lett.*, **1987**, *28*, 4437 .

18 S. Takano, Y. Shimazaki, Y. Sekiguchi, and K. Ogasawara, *Synthesis*, **1989**, 539; S. Takano, Y. Shimazaki, Y. Iwabuchi, and K. Ogasawara, *Tetrahedron Lett.*, **1990**, *31*, 3619; N. Sakai and Y. Ohfune, *Tetrahedron Lett.*, **1990**, *31*, 4151; S. Takano, M. Setoh, and K. Ogasawara, *Tetrahedron: Asymmetry*, **1992**, *3*, 533; N. Sakai and Y. Ohfune, *J. Am. Chem. Soc.*, **1992**, *114*, 998; S. Takano, T. Kamikubo, T. Sugihara, M. Suzuki, and K. Ogasawara, *Tetrahedron: Asymmetry*, **1993**, *4*, 201.

19 Ordinary EtOH is sufficient for use instead of absolute EtOH employed in the original paper, ref. 1.

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