THE UNIVERSITY OF CALGARY

Asymmetric Reactions with Camphorseleno Chiral Auxiliaries

by

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Abstract

This Thesis describes a variety of asymmetric reactions with a series of camphorseleno chiral auxiliaries derived from di[(1*R*)-*endo*-3-camphoryl] diselenide and C(2) modified analogues.

The asymmetric oxidations of camphor-derived methyl selenides proceeded with high diastereoselectivities (up to 97% diastereomeric excess (d.e.)). The asymmetric [2,3]sigmatropic rearrangements of camphor-derived neryl and geranyl selenoxides afforded excesses of licareol or coriandrol in 4-34% enantiomeric excesses (e.e.'s). Double differentiation was observed when chiral oxaziridines were used to generate the required selenoxides. Interestingly, the absolute stereochemistry of the products was controlled by the type of chiral auxiliary, and not by the *E,Z*-geometry of the allylic selenide or the configuration of the oxidant. Poor enantioselectivities (2-19% e.e.'s) were observed in asymmetric selenoxide eliminations of vinyl selenides to chiral allenes.

Moderate to high facial selectivities (47-90% d.e.) were obtained from asymmetric methoxyselenenylations using camphor-derived selenenyl chlorides and triflates. Cyclofunctionalization of 4-pentenamide under neutral conditions resulted in selenenyl chloride 1,2-addition in 90% d.e. The corresponding 4-(camphorselenomethyl)-butyrolactone and 4-(camphorseleno)-3-hydroxypentanenitrile were formed under acidic or basic conditions, respectively, with excellent d.e.'s (90-97%) via an imminium cation intermediate. Cyclofunctionalization of methyl N-(4-pentenyl)carbamate afforded the corresponding ϒ-lactam with moderate stereoselectivity (44% e.e.). Selenenyl azide additions to alkenes with camphor-derived diselenides provided the corresponding 1,2-adducts in good yields, but poor d.e.'s (4-37%).

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To my family, for their endless help and encouragement

致我的全家

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List of Abbreviations

Å	Ångström
α	the position adjacent to a funtionality
Ac	Acetyl
$[\alpha]_D$	specific optical rotation
AIBN	2,2'-azobis(2-methylpropionitrile)
Ar	generalized aryl group
β	second position from a functional group
bp	boiling point
br	broad
Bu	butyl
c	concentration
°C	degrees Celsius
^{13}C	carbon-13
cal	calories
C.M.	complex mixture
cm^{-1}	wavenumbers
d	doublet or days
DBU	1,8-diaza-7-bicyclo[5.4.0]undecene
dd	doublet of doublets
ddd	doublet of doublet of doublets
d.e.	diastereomeric excess
DMF	N, N-dimethylformamide
DMSO	dimethyl sulfoxide
δ	chemical shift
e.e.	enantiomeric excess
Et	ethyl
g	grams
GC	gas chromatography

h	hours
HSABT	Hard Soft Acid Base Theory
HOMO	highest occupied molecular orbital
Hz	Hertz
IR	Infrared
J	coupling constant or Joules
k	kilo
LDA	lithium diisopropylamide
lit.	literature
M	molar
m	multiplet
M^+	molecular ion
m/z	mass to charge ratio
MCPBA	3-chloroperoxybenzoic acid
Me	methyl
mg	milligrams
MHz	megaHertz
min	minutes
mL	milliliters
mmol	millimoles
mol	moles
MOM	methoxymethyl
MS	mass spectrometry
μL	microliters
n-	straight chain (normal)
NMR	nuclear magnetic resonance
Nu	generalized nucleophile
ox.	oxidation
p.	page
Ph	phenyl

R	generalized alkyl group
R^*	generalized chiral alkyl or aryl group
Ref.	reference
rt	room temperature
s	singlet
^{77}Se	selenium-77
t	triplet
t-	tertiary
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
Ts	4-toluenesufonyl
vs.	versus

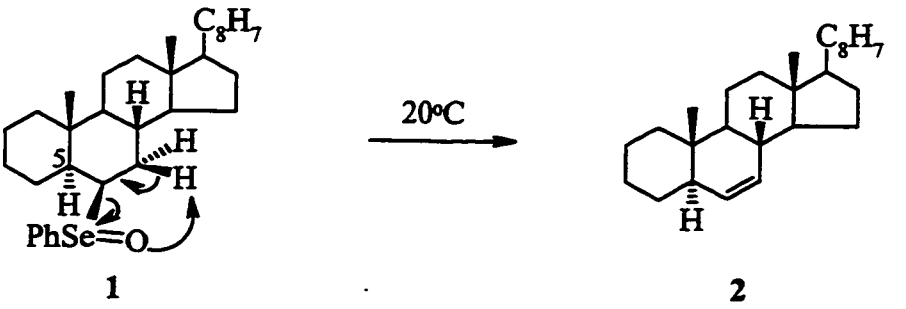
Chapter One

Introduction

1.1 Historical Background of Organoselenium Chemistry

The element selenium was discovered by Berzelius in 1818,[1] and the first organoselenium compounds were prepared by organic chemists shortly thereafter [e.g. diethyl selenide (1836),[2] ethaneselenol (1847),[3] dimethyl selenide (1857),[4] the first selenoxides (1893),[5] and some heterocyclic compounds containing N and Se (1889-1890[6])]. Most of these compounds were highly malodorous (selenols, selenides) or unstable (selenoxides) and so they remained little studied for many decades. By the 1940's selenium dioxide was found to have synthetic usefulness in the oxidation of olefins to form allylic alcohols,[7] and elemental selenium was employed in the dehydrogenation and aromatization of hydrocarbons.[8] The list of known selenium compounds grew rapidly over the next decades, and in 1973, Klayman and Gunther's book[9] summarized their biological and chemical properties. However, organoselenium chemistry didn't play a major role in organic synthesis until after 1970, when Jones et. al.[10] observed that the *syn*-elimination of steroidal selenoxide **1** produced the corresponding olefin **2.** The reactions of both (*R*)- and (*S*)-6-β-phenylseleninylcholestane (**1**) produced only cholest-6-ene (**2**) in high yield, under exceptionally mild conditions, without even a trace of cholest-5-ene (Scheme 1.1). The regiochemistry depends on the *syn* nature of the elimination. Compound **1** has no proton at C(5) that is *cis* to the selenoxide, which would be required for the formation of cholest-5-ene.

Scheme 1.1 *Syn*-Elimination of a Steroidal Selenoxide

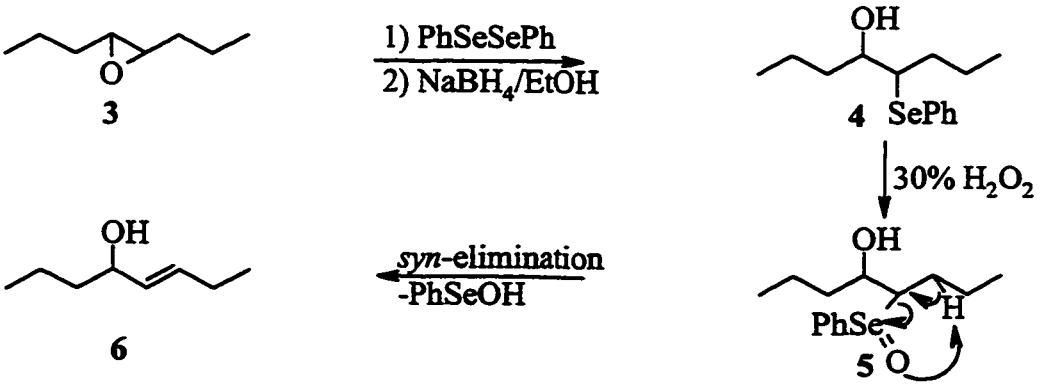


1 2

Because the carbon-carbon double bond is one of the most important functional groups in organic chemistry, and because this reaction requires much lower temperatures than other *syn*-eliminations, it promoted an increased interest in this area.

Since 1970 there has been an explosive growth in many aspects of organoselenium chemistry and its applications in synthesis. The leap forward was initiated in 1973 by Clive,[11] Reich,[12] and Sharpless'[13] (Scheme 1.2) independent work in finding applications of Jones' observation in the preparation of olefins and other unsaturated compounds. An example of this early work is shown in Scheme 1.2, where a selenoxide elimination was a key step in the preparation of allylic alcohol **6** from epoxide **3**.[13]

Scheme 1.2 Sharpless' Application of the Selenoxide *Syn*-Elimination to the Preparation of Allylic Alcohols



98% overall yield

This process involves three distinct steps: 1) nucleophilic opening of the epoxide 3 with benzeneselenolate anion, followed by 2) oxidation of the phenylseleno group to form the corresponding selenoxide 5, and 3) regioselective *syn*-elimination of the selenoxide.

1.2 Organoselenium Chemistry

The recognition of the selenoxide *syn*-elimination as a powerful synthetic method started a renaissance of organoselenium chemistry, which led to the discovery of other useful selenium reagents and reactions. An extensive investigation of organoselenium compounds indicated that selenium moieties could be introduced into numerous organic substrates in both nucleophilic and electrophilic reactions. Since selenium is one of the group VI elements, its chemistry is often compared to that of sulfur. However, several unique characteristics of organoselenium species make them more suitable for synthetic transformations, despite the more extensively established chemistry of sulfur, as well as other factors such as higher stability, lower cost and lower toxicity of most sulfur compounds compared to their selenium analogues.

First, as a fourth row element, selenium has a larger radius (Van Der Waals radius of selenium: 2.00 Å; sulfur: 1.85 Å).[14] According to Hard Soft Acid Base Theory (HSABT),[15,16] organoselenium anions possess low ionization potentials and very polarizable HOMO's. Therefore, compared with their sulfur counterparts, they are weaker bases and more powerful nucleophiles that exhibit a strong preference for reactions with soft Lewis acids. Similarly, selenium species behave as better soft electrophiles than analogous sulfur electrophiles.[17]

On the other hand, due to the lower bond dissociation energy of the selenium-carbon bond (C-Se: 71 kcal/mol;[18] C-S: 84.2 kcal/mol[19]), reactions requiring the cleavage of a C-Se bond occur under much milder conditions than those of sulfur compounds. β-elimination of selenoxides takes place at or below room temperature, whereas *syn*-elimination of similar sulfoxides requires elevated temperatures of more than 100 °C.[20]

[2,3]Sigmatropic rearrangements of allylic selenoxides and reductive deselenizations are also observed under milder conditions than those in the sulfur series.[21]

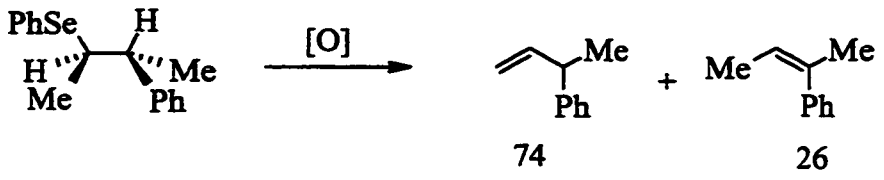
Reactions of selenium compounds are often more regioselective and stereoselective than those of sulfur compounds, which fits the requirements of modern organic synthesis. A more detailed description of the regiochemistry and stereochemistry of certain selenium reactions that are of direct relevance to this Thesis will be provided in sections 1.2.1-1.2.5. For more detailed information, the reader is directed to several excellent review articles on synthetic organoselenium chemistry by Sharpless,[22] Clive[23] and Reich[21,24] in the 1970s. Exhaustive reviews of the literature up to 1987 were also covered in monographs by Liotta,[25] Back,[26] Nicolaou[27] and Paulmier.[28]

1.2.1 Selenoxide Elimination

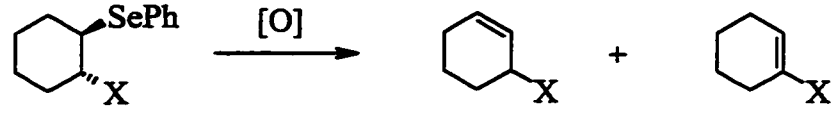
As seen earlier, the *syn*-elimination reaction of alkyl aryl selenoxides is an extremely powerful method for the introduction of carbon-carbon double bonds into organic molecules. Generally, this type of fragmentation shows a preference for abstraction of hydrogen from the less substituted carbon.[29] The regiochemistry can be affected by β-substituents. Normally, the elimination is away from oxygen functions[30] or amido groups[31] in the β-position to afford allylic products, whereas the β-sulfone[32] group directs the elimination toward the vinylic site. Azides[33] and halides[30] show low regioselectivity (for examples, see Scheme 1.3).

From many examples of this olefin-forming process, α-alkyl substituents have been found to accelerate the rate, while β-substituents decrease the rate of elimination. Improvements to the reaction can be achieved by the use of a 2-pyridylseleno group[34] or an aromatic group with an electron-withdrawing substituent (NO_2 or Cl)[35] instead of a phenylseleno group. The byproduct selenenic acid (ArSeOH) can add to the newly formed double bonds. This problem can be overcome by employing an excess of oxidant to oxidize the selenenic acid into it's corresponding seleninic acid ($ArSeO_2H$), or by trapping the selenenic acid with a secondary amine.[35,36] For most of the selenoxide *syn*-elimination reactions, non-polar aprotic solvents are recommended.

Scheme 1.3 Regiochemistry of *Syn*-Eliminations of Selenoxides

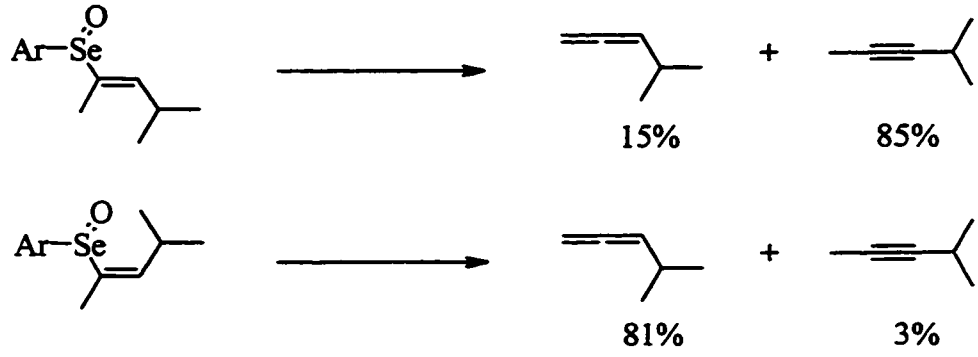


74 26 Ref. 29



X=			
OAc	97	3	Ref. 30
OH	99	<1	Ref. 30
OMe	98	2	Ref. 30
Cl	51	49	Ref. 30
N_3	60	40	Ref. 33
NHAc	100	0	Ref. 31
SO_2Ar	0	100	Ref. 32

Scheme 1.4 *Syn*-Elimination of Vinylic Selenoxides

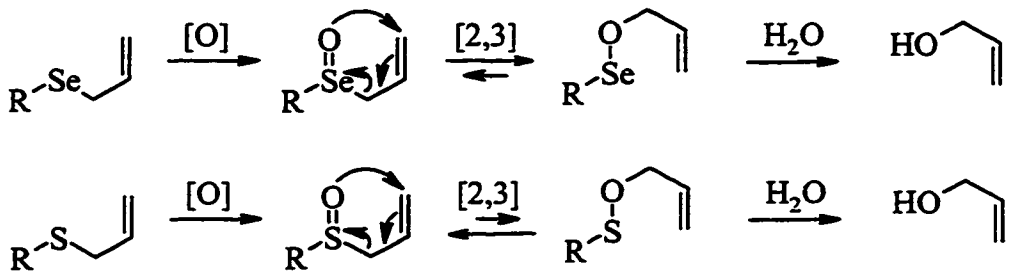


Vinylic selenoxides also undergo *syn*-eliminations to afford acetylenes, which require higher temperatures. The eliminated proton has to be in a *cis* position to the selenoxide group. When this is not the case, the corresponding allene is formed instead (Scheme 1.4).[37]

1.2.2 [2,3]Sigmatropic Rearrangement of Selenoxides

Another important transformation of selenium compounds is the [2,3]sigmatropic rearrangement of allylic selenoxides[38] or selenimides.[39] This reaction has been developed as a protocol for transposition of oxygen or nitrogen functions from selenium to carbon. Three steps are involved in the [2,3]sigmatropic rearrangement of a selenoxide (Scheme 1.5): 1) oxidation of an allylic selenide, 2) formation of the corresponding selenenate ester by a [2,3]shift of the allylic selenoxide, 3) hydrolysis of the selenenate to form the desired allylic alcohol. The equilibrium between the selenoxide and selenenate favors the latter because of the cleavage of a weak carbon-selenium bond and the formation of a more stable carbon-oxygen bond, which make this process effectively irreversible.[40] This is in contrast to the sulfur series, where the sulfoxide is more stable than the corresponding sulfenate ester. Hence, the treatment of allylic alcohols with sulfenyl halides is a method for the preparation of sulfoxides via reverse rearrangement of the resulting sulfenate esters.[41]

Scheme 1.5 [2,3] Sigmatropic Rearrangements of Allylic Selenoxides and Sulfoxides



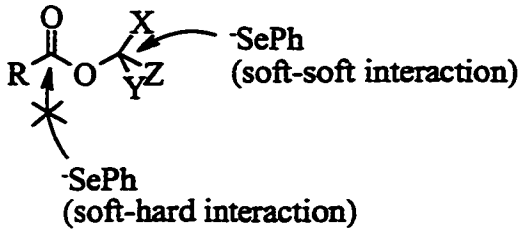
1.2.3 Reactions of Selenium Nucleophiles

The most widely used and studied selenium nucleophile is benzeneselenolate anion. As discussed previously (see Scheme 1.2), it was Sharpless who first reported the potential usefulness of this nucleophile in the conversion of epoxides to alcohols. A range

of other valuable chemical transformations of selenium nucleophiles have also been subsequently utilized in organic synthesis.

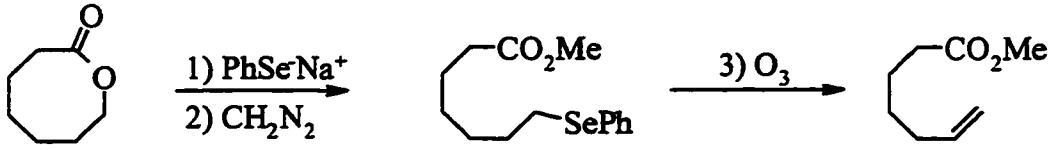
Liotta reported that this soft nucleophile could be an effective reagent for the S_N2 cleavage of esters and lactones. As expected from HSABT, benzeneselenolate anion should show a preference for attack at the carbinol carbon of an ester or lactone (soft-soft interaction) rather than the carbonyl carbon (soft-hard interaction)[17] (Scheme 1.6).

Scheme 1.6 Cleavage of an Ester with a Selenium Nucleophile



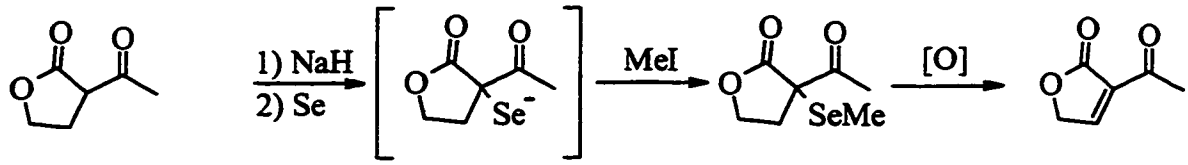
Thus, benzeneselenolate anion has been found to be an efficient reagent for carrying out S_N2 type ester and lactone cleavage reactions, and the reaction shows high selectivity with respect to the bulk of the ester group (e.g. methyl esters are cleaved faster than more hindered esters), and with respect to other functional groups (e.g. ethers and amides are inert to benzeneselenolate anion). When applied to lactones and used in conjunction with a subsequent selenoxide elimination, this process provides a general methodology for the preparation of ω-olefinic carboxylic acids and esters.[42] (e.g. see Scheme 1.7)

Scheme 1.7 Preparation of an ω-Olefinic Ester from a Lactone



Reactions of selenium nucleophiles can also be employed to generate α,β-unsaturated carbonyl compounds. This strategy involves the reaction of an enolate with elemental selenium to form the α-selenolate, followed by alkylation with an alkyl halide and oxidative elimination to afford the desired unsaturated products[43] (Scheme 1.8).

Scheme 1.8 Dehydrogenation of a Carbonyl Compound with Elemental Selenium via a Selenolate



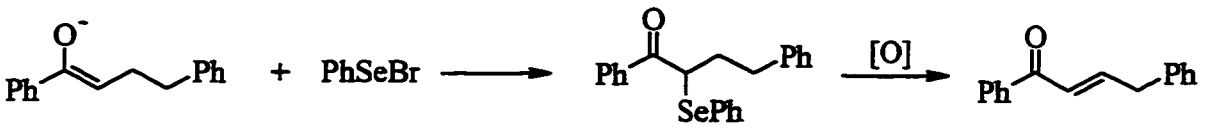
82% 97%

1.2.4 Reactions of Selenium Electrophiles

Various selenium electrophiles have also been investigated. Benzeneselenenyl chloride and benzeneselenenyl bromide are the most popular, and both are commercially available. More reactive selenium electrophiles can be obtained by treatment of benzeneselenenyl halides with various silver salts such as AgOTf, $AgPF_6$, $AgBF_4$, $AgSbF_6$, etc. This results in precipitation of AgCl or AgBr and generates the selenenyl species with a much less nucleophilic counterion than the original chloride or bromide.

Based on HSABT, electrophilic selenium species are expected to react readily with soft nucleophiles, which have low ionization potentials and charge densities. Consequently, reactions with the enol forms of ketones or aldehydes, with ketone enolate anions[44] (e.g. see Scheme 1.9), enol acetates,[45] or enol silyl ethers[46] etc. occur at the softer carbon centre. The resulting α-phenylselenocarbonyl compounds undergo oxidative elimination to form the corresponding α,β-unsaturated compounds. This methodology provides a means for the dehydrogenation of carbonyl compounds.

Scheme 1.9 Conversion of an Enolate to an Enone

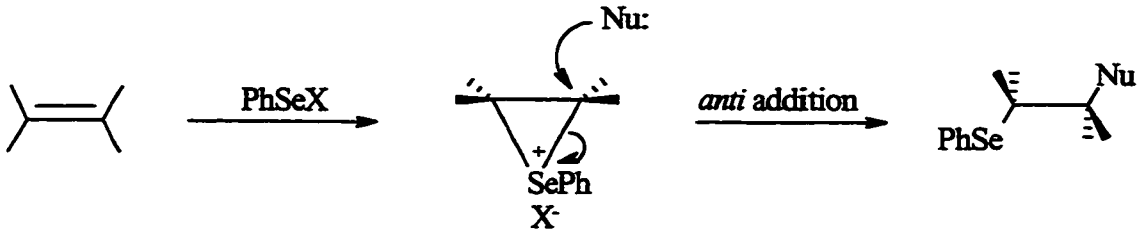


Generally, new methods for introducing functional groups to olefins are welcome, especially if they show advantage over existing approaches and proceed in a stereo- and regio-controlled manner. The additions of electrophilic selenium reagents to alkenes are of significant synthetic interest because they are *anti* stereospecific, usually highly regioselective, and capable of further transformations of the newly incorporated functional groups. Scheme 1.10[47] illustrates the general sequence of this process. First, addition of the selenium electrophile to the alkene generates the corresponding bridged intermediate. Then, nucleophiles attack the three-membered intermediate by an S_N2 mechanism to form products of *anti* addition. The bridged intermediate, known as a seleniranium ion, was postulated by Schmid and Garratt[48] to explain the stereochemistry and kinetic phenomena associated with this reaction.

The addition of electrophilic selenium reagents across double bonds is of synthetic importance not only because it is *anti* stereospecific in most cases, but also because it permits the introduction of a variety of synthetically useful nucleophilic functional groups. Thus, when the nucleophile is water, alcohol, azide, halide, or sulfinate anion, the corresponding reactions are hydroxyselenenylation, alkoxyselenenylation,[49] selenenyl azide addition,[50] selenenyl halide addition,[51] and selenosulfonation.[32,52] Generally, additions of selenium electrophiles to carbon-carbon double bonds proceed with Markovnikov regiochemistry and, as indicated earlier, *anti* stereochemistry. However the regiochemistry of selenenyl halide additions also depends on the reaction temperature. Under thermodynamic conditions, the reaction gives mainly Markovnikov products, whereas *anti*-Markovnikov products are obtained by applying kinetic control.[51] Scheme 1.11 shows representative examples of these reactions. Intramolecular ring-closure is achieved by using unsaturated nucleophiles (e.g. unsaturated alcohols,[53,54] carboxylic

acids,[55] and carbamates[56] etc.). The term "cyclofunctionalization"[57] was proposed by Clive to describe this type of synthetic operation.

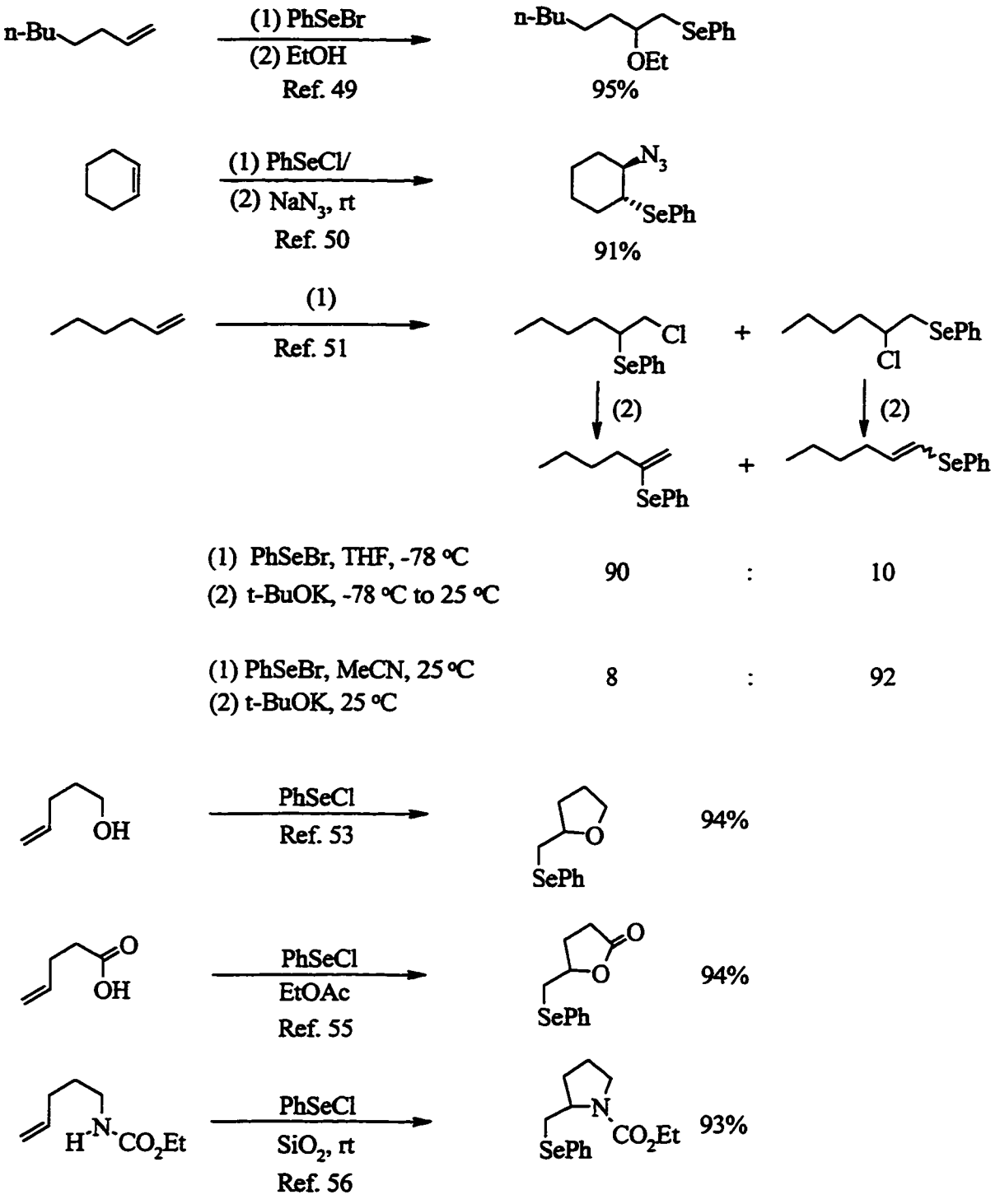
Scheme 1.10 Addition of Selenium Electrophiles to Olefins



X= Cl, Br, OTf, Ts, etc.

Nu= ROH, H_2O, N_3^-, X^-, etc.

Scheme 1.11 Additions of Selenium Electrophiles to Double Bonds



1.2.5 Deselenization

The widespread growth of organoselenium chemistry in synthesis generated an urgent requirement for efficient methods to remove selenium moieties at the end of transformations effected by them, since selenium generally does not exist in the target compounds. As discussed earlier, selenoxide elimination provides a means for the oxidative removal of selenium, but unsaturated compounds are not always desired. Consequently, it was necessary to also find methodology to remove selenium reductively.

Clive reported the reduction of selenides and selenoacetals to the corresponding hydrocarbons with triphenyltin hydride[58] (Scheme 1.12). The typical procedure was carried out in a refluxing toluene solution of triphenyltin hydride and the selenide. The reductive deselenization of selenium-containing substrates can be accomplished in the presence of numerous functionalities, such as hydroxyl, lactone, ether, phenol, and urethane groups. Tri-*n*-butyltin hydride can be similarly employed.[59] A free-radical mechanism is involved in this process.

Scheme 1.12 Reduction of Selenium Compounds with a Tin Hydride

$$RSeR' \xrightarrow[\text{Toluene, reflux}]{\text{AIBN/Ph}_3\text{SnH}} RH + R'H$$

Although tin hydrides offer an attractive method for cleaving selenium-carbon bonds, the tin byproducts are toxic and hard to remove from the desired products by chromatography. Thus, alternative methods are also required.

Back and coworkers developed a nickel boride deselenization procedure[60] (Scheme 1.13), which proceeds rapidly at 0°C, and provides solid byproducts that are easily removed by filtration. The reduction is typically performed in an open Erlenmeyer flask by treating nickel chloride and the selenide with excess sodium borohydride in methanolic THF solution. This straightforward method is compatible with many other functional groups as well.

Scheme 1.13 Reductive Cleavage of Selenides with Nickel Boride

$$NaBH_4 + NiCl_2 \cdot H_2O \xrightarrow{MeOH/THF} (Ni_2B)_2H_3$$

$$(Ni_2B)_2H_3 + RSeAr \xrightarrow{0^oC/15\ min} RH + ArH$$

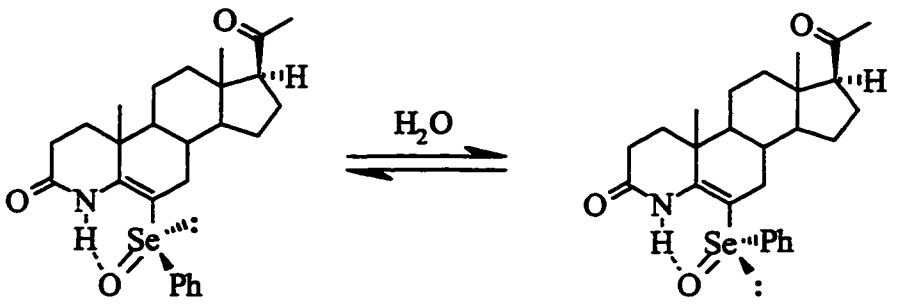
1.3 Asymmetric Organoselenium Chemistry

The extensive development of synthetic methodology based on organoselenium chemistry during the past twenty-five years, and the increasing interest in enantioselective synthesis, promoted efforts to extend selenium chemistry into the asymmetric realm. So far, there are two approaches to this goal. One can either use chiral oxidants to form optically active selenoxides, which can then be used in chirality transfer to other sites in the molecule, or by attaching chiral auxiliaries directly to the selenium atom. Recent advances in asymmetric organoselenium chemistry in the above two areas will be discussed in the following sections.

1.3.1 Asymmetric Oxidation of Prochiral Selenides

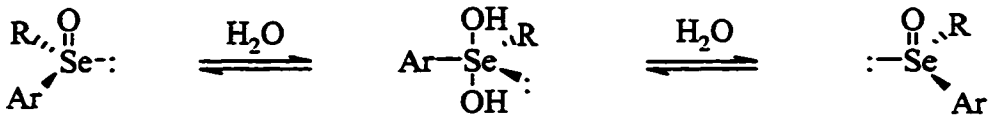
The oxidation of an unsymmetrical selenide creates a new chiral center at the selenium atom of the resulting selenoxide. Back and coworkers[61] showed that selenoxide **7a** and its diastereomer **7b** (Scheme 1.14) are configurationally stable at 80 °C, while subsequent work by Kobayashi et. al.[62] indicated that the barrier to inversion in a typical selenoxide is 15-17 kcal/mol. However, the major impediment to synthetic applications of chiral selenoxides is their poor configurational stability in the presence of water, which causes them to racemize via formation of achiral hydrates[61,63] (Scheme 1.15).

Scheme 1.14 Interconversion of Stereoisomers of the Selenoxides



7a **7b**

Scheme 1.15 Racemization of Selenoxides by Water

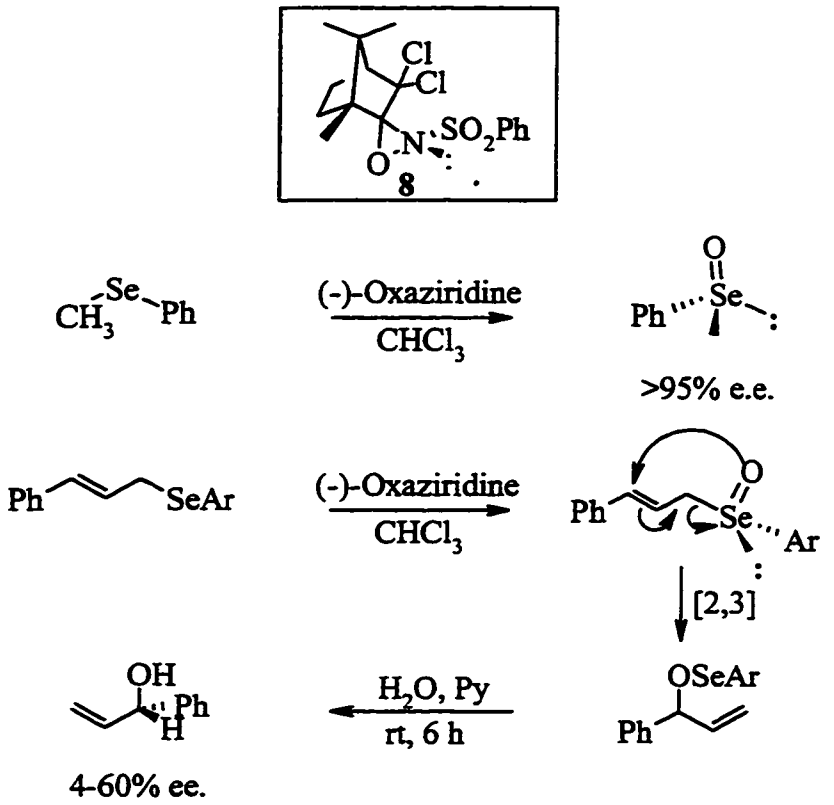


Chiral selenoxides are potentially valuable intermediates in asymmetric transfer from selenium to carbon by [2,3]sigmatropic rearrangement or by asymmetric selenoxide elimination. However, nonracemic selenoxides were not investigated until the beginning of the 1980's, whereas nonracemic sulfoxides have been known since the mid-1920s,[64] and can be prepared in high e.e. by enantioselective oxidation,[65] thermodynamic preference in diastereoselective oxidation,[66] or by enzymatic oxidation.[67] These sulfoxides have been exploited in asymmetric synthesis.

The first highly enantioenriched alkyl aryl selenoxide was prepared by Davis et. al.[68,69] by asymmetric oxidation of prochiral methyl phenyl selenide with oxaziridine **8** in up to 95% e.e. (Scheme 1.16). Such selenoxides are more stable in solution than in the solid state, and exhibit high enantiopurity as long as acid and moisture are excluded. Since the formation of selenoxides can be achieved with high stereoselectivity, Davis and

coworkers investigated the potential for chirality transfer in [2,3]sigmatropic rearrangements of (*E*)- and (*Z*)-aryl cinnamyl selenoxides.[68] Unfortunately, the corresponding allylic alcohols were produced with much lower e.e.'s (4-60%) than their selenoxide precursors (Scheme 1.16). Obviously, it was the asymmetry-transfer step, and not the original oxidation, that limited the enantioselectivity of the overall process.

Scheme 1.16 Oxidation of Allylic Selenides and [2,3]Sigmatropic Shifts Effected with a Davis Oxaziridine



Walsh et. al. studied the [2,3]sigmatropic rearrangement of the chiral selenoxides generated by enzymes,[70] which gave the product allylic alcohols as racemic mixtures. No doubt the use of aqueous media resulted in rapid racemization of the intermediate selenoxides via Scheme 1.15. In our group, Jones performed some asymmetric oxidations of allyl aryl selenides with both Davis oxaziridines and Sharpless oxidation reagents,[71] but also observed poor enantioselectivity. Subsequently, Uemura and coworkers reported

that the efficiency of chirality transfer can be increased by the introduction of an *o*-nitro group to the arylseleno moiety. Thus, Sharpless oxidation of *o*-nitrophenyl allylic selenides afforded the corresponding allylic alcohols with up to 92% e.e. in one example,[72] although the results were highly variable (16-92% e.e.). This suggests that the efficiency of chirality transfer is highly dependent on the structure of the allylic selenoxide and that enantioselectivity can potentially be improved by rational modification of the allylic selenide.

Since *syn*-elimination of a vinyl selenoxide can produce an allene, the application of a chiral selenoxide provides a potential route to optically active allenes with axial chirality. Independent work by both Jones[71] and Uemura[73] indicated that again it's the chirality transfer step that is responsible for low efficiency in the overall process (8-28 % e.e.).[71,73]

1.3.2 Asymmetric Selenium Reactions with Chiral Auxiliaries

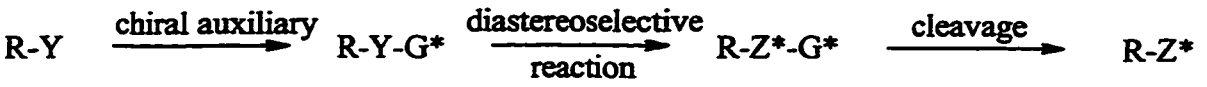
In asymmetric synthesis, the use of enantiomerically pure chiral auxiliaries involves the temporary introduction of a chiral group G* onto an achiral substrate R-Y. The modified substrate R-Y-G* is subsequently transformed, ideally through a highly diastereoselective process, into a new product R-Z*-G*. After cleavage of the chiral auxiliary, the final product R-Z* is obtained with a new stereocenter.[74] (Scheme 1.17) Basic requirements for asymmetric reactions using chiral auxiliaries are as follows:

1) The transformation from R-Y-G* to R-Z*-G* should be highly diastereoselective, and the purification of R-Z*-G* must be straightforward.

2) Cleavage of the chiral auxiliary from the product should be possible under relatively mild conditions without epimerization of the new stereocenter.

3) Both enantiomers of the chiral auxiliary should be readily available from cheap starting materials, or easily recycled after the cleavage step.

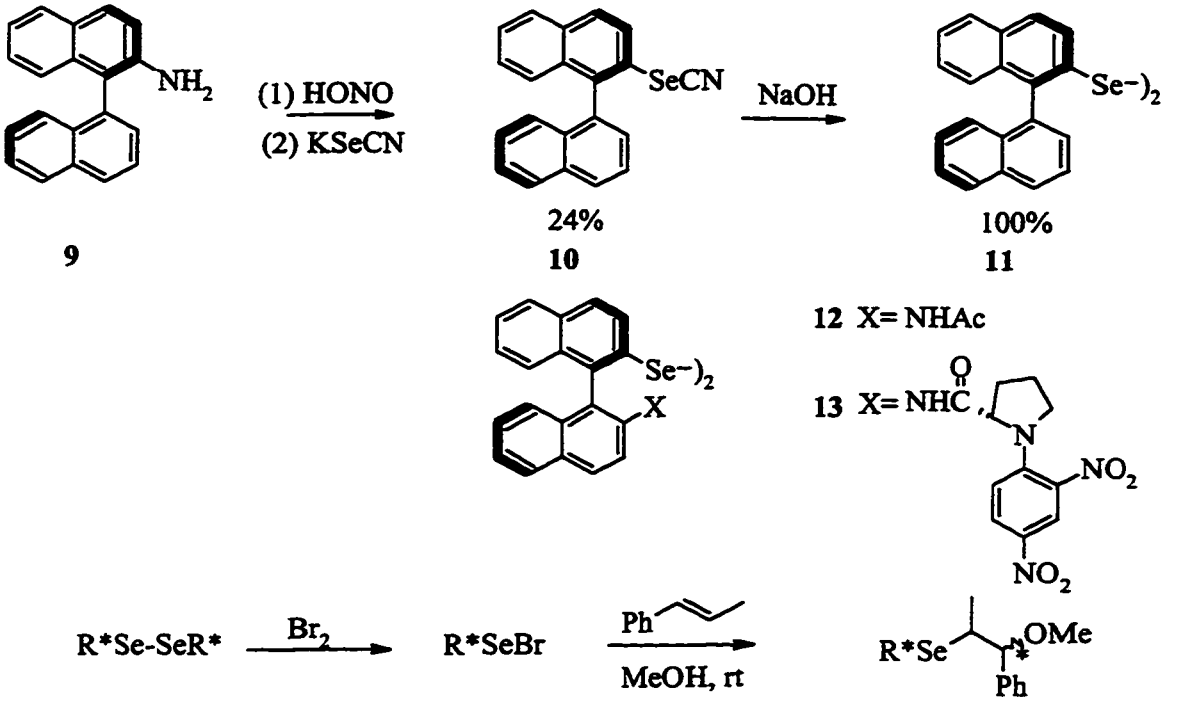
Scheme 1.17 Enantioselective Reactions with a Chiral Auxiliary



In the present section, selenium-based chiral auxiliaries and their applications in asymmetric reactions will be described.

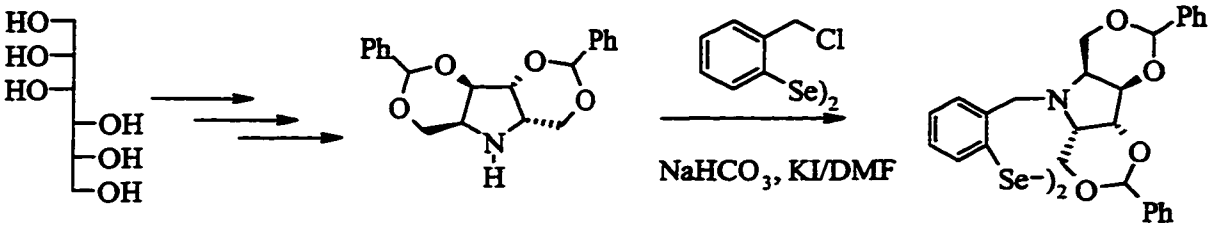
In 1988, Tomoda synthesized the first successful chiral auxiliary, which was derived from 2-amino-1,1'-binapthyl (**9**).[75] Binapthylamine was treated with nitrous acid, followed by potassium selenocyanate to form the corresponding selenocyanate **10**, and the desired diselenide **11** was generated by treatment of **10** with sodium hydroxide solution. The related diselenides **12** and **13** were prepared in a similar manner. Reactions of the diselenides with bromine produced selenium electrophiles, which underwent stereospecific *trans*-addition to alkenes in the presence of methanol, in a so-called methoxyselenenylation process (see Section 1.2.4). Tomoda demonstrated that asymmetric methoxyselenenylation with chiral auxiliaries **11** and **12** afforded only moderate asymmetric induction (17-54% d.e.), whereas, diselenide **13** bearing a chiral (*S*)-amide group at the 2' position of the (*R*)-binapthyl skeleton enhanced diastereoselectivity up to 79% d.e. with *trans*-β-methylstyrene (Scheme 1.18). Double asymmetric induction[74] of the (*S*)-amide group and the (*R*)-binapthyl skeleton was reported to play a role in the improvement of facial selectivity in the case of **13**. Although 79% d.e. is synthetically noteworthy, the reaction lacks consistency in stereoselectivity and gives poor yields for most of the substrates.

Scheme 1.18 Preparation and Applications of Tomoda's Chiral Auxiliaries



Tomoda also designed another chiral diaryl diselenide **16**, possessing an enantiomerically pure cyclic amine with C_2 symmetry at the *o*-benzylic position of the arylseleno group. Diselenide **16** was made from D-mannitol **14**[76] (Scheme 1.19). First, the C_2 symmetric pyrrolidine **15** was obtained in four steps from D-mannitol. Then, **15** was coupled with di(2-chloromethylphenyl) diselenide to form diselenide **16** in 99% yield. It was suggested that an enhancement of diastereoselectivity in electrophilic reactions would occur due to intramolecular coordination of the pyrrolidine nitrogen atom with the electrophilic selenium center. Methoxyselenenylation with **16** was then applied to a variety of olefins. Two *trans*-disubstituted styrenes were obtained with high d.e. (97%), but this chiral auxiliary afforded lower d.e.'s (28-57%) in similar reactions with other olefins.

Scheme 1.19 Preparation of a D-mannitol-Derived Diselenide



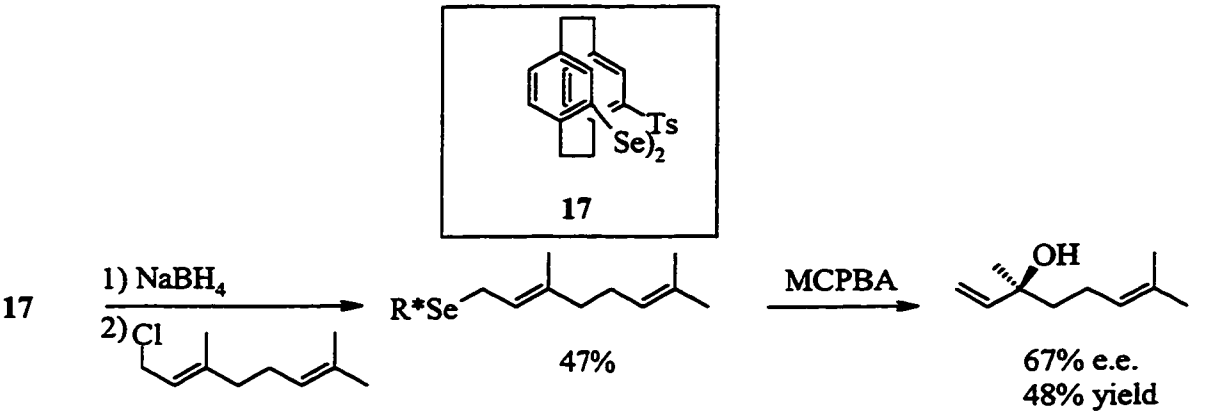
55%

99%

14 **15** **16**

Reich and Yelm[77] synthesized a chiral paracyclophane diselenide **17** (Scheme 1.20) from paracyclophane, and they applied their chiral auxiliary to [2,3]sigmatropic rearrangements of the geranyl selenide **18**. Unfortunately, the highest e.e. obtained for the resulting linaool (**19**) was only 67%, and the preparation and purification of the diselenide was rather lengthy.

Scheme 1.20 Reich and Yelm's Chiral Auxiliary



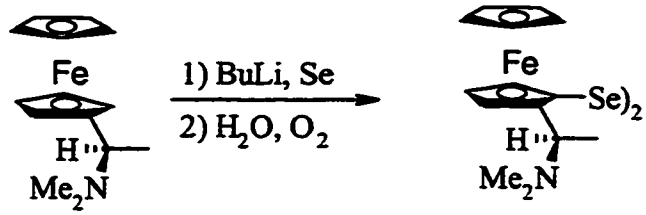
47%

67% e.e.
48% yield

18 **19**

Uemura's group reported the synthesis of an effective diferrocenyl chiral diselenide **21**, which was made by lithiation of commercially available 1-(N,N'-dimethylamino)ethylferrocene (**20**), followed by treatment with elemental selenium and air oxidation to afford diselenide **21** in 80% yield (Scheme 1.21).

Scheme 1.21 Uemura's Chiral Auxiliary



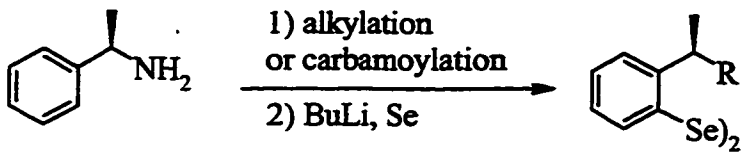
80%

20 **21**

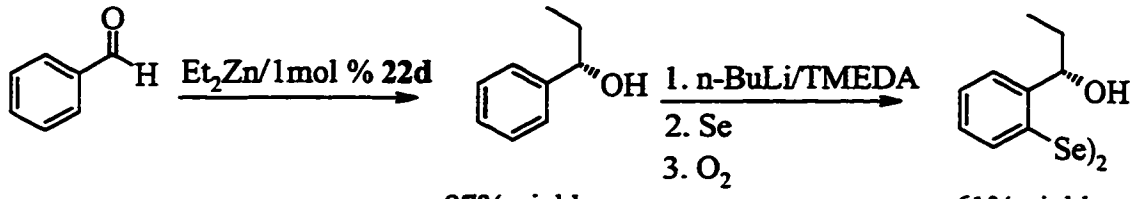
They investigated a series of asymmetric reactions (Scheme 1.21) with this diselenide, including [2,3]sigmatropic rearrangements of selenoxides and selenimides,[78] and asymmetric *syn*-eliminations of selenoxides.[79] These reactions gave relatively high e.e.'s in some cases, but again proved inconsistent. Methoxyselenenylation[80,81] with **21** resulted in good and occasionally high facial selectivity (40-98% d.e.) and good yield. Cyclofunctionalizations[82] proceeded with occasionally good stereoselectivity with phenyl substituted olefins, but in poor yield. Low diastereoisomeric excesses were obtained from the ring opening of *meso*-epoxides with the related selenolate nucleophile (13-60% d.e.).[83] If the high expense[84] ($ 388/g) of the ferrocene-based starting material is taken into account, this approach has drawbacks to synthetic chemists.

Wirth reported a series of new chiral diselenides with a nitrogen atom in side chains attached to the aromatic moiety that can coordinate with the selenium atom. Chiral diselenides **22a-e** were all prepared in a short synthetic sequence from optically pure phenylethylamine.[85] (Scheme 1.22) These chiral diselenides serve as efficient catalysts in the diethylzinc addition to aldehydes, yielding secondary alcohols in up to 98% e.e. Access to numerous chiral alcohols becomes possible by employing different organozinc reagents. Diselenide **22d** was applied as a catalyst to make the new diselenide **22g**, bearing a benzylic hydroxyl group, in high optical purity and satisfactory overall yield. Compound **22g** displayed high diastereoselectivity in oxyselenenylations (over 80% d.e.). It was concluded that the stereoselectivity depends on the intramolecular interaction between the oxygen and electrophilic selenium atoms.

Scheme 1.22 Wirth's Chiral Diselenides



22a R=Me_2N (66%)
b R=MeNH (29%)
c R=Et_2N (53%)
d R=pyrrolidin-1-yl (83%)
e R=$Me_2NC(O)NH$ (39%)

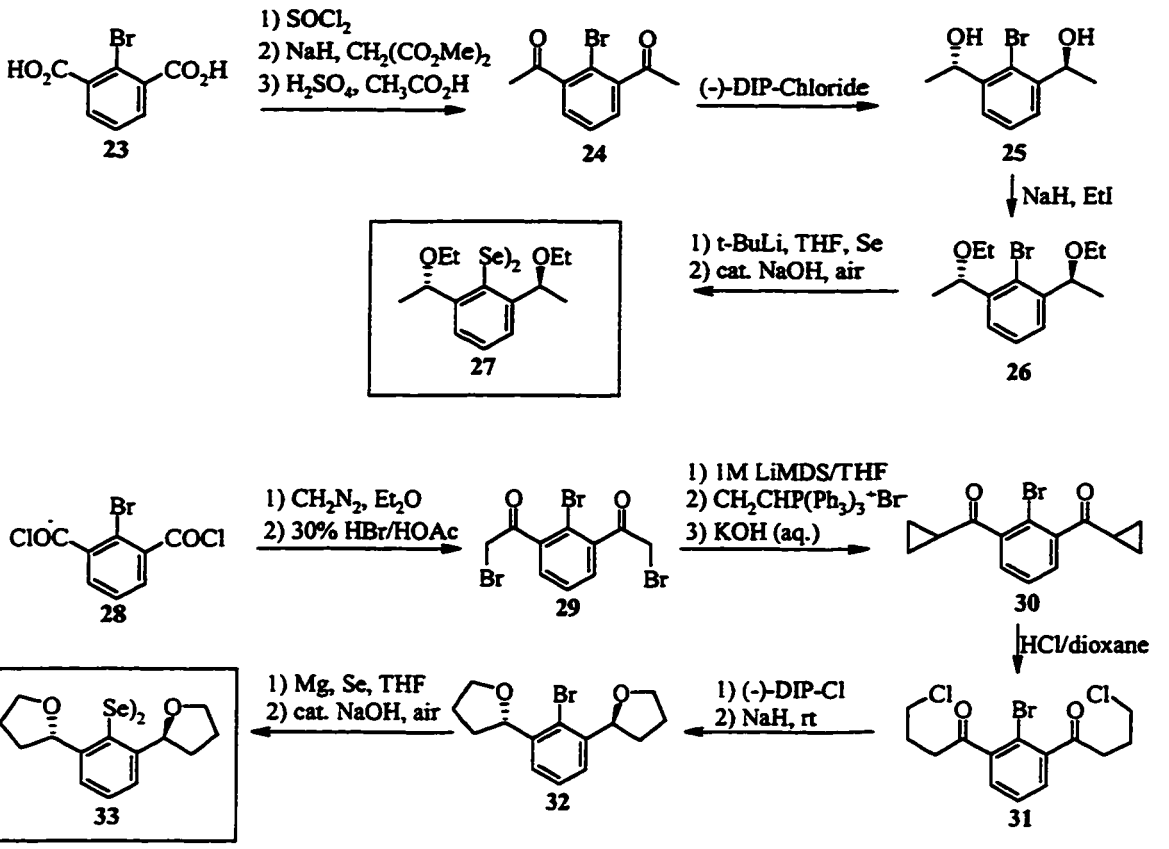


97% yield
98% e.e.

61% yield
22g

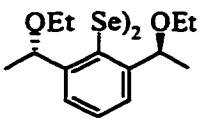
More recently, two novel chiral auxiliaries **27**[86] and **33**[87] with C_2 symmetry were synthesized by Déziel et. al. (Scheme 1.23). The diacid **23** was converted into its diacyl chloride **28** by the addition of thionyl chloride, followed by condensation with the sodium salt of dimethyl malonate, hydrolysis and decarboxylation to afford 2,6-diacetylbromobezene (**24**). The chiral diol **25** was obtained from asymmetric reduction of diketone **24** with commercially available enantiopure DIP-chloride. Treatment of the diol **25** with sodium hydride and ethyl iodide produced bis(ethoxyethyl)bromobenzene (**26**). The desired diselenide **27** was prepared by lithiation, selenenylation and air oxidation of the resulting selenolate. The related diselenide **33** is the rigidified analogue of **27**. The major difference in its synthesis is the use of the bis(cyclopropane) intermediate **30**, obtained from the bis(α-bromoketone) **29**, according to a route developed earlier by Posner.[88]

Scheme 1.23 Déziel's Chiral Auxiliaries

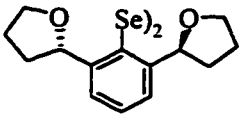


Asymmetric methoxyselenenylations and cyclofunctionalizations have been carried out with both diselenides **27** and **33** via their corresponding selenenyl triflates. Examples are shown in Table 1.1. Diselenide **27** provides high facial selectivity only with phenyl-substituted substrates, whereas the more rigid bis(tetrahydrofuranyl) chiral auxiliary **33** showed excellent stereocontrol with most of the olefins studied. However, this chiral auxiliary still suffers from its lengthy preparation sequence, which limits its practical value, especially in large scale syntheses.

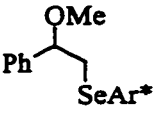
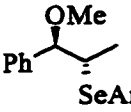
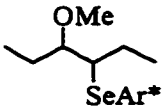
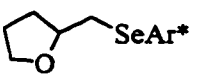
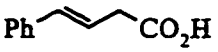
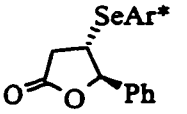
Table 1.1 Asymmetric Reactions with Déziel's Chiral Auxiliaries



27



33

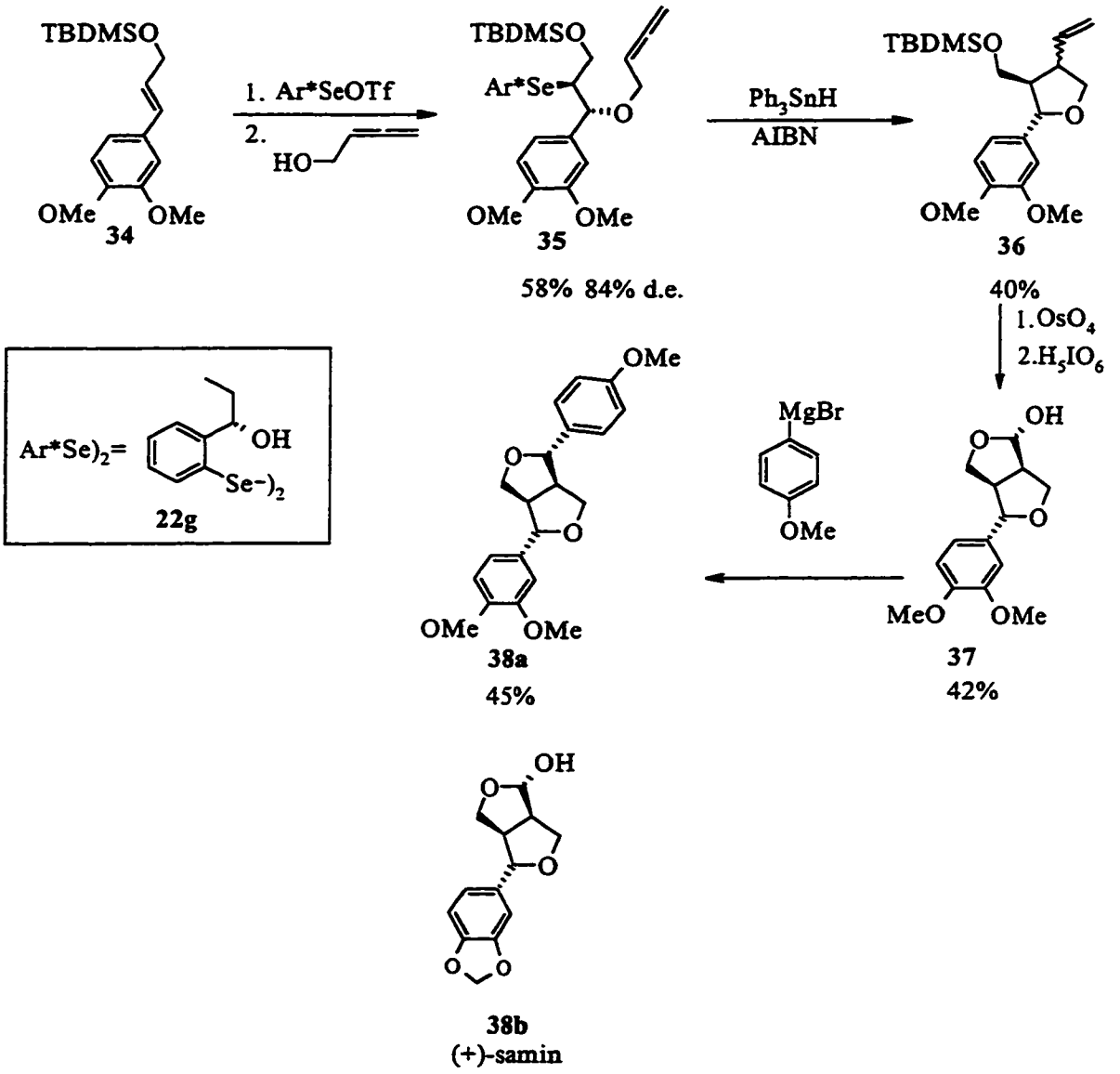
Olefin	Product	Diastereomeric Ratio with 27 (yield)	Diastereomeric Ratio with 33 (yield)
		8:1 (88)	30:1 (73)
		13:1 (82)	>100:1 (81)
		3:1 (91)	8:1 (67)
		2:1 (96)	10:1 (84)
		13:1 (72)	>100:1 (62)

1.3.3 Applications of Asymmetric Organoselenium Chemistry to Total Synthesis

Asymmetric organoselenium chemistry is now commonly accepted as a new and potentially powerful tool for introducing functional groups and regulating new chiral centers in a variety of organic substrates. Recently, Wirth[89] exploited this strategy in an enantioselective total synthesis of (+)-membrine (**38a**) (Scheme 1.24). The key step of the total synthesis was the alkoxyselenenylation of styrene **34** with the chiral diselenide **22g**. The reaction resulted in the *trans*-addition product **35** with 84% d.e. The synthesis was completed by the following steps. Intramolecular radical cyclization of **35** mediated by triphenyltin hydride produced **36**, containing the tetrahydrofuran functionality. The

double bond was oxidized by osmium tetroxide, yielding the corresponding diol, which was treated with periodic acid *in situ* to form an aldehyde. The TBDMS protecting group was simultaneously removed under these conditions and the resulting hydroxy aldehyde cyclized to the furofuran derivative **37** in 42% yield. The last step was effected by means of a Grignard reaction. Wirth also accomplished the synthesis of (+)-samin (**38b**)[90] with a similar protocol.

Scheme 1.24 First Total Synthesis of (+) Membrine



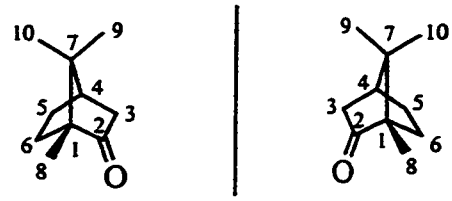
1.4 Conclusions and Objectives

Substantial progress has been achieved in recent years in asymmetric organoselenium chemistry. Chiral selenoxides are of potential usefulness in [2,3]sigmatropic rearrangements and asymmetric *syn*-eliminations, but they suffer from limited scope and, to date, poor stereoselectivity. In contrast, selenium-based chiral auxiliaries can be applied to a much broader range of transformations. Because of this obvious advantage over asymmetric oxidations, the investigation of new chiral auxiliaries has piqued the interest of many research groups.

Unfortunately, the existing chiral auxiliaries all have their drawbacks. These include expensive starting materials (e.g. Uemura's chiral auxiliaries), lengthy preparations (e.g. Déziel's and Reich's chiral auxiliaries), or inconsistent stereoselectivities (virtually all chiral auxiliaries studied to date). These three factors limit their synthetic utility, and consequently there is a continued need for the development of improved chiral auxiliaries for selenium chemistry.

Our group has been attempting to design more efficient chiral auxiliaries, which could be readily prepared from cheap optically pure starting materials, and would demonstrate high stereoselectivity for diverse asymmetric reactions with improved consistency. Very recently, we have been investigating the use of new chiral auxiliaries derived from camphor (**39**) and (**40**) (Scheme 1.25). These compounds have several obvious attractive features: 1) both enantiomers of camphor are commercially available and relatively inexpensive, 2) selenium can be introduced in one step at C(3) via the enolate of camphor (*vide infra*), 3) the camphor skeleton is relatively rigid, thereby restricting the degrees of freedom of the auxiliary, 4) the C(3) selenoxide of camphor should be prevented from fragmentation via selenoxide elimination because the only available β-proton would produce a highly strained olefin in violation of Bredt's Rule, 5) the ketone at C(2) provides a site for further transformation of the camphor moiety, for example to introduce bulky groups or groups that could coordinate with the selenium atom of the chiral auxiliary (an effect that was shown to be of importance by others; see Tomoda's and Wirth's work in section 1.3.2)

Scheme 1.25 (+) and (-)-Camphor



(+) (-)

39 **40**

To date, B. Dyck in this laboratory has prepared a series of camphor diselenides for this purpose, and has investigated their use in a limited number of reactions, including cyclofunctionalizations of unsaturated alcohols and carboxylic acids and a few oxyselenenylations.[91]

The objective of this Thesis is to extend these studies of camphorseleno auxiliaries to a broader range of substrates and to optimize the conditions for obtaining the best stereoselectivity. Specifically, the following types of processes will be described: 1) [2,3]sigmatropic rearrangements of allyl selenides, 2) selenoxide eliminations of vinyl selenides, 3) methoxyselenenylations of olefins, 4) additions of selenenyl azides to olefins, 5) cyclofuntionalizations of unsaturated amides and carbamates.

Chapter Two

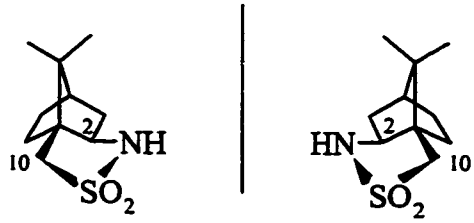
Asymmetric Reactions with Camphorseleno Chiral Auxiliaries

2.1 Introduction

Enantiopure (+)- and (-)-camphor (**39**) and (**40**), respectively (Scheme 1.25), have attracted considerable interest in organic chemistry as both chiral templates and chiral auxiliaries for several decades. First, (+)- and (-)-camphor can serve as versatile, and practical chiral starting materials by means of numerous synthetic transformations, including various rearrangements and functionalization at C(3), C(5), C(8), C(9) and C(10), as well as the cleavage of C(1)/C(2) and C(2)/C(3) bonds. This topic has been reviewed by Money.[92]

On the other hand, these two commercially available cheap compounds, and their derivatives, can also be used as efficient chiral auxiliaries in asymmetric reactions. For example, among the numerous existing camphor-based auxiliaries, the readily available enantiomers of bornane-10,2-sultam (**41**) and (**42**) (Scheme 2.1) and their derivatives have been widely studied and applied to natural product synthesis (e.g. α-amino acids).[93]

Scheme 2.1 (+)- and (-)-Bornane-(10,2) sultam

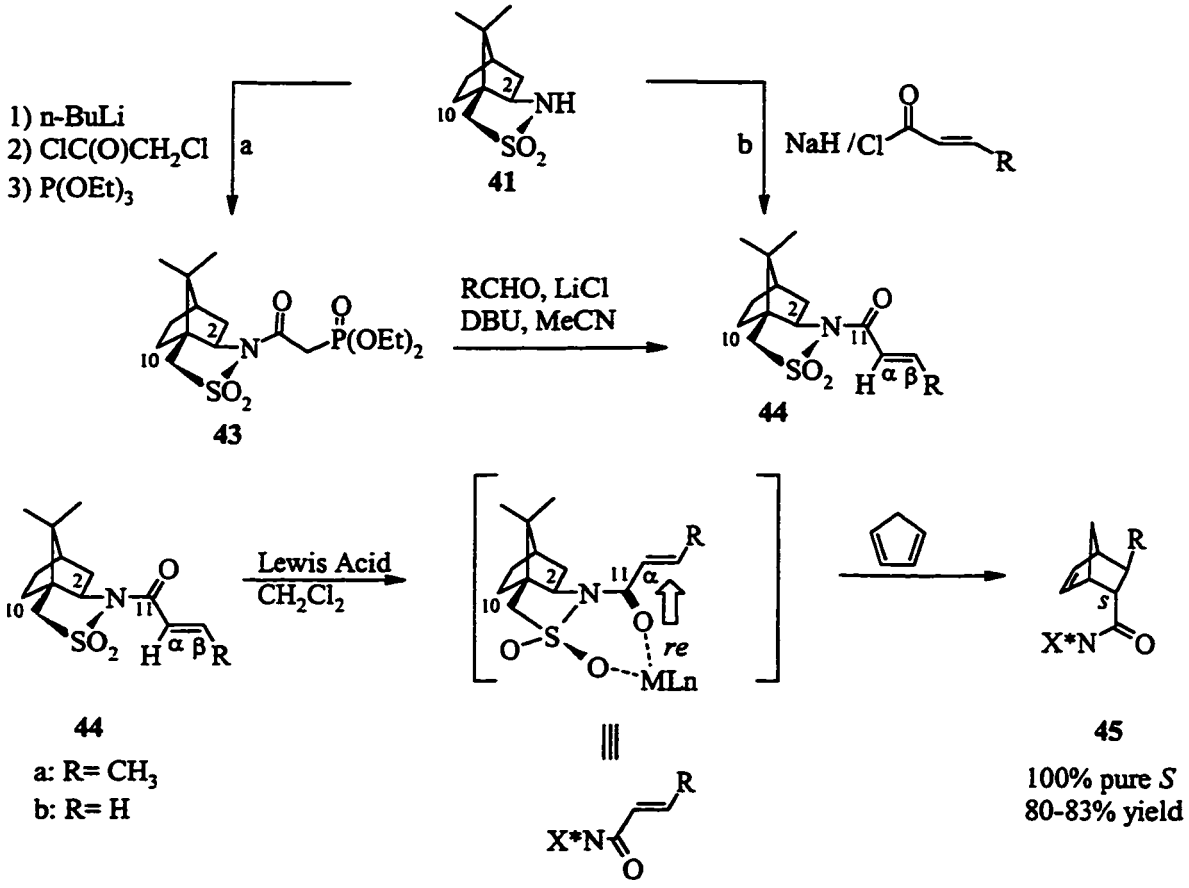


(-) **41** (+) **42**

A variety of reactions with high π-facial selectivity of their N-enoyl derivatives (Diels-Alder additions, dihydroxylations, 1,4-additions), as well as of their O-metalated

N,O-ketene acetals (aldolizations, alkylations, brominations, aminations) have been reported and reviewed by Oppolzer.[94,95] Scheme 2.2 shows one example of an application of N-enoyl sultam **44**, which was readily prepared from sultam **41** by direct N-acylation (route b) or via phosphonates **43** by means of a modified Wittig-Horner reaction (route a). The N-enoyl sultam **44** reacted as a chiral dienophile in asymmetric Diels-Alder reactions. In the presence of $TiCl_4$, $EtAlCl_2$, or Me_2AlCl, cyclopentadiene added to the acryloyl sultam to form adduct **45** with excellent *endo*- as well as π-facial selectivities in satisfactory yields.

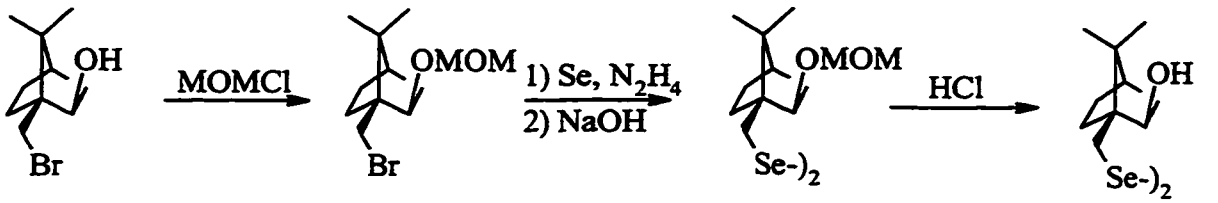
Scheme 2.2 Facially Selective Diels-Alder Reaction of an N-α,β-Enoyl Sultam



The successful earlier investigation of camphor-derived auxiliaries suggested the extension of this chemistry into the organoselenium realm. Simultaneously with our work

in this area,[91,96] Koizumi and coworkers[97] independently reported the preparation of C(2)-hydroxy C(8)-camphor diselenide **49** (Scheme 2.3). They treated 7-bromoisoborneol (**46**) with methoxymethyl chloride to protect the C(2)-hydroxyl group. Then, selenenylation of bromide **47** by reaction with elemental selenium and hydrazine, followed by aerial oxidation, afforded diselenide **48**. Diselenide **49** was obtained by removing the methoxymethyl ether group with hydrochloric acid.

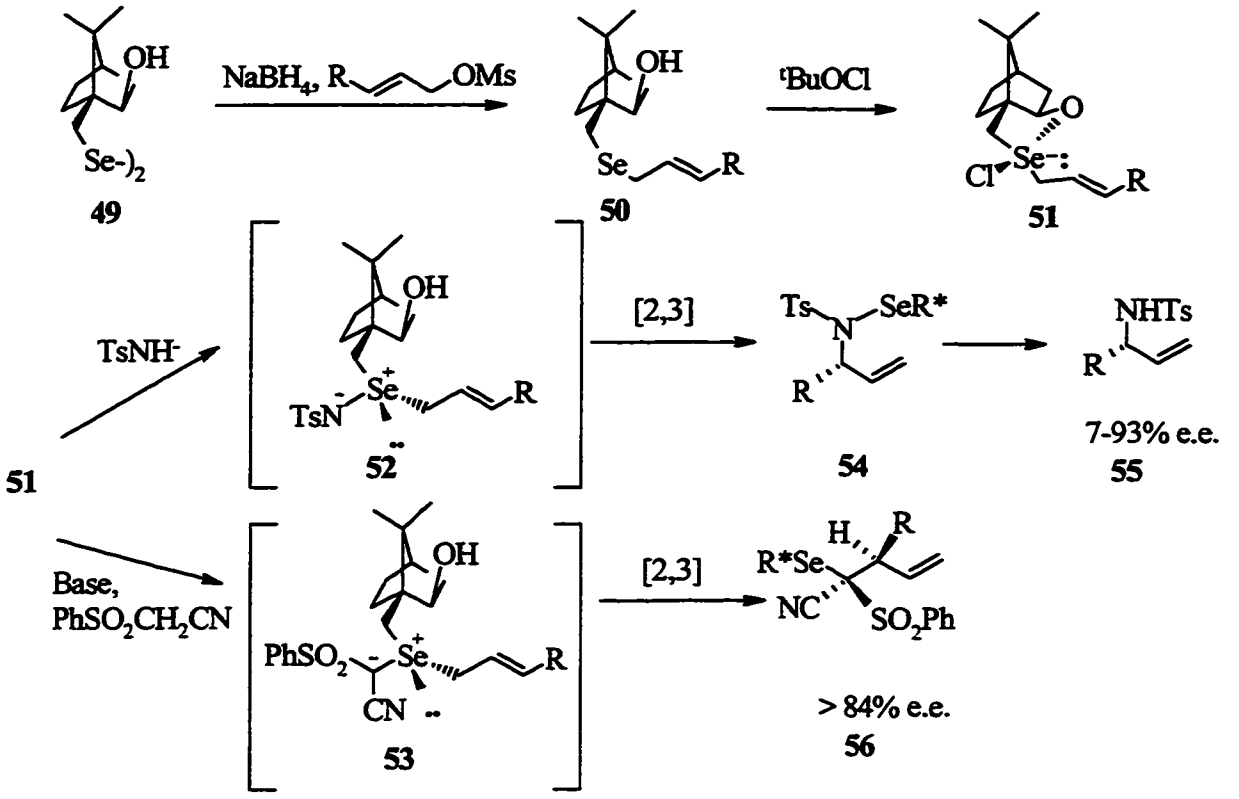
Scheme 2.3 Koizumi's Chiral Auxiliary



46 **47** **48** **49**

Koizumi et. al.[98] investigated the application of the chiral auxiliary **49** to [2,3]sigmatropic rearrangements of both the corresponding allylic selenimides **52** and allylic selenonium ylides **53** (Scheme 2.4). Treatment of diselenide **49** with sodium borohydride, followed by reaction with allylic mesylates gave the corresponding allylic selenides **50**, which were oxidized by t-butyl hypochlorite to yield chloroselenurane **51** in unspecified yield. Nucleophilic substitution reactions of **51** with either amine derivatives or carbon nucleophiles generated allylic selenimides **52** or allylic selenonium ylides **53** *in situ*, respectively, with retention of configuration. The [2,3] sigmatropic rearrangements of **52** and **53** proceeded in a stereoselective manner to form chiral amines **55** and selenides **56**. The latter reaction provides a new method for the formation of carbon-carbon bonds with asymmetric induction at the C(3) center of the original allylic mesylate.

Scheme 2.4 Applications of Koizumi's Chiral Auxiliaries in Asymmetric Reactions

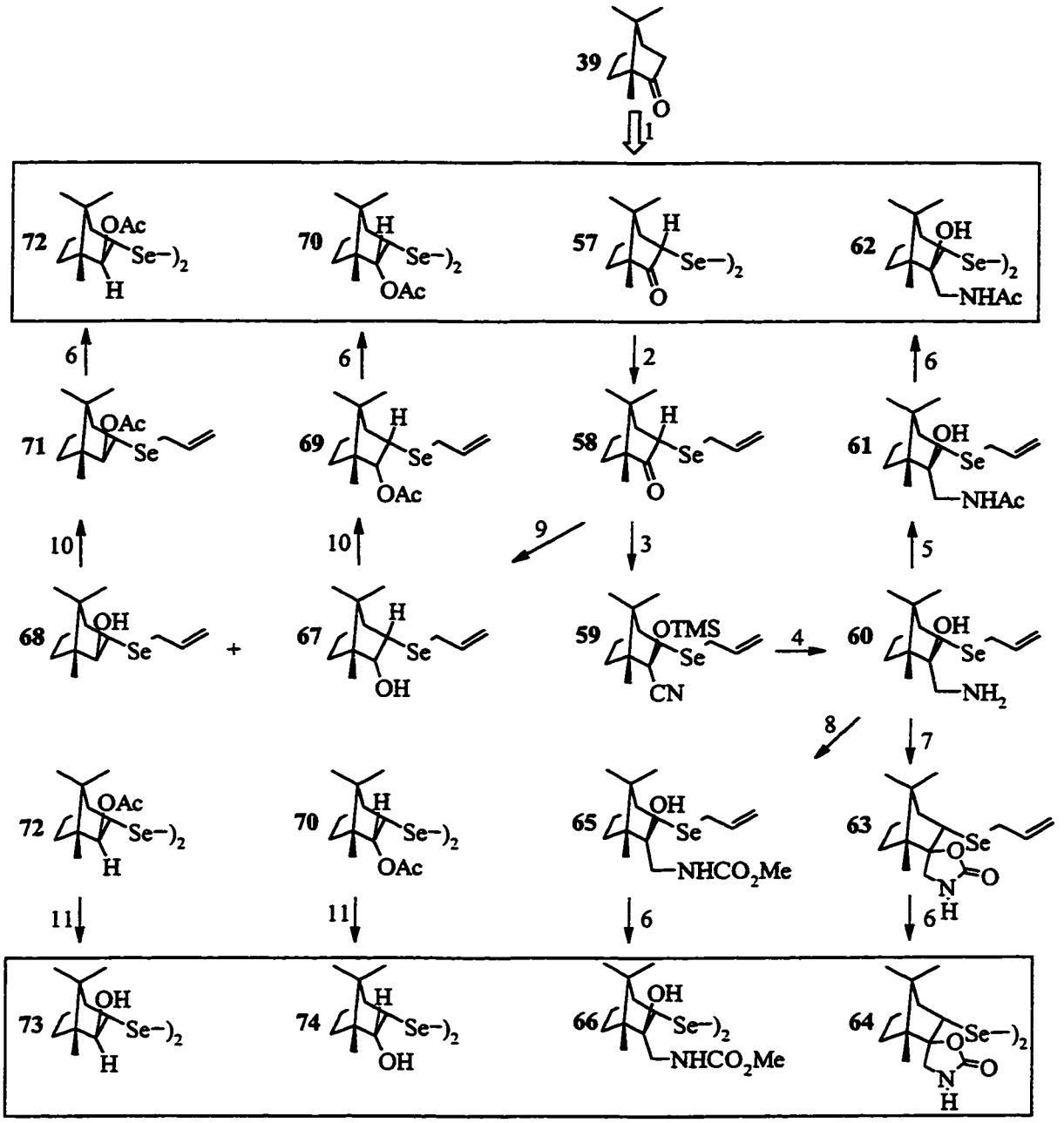


2.2 First Preparations of 3-Camphorseleno Chiral Auxiliaries

In our group, B. P. Dyck[91b, 99,100] achieved the first preparations of camphor-based diselenides, in which the selenium moiety was introduced at C(3) (Scheme 2.5), in contrast to the C(8)-functionalized analogues prepared by Koizumi (Scheme 2.3). The synthesis started from (1*R*)-(+)-camphor (**39**), which was treated with LDA to form the corresponding camphor enolate, followed by selenenylation with elemental selenium and then air oxidation to afford 76% of the di(*endo*-3-camphoryl) diselenide (**57**). Moreover, in order to modify the structure at C(2) with bulky groups or ones capable of coordinating with the selenium atom in subsequent applications, he first protected the selenium moiety as an allyl selenide in order to prevent C-Se cleavage in subsequent required reduction steps (*vide infra*). The allyl selenide **58** was then used as a key intermediate for further

functionalizations to produce other diselenides to be investigated as chiral auxiliaries. In order to introduce a nitrogen moiety directly to C(2), **58** was converted to cyanohydrin **59** by the general procedure of Evans[101] in 99% yield. Cyanohydrin **59** was then reduced to amino alcohol **60** in quantitative yield with lithium aluminum hydride. The amino alcohol **60** was readily converted into the N-acylated selenide **61**, carbamate **65**, or oxazolidinone **63** by treatment with acetic anhydride, methyl chloroformate, or N,N'-carbonyl(diimidazole), respectively. All three allyl selenides were easily converted into their corresponding diselenides **62**, **66** and **64**, respectively, by means of one-pot oxidation-[2,3]sigmatropic rearrangements followed by hydrazinolysis of the intermediate selenenic acids. The *exo* and *endo* hydroxyl functionalities were introduced into the C(2) position by reduction of allyl selenide **58** with lithium aluminum hydride. The reaction afforded a mixture of C(2) epimers **67** and **68**. Presumably because of hydrogen-bonding between the hydroxyl groups and the selenoxide oxygens, [2,3]shifts of the corresponding selenoxides didn't go smoothly. The problem was solved by protecting the hydroxyl groups as acetates **69** and **71**, respectively. Preparations of diselenides **70** and **72** were accomplished by applying the standard deprotection conditions to selenides **69** and **71**. Treatment of diselenides **70** and **72** with sodium hydroxide afforded diselenides **73** and **74**, each in 92% yield.

Scheme 2.5 Preparation of Camphor-Based Diselenides



1. LDA/Se/H^+, O_2 (76%)
2. $NaBH_4$/Allyl Iodide (92%)
3. TMSCN/ZnI_2 (99%)
4. $LiAlH_4/Et_2O$ (100%)
5. Ac_2O/Py (90%)
6. MCPBA/Et_3N/H_2NNH_2 (60-90%)
7. N,N'-Carbonyl(diimidazole) (80%)
8. Methyl chloroformate/Py (89%)
9. $LiAlH_4/Et_2O$ (30% *endo*, 59% *exo*)
10. Ac_2O/Py (99%)
11. NaOH/dioxane (92%)

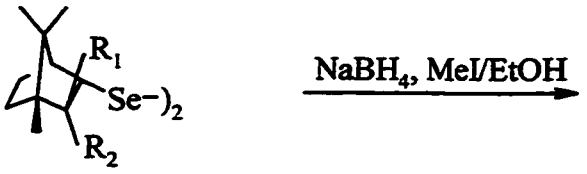
2.3 Asymmetric Reactions of Camphorseleno Chiral Diselenides

To date, Dyck has thus effectively synthesized eight chiral diselenides **57**, **62**, **64**, **66**, **70**, **72**, **73** and **74** from cheap starting materials in good yields. The nitrogen atom and the oxygen atom at C(2) of some of these chiral auxiliaries are potential sites for intramolecular coordination with the selenium atom, and for hydrogen bonding to selenoxide moieties at C(3) in later transformations, which might play a role in enhancing stereoselectivity. Diselenide **64** with a *spiro*-oxazolidinone group at C(2) is of potential interest if the five-membered ring blocks access to one side of the selenium atom. The subsequent applications of these chiral diselenides in asymmetric reactions will be discussed in the following sections.

2.3.1 Asymmetric Oxidations of Methyl Selenides

Although there have been several reports of the isolation of enantioenriched chiral selenoxides, and of their applications to asymmetric reactions, the latter are limited to a few examples of [2,3]sigmatropic rearrangements and asymmetric selenoxide eliminations with low to moderate stereoselectivities (see section 1.3.1). In general, the common step for these processes is the oxidation of a prochiral selenide with a chiral oxidant to form the chiral selenoxide. However, the possibility exists of using achiral oxidants when the selenium atom is attached to a chiral auxiliary group, or of employing chiral oxidants in double differentiation experiments,[102] where the asymmetric properties of both the auxiliary group and the oxidant can either synergize or oppose asymmetric induction at the newly created chiral selenium center. We therefore prepared methyl selenides from several of the camphor diselenides in order to perform some model oxidations. Diselenides **57**, **62** and **64** were treated with sodium borohydride to form the corresponding selenolates, followed by reaction with methyl iodide to provide methyl selenides **75**, **76** and **77** in good yields (see Scheme 2.6).

Scheme 2.6 Preparation of Methyl Selenides

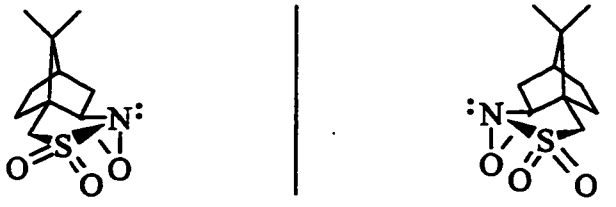


57: R_1, R_2= O
64: oxazolidinone
62: R_1= OH, R_2= CH_2NHAc

75: R_1, R_2= O
76: oxazolidinone
77: R_1= OH, R_2= CH_2NHAc

As shown in Table 2.1, the oxidations of methyl selenides **75**, **76**, and **77** should result in a mixture of two diastereomers, the diastereomeric excesses of which can be easily determined by proton NMR spectroscopy. After oxidation, the Se-methyl groups shifted downfield and were sufficiently separated to permit accurate integration. For example, selenoxide **81** showed two singlets at δ 2.82 ppm (minor) and 2.88 ppm (major), respectively, for the two stereoisomers, instead of the singlet at 2.05 ppm for the selenide **76**. Similarly, selenoxide **82** showed singlets at δ 2.60 (major) and δ 2.73 (minor). Thus, the oxidations were performed in NMR tubes using $CDCl_3$ as the solvent. Because the resulting selenoxides are sensitive to moisture, all of the reagents including the solvent were freshly dried to avoid epimerization of the chiral selenoxides. An achiral oxidant (MCPBA), as well as chiral oxidants (Davis oxaziridines **78** and **79**; see Scheme 2.7) were employed in this investigation.

Scheme 2.7 Davis Oxaziridines Used in Oxidations of Selenides

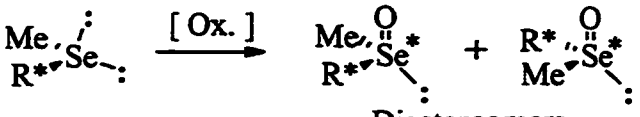


(+)-(2*R*, 8a*S*)
78

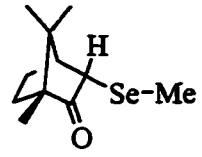
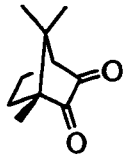
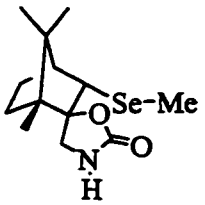
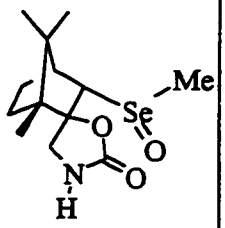
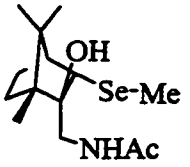
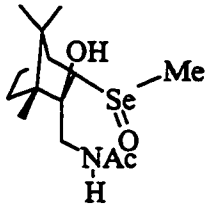
(-)-(2*S*, 8a*R*)
79

The results of the methyl selenide oxidations are listed in Table 2.1. The oxidation of selenide **75** with MCPBA resulted in a Pummerer rearrangement to form the diketone **80**. Oxidation of selenide **76** with MCPBA led to selenoxide **81** in only 27% d.e., while oxidation of selenide **77** under the same conditions gave selenoxide **82** with 78% d.e.

Table 2.1 Asymmetric Oxidations of Selenides **75-77**



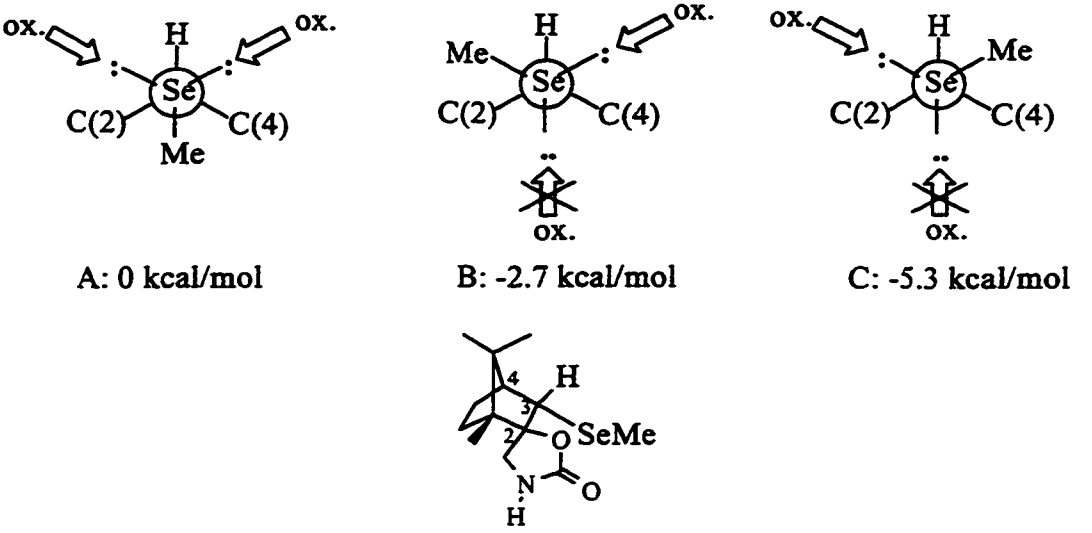
Diastereomers

Selenide	Entry	Oxidant	d.e.%	Major Product
75 	1	MCPBA		**80** 
76 	2	MCPBA	27	**81** 
	3	(+)-Oxaziridine **78**	68	
	4	(-)-Oxaziridine **79**	33	
77 	5	MCPBA	78	**82** 
	6	(+)-Oxaziridine **78**	56	
	7	(-)-Oxaziridine **79**	>97	

From Table 2.1, results from the oxidation of selenide **76** with chiral oxidants indicated that the (+)-oxaziridine **78** showed double differentiation with a d.e. of 68%, whereas reaction with the (-)-oxaziridine **79** gave similar stereoselectivity (33%) compared with that of MCPBA. In the case of selenide **77**, over 97% d.e. was observed from the oxidation by (-)-oxaziridine **79**, and (+)-oxaziridine **78** diminished the d.e. drastically (56%). In all of Entries 2-4, it was the same selenoxide with the methyl signal

at δ 2.88 that was the major diastereomer. Similarly, in Entries 5-7, it was the same selenoxide with the methyl signal at δ 2.60 that was the major diastereomer. It was noteworthy that double differentiation in the formation of selenide **81** was observed with (+)-oxaziridine **78**, whereas it was (-)-oxaziridine **79** that achieved double differentiation in selenoxide **82**. The mechanism for this double differentiation is not clear, since the interactions of the selenides **76** and **77** with chiral oxaziridines **78** and **79** are extremely complex, with many possibilities for hydrogen-bonded and nonbonded interactions.

Scheme 2.8 Conformational Isomers and Relative Energies of Methyl Selenide **76**



A: 0 kcal/mol B: -2.7 kcal/mol C: -5.3 kcal/mol

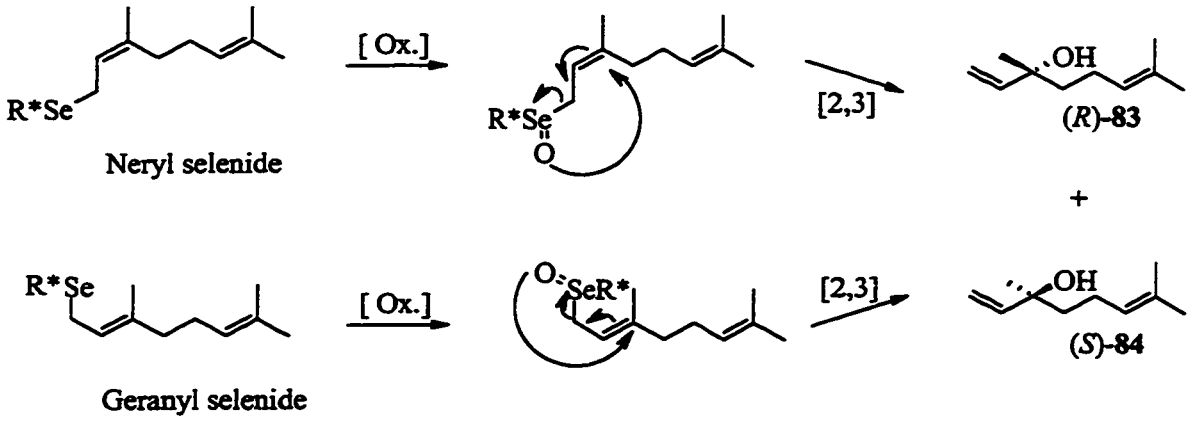
Unfortunately, it was not possible to determine the absolute configuration of the selenium atoms in selenoxides **81** and **82**. Conformational analysis of selenide **76**, with respect to rotation about the C(3)-Se bond, indicates that conformers A and B (Scheme 2.8) suffer from steric interactions with the bulky C(2) substituents, suggesting that conformer C might be preferred in the oxidation. Molecular modeling of these three rotamers for selenide **76** (Spartan Version 4.1.1, *ab initio* using the 3-21G* basis set, Hartree Fock method) confirmed their relative stabilities, as shown in Scheme 2.8. Moreover, in C, approach of the oxidant from the indicated *exo* side appears to be preferable. However, consideration of the Curtin-Hammet principle,[103] as well as

complications from the possibility of stabilizing Se-O or Se-N interactions in the selenoxide-forming transition state, as well as hydrogen-bonding interactions, make such assumptions regarding the absolute stereochemistry tenuous at best. (Scheme 2.8).

2.3.2 [2,3]Sigmatropic Rearrangements of Allyl Selenides

Since moderate and high stereoselectivities were achieved in the oxidations of methyl selenides **76** and **77**, respectively, we attempted to extend the asymmetric oxidations to allyl selenides containing these same camphor-derived auxiliaries. We thus investigated the [2,3]sigmatropic rearrangements of geranyl and neryl selenides, which are geometric isomers (Scheme 2.9). There are several reasons for choosing the geraniol and nerol test system. First, oxidation-[2,3]shifts of both selenides are expected to produce the enantiomeric alcohols: (*R*)-(-)-licareol (**83**) and (*S*)-(+)-coriandrol (**84**), which are natural products with known specific rotations[104] (the racemic mixture of **83** and **84** is sometimes referred to as linalool). Moreover, they can also be separated by GC with a chiral column, thereby facilitating measurement of e.e.'s and making it possible to establish the absolute configurations of the products. Furthermore, the ready availability of both geometric isomers could provide insight into the effect of *E,Z*-configuration upon the stereoselectivity of the process.

Scheme 2.9 [2,3]Sigmatropic Rearrangements of Neryl and Geranyl Selenides

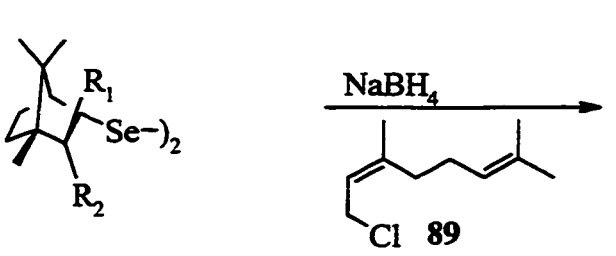


Neryl selenide

Geranyl selenide

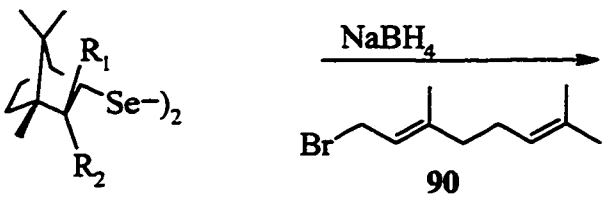
Finally, the required allyl selenides can be readily obtained from the corresponding camphor diselenides in a similar mode to the preparations of methyl selenides **76** and **77**. Thus, the camphor selenolates were generated *in situ* by treating diselenides **62** and **64** with sodium borohydride, followed by additions of neryl chloride (**89**) or geranyl bromide (**90**) to afford selenides **85**, **86**, **87** and **88** in satisfactory yields (see Scheme 2.10).

Scheme 2.10 Preparation of Neryl and Geranyl Selenides



64: R_1, R_2= oxazolidinone
62: R_1= OH, R_2= CH_2NHAc

85: R_1, R_2= oxazolidinone
87: R_1= OH, R_2= CH_2NHAc



64: R_1, R_2=oxazolidinone
62: R_1= OH, R_2= CH_2NHAc

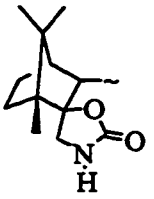
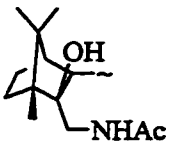
86: R_1, R_2= oxazolidinone
88: R_1= OH, R_2= CH_2NHAc

We then proceeded to investigate the enantioselectivities of the [2,3]sigmatropic rearrangements of their respective selenoxides. The results are shown in Table 2.2. The e.e.'s in the table were obtained by GC measurements with a Cyclodex B chiral column, under conditions where commercially available racemic linalool showed two peaks with different retention times and identical integrations for the two respective enantiomers, whereas a nonracemic mixture (Entry 6) showed the same two peaks with different area integrations (Figure 2.1). Absolute configurations of the products were determined by

polarimetry, since it is known[104] that the (*S*) and (*R*) enantiomers of linalool are dextro- and levorotatory, respectively.

[2,3]Sigmatropic rearrangements of selenoxides derived from selenides **85** and **86** all gave excesses of *S*-(+)-coriandrol (**84**) (Entry 1-5), while the excesses of *R*-(-)-licareol were obtained from all of the reactions of selenoxides derived from selenides **87** and **88** (Entry 6-12). It can be seen that the absolute configurations of the products were controlled by the C(2)-substituents of the camphor moiety, and not by the choice of oxidant or the geometry of allylic substituents.

Table 2.2 [2,3]Sigmatropic Rearrangements of Neryl and Geranyl Selenides

R*	Selenide	Oxidant	Entry	Solvent	Configuration of major product	e.e.% (yield%)
	**85** (*Z*)	(-)-Oxaziridine	1	CH_2Cl_2	*S*	5(66)
		(+)-Oxaziridine	2	CH_2Cl_2	*S*	27(69)
			3	MeOH	*S*	28(67)
	86 (*E*)	(-)-Oxaziridine	4	CH_2Cl_2	*S*	4(65)
		(+)-Oxaziridine	5	CH_2Cl_2	*S*	25(66)
	**87** (*Z*)	(-)-Oxaziridine	6	CH_2Cl_2	*R*	32(67)
			7	Et_2O	*R*	30(56)
			8	CCl_4	*R*	34(70)
			9	MeOH	*R*	6(78)
		(+)-Oxaziridine	10	CH_2Cl_2	*R*	18(64)
	88 (*E*)	(-)-Oxaziridine	11	CH_2Cl_2	*R*	27(63)
		(+)-Oxaziridine	12	CH_2Cl_2	*R*	10(69)

Higher e.e.'s of *S*-(+)-coriandrol were obtained by oxidation of either (*Z*) or (*E*)-selenides **85** and **86**, respectively, containing the oxazolidinone moiety at C(2), with the (+)-oxaziridine **78** (compare Entry 2 and 3 vs. 1, and Entry 5 vs. 4). On the other hand, higher e.e.'s of *R*-(-)-licareol were obtained from (*Z*)-**87** and (*E*)-**88** with the (-)-oxaziridine **79** (compare Entry 6-8 vs. 10, and Entry 11 vs. 12). By analogy to the oxidations of the methyl selenides **76** and **77** described earlier, these results suggest that

double differentiation occurs when (+)-**78** is used with the oxazolidinone moiety at C(2), and when (-)-**79** is employed with the hydroxy acetamide group at C(2). Surprisingly, the absolute stereochemistry of the products was not effected by the (*E*) or (*Z*) geometry of the selenides.

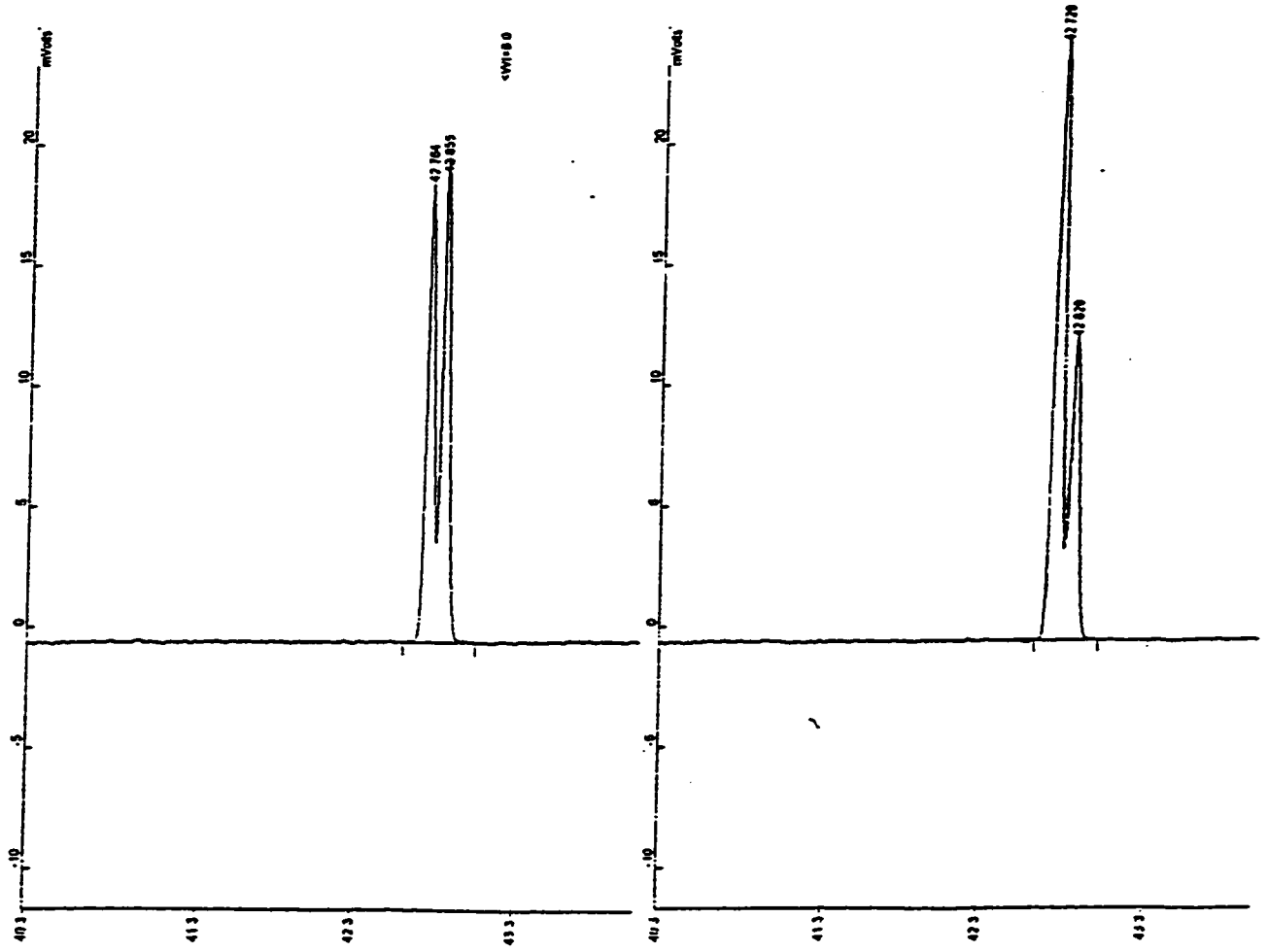
The reactions of hydroxy acetamide-containing selenide **87** also revealed a dependence on the solvent, where the e.e. decreased to 6% with the protic solvent methanol (Entry 9). The oxazolidinone-containing selenide **85** showed no such effect (Entry 3). This is consistent with a scenario where the selenoxide obtained from **87**, but not that from **85**, is subjected to intramolecular hydrogen bonding which is disrupted in a protic solvent such as methanol.

Scheme 2.11 illustrates a typical analysis of the sigmatropic rearrangement of the selenoxides derived from the oxidation of oxazolidinone-substituted (*Z*)-and (*E*)-selenides **85** and **86**, respectively. The (*S*)-selenoxide is shown arbitrarily, since firm conclusions about its absolute configuration could not be made. Let us assume, again arbitrarily, that the selenoxide oxygen atom approaches the allylic π-bond from above. Two possible modes, termed *exo* and *endo*,[68,105] can then lead to the respective products, and the e.e. depends on the energy difference between the transition states preceding them. Since (*S*)-(+)-coriandrol was the principal product from the oxidation of both **85** and **86**, we can conclude that the neryl selenoxide reacts preferentially by the *endo* pathway, and the geranyl selenoxide by the *exo* route. However, it must be kept in mind that if the oxidation produced the (*R*)-selenoxide instead of the (*S*)-diastereomer shown in Scheme 2.11, or if the selenoxide oxygen atom of the (*S*)-selenoxide attacked the allylic π-system from below, then the assignment of *endo* and *exo* pathways for the neryl and geranyl systems, respectively, could be reversed.

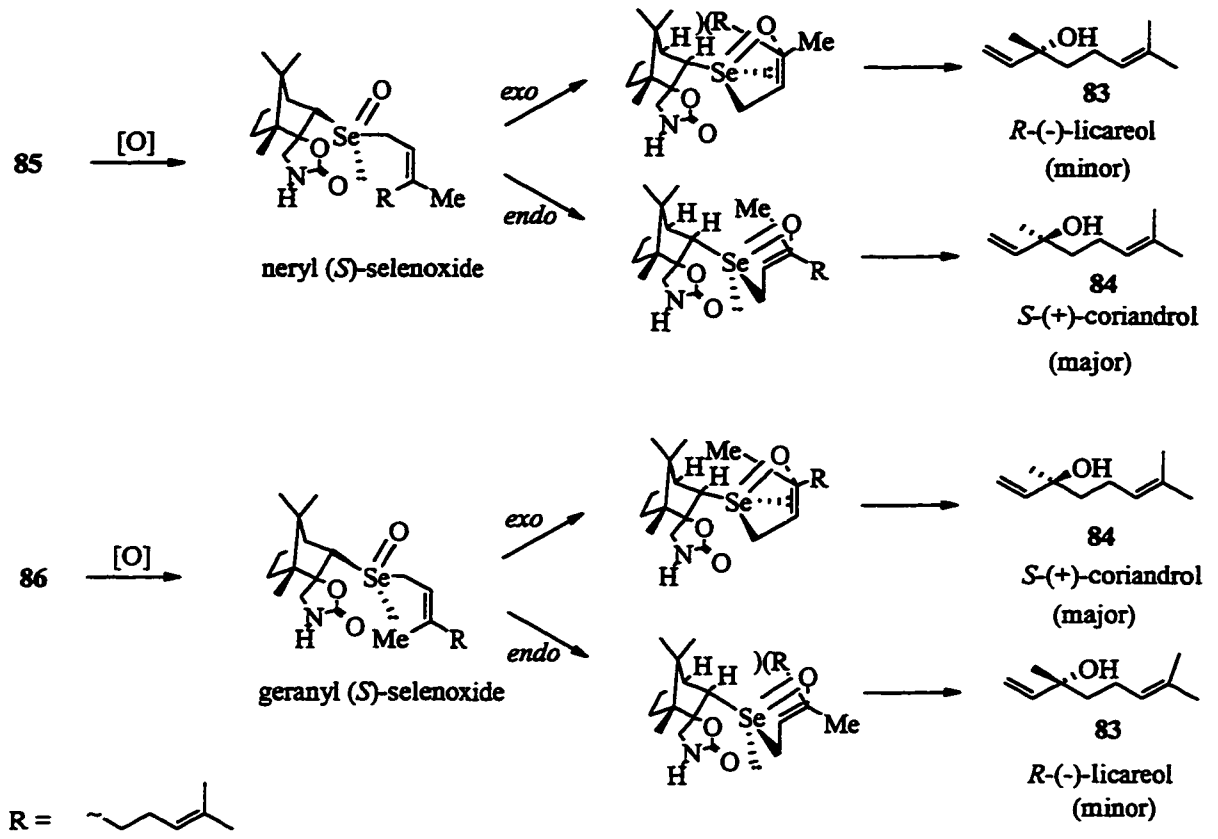
Selenides **87** and **88**, where hydroxyl and acetamido substituents replace the oxazolidinone moiety at C(2) of **85** and **86** showed the opposite stereoselectivity, producing (*R*)-(-)-licareol as the principal product. This may be due to the preferential formation of the selenoxide of opposite configuration to that obtained from **85** and **86**, or to more complex phenomena related to N-Se or O-Se interactions or hydrogen-bonding.

Since the oxidation step was found to proceed with high stereoselectivity (up to >97% d.e.) in the model methyl selenoxide system when double differentiation was possible, the poor e.e's in even the most stereoselective entries in Table 2.2 must be from inefficient chirality transfer in the sigmatropic rearrangements of the selenoxides and not from poor diastereoselectivity in the oxidation itself.

Figure 2.1 GC of Racemic and Nonracemic Linalool on a Cyclodex B Column



Scheme 2.11 Sigmatropic Rearrangements of Neryl and Geranyl Selenoxides

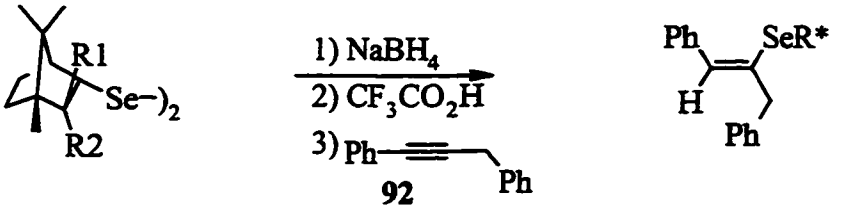


2.3.3 Asymmetric Selenoxide Elimination of Vinyl Selenides

Another potential application of chiral selenoxides is the asymmetric selenoxide elimination. For vinyl selenoxides without any *cis* hydrogens available, such eliminations give the corresponding allenes preferentially (see Scheme 1.4). If the product is itself chiral, then its formation via *syn* elimination of a nonracemic selenoxide, in principle, can produce a nonracemic allene. As stated in the previous section, the chiral selenoxide can be formed by asymmetric oxidation. 1,3-Diphenyl-2-(camphorseleno)propenes **89-91** were chosen as the test system because they can be made simply from the available camphor diselenides and 1,3-diphenylpropyne (**92**) as shown in Scheme 2.12 Moreover, the expected product, 1,3-diphenylallene, has a strong specific rotation ($[\alpha]_D$ = +1020, *S*-

enantiomer) that has been reported in the literature.[106] Diselenides **62**, **64** and **72** were treated with sodium borohydride to afford the corresponding camphor selenolates *in situ*. Camphor selenols were formed by adding trifluoroacetic acid to the reaction mixture, and their addition to diphenylpropyne (**92**) was achieved according to the general method of Tierce and Montana.[107] Only the (*Z*)-isomers of selenides **89**, **90** and **91** were obtained in significant yields by this method.

Scheme 2.12 Preparation of Chiral Vinyl Selenides

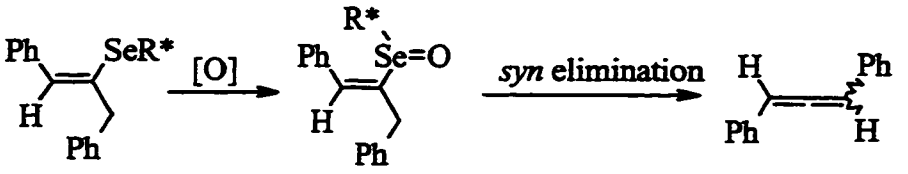


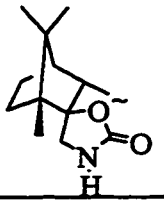
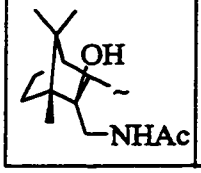
72: R_1= OAc, R_2= H
62: R_1= OH, R_2= CH_2NHAc
64: R_1, R_2= oxazolidinone

89: R_1=OAc, R_2= H
90: R_1= OH, R_2= CH_2NHAc
91: R_1, R_2= oxazolidinone

The results of the oxidation-elimination reactions of vinyl selenides **89-91** are shown in Table 2.3. All of the e.e's were measured by polarimetry. Both achiral and chiral oxidants were examined, but all of the e.e's are too low to be practical. From the preliminary studies of methyl selenide oxidations (see Section 2.3.1), it is assumed that the low enantioselectivities are the result of inefficient chirality transfer during the elimination step and not the oxidation step. It is noteworthy that the chiral auxiliaries in selenides **89** and **91** afforded the (*S*)-enantiomer in excess, while again, the oxazolidinone auxiliary had the opposite effect. Very slight double differentiation appears to have taken place with the (+)-oxaziridine **78** in the case of **89** and **90**, but is insignificant with **91**. In view of the extremely low e.e's, further experiments were abandoned.

Table 2.3 Selenoxide Eliminations of Chiral Vinyl Selenides



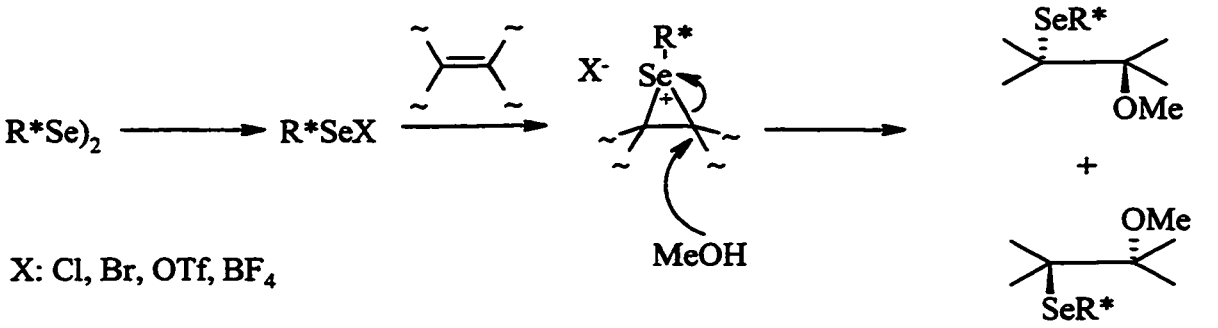
R*	Selenide	Oxidant	Isolated Yield %	e.e. % (Config. of major product)
	**89**	MCPBA	64	4.0 (S)
		(+)-Oxaziridine **78**	63	19.2 (S)
		(-)-Oxaziridine **79**	56	2.6 (S)
	**90**	MCPBA	69	5.7 (R)
		(+)-Oxaziridine **78**	56	11.3 (R)
		(-)-Oxaziridine **79**	61	6.1 (R)
	**91**	MCPBA	63	7.8 (S)
		(+)-Oxaziridine **78**	50	6.3 (S)
		(-)-Oxaziridine **79**	52	9.6 (S)

2.3.4 Methoxyselenenylations

As mentioned in Chapter 1, the stereospecific *trans*-addition reactions of selenenic electrophiles provides a useful strategy for the fuctionalization of simple olefins. In the case of methoxyselenenylation, if the *trans*-addition also proceeds with high facial selectivity, it would offer an effective approach to the enantioselective introduction of a methyl ether function. This objective can be achieved by applying chiral organoselenium auxiliaries. It will be recalled from Chapter 1 that there have been numerous examples of methoxyselenenylations employing chiral auxiliaries, but problems such as difficult access to the required chiral organoselenium reagents and inconsistent diastereoselectivities still exist. Thus, it was considered worthwhile to

investigate some asymmetric methoxyselenenylations of alkenes with camphor-derived diselenides. This would involve conversion of the camphor-derived diselenides to selenenic electrophiles, followed by addition of the electrophile to the alkene to generate the three-membered seleniranium ion. Finally, attack by methanol would open the three-membered ring, and form the corresponding β-methoxy selenide (Scheme 2.13). The d.e.'s can be measured by NMR spectroscopy, and reductive deselenization leads, in some examples, to compounds with known specific rotations, which provides the opportunity to determine the absolute stereochemistry.

Scheme 2.13 Asymmetric Methoxyselenenylation



Attempts were first made to optimize the chiral auxiliary and conditions for this process by varying one parameter at a time. The following experiment was chosen as a reference point for comparison. The original 2-keto camphor diselenide **57** and the commercially available *trans*-5-decene were used as the test reagent and substrate, and the triflate was chosen as the leaving group X because it generates a strong electrophile with a nonnucleophilic counterion. Thus, after the diselenide was stirred with 1 molar equivalent of bromine in dichloromethane solution at -78 °C for 15 min, 1.4 equivalents of methanolic silver triflate solution were added to generate the selenenyl triflate *in situ,* followed by the addition of 2.5 molar equivalents of *trans*-5-decene. The solution was kept at -78 °C for 1 h, after which aqueous work-up, purification by column chromatography, and analysis by proton NMR spectroscopy was performed to determine the d.e. of the reaction. The methoxy protons as well as the protons from C(3) and

sometimes C(4) of the camphor moiety were generally well separated. Figure 2.2 shows the spectrum of the diastereomers from this experiment. Thus, the signals assigned to C(3)-H for the major and minor diastereomers occur at δ 3.78 and 3.99 ppm, respectively, while those from their methoxy groups are present at δ 3.42 and 3.39 ppm, respectively. The next stage was to thus compare the effectiveness of different chiral auxiliaries under a standard set of conditions. The results are shown in Table 2.4. for seven chiral auxiliaries that were tested, where the above experiment is shown in Entry 1.

From the data in Table 2.4, it can be seen that the highest diastereoselectivity and best yield were obtained with the C(2) keto diselenide **57** (Entry 1), while the results of reactions with the C(2) *exo* hydroxy and C(2) *exo* acetoxy diselenides **72** and **73** (Entry 3, and 6) demonstrated comparable stereoselectivities. It's possible that an intramolecular interaction between the ketone oxygen atom and the selenium atom of the seleniranium ion in Entry 1 contributes to the relatively high d.e. A similar interaction may be possible with the *exo* carbonyl oxygen atom of the acetate in Entry 6, but not with the *exo*-alcohol in Entry 3, where the *trans* orientation of the of the C(2) and C(3) substituents prevent their close proximity. The C(2) *endo*-hydroxy (Entry 2) and acetoxy diselenides (Entry 5) **74** and **70** were expected to provide improved interaction with the selenium atom and therefore more efficient chirality transfer, but unfortunately, no reaction was observed with either of them. This may be due to strong coordination between the hydroxy or acetoxy oxygen atoms with the selenium atom in Entry 2 and 5, where both the C(2)-substituents and the selenium moiety are *endo* and therefore *cis*. The C(2) oxazolidinone diselenide **64** (Entry 4) gave poor diastereoselectivity. It's fortunate that the most effective diselenide is also the one that can be most readily prepared in one step from camphor on a large scale. The C(2) hydroxy acetamido diselenide **62** (Scheme 2.14) produced selenenamide **94** under these conditions, the chemistry of which has been studied by B. Dyck, who determined that it acts as a glutathione peroxidase mimic.[108] In view of the significance of this compound, suitable crystals were grown for X-ray crystallography and the resulting structure was obtained by Dr. M. Parvez and is given in Appendix A, as well as in a recent publication.[109] Since the reaction of the C(2) keto

diselenide **57** proceeded with the highest stereoselectivity, this chiral auxiliary was chosen for further optimization.

Figure 2.2 ^{1}H NMR Spectrum of Entry 1 in Table 2.4

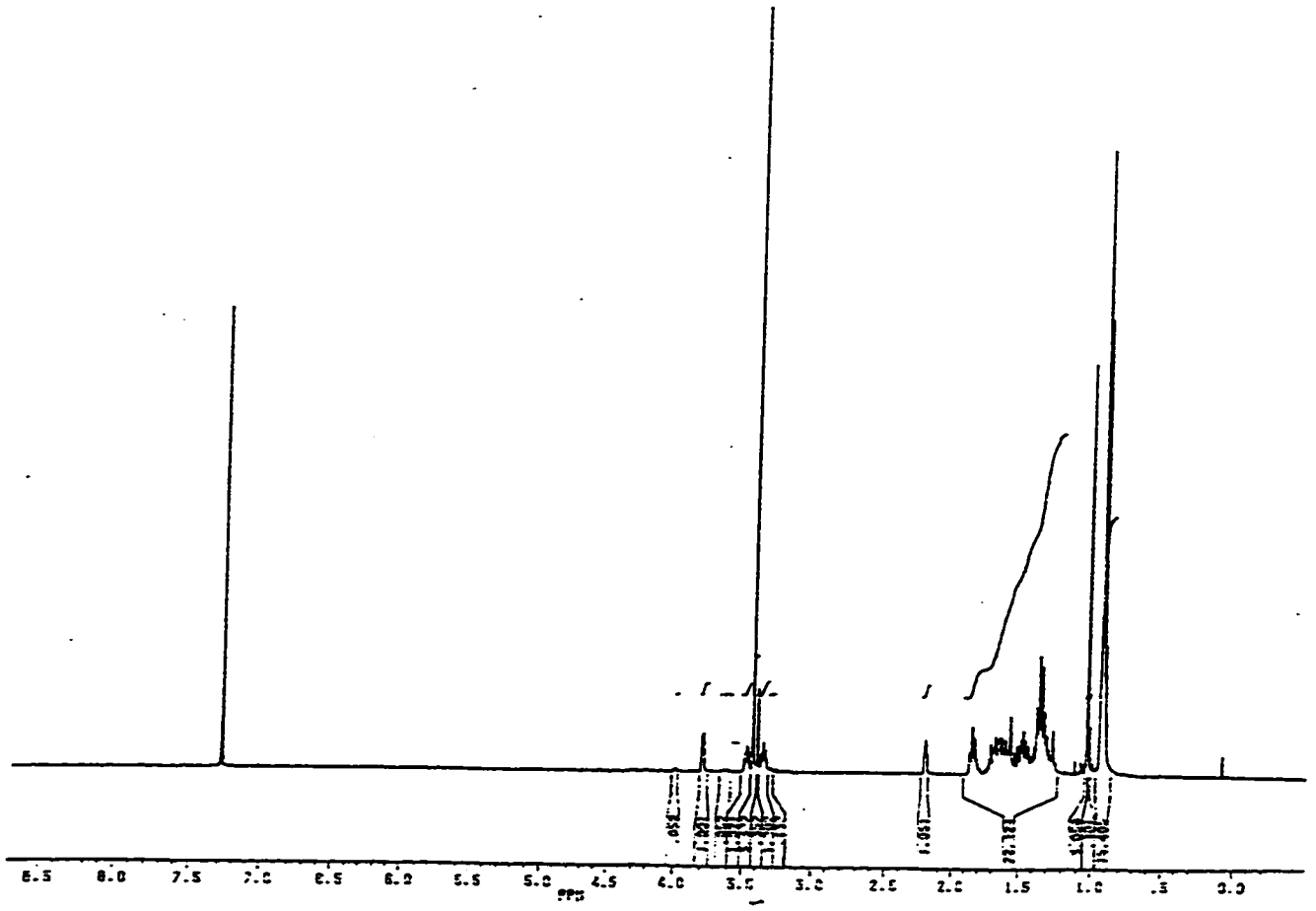
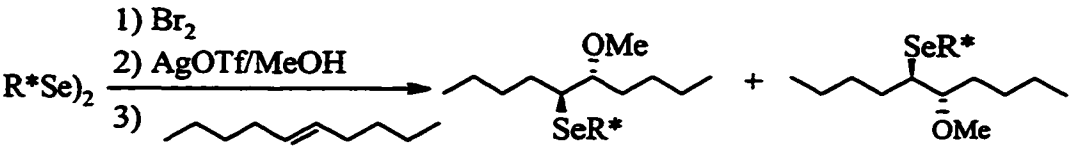
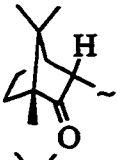
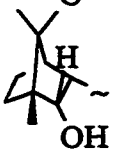
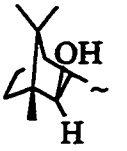
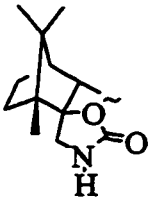
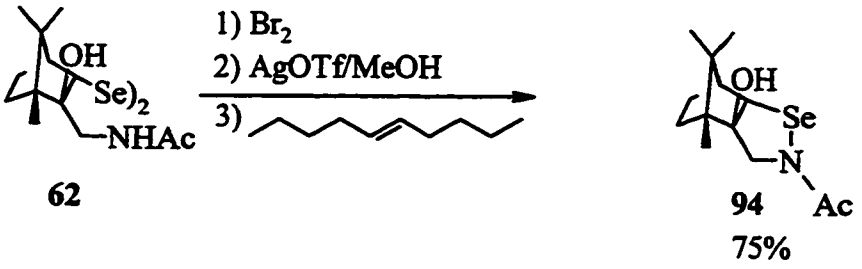


Table 2.4 Methoxyselenenylation of *trans*-5-Decene with Different Chiral Auxiliaries



Entry	R*	Diselenide	Isolated Yield %	d.e. %
1		**57**	77	87
2		**74**	N.R.	N.R.
3		**73**	63	64
4		**64**	65	32
5		**70**	N.R.	N.R.
6		**72**	51	69

Scheme 2.14 Formation of a Cyclic Selenenamide from **62**

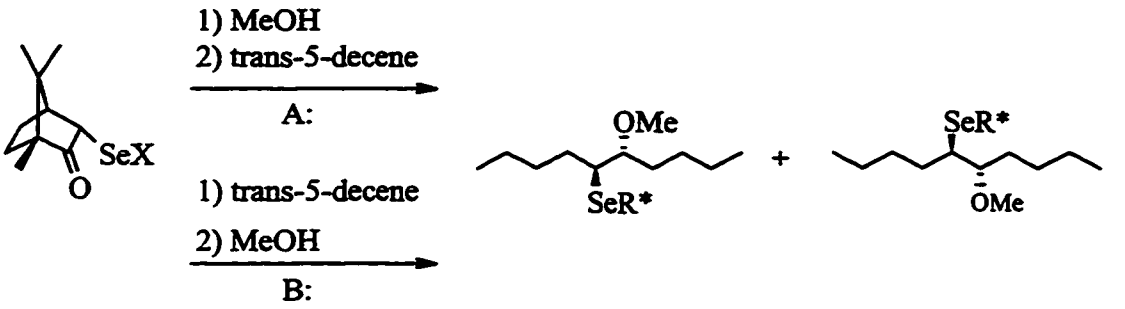


62 **94** 75%

The optimization of the methoxyselenenylation of *trans*-5-decene with the C(2) keto diselenide **57** was accomplished by changing one parameter at a time (Table 2.5). First of all, two general procedures for adding reagents were investigated. Procedure A involved the addition of methanol before the olefin, and vice versa in procedure B. The application of procedure B decreased the stereoselectivity drastically (Entry 2). By varying the temperature (Entry 1, 3, 4), we can see that low temperatures produced the highest d.e.'s. The use of other solvents such as ether and toluene (Entry 5 and 6) provided comparable results to dichloromethane. Counterions other than triflate, including BF_4^-, Br^- and Cl^-, were also tested (Entry 7, 8, 9). Tetrafluoroborate showed similar selectivity to triflate, whereas reactions with bromide and chloride produced complex mixtures. When the selenenyl chloride was employed (Entry 9), no reaction occurred at low temperatures and so the procedure was performed at room temperature.

From the above results, it appears that the best conditions for methoxyselenenylations include: the 2-keto camphor chiral auxiliary, low temperatures, non-nucleophilic counterions such as triflate or tetrafluoroborate, and either dichloromethane, ether or toluene as the solvent. The conditions of Entry 1 or 3 were therefore used in subsequent experiments.

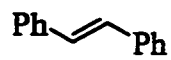
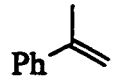
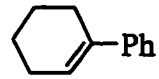
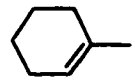
Table 2.5 Optimization of the Methoxyselenenylation Reaction



Entry	Procedure	X	Solvent	Temperature, °C	% d.e.
1	A	OTf	CH_2Cl_2	-78	87
2	B	OTf	CH_2Cl_2	-78	30
3	A	OTf	CH_2Cl_2	-95	90
4	A	OTf	CH_2Cl_2	-42	65
5	A	OTf	Et_2O	-78	84
6	A	OTf	Toluene	-78	85
7	A	BF_4	CH_2Cl_2	-78	84
8	A	Br	CH_2Cl_2	-78	C.M.
9	A	Cl	CH_2Cl_2	23	C.M.

Next, we investigated the methoxyselenenylations of a variety of other commercially available olefins with the optimized conditions determined above. The results are shown in Table 2.6. The substrates were chosen to examine the effects of various substitution patterns and *E,Z* geometry. Under the conditions employed, methoxyselenenylations of *trans*-alkenes demonstrated higher stereoselectivities compared with *cis*-alkenes (Entry 1 and 8 vs. 2 and 11, Entry 3 vs. 4). Similarly, 1,1-di-substituted and tri-substituted olefins also showed moderate facial selectivities of 66-72% d.e. (Entry 6, 9, 10). The monosubstituted olefin in Entry 7 gave only a low d.e. The regiochemistry of additions to mono- and trisubstituted olefins afforded Markovnikov products as the only isolable adducts, in accordance with literature precedents.[48]

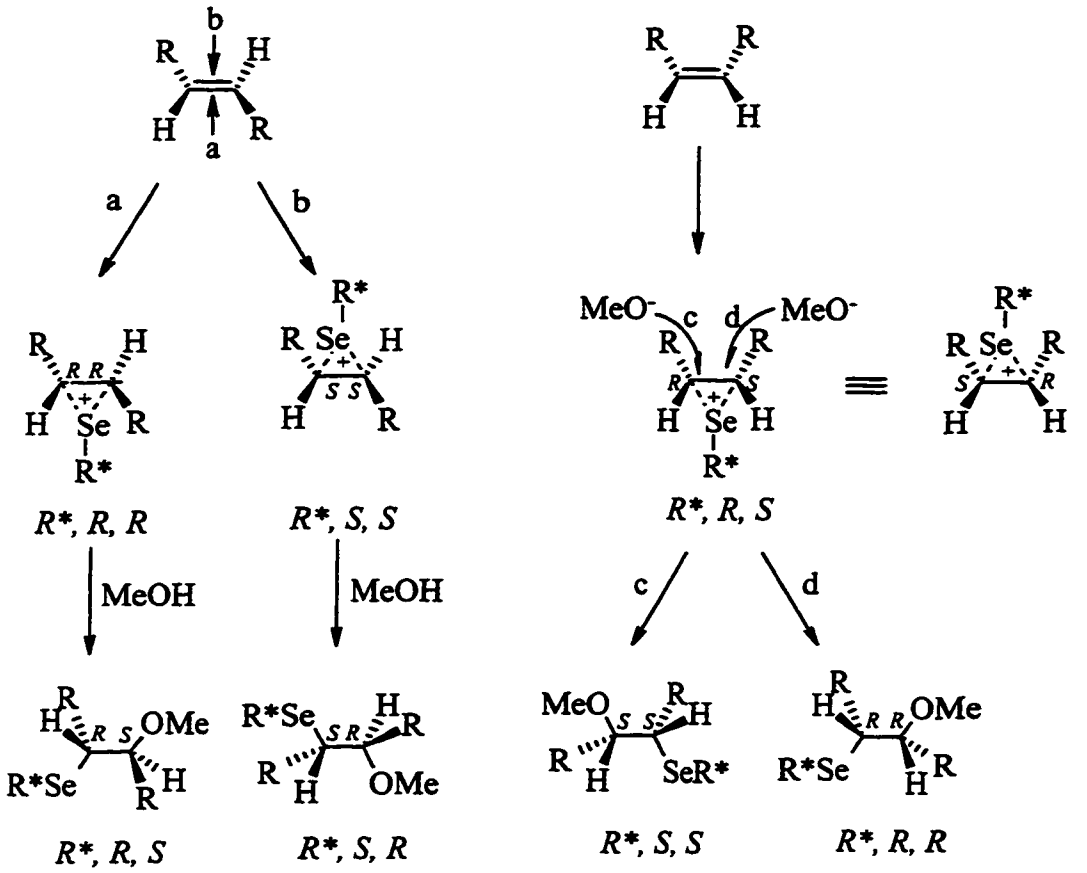
Table 2.6 Methoxyselenenylations with the 2-Keto Camphor Auxiliary

Entry	Substrates	% Yield	% d. e.
1		72	90
2		88	50
3		65	68
4		66	38
5		71	63
6		88	66
7		77	47
8		69	74
9		73	71
10		90	68
11		71	49

It should be mentioned that the stereo-determining step for *cis*- and *trans*-alkenes is not the same[110] (Scheme 2.15). If we assume that the mechanism of methoxyselenenylation involves the three-membered seleniranium cation intermediate, two diastereomeric intermediates can be generated from a *trans*-alkene by attacking opposite faces of the double bond by the selenium electrophile, whereas attack of the selenium electrophile upon the two faces of a *cis*-alkene produces the same cation intermediate. In the case of *trans* alkenes, attack of methanol at either carbon of the seleniranium cation in the second step affords the same stereoisomer, while attack at the

two carbon atoms of the intermediate derived from the *cis*-alkene produces different diastereomers. Thus, the stereochemistry-determining step for *trans*-alkenes is the cation-forming step, and for *cis*-alkenes it's the step involving capture of the nucleophile.

Scheme 2.15 Mechanism for Methoxyselenenylation of *trans*- and *cis*-Alkenes[a]

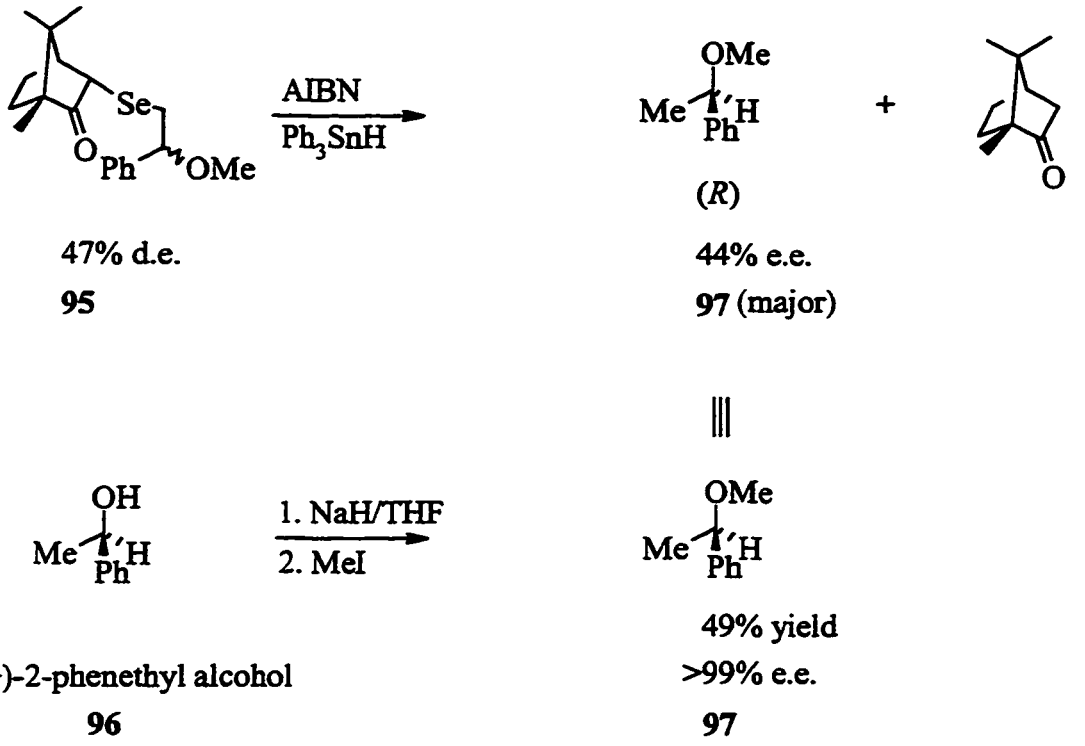


[a] *R*, *S* configurations are based on the assumption that the substituents have the following order of priority according to the CIP rules regardless of the actual identity of R: R*Se > OMe > CHRSeR* > CHROMe > R > H.

The absolute stereochemistry of the methyl ether **95**, produced from diselenide **57** and styrene (Table 2.6, Entry 7) was determined by reductive removal of the chiral organoselenium moiety and comparison of the GC retention time on a chiral column of the product with that of an authentic sample prepared from commercially available *R*-(+)-

2-phenethyl alcohol. Thus, the reduction of **95** with triphenyltin hydride in the presence of a trace of AIBN in refluxing toluene solution afforded methyl ether **97** with nearly the same e.e. as the d.e. of the precursor **95**. (*R*)-(+)-2-Phenethyl alcohol (**96**) was then treated with sodium hydride, followed by methyl iodide, to provide methyl ether **97** in almost 100% e.e., which had the same retention time as the major isomer of the product obtained from the methoxyselenenylation experiment. Therefore, we can conclude that the absolute configuration of the chiral center α to the ether moiety is *R* in the major stereoisomer of **97** and *S* in its precursor **95**. (Scheme 2.16).

Scheme 2.16 Absolute Configuration of Selenide **95**

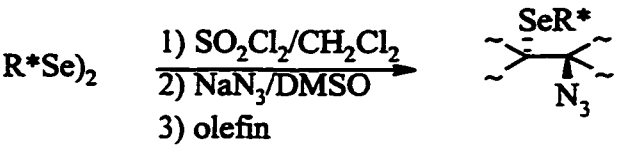


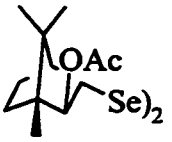
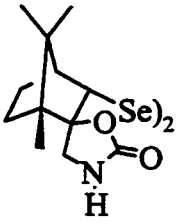
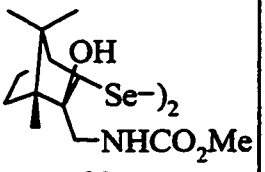
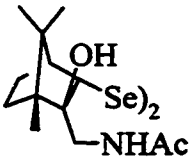
Very recently, while the writing of this Thesis was underway, Tiecco[111] et al. reported that the selenenyl sulfate derived from diselenide **57** can also be used for asymmetric methoxyselenenylations. However the corresponding selenenyl triflate used in this work provides comparable or higher d.e.'s than the sulfate.

2.3.5 Selenenyl Azide Additions

The first examples of the direct introduction of PhSe and N_3 functions by addition to unactivated olefins were reported by Hassner.[50] We attempted to extend this reaction into the asymmetric realm by employing camphor-derived diselenides. Diselenides **62**, **64**, **66** and **72** were treated with sulfuryl chloride to generate the corresponding camphorselenenyl chlorides *in situ*. A sodium azide solution in DMSO was added in one portion, followed by the olefin to afford the β-phenylseleno azide in good yield. The presence of the azide function in the products was obvious from the characteristic IR absorption at ca. 2100 cm^{-1}, and both low resolution and high resolution mass spectra were consistent with the desired products. All of the d.e.'s were determined by NMR spectroscopy, since signals from the protons at C(3) and C(4) of the camphor moiety were well separated. For example, in the ^1H NMR spectrum of the product from Entry 3 in Table 2.7, the signal from C(3)-H of the major isomer occurs at δ 3.89-3.92 ppm, whereas that of the minor isomer produces a signal at δ 3.81-3.84 ppm. It was reported by Hassner[50] that the additions of selenenyl azides to alkenes proceed via a three-membered seleniranium ion intermediate and give *trans*-addition adducts stereospecifically. Unfortunately, among all four diselenides explored, none demonstrated satisfactory stereoselectivities. This may be because DMSO disrupts the intramolecular interactions between the heteroatoms at the C(2) position and the selenium atom. An attempt to use diselenide **57** in a similar manner produced a complex mixture in which the α-diketone **80** was a major product.

Table 2.7 Selenenyl Azide Additions to Alkenes



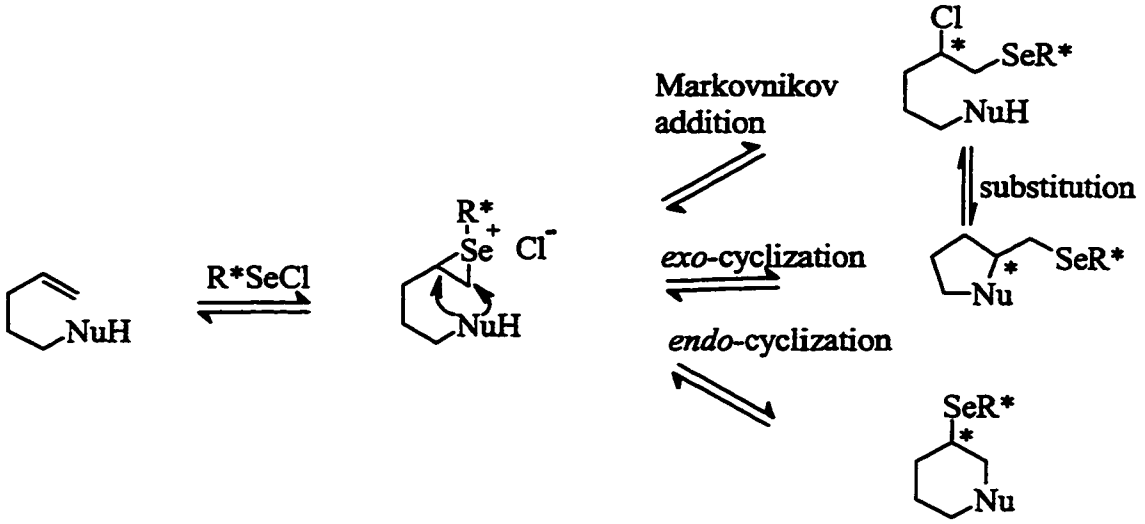
R*Se)$_2$	Entry	Substrate	Isolated Yield %	d.e. %
 **72**	1	cyclohexene	63	6
	2	*trans*-5-decene	73	37
 **64**	3	cyclohexene	97	19
	4	*trans*-5-decene	91	4
 **66**	5	cyclohexene	90	11
 **62**	6	*trans*-5-decene	88	25

2.3.6 Cyclofuntionalizations

Heterocycles and carbocycles feature greatly in the structure of natural products, which makes the asymmetric construction of rings one of the important and challenging objectives in modern organic synthesis. Among the most practical ring-forming reactions

are those based on the intramolecular reaction of a nucleophilic group and an electrophilic site elsewhere in the molecule. Chiral organoselenium auxiliaries can be exploited in this way in cyclofunctionalizations.[82,86,87] The sequential steps are shown in Scheme 2.17.

Scheme 2.17 Asymmetric Cyclofuntionalization

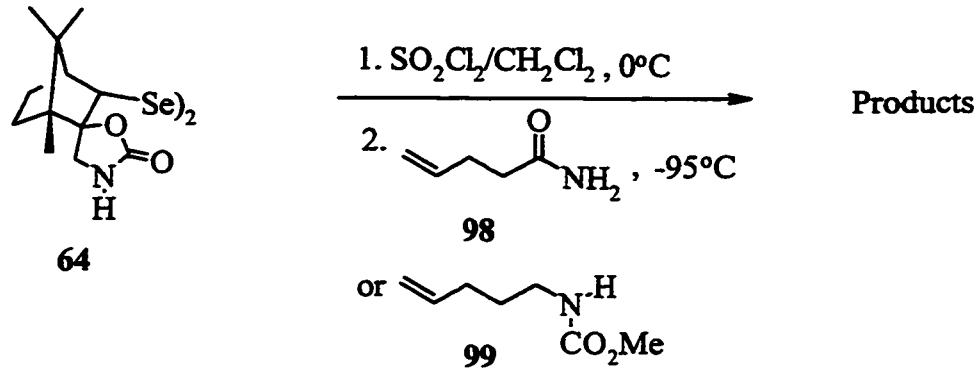


First, the electrophilic site is generated by the addition of a selenium electrophile. The resulting seleniranium ion intermediate can either react further with the counterion, (e.g. chloride ion) via 1,2 addition, or be attacked by the internal nucleophile to produce the cyclized product. The cyclization step can take place either via an *exo* transition state or an *endo* transition state, depending on the ring size. Baldwin has formulated a series of rules to predict the regiochemistry of such processes,[112] but they are sometime unreliable when applied to attack at three-membered rings because of the severely distorted orbitals required to accommodate the small bond angles of approximately 60° instead of the 109° preferred at a saturated carbon atom.

To date, several successful asymmetric ring-closure reactions mediated by chiral organoselenium reagents have been reported and are described in Chapter 1. B. Dyck[91] of this laboratory succeeded in the diastereoselective cyclization of a series of unsaturated alcohols and carboxylic acids with camphor-based selenenyl chlorides. Among the

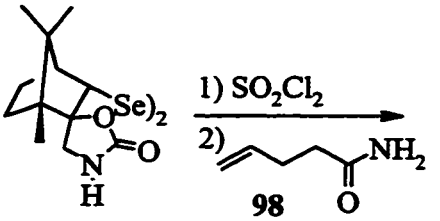
auxiliaries that were tested, the selenenyl chloride containing the C(2) oxazolidinone moiety proved to be the most efficient chiral auxiliary (70-90% d.e.). The optimized conditions were found to be: a) treatment of the diselenide with sulfuryl chloride at 0 °C, b) cooling to -95 °C and addition of 2.2 equivalents of the olefin, c) allowing the solution to stir at -95 °C for 45 min. Since asymmetric cyclofunctionalizations involving nitrogen nucleophiles have not been widely reported, we investigated such reactions of amide **98** and carbamate **99**, using the diselenide **64** (Scheme 2.18).

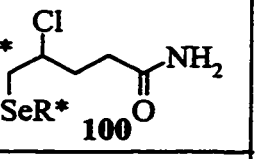
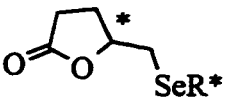
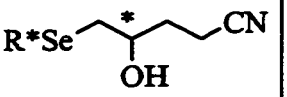
Scheme 2.18 Attempted Cyclofunctionalizations of Amide Nucleophiles



The cyclization procedure was applied to amide **98** under various conditions, and the products, along with their d.e.'s are shown in Table 2.8. The results were unexpected, since none of the reactions studied produced the desired lactam. Under neutral conditions (Entry 1), chloride **100** was isolated but was not stable enough for full characterization. Addition of *p*-TsOH to the reaction mixture produced the five-membered lactone **101** in greater than 97% d.e. (Entry 2). This product had formerly been obtained by Dyck in 90% d.e. by the cyclization of 4-pentenoic acid. Finally, the nitrile **102** was generated in 90% d.e. by the addition of potassium *t*-butoxide to the reaction mixture (Entry 3).

Table 2.8 Reactions of Amide **98**

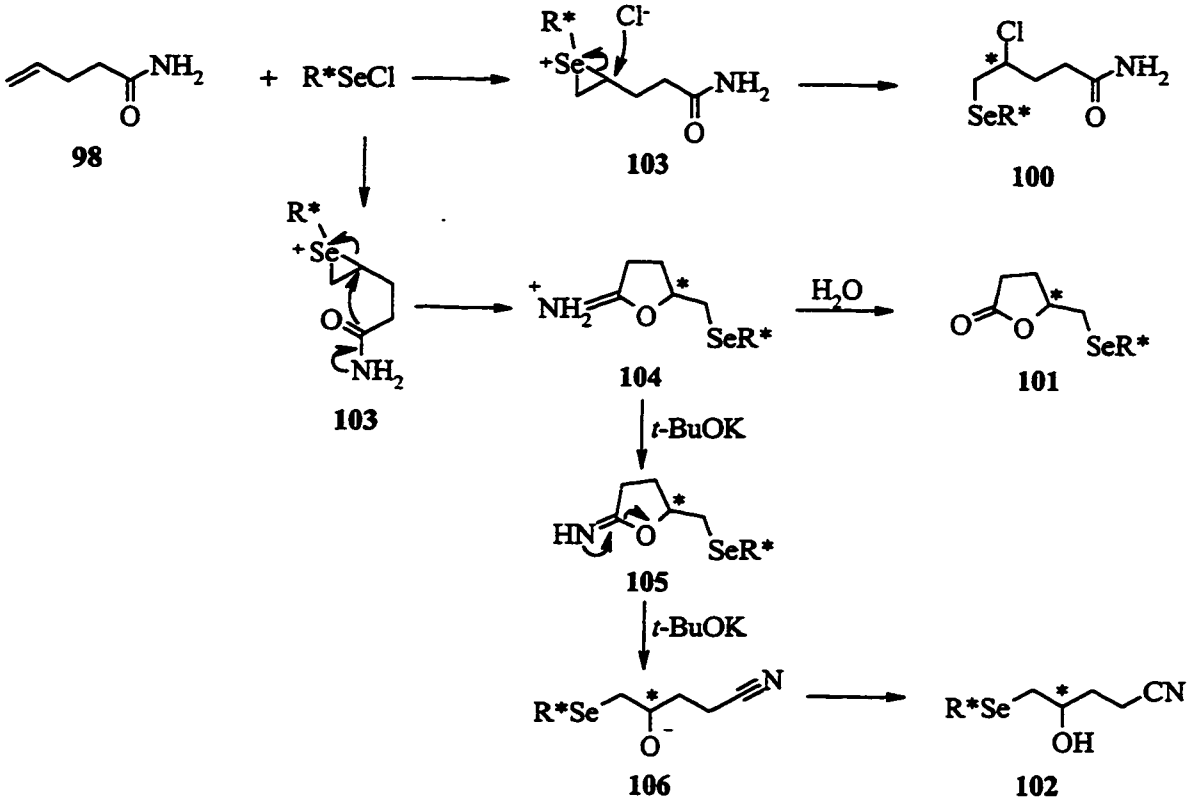


Conditions	Entry	Time (h)	d.e.% (yield)	Products
1. SO_2Cl_2, 0 °C 2. **98**, -78°C	1	1	90	 **100**
1. SO_2Cl_2, 0 °C 2. **98**, -95 °C 3. p-TsOH, rt	2	1 16	>97 (88)	 **101**
1. SO_2Cl_2, 0 °C 2. **98**, -95 °C 3. t-BuOK, rt	3	1 4	90 (67)	 **102**

The yields listed in Entry 2 and 3 in Table 2.8 refer to isolated yields after column chromatography, and the products were characterized by their ^1H NMR, ^{13}C NMR, IR and mass spectra. The IR spectrum of chloride **100** showed a strong absorption at 751 cm^{-1}, which indicated the existence of a carbon-chlorine bond. The IR spectrum of nitrile **102** had a strong signal at 2300 cm^{-1}, attributed to the triple bond of the CN group, whereas the OH stretch appeared at 3400 cm^{-1}. Diastereomeric excesses were determined by ^1H NMR spectroscopy. Lactone **101** was identical to the sample characterized by Dyck. A possible explanation for the formation of these three products is shown in Scheme 2.19. First, the selenium electrophile adds to the double bond to form the

seleniranium cation **103**. Ring-opening and overall 1,2-addition of the chloride counterion produced Markovnikov adduct **100** under neutral conditions. With acid catalysis, the oxygen atom of the amide functionality of **103** preferentially attacked the developing electrophilic center to form the imminium cation **104**, which subsequently hydrolyzed during workup to the corresponding lactone **101**. On the other hand, in the presence of potassium t-butoxide, the imine moiety of **105** underwent elimination to afford the corresponding nitrile **102**.

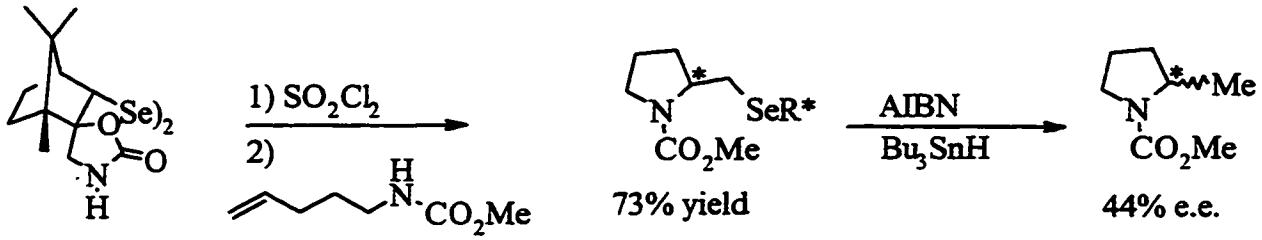
Scheme 2.19 Mechanism for the Reactions of Amide **98**



Some earlier work on the organoselenium-mediated synthesis of nitrogen heterocycles was reported by Clive with benzeneselenenyl chloride.[56] It was found that ω-unsaturated primary amines do not cyclize easily, but their urethane derivatives do. Also, the presence of silica-gel in the reaction mixture was reported to increase the yields of the

cyclic products. We attempted to apply this chemistry to the asymmetric cyclofunctionalizations of urethane **99** (Scheme 2.20). The cyclized product **107** was isolated and purified by chromatography. The structure was consistent with its IR and mass spectra, but unfortunately, the ^{1}H-NMR spectrum showed overlapping signals, making it impossible to determine the d.e. The product was therefore subjected to free-radical deselenization with tri-n-butyltin hydride in the presence of AIBN to afford carbamate **108**, the e.e. of which was then measured by GC on a chiral column. We thus obtained moderate stereoselectivity in the first example of an asymmetric urethane cyclization induced by a selenium electrophile.

Scheme 2.20 Cyclofunctionalization of the Urethane **99**



64 **99** **107** **108**

2.4 Conclusions and Future Work

This chapter summarizes the investigation of camphor-derived chiral auxiliaries in a variety of asymmetric reactions. A study of [2,3]sigmatropic rearrangements of neryl and geranyl selenides indicated that, although the oxidation step proceeds with high stereodifferentiation, the [2,3]shift lacks high stereoselectivity. Even though the results were disappointing, it was nevertheless possible to conclude that the C(2) substituent plays a major role in asymmetric induction. This is evident from the fact that C(2) oxazolidinone selenides **85** and **86** gave mainly the (*S*)-allylic alcohol, whereas the C(2) hydroxy acetamido selenides **87** and **88** produced an excess of the (*R*)-allylic alcohol. It was interesting to note that neither the configuration of the oxidant, nor the *E,Z*-

configuration of the allylic substituent had an effect upon the absolute configuration of the major product. Asymmetric oxidation-elimination reactions showed very poor enantioselectivity, making the protocol of little value for the preparation of chiral allenes.

Among the electrophilic addition reactions studied, moderate to good stereoselectivities were obtained in methoxyselenenylations, and the conditions were optimized. The C(2) keto camphor moiety was found to be the most effective auxiliary, and the required diselenide **57** can be readily made in one step from camphor. However, poor diastereomeric excesses were obtained from the selenenyl azide additions using this chiral auxiliary.

The C(2) oxazolidinone auxiliary proved to be the most effective in cyclofunctionalizations. Although no lactam was observed from the reaction with an ω-unsaturated primary amide, the resulting products, a lactone and nitrile, were formed in high d.e. and the mechanism itself is of interest. Cyclization of the carbamate from an ω-unsaturated N-carbamoyl amine produced the corresponding lactam with moderate d.e.

For some of the reactions described above, the low e.e's were probably due to the relatively long C-Se bond, which results in relatively loose transition states, thereby diminishing energy difference between them and decreasing enantioselectivity in kinetically controlled processes. Similarly, the long C-Se bond in asymmetric selenium reactions would minimize energy differences of the products, thereby decreasing the enantioselectivity of reactions under thermodynamic control.

In the future, the optimization of conditions for lactam cyclofunctionalization should be carried out, and the extension of this reaction to other ω-unsaturated amides and carbamates is recommended. Since C(2)-substituents play a key role in chirality transfer, more efficient auxiliaries should be designed by introducing bulkier or much strongly coodinating groups to the C(2) position.

Chapter Three

Experimental Section

3.1 General Comments

IR Spectra were recorded on a Nicolet 5DX or a Mattson 4030 spectrophotometer, using thin films deposited from chloroform solution on to NaCl plates, unless otherwise stated. ^{1}H and decoupled ^{13}C NMR spectra were taken on a Bruker AC-E 200 (^{1}H, 200 MHz; ^{13}C, 50 MHz) or a Bruker AM 400 (^{1}H, 400 MHz; ^{13}C, 100 MHz) spectrometer. Deuteriochloroform was used as the solvent, unless otherwise stated, with either residual chloroform (^{1}H δ 7.27, ^{13}C δ 77.16 ppm) or TMS (^{1}H δ 0.0 ppm) as the internal standard. ^{77}Se NMR spectra were obtained at 400 MHz on a Bruker AM 400 spectrometer, with diphenyl diselenide (δ 461 ppm[113]) as an external standard with signals reported relative to dimethyl selenide (δ 0.0 ppm). All of the ^{1}H NMR spectra have the following format: δ chemical shift (in ppm), (multiplicity, coupling constant (Hz), relative number of protons, assignment). ^{13}C NMR spectra have the following format: δ chemical shift (in ppm).

Low and high resolution mass spectra were acquired on a Kratos MS80 or a VG 7070 mass spectrometer by Ms. Q. Wu and Ms. D. Fox at the University of Calgary. The spectra have the format: m/z (assignment, relative intensity %). Chiral GC spectra were obtained on a Varian Star 3400 CX instrument with a Cyclodex B 30 m X 0.32 mm column. Optical rotations were measured on a Rudolph III polarimeter or an AutoPol IV polarimeter. Elemental analyses were determined by Ms. D. Fox at the University of Calgary. TLC was performed on aluminum sheets coated with 0.2 mm of Merck silica-gel 60 F-254, and the spots were visualized under UV light or by spraying with 2% ceric sulfate in 12% sulfuric acid solution. Flash chromatography was performed by a similar method to that reported by Still,[114] using Merck silica gel (230-400 mesh).

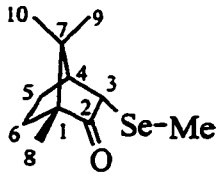
Solvents used were reagent grade, and dry dichloromethane, THF and toluene were distilled from phosphorus pentoxide, lithium aluminum hydride, and calcium

hydride respectively. Anhydrous diethyl ether and DMSO were stored in septum-sealed bottles. Concentrated aqueous solutions of NaCl, Na_2CO_3, $NaHCO_3$, K_2CO_3, NH_4Cl, 5% HCl, and 1.5 M NaOH were used for washing organic solutions. Anhydrous $MgSO_4$ or Na_2SO_4 were used as drying agents. Ice-water (0 °C), acetone-dry ice (-78 °C), and acetone-liquid nitrogen (-95 °C) were used in the cooling baths. All of the diselenides were prepared by following B. Dyck's procedure.[91b] MCPBA was purified by the procedure of Schwartz and Blumbergs.[115] The (*R*)-(+)-camphor starting material had $[\alpha]_D$ = +43.7° (c= 10, EtOH) compared to the literature value of +43.8°.[116] All other chemicals were commercially available and used without further purification unless otherwise noted.

The X-ray structure of selenenamide **94** was solved by Dr. M. Parvez. The ORTEP diagram, experimental details, atomic coordinates, bond lengths, bond angles and torsion angles are presented in Appendix A, which was also provided by Dr. Parvez.

3.2 Experiments Related to Section 2.3.1

3.2.1 Preparation of (1*R*)-*endo*-3-Camphoryl Methyl Selenide (75)

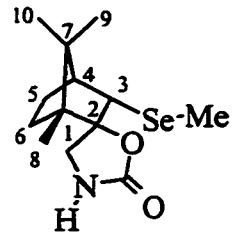


75

This compound was first prepared by B. Dyck in our laboratory, but its characterization has not yet been reported. Sodium borohydride (0.41 g, 5.4 mmol) was added in portions to an ice-cooled solution of diselenide **57** (1.0 g, 2.2 mmol) in 1.0 mL of absolute ethanol. After the addition was complete, the ice bath was removed and the mixture was stirred under argon at rt for 1 h. Methyl iodide (0.41 mL, 6.5 mmol) was added, and the mixture was stirred for 1.5 h. The mixture was poured into 100 mL of

ether, washed three times with 200 mL of water and once with 100 mL of aqueous NaCl, dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was chromatographed (elution with 5% ethyl acetate/hexane) to afford 0.78 g (73%) of **75** as a pale yellow oil; IR (nujol), 1732 (C=O), 1040 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 3.66-3.63 (m, 1H, C(3)-H), 2.23-2.17 (m, 1H, C(4)-H), 2.20 (s, 3H, SeMe), 1.89-1.39 (m, 4H, C(5) and C(6)-H), 1.03 (s, 3H, C(8)-H), 0.93 (s, 3H, C(9)-H), 0.91 (s, 3H, C(10)-H); mass spectrum, m/z (relative intensity) 246 (M^+, 21), 151 (R^{*+}, 8), 123 (57), 41 (100). Elemental analysis calculated for $C_{11}H_{18}OSe$: C, 53.88; H, 7.40; N, 0.00. Found: C, 53.83; H, 7.43; N, 0.17.

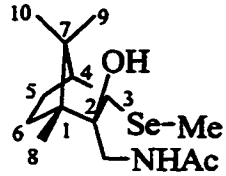
3.2.2 Preparation of (1*R*)-N,O-Carbonyl-*endo*-2-aminomethyl-*exo*-2-hydroxy-*endo*-3-bornyl Methyl Selenide (**76**)



76

This compound was first prepared by B. Dyck in our laboratory, but its characterization has not yet been reported. Compound **76** was prepared in 78% yield from diselenide **64** according to the procedure in Section 3.2.1: white foam; IR (nujol), 3275 (NH), 1747 (C=O), 1040 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 5.40 (br s, 1H, NH), 4.11 (d, J= 9.1 Hz, 1H, NCH_2), 3.66 (m, 1H, C(3)-H), 3.56 (d, J= 9.2 Hz, 1H, NCH_2), 2.16-2.01 (m, 1H, C(4)-H), 2.05 (s, 3H, SeMe), 1.68-1.01 (m, 4H, C(5)and C(6)-H), 1.66 (s, 3H, C(8)-H), 0.94 (s, 3H, C(9)-H), 0.93 (s, 3H, C(10)-H); mass spectrum, m/z (relative intensity) 303 (M^+, 50), 288 (R^*Se^+, 7), 208 (R^{*+}, 66), 83 (100). Elemental analysis calculated for $C_{13}H_{21}NO_2Se$: C, 51.66; H, 7.00; N, 4.63. Found: C, 51.38; H, 6.98; N, 4.65.

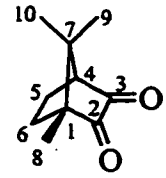
3.2.3 Preparation of (1*R*)-N-Acetyl-*endo*-2-aminomethyl-*exo*-2-hydroxy-*endo*-3-bornyl Methyl Selenide (77)



77

This compound was first prepared by B. Dyck in our laboratory, but its characterization has not yet been reported. The title compound was prepared in 78% yield from diselenide **62** using the same procedure as described in section 3.2.1: white foam; IR (nujol), 3290 (OH), 1642 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 6.60 (br s, 1H, NH), 3.80 (dd, J= 14.4, 7.6 Hz, 1H, NCH_2), 3.41 (m, 2H, OH and C(3)-H), 3.19 (dd, J= 14.1, 5.0 Hz, 1H, NCH_2), 2.07 (s, 3H, SeMe or Ac), 2.04 (s, 3H, SeMe or Ac), 1.90-1.86 (m, 1H, C(4)-H), 1.68-1.26 (m, 4H, C(5)and C(6)-H), 1.15 (s, 3H, C(8)-H), 0.94 (s, 3H, C(9)-H), 0.90 (s, 3H, C(10)-H); mass spectrum, m/z (relative intensity) 319 (M^+, 2), 304 ($R^{\bullet}Se^+$, 1) 224 ($R^{\bullet+}$, 36), 109 (87), 43 (100). Elemental analysis calculated for $C_{14}H_{25}NO_2Se$: C, 52.83; H, 7.92; N, 4.40. Found: C, 52.72; H, 7.93; N, 4.45.

3.2.4.1 Asymmetric Oxidations of Selenides. Table 2.1, Entry 1

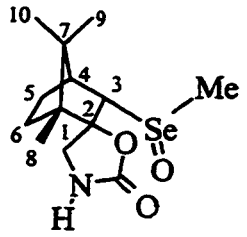


80

Selenide **75** (24 mg, 0.098 mmol) and MCPBA (16.9 mg, 0.098 mmol) were dissolved in 1 mL of $CDCl_3$ in an NMR tube at rt to get a homogeneous yellow solution:

IR (nujol), 1771 (C=O), 1754 (C=O); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.64 (d, J= 5.4 Hz, 1H, C(4)-H), 2.26-1.12 (m, 4H), 1.12 (s, 3H, C(8)-H), 1.07 (s, 3H, C(9)-H), 0.95 (s, 3H, C(10)-H). These spectra compare favourably with those reported in the literature[117] for **80**.

3.2.4.2 Table 2.1 Entry 2



81

Selenide **76** (12 mg, 0.042 mmol) and MCPBA (7.3 mg, 0.042 mmol) were dissolved in 1 mL of $CDCl_3$ in an NMR tube at rt to get a homogeneous colourless solution: ^{1}H NMR ($CDCl_3$, 200 MHz), major diastereomer: δ 6.33 (br s, 1H, NH), 3.97-3.96 (m, 1H, C(3)-H), 3.71(d, J= 17.1 Hz, 1H, NCH_2), 3.57 (d, J= 17.1 Hz, 1H, NCH_2), 2.88 (s, 3H, SeMe), 2.54 (m, 1H, C(4)-H), 1.78-1.25 (m, 4H, C(5)and C(6)-H), 1.15 (s, 3H, C(8)-H), 0.98 (s, 3H, C(9)-H), 0.97 (s, 3H, C(10)-H); minor diastereomer: δ 6.43 (br s, 1H, NH), 2.82 (s, 3H, SeMe), 2.20-2.25 (m, 1H, C(4)-H), 1.18 (s, 3H, C(8)-H), 0.99 (s, 3H, C(9)-H).

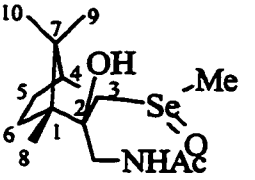
3.2.4.3 Table 2.1 Entry 3

A solution of selenide **76** (13 mg, 0.047 mmol) and (+)-oxaziridine **78** (13 mg, 0.057 mmol) in 1 mL of $CDCl_3$ in an NMR tube was prepared at rt to afford a colourless solution, in which signals of the Se-methyl group at δ 2.88 ppm (major) and 2.82 ppm (minor) were sufficiently separated to permit integration.

3.2.4.4 Table 2.1 Entry 4

A solution of selenide **76** (11 mg, 0.039 mmol) and (-)-oxaziridine **79** (11 mg, 0.047 mmol) mmol in 1 mL of $CDCl_3$ in an NMR tube was prepared at rt to afford a colourless solution, in which signals of the Se-methyl group at δ 2.88 ppm (major) and 2.82 ppm (minor) were sufficiently separated to permit integration.

3.2.4.5 Table 2.1 Entry 5



82

Selenide **77** (18 mg, 0.056 mmol) and MCPBA (11 mg, 0.062 mmol) were dissolved in 1 mL of $CDCl_3$ in an NMR tube at rt to get a homogeneous colourless solution: ^1H NMR ($CDCl_3$, 200 Hz) major diastereomer: δ 4.10 (dd, J= 14.2, 8.8 Hz, 1H, NCH_2), 3.65-3.62 (m, 1H, C(3)-H), 3.38 (dd, J= 14.3, 3.5 Hz, 1H, NCH_2), 2.60 (s, 3H, SeMe), 2.02 (s, 3H, Ac), 2.57-1.27 (m, 5H, C(4), C(5) and C(6)-H), 1.27 (s, 3H, C(8)-H), 0.98 (s, 3H, C(9)-H), 0.90 (s, 3H, C(10)-H); minor diastereomer: δ 2.73 (s, 3H, SeMe), 1.24 (s, 3H, C(8)-H).

3.2.4.6 Table 2.1 Entry 6

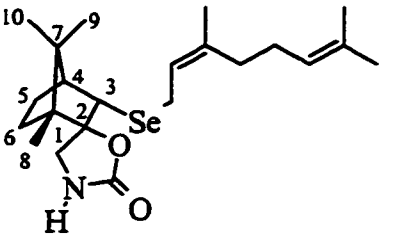
A solution of selenide **77** (20 mg, 0.063 mmol) and (+)-oxaziridine **78** (22 mg, 0.094 mmol) in 1 mL of $CDCl_3$ in an NMR tube was prepared at rt to afford a colourless solution, in which signals of the Se-methyl group at δ 2.60 ppm (major) and 2.73 ppm (minor) were sufficiently separated to permit integration.

3.2.4.7 Table 2.1 Entry 7

A solution of selenide **77** (13 mg, 0.041 mmol) and (-)-oxaziridine **79** (14 mg, 0.061 mmol) mmol in 1 mL of $CDCl_3$ in an NMR tube was prepared at rt to afford a colourless solution, in which signals of the Se-methyl group at δ 2.60 ppm (major) and 2.73 ppm (minor) were sufficiently separated to permit integration.

3.3 Experiments Related to Section 2.3.2

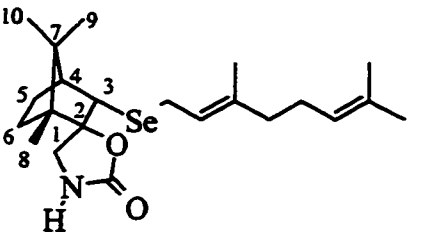
3.3.1 Preparation of (1*R*)-N,O-Carbonyl-*endo*-2-aminomethyl-*exo*-2-hydroxy-*endo*-3-bornyl Neryl Selenide (**85**)[91b]



85

Sodium borohydride (0.32 g, 8.5 mmol) was added in portions to an ice-cooled solution of diselenide **64** (1.0 g, 1.7 mmol) in 10 mL of absolute ethanol. After the addition was complete, the ice bath was removed and the mixture was stirred under argon at rt for 1 h. Neryl chloride (0.41 mL, 5.1 mmol) was added, and the mixture was stirred for 1.5 h at rt. The mixture was poured into 100 mL of ether, washed three times with 200 mL of water and one time with 100 mL of aqueous NaCl, dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was chromatographed (elution with 50% ethyl acetate/hexane) to afford 1.3 g (87%) of **85** as a pale yellow oil, with spectra identical to those reported earlier.[91b]

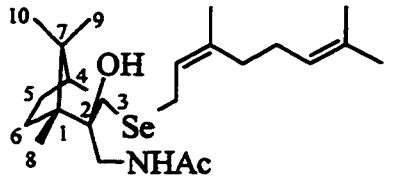
3.3.2 Preparation of (1*R*)-N,O-Carbonyl-*endo*-2-aminomethyl-*exo*-2-hydroxy-*endo*-3-bornyl Geranyl Selenide (**86**)



86

Sodium borohydride (0.31 g, 8.2 mmol) was added in portions to an ice-cooled solution of diselenide **62** (1.0 g, 1.6 mmol) in 10 mL of absolute ethanol. After the addition was complete, the ice bath was removed and the mixture was stirred under argon at rt for 1 h. Geranyl bromide (0.95 mL, 4.8 mmol) was added, and the mixture was stirred for 1.5 h at rt. The mixture was poured into 100 mL of ether, washed three times with 200 mL of water and one time with 100 mL of aqueous NaCl, dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was chromatographed (elution with 50% ethyl acetate/hexane) to afford 1.4 g (90%) of **87** as a pale yellow oil: IR (neat) 3284 (NH), 1754 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.29 (br s, 1H, NH), 5.33-5.40 (m, 1H, C=CH), 5.16-5.06 (m, 1H, C=CH), 3.85 (dd, J= 14.5, 8.0 Hz, 1H, NCH_2), 3.33-3.12 (m, 1H, C(3)-H), 3.35-3.10 (m, 3H, $SeCH_2$, 1H from NCH_2), 2.10-2.06 (m, 4H), 1.83-1.82 (m, 1H, C(4)-H), 1.70 (s, 3H, C=CMe), 1.61 (s, 3H, C=CMe), 1.57 (s, 3H, C=CMe), 1.56-1.43 (m, 4H, C(5) and C(6)-H), 1.14 (s, 3H, C(8)-H), 0.94 (s, 3H, C(9)-H), 0.88 (s, 3H, C(10)-H); mass spectrum, m/z (relative intensity) 425 (M^+, 1), 289 (R^*Se^+, 52), 208 (R^{*+}, 55), 81 (100). Elemental analysis calculated for $C_{22}H_{35}NO_2Se$: C, 62.25; H, 8.31; N, 3.30. Found: C, 62.54; H, 8.31; N, 3.31.

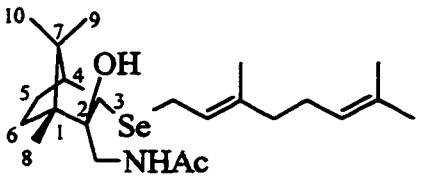
3.3.3 Preparation of (1*R*)-N-Acetyl-*endo*-2-aminomethyl-*exo*-2-hydroxy-*endo*-3-bornyl Geranyl Selenide (**87**)[91b]



87

Compound **87** was prepared in 91% yield from diselenide **64** according to the procedure of Section 3.3.1: colourless oil, with spectra identical to those reported earlier.[91b]

3.3.4 Preparation of (1*R*)-N-Acetyl-*endo*-aminomethyl-*exo*-2-hydroxy-*endo*-3-bornyl Geranyl Selenide (**88**)



88

Compound **88** was prepared in 87% yield from diselenide **64** according to the procedure of Section 3.3.2: colourless oil; IR (neat) 3290 (OH), 1651 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.29 (br s, 1H, NH), 5.36 (m, 1H, C=CH), 5.10 (m, 1H, C=CH), 3.83 (dd, J= 14.5, 8.0 Hz, 1H, NCH_2), 3.40-3.38 (m, 1H, C(3)-H), 3.35-3.10 (m, 4H, $SeCH_2$, OH, 1H from NCH_2), 2.10-2.06 (m, 2H), 2.04 (s, 3H, Ac), 1.83-1.81 (m, 1H, C(4)-H), 1.70 (s, 3H, C=CMe), 1.61 (s, 3H, C=CMe), 1.57 (s, 3H, C=CMe), 1.56-1.24 (m, 4H, C(5)and C(6)-H), 1.14 (s, 3H, C(8)-H), 0.94 (s, 3H, C(9)-H), 0.89 (s, 3H, C(10)-H); mass spectrum, m/z (relative intensity) 441 (M^+, 3), 304 (R^*Se^+, 28), 224 (R^{*+}, 41), 69

(100). Elemental analysis calculated for $C_{24}H_{41}NO_2Se$: C, 62.71; H, 8.92; N, 3.18. Found: C, 62.34; H, 8.54; N, 3.13.

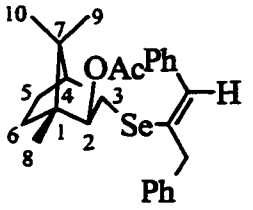
3.3.5 [2,3]Sigmatropic Rearrangements with Neryl and Geranyl Selenides. Table 2.2, Entry 1 (Typical Procedure)

(*R*)-**83** + (*S*)-**84**

Neryl selenide **85** (50 mg, 0.12 mmol) and 20 mg of 4 Å molecular sieves were placed in an oven-dried flask under an argon atmosphere. To this was added (-)-oxaziridine **79** (41 mg, 0.18 mmol) in 2 mL of distilled dichloromethane via syringe, and the reaction mixture was stirred at rt for 1 h. The solution was then filtered to remove the sulfonimine, and the filtrate was diluted with 5 mL of dichloromethane. The resulting solution was washed with aqueous NaCl solution and dried over $MgSO_4$. The solvent was removed by simple distillation, followed by Kugelrohr distillation to afford 12 mg (66%) of a mixture of *R*-(-)-licareol (**83**) and *S*-(+)-coriandrol (**84**) as a colourless oil (bp 82-87 °C/ 13 mmHg). The product was analyzed by GC on a Cyclodex B column. The ^{1}H NMR spectrum was consistent with that of an authentic sample of linalool (racemic **83**, **84**).

3.4 Experiments related to Section 2.3.3

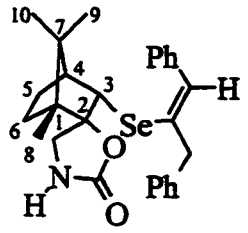
3.4.1 Preparation of (*Z*)-1,3-Diphenyl-2-[(1*R*)-*exo*-2-acetoxy-*endo*-3-bornylseleno]-1-propene (**89**)



89

Diselenide **72** (100 mg, 0.18 mmol) was dissolved in 5 mL of absolute ethanol and the mixture was cooled to 0 °C with an ice-water bath. To this solution was added sodium borohydride (14 mg, 0.36 mmol) under argon. The ice bath was removed, and the mixture was stirred at rt for 1 h. Trifluoroacetic acid (47 μL, 0.20 mmol) was added, and the reaction mixture was allowed to stir for another 1 h, followed by the addition of diphenylpropyne (**92**) (70 mg, 0.37 mmol). The mixture was heated in an oil bath at 50-60 °C for 6 h. The solution was cooled to rt and diluted with 20 mL of diethyl ether, then it was washed with 5% NaOH, 10% HCl, aqueous Na_2CO_3 and NaCl solutions, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed (elution with 5% ethyl acetate/hexane) to afford 119 mg (70%) of vinyl selenide **89** as colourless oil: IR (neat) 1741 (C=O), 1600 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.50-7.22 (m, 10H, aromatic) 6.74 (s, 1H, C=CH), 4.65 (d, J= 4.4 Hz, C(2)-H), 3.85 (s, 2H, CH_2Ph), 3.62-3.60 (m, 1H, C(3)-H), 1.99 (s, 3H, Ac), 1.88-0.88 (m, 5H), 0.84 (s, 3H, C(8)-H), 0.82 (s, 3H, C(9)-H), 0.71 (s, 3H, C(10)-H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.2 (C=O), 139.2, 133.1, 132.6, 129.2 (two signals), 128.9, 128.7, 128.4, 128.2, 127.2, 126.7, 86.1, 50.9, 50.5, 48.5, 47.4, 33.6, 23.1, 21.3, 20.7, 19.5, 11.4; mass spectrum, m/z (relative intensity) 468 (M^+, 35), 408 (M^+-AcOH, 16), 272 (25), 91 (CH_2Ph, 100). Elemental analysis calculated for $C_{27}H_{32}O_2Se$: C, 69.37; H, 6.90; N, 0.00. Found: C, 69.46; H, 6.96; N, 0.16.

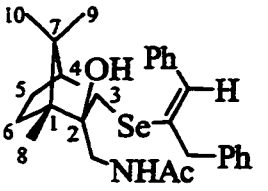
3.4.2 Preparation of (*Z*)-1,3-Diphenyl-2-[(1*R*)-N,O-carbonyl-*endo*-2-aminomethyl-*exo*-2-hydroxy-*endo*-3-bornylseleno]-1-propene (**90**)



90

Sodium borohydride (30 mg, 0.78 mmol) was placed in a round-bottomed flask under argon, and cooled to 0 °C. Diselenide **64** (150 mg, 0.26 mmol) was added in 2 mL of ethanol via syringe. The solution was refluxed for 0.5 h, then cooled to rt, followed by the addition of trifluroacetic acid (60 μL, 0.78 mmol). The reaction mixture was allowed to stir for another 1 h, followed by the addition of diphenylpropyne (**92**) (120 mg, 0.62 mmol). The solution was refluxed for 16 h. The solution was diluted with 30 mL of diethyl ether after cooling to rt, washed with 5% NaOH, 10% HCl aqueous Na_2CO_3 and NaCl, dried ($MgSO_4$), and was then concentrated *in vacuo*. The residue was chromatographed (elution with 70% diethyl ether/hexane) to afford 178 mg (71%) of vinyl selenide **90** as a colourless oil: IR (neat) 1753 (C=O), 1670 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.49-7.23 (m, 10H, aromatic), 6.85 (s, 1H, C=CH), 3.91 (dd, J= 3.9, 2.6 Hz, 1H, C(3)-H), 3.87 (d, J= 9.3 Hz, 2H, CH_2Ph), 3.79 (d, J= 8.7 Hz, 1H, NCH_2), 3.38 (d, J= 9.2 Hz, 1H, NCH_2), 1.71-1.69 (m, 1H, C(4)-H), 1.57-0.96 (m, 4H), 0.92 (s, 3H, C(8)-H), 0.86 (s, 3H, C(9)-H), 0.83 (s, 3H, C(10)-H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.8 (C=O), 139.0, 137.7, 133.9, 132.4, 129.4, 129.3, 128.7, 128.3, 127.5, 126.8, 93.2, 55.1, 53.1, 52.1, 48.4, 47.3, 46.7, 29.0, 22.7, 20.4, 20.07, 11.0; mass spectrum, m/z (relative intensity) 481 (M^+, 10), 289 (R^*Se^+, 9), 191 (100), 91 (CH_2Ph, 73). Exact mass calculated for $C_{27}H_{31}NO_2Se$: 481.1524. Found: 481.1502.

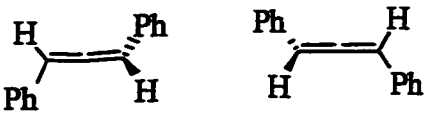
3.4.3 Preparation of (*Z*)-1,3-Diphenyl-2-[(1*R*)-N-acetyl-*endo*-2-aminomethyl-*exo*-2-hydroxy-*endo*-3-bornylseleno]-1-propene (**91**)



91

Sodium borohydride (16 mg, 0.43 mmol) was placed in a round-bottomed flask under argon, and cooled to 0 °C. Diselenide **64** (100 mg, 0.16 mmol) was added in 2 mL of ethanol via syringe. The solution was refluxed for 0.5 h, followed by the addition of diphenylpropyne **92** (76 mg, 0.40 mmol). The solution was refluxed for 16 h. then cooled to rt, followed by the addition of trifluroacetic acid (32 μL, 0.43 mmol). The colour of the mixture changed from orange to yellow. The solution was diluted with 10 mL of diethyl ether after cooling to rt, washed with 5% NaOH, 10% HCl aqueous Na_2CO_3 and NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed (elution with diethyl ether) to afford 136 mg (83%) of vinyl selenide **91** as a colourless oil: IR (neat) 3330 (OH), 1653 (C=O), 1633 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.59-7.27 (m, 10H, aromatic), 6.80 (s, 1H, C=CH), 5.91 (br s, 1H, NH), 3.85 (dd, J= 14.4, 7.6 Hz, 1H, NCH_2), 3.42 (m, 2H, OH and C(3)-H), 3.21 (dd, J= 14.1, 5.0 Hz, 1H, NCH_2), 2.17 (s, 3H, Ac), 1.92-1.88 (m, 1H, C(4)-H), 1.68-1.36 (m, 4H, C(5)and C(6)-H), 1.15 (s, 3H, C(8)-H), 0.94 (s, 3H, C(9)-H), 0.89 (s, 3H, C(10)-H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 158.8 (C=O), 139.0, 137.7, 133.9, 132.4, 129.4, 128.9, 128.6, 128.3, 127.5, 126.8, 93.2, 55.1, 53.1, 52.1, 48.4, 47.3, 46.7, 29.0, 22.7, 20.4, 20.1, 11.0; mass spectrum, m/z (relative intensity) 497 (M^+, 4), 305 (R^*Se^+, 24), 224 (R^{*+}, 88), 91 (CH_2Ph, 100). Exact mass calculated for $C_{28}H_{35}NO_2Se$: 497.1833. Found: 497.1843.

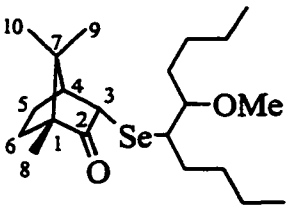
3.4.4 Selenoxide Eliminations of Chiral Vinyl Selenides. Table 2.3 Entry 1 (Typical Procedure)



Selenide **89** (50 mg, 0.11 mmol) was dissolved in 1 mL of distilled dichloromethane, and MCPBA (20 mg, 0.11 mmol) in 2 mL of dichloromethane was added. The mixture was stirred at rt for 48 h. The solution was concentrated *in vacuo* and the residue was purified by chromatography (elution with 100% pentane) to afford 13 mg (64%) of the product 1,3-diphenylallene as a white solid. The e.e. was measured by polarimetry in ethanol solution ($[\alpha]_D$ = + 40°, (c=0.0055); lit.[106] $[\alpha]_D$ = +1020°, *S*-enantiomer); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.44-7.28 (m, 10H, aromatic), 6.61 (s, 2H, C=CH); GC-mass spectrum, m/z (relative intensity) 192 (M^+, 100), 165 (20). The ^{1}H NMR spectrum is consistent with that reported in the literature.[118]

3.5 Experiments related to Section 2.3.4

3.5.1.1 Methoxyselenenylation of *trans*-5-Decene. Table 2.4, Entry 1(Typical Procedure)



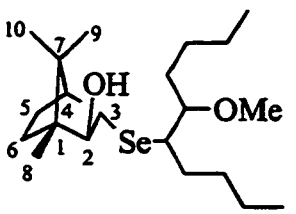
Diselenide **57** (50 mg, 0.11 mmol) was dissolved in 3 mL of redistilled dichloromethane in the presence of 4 Å molecular sieves (100 mg). A 1M tetrachloromethane solution of bromine (0.11 mL, 0.11 mmol) was added dropwise at -78 °C under a nitrogen atmosphere, while stirring. After 15 min, a 0.70 M methanol solution

of silver triflate (0.45 mL, 0.30 mmol) was added. After another 15 min, *trans*-5-decene (0.10 mL, 0.54 mmol) was added to the colourless heterogeneous mixture. The resulting mixture was stirred for 1 h at -78 °C. It was quenched with aqueous $NaHCO_3$ solution, diluted with 10 mL of dichloromethane, washed with water, and aqueous NaCl solution, dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The residue was chromatographed (elution with 5% ethyl acetate/hexane) to afford 78 mg (88%) of the addition product as a pale yellow oil: IR (neat), 1738 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz), major diastereomer: δ 3.78 (d, J= 4.7 Hz, 1H, C(3)-H), 3.42 (s, 3H, OMe), 3.49-3.32 (m, 2H, SeCH and MeOCH), 2.21-2.19 (m, 1H, C(4)-H), 1.86-1.25 (m, 16H), 1.02 (s, 3H, C(8)-H), 0.93 (s, 3H, C(9)-H), 0.92 (s, 3H, C(10)-H), 0.92-0.89 (m, 6H, CH_3CH_2); minor diastereomer: δ 3.99 (d, J= 4.8 Hz, 1H, C(3)-H), 3.39 (s, 3H, OMe); ^{13}C NMR ($CDCl_3$, 100 MHz), major diastereomer: δ 218.5 (C=O), 85.4, 58.4, 58.2, 48.9, 47.0, 46.6, 46.0, 31.7, 31.4, 30.9, 30.6, 28.5, 23.7, 23.1, 22.8, 19.8, 14.3 (two signals), 14.2, 10.0; minor diastereomer: δ 85.8, 57.9, 30.7 (two signals), 23.5, 19.8; mass spectrum, m/z (relative intensity) 402 (M^+, 21), 370 (M^+-MeOH, 19), 230 (R^*Se^+, 50), 151 (R^{*+}, 65), 101 (100), 69 (99). Exact mass calculated for $C_{21}H_{38}O_2Se$: 402.2040. Found: 402.2059.

3.5.1.2 Table 2.4, Entry 2

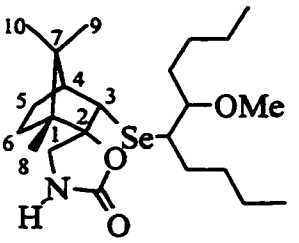
The same procedure as for Entry 1 of Table 2.4 was followed with diselenide **74**. No reaction occurred as evident from the TLC and ^1H NMR spectrum of the reaction mixture.

3.5.1.3 Table 2.4, Entry 3



The procedure of Entry 1 was followed with diselenide **73** to afford the corresponding adduct: IR (neat) 3443 (OH) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz), major diastereomer: δ 3.72 (d, J= 3.7 Hz, 1H, C(2)-H), 3.55-3.21 (m, 4H, OH, C(3)-H, SeCH and MeOCH), 3.41 (s, 3H, OMe), 1.89-1.85 (m, 1H, C(4)-H), 1.83-1.26 (m, 16H), 1.10 (s, 3H, C(8)-H), 0.92 (two t, 6H, CH_3CH_2), 0.90 (s, 3H, C(9)-H), 0.87 (s, 3H, C(10)-H); minor diastereomer: δ 3.40 (s, 3H, Ome), 1.08 (s, 3H, C(8)-H); ^{13}C NMR ($CDCl_3$, 50 MHz), major diastereomer: δ 89.9, 86.6, 57.8, 52.5, 52.2, 50.4, 48.1, 46.1, 34.6, 33.0, 32.3, 31.1, 28.8, 23.4, 23.1, 22.8, 20.7, 20.1, 14.3, 14.2, 11.6; minor diastereomer: δ 89.1, 85.9, 34.4, 32.4, 31.9, 28.7, 20.9, 20.2, 20.1; mass spectrum, m/z (relative intensity) 404 (M^+, 12), 303 (11), 101(95), 69 (100). Exact mass calculated for $C_{21}H_{40}O_2Se$: 404.2196. Found: 404.2173.

3.5.1.4 Table 2.4, Entry 4



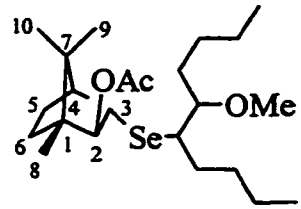
The procedure of Entry 1 was followed with diselenide **64** to afford the corresponding adduct: IR (neat) 3263 (NH), 1753 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz), major diastereomer: δ 5.01 (br s, 1H, NH), 4.10 (d, J= 8.9 Hz, 1H NCH_2), 4.02 (dd, J= 3.8, 2.6 Hz, 1H, C(3)-H), 3.56 (d, J= 8.9 Hz, 1H, NCH_2), 3.38 (s, 3H, OMe), 3.21-3.17 (m, 2H, MeOCH and SeCH), 2.02-2.00 (m, 1H, C(4)-H), 1.72-1.25 (m, 16H), 1.15 (s, 3H, C(8)-H), 1.11-0.93 (m, 6H, CH_3CH_2), 0.92 (s, 3H, C(9)-H), 0.91(s, 3H, C(10)-H); minor diastereomer: δ 4.07 (d, J= 9.0 Hz, 1H NCH_2), 3.75-3.73 (m, 1H, C(3)-H), 3.39 (s, 3H, OMe), 1.99-1.97 (m, 1H, C(4)-H); ^{13}C NMR ($CDCl_3$, 100 MHz), major diastereomer: δ 159.2 (C=O), 93.4, 85.5, 58.0, 54.5, 53.2, 52.7, 48.3, 47.5, 46.9, 45.9, 31.6, 30.8, 29.0, 28.7, 28.6, 23.1, 22.8, 22.6, 20.2, 14.3, 14.2, 11.1; minor diastereomer: 159.2 (C=O),

93.2, 54.9, 53.3, 52.9, 46.8, 32.7, 32.3, 30.8, 23.0, 22.8, 20.7, 20.6, 11.1.; mass spectrum, m/z (relative intensity) 459 (M^+, 58), 288 (R^*Se^+, 64), 208 (R^{*+}, 73), 69 (100). Exact mass calculated for $C_{23}H_{41}NO_3Se$: 459.2255. Found: 459.2253.

3.5.1.5 Table 2.4, Entry 5

The same procedure as for Entry 1 of Table 2.4 was followed with diselenide 70. No reaction occurred as evident from the TLC and ^1H NMR spectrum of the reaction mixture.

3.5.1.6 Table 2.4, Entry 6



The procedure of Entry 1 was followed with diselenide **72** to afford the corresponding adduct: IR (neat) 1742 (C=O), 1233 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz), major diastereomer: δ 4.81 (d, J= 4.1 Hz, 1H, C(2)-H), 3.59-3.56 (m, 1H, C(3)-H), 3.39 (s, 3H, OMe), 3.30-3.20 (m, 1H, MeOCH), 2.95-2.07 (m, 1H, SeCH), 2.05 (s, 3H, Ac), 1.87-1.85 (m, 1H, C(4)-H), 1.81-1.22 (m, 16H), 1.05 (s, 3H, C(8)-H), 0.94-0.92 (m, 6H, CH_3CH_2), 0.90 (s, 3H, C(9)-H), 0.78 (s, 3H, C(10)-H); minor diastereomer: δ 4.85 (d, J= 4.2 Hz, 1H, C(2)-H), 3.39 (s, 3H, OMe), 2.06 (s, 3H, Ac), 1.04 (s, 3H, C(8)-H), 0,89 (s, 3H, C(9)-H); ^{13}C NMR ($CDCl_3$, 100 MHz), major diastereomer: δ 170.2 (C=O), 88.1, 58.1, 51.1, 50.8, 48.0, 46.8, 45.3, 33.7, 31.9, 31.7, 30.9, 28.5, 23.4, 23.1, 22.8, 21.3, 20.7, 19.7, 14.3 (two signals), 11.5; minor diastereomer: δ 85.4, 58.0, 51.2, 48.1, 45.6, 32.3, 31.8, 30.8, 23.3, 20.6, 14.2; mass spectrum, m/z (relative intensity) 446 (M^+, 6), 386 (M^+-

AcOH, 6), 285 (36), 215 ($R^{+}Se$-$AcOH^{+}$, 59), 101 (88), 69(97), 43 (100). Exact mass calculated for $C_{23}H_{42}O_3Se$: 446.2303. Found: 446.2279.

3.5.2.1 Optimization of Conditions for the Methoxyselenenylation of *trans*-5-decene. Table 2.5, Entry 1

This Entry is identical to Entry 1 in Table 2.4 (Section 3.5.1.1).

3.5.2.2 Table 2.5, Entry 2

Diselenide **57** (50 mg, 0.11 mmol) was dissolved in 3 mL of dry dichloromethane and a 1M tetrachloromethane solution of bromine (0.11 mL, 0.11 mmol) was added dropwise at -78 °C under a nitrogen atmosphere with stirring. After 15 min, *trans*-5-decene (0.10 mL, 0.540 mmol) was added to the heterogeneous mixture of the selenenyl bromide. After 15 min, a 0.70 M methanol solution of silver triflate (0.45 mL, 0.30 mmol) was added. The resulting mixture was stirred for 1 h at -78 °C. It was quenched with aqueous $NaHCO_3$ solution, diluted with 10 mL of dichloromethane, washed with water and aqueous NaCl solution, dried ($MgSO_4$), filtered, and concentrated *in vacuo* to afford the product as a pale yellow oil, which gave an identical ^1H NMR spectrum to that of the mixture from Table 2.4, Entry 1 (Section 3.5.1), except for the ratio of signals from the major and minor diastereomers.

3.5.2.3 Table 2.5, Entry 3

The reaction was performed according to the procedure in Section 3.5.1.1 at -95 °C instead of -78 °C.

3.5.2.4 Table 2.5, Entry 4

The reaction was performed according to the procedure in Section 3.5.1.1 at -42 °C instead of -78 °C.

3.5.2.5 Table 2.5, Entry 5

The reaction was performed according to the procedure in Section 3.5.1.1, using dry diethyl ether instead of dichloromethane as the reaction solvent.

3.5.2.6 Table 2.5, Entry 6

The reaction was performed according to the procedure in Section 3.5.1.1, using dry toluene instead of dichloromethane as the reaction solvent.

3.5.2.7 Table 2.5, Entry 7

The reaction was performed according to the procedure in Section 3.5.1.1, using silver tetrafluoroborate instead of silver triflate as the silver salt.

3.5.2.8 Table 2.5, Entry 8

Diselenide **57** (50 mg, 0.11 mmol) was dissolved in 3 mL of dry dichloromethane and a 1M tetrachloromethane solution of bromine (0.11 mL, 0.11 mmol) was added dropwise at -78 °C under a nitrogen atmosphere with stirring. After 15 min, *trans*-5-decene (0.10 mL, 0.540 mmol) was added to the brown solution. The resulting mixture was stirred for 1 h at -78 °C. It was quenched with aqueous $NaHCO_3$ solution, diluted with 10 mL of dichloromethane, washed with water and aqueous NaCl solution, dried ($MgSO_4$), filtered, and concentrated *in vacuo* to afford a brown oil. TLC and ^1H NMR analysis indicated the formation of a complex mixture.

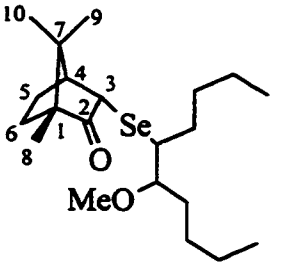
3.5.2.9 Table 2.5, Entry 9

Diselenide **57** (50 mg, 0.11 mmol) was dissolved in 3 mL of dry dichloromethane and a 1M tetrachloromethane solution of sulfuryl chloride (7.0 μL, 0.11 mmol) was added dropwise at -78 °C under a nitrogen atmosphere. After 15 min, *trans*-5-decene (0.10 mL, 0.54 mmol) was added to the orange solution. The resulting mixture was stirred for 1 h at -78 °C. It was quenched with aqueous $NaHCO_3$ solution, diluted with 10 mL of dichloromethane, washed with water and aqueous NaCl solution, dried ($MgSO_4$), filtered, and concentrated *in vacuo* to afford a brown oil. TLC and ^1H NMR analysis indicated the formation of a complex mixture.

3.5.3.1 Methoxyselenenylations with the 2-Keto Camphor Auxiliary. Table 2.6, Entry 1

This Entry is identical to Entry 1 in Table 2.4 (Section 3.5.1.1).

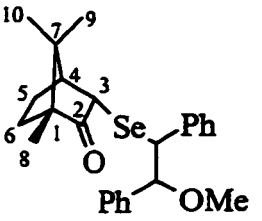
3.5.3.2 Table 2.6, Entry 2



The procedure of Entry 1 was followed with *cis*-5-decene to afford the corresponding adduct: IR (neat) 1738 (C=O), 1096 (C-OMe) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz), major diastereomer: δ 3.65 (d, J= 4.6 Hz, 1H, C(3)-H), 3.40 (s, 3H, OMe), 3.48-3.25 (m, 2H, SeCH and MeOCH), 2.25-2.21 (m, 1H, C(4)-H), 1.91-1.01 (m, 16H), 1.02 (s, 3H, C(8)-H), 0.93 (s, 3H, C(9)-H), 0.91 (s, 3H, C(10)-H), 0.99-0.61 (m, 6H); minor diastereomer: δ 3.75 (d, J= 3.4 Hz, 1H, C(3)-H), 3.38 (s, 3H, OMe), 2.18-2.17 (m, 1H,

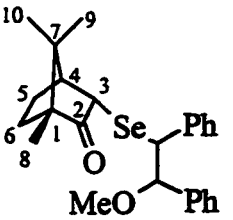
C(4)-H); ^{13}C NMR ($CDCl_3$, 100 MHz); major diastereomer: δ 218.6 (C=O), 84.9, 58.4, 57.9, 49.0, 48.9, 46.7, 45.6, 32.0, 31.1, 30.9, 30.6, 28.9, 28.8, 23.7, 22.8, 19.8 (two signals), 14.3 (two signals), 10.0; minor diastereomer: δ 84.8, 58.3, 58.0, 47.0, 45.5, 31.7, 31.1, 30.6, 29.9, 23.6, 23.0, 19.9, 14.2; mass spectrum, m/z (relative intensity) 402 (M^+, 10), 370 (M^+-MeOH, 5), 230 ($R^{\bullet}Se^+$, 14), 151 ($R^{\bullet+}$, 17), 302 (4), 171 (29), 101 (100), 41 (86). Exact mass calculated for $C_{21}H_{38}SeO_2$: 402.2040. Found: 402.2055.

3.5.3.3 Table 2.6, Entry 3



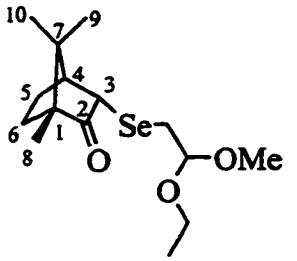
The procedure of Entry 1 was followed with *trans*-stilbene to afford the corresponding adduct. This compound could not be separated by column chromatography, and the yield given in Table 2.6 is based on NMR integration: ^1H NMR ($CDCl_3$, 200 MHz), major diastereomer: δ 7.55-7.13 (m, 10H, aromatic), 4.71 (d, J= 9.3 Hz, 1H, SeCH or MeOCH), 4.55 (d, J= 9.2 Hz, 1H, SeCH or MeOCH), 3.12 (s, 3H, OMe), 2.72-2.69 (m, 1H, C(3)-H), 2.04-1.26 (m, 5H, C(4), C(5) and C(6)-H), 0.88 (s, 3H, C(8)-H), 0.83 (s, 3H, C(9)-H), 0.51 (s, 3H, C(10)-H); minor diastereomer: 3.11-2.99 (m, 3H, C(3)-H), 0.60 (s, 3H, C(10)-H).

3.5.3.4 Table 2.6, Entry 4



The procedure of Entry 1 was followed with *cis*-stilbene to afford the corresponding adduct. This compound could not be separated by column chromatography, and the yield given in Table 2.6 is based on NMR integration: ^{1}H NMR ($CDCl_3$, 200 MHz), major diastereomer: δ 7.23-7.09 (m, 10H, aromatic), 4.87 (d, J= 9.4 Hz, 1H, SeCH or MeOCH), 4.55 (d, J= 9.4 Hz, 1H, SeCH or MeOCH), 3.27 (s, 3H, OMe), 3.05-3.00 (m, 1H, C(3)-H), 2.00-0.93 (m, 5H, C(4), C(5) and C(6)-H), 0.88 (s, 3H, C(8)-H), 0.84 (s, 3H, C(9)-H), 0.54 (s, 3H, C(10)-H); minor diastereomer: δ 3.5 (m, 1H, C(3)-H), 3.29 (s, 3H, OMe), 0.92 (s, 3H, C(8)-H).

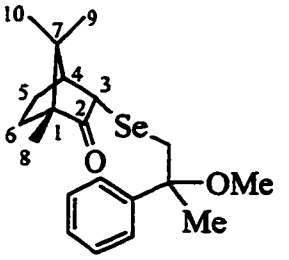
3.5.3.5 Table 2.6, Entry 5



The procedure of Entry 1 was followed with ethyl vinyl ether to afford the corresponding adduct: IR (neat) 1746 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz), major diastereomer: δ 4.70 (t, J= 5.5 Hz, 1H, MeOCH), 3.89 (dd, J= 4.4, 1.9 Hz, 1H, C(3)-H), 3.76-3.71 (m, 1H, $SeCH_2$), 3.59-3.54 (m, 1H, $SeCH_2$), 3.37 (s, 3H, OMe), 3.01 (dd, J=12.8, 5.8 Hz, 1H, OCH_2Me), 2.91 (dd, J=12.8, 5.2 Hz, 1H, OCH_2Me), 2.21-2.20 (m, 1H, C(4)-H), 1.80-1.40 (m, 4H, C(6) and C(5)-H), 1.21 (t, J= 7.1 Hz, 3H, CH_2CH_3), 1.01 (s, 3H, C(8)-H), 0.92 (s, 3H, C(9)-H), 0.90 (s, 3H, C(10)-H); minor diastereomer: δ 3.36 (s, 3H, OMe), 0.93 (s, 3H, C(9)-H); ^{13}C NMR ($CDCl_3$, 100 MHz), major diastereomer: δ 218.5 (C=O), 104.6, 62.5, 58.4, 53.8, 48.5, 47.2, 47.0, 30.7, 26.8, 23.5, 19.8 (two signals), 15.5, 9.9; minor diastereomer: δ 62.7, 53.5, 29.9. ^{77}Se NMR ($CDCl_3$, 400 MHz), major diastereomer: δ 191.6; minor diastereomer: δ 193.7; mass spectrum: m/z (relative

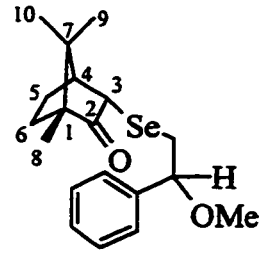
intensity) 334 (M^+, 1), 302 (M^+-MeOH, 4), 230 (R^*Se^+, 1), 151 (R^{*+}, 3), 89 (100), 61 (53). Exact mass calculated for $C_{15}H_{26}SeO_3$: 334.1049. Found: 334.1053.

3.5.3.6 Table 2.6, Entry 6



The procedure of Entry 1 was followed with α-methyl styrene to afford the corresponding adduct: IR (neat) 1740 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz), major diastereomer: δ 7.39-7.14 (m, 5H, aromatic), 3.31-3.05 (m, 3H, C(3)-H and $SeCH_2$), 3.06 (s, 3H, OMe), 1.95-1.93 (m, 1H, C(4)-H), 1.65 (s, 3H, α-methyl), 1.72-1.26 (m, 4H, C(5) and C(6)-H), 0.89 (s, 3H, C(8)-H), 0.79 (s, 3H, C(9)-H), 0.66 (s, 3H, C(10)-H); minor diastereomer: δ 3.04 (s, 3H, OMe), 1.89-1.85 (m, 1H, C(4)-H), 1.63 (s, 3H, α-methyl), 0.87 (s, 3H, C(8)-H); ^{13}C NMR ($CDCl_3$, 100 MHz), major diastereomer: δ 218.6 (C=O), 144.0, 128.4, 127.5, 126.5, 79.6, 79.2, 58.3, 51.1, 48.3, 46.8, 46.6, 38.2, 30.7, 23.4, 23.2, 19.8, 9.8; minor diastereomer: δ 127.6, 126.7, 58.2, 51.1, 48.4, 46.8, 38.0, 30.6, 23.5, 19.7; mass spectrum, m/z (relative intensity) 380 (M^+, 6), 348 (M^+-MeOH, 5), 230 (R^*Se^+, 13), 151 (R^{*+}, 3), 135 (100), 43 (47). Exact mass calculated for $C_{20}H_{28}SeO_2$: 380.1257. Found: 380.1271.

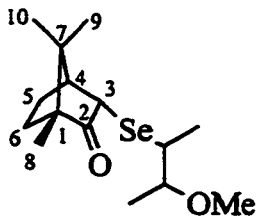
3.5.3.7 Table 2.6, Entry 7



95

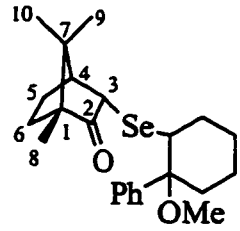
The procedure of Entry 1 was followed with styrene to afford the corresponding adduct: IR (neat) 1735 (C=O) cm^{-1}, 702 and 767 (monosubstituted aromatic) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz), major diastereomer: δ 7.37-7.26 (m, 5H, aromatic H), 4.48 (dd, J= 8.6, 4.5 Hz, 1H, MeOCH), 3.56-3.54 (m, 1H, C(3)-H), 3.27 (s, 3H, OMe), 3.26-2.96 (m, 2H, $SeCH_2$), 2.14-2.10 (m, 1H, C(4)-H), 1.82-1.38 (m, 4H), 0.99 (s, 3H, C(8)-H), 0.91 (s, 3H, C(9)-H), 0.81 (s, 3H, C(10)-H); minor diastereomer: δ 4.39-4.42 (t, J=7.1 Hz, 1H, MeOCH), 3.25 (s, 3H, OMe), 2.06-2.04 (m, 1H, C(4)-H), 0.98 (s, 3H, C(8)-H), 0.89 (s, 3H, C(9)-H), 0.79 (s, 3H, C(10)-H); ^{13}C NMR ($CDCl_3$, 100 MHz), major diastereomer: δ 218.7 (C=O), 141.4, 128.7, 126.8, 84.4, 57.2, 48.6, 48.5, 47.3, 46.9, 32.0, 30.7, 29.9, 23.5, 19.8 (two signals), 9.9; minor diastereomer: δ 128.3, 127.2, 84.6, 31.2, 30.7, 23.5, 19.7; mass spectrum, m/z (relative intensity) 366 (M^+, 9), 334 (M^+-MeOH, 16), 230 (R^*Se^+, 11), 151 (R^{*+}, 4), 121 (100). Exact mass calculated for $C_{19}H_{26}SeO_2$: 366.1100. Found: 366.1063.

3.5.3.8 Table 2.6, Entry 8



The procedure of Entry 1 was followed with *trans*-2-butene to afford the corresponding adduct: IR (neat): 1729 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz), major diastereomer: δ 3.77 (d, J= 4.8 Hz, 1H, C(3)-H), 3.38-3.72 (m, 2H, SeCH and MeOCH), 3.37 (s, 3H, OMe), 2.21-2.20 (m, 1H, C(4)-H), 2.05-1.50 (m, 4H, C(5) and C(6)-H), 1.46 (d, J=7.0 Hz, 3H, SeCHMe), 1.21 (d, J= 6.2 Hz, 3H, MeOCHMe), 1.03 (s, 3H, C(8)-H), 0.93 (s, 3H, C(9)-H), 0.92 (s, 3H, C(10)-H); minor diastereomer: δ 3.95 (d, J =4.6 Hz, 1H, C(3)-H), 3.36 (s, 3H, OMe), 1.02 (s, 3H, C(8)-H), 0.91 (s, 3H, C(10)-H); ^{13}C NMR ($CDCl_3$, 50 MHz), 218.7 (C=O), 80.9, 58.3, 57.0, 49.0, 47.1, 45.7, 41.0, 30.7, 23.8, 19.9, 19.8, 17.4, 16.8, 9.9; minor diastereomer: δ 81.5, 58.3, 56.9, 49.0, 46.2, 41.1, 41.0, 23.6, 19.8, 18.4, 16.8, 16.4; mass spectrum, m/z (relative intensity) 318 (M^+, 5), 230 (R^*Se^+, 8), 152 (R^{*+}, 33), 87 (46), 41 (100). Exact mass calculated for $C_{15}H_{26}SeO_2$: 318.1100. Found: 318.1078.

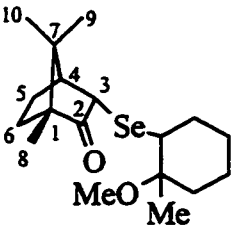
3.5.3.9 Table 2.6, Entry 9



The procedure of Entry 1 was followed with 1-phenyl-1-cyclohexene to afford the corresponding adduct: IR (neat) 1737 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz), major diastereomer: δ 7.50-7.21 (m, 5H, aromatic), 3.14-3.01 (m, 1H, C(3)-H), 2.99 (s, 3H, OMe), 2.69-2.36 (m, 2H, MeOCCH_2), 2.32 (dd, J= 4.5, 1.4 Hz, 1H, SeCH), 2.10-1.00 (m, 11H), 0.93 (s, 3H, C(8)-H), 0.77 (s, 3H, C(9)-H), 0.48 (s, 3H, C(10)-H); minor diastereomer: δ 3.76-3.57 (m, 1H, C(3)-H), 2.96 (s, 3H, OMe), 2.29-2.19 (m, 1H, SeCH); ^{13}C NMR ($CDCl_3$, 50 MHz), major diastereomer: δ 216.9 (C=O), 143.8, 128.2, 128.0, 127.5, 80.8, 58.2, 50.6, 49.1, 48.7, 47.4, 46.5, 30.8, 30.2, 25.4, 23.0, 22.2, 21.1, 20.4, 19.8, 9.7; minor diastereomer: δ 144.1, 128.1, 127.4, 80.6, 58.1, 51.0, 50.5, 48.5, 46.8, 46.7, 30.6, 30.0, 25.4, 25.3, 23.4, 22.2, 19.5, 9.8; mass spectrum, m/z (relative intensity)

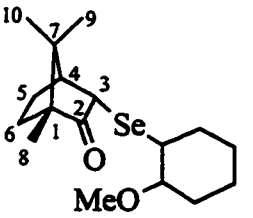
420 (M^+, 28), 388 (M^+-MeOH, 30), 269 (100), 189 (56), 91 (97). Exact mass calculated for $C_{23}H_{32}SeO_2$: 420.1570. Found: 420.1552.

3.5.3.10 Table 2.6, Entry 10



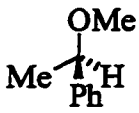
The procedure of Entry 1 was followed with 1-methyl-1-cyclohexene to afford the corresponding adduct: IR (neat) 1734 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz), major diastereomer: δ 3.91 (d, J= 4.7 Hz, 1H, C(3)-H), 3.57 (dd, J= 9.1, 3.9 Hz, 1H, SeCH), 3.26 (s, 3H OMe), 2.23-2.17 (m, 1H, C(4)-H), 1.89-1.40 (m, 12H), 1.31 (s, 3H, Me), 1.02 (s, 3H, C(8)-H), 0.92 (s, 6H, C(9) and C(10)-H); minor diastereomer: δ 3.42 (dd, J= 10.1, 3.8 Hz, 1H, SeCH) 3.22 (s, 3H, OMe), 1.27 (s, 3H, Me) 0.90 (s, 6H, C(9) and C(10)-H); ^{13}C NMR ($CDCl_3$, 50 MHz), major diastereomer: δ 218. 5 (C=O), 68.0, 58.3, 48.7, 48.6, 47.1, 47.0, 46.5, 34.9, 30.7, 29.9, 25.1, 23.7, 22.6, 21.6, 19.9, 10.0, 9.9; minor diastereomer: δ 48.9, 23.6, 22.8, 19.8; mass spectrum, m/z (relative intensity) 358 (M^+, 14), 326 (M^+-MeOH, 12), 230 ($R^•Se^+$, 8), 151 ($R^{•+}$, 5), 95 (100), 41 (61). Exact mass calculated for $C_{18}H_{30}SeO_2$: 358.1413. Found: 358.1403.

3.5.3.11 Table 2.6, Entry 11



The procedure of Entry 1 was followed with cyclohexene to afford the corresponding adduct: IR (neat) 1739 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz), major diastereomer: δ 4.09-4.07 (m, 1H, C(3)-H), 3.38 (s, 3H, OMe), 3.36-3.18 (m, 2H, MeOCH and SeCH), 2.21-1.25 (m, 13H), 1.02 (s, 3H, C(8)-H), 0.92 (s, 6H, C(9) and C(10)-H); minor diastereomer: δ 3.99-3.40 (m, 1H, C(3)-H), 1.01 (s, 3H, C(8)-H), 0.90 (s, 6H, C(9) and C(10)-H); ^{13}C NMR ($CDCl_3$, 50 MHz), major diastereomer: δ 218.2 (C=O), 83.6, 58.3, 56.5, 48.8, 47.1 (two signals), 43.0, 31.4, 30.8, 30.1, 25.5, 23.6, 23.3, 20.0, 19.9, 9.9; minor diastereomer: δ 85.0, 56.8, 49.2, 47.3, 44.5, 32.6, 31.0, 26.3, 24.0, 23.7, 20.0, 19.8; mass spectrum, m/z (relative intensity) 344 (M^+, 8), 312 (M^+-MeOH, 11), 230 (R^*Se^+, 12), 151 (R^{*+}, 11), 81 (100), 45 (53). Exact Mass calculated for $C_{17}H_{28}SeO_2$: 334.1257. Found: 334.1242.

3.5.4 Preparation of Authentic *R*-(+)-2-Phenethyl Methyl Ether (**97**)



(*R*)

97

R-(+)-2-Phenethyl alcohol (200 mg, 1.6 mmol) was dissolved in 5 mL of dry THF at 0 °C, followed by addition of NaH (67 mg, 60%, 1.7 mmol). The mixture was stirred for 45 min at 0 °C, and then methyl iodide (102 μL, 1.6 mmol) was added via syringe. The solution was allowed to stir for another 2 h, it was then warmed to rt and was stirred for another 1 h. The solution was diluted with 10 mL of ether, washed with H_2O and aqueous NaCl solution, and dried ($MgSO_4$). The solvent was removed by simple distillation to afford 109 mg (49%) of a residue consisting of a colourless oil: ^1H NMR ($CDCl_3$, 200 MHz) δ 7.38-7.27 (m, 5H, aromatic), 4.30 (q, J= 6.5 Hz, 1H, CH), 3.24 (s, 3H, OMe), 1.45 (d, J= 6.5 Hz, 3H, Me); GC-mass spectrum, m/z (relative intensity) 136 (M^+, 7), 121 (M^+-Me, 100), 105 (M^+-OMe, 20).

3.5.5 Deselenization of the Product from Table 2.6, Entry 7

(*R*)

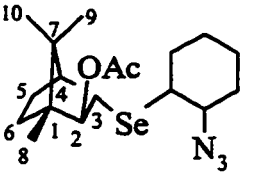
97

39

A mixture of AIBN (10 mg) and triphenyltin hydride (192 mg, 0.55 mmol) was added dropwise to a refluxing solution of selenide **95** (100 mg, 0.27 mmol) in 2 mL of toluene. After 2 h, additional of triphenyltin hydride (96 mg, 0.27 mmol) and AIBN (5 mg) were added, and heating was continued for 1 h. The reaction mixture was separated by chromatography (elution with hexane), followed by (10% diethyl ether/hexane). The solvent was removed by simple distillation, followed by Kugelrohr distillation (70-90 °C, 130 mmHg) to afford the methyl ether **97** as a colourless oil, the e.e. of which was determined on a chiral Cyclodex B GC column. The absolute configuration was assigned by comparison with the authentic sample. The white solid remaining after distillation was (*R*)-(+)-camphor (**39**). Both **97** and **39** had ^{1}H NMR spectra identical to those of authentic samples.

3.6 Experiments Related to Section 2.3.5

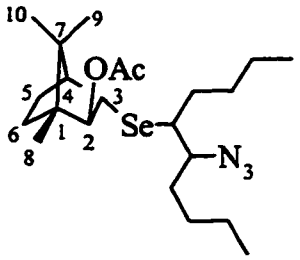
3.6.1 Selenenyl Azide Additions to Alkenes. Table 2.7, Entry 1 (Typical Procedure)



Diselenide **72** (50 mg, 0.09 mmol) was dissolved in 3 mL of dichloromethane, cooled to 0 °C, and 7.0 μL of SO_2Cl_2 were added. The mixture was stirred for 10 min at 0

°C. The solvent was removed *in vacuo*, and the orange solid residue was redissolved in 1 mL of dry DMSO containing NaN_3 (23 mg, 0.36 mmol). Cyclohexene (50 μL, 0.49 mmol) was added via syringe. The resulting orange solution was stirred at rt overnight, diluted with 10 mL of ether, washed with H_2O and aqueous NaCl solution, dried ($MgSO_4$), concentrated *in vacuo*, and the residue was chromatographed (elution with 10% diethyl ether/hexane) to afford 70 mg (97%) of the addition product as a colourless oil: IR (neat) 2096 (N_3), 1741 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz), major diastereomer: δ 4.82 (d, J= 4.0 Hz, 1H, C(2)-H), 3.65-3.61 (m, 1H, C(3)-H), 3.44-3.28 (m, 1H, CHN_3), 2.81-2.69 (m, 1H, SeCH), 2.26-1.21 (m, 13H), 2.06 (s, 3H, Ac), 1.06 (s, 3H, C(8)-H), 0.89 (s, 3H, C(9)-H), 0.78 (s, 3H, C(10)-H); minor diastereomer: δ 4.75 (d, J= 4.2 Hz, 1H, C(2)-H), 3.70-3.67 (ddd, J= 4.1, 4.1, 1.8 Hz, 1H, C(3)-H); ^{13}C NMR ($CDCl_3$, 50 MHz), major diastereomer: δ 170.4 (C=O), 88.2 (CN_3), 66.1, 50.9, 50.7, 48.1, 47.8, 43.0, 33.7 33.4, 31.8, 25.9, 24.0, 23.4, 21.3, 20.8, 19.8, 11.5; minor diastereomer: δ 87.4, 66.0, 51.2, 50.6, 48.0, 47.6, 43.2, 32.9, 31.5, 25.7, 23.8, 23.3, 21.4, 20.6. Some NMR assignments to major/minor diastereomers were tentative due to almost equal amounts of the two being present. Mass spectrum, m/z (relative intensity) 399 (M^+, 7), 371 (M^+-N_2, 2), 215 (R^*Se-OAc, 51), 43 (100). Exact mass calculated for $C_{18}H_{29}N_3O_2Se$: 399.1429. Found: 399.1429.

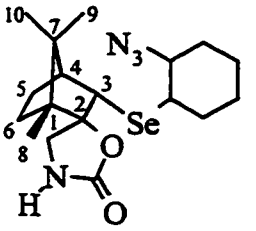
3.6.2 Table 2.7, Entry 2



The procedure of Entry 1 was followed with *trans*-5-decene to afford the corresponding adduct: IR (neat) 2097 (N_3), 1742 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200

MHz), major diastereomer: δ 4.76 (d, J= 4.2 Hz, 1H, C(2)-H), 3.55-3.39 (m, 2H, C(3)-H and CHN_3), 2.85-2.73 (m, 1H, SeCH), 2.04 (s, 3H, Ac), 1.87-0.88 (m, 23H), 1.04 (s, 3H, C(8)-H), 0.89 (s, 3H, C(9)-H), 0.77 (s, 3H, C(10)-H); minor diastereomer: δ 4.83 (d, J= 4.1 Hz, 1H, C(2)-H),), 2.05 (s, 3H, Ac); ^{13}C NMR ($CDCl_3$, 50 MHz), major diastereomer: δ 170.0 (C=O), 87.4 (CN_3), 68.0, 50.9, 50.7, 50.7, 48.0, 47.9, 47.2, 33.7, 32.1, 32.1, 30.4, 28.9, 23.4, 23.1, 22.6, 21.2, 20.6, 19.7, 14.1, 11.4; minor diastereomer: δ 88.2, 67.7, 51.2, 48.1, 47.2, 32.4, 32.0, 30.4, 21.2, 20.5; mass spectrum, m/z (relative intensity) 457 (M^+, 1), 215 (R^*Se-OAc, 26), 154 (100). Exact mass calculated for $C_{22}H_{39}N_3O_2Se$: 457.2212. Found: 457.2221.

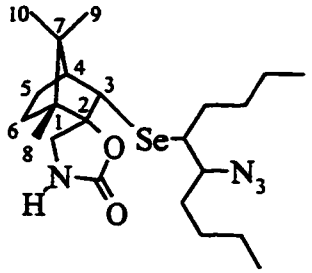
3.6.3 Table 2.7, Entry 3



The procedure of Entry 1 was followed with diselenide **64** and cyclohexene to afford the corresponding adduct: IR (neat) 2093 (N_3), 1752 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz), major diastereomer: δ 5.65 (br s, 1H, NH), 3.98 (d, J= 9.1 Hz, 1H, NCH_2), 3.90 (dd, J= 4.0, 2.5 Hz, 1H, C(3)-H), 3.55 (d, J= 9.1 Hz, 1H, NCH_2), 3.38-3.19 (m, 1H, CHN_3), 2.92-2.62 (m, 1H, SeCH), 2.20-0.96 (m, 12H), 2.06-2.02 (m, 1H, C(4)-H), 1.16 (s, 3H, C(8)-H), 0.92 (s, 6H, C(9)-H and C(10)-H); minor diastereomer: 5.56 (br s, 1H, NH), 4.08 (d, J= 9.2 Hz, 1H, CH_2NH), 3.83 (dd, J= 3.9, 2.3 Hz, 1H, C(3)-H), 1.98-1.94 (m, 1H, C(4)-H), 1.16 (s, 3H, C(8)-H), 0.92 (s, 6H, C(9)-H and C(10)-H); ^{13}C NMR ($CDCl_3$, 50 MHz), major diastereomer: δ 159.6 (C=O), 93.1 (C-N_3), 66.8, 55.6, 53.2, 52.9, 48.3, 46.9, 45.8, 33.8, 32.2, 29.0, 26.2, 24.2, 22.9, 20.6, 20.2, 11.0; minor diastereomer: δ 159.3, 65.3, 53.2, 53.0, 52.9, 52.7, 48.4, 46.7, 43.9, 33.6, 32.0, 29.0, 26.0, 24.2, 22.9, 20.6, 20.3; mass spectrum, m/z (relative intensity) 412 (M^+, 12), 384 (M^+-N_2,

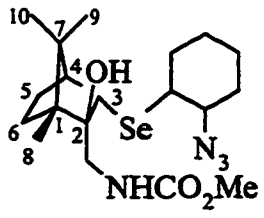
7), 288 ($R^{\bullet}Se^{+}$, 76), 208 ($R^{\bullet+}$, 63), 41 (100). Exact mass calculated for $C_{18}H_{28}N_4O_2Se$: 412.1380. Found: 412.1387.

3.6.4 Table 2.7, Entry 4



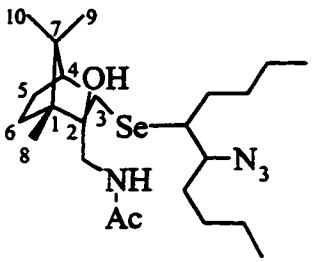
The procedure of Entry 1 was followed with diselenide **64** and *trans*-5-decene to afford the corresponding adduct: IR (neat) 2096 (N_3), 1754 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz), major diastereomer: δ 5.20 (br s, 1H, NH), 4.00 (d, J= 9.1 Hz, 1H, NCH_2), 3.76 (dd, J= 3.9, 2.4 Hz, 1H, C(3)-H), 3.69-3.46 (m, 2H, NCH_2 and CHN_3), 3.02-2.88 (m, 1H, SeCH), 2.03-1.89 (m, 1H, C(4)-H), 1.71-0.96 (m, 22H), 1.16 (s, 3H, C(8)-H), 0.93 (s, 6H, C(9)-H and C(10)-H); minor diastereomer: 4.01 (d, J= 9.0 Hz, 1H, CH_2N), 3.71 (dd, J= 4.1, 2.5 Hz, 1H, C(3)-H), ^{13}C NMR ($CDCl_3$, 50 MHz), major diastereomer: δ 159.0 (C=O), 93.1 (C-N_3), 69.0, 68.3, 67.4, 55.7, 52.8, 49.0, 48.6, 46.9, 32.3, 32.0, 30.4, 29.0 (two signals), 22.8, 22.7, 20.6, 20.2, 14.2, 14.1, 11.1; minor diastereomer: δ 159.9, 93.0, 55.9, 53.2, 52.8, 48.3, 46.9, 32.0, 29.1, 28.9, 22.9, 22.8, 14.2; mass spectrum, m/z (relative intensity) 470 (M^+, 12), 288 ($R^{\bullet}Se^{+}$, 33), 208 ($R^{\bullet+}$, 31), 41 (90). Exact mass calculated for $C_{22}H_{38}N_4O_2Se$: 470.2163. Found: 470.2146.

3.6.5 Table 2.7, Entry 5



The procedure of Entry 1 was followed with diselenide **66** and cyclohexene to afford the corresponding adduct: IR (neat) 3339 (OH), 2095 (N_3), 1698 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz), major diastereomer: δ 5.75 (br s, 1H, NH), 3.69 (s, 3H CO_2Me), 3.66-3.11 (m, 5H, OH, NCH_2, CHN_3, and C(3)-H), 2.74 (m, 1H, SeCH), 2.27-1.26 (m, 13H), 1.18 (s, 3H, C(8)-H), 0.94 (s, 3H, C(9)-H), 0.89 (s, 3H, C(10)-H); minor diastereomer: 6.25 (br s, 1H, NH), 0.88 (s, 3H, C(10)-H); ^{13}C NMR ($CDCl_3$, 50 MHz), major diastereomer: δ 170.0 (C=O), 80.9 (CN_3), 62.3, 55.8, 53.2, 53.2, 52.4, 48.6, 47.4, 44.4, 33.8, 31.7, 29.1, 26.2, 24.1, 20.8, 20.7, 20.6, 10.7; minor diastereomer: δ 62.1, 58.5, 53.4, 53.2, 52.4, 48.5, 47.3, 45.3, 34.7, 31.8, 29.0, 26.1, 24.1, 22.9, 20.7, 20.5. Some NMR assignments to major/minor diastereomers were tentative due to almost equal amounts of the two being present. Mass spectrum, m/z (relative intensity) 444 (M^+, 3), 319 (R^*Se^+, 6), 240 (R^{*+}, 32), 97 (100). Exact mass calculated for $C_{19}H_{32}N_4O_3Se$: 444.1643. Found: 444.1627.

3.6.6 Table 2.7, Entry 6

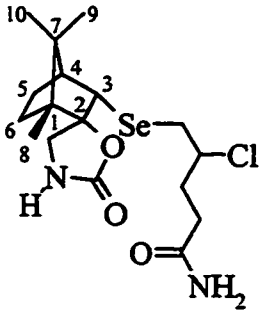


The procedure of Entry 1 was followed with diselenide **62** and *trans*-5-decene to afford the corresponding adduct: IR (neat) 3343 (OH), 2096 (N_3), 1637 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz), major diastereomer: δ 6.42 (br s, 1H, NH), 3.94-3.46 (m, 3H, OH, NCH_2, CHN_3), 3.32-3.30 (m, 1H, C(3)-H), 3.23-2.95 (m, 2H, NCH_2 and SeCH), 2.02 (s, 3H, Ac), 1.97-1.90 (m, 1H, C(4)-H), 1.84-1.15 (m, 22H), 0.94 (s, 3H, C(8)-H), 0.90 (s, 6H, C(9)-H, and C(10)-H); minor diastereomer: 6.81 (br s, 1H., NH), 2.03 (s, 3H, Ac); ^{13}C NMR ($CDCl_3$, 50 MHz), major diastereomer: δ 173.0 (C=O), 82.3 (C-N_3), 67.7, 56.3, 53.4, 52.9, 48.8, 48.7, 47.1, 32.2, 32.0, 30.8, 29.2 (two signals), 29.1, 23.4, 23.1, 22.8,

22.6, 21.0, 20.9, 14.2, 11.1; minor diastereomer: δ 173.4, 82.1, 67.5, 57.0, 53.7, 53.2, 49.8, 48.7, 46.4, 32.6, 31.5, 30.7, 29.1, 23.2, 22.9, 22.7, 10.9. Some NMR assignments to major/minor diastereomers were tentative due to almost equal amounts of the two being present. Mass spectrum, m/z (relative intensity) 486 (M^+, 1), 304 (R^*Se^+, 12), 224 (R^{*+}, 65), 43 (100). Exact mass calculated for $C_{23}H_{42}N_4O_2Se$: 486.2473. Found: 486.2454

3.7 Experiments Related to Section 2.3.6

3.7.1 Reaction of Amide **98**. Table 2.8, Entry 1

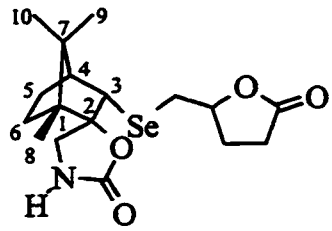


100

Diselenide **64** (50 mg, 0.087 mmol) was dissolved in 3 mL of dichloromethane. The mixture was cooled to 0 °C, SO_2Cl_2 (6.9 μL, 0.087 mmol) was added, and stirring was continued for 10 min. The resulting solution was cooled to -78 °C, amide **98** (21 mg, 0.21 mmol) was added, and the orange color was discharged immediately. After stirring for 1 h, the mixture was concentrated *in vacuo*, and was rapidly chromatographed (elution with ethyl acetate) to afford chloride **100** as a colourless oil, which decomposed readily into lactone **101** upon prolonged standing or slow chromatography; IR (neat) 3228 (NH), 1752 (C=O), 1668 (C=O), 751 (CCl) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz), major diastereomer: δ 6.25 (br s, 1H, NH), 6.01 (br s, 2H, NH_2), 4.14-4.05 (m, 1H, CHCl), 4.02 (d, J= 8.9 Hz, 1H, NCH_2), 3.58 (m, 2H, NCH_2 and C(3)-H), 3.13 (dd, J= 13.1, 5.1 Hz, 1H, $SeCH_2$), 2.93 (m, 1H, $SeCH_2$), 2.50-2.43 (m, 2H, CH_2NH_2), 2.18-1.23 (m, 7H), 1.15

(s, 3H, C(8)-H), 0.94 (s, 3H, C(9)-H), 0.93 (s, 3H, C(10)-H); minor diastereomer: δ 6.18 (br s, 1H, NH).

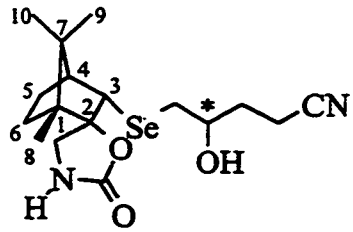
3.7.2 Table 2.8, Entry 2



101

Diselenide **64** (100 mg, 0.17 mmol) was dissolved in 3 mL of dichloromethane, cooled to 0 °C, SO_2Cl_2 (14 μL, 0.17 mmol) was added, and stirring was continued for 10 min. The resulting solution was cooled to -95 °C, amide **98** (41 mg, 0.41 mmol) was added, and the orange colour was discharged immediately. After being stirred at -95 °C for 1 h, the mixture was warmed to rt, and TsOH (10 mg) was added. After 10 h, the solution was concentrated *in vacuo*, and was chromatographed (elution with ethyl acetate) to afford 118 mg (88%) **101** as a colourless oil, which had ^{1}H NMR and ^{13}C NMR spectra identical to those obtained by B. Dyck.[91b] Only one diastereomer was detected.

3.7.3 Table 2.8, Entry 3

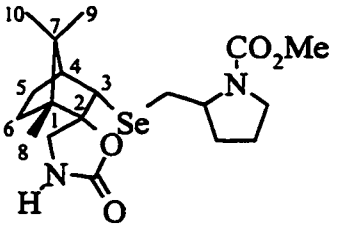


102

Diselenide **64** (100 mg, 0.17 mmol) was dissolved in 3 mL of dichloromethane, cooled to 0 °C, SO_2Cl_2 (14 μL, 0.17 mmol) was added, and stirring was continued for 10

min. The resulting solution was cooled to -95 °C, amide **98** (41 mg, 0.41 mmol) was added, and the orange colour was discharged immediately. After being stirred at -95 °C for 1 h, the mixture was warmed to rt, and potassium t-butoxide (117 mg, 1.05 mmol) was added to the mixture. After 4 h of stirring, the solution was concentrated *in vacuo*, and was chromatographed (elution with ethyl acetate) to afford 90 mg (67%) of **102** as a colourless oil: IR (neat) 3360 (OH), 2247 (C≡N), 1749 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz), major diastereomer: δ 5.71 (br s, 1H, NH), 4.06 (d, J= 9.3 Hz, 1H, NCH_2), 3.85 (br s, 1H, OH), 3.77 (dd, J= 3.9, 2.4 Hz, 1H, C(3)-H), 3.59 (d, J= 9.4 Hz, 1H, NCH_2), 3.09-3.07 (m, 1H, CHOH), 2.84 (dd, J= 12.6, 5.1 Hz, 1H, $SeCH_2$), 2.70 (dd, J= 12.6, 7.4 Hz, 1H, $SeCH_2$), 2.54 (dd, J= 7.7, 6.7 Hz, 2H, CH_2CN), 2.07-2.00 (m, 1H, C(4)-H), 1.97-1.21 (m, 6H), 1.16 (s, 3H, C(8)-H), 0.94 (s, 3H, C(9)-H), 0.93 (s, 3H, C(10)-H); minor diastereomer: 5.80 (br s, 1H, NH); ^{13}C NMR (C_6D_6, 50 MHz), major diastereomer: δ 160.2 (C=O), 120.5 (C≡N), 93.2, 70.0, 57.2, 53.2, 53.0, 48.6, 47.2, 33.2, 32.6, 29.2, 23.0, 20.6, 20.5, 14.1, 11.1; minor diastereomer: none of the signals could be identified; mass spectrum, m/z (relative intensity) 386 (M^+, 16), 288 ($R^•Se^+$, 34), 208 ($R^{•+}$, 77), 83 (100). Exact mass calculated for $C_{17}H_{26}N_2O_3Se$: 386.1102. Found: 386.1102.

3.8.1 Preparation of Carbamate **107**

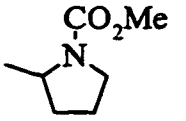


107

Diselenide **64** (100 mg, 0.17 mmol) was dissolved in 3 mL of dichloromethane, cooled to 0 °C, SO_2Cl_2 (14 μL, 0.17 mmol) was added, and stirring was continued for 10 min. The resulting solution was cooled to -78 °C, and carbamate **99** (60 mg, 0.42 mmol) was added, and the orange colour was discharged immediately. After being stirred at -78

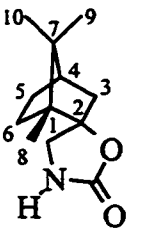
°C for 1 h, the mixture was warmed to rt and oven dried silica-gel (100 mg) was added to the mixture. It was stirred at rt overnight, and then was washed with aqueous NaCl solution, dried ($MgSO_4$), and purified by column chromatography (elution with 80% ethyl acetate/hexane) to afford product **107** as a colourless oil: IR (neat) 3377 (NH), 1774 (C=O), 1701 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz), major diastereomer: δ 5.50 (br s, 1H, NH); both diastereomers: 4.09-3.95 (m, 3H, $SeCH_2CH$, C(3)-H and NCH_2), 3.71-3.65 (m, 3H, CO_2Me), 3.55 (d, J= 5.1 Hz, 1H, NCH_2), 2.00-1.20 (m, 13H), 1.15 (s, 3H, C(8)-H), 0.92 (s, 6H, C(9) and C(10)-H); minor diastereomer: 5.72 (br s, 1H, NH); ^{13}C NMR (C_6D_6, 50 MHz), major diastereomer: δ 170.0 (C=O), 155.5 (C=O), 88.0, 59.1, 51.6, 51.3, 50.8, 48.5, 47.9, 47.2, 34.2, 30.7, 30.6, 27.8, 24.0, 23.9, 21.3, 20.1, 11.8; minor diastereomer: δ 58.8, 58.3, 52.1, 51.1, 49.3, 48.2, 47.4, 31.5, 29.3, 24.1, 23.8, 23.2, 20.9, 20.1; mass spectrum, m/z (relative intensity) 430 (M^+, 5), 288 ($R^•Se^+$, 15), 208 ($R^{•+}$, 10), 128 (100). Exact mass calculated for $C_{19}H_{30}N_2O_4Se$: 430.1374. Found: 430.1366.

3.8.2 Deselenization of Product **107**



108

+



109

A mixture of AIBN (10 mg) and tri-n-butyltin hydride (138 μL, 0.52 mmol) in toluene was added dropwise to a refluxing solution of selenide **107** (110 mg, 0.26 mmol) in 2 mL of toluene. After 2 h, additional triphenyltin hydride (69 μL, 0.26 mmol) and AIBN (5 mg) were added, and heating was continued for 1 h. The reaction mixture was separated by chromatography (elution with hexane followed by 10% diethyl ether/hexane). The solvent was removed by simple distillation, followed by further column chromatography (elution with 100% hexane to remove the tin residue, followed by elution with 50% diethyl ether/hexane) to afford carbamate **108** as yellow oil and 49

mg (91%) of oxazolidinone **109** as a white solid. The e.e. of **108** was determined on a chiral Cyclodex B GC column. Oxazolidinone **109** had a ^{1}H NMR spectrum identical to that of an authentic sample prepared by B. Dyck.[91b] Compound **108**: ^{1}H NMR ($CDCl_3$, 200 MHz), δ 4.00 (br s, 1H, NCH), 3.40 (br s, 2H, NCH_2), 3.70 (s, 3H, CO_2Me), 2.18-1.63 (m, 4H), 1.56 (d, J= 3.3 Hz, 3H, Me). GC-mass spectrum, m/z (relative intensity) 143 (M^+, 11), 128 (M^+-Me, 100). The NMR spectrum of **108** was in close agreement with that reported in the literature.[56]

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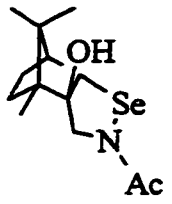
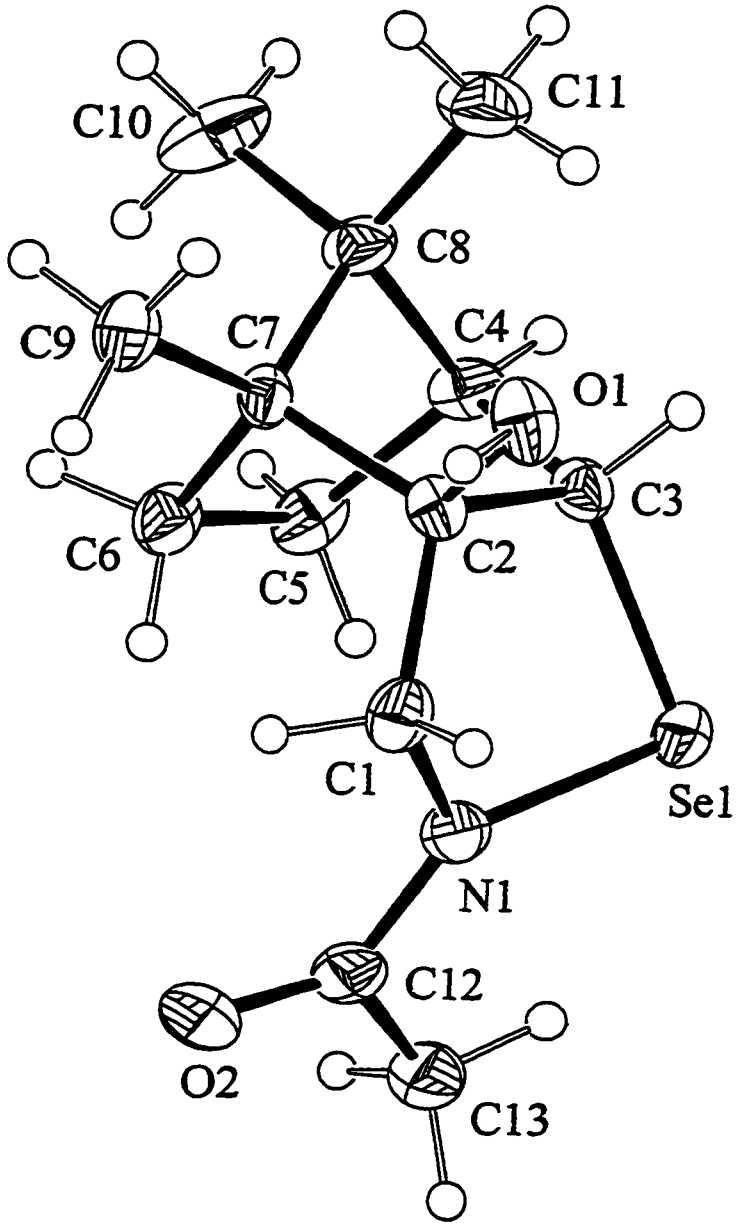
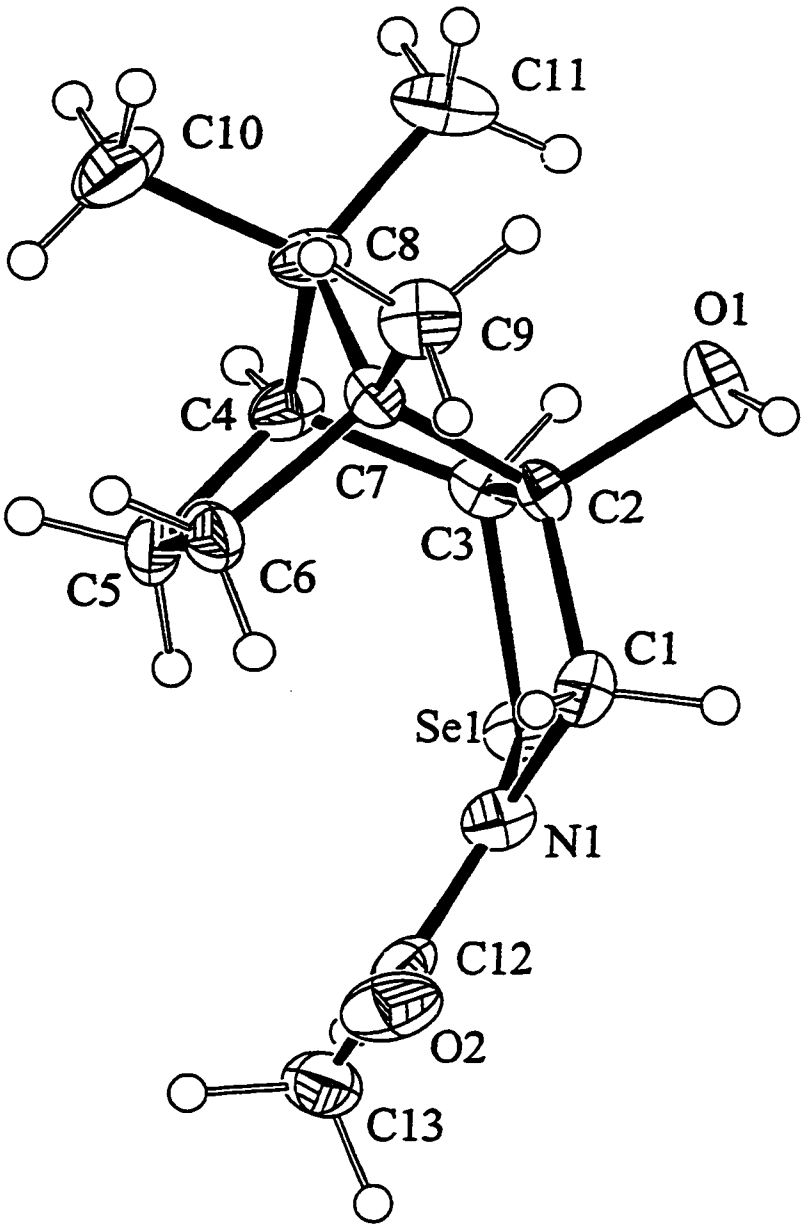
Apendix A

X-ray Crystal Structure of Selenenamide **94**



94




C11
C10
C8
C9
O1
C4
C7
C2
C3
C5
C6
C1
Se1
N1
C12
O2
C13

Experimental

Data Collection

A colourless, needle-shaped crystal of $C_{13}H_{21}NO_2Se$ having approximate dimensions of 0.30 x 0.12 x 0.10 mm was mounted on a glass fiber. All measurements were made on an Enraf-Nonius CAD-4 diffractometer with graphite monochromated Cu-Kα radiation.

Cell constants and an orientation matrix for data collection , obtained from a least-squares refinement using the setting angles of 25 carefully centered reflections in the range $20.0 < \theta < 30.0°$ corresponded to a primitive orthorhombic cell with dimensions:

a = 6.868(1) $\AA$

b = 11.537(2) $\AA$

c = 17.079(3) $\AA$

V = 1353.3(3) $\AA^3$

For Z = 4 and F.W. = 302.27, the calculated density is 1.48 g/cm^3. The systematic absences of:

h00: h $\neq$ 2n

0k0: k $\neq$ 2n

00l: l $\neq$ 2n

uniquely determine the space group to be:

$P2_12_12_1$ (#19)

The data were collected at a temperature of 23 $\pm$ 1°C using the ω scan technique to a maximum 2θ value of 135.8°. Omega scans of several intense reflections, made prior to data collection, had an average width at half-height of 0.00° with a take-off angle of 2.8°. Scans of (0.80 + 0.35 tan θ)° were made at a variable speed. Moving-crystal moving counter background measurements were made by scanning an additional 25% above and below the scan range. For intense reflections an attenuator was automatically inserted in front of the detector.

Data Reduction

Of the 2830 reflections which were collected, 1530 were unique (R_{int} = 0.032); equivalent reflections were merged. Over the course of data collection, the standards decreased by 4.6%. A linear correction factor was applied to the data to account for this phenomenon.

The linear absorption coefficient, μ, for Cu-Kα radiation is 36.8 cm^{-1}. An empirical absorption correction based on azimuthal scans of several reflections was applied which resulted in transmission factors ranging from 0.87 to 1.00. The data were corrected for Lorentz and polarization effects.

Structure Solution and Refinement

The structure was solved by direct methods[1] and expanded using Fourier techniques[2]. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included at geometrically idealized positions with C-H and N-H 0.95 Å but were not refined. The final cycle of full-matrix least-squares refinement[3] was based on 1299 observed reflections ($I > 3.00\sigma(I)$) and 154 variable parameters and converged (largest parameter shift was 0.01 times its esd) with unweighted and weighted agreement factors of:

$$R = \Sigma||Fo| - |Fc||/\Sigma|Fo| = 0.032$$

$$R_w = \sqrt{(\Sigma w(|Fo| - |Fc|)^2/\Sigma wFo^2)}] = 0.030$$

The standard deviation of an observation of unit weight[4] was 2.68. The weighting scheme was based on counting statistics. Plots of $\Sigma w(|Fo| - |Fc|)^2$ versus $|Fo|$, reflection order in data collection, $\sin\theta/\lambda$ and various classes of indices showed no unusual trends. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.31 and -0.53 $e^-/Å^3$, respectively.

Neutral atom scattering factors were taken from Cromer and Waber[5] . Anomalous dispersion effects were included in Fcalc[6]; the values for $\Delta f'$ and $\Delta f''$ were those of Creagh and McAuley[7]. The values for the mass attenuation coefficients are those of Creagh and Hubbel[8]. All calculations were performed using the teXsan[9] crystallographic software package of Molecular Structure Corporation.

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(3) Least-Squares:

Function minimized: $\Sigma w(|Fo| - |Fc|)^2$

where w = $\frac{1}{\sigma^2(Fo)} = [\sigma_c^2(Fo) + \frac{p^2}{4}Fo^2]^{-1}$

$\sigma_c(Fo)$ = e.s.d. based on counting statistics

p = p-factor

(4) Standard deviation of an observation of unit weight:

$$\sqrt{\Sigma w(|Fo| - |Fc|)^2/(No - Nv)}$$

where: No = number of observations

Nv = number of variables

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EXPERIMENTAL DETAILS

A. Crystal Data

Empirical Formula	$C_{13}H_{21}NO_2Se$
Formula Weight	302.27
Crystal Color, Habit	colourless, needle
Crystal Dimensions	0.30 X 0.12 X 0.10 mm
Crystal System	orthorhombic
No. of Reflections Used for Unit Cell Determination (θ range)	25 (20.0 - 30.0°)
Lattice Parameters	a = 6.868(1)Å b = 11.537(2) Å c = 17.079(3) Å V = 1353.3(3) Å^3
Space Group	$P2_12_12_1$ (#19)
Z value	4
D_{calc}	1.483 g/cm^3
F_{000}	624.00
μ(CuKα)	36.81 cm^{-1}

B. Intensity Measurements

Diffractometer	Enraf-Nonius CAD-4
Radiation	CuKα (λ = 1.54178 Å) graphite monochromated
Attenuator	Ni foil (factor = 26.50)
Temperature	23.0°C
$2\theta_{max}$	135.8°

No. of Reflections Measured	Total: 2830 Unique: 1530 (R_{int} = 0.032)
Corrections	Lorentz-polarization Absorption (trans. factors: 0.8737 - 1.0000) Decay (4.62%)

C. Structure Solution and Refinement

Structure Solution	Direct Methods (SIR92)
Refinement	Full-matrix least-squares
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (I>3.00σ(I))	1299
No. Variables	154
Reflection/Parameter Ratio	8.44
Residuals: R; Rw	0.032 ; 0.030
Goodness of Fit Indicator	2.68
Max Shift/Error in Final Cycle	0.01
Maximum peak in Final Diff. Map	0.31 $e^-/\AA^3$
Minimum peak in Final Diff. Map	-0.53 $e^-/\AA^3$

Table 1. Atomic coordinates and B_{iso}/B_{eq}

atom	x	y	z	B_{eq}
Se(1)	0.52880(8)	0.22729(5)	0.81766(4)	3.22(1)
O(1)	0.3264(5)	-0.0640(3)	0.7846(2)	3.59(9)
O(2)	-0.0272(6)	0.3312(4)	0.7992(2)	5.0(1)
N(1)	0.2603(6)	0.2405(4)	0.7993(3)	3.2(1)
C(1)	0.1821(9)	0.1265(5)	0.7811(3)	3.2(1)
C(2)	0.2788(8)	0.0331(5)	0.8331(3)	2.5(1)
C(3)	0.4725(8)	0.0796(4)	0.8673(3)	2.8(1)
C(4)	0.4413(9)	0.0747(5)	0.9565(3)	3.1(1)
C(5)	0.2898(10)	0.1645(5)	0.9793(3)	3.7(1)
C(6)	0.0995(9)	0.1098(5)	0.9484(3)	3.4(1)
C(7)	0.1671(8)	-0.0028(5)	0.9093(3)	2.6(1)
C(8)	0.3334(9)	-0.0410(5)	0.9646(4)	3.3(1)
C(9)	0.0034(9)	-0.0894(5)	0.8948(3)	3.9(1)
C(10)	0.2613(12)	-0.0624(6)	1.0503(4)	5.6(2)
C(11)	0.4465(11)	-0.1482(5)	0.9400(4)	5.1(2)
C(12)	0.1517(9)	0.3355(6)	0.8092(4)	3.5(1)
C(13)	0.2556(10)	0.4453(5)	0.8293(4)	4.6(2)
H(1)	0.2222	-0.0786	0.7494	4.2950
H(2)	0.0456	0.1265	0.7901	3.8849
H(3)	0.2068	0.1092	0.7276	3.8849
H(4)	0.5733	0.0267	0.8540	3.3294
H(5)	0.5582	0.0790	0.9861	3.6990
H(6)	0.2854	0.1749	1.0345	4.3964
H(7)	0.3150	0.2369	0.9548	4.3964

Table 1. Atomic coordinates and B_{iso}/B_{eq} (continued)

atom	x	y	z	B_{eq}
H(8)	0.0123	0.0939	0.9903	4.1392
H(9)	0.0381	0.1594	0.9116	4.1392
H(10)	-0.0540	-0.1109	0.9432	4.6668
H(11)	-0.0924	-0.0551	0.8620	4.6668
H(12)	0.0548	-0.1565	0.8698	4.6668
H(13)	0.1884	0.0028	1.0676	6.7524
H(14)	0.1809	-0.1294	1.0514	6.7524
H(15)	0.3699	-0.0735	1.0837	6.7524
H(16)	0.3633	-0.2139	0.9420	6.1170
H(17)	0.4936	-0.1382	0.8883	6.1170
H(18)	0.5531	-0.1594	0.9747	6.1170
H(19)	0.3913	0.4304	0.8334	5.4974
H(20)	0.2336	0.5010	0.7892	5.4974
H(21)	0.2083	0.4743	0.8776	5.4974

$$B_{eq} = \frac{8}{3}\pi^2(U_{11}(aa^*)^2 + U_{22}(bb^*)^2 + U_{33}(cc^*)^2 + 2U_{12}aa^*bb^* \cos\gamma + 2U_{13}aa^*cc^* \cos\beta + 2U_{23}bb^*cc^* \cos\alpha)$$

Table 2. Anisotropic Displacement Parameters

atom	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
Se(1)	0.0328(3)	0.0412(3)	0.0482(3)	-0.0055(3)	0.0019(3)	0.0074(3)
O(1)	0.035(2)	0.049(2)	0.052(2)	-0.001(2)	0.003(2)	-0.024(2)
O(2)	0.042(2)	0.069(3)	0.078(3)	0.015(3)	-0.007(3)	0.028(3)
N(1)	0.038(2)	0.039(3)	0.045(3)	-0.004(2)	-0.005(2)	0.007(2)
C(1)	0.041(4)	0.051(4)	0.031(3)	-0.005(3)	0.003(3)	-0.002(3)
C(2)	0.030(3)	0.030(3)	0.034(3)	0.000(2)	-0.001(3)	-0.010(2)
C(3)	0.027(3)	0.031(3)	0.048(3)	-0.001(3)	-0.001(3)	-0.002(2)
C(4)	0.042(4)	0.039(3)	0.036(3)	-0.008(3)	-0.015(3)	0.004(3)
C(5)	0.067(4)	0.043(4)	0.029(3)	-0.006(3)	0.008(3)	-0.007(3)
C(6)	0.050(4)	0.039(3)	0.042(3)	0.002(3)	0.017(3)	-0.005(3)
C(7)	0.032(3)	0.029(3)	0.039(3)	-0.002(3)	0.006(3)	-0.004(3)
C(8)	0.040(3)	0.035(3)	0.050(4)	-0.010(3)	-0.008(3)	0.011(3)
C(9)	0.034(4)	0.053(3)	0.060(4)	-0.012(3)	0.001(3)	0.001(3)
C(10)	0.105(6)	0.063(5)	0.046(4)	-0.027(5)	-0.012(4)	0.019(4)
C(11)	0.061(5)	0.035(3)	0.098(5)	0.001(4)	-0.013(4)	0.013(4)
C(12)	0.053(4)	0.052(4)	0.028(3)	0.009(3)	0.001(3)	0.012(3)
C(13)	0.063(5)	0.043(4)	0.067(5)	0.013(3)	0.019(4)	0.010(4)

The general temperature factor expression:

$$\exp(-2\pi^2(a^{*2}U_{11}h^2 + b^{*2}U_{22}k^2 + c^{*2}U_{33}l^2 + 2a^*b^*U_{12}hk + 2a^*c^*U_{13}hl + 2b^*c^*U_{23}kl))$$

Table 3. Bond Lengths(Å)

atom	atom	distance	atom	atom	distance
Se(1)	N(1)	1.877(4)	Se(1)	C(3)	1.942(5)
O(1)	C(2)	1.431(6)	O(2)	C(12)	1.241(7)
N(1)	C(1)	1.454(7)	N(1)	C(12)	1.337(7)
C(1)	C(2)	1.546(8)	C(2)	C(3)	1.548(7)
C(2)	C(7)	1.566(7)	C(3)	C(4)	1.540(6)
C(4)	C(5)	1.519(8)	C(4)	C(8)	1.532(7)
C(5)	C(6)	1.544(8)	C(6)	C(7)	1.532(7)
C(7)	C(8)	1.546(7)	C(7)	C(9)	1.525(7)
C(8)	C(10)	1.564(8)	C(8)	C(11)	1.520(8)
C(12)	C(13)	1.494(9)			

Table 4. Bond Angles(°)

atom	atom	atom	angle	atom	atom	atom	angle
N(1)	Se(1)	C(3)	87.1(2)	Se(1)	N(1)	C(1)	109.0(4)
Se(1)	N(1)	C(12)	126.4(4)	C(1)	N(1)	C(12)	124.2(5)
N(1)	C(1)	C(2)	110.4(4)	O(1)	C(2)	C(1)	108.1(4)
O(1)	C(2)	C(3)	107.0(4)	O(1)	C(2)	C(7)	112.7(4)
C(1)	C(2)	C(3)	110.1(4)	C(1)	C(2)	C(7)	116.8(5)
C(3)	C(2)	C(7)	101.5(4)	Se(1)	C(3)	C(2)	108.1(4)
Se(1)	C(3)	C(4)	119.5(4)	C(2)	C(3)	C(4)	103.9(4)
C(3)	C(4)	C(5)	108.9(4)	C(3)	C(4)	C(8)	100.9(4)
C(5)	C(4)	C(8)	103.9(5)	C(4)	C(5)	C(6)	102.3(4)
C(5)	C(6)	C(7)	103.8(5)	C(2)	C(7)	C(6)	106.7(4)
C(2)	C(7)	C(8)	102.8(4)	C(2)	C(7)	C(9)	113.5(4)
C(6)	C(7)	C(8)	101.5(5)	C(6)	C(7)	C(9)	113.8(5)
C(8)	C(7)	C(9)	117.2(5)	C(4)	C(8)	C(7)	93.1(4)
C(4)	C(8)	C(10)	112.1(5)	C(4)	C(8)	C(11)	115.9(5)
C(7)	C(8)	C(10)	112.5(5)	C(7)	C(8)	C(11)	116.1(5)
C(10)	C(8)	C(11)	106.9(5)	O(2)	C(12)	N(1)	120.1(6)
O(2)	C(12)	C(13)	122.6(6)	N(1)	C(12)	C(13)	117.2(5)

Table 5. Torsion Angles(°)

atom	atom	atom	atom	angle	atom	atom	atom	atom	angle
Se(1)	N(1)	C(1)	C(2)	39.0(6)	Se(1)	N(1)	C(12)	O(2)	-175.8(4)
Se(1)	N(1)	C(12)	C(13)	6.5(8)	Se(1)	C(3)	C(2)	O(1)	109.1(4)
Se(1)	C(3)	C(2)	C(1)	-8.2(5)	Se(1)	C(3)	C(2)	C(7)	-132.5(3)
Se(1)	C(3)	C(4)	C(5)	51.8(6)	Se(1)	C(3)	C(4)	C(8)	160.7(4)
O(1)	C(2)	C(1)	N(1)	-135.8(4)	O(1)	C(2)	C(3)	C(4)	-123.0(4)
O(1)	C(2)	C(7)	C(6)	-171.6(5)	O(1)	C(2)	C(7)	C(8)	82.1(5)
O(1)	C(2)	C(7)	C(9)	-45.5(6)	O(2)	C(12)	N(1)	C(1)	-4(1)
N(1)	Se(1)	C(3)	C(2)	24.6(3)	N(1)	Se(1)	C(3)	C(4)	-93.8(5)
N(1)	C(1)	C(2)	C(3)	-19.2(6)	N(1)	C(1)	C(2)	C(7)	95.9(6)
C(1)	N(1)	Se(1)	C(3)	-36.6(4)	C(1)	N(1)	C(12)	C(13)	178.7(5)
C(1)	C(2)	C(3)	C(4)	119.7(5)	C(1)	C(2)	C(7)	C(6)	-45.5(6)
C(1)	C(2)	C(7)	C(8)	-151.8(5)	C(1)	C(2)	C(7)	C(9)	80.6(6)
C(2)	C(1)	N(1)	C(12)	-134.4(5)	C(2)	C(3)	C(4)	C(5)	-68.7(5)
C(2)	C(3)	C(4)	C(8)	40.2(5)	C(2)	C(7)	C(6)	C(5)	-70.7(5)
C(2)	C(7)	C(8)	C(4)	55.3(5)	C(2)	C(7)	C(8)	C(10)	170.8(5)
C(2)	C(7)	C(8)	C(11)	-65.5(6)	C(3)	Se(1)	N(1)	C(12)	136.6(5)
C(3)	C(2)	C(7)	C(6)	74.3(5)	C(3)	C(2)	C(7)	C(8)	-32.0(5)
C(3)	C(2)	C(7)	C(9)	-159.6(4)	C(3)	C(4)	C(5)	C(6)	72.8(5)
C(3)	C(4)	C(8)	C(7)	-57.8(5)	C(3)	C(4)	C(8)	C(10)	-173.6(5)
C(3)	C(4)	C(8)	C(11)	63.3(6)	C(4)	C(3)	C(2)	C(7)	-4.7(5)
C(4)	C(5)	C(6)	C(7)	-1.8(5)	C(4)	C(8)	C(7)	C(6)	-54.9(5)
C(4)	C(8)	C(7)	C(9)	-179.4(5)	C(5)	C(4)	C(8)	C(7)	55.0(5)
C(5)	C(4)	C(8)	C(10)	-60.8(6)	C(5)	C(4)	C(8)	C(11)	176.1(5)
C(5)	C(6)	C(7)	C(8)	36.5(5)	C(5)	C(6)	C(7)	C(9)	163.3(5)

Table 5. Torsion Angles(°) (continued)

atom	atom	atom	atom	angle	atom	atom	atom	atom	angle
C(6)	C(5)	C(4)	C(8)	-34.1(5)	C(6)	C(7)	C(8)	C(10)	60.5(6)
C(6)	C(7)	C(8)	C(11)	-175.8(5)	C(9)	C(7)	C(8)	C(10)	-64.0(7)
C(9)	C(7)	C(8)	C(11)	59.7(7)					

Table 6. Non-bonded Contacts out to 3.60 Å

atom	atom	distance	ADC	atom	atom	distance	ADC
Se(1)	O(1)	3.136(3)	65604	Se(1)	O(2)	3.292(4)	65501
O(1)	O(2)	2.782(5)	54604	O(1)	C(13)	3.469(8)	64604
O(2)	C(9)	3.442(7)	55604	C(5)	C(6)	3.581(8)	55703

The ADC (atom designator code) specifies the position of an atom in a crystal. The 5-digit number shown in the table is a composite of three one-digit numbers and one two-digit number: TA (first digit) + TB (second digit) + TC (third digit) + SN (last two digits). TA, TB and TC are the crystal lattice translation digits along cell edges a, b and c. A translation digit of 5 indicates the origin unit cell. If TA = 4, this indicates a translation of one unit cell length along the a-axis in the negative direction. Each translation digit can range in value from 1 to 9 and thus ± 4 lattice translations from the origin (TA=5, TB=5, TC=5) can be represented.

The SN, or symmetry operator number, refers to the number of the symmetry operator used to generate the coordinates of the target atom. A list of symmetry operators relevant to this structure are given below.

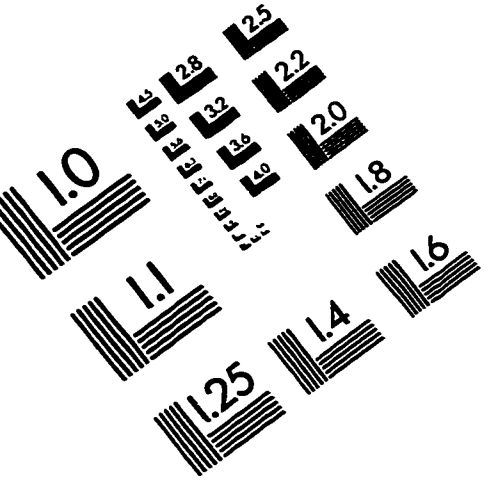
For a given intermolecular contact, the first atom (origin atom) is located in the origin unit cell and its position can be generated using the identity operator (SN=1). Thus, the ADC for an origin atom is always 55501. The position of the second atom (target atom) can be generated using the ADC and the coordinates of the atom in the parameter table. For example, an ADC of 47502 refers to the target atom moved through symmetry operator two, then translated -1 cell translations along the a axis, +2 cell translations along the b axis, and 0 cell translations along the c axis.

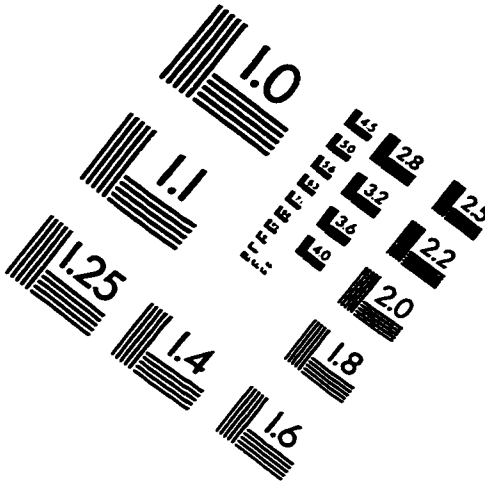
An ADC of 1 indicates an intermolecular contact between two fragments (eg. cation and anion) that reside in the same asymmetric unit.

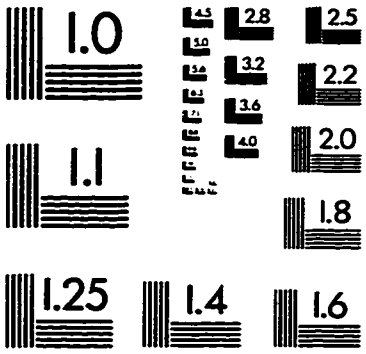
Symmetry Operators:

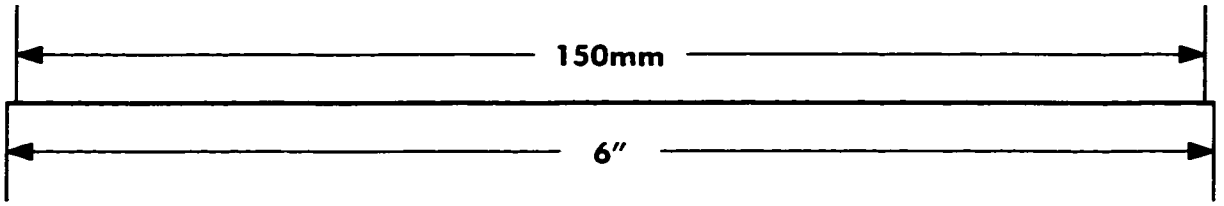
(1)	X,	Y,	Z	(2)	1/2-X,	-Y,	1/2+Z
(3)	1/2+X,	1/2-Y,	-Z	(4)	-X,	1/2+Y,	1/2-Z

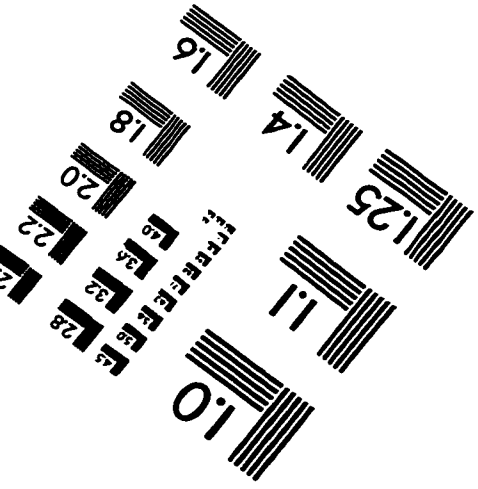
IMAGE EVALUATION
TEST TARGET (QA-3)

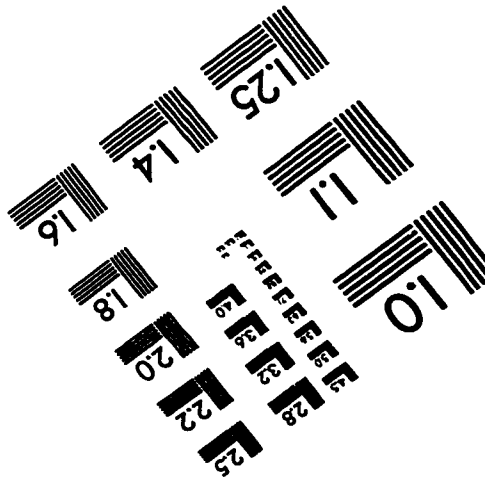












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